Chapter 706

Non-Inferiority Logrank Tests

Introduction

This module computes the sample size and power for *non-inferiority* tests under the assumption of proportional hazards. Accrual time and follow-up time are included among the parameters to be set. The non-inferiority logrank test is used for data analysis.

Sometimes, the objective of a study is to show that an experimental therapy is not inferior to (no worse than) the standard therapy. The experimental therapy may be cheaper, less toxic, or have fewer side effects. Such studies are often called non-inferiority trials and have a one-sided hypothesis.

Power and sample size calculations for the non-inferiority logrank test have been developed by Jung et al. (2005), and we use their results. These calculations assume an underlying exponential survival distribution with a uniform patient accrual pattern during the accrual period.

Technical Details

Test Statistic

Suppose a clinical trial consists of two independent groups. Designate group one as the standard group with hazard rate h_1 and sample size n_1. Designate group two as the experimental group with hazard rate h_2 and sample size n_2. The total sample size is $N = n_1 + n_2$. Usually, you would plan to have $n_1 = n_2$.

Define the proportion of the total sample in each group as

$$Q_i = \frac{n_i}{N}, \quad i = 1,2$$

Individuals are recruited during an accrual period of R years (or months or days). They are followed for an additional period of time until a total of T years is reached. Hence, the follow-up period is T-R years. At the end of the study, the non-inferiority logrank test is conducted at significance level α with power $1-\beta$. Under the proportion hazards assumption, the hazard ratio $HR = h_2 / h_1$ is constant across time.

For a given non-inferiority margin HR_0 (>1) (the maximum ratio of clinical insignificance), the statistical hypotheses tested are

$$H_0 : HR \geq HR_0 \text{ vs. } H_1 : HR < HR_0$$

Define the partial score function as

$$W(HR) = HR\sum_{i=1}^{n_1}\frac{\delta_{1i}\sum_{j=1}^{n_2} I(X_{2j} \ge X_{1i})}{\sum_{j=1}^{n_1} I(X_{1j} \ge X_{1i}) + HR\sum_{j=1}^{n_2} I(X_{2j} \ge X_{1i})} - \sum_{i=1}^{n_2}\frac{\delta_{2i}\sum_{j=1}^{n_2} I(X_{1j} \ge X_{2i})}{\sum_{j=1}^{n_1} I(X_{1j} \ge X_{2i}) + HR\sum_{j=1}^{n_2} I(X_{2j} \ge X_{2i})}$$

and the information function as

$$\sigma_N^2(HR) = HR\sum_{k=1}^{2}\sum_{i=1}^{n_k}\frac{\delta_{ki}\left\{\sum_{j=1}^{n_1} I(X_{1j} \ge X_{ki})\right\}\left\{\sum_{j=1}^{n_2} I(X_{2j} \ge X_{ki})\right\}}{\left\{\sum_{j=1}^{n_1} I(X_{1j} \ge X_{ki}) + HR\sum_{j=1}^{n_2} I(X_{2j} \ge X_{ki})\right\}^2}$$

where X_{ki} is the minimum of the survival time, and the censoring time, δ_{ki} ,is an event indicator taking 1 if there was an event or 0 otherwise, and $I(.)$ is an indicator function. Note that $W(1)$ is the standard logrank test statistic. Under H_0, $W(HR_0)/\sigma_N(HR_0)$ is asymptotically normal with mean 0 and variance 1. Reject H_0 in favor of H_1 if $W(HR_0)/\sigma_N(HR_0) > z_{1-\alpha}$ with one-sided type I error probability α.

The partial MLE, $\hat{HR}$, is obtained by solving $W(HR) = 0$. Let $HR*$ denote the true value of HR. It can be shown that $\hat{HR}$ is asymptotically normal with mean $HR*$ and variance $\sigma_N^{-2}(HR*)$.

An asymptotic $100(1-\alpha)\%$ confidence interval for HR is $\hat{HR} \pm z_{1-\alpha/2}\sigma_N^{-1}(\hat{HR})$.

Power Calculations

Jung (2005) shows that the power of the non-inferiority logrank test can be expressed as

$$1-\beta = \Phi\left(\frac{(HR_0 - 1)DQ_1Q_2 - z_{1-\alpha}\sqrt{HR_0}}{Q_1 + Q_2 HR_0}\right)$$

where D is the observed number of deaths (events). The total sample size N is obtained by inflating D according to the relationship $E(d)N = D$, where $E(d)$ is the expected death rate for the trial.

Following the proposal of Yateman and Skene (1992) and the results of Lakatos (1988), we compute $E(d)$ using the Markov Model given in chapter 715 as

$$E(d) = Q_1 S_{1,2} + Q_2 S_{2,2}$$

where $S_{1,2}$ and $S_{2,2}$ are the occupancy probabilities for the event state for the standard and experimental groups, respectively. This formulation allows the inclusion of loss to follow-up, noncompliance, and drop-in along with various accrual patterns.

Procedure Options

This section describes the options that are specific to this procedure. These are located on the Design tab. For more information about the options of other tabs, go to the Procedure Window chapter.

Design Tab

The Design tab contains most of the parameters and options that you will be concerned with.

Solve For

Solve For

This option specifies the parameter to be solved for from the other parameters. The parameters that may be selected are *Power* or *Sample Size*. Select *Sample Size* when you want to calculate the sample size needed to achieve a given power and alpha level. Select *Power* when you want to calculate the power.

Power and Alpha

Power

This option specifies one or more values for power. Power is the probability of rejecting a false null hypothesis, and is equal to one minus Beta. Beta is the probability of a type-II error, which occurs when a false null hypothesis is not rejected. In this procedure, a type-II error occurs when you do not reject the null hypothesis that the hazard ratio is greater than *HR*0 when in fact it is.

Values must be between zero and one. Historically, the value of 0.80 (Beta = 0.20) was used for power. Now, 0.90 (Beta = 0.10) is also commonly used.

A single value may be entered here or a range of values such as *0.8 to 0.95 by 0.05* may be entered.

Alpha

This option specifies one or more values for the probability of a type-I error. A type-I error occurs when you reject the null hypothesis that the hazard ratio is greater than *HR*0 when in fact it is not.

Values of alpha must be between zero and one. Historically, the value of 0.05 has been used for alpha. This means that about one test in twenty will falsely reject the null hypothesis. You should pick a value for alpha that represents the risk of a type-I error you are willing to take in your experimental situation.

You may enter a range of values such as *0.01 0.05 0.10* or *0.01 to 0.10 by 0.01*.

Sample Size

Total Sample Size (N)

This is the combined sample size of both groups. This amount is divided between the two groups using the value of the Proportion in Reference Group.

Percent in Group 1

This is the percent of *N* in the reference (control) group. If this value is labeled Q_1, the sample size of group one is NQ_1 and the sample size of group two is $N - NQ_1$. Note that the value of NQ_1 is rounded to the nearest integer.

Effect Size

HR0 (Non-Inferiority Hazard Ratio)

Enter the non-inferiority bound for the hazard ratio. This value is used to construct the hypotheses.

Higher Hazards Worse

When events are bad (such as death), then this number should be > 1. The alternative hypothesis is H1: HR < HR0.

Enter the maximum hazard ratio for which the treatment group will be considered non-inferior to the reference group. For example, if you enter 1.20 here, you are saying that hazard ratios < 1.20 will result in the conclusion of non-inferiority when H0 is rejected. In other words, hazard ratios up to 1.20 indicate that the treatment group is no worse than the reference group.

Higher Hazards Better

When events are good, then this number should be < 1. The alternative hypothesis is H1: HR > HR0.

Enter the minimum hazard ratio for which the treatment group will be considered non-inferior to the reference group. For example, if you enter 0.8 here, you are saying that hazard ratios > 0.8 will result in the conclusion of non-inferiority when H0 is rejected. In other words, hazard ratios down to 0.8 indicate that the treatment group is no worse than the reference group.

h1 (Hazard Rate of Reference Group)

Specify one or more hazard rates (instantaneous failure rate) for the reference group. For an exponential distribution, the hazard rate is the inverse of the mean survival time. An estimate of the hazard rate may be obtained from the median survival time or from the proportion surviving to a certain time point. This calculation is automated by pressing the *Parameter Conversion* button.

Hazard rates must be greater than zero. Constant hazard rates are specified by entering them directly. Variable hazard rates are specified as columns of the spreadsheet. When you want to specify different hazard rates for different time periods, you would enter those rates into a column of the spreadsheet, one row per time period. You specify the column (or columns) by beginning the entry with an equals sign. For example, if you have entered the hazard rates in column 2, you would enter *=2* here.

Duration

Accrual Time (Integers Only)

Enter one or more values for the number of time periods (months, years, etc.) during which subjects are entered into the study. The total duration of the study is equal to the Accrual Time plus the Follow-Up Time. These values must be integers.

Accrual times can range from 0 to the Total Time. That is, the accrual time must be less than or equal to the Total Time. Otherwise, the scenario is skipped.

Enter *0* when all subjects begin the study together.

Accrual Pattern

Specify the type of accrual (patient entry) pattern. Two types of entries are possible:

- **Uniform or Equal**

  If you want to specify a uniform accrual rate for all time periods, enter *Equal* here.

- **Non-Uniform (Spreadsheet Entry)**

  Use this option when you want to specify one or more accrual patterns with different accrual rates per time period. You will specify the different accrual rates for each time period in the spreadsheet.

Accrual Values in Columns

Specify the columns of the spreadsheet containing the different accrual (patient entry) rates. One value per row is entered in spreadsheet cells for each time period. Each value is the proportion of the total number of subjects that enroll during the corresponding time period.

Syntax

Enter an equals sign followed by a list of columns containing the accrual patterns. For example, if you have entered two sets of accrual patterns in columns 1 and 2, you would enter "=C1 C2."

Standardized

Note that cell values in a column are standardized so they sum to one. Thus, the accrual patterns 2 1 1 and 50 25 25 both result in the same accrual pattern as 0.50 0.25 0.25 .

Number of Rows and Columns

The number of rows in each column should equal the Accrual Time. The number of columns is up to you. A separate analysis is conducted for each column.

Spreadsheet Cells

In a specified column, the proportion of all subjects that are expected to enroll during the first time period is specified in row one. The proportion of all subjects that are expected during the second time period is specified in row two. And so on.

For example, if you had specified three accrual-time periods and you wanted to specify double the accrual rate in the first period than in the other two, the spreadsheet would appear as

C1
2
1
1

Total Time (Integers Only)

Enter one or more values for the number of time periods (months, years, etc.) in the study. The follow-up time is equal to the Total Time minus the Accrual Time. These values must be integers.

Proportion Lost or Switching Groups

Reference (or Treatment) Lost

This is the proportion of subjects in the reference (treatment) group that are lost to follow up (i.e. censored) during a single time period (month, year, etc.). Multiple entries, such as *0.01 0.03 0.05*, are allowed.

When you want to specify different proportions for different time periods, you would enter those proportions into a column of the spreadsheet, one row per time period. You specify the column of the spreadsheet by beginning your entry with an equals sign. For example, if you have entered the proportions in column 5, you would enter *=C5* here.

Reference Switching to Treatment

This is the proportion of subjects in the reference group that change to a treatment regime similar in efficacy to the treatment group during a single time period (month, year, etc.). This is sometimes referred to as *drop in*. Multiple entries, such as *0.01 0.03 0.05*, are allowed.

When you want to specify different proportions for different time periods, you would enter those values into a column of the spreadsheet, one row per time period. You specify the column of the spreadsheet by beginning your entry with an equals sign. For example, if you have entered the proportions in column 1, you would enter *=C1* here.

Treatment Switching to Reference

This is the proportion of subjects in the treatment group that change to a treatment regime similar in efficacy to the reference group during a single time period (month, year, etc.). This is sometimes referred to as *noncompliance*. Multiple entries, such as *0.01 0.03 0.05*, are allowed.

When you want to specify different proportions for different time periods, you would enter those values into a column of the spreadsheet, one row per time period. You specify the column of the spreadsheet by beginning your entry with an equals sign. For example, if you have entered the proportions in column 2, you would enter *=C2* here.

Reports Tab

The Reports tab contains additional settings for this procedure.

Report Column Width

Report Column Width

This option sets the width of the each column of the numeric report.

The numeric report for this option necessarily contains many columns, so the maximum number of decimal places that can be displayed is four. If you try to increase that number, the numbers may run together. You can increase the width of each column using this option.

The recommended report column width for scenarios without large numbers of decimal places or extremely large sample sizes is 0.49.

Options Tab

The Options tab contains additional settings for this procedure.

Options

Number of Intervals within a Time Period

The algorithm requires that each time period be partitioned into a number of equal-width intervals. Each of these subintervals is assumed to follow an exponential distribution. This option controls the number of subintervals. All parameters such as hazard rates, loss to follow-up rates, and noncompliance rates are assumed to be constant within a subinterval.

Lakatos (1988) gives little input as to how the number of subintervals should be chosen. In a private communication, he indicated that 100 ought to be adequate. This seems to work when the hazard rate is less than 1.0.

As the hazard rate increases above 1.0, this number must increase. A value of 2000 should be sufficient as long as the hazard rates (h1 and h2) are less than 10. When the hazard rates are greater than 10, you may want to increase this value to 5000 or even 10000.

Example 1 – Finding the Power

A non-inferiority trial is planned in which the primary analysis will use the non-inferiority logrank test. After extensive discussion, the researchers have decided that the upper bound on non-inferiority is 1.3.

The trial will include a recruitment period of two-years after which participants will be followed for three more years. It is assumed that patients will enter the study uniformly over the accrual period. The researcher estimates a loss-to-follow rate of 5% per year in both the reference and experimental groups. Past experience leads to a base line hazard rate of 0.04. An equal sample allocation design will be used with a target power of 0.90 and significance level of 0.05.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Non-Inferiority Logrank Tests** procedure window by expanding **Survival**, then **Two Survival Curves**, then clicking on **Non-Inferiority**, and then clicking on **Non-Inferiority Logrank Tests**. You may then make the appropriate entries as listed below, or open **Example 1** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Power**
Alpha	**0.05**
Group Allocation	**Enter total sample size and percentage in Group 1**
Total Sample Size (N)	**1000 to 5000 by 1000**
Percent in Group 1	**50**
HR0 (Non-Inferiority Hazard Ratio)	**1.3**
h1 (Hazard Rate of Reference Group)	**0.04**
Accrual Time (Integers Only)	**2**
Accrual Pattern	**Uniform or Equal**
Total Time (Integers Only)	**5**
References Lost	**0.05**
References Switch to Treatment	**0.0**
Treatments Lost	**0.0**
Treatments Switch to Reference	**0.0**
Reports Tab	
Show Detail Numeric Reports	**Checked**

Annotated Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Results

Numeric Results in Terms of Sample Size
Hypotheses: H0: HR ≥ HR0 vs. H1: HR < HR0

Power	N1	N2	N	Non-Inf Haz Ratio HR0	Actual Haz Ratio HR1	Ref Haz Rate h1	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ref Loss	Trt Loss	Ref to Trt	Trt to Ref	Alpha	Beta
0.4665	500	500	1000	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0000	0.0000	0.0000	0.0500	0.5335
0.7111	1000	1000	2000	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0000	0.0000	0.0000	0.0500	0.2889
0.8528	1500	1500	3000	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0000	0.0000	0.0000	0.0500	0.1472
0.9282	2000	2000	4000	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0000	0.0000	0.0000	0.0500	0.0718
0.9662	2500	2500	5000	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0000	0.0000	0.0000	0.0500	0.0338

References

Jung,Sin-Ho; Kang, Sun J.; McCall, Linda M.; Blumenstein, Brent. 2005. 'Sample Sizes Computation for Two-Sample Noninferiority Log-Rank Test', J. of Biopharmaceutical Statistics, Volume 15, pages 969-979.
Lakatos, Edward. 1988. 'Sample Sizes Based on the Log-Rank Statistic in Complex Clinical Trials', Biometrics, Volume 44, March, pages 229-241.

Report Definitions

Power is the probability of rejecting a false null hypothesis. Power should be close to one.
N1|N2|N are the sample sizes of the reference group, treatment group, and both groups, respectively.
E1|E2|E are the number of events in the reference group, the treatment group, and both groups, respectively.
Non-Inferiority Haz Ratio (HR0) is the upper bound for the hazard ratio that still leads to the conclusion of non-inferiority.
Actual Haz Ratio (HR1) is assumed to be the actual value of the hazard ratio. This is always set to 1.
Ref Haz Rate (h1) is the hazard (instantaneous failure) rate of the reference group. Its scale is events per time period.
Accrual Time is the number of time periods (years or months) during which accrual takes place.
Total Time is the total number of time periods in the study. Follow-up time = (Total Time) - (Accrual Time).
Ref Loss is the proportion of the reference group that is lost (drop out) during a single time period (year or month).
Trt Loss is the proportion of the treatment group that is lost (drop out) during a single time period (year or month).
Ref to Trt (drop in) is the proportion of the reference group that switch to a group with a hazard rate equal to the treatment group.
Trt to Ref (noncompliance) is the proportion of the treatment group that switch to a group with a hazard rate equal to the reference group.
Alpha is the probability of rejecting a true null hypothesis. It should be small.
Beta is the probability of accepting a false null hypothesis. It should be small.

This report shows the values of each of the parameters, one scenario per row. We see that almost 4000 subjects will be required for this study.

Next, a report displaying the number of required events rather than the sample size is displayed.

Numeric Results in Terms of Events
Hypotheses: H0: HR ≥ HR0 vs. H1: HR < HR0

Power	Ref Evts E1	Trt Evts E2	Total Evts E	Non-Inf Haz Ratio HR0	Actual Haz Ratio HR1	Ref Haz Rate h1	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ref Loss	Trt Loss	Ref to Trt	Trt to Ref	Alpha	Beta
0.4665	66.8	73.8	140.6	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0000	0.0000	0.0000	0.0500	0.5335
0.7111	133.6	147.6	281.3	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0000	0.0000	0.0000	0.0500	0.2889
0.8528	200.4	221.5	421.9	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0000	0.0000	0.0000	0.0500	0.1472
0.9282	267.3	295.3	562.5	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0000	0.0000	0.0000	0.0500	0.0718
0.9662	334.1	369.1	703.2	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0000	0.0000	0.0000	0.0500	0.0338

Most of this report is identical to the last report, except that the sample sizes are replaced by the number of required events.

Next, reports displaying the individual settings year-by-year for each scenario are displayed.

Detailed Input when Power=0.4510 HR0=1.30 HR=1.00 N=1000 Alpha=0.0500 Accrual/Total Time=2 / 5

Time Period	Reference Hazard Rate h1 (0.0400)	Percent Accrual (Equal)	Percent Admin. Censored (Calc.)	Reference Loss (0.0500)	Treatment Loss (0.0000)	Switch Reference to Treatment (0.0000)	Switch Treatment to Reference (0.0000)
1	0.0400	50.00	0.00	0.0500	0.0000	0.0000	0.0000
2	0.0400	50.00	0.00	0.0500	0.0000	0.0000	0.0000
3	0.0400	0.00	0.00	0.0500	0.0000	0.0000	0.0000
4	0.0400	0.00	50.00	0.0500	0.0000	0.0000	0.0000
5	0.0400	0.00	100.00	0.0500	0.0000	0.0000	0.0000

This report shows the individual settings for each time period (year). It becomes very useful when you want to document a study in which these parameters vary from year to year.

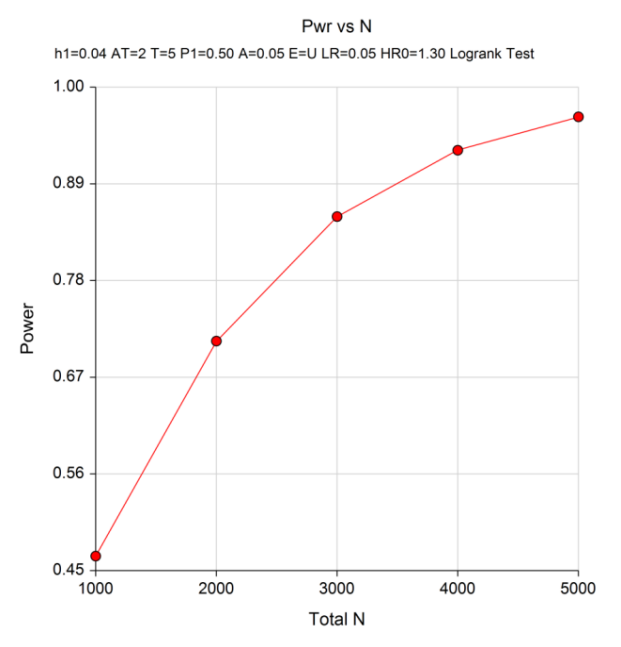
Next, summary statements are displayed.

Summary Statements

A logrank test for non-inferiority against an upper hazard ratio bound of 1.30 with an overall sample size of 1000 subjects (500 in the reference group and 500 in the treatment group) achieves 46.65% power at a 0.050 significance level when the actual hazard ratio is 1.00 and the reference group hazard rate is 0.0400. The study lasts for 5 time periods of which subject accrual (entry) occurs in the first 2 time periods. The accrual pattern across time periods is uniform (all periods equal). The proportion dropping out of the reference group is 0.0500. No subjects drop out of the treatment group. The proportion switching from the reference group to another group with a hazard rate equal to the treatment group is 0.0000. The proportion switching from the treatment group to another group with a hazard rate equal to the reference group is 0.0000.

Finally, a scatter plot of the results is displayed.

Plots Section



This plot shows the relationship between sample size and. Note that for 90% power, a total sample size of about 4000 is required. The exact number will be found in Example 2.

Example 2 – Finding the Sample Size

Continuing with the previous example, the researcher wants to investigate the sample sizes necessary to achieve 80% and 90% power. All other parameters will remain the same as in Example 1.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Non-Inferiority Logrank Tests** procedure window by expanding **Survival**, then **Two Survival Curves**, then clicking on **Non-Inferiority**, and then clicking on **Non-Inferiority Logrank Tests**. You may then make the appropriate entries as listed below, or open **Example 2** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Sample Size**
Power	**0.80 0.90**
Alpha	**0.05**
Group Allocation	**Equal (N1 = N2)**
HR0 (Non-Inferiority Hazard Ratio)	**1.3**
h1 (Hazard Rate of Reference Group)	**0.04**
Accrual Time (Integers Only)	**2**
Accrual Pattern	**Uniform or Equal**
Total Time (Integers Only)	**5**
References Lost	**0.05**
References Switch to Treatment	**0.0**
Treatments Lost	**0.05**
Treatments Switch to Reference	**0.0**

Output

Click the Run button to perform the calculations and generate the following output.

Numeric Results

Numeric Results in Terms of Sample Size

Hypotheses: H0: HR ≥ HR0 vs. H1: HR < HR0

Power	N1	N2	N	Non-Inf Haz Ratio HR0	Actual Haz Ratio HR1	Ref Haz Rate h1	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ref Loss	Trt Loss	Ref to Trt	Trt to Ref	Alpha	Beta
0.8000	1344	1345	2689	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0500	0.0000	0.0000	0.0500	0.2000
0.9000	1865	1866	3731	1.30	1.00	0.0400	Equal	2 / 5	0.0500	0.0500	0.0000	0.0000	0.0500	0.1000

Example 3 – Validation using Jung (2005)

Jung et al. (2005) pages 974-975 present an example that will be used to validate this procedure. In this article, an 8.8-year trial is presented in which patient accrual occurs the first 3.8 years. The baseline hazard rate is 0.0446. The value of *HR*0 is 1.3 and the value of *HR* is 1.0. Equal allocation between groups is used and uniform accrual is assumed. The significance level is 0.05 and the desired power is 0.90. Given these values, the number of events is found to be 499 and the sample size is 1891.

Since this procedure using integer values for the accrual and trial time, the accrual time and total time will be set to 4 and 9 years, respectively.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Non-Inferiority Logrank Tests** procedure window by expanding **Survival**, then **Two Survival Curves**, then clicking on **Non-Inferiority**, and then clicking on **Non-Inferiority Logrank Tests**. You may then make the appropriate entries as listed below, or open **Example 3** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Find (Solve For)	**Sample Size**
Power	**0.90**
Alpha	**0.05**
Group Allocation	**Equal (N1 = N2)**
HR0	**1.3**
h1	**0.0446**
Accrual Time	**4**
Accrual Pattern	**Uniform or Equal**
Total Time	**9**
References Lost	**0.0**
References Switch to Treatment	**0.0**
Treatments Lost	**0.0**
Treatments Switch to Reference	**0.0**

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Results

Numeric Results in Terms of Sample Size

Hypotheses: H0: HR ≥ HR0 vs. H1: HR < HR0

Power	N1	N2	N	Non-Inf Haz Ratio HR0	Actual Haz Ratio HR1	Ref Haz Rate h1	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ref Loss	Trt Loss	Ref to Trt	Trt to Ref	Alpha	Beta
0.9000	933	933	1866	1.30	1.00	0.0446	Equal	4 / 9	0.0000	0.0000	0.0000	0.0000	0.0500	0.1000

Numeric Results in Terms of Events
Hypotheses: H0: HR ≥ HR0 vs. H1: HR < HR0

Power	Ref Evts E1	Trt Evts E2	Total Evts E	Non-Inf Haz Ratio HR0	Actual Haz Ratio HR1	Ref Haz Rate h1	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ref Loss	Trt Loss	Ref to Trt	Trt to Ref	Alpha	Beta
0.9000	249.3	249.3	**498.6**	1.30	1.00	0.0446	Equal	4 / 9	0.0000	0.0000	0.0000	0.0000	0.0500	0.1000

Note that the number of events (499) matches Jung's results exactly. The sample size of 1866 is slightly less than Jung's 1891. This difference occurs because these results were obtained for 4 years of accrual, not 3.8, and because we used Lakatos' method for transforming the number of events into the sample size.

Example 4 – Inputting Time-Dependent Hazard Rates from a Spreadsheet

Time-dependent parameters (hazard rates, losses to follow-up, etc) may be entered. See Example 4 of Chapter 715 (Logrank Tests) for an extensive example of how this is done for the logrank test.