

Chapter 560

Cumulative Incidence

Introduction

This routine calculates nonparametric, maximum-likelihood estimates and confidence limits of the probability of failure (the *cumulative incidence*) for a particular cause in the presence of other causes. This is sometimes called the problem of *competing risks*. This procedure also calculates Gray's Test and the Pepe and Mori Test for comparing groups while accounting for competing risks.

An often used, though incorrect, approach is to treat all failures from causes other than that of interest as censored observations and estimate the cumulative incidence using 1 - *KM* (Kaplan-Meier estimate). The problem with this approach is that it makes the incorrect assumption that the probability of failing prior to time t from other causes is zero. This leads to overestimation of the cumulative incidence. This overestimation can be quite substantial if there are many failures from other causes in the data.

Technical Details

Estimation and Confidence Intervals

The following results are summarized from Marubini and Valsecchi (1996). Suppose that one of K mutually exclusive events may occur to a subject. These events may be failure, death, etc. When an event occurs, the time until it occurred T and the type of event k is recorded. The experiment may be terminated before any event occurs for some subjects in which case they are called *censored* observations and the time until censoring is recorded. The cause-specific hazard functions are defined as

$$h_k(t) = \lim_{\Delta t \rightarrow 0^+} \frac{\Pr\{t \leq T < t + \Delta t, K = k | T \geq t\}}{\Delta t}, \quad k = 1, 2, \dots, K$$

The overall survival function is denoted by

$$S(t) = \Pr(T > t)$$

and the probability of failing for cause k is denoted by

$$I_k(t) = \Pr(T \leq t, k = K), \quad k = 1, 2, \dots, K$$

These cause-specific failure probabilities, also known as the cumulative incidence functions, are defined as

$$I_k(t) = \int_0^t h_k(u) S(u) du, \quad k = 1, 2, \dots, K$$

where

$$S(u) = \exp\left\{-\int_0^u \left(\sum_{k=1}^K h_k(y)\right) dy\right\}$$

This makes use of the assumption that a subject must be event free up to time u to then fail of cause k at time u .

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If we let d_{kj} denote the number of subjects having event k and time t_j , $d_j = \sum_{k=1}^K d_{kj}$, and n_j denote the number of subjects at risk at time t_j , the likelihood may be written as

$$L = \prod_{j=1}^J \left[\left(\prod_{k=1}^K h_{kj}^{d_{kj}} \right) \left(1 - \sum_{k=1}^K h_{kj} \right)^{n_j - d_j} \right]$$

The ML estimate of the cause-specific hazard is

$$\hat{h}_{kj} = \frac{d_{kj}}{n_j}$$

and the estimated crude cumulative incidence for event k is

$$\hat{I}_k(t) = \sum_{j|t_j \leq t} \hat{S}(t_{j-1}) \frac{d_{kj}}{n_j}$$

where $\hat{S}(t_{j-1})$ is the usual Kaplan-Meier estimate of survival until time t_{j-1} .

The variance of the crude cumulative incidence is estimated by

$$\begin{aligned} \text{Var}[\hat{I}_k(t_j)] &= \sum_{i=1}^j \left\{ \left[\hat{I}_k(t_j) - \hat{I}_k(t_i) \right]^2 \frac{d_i}{n_i(n_i - d_i)} \right\} + \sum_{i=1}^j \left[\hat{S}(t_{i-1}) \right]^2 \left(\frac{n_i - d_{ki}}{n_i} \right) \left(\frac{d_{ki}}{n_i^2} \right) \\ &\quad - 2 \sum_{i=1}^j \left\{ \left[\hat{I}_k(t_j) - \hat{I}_k(t_i) \right] \hat{S}(t_{i-1}) \frac{d_{ki}}{n_i^2} \right\} \end{aligned}$$

Finally, using the above estimate cumulative incidence and its estimated variance, approximate $100(1 - \alpha)\%$ confidence intervals may be calculated using

$$\exp \left\{ \log[\hat{I}_k(t)] \pm z_{1-\alpha/2} \frac{\sqrt{\text{Var}[\hat{I}_k(t)]}}{\hat{I}_k(t)} \right\}$$

This expression guarantees that the resulting values will be between zero and one.

Hypothesis Tests

The following results are summarized from Pintilie (2006). In the absence of competing risks, the logrank test is often used to compare the 2 or more groups with respect to a particular outcome. If competing risks are present, the logrank test can still be used to compare the cause-specific hazards, but it does not account for competing risks. The logrank test for cause-specific hazards is conducted by assigning a “1” to the event of interest and a “0” to all competing risk events and censored observations. Thus, the logrank test effectively ignores the competing risks and focuses only on the event of interest. This can result in very misleading results if not interpreted correctly. Please see the Kaplan-Meier (Logrank tests) procedure and documentation for more information about the logrank test; it will not be repeated here.

In the presence of competing risks, you should use Gray’s test for K samples or Pepe and Mori’s test for 2 samples as a direct approach to compare groups with respect to the event of interest while accounting for the effects of the other competing risk events. Gray’s test compares the weighted averages of the subdistribution hazards across groups for the event of interest. Pepe and Mori’s test compares the cumulative incidence functions (CIF’s) directly.

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Both are appropriate for comparing groups with respect to an outcome of interest while accounting for competing risks.

Gray's Test

Gray's test is a K -sample test that was introduced by Gray (1988). It compares the weighted averages of the subdistribution hazards across groups for the event of interest. The null hypothesis is that there is no difference among the K groups. The test is based on the $K - 1$ score statistics

$$Z_K(\tau) = \int_{t=0}^{\tau} W_K(t) \{ \gamma_K(t) - \gamma_0(t) \} dt,$$

where τ is taken to be the largest observed time in the study and $\gamma(t)$ is the subdistribution hazard with

$$\gamma_K(t) = \frac{i_K(t)}{1 - I_K(t)}.$$

In these equations $i_K(t)$ is the subdensity and $I_K(t)$ is the subdistribution function in group K for the event of interest, $W_K(t)$ is a weight function, and $\gamma_0(t)$ is the subdistribution hazard for all groups taken together.

If we let Z represent the vector of $K - 1$ score statistics and represent the variance-covariance matrix for Z , the test statistic, Q , is given by

$$Q_{Gray} = Z' \Sigma^{-1} Z$$

For large samples, Q_{Gray} is approximately distributed as a chi-squared random variable with $K - 1$ degrees of freedom. The formula for Σ is complex and is not given here. See Pintilie (2006) and Gray (1988) for more information about this test.

Pepe and Mori's Test

Pepe and Mori's test is a 2-sample test that was introduced by Pepe and Mori (1993). This test compares the cumulative incidence functions (CIF's) directly for the event of interest. The null hypothesis is that there is no difference between the 2 groups.

For groups 1 and 2, respectively, define $\hat{I}_1(t)$ and $\hat{I}_2(t)$ as the cumulative incidence function estimates for the event of interest, $\hat{I}_{cr,1}(t)$ and $\hat{I}_{cr,2}(t)$ as the cumulative incidence function estimates for competing risks, $\hat{C}_1(t)$ and $\hat{C}_2(t)$ as the Kaplan-Meier estimate of survival where the events are defined as observations that are either competing risk events or censored, and N_1 and N_2 as the total sample sizes. For both groups, also define $n_1(t_j)$ and $n_2(t_j)$ as the number at risk at time t_j , $d_1(t_j)$ and $d_2(t_j)$ as the number of events of interest or competing risk events at time t_j , and $d_{ev,1}(t_j)$ and $d_{ev,2}(t_j)$ as the number of events of interest at time t_j . Further define $W(t)$ as a weight function that decreases with time.

For ordered unique times representing either events or censored observations, t_1, t_2, \dots, t_n , Pepe and Mori's test statistic is given by

$$Q_{PM} = \frac{s^2}{\hat{\sigma}^2},$$

where

$$s = \sqrt{\frac{N_1 N_2}{N_1 + N_2} \sum_{\text{all } t_j} W(t_j) [\hat{I}_1(t_j) - \hat{I}_2(t_j)] (t_{j+1} - t_j)}$$

$$\hat{\sigma}^2 = \frac{N_1 N_2 (\hat{\sigma}_1^2 + \hat{\sigma}_2^2)}{N_1 + N_2}$$

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with

$$W(t_j) = \frac{(N_1 + N_2)\hat{C}_1(t_{j-1})\hat{C}_2(t_{j-1})}{N_1\hat{C}_1(t_{j-1}) + N_2\hat{C}_2(t_{j-1})}$$

$$\hat{\sigma}_K^2 = \sum_{\text{all } t_j} \frac{[v_{1,K}(t_j) - \hat{I}_{cr,K}(t_j)v_{2,K}(t_j)]^2 d_{ev,K}(t_j) + v_{3,K}(t_j)^2 (d_K(t_j) - d_{ev,K}(t_j))}{n_K(t_j)(n_K(t_j) - 1)}$$

$$v_{1,K}(t_j) = \sum_{t_k \geq t_j} W(t_k) (t_{k+1} - t_k) (1 - \hat{I}_K(t_k))$$

$$v_{2,K}(t_j) = \sum_{t_k \geq t_j} W(t_k) (t_{k+1} - t_k)$$

$$v_{3,K}(t_j) = \sum_{t_k \geq t_j} W(t_k) (t_{k+1} - t_k) \hat{I}_K(t_k)$$

For large samples, Q_{PM} is approximately distributed as a chi-squared random variable with 1 degree of freedom. See Pintilie (2006) and Pepe and Mori (1993) for more information about this test.

Data Structure

This routine requires at least two variables: one containing the elapsed time values and another containing the type of event. Optional variables include a group identification variable and a frequency variable.

Marubini and Valsecchi (1996) include an example of hypothetical data consisting of two treatment groups and two events. The events are local relapse (1) and distant metastases (2). Censored observations are represented with a zero. Information is available on 35 subjects in each group. These data are stored in the Marubini database. The table below shows the data.

Marubini dataset

| Time | Treatment | Event |
|------|-----------|-------|
| 1 | A | 1 |
| 13 | A | 1 |
| 17 | A | 1 |
| 30 | A | 1 |
| 34 | A | 1 |
| 41 | A | 1 |
| 78 | A | 1 |
| 100 | A | 1 |
| 119 | A | 1 |
| 169 | A | 1 |
| 1 | A | 2 |
| 6 | A | 2 |
| 8 | A | 2 |
| 13 | A | 2 |
| 13 | A | 2 |
| 15 | A | 2 |
| . | . | . |
| . | . | . |
| . | . | . |

| Time | Treatment | Event |
|------|-----------|-------|
| 7 | B | 1 |
| 16 | B | 1 |
| 16 | B | 1 |
| 20 | B | 1 |
| 39 | B | 1 |
| 49 | B | 1 |
| 56 | B | 1 |
| 73 | B | 1 |
| 93 | B | 1 |
| 113 | B | 1 |
| 1 | B | 2 |
| 2 | B | 2 |
| 4 | B | 2 |
| 6 | B | 2 |
| 8 | B | 2 |
| 9 | B | 2 |
| . | . | . |
| . | . | . |
| . | . | . |

Example 1 – Cumulative Incidence

This section presents an example of how to generate cumulative incidence reports. The data used were shown above and are found in the Marubini dataset.

Setup

To run this example, complete the following steps:

- 1 **Open the Marubini example dataset**
 - From the File menu of the NCSS Data window, select **Open Example Data**.
 - Select **Marubini** and click **OK**.
- 2 **Specify the Cumulative Incidence procedure options**
 - Find and open the **Cumulative Incidence** procedure using the menus or the Procedure Navigator.
 - The settings for this example are listed below and are stored in the **Example 1** settings template. To load this template, click **Open Example Template** in the Help Center or File menu.

| Option | Value |
|--|-------------------------------------|
| Variables Tab | |
| Time Variable..... | Time |
| Event (Censor) Variable | Event |
| Event Types..... | 1 2 |
| Censor Types | 0 |
| Group Variable..... | Treatment |
| Reports Tab | |
| Events Reported On | 1 |
| Summary Reports Times..... | 25 50 75 100 125 150 175 200 |
| Confidence Level..... | 95 |
| Logrank Test (K Groups) | Checked |
| Plots Tab | |
| Two Plots Per Line..... | Checked |
| Cumulative Incidence Plot Format (<i>Click the Button</i>) | |
| Cumulative Incidence Line | Checked |
| Confidence Limits..... | Checked |
| Survival Plot Format (<i>Click the Button</i>) | |
| Kaplan-Meier Survival Line | Checked |
| Confidence Limits..... | Checked |

- 3 **Run the procedure**
 - Click the **Run** button to perform the calculations and generate the output.

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Data Summary Section

Data Summary Report for Treatment = A

| Type of Observation | Values | Count | Percent (%) | Minimum | Maximum |
|---------------------|--------|-------|-------------|---------|---------|
| Censored | 5 | 5 | 14.29% | 34 | 207 |
| Event = 1 | 10 | 10 | 28.57% | 1 | 169 |
| Event = 2 | 18 | 20 | 57.14% | 1 | 240 |
| Total | 33 | 35 | 100.00% | 1 | 240 |

This section of the report displays information about the database. It is especially useful to allow you to check for obvious data-entry errors. The Values column gives the number of unique time values. The Count column uses the values in the Frequency Variable when it was used.

Cumulative Incidence Detail Report

Cumulative Incidence Detail Report for Event = 1 and Treatment = A

| Time | Number At Risk | Events of Type 1 | Events of All Types | Cumulative Incidence | Lower 95% C.L. Cum. Inc. | Upper 95% C.L. Cum. Inc. | Standard Error of Cum. Inc. | 1 - Product Limit |
|-------|----------------|------------------|---------------------|----------------------|--------------------------|--------------------------|-----------------------------|-------------------|
| 1.0 | 35 | 1 | 2 | 0.0286 | 0.0041 | 0.1972 | 0.0282 | 0.0571 |
| 6.0 | 33 | 0 | 1 | 0.0286 | 0.0041 | 0.1972 | 0.0282 | 0.0857 |
| 8.0 | 32 | 0 | 1 | 0.0286 | 0.0041 | 0.1972 | 0.0282 | 0.1143 |
| 13.0 | 31 | 1 | 3 | 0.0571 | 0.0149 | 0.2195 | 0.0392 | 0.2000 |
| 15.0 | 28 | 0 | 1 | 0.0571 | 0.0149 | 0.2195 | 0.0392 | 0.2286 |
| . | . | . | . | . | . | . | . | . |
| . | . | . | . | . | . | . | . | . |
| 240.0 | 1 | 0 | 1 | 0.3144 | 0.1871 | 0.5285 | 0.0833 | 1.0000 |

This report displays the cumulative incidence values along with their confidence intervals and standard errors.

Time

This is the time value, t_j , being reported on. These values are from the dataset being analyzed. Note that tied values are combined.

Number at Risk

This is the number of individuals at risk, n_j , just before time t_j .

Events of Type 1

This is the number of events of the type indicated (in this report, the type is 1), d_{kj} , that occurred at t_j .

Events of All Types

This is the number of events of all types, d_{kj} , that occurred at time t_j . Note that censored observations have a zero in this column.

Cumulative Incidence

This is the cumulative incidence, $\hat{I}_k(t_j)$. This is the cumulative probability of event k up through the current time value, accounting for all other events. The formula used to calculate this value was given in the Technical Details section earlier in this chapter.

Cumulative Incidence

Lower and Upper 95% C.L. Cum. Inc.

These are confidence limits for the above cumulative incidence.

Standard Error of Cum. Inc.

This is the estimated standard error of the cumulative incidence. It is calculated using $\sqrt{\text{Var}[\hat{I}_k(t_j)]}$.

1 – Product Limit

This is one minus the Kaplan-Meier product limit estimate. This is a cumulative incidence measure calculated assuming that there are no other possible events other than the event of interest.

Cumulative Survival Detail Report

Cumulative Survival Detail Report for Event = 1 and Treatment = A

| Time | Number At Risk | Events of Type 1 | Events of All Types | Cumulative Survival | Lower 95% C.L. Cum. Surv. | Upper 95% C.L. Cum. Surv. | Standard Error of Cum. Surv. | Product Limit |
|-------|----------------|------------------|---------------------|---------------------|---------------------------|---------------------------|------------------------------|---------------|
| 1.0 | 35 | 1 | 2 | 0.9714 | 0.8028 | 0.9959 | 0.0282 | 0.9429 |
| 6.0 | 33 | 0 | 1 | 0.9714 | 0.8028 | 0.9959 | 0.0282 | 0.9143 |
| 8.0 | 32 | 0 | 1 | 0.9714 | 0.8028 | 0.9959 | 0.0282 | 0.8857 |
| 13.0 | 31 | 1 | 3 | 0.9429 | 0.7805 | 0.9851 | 0.0392 | 0.8000 |
| 15.0 | 28 | 0 | 1 | 0.9429 | 0.7805 | 0.9851 | 0.0392 | 0.7714 |
| . | . | . | . | . | . | . | . | . |
| . | . | . | . | . | . | . | . | . |
| 240.0 | 1 | 0 | 1 | 0.6856 | 0.4715 | 0.8129 | 0.0833 | 0.0000 |

This report displays the cumulative survival values along with their confidence intervals and standard errors. The cumulative survival values are equal to one minus the cumulative incidence values.

Cumulative Incidence Summary Report

Cumulative Incidence Summary Report for Event = 1 and Treatment = A

| Time | Number At Risk | Events of Type 1 | Events of All Types | Cumulative Incidence | Lower 95% C.L. Cum. Inc. | Upper 95% C.L. Cum. Inc. | Standard Error of Cum. Inc. | 1 - Product Limit |
|-------|----------------|------------------|---------------------|----------------------|--------------------------|--------------------------|-----------------------------|-------------------|
| 25.0 | 26 | 0 | 0 | 0.0857 | 0.0290 | 0.2529 | 0.0473 | 0.2571 |
| 50.0 | 18 | 0 | 0 | 0.1727 | 0.0834 | 0.3578 | 0.0642 | 0.4623 |
| 75.0 | 15 | 0 | 0 | 0.1727 | 0.0834 | 0.3578 | 0.0642 | 0.4940 |
| 100.0 | 10 | 1 | 1 | 0.2402 | 0.1308 | 0.4411 | 0.0745 | 0.6964 |
| 125.0 | 8 | 0 | 0 | 0.2739 | 0.1564 | 0.4797 | 0.0783 | 0.7301 |
| 150.0 | 5 | 0 | 0 | 0.2739 | 0.1564 | 0.4797 | 0.0783 | 0.7976 |
| 175.0 | 3 | 0 | 0 | 0.3144 | 0.1871 | 0.5285 | 0.0833 | 0.8786 |
| 200.0 | 2 | 0 | 0 | 0.3144 | 0.1871 | 0.5285 | 0.0833 | 0.9190 |

This report displays the cumulative incidence values at designated time values. All definitions are the same as in the Cumulative Incidence report. The number at risk and the numbers of events are for the last actual time value in the data before the current time value. For example, the values shown for the time of 75.0 are actually the values for the time of 63.0 on the database since 63.0 is the largest time value before 75.0.

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Cumulative Survival Summary Report

Cumulative Survival Summary Report for Event = 1 and Treatment = A

| Time | Number At Risk | Events of Type 1 | Events of All Types | Cumulative Survival | Lower 95% C.L. Cum. Surv. | Upper 95% C.L. Cum. Surv. | Standard Error of Cum. Surv. | Product Limit |
|-------|----------------|------------------|---------------------|---------------------|---------------------------|---------------------------|------------------------------|---------------|
| 25.0 | 26 | 0 | 0 | 0.9143 | 0.7471 | 0.9710 | 0.0473 | 0.7429 |
| 50.0 | 18 | 0 | 0 | 0.8273 | 0.6422 | 0.9166 | 0.0642 | 0.5377 |
| 75.0 | 15 | 0 | 0 | 0.8273 | 0.6422 | 0.9166 | 0.0642 | 0.5060 |
| 100.0 | 10 | 1 | 1 | 0.7598 | 0.5589 | 0.8692 | 0.0745 | 0.3036 |
| 125.0 | 8 | 0 | 0 | 0.7261 | 0.5203 | 0.8436 | 0.0783 | 0.2699 |
| 150.0 | 5 | 0 | 0 | 0.7261 | 0.5203 | 0.8436 | 0.0783 | 0.2024 |
| 175.0 | 3 | 0 | 0 | 0.6856 | 0.4715 | 0.8129 | 0.0833 | 0.1214 |
| 200.0 | 2 | 0 | 0 | 0.6856 | 0.4715 | 0.8129 | 0.0833 | 0.0810 |

This report displays the survival values at designated time values. All definitions are the same as in the Cumulative Survival report. The number at risk and the numbers of events are for the last actual time value in the data before the current time value. For example, the values shown for the time of 75.0 are actually the values for the time of 63.0 on the database since 63.0 is the largest time value before 75.0.

Gray's Test Report

Gray's Test

This test compares K groups while accounting for competing risks using the subdistribution hazards.

| Event Type | Chi-Square Value | DF | P-Value | Reject H0 at $\alpha = 0.05?$ |
|------------|------------------|----|---------|-------------------------------|
| Event = 1 | 0.2225 | 1 | 0.63711 | No |

This report displays the results of Gray's test, which accounts for competing risks. With a p-value of 0.63711, we would fail to reject the null hypothesis of no difference between the two groups for event 1.

Pepe and Mori's Test Report

Pepe and Mori's Test

This test compares 2 groups while accounting for competing risks using the cumulative incidence functions (CIF's).

| Event Type | Chi-Square Value | DF | P-Value | Reject H0 at $\alpha = 0.05?$ |
|------------|------------------|----|---------|-------------------------------|
| Event = 1 | 0.0575 | 1 | 0.81043 | No |

This report displays the results of Pepe and Mori's test, which accounts for competing risks. With a p-value of 0.81043, we would fail to reject the null hypothesis of no difference between the two groups for event 1. This is consistent with the results of Gray's test.

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Logrank Test Report

Logrank Test

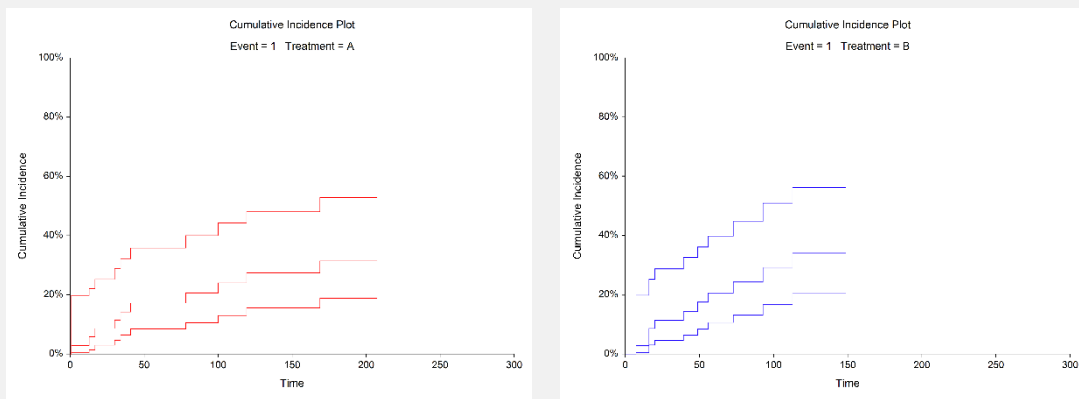
This test compares the cause-specific hazards for K groups without accounting for competing risks. All competing risk events are considered censored by this test.

| Event Type | Chi-Square Value | DF | P-Value | Reject H0 at $\alpha = 0.05$? |
|------------|------------------|----|---------|--------------------------------|
| Event = 1 | 2.0392 | 1 | 0.15329 | No |

This report displays the results of the logrank test, which does not account for competing risks. With a p-value of 0.15329, we would fail to reject the null hypothesis of no difference between the two groups for event 1.

Individual Cumulative Incidence Plots

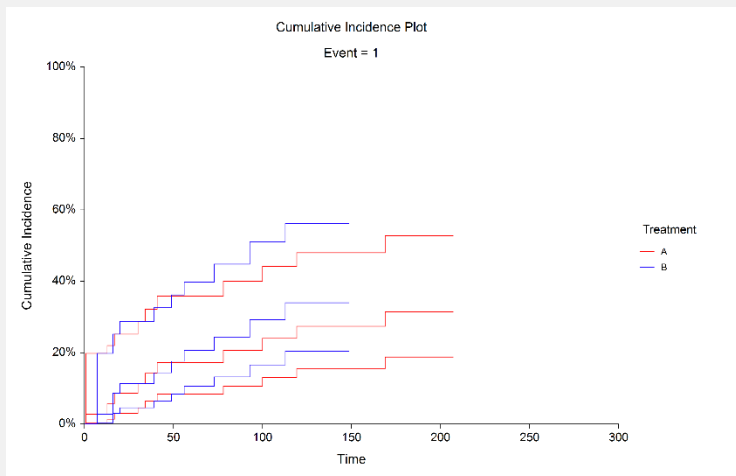
Individual Cumulative Incidence Plots



These plots show the cumulative incidence curve surrounded by the 95% confidence interval. Note that only Event = 1 is shown because this was the selection of the Events Reported On option under the Reports tab.

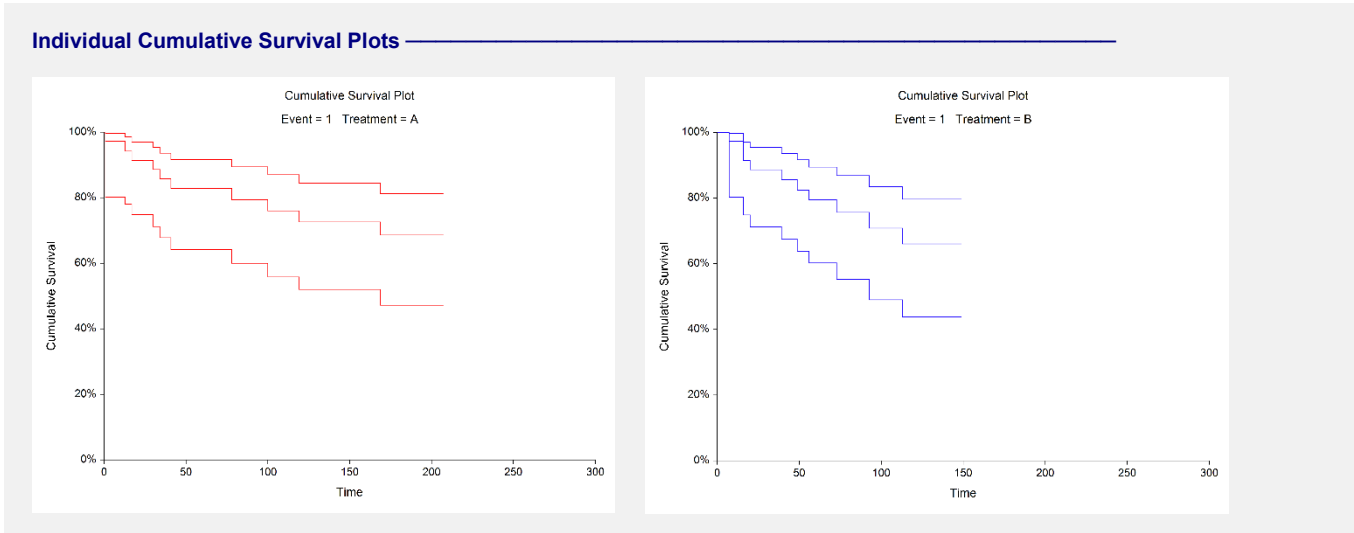
Combined Cumulative Incidence Plots By Event

Combined Cumulative Incidence Plots By Event



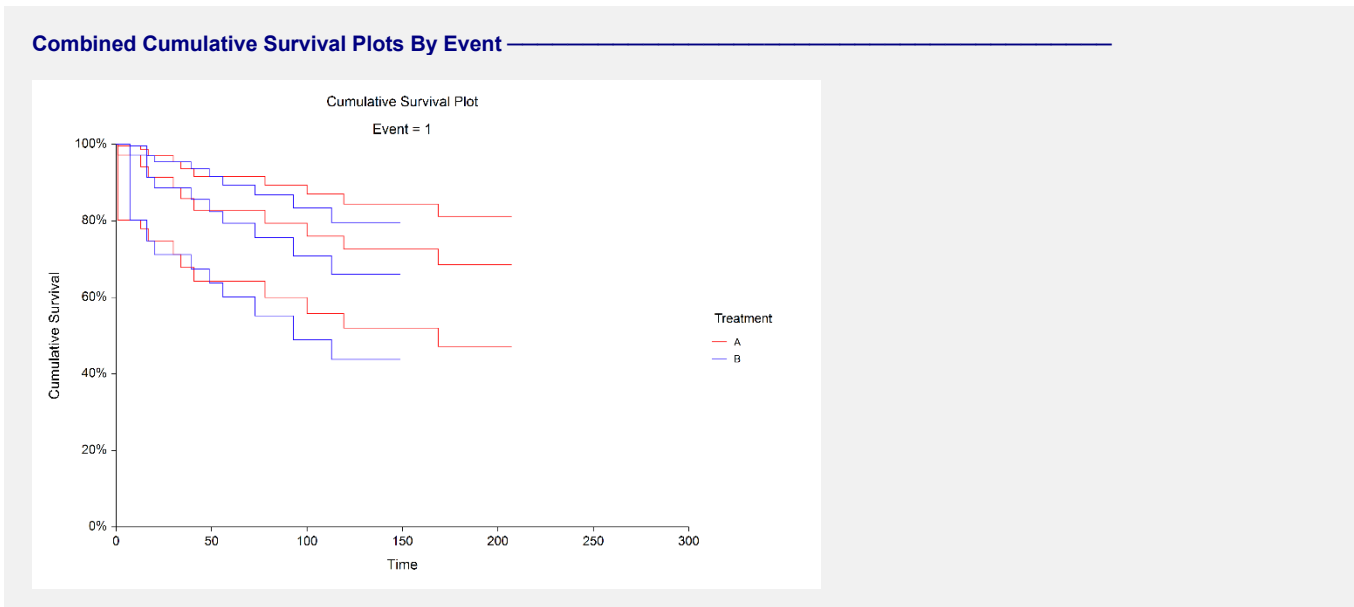
This plot shows the cumulative incidence for each of the two groups. Note that only Event = 1 is shown because this was the selection of the Events Reported On option under the Reports tab.

Individual Cumulative Survival Plots



These plots display the cumulative survival values and confidence intervals for each group, one group per plot. Note that only Event = 1 is shown because this was the selection of the Events Reported On option under the Reports tab.

Combined Cumulative Survival Plots By Event



This plot displays the cumulative survival values for both groups. Note that only Event = 1 is shown because this was the selection of the Events Reported On option under the Reports tab.

Example 2 – Validation of Cumulative Incidence Estimation Values and Gray’s Test using Marubini and Valsecchi (1996)

Marubini and Valsecchi (1996) reported cumulative incidence values calculated for the data in the Marubini dataset. For event 1 and group B at Time = 16 they calculated the cumulative incidence as 0.08571, with a standard error of 0.04732 and confidence limits of 0.02905 to 0.25292. They also report the Gray’s test statistic for event 1 to be 0.222 with a p-value of 0.634.

Setup

To run this example, complete the following steps:

1 Open the Marubini example dataset

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Select **Marubini** and click **OK**.

2 Specify the Cumulative Incidence procedure options

- Find and open the **Cumulative Incidence** procedure using the menus or the Procedure Navigator.
- The settings for this example are listed below and are stored in the **Example 2** settings template. To load this template, click **Open Example Template** in the Help Center or File menu.

| <u>Option</u> | <u>Value</u> |
|--|------------------|
| Variables Tab | |
| Time Variable..... | Time |
| Event (Censor) Variable | Event |
| Event Types..... | 1 2 |
| Censor Types | 0 |
| Group Variable..... | Treatment |
| Reports Tab | |
| Events Reported On | 1 |
| Cumulative Incidence Detail Report | Checked |
| Confidence Level..... | 95 |
| Gray's Test (K Groups)..... | Checked |
| Plots Tab | |
| All Plots..... | Unchecked |

3 Run the procedure

- Click the **Run** button to perform the calculations and generate the output.

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Output

Cumulative Incidence Detail Report for Event = 1 and Treatment = B

| Time | Number At Risk | Events of Type 1 | Events of All Types | Cumulative Incidence | Lower 95% C.L. Cum. Inc. | Upper 95% C.L. Cum. Inc. | Standard Error of Cum. Inc. | 1 - Product Limit |
|-------|----------------|------------------|---------------------|----------------------|--------------------------|--------------------------|-----------------------------|-------------------|
| 1.0 | 35 | 0 | 1 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0286 |
| 2.0 | 34 | 0 | 1 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0571 |
| 4.0 | 33 | 0 | 1 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.0857 |
| 6.0 | 32 | 0 | 1 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | 0.1143 |
| 7.0 | 31 | 1 | 1 | 0.0286 | 0.0041 | 0.1972 | 0.0282 | 0.1429 |
| 8.0 | 30 | 0 | 1 | 0.0286 | 0.0041 | 0.1972 | 0.0282 | 0.1714 |
| 9.0 | 29 | 0 | 1 | 0.0286 | 0.0041 | 0.1972 | 0.0282 | 0.2000 |
| 10.0 | 28 | 0 | 1 | 0.0286 | 0.0041 | 0.1972 | 0.0282 | 0.2286 |
| 13.0 | 27 | 0 | 1 | 0.0286 | 0.0041 | 0.1972 | 0.0282 | 0.2571 |
| 16.0 | 26 | 2 | 2 | 0.0857 | 0.0290 | 0.2529 | 0.0473 | 0.3143 |
| 17.0 | 24 | 0 | 3 | 0.0857 | 0.0290 | 0.2529 | 0.0473 | 0.4000 |
| 18.0 | 21 | 0 | 2 | 0.0857 | 0.0290 | 0.2529 | 0.0473 | 0.4571 |
| 20.0 | 19 | 1 | 1 | 0.1143 | 0.0454 | 0.2874 | 0.0538 | 0.4857 |
| 27.0 | 18 | 0 | 1 | 0.1143 | 0.0454 | 0.2874 | 0.0538 | 0.5143 |
| 29.0 | 17 | 0 | 1 | 0.1143 | 0.0454 | 0.2874 | 0.0538 | 0.5429 |
| 34.0 | 16 | 0 | 0 | 0.1143 | 0.0454 | 0.2874 | 0.0538 | 0.5429 |
| 39.0 | 15 | 1 | 2 | 0.1448 | 0.0643 | 0.3259 | 0.0599 | 0.6038 |
| 49.0 | 13 | 1 | 1 | 0.1752 | 0.0847 | 0.3627 | 0.0650 | 0.6343 |
| 50.0 | 12 | 0 | 1 | 0.1752 | 0.0847 | 0.3627 | 0.0650 | 0.6648 |
| 56.0 | 11 | 1 | 1 | 0.2057 | 0.1063 | 0.3983 | 0.0693 | 0.6952 |
| 60.0 | 10 | 0 | 0 | 0.2057 | 0.1063 | 0.3983 | 0.0693 | 0.6952 |
| 63.0 | 9 | 0 | 0 | 0.2057 | 0.1063 | 0.3983 | 0.0693 | 0.6952 |
| 69.0 | 8 | 0 | 1 | 0.2057 | 0.1063 | 0.3983 | 0.0693 | 0.7333 |
| 73.0 | 7 | 1 | 1 | 0.2438 | 0.1329 | 0.4473 | 0.0755 | 0.7714 |
| 76.0 | 6 | 0 | 1 | 0.2438 | 0.1329 | 0.4473 | 0.0755 | 0.8095 |
| 78.0 | 5 | 0 | 0 | 0.2438 | 0.1329 | 0.4473 | 0.0755 | 0.8095 |
| 93.0 | 4 | 1 | 1 | 0.2914 | 0.1666 | 0.5098 | 0.0832 | 0.8571 |
| 110.0 | 3 | 0 | 1 | 0.2914 | 0.1666 | 0.5098 | 0.0832 | 0.9048 |
| 113.0 | 2 | 1 | 1 | 0.3390 | 0.2045 | 0.5621 | 0.0874 | 0.9524 |
| 149.0 | 1 | 0 | 0 | 0.3390 | 0.2045 | 0.5621 | 0.0874 | 0.9524 |

Gray's Test

This test compares K groups while accounting for competing risks using the subdistribution hazards.

| Event Type | Chi-Square Value | DF | P-Value | Reject H0 at $\alpha = 0.05$? |
|------------|------------------|----|---------|--------------------------------|
| Event = 1 | 0.2225 | 1 | 0.63711 | No |

The cumulative incidence value (0.0857), the standard error (0.0473), and confidence limits (0.0290,0.2529) for Time = 16 match those reported by Marubini and Valsecchi (1996). The test statistic (0.2225) and p-value (0.63711) match as well with slight differences due to rounding.

Example 3 – Validation of Gray’s Test, Pepe and Mori’s Test, and the Logrank Test using Pintilie (2006)

Pintilie (2006) uses the R package “cmprsk” (written by Bob Gray, the author of Gray (1998)) to compute Gray’s test for a Follicular cell lymphoma dataset. The author reports the test statistics and p-values obtained from R “cmprsk” to be 2.631747 and 1.047464e-01, respectively, for event 1 and 39.309879 and 3.616071e-10, respectively, for event 2.

For event 1, Pintilie (2006) further computes Pepe and Mori’s test (test statistic = 2.617415, p-value = 0.1056965) and the logrank test (test statistic = 6.941658, p-value = 0.008421103).

This example will demonstrate that NCSS gets the same results.

Setup

To run this example, complete the following steps:

1 Open the Follic example dataset

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Select **Follic** and click **OK**.

2 Specify the Cumulative Incidence procedure options

- Find and open the **Cumulative Incidence** procedure using the menus or the Procedure Navigator.
- The settings for this example are listed below and are stored in the **Example 3** settings template. To load this template, click **Open Example Template** in the Help Center or File menu.

| <u>Option</u> | <u>Value</u> |
|--|------------------|
| Variables Tab | |
| Time Variable..... | dftime |
| Event (Censor) Variable | event |
| Event Types..... | 1 2 |
| Censor Types | 0 |
| Group Variable..... | group |
| Reports Tab | |
| Events Reported On | ALL |
| Data Summary Report..... | Unchecked |
| Cumulative Incidence Detail Report | Unchecked |
| Cumulative Survival Detail Report..... | Unchecked |
| Cumulative Incidence Summary..... | Unchecked |
| Report | |
| Cumulative Survival Summary | Unchecked |
| Report | |
| Gray's Test (K Groups)..... | Checked |
| Pepe and Mori's Test (2 Groups) | Checked |
| Logrank Test (K Groups) | Checked |
| Plots Tab | |
| All Plots..... | Unchecked |

3 Run the procedure

- Click the **Run** button to perform the calculations and generate the output.

Cumulative Incidence

Output

Gray's Test

This test compares K groups while accounting for competing risks using the subdistribution hazards.

| Event Type | Chi-Square Value | DF | P-Value | Reject H0 at $\alpha = 0.05$? |
|------------|------------------|----|---------|--------------------------------|
| event = 1 | 2.6317 | 1 | 0.10475 | No |
| event = 2 | 39.3470 | 1 | 0.00000 | Yes |

Pepe and Mori's Test

This test compares 2 groups while accounting for competing risks using the cumulative incidence functions (CIF's).

| Event Type | Chi-Square Value | DF | P-Value | Reject H0 at $\alpha = 0.05$? |
|------------|------------------|----|---------|--------------------------------|
| event = 1 | 2.6174 | 1 | 0.10570 | No |
| event = 2 | 17.7670 | 1 | 0.00002 | Yes |

Logrank Test

This test compares the cause-specific hazards for K groups without accounting for competing risks. All competing risk events are considered censored by this test.

| Event Type | Chi-Square Value | DF | P-Value | Reject H0 at $\alpha = 0.05$? |
|------------|------------------|----|---------|--------------------------------|
| event = 1 | 6.9417 | 1 | 0.00842 | Yes |
| event = 2 | 66.1370 | 1 | 0.00000 | Yes |

The test statistics and p-values reported by NCSS all match Pintilie (2006) except for Gray's Test for event 2... there is a slight difference there. As was stated in the introduction, Pintilie (2006) uses the R package "cmprsk" to compute Gray's test. We reran the example from the book using the most recent version of "cmprsk", version 2.2-7, and found that the results from "cmprsk" in R match the values reported by NCSS.

Example 4 – Adding an At-Risk Table to a Cumulative Incidence Plot and a Survival 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 cumulative incidence plot and a survival plot. The survival plot will be created with default settings, but we'll modify the cumulative incidence plot to highlight some of the available options. The data used in this example are contained in the Marubini dataset.

Setup

To run this example, complete the following steps:

- 1 **Open the Marubini example dataset**
 - From the File menu of the NCSS Data window, select **Open Example Data**.
 - Select **Marubini** and click **OK**.
- 2 **Specify the Cumulative Incidence procedure options**
 - Find and open the **Cumulative Incidence** procedure using the menus or the Procedure Navigator.
 - The settings for this example are listed below and are stored in the **Example 4** settings template. To load this template, click **Open Example Template** in the Help Center or File menu.

| <u>Option</u> | <u>Value</u> |
|--|--|
| Variables Tab | |
| Time Variable..... | Time |
| Event (Censor) Variable | Event |
| Event Types..... | 1 2 |
| Censor Types | 0 |
| Group Variable..... | Treatment |
| Reports Tab | |
| Events Reported On | 1 |
| All Reports | Unchecked |
| Report Options Tab | |
| Value Labels | Value Labels |
| Plots Tab | |
| Combined Incidence Plots (By Event) | Checked |
| Combined Survival Plots (By Event)..... | Checked |
| Cumulative Incidence Plot Format (<i>Click the Button</i>) | |
| <i>Cum. Incidence Tab</i> | |
| Cumulative Incidence Line | Checked |
| Tick Marks at Censor Points | Checked |
| <i>At-Risk Table Tab</i> | |
| General Sub-Tab | |
| Show At-Risk Table..... | Checked |
| Display..... | Number At Risk (Number Censored) (Number of Events) |
| Layout Sub-Tab | |
| Top Outside Margin..... | 0 |

Cumulative Incidence

Groups Sub-Tab

Display (Group Headings)..... **Line + Symbol + Label**

Add a Label Prefix..... **Unchecked**

Label Colors From..... **Line Fill**

Value Colors From **Line Fill**

Value Layout (*Click the Button*)

Alignment..... **Center**

Survival Plot Format (*Click the Button*)

Survival Tab

Kaplan-Meier Survival Line **Checked**

At-Risk Table Tab

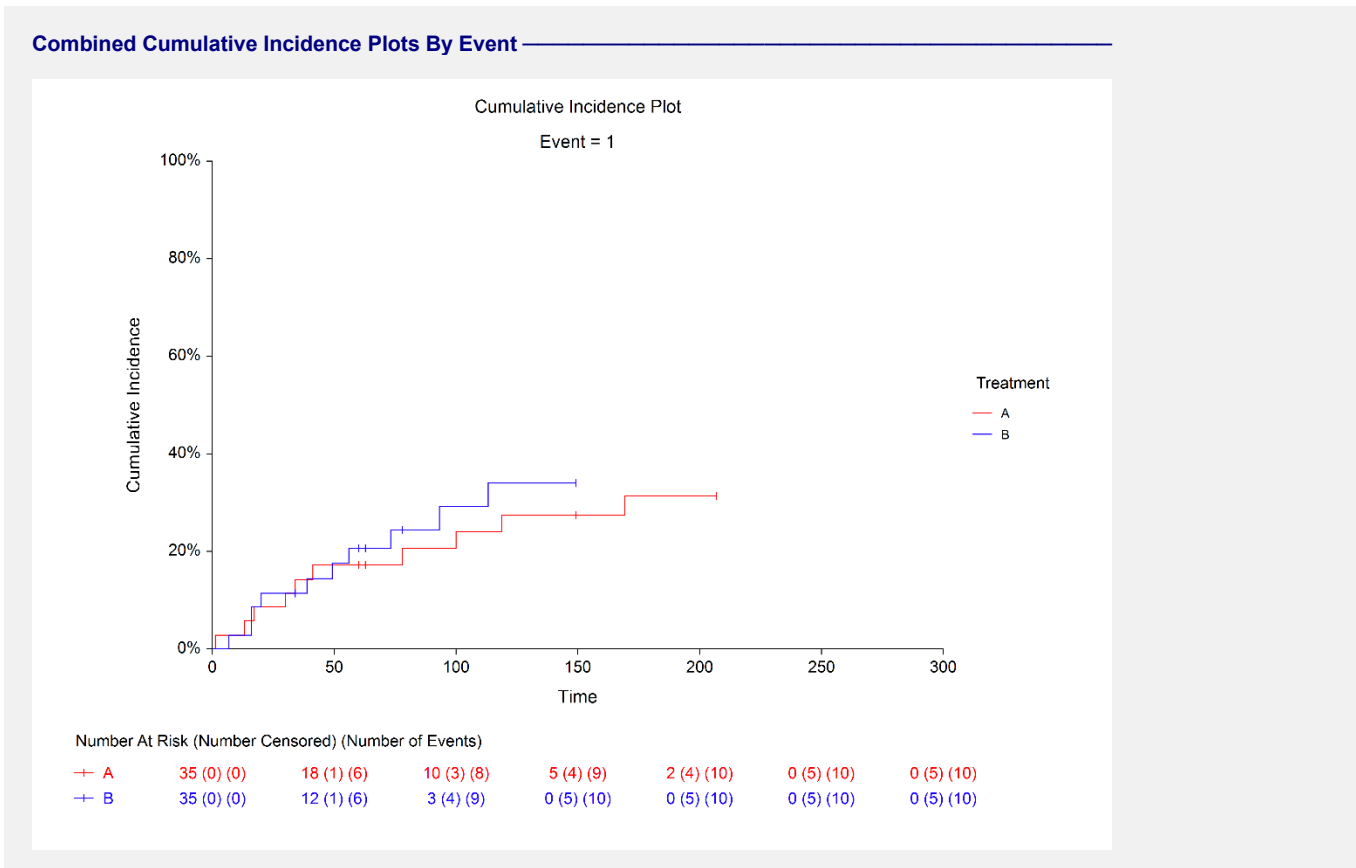
General Sub-Tab

Show At-Risk Table..... **Checked**

3 Run the procedure

- Click the **Run** button to perform the calculations and generate the output.

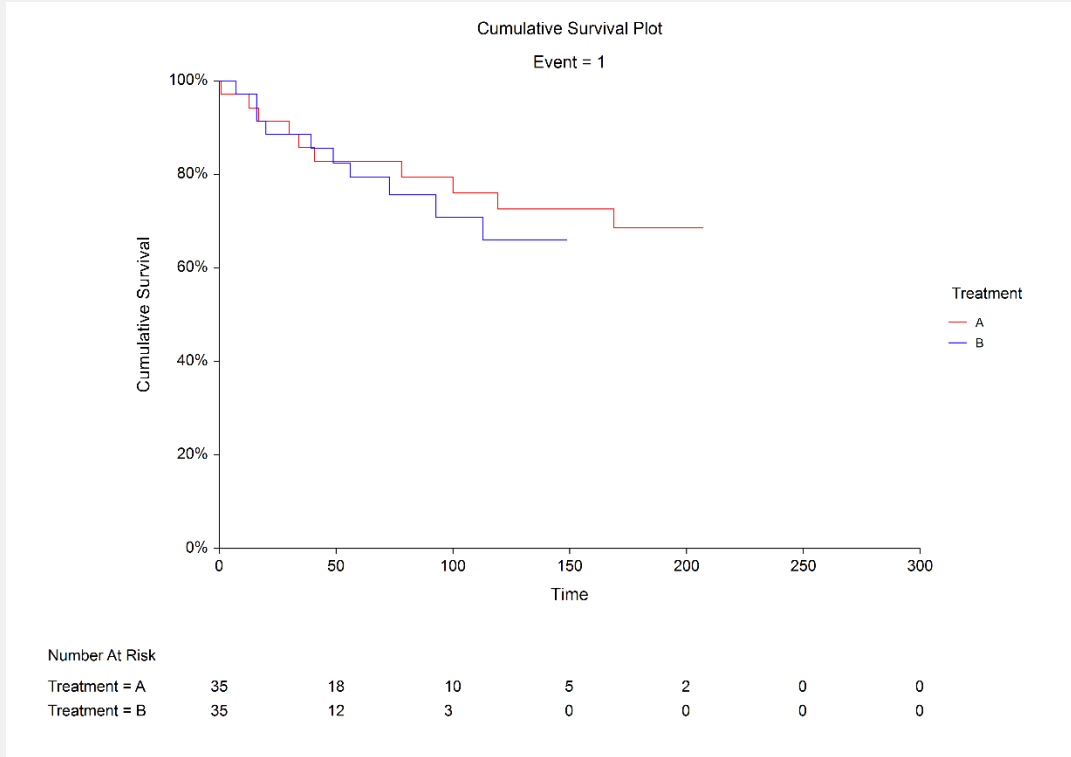
Output



The modified cumulative incidence 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.

Cumulative Incidence

Combined Cumulative Survival Plots By Event



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.