Chapter 715

Logrank Tests

Introduction

This procedure computes the sample size and power of the logrank test for equality of survival distributions under very general assumptions. Accrual time, follow-up time, loss during follow up, noncompliance, and time-dependent hazard rates are parameters that can be set.

A clinical trial is often employed to test the equality of survival distributions for two treatment groups. For example, a researcher might wish to determine if Beta-Blocker A enhances the survival of newly diagnosed myocardial infarction patients over that of the standard Beta-Blocker B. The question being considered is whether the pattern of survival is different.

The two-sample t-test is not appropriate for two reasons. First, the data consist of the length of survival (time to failure), which is often highly skewed, so the usual normality assumption cannot be validated. Second, since the purpose of the treatment is to increase survival time, it is likely (and desirable) that some of the individuals in the study will survive longer than the planned duration of the study. The survival times of these individuals are then said to be *censored*. These times provide valuable information, but they are not the actual survival times. Hence, special methods have to be employed which use both regular and censored survival times.

The logrank test is one of the most popular tests for comparing two survival distributions. It is easy to apply and is usually more powerful than an analysis based simply on proportions. It compares survival across the whole spectrum of time, not just at one or two points. This module allows the sample size and power of the logrank test to be analyzed under very general conditions.

Power and sample size calculations for the logrank test have been studied by several authors. This PASS module uses the method of Lakatos (1988) because of its generality. This method is based on a Markov model that yields the asymptotic mean and variance of the logrank statistic under very general conditions.

Four Different Effect Size Parameterizations

There are four closely-related effect size parameterizations that are available in this procedure and documented in this chapter. The parameterization can be in terms of hazard rates, median survival time, proportion surviving, and mortality (proportion dying).

The Markov process methodology divides the total study time into K equal-length intervals. The value of K is large enough so that the distribution within an interval can be assumed to follow the exponential distribution. The next section presents pertinent results for the exponential distribution.

Exponential Distribution

The density function of the exponential is defined as

$$f(t) = he^{-ht}$$

The probability of surviving the first t years is

$$S(t) = e^{-ht}$$

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The mortality (probability of dying during the first t years) is

$$M(t) = 1 - e^{-ht}$$

For an exponential distribution, the mean survival is $1/h$ and the median is $\ln(2)/h$.

Notice that it is easy to translate between the hazard rate, the proportion surviving, the mortality, and the median survival time. The choice of which parameterization is used is arbitrary and is selected according to the convenience of the user.

Hazard Rate Parameterization

In this case, the hazard rates for the control and treatment groups are specified directly.

Median Survival Time Parameterization

Here, the median survival time is specified. These are transformed to hazard rates using the relationship $h = \ln(2) / MST$.

Proportion Surviving Parameterization

In this case, the proportion surviving until a given time $T0$ is specified. These are transformed to hazard rates using the relationship $h = -\ln(S(T0)) / T0$. Note that when separate proportions surviving are given for each time period, $T0$ is taken to be the time period number.

Mortality Parameterization

Here, the mortality until a given time $T0$ is specified. These are transformed to hazard rates using the relationship $h = -\ln(1 - M(T0)) / T0$. Note that when separate mortalities are given for each time period, $T0$ is taken to be the time period number.

Comparison of Lakatos Procedures to other *PASS* Logrank Procedures

The follow chart lists the capabilities and assumptions of each of the logrank procedures available in ***PASS***.

	Algorithm		
Feature/Capability	**Simple (Freedman)**	**Advanced (Lachin)**	**Markov Process (Lakatos)**
Test Statistic	Logrank statistic	Mean hazard difference*	Logrank statistic
Hazard Ratio	Constant	Constant	Any pattern including time-dependent
Basic Time Distribution	Constant hazard ratio**	Constant hazard ratio (exponential)	Any distribution
Loss to Follow Up Parameters	Yes	Yes	Yes
Accrual Parameters	No	Yes	Yes
Drop In Parameters	No	No	Yes
Noncompliance Parameters	No	No	Yes
Duration Parameters	No	Yes	Yes
Input Hazard Ratios	No	No	Yes
Input Median Survival Times	No	No	Yes
Input Proportion Surviving	Yes	Yes	Yes
Input Mortality Rates	No	No	Yes

*Simulation shows power similar to logrank statistic
**Not necessarily exponential

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Comparison of Results

It is informative to calculate sample sizes for various scenarios using several of the methods. The scenario used to compare the various methods was S1 = 0.5, S2 = 0.7, T0 = 4, Loss to Follow Up = 0.05, Accrual Time = 2, Total Time = 4, and N = 200. Note that the Freedman method in ***PASS*** does not allow the input of T0, Accrual Time, or Total Time, so it is much less comparable. The Lachin/Foulkes and Lakatos values are very similar.

Computation Method	S1	S2	T0	Loss to Follow Up	Accrual Time	Total Time	N	Power
PASS (Freedman)	0.5	0.7	?	0.05	0	?	200	0.7979
PASS (Lachin/Foulkes)	0.5	0.7	4	0.05	2	4	200	0.7219
PASS (Lakatos)	0.5	0.7	4	0.05	2	4	200	0.7144

Technical Details

The logrank statistic L is defined as

$$L = \frac{\sum_{i=1}^{d}\left(X_i - \frac{n_{2i}}{n_{1i}+n_{2i}}\right)}{\left[\sum_{i=1}^{d}\frac{n_{1i}n_{2i}}{(n_{1i}+n_{2i})^2}\right]^{1/2}}$$

where X_i is an indicator for the control group, n_{2i} is the number at risk in the experimental group just before the i^{th} event (death), and n_{1i} is the number at risk in the control group just before the i^{th} event (death).

Following Freedman (1982) and Lakatos (1988), the trial is partitioned into K equal intervals. The distribution of L is asymptotically normal with mean E and variance V given by

$$E = \frac{\sum_{k=1}^{K}\sum_{i=1}^{d_k}\left(\frac{\phi_{ki}\theta_{ki}}{1+\phi_{ki}\theta_{ki}} - \frac{\phi_{ki}}{1+\phi_{ki}}\right)}{\left[\sum_{k=1}^{K}\sum_{i=1}^{d_k}\frac{\phi_{ki}}{(1+\phi_{ki})^2}\right]^{\frac{1}{2}}}$$

$$V = \frac{\sum_{k=1}^{K}\sum_{i=1}^{d_i}\frac{\phi_{ki}\theta_{ki}}{(1+\phi_{ki}\theta_{ki})^2}}{\sum_{k=1}^{K}\sum_{i=1}^{d_k}\frac{\phi_{ki}}{(1+\phi_{ki})^2}}$$

where

$$\phi_{ki} = \frac{n_{2i}}{n_{1i}}$$

$$\theta_{ki} = \frac{h_{2i}}{h_{1i}}$$

and h_{1ki} and h_{2ki} are the hazards of dying in the control and treatment groups respectively, just before the i^{th} death in the k^{th} interval. d_k is the number of deaths in the k^{th} interval.

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Next, assume that the intervals are short enough so that the parameters are constant within an interval. That is, so that

$$\phi_{ki} = \phi_k\,,\ \theta_{ki} = \theta_k\,,\ h_{1ki} = h_{1k}\,,\ h_{2ki} = h_{2k}$$

The values of *E* and *V* then reduce to

$$E = \sqrt{d}\,\frac{\sum_{k=1}^{K}\left[\left(\frac{d_k}{d}\right)\left(\frac{\phi_k\theta_k}{1+\phi_k\theta_k} - \frac{\phi_k}{1+\phi_k}\right)\right]}{\sqrt{\sum_{k=1}^{K}\left[\left(\frac{d_k}{d}\right)\left(\frac{\phi_k}{(1+\phi_k)^2}\right)\right]}} \qquad V = \frac{\sum_{k=1}^{K}\left[\left(\frac{d_k}{d}\right)\frac{\phi_k\theta_k}{(1+\phi_k\theta_k)^2}\right]}{\sum_{k=1}^{K}\left[\left(\frac{d_k}{d}\right)\frac{d_k\phi_k}{(1+\phi_k)^2}\right]}$$

$$= \sqrt{d}\,\frac{\sum_{k=1}^{K}\left[\rho_k\left(\frac{\phi_k\theta_k}{1+\phi_k\theta_k} - \frac{\phi_k}{1+\phi_k}\right)\right]}{\sqrt{\sum_{k=1}^{K}\left[\rho_k\left(\frac{\phi_k}{(1+\phi_k)^2}\right)\right]}} \qquad = \frac{\sum_{k=1}^{K}\left[\rho_k\frac{\phi_k\theta_k}{(1+\phi_k\theta_k)^2}\right]}{\sum_{k=1}^{K}\left[\rho_k\frac{d_k\phi_k}{(1+\phi_k)^2}\right]}$$

where

$$d = \sum_{k=1}^{K} d_k$$

and ρ_k is the proportion of the events (deaths) that occur in interval *k*.

The intervals mentioned above are constructed to correspond to a non-stationary Markov process, one for each group. This Markov process is defined as follows

$$S_{1,k} = T_{1,k,k-1}S_{1,k-1}$$

where $S_{1,k}$ is a vector giving the occupancy probabilities for each of the four possible states of the process: lost, dead, active complier, or active non-complier and $T_{1,k,k-1}$ is the transition matrix constructed so that each element gives the probability of transferring from state *j1* to state *j2* in the control group. A similar formulation is defined for the treatment group.

At each iteration

$$S_{1,k} = \begin{bmatrix} s_{1,k,1} \\ s_{1,k,2} \\ s_{1,k,3} \\ s_{1,k,4} \end{bmatrix},\ S_{2,k} = \begin{bmatrix} s_{2,k,1} \\ s_{2,k,2} \\ s_{2,k,3} \\ s_{2,k,4} \end{bmatrix}$$

At the beginning of the trial

$$S_{1,0} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ q_1 \end{bmatrix},\ S_{2,0} = \begin{bmatrix} 0 \\ 0 \\ 1-q_1 \\ 0 \end{bmatrix}$$

where q_1 is the control proportion of the total sample.

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The transition matrices may be different for each group, but this does not need to be so. Its elements are as follows (the first row and column contains labels which are not part of the actual matrix).

$$T_{1,k,k-1} = \begin{bmatrix} States & Lost & Event & Complier & Non-complier \\ Lost & 1 & 0 & p_{loss,k} & p_{loss,k} \\ Event & 0 & 1 & p_{event1,k} & p_{event2,k} \\ Complier & 0 & 0 & 1-sum_c & p_{drop-in,k} \\ Non-complier & 0 & 0 & p_{noncomp,k} & 1-sum_n \end{bmatrix}$$

where sum_c and sum_n represent the sum of the other elements of their columns.

These values represent parameters of the population such as event rates, loss to follow-up rates, and recruitment rates.

The parameters ϕ_k , θ_k, and d_k are estimated from the occupancy probabilities as follows

Events (deaths)

$$d_{1,k} = s_{1,k,2} - s_{1,k-1,2}$$

$$d_{2,k} = s_{2,k,2} - s_{2,k-1,2}$$

Censored

$$c_{1,i} = s_{1,k,1} - s_{1,k-1,1}$$

$$c_{2,i} = s_{2,k,1} - s_{2,k-1,1}$$

At Risk

$$a_{1,k} = \left(s_{1,k-1,3} + s_{1,k-1,4}\right)$$

$$a_{2,k} = \left(s_{2,k-1,3} + s_{2,k-1,4}\right)$$

Hazard

$$h_{1,k} = d_{1,k} / a_{1,k}$$

$$h_{2,k} = d_{2,k} / a_{2,k}$$

Finally, the interval parameters are given by

$$\phi_k = \frac{s_{2,k-1,3} + s_{2,k-1,4}}{s_{1,k-1,3} + s_{1,k-1,4}}$$

$$\theta_k = \frac{h_{2,k,3}}{h_{1,k,3}}$$

$$d_k = d_{1,k} + d_{2,k}$$

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Power Calculation

1. Find z_α such that $1-\Phi(z_\alpha)=\alpha$, where $\Phi(x)$ is the area under the standardized normal curve to the left of *x*.
2. Calculate E_0 and V_0 assuming the two transition matrices are the same (H0). Also, calculate E_1 and V_1 assuming the two transition matrices are different (H1)
3. Calculate: $X_\alpha = E_0 + z_\alpha V_0$
4. Calculate: $z_\beta = \dfrac{X_\alpha - E_1}{V_1}$
5. Calculate beta and power: $\beta = \Phi(z_\beta)$.

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. This chapter covers four procedures, each of which has different effect size options. However, many of the options are common to all four procedures. These common options will be displayed first, followed by the various effect size options.

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*, *Sample Size*, and *Effect size (HR or MR)*. Note that the effect size corresponds to the parameterization that is chosen.

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.

Test

Alternative

Specify whether the statistical test is two-sided or one-sided.

- **Two-Sided**

  This option tests whether the two hazards rates, median survival times, survival proportions, or mortalities are different (H1: h1 ≠ h2). This is the option that is usually selected.

- **One-Sided**

  When this option is used and the value of h1 is less than h2, rejecting the null hypothesis results in the conclusion that the control hazard rate (h1) is less than the treatment hazard rate (h2). When h1 is greater than h2, rejecting the null hypothesis results in the conclusion that the control hazard rate (h1) is greater than the treatment hazard rate (h2). When you use a one-sided test, you should divide your alpha level by two.

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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 fail to reject the null hypothesis of equal survival curves when in fact the curves are different.

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 of equal survival curves when in fact the curves are equal.

Values of alpha must be between zero and one. Historically, the value of 0.05 has been used for a two-sided test and 0.025 has been used for a one-sided test. 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 (When Solving for Sample Size)

Group Allocation

Select the option that describes the constraints on *N1* or *N2* or both.

The options are

- **Equal (N1 = N2)**

  This selection is used when you wish to have equal sample sizes in each group. Since you are solving for both sample sizes at once, no additional sample size parameters need to be entered.

- **Enter R = N2/N1, solve for N1 and N2**

  For this choice, you set a value for the ratio of *N2* to *N1*, and then PASS determines the needed *N1* and *N2*, with this ratio, to obtain the desired power. An equivalent representation of the ratio, *R*, is

  $$N2 = R * N1.$$

- **Enter percentage in Group 1, solve for N1 and N2**

  For this choice, you set a value for the percentage of the total sample size that is in Group 1, and then PASS determines the needed *N1* and *N2* with this percentage to obtain the desired power.

R (Group Sample Size Ratio)

This option is displayed only if Group Allocation = "Enter R = N2/N1, solve for N1 and N2."

R is the ratio of *N2* to *N1*. That is,

$$R = N2 / N1.$$

Use this value to fix the ratio of *N2* to *N1* while solving for *N1* and *N2*. Only sample size combinations with this ratio are considered.

N2 is related to *N1* by the formula:

$$N2 = [R \times N1],$$

where the value *[Y]* is the next integer $\geq Y$.

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For example, setting $R = 2.0$ results in a Group 2 sample size that is double the sample size in Group 1 (e.g., $N1 = 10$ and $N2 = 20$, or $N1 = 50$ and $N2 = 100$).

R must be greater than 0. If $R < 1$, then $N2$ will be less than $N1$; if $R > 1$, then $N2$ will be greater than $N1$. You can enter a single or a series of values.

Percent in Group 1

This option is displayed only if Group Allocation = "Enter percentage in Group 1, solve for N1 and N2."

Use this value to fix the percentage of the total sample size allocated to Group 1 while solving for $N1$ and $N2$. Only sample size combinations with this Group 1 percentage are considered. Small variations from the specified percentage may occur due to the discrete nature of sample sizes.

The Percent in Group 1 must be greater than 0 and less than 100. You can enter a single or a series of values.

Sample Size (When Not Solving for Sample Size)

Group Allocation

Select the option that describes how individuals in the study will be allocated to Group 1 and to Group 2.

The options are

- **Equal (N1 = N2)**
  This selection is used when you wish to have equal sample sizes in each group. A single per group sample size will be entered.

- **Enter N1 and N2 individually**
  This choice permits you to enter different values for $N1$ and $N2$.

- **Enter N1 and R, where N2 = R * N1**
  Choose this option to specify a value (or values) for $N1$, and obtain $N2$ as a ratio (multiple) of $N1$.

- **Enter total sample size and percentage in Group 1**
  Choose this option to specify a value (or values) for the total sample size (N), obtain $N1$ as a percentage of N, and then $N2$ as $N - N1$.

Sample Size Per Group

This option is displayed only if Group Allocation = "Equal (N1 = N2)."

The Sample Size Per Group is the number of items or individuals sampled from each of the Group 1 and Group 2 populations. Since the sample sizes are the same in each group, this value is the value for $N1$, and also the value for $N2$.

The Sample Size Per Group must be ≥ 2. You can enter a single value or a series of values.

N1 (Sample Size, Group 1)

*This option is displayed if Group Allocation = "Enter N1 and N2 individually" or "Enter N1 and R, where N2 = R * N1."*

$N1$ is the number of items or individuals sampled from the Group 1 population.

$N1$ must be ≥ 2. You can enter a single value or a series of values.

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N2 (Sample Size, Group 2)

This option is displayed only if Group Allocation = "Enter N1 and N2 individually."

N2 is the number of items or individuals sampled from the Group 2 population.

N2 must be ≥ 2. You can enter a single value or a series of values.

R (Group Sample Size Ratio)

*This option is displayed only if Group Allocation = "Enter N1 and R, where N2 = R * N1."*

R is the ratio of *N2* to *N1*. That is,

$$R = N2/N1$$

Use this value to obtain *N2* as a multiple (or proportion) of *N1*.

N2 is calculated from *N1* using the formula:

$$N2=[R \times N1],$$

where the value *[Y]* is the next integer ≥ *Y*.

For example, setting *R* = 2.0 results in a Group 2 sample size that is double the sample size in Group 1.

R must be greater than 0. If *R* < 1, then *N2* will be less than N1; if *R* > 1, then *N2* will be greater than *N1*. You can enter a single value or a series of values.

Total Sample Size (N)

This option is displayed only if Group Allocation = "Enter total sample size and percentage in Group 1."

This is the total sample size, or the sum of the two group sample sizes. This value, along with the percentage of the total sample size in Group 1, implicitly defines *N1* and *N2*.

The total sample size must be greater than one, but practically, must be greater than 3, since each group sample size needs to be at least 2.

You can enter a single value or a series of values.

Percent in Group 1

This option is displayed only if Group Allocation = "Enter total sample size and percentage in Group 1."

This value fixes the percentage of the total sample size allocated to Group 1. Small variations from the specified percentage may occur due to the discrete nature of sample sizes.

The Percent in Group 1 must be greater than 0 and less than 100. You can enter a single value or a series of values.

Effect Size

Input Type

Indicate what type of values to enter to specify the effect size. Regardless of the entry type chosen, the test statistics used in the power and sample size calculations are the same. This option is simply given for convenience in specifying the effect size.

The choices are

- **Hazard Rate**

  Enter h1, the hazard rate of the control group, and either h2, the hazard rate of the treatment group, or HR = h2/h1, the hazard ratio.

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- **Median Survival Time**

  Enter T1, the median survival time of the control group, and either T2, the median survival time of the treatment group, or HR = T1/T2, the hazard ratio.

- **Proportion Surviving**

  Enter S1, the proportion surviving past time T0 in the control group, and either S2, the proportion surviving past time T0 in the treatment group, or HR, the hazard ratio.

- **Mortality**

  Enter M1, the mortality rate through time T0 in the control group, and either M2, the mortality rate through time T0 in the treatment group, or MR = M2/M1, the mortality ratio.

Effect Size = Hazard Rate

h1 (Hazard Rate of Control Group)

Specify one or more hazard rates (instantaneous failure rate) for the control 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.

The following examples assume an exponential survival distribution.

Median Survival Time	Hazard Rate
0.5	1.386
1.0	0.693
2.0	0.347
3.0	0.231
4.0	0.173
5.0	0.139

Treatment Group Parameter

Specify which of the parameters below will be used to specify the treatment group hazard rate.

h2 (Hazard Rate – Treatment Group)

Specify one or more hazard rates (instantaneous failure rate) for the treatment group. 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 3, you would enter *=3* here.

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HR (Hazard Ratio = h2/h1)

Specify one or more values for the hazard ratio, HR = h2/h1. Hazard ratios must be greater than zero. The null hypothesis is that the hazard ratio is 1.0. Typical values of the hazard ratio are from 0.25 to 4.0.

Constant hazard ratios are specified by entering them directly. Variable hazard ratios are specified as columns of the spreadsheet.

An estimate of the hazard ratio may be obtained from the median survival times, from the hazard rates, or from the proportion surviving past a certain time point by pressing the *Parameter Conversion* button.

When you want to specify different hazard ratios for different time periods, you would enter those values into a column of the spreadsheet, one row per time period. You specify the column (or columns) by beginning your entry with an equals sign.

For example, if you have entered the hazard ratios in column 3, you would enter *=3* here.

Effect Size = Median Survival Time

T1 (Median Survival Time – Control)

Specify one or more median survival times for the control group. These values must be greater than zero.

Constant median survival times are specified by entering them directly. Variable median survival times are specified as columns of the spreadsheet. When you want to specify different median survival times for different time periods, you would enter those times 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 median survival times in column 2, you would enter =2 here.

The following examples assume an exponential survival distribution.

Median Survival Time	Hazard Rate
0.5	1.386
1.0	0.693
2.0	0.347
3.0	0.231
4.0	0.173
5.0	0.139

Treatment Group Parameter

Specify which of the parameters below will be used to specify the treatment group median survival time.

T2 (Median Survival Time – Treatment)

Specify one or more median survival times for the treatment group. These values must be greater than zero.

Constant median survival times are specified by entering them directly. Variable median survival times are specified as columns of the spreadsheet. When you want to specify different median survival times for different time periods, you would enter those times 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 median survival times in column 1, you would enter *=1* here.

HR (Hazard Ratio = T1/T2)

Specify one or more values for the hazard ratio, HR = T1/T2 = h2/h1. Hazard ratios must be greater than zero. The null hypothesis is that the hazard ratio is 1.0. Typical values of the hazard ratio are from 0.25 to 4.0.

Constant hazard ratios are specified by entering them directly. Variable hazard ratios are specified as columns of the spreadsheet.

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An estimate of the hazard ratio may be obtained from the median survival times, from the hazard rates, or from the proportion surviving past a certain time point by pressing the *Parameter Conversion* button.

When you want to specify different hazard ratios for different time periods, you would enter those values into a column of the spreadsheet, one row per time period. You specify the column (or columns) by beginning your entry with an equals sign.

For example, if you have entered the hazard ratios in column 3, you would enter *=3* here.

Effect Size = Proportion Surviving

S1 (Proportion Surviving – Control)

Specify one or more proportions surviving for the control group. These values must be between zero and one. Constant proportions surviving are specified by entering them directly. The values represent the proportions surviving until time T0.

Variable proportions surviving are specified as columns of the spreadsheet. When you want to specify different proportions surviving for different time periods, you would enter those times 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 proportions surviving in column 2, you would enter *=2* here.

Treatment Group Parameter

Specify which of the parameters below will be used to specify the proportion surviving in the treatment group.

S2 (Proportion Surviving – Treatment)

Specify one or more proportions surviving for the treatment group. These values must be between zero and one. Constant proportions surviving are specified by entering them directly. The values represent the proportions surviving until time T0.

Variable proportions surviving are specified as columns of the spreadsheet. When you want to specify different proportions surviving for different time periods, you would enter those times 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 proportions surviving in column 3, you would enter *=3* here.

HR (Hazard Ratio)

Specify one or more values for the hazard ratio, HR = h2/h1. Hazard ratios must be greater than zero. The null hypothesis is that the hazard ratio is 1.0. Typical values of the hazard ratio are from 0.25 to 4.0.

Constant hazard ratios are specified by entering them directly. Variable hazard ratios are specified as columns of the spreadsheet.

An estimate of the hazard ratio may be obtained from the median survival times, from the hazard rates, or from the proportion surviving past a certain time point by pressing the *Parameter Conversion* button.

When you want to specify different hazard ratios for different time periods, you would enter those values into a column of the spreadsheet, one row per time period. You specify the column (or columns) by beginning your entry with an equals sign.

For example, if you have entered the hazard ratios in column 3, you would enter *=3* here.

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T0 (Survival Time)

This is the time corresponding to the proportions surviving. It must be a value greater than zero.

When you say 0.40 survive, you must indicate the number of time periods (years) to which they survive. That is, you must say 40% survive over five years. For example, a value of 3 here and proportion surviving of 0.4 means that 40% survive over three years.

This value is only used when S1 and S2 are entered as numbers. It is not used when a proportion surviving is entered as a column because, in that case, the time period is different for each row.

Effect Size = Mortality

M1 (Mortality – Control)

Specify one or more mortality values for the control group. These values must be between zero and one. Constant mortalities are specified by entering them directly. The values represent the proportions dying until time T0.

Variable mortalities are specified as columns of the spreadsheet. When you want to specify different mortalities for different time periods, you would enter those times 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 mortalities in column 2, you would enter *=2* here.

Treatment Group Parameter

Specify which of the parameters below will be used to specify the proportion dying in the treatment group.

M2 (Mortality – Treatment)

Specify one or more mortalities (proportions dying) for the treatment group. These values must be between zero and one. Constant mortalities are specified by entering them directly. The values represent the mortalities until time T0.

Variable mortalities are specified as columns of the spreadsheet. When you want to specify different mortalities for different time periods, you would enter those times 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 mortalities in column 3, you would enter *=3* here.

MR (Mortality Ratio = M2/M1)

Specify one or more values for the mortality ratio, MR = M2/M1. Mortality ratios must be greater than zero. The null hypothesis is that the mortality ratio is 1.0. Typical values of the mortality ratio are from 0.25 to 4.0.

Constant mortality ratios are specified by entering them directly. Variable mortality ratios are specified as columns of the spreadsheet.

An estimate of the mortality ratio may be obtained from median survival times, from hazard rates, or from the proportions surviving past a certain time point by pressing the *Parameter Conversion* button.

When you want to specify different mortality ratios for different time periods, you would enter those values into a column of the spreadsheet, one row per time period. You specify the column (or columns) by beginning your entry with an equals sign.

For example, if you have entered the hazard ratios in column 3, you would enter *=3* here.

T0 (Survival Time)

This is the time corresponding to the mortality. It must be a value greater than zero.

When you say 0.40 die, you must indicate the number of time periods (years) on which this is based. For example, a value of 3 here and mortality of 0.4 means that 40% die over the first three years.

This value is only used when M1 and M2 are entered as numbers. It is not used when mortality is entered as a column because, in that case, the time period is different for each row.

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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.

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Proportion Lost or Switching Groups

Controls (or Treatment) Lost

This is the proportion of subjects in the control (treatment) group that disappear from the study 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 rates 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.

Controls Switching to Treatments

This is the proportion of subjects in the control 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.

Treatments Switching to Controls

This is the proportion of subjects in the treatment group that change to a treatment regime similar in efficacy to the control 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.

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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 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.

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Example 1 – Finding the Power using Proportion Surviving

A researcher is planning a clinical trial using a parallel, two-group, equal sample allocation design to compare the survivability of a new treatment with that of the current treatment. The proportion surviving one-year after the current treatment is 0.50. The new treatment will be adopted if the proportion surviving after one year can be shown to be higher than the current treatment. The researcher wishes to determine the power of the logrank test to detect a difference in survival when the true proportion surviving in the new treatment group at one year is 0.70. To obtain a better understanding of the relationship between power and survivability, the researcher also wants to see the results when the proportion surviving is 0.65 and 0.75.

The trial will include a recruitment period of one-year after which participants will be followed for an additional two-years. It is assumed that patients will enter the study uniformly over the accrual period. The researcher estimates a loss-to-follow-up rate of 5% per year in both the control and the experimental groups. Past experience has led to estimates of noncompliance and drop in of 4% and 3%, respectively.

The researcher decides to investigate various sample sizes between 50 and 250 at a 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 **Logrank Tests** procedure window by expanding **Survival**, then **Two Survival Curves**, then clicking on **Test (Inequality)**, and then clicking on **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**
Alternative Hypothesis	**Two-Sided**
Alpha	**0.05**
Group Allocation	**Enter total sample size and percentage in Group 1**
Total Sample Size (N)	**50 to 250 by 50**
Percent in Group 1	**50**
Input Type	**Proportion Surviving**
S1	**0.50**
Treatment Group Parameter	**S2**
S2	**0.65 0.70 0.75**
T0	**1**
Accrual Time	**1**
Accrual Pattern	**Uniform or Equal**
Total Time	**3**
Controls Lost	**0.05**
Treatments Lost	**0.05**
Controls Switch to Treatments	**0.03**
Treatments Switch to Controls	**0.04**
Reports Tab	
Show Detail Numeric Reports	**Checked**

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Annotated Output

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

Numeric Results

Numeric Results for the Logrank Test in Terms of Sample Size
Alternative Hypothesis: Two-Sided
T0 = 1

Power	N1	N2	N	Haz Ratio (HR)	Ctrl Prop Surv (S1)	Trt Prop Surv (S2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.2608	25	25	50	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.7392
0.4615	50	50	100	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.5385
0.6262	75	75	150	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.3738
0.7500	100	100	200	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.2500
0.8378	125	125	250	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.1622
0.4320	25	25	50	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.5680
0.7162	50	50	100	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.2838
0.8732	75	75	150	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.1268
0.9477	100	100	200	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0523
0.9796	125	125	250	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0204
0.6293	25	25	50	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.3707
0.9010	50	50	100	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0990
0.9784	75	75	150	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0216
0.9959	100	100	200	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0041
0.9993	125	125	250	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0007

References

Lakatos, Edward. 1988. 'Sample Sizes Based on the Log-Rank Statistic in Complex Clinical Trials', Biometrics, Volume 44, March, pages 229-241.
Lakatos, Edward. 2002. 'Designing Complex Group Sequential Survival Trials', Statistics in Medicine, Volume 21, pages 1969-1989.

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 control group, treatment group, and both groups, respectively.
Hazard Ratio (HR) is the treatment group's hazard rate divided by the control group's hazard rate.
Proportion Surviving is the proportion surviving past time T0.
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).
Ctrl Loss is the proportion of the control 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).
Ctrl to Trt (drop in) is the proportion of the control group that switch to a group with a hazard rate equal to the treatment group.
Trt to Ctrl (noncompliance) is the proportion of the treatment group that switch to a group with a hazard rate equal to the control 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. In addition to the parameters that were set on the template, the hazard ratio is displayed.

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Logrank Tests

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

Numeric Results for the Logrank Test in Terms of Events
Alternative Hypothesis: Two-Sided
T0 = 1

Power	Ctrl Evts E1	Trt Evts E2	Total Evts E	Haz Ratio (HR)	Ctrl Prop Surv (S1)	Trt Prop Surv (S2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.2608	19.5	15.8	35.2	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.7392
0.4615	38.9	31.6	70.5	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.5385
0.6262	58.4	47.4	105.7	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.3738
0.7500	77.8	63.1	140.9	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.2500
0.8378	97.3	78.9	176.2	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.1622
0.4320	19.4	14.2	33.6	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.5680
0.7162	38.8	28.4	67.2	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.2838
0.8732	58.2	42.7	100.9	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.1268
0.9477	77.6	56.9	134.5	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0523
0.9796	97.0	71.1	168.1	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0204
0.6293	19.4	12.5	31.8	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.3707
0.9010	38.7	25.0	63.7	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0990
0.9784	58.1	37.5	95.5	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0216
0.9959	77.4	49.9	127.4	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0041
0.9993	96.8	62.4	159.2	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0007

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=0.2608 N1=25 N2=25 N=50 Alpha=0.0500 Accrual/Total Time=1 / 3
T0 = 1

Time Period	Control Prop Surviving (.5000)	Treatment Prop Surviving (.6500)	Hazard Ratio (HR) (.6215)	Percent Accrual (Equal)	Percent Admin. Censored (Calc.)	Control Loss (.0500)	Treatment Loss (.0500)	Control to Treatment (.0300)	Treatment to Control (.0400)
1	0.5000	0.6500	0.6215	100.00	0.00	0.0500	0.0500	0.0300	0.0400
2	0.2500	0.4225	0.6215	0.00	0.00	0.0500	0.0500	0.0300	0.0400
3	0.1250	0.2746	0.6215	0.00	100.00	0.0500	0.0500	0.0300	0.0400

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.

Percent Administrative Censored

The percent administrative censored is the percent of those who have been in the study that number of years who are censored because the study ends. The value is calculated solely from the accrual proportions.

For example, suppose a study runs 9 years and accrual occurs for the first 7 years. Hence, there are two years of follow-up. The following table shows how the Percent Admin. Censored is calculated if the accrual amounts are as given.

Year	Accrual	Admin. Censored	% Admin. Censored	Denominator
1	0.08	0	0.00	
2	0.10	0	0.00	
3	0.10	0.2/1	20.00	1.0 = 1.0
4	0.17	0.2/0.8	25.00	0.8 = 1 - 0.2
5	0.15	0.15/0.6	25.00	0.6 = 0.8 - 0.2
6	0.20	0.17/0.45	37.78	0.45 = 0.6 - 0.15
7	0.20	0.1/0.28	35.71	0.28 = 0.45 - 0.17
8	0.00	0.1/0.18	55.56	0.18 = 0.28 - 0.10
9	0.00	0.08/0.08	100.00	0.08 = 0.18 - 0.10

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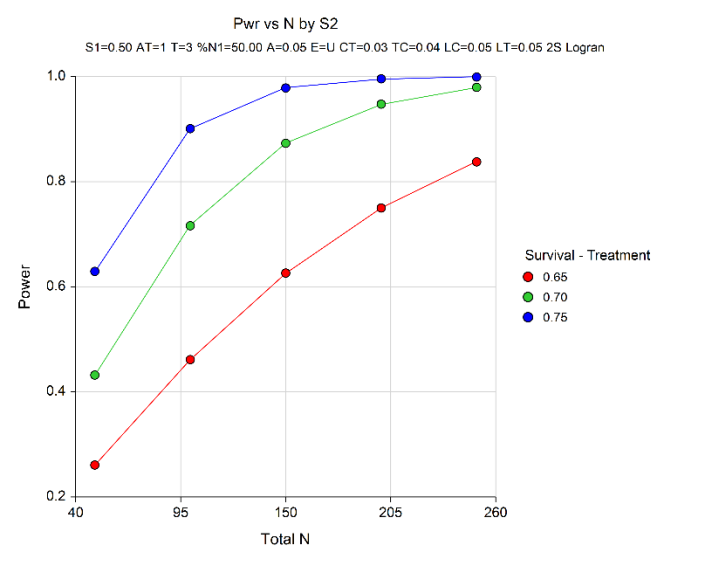
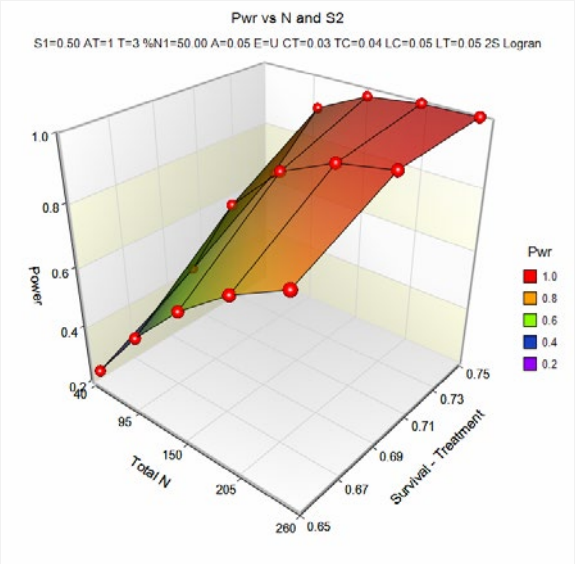
Next, summary statements are displayed.

Summary Statements
A two-sided logrank test with an overall sample size of 50 subjects (25 in the control group and 25 in the treatment group) achieves 26.1% power at a 0.050 significance level to detect a hazard ratio of 0.6215 when the proportion surviving in the control group is 0.5000. The study lasts for 3 time periods of which subject accrual (entry) occurs in the first time period. The proportion dropping out of the control group is 0.0500. The proportion dropping out of the treatment group is 0.0500. The proportion switching from the control group to another group with a survival proportion equal to that of the treatment group is 0.0300. The proportion switching from the treatment group to another group with a survival proportion equal to that of the control group is 0.0400.

Finally, a scatter plot of the results is displayed.

Plots Section





These plots show the relationship between sample size and power for the three values of S2. Note that for 90% power, a total sample size of about 160 is required. The exact number will be found in Example 2.

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Example 2 – Finding the Sample Size using Proportion Surviving

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 **Logrank Tests** procedure window by expanding **Survival**, then **Two Survival Curves**, then clicking on **Test (Inequality)**, and then clicking on **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**
Alternative Hypothesis	**Two-Sided**
Power	**0.80 0.90**
Alpha	**0.05**
Group Allocation	**Equal (N1 = N2)**
Input Type	**Proportion Surviving**
S1	**0.50**
Treatment Group Parameter	**S2**
S2	**0.65 0.70 0.75**
T0	**1**
Accrual Time	**1**
Accrual Pattern	**Uniform or Equal**
Total Time	**3**
Controls Lost	**0.05**
Treatments Lost	**0.05**
Controls Switch to Treatments	**0.03**
Treatments Switch to Controls	**0.04**

Output

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

Numeric Results

Numeric Results in Terms of Sample Size when the Test is Two-Sided and T0 is 1
Alternative Hypothesis: Two-Sided
T0 = 1

Power	N1	N2	N	Haz Ratio (HR)	Ctrl Prop Surv (S1)	Trt Prop Surv (S2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.8014	113	114	227	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.1986
0.9002	151	152	303	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0998
0.8019	61	62	123	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.1981
0.9004	82	82	164	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0996
0.8022	37	38	75	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.1978
0.9010	50	50	100	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0990

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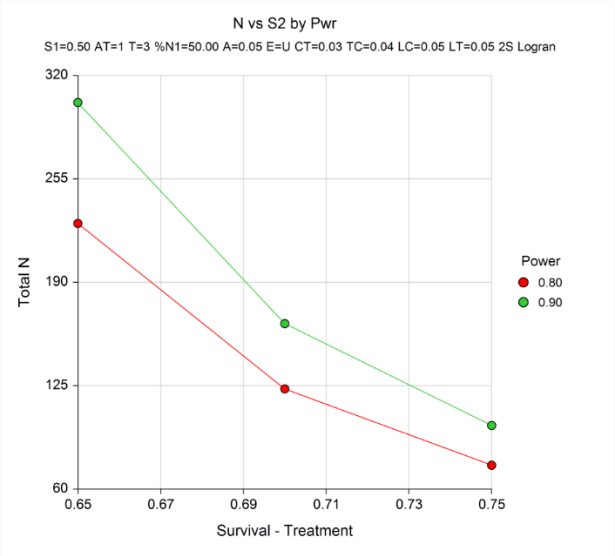
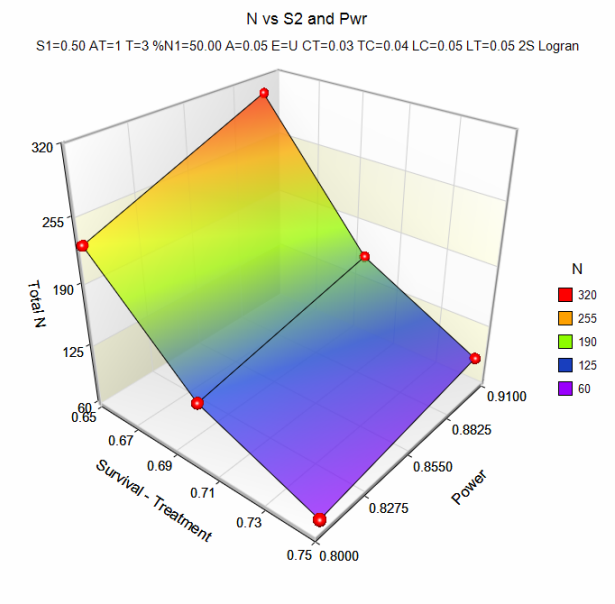
Logrank Tests

Numeric Results for the Logrank Test in Terms of Events
Alternative Hypothesis: Two-Sided
T0 = 1

Power	Ctrl Evts E1	Trt Evts E2	Total Evts E	Haz Ratio (HR)	Ctrl Prop Surv (S1)	Trt Prop Surv (S2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.8014	88.3	71.7	160.0	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.1986
0.9002	117.9	95.7	213.5	0.6215	0.5000	0.6500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0998
0.8019	47.7	35.0	82.7	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.1981
0.9004	63.7	46.6	110.3	0.5146	0.5000	0.7000	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0996
0.8022	29.0	18.7	47.8	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.1978
0.9010	38.7	25.0	63.7	0.4150	0.5000	0.7500	Equal	1 / 3	0.0500	0.0500	0.0300	0.0400	0.0500	0.0990

Chart Section





The total sample size need to achieve 90% power when the proportion surviving with the new treatment is 0.70, is 164. It is apparent that as the proportion surviving (effect size) increases, the sample size decreases.

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Example 3 – Validation using Lakatos (1988)

Lakatos (1988) pages 231-234 presents an example that will be used to validate this procedure. In this example, a two-year trial is investigated. All subjects begin the trial together, so there is no accrual period. The hazard rates are 1.0 and 0.5 for the control and treatment groups, respectively. The yearly loss to follow-up is 3% per year in both groups. Noncompliance and drop-in rates are assumed to be 4% and 5%, respectively. The power is set to 90%. A two-sided logrank test with alpha set to 0.05 is assumed. Equal allocation of the sample to both control and experiment groups is used. Lakatos obtains a sample size of 139.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Logrank Tests** procedure window by expanding **Survival**, then **Two Survival Curves**, then clicking on **Test (Inequality)**, and then clicking on **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	
Solve For	**Sample Size**
Alternative Hypothesis	**Two-Sided**
Power	**0.90**
Alpha	**0.05**
Group Allocation	**Equal (N1 = N2)**
Input Type	**Hazard Rate**
h1	**1.0**
Treatment Group Parameter	**h2**
h2	**0.5**
Accrual Time	**0**
Accrual Pattern	**Uniform or Equal**
Total Time	**2**
Controls Lost	**0.03**
Treatments Lost	**0.03**
Controls Switch to Treatments	**0.04**
Treatments Switch to Controls	**0.05**

Output

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

Numeric Results

Numeric Results for the Logrank Test in Terms of Sample Size
Alternative Hypothesis: Two-Sided

Power	N1	N2	N	Haz Ratio (HR)	Ctrl Haz Rate (h1)	Trt Haz Rate (h2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.9014	69	70	139	0.5000	1.00	0.5000	Equal	0 / 2	0.0300	0.0300	0.0400	0.0500	0.0500	0.0986

The total sample size of 139 matches the value published in Lakatos' article.

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

This example shows how time-dependent hazard rates and other parameters can be input directly from a spreadsheet.

A pre-trial study indicates that a newly developed treatment will cut the hazard rate in half, when compared to the current treatment. A 5-year trial is being designed to confirm the finding of the pre-trial study. The goal for this portion of the study design is to determine the sample size needed to detect a decrease in hazard rate with 90% power.

The pre-trial study showed that the hazard rate immediately following either treatment (during the first year) is high, drops considerably during the second year, and then gradually increases. Fifty percent of the study participants will be enrolled during the first year, followed by 25% each of the second and third years. The following table shows the time-dependent parameters for the 5-year trial, based on the pre-trial study.

PRETRIAL dataset

Year	H1	Ls1	Ls2	NCom	Acc
1	0.08	0.04	0.06	0.04	50
2	0.04	0.04	0.06	0.04	25
3	0.05	0.05	0.07	0.05	25
4	0.06	0.06	0.07	0.06	
5	0.07	0.07	0.08	0.07	

The column H1 refers to the anticipated hazard rates for each of the five years. Ls1 and Ls2 refer to the proportions lost to follow-up in the control group and the treatment group, respectively. The proportion that are noncompliant are also expected to increase after the second year according the proportions shown. The final column specifies the accrual rate as outlined in the previous paragraph.

Following the 5-year trial, a two-sided logrank test with alpha equal to 0.05, will be used to determine the evidence of difference among the current and new treatments.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Logrank Tests** procedure window by expanding **Survival**, then **Two Survival Curves**, then clicking on **Test (Inequality)**, and then clicking on **Logrank Tests**. You may then make the appropriate entries as listed below, or open **Example 4** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Sample Size**
Alternative Hypothesis	**Two-Sided**
Power	**0.90**
Alpha	**0.05**
Group Allocation	**Equal (N1 = N2)**
Input Type	**Hazard Rate**
h1	**=H1**
Treatment Group Parameter	**HR (Hazard Ratio = h2/h1)**
HR	**0.5**

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Logrank Tests

Design Tab (continued)

Accrual Time **3**
Accrual Pattern ..... **Non-Uniform (Spreadsheet Entry)**
Accrual Values in Columns..... **=Acc**
Total Time **5**
Controls Lost..... **=Ls1**
Treatments Lost..... **=Ls2**
Controls Switch to Treatments **0.02**
Treatments Switch to Controls ..... **=NCom**

Reports Tab

Show Detail Numeric Reports ..... **Checked**

Output

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

Numeric Results

Numeric Results for the Logrank Test in Terms of Sample Size
Alternative Hypothesis: Two-Sided

Power	N1	N2	N	Haz Ratio (HR)	Ctrl Haz Rate (h1)	Trt Haz Rate (h2)	Accrual Pat'n	Accrual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.9001	418	419	837	0.5000	H1	Calc.	Acc	3 / 5	Ls1	Ls2	0.0200	NCom	0.0500	0.0999

Numeric Results for the Logrank Test in Terms of Events
Alternative Hypothesis: Two-Sided

Power	Ctrl Evts (E1)	Trt Evts (E2)	Total Evts (E)	Haz Ratio (HR)	Ctrl Haz Rate (h1)	Trt Haz Rate (h2)	Accrual Pat'n	Accrual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.9001	74.4	41.2	115.6	0.5000	H1	Calc.	Acc	3 / 5	Ls1	Ls2	0.0200	NCom	0.0500	0.0999

Detailed Input when Power=0.9001 N1=418 N2=419 N=837 Alpha=0.0500 Accrual/Total Time=3 / 5

Time Period	Control Hazard Rate (H1)	Treatment Hazard Rate (Calc.)	Hazard Ratio (HR) (0.5000)	Percent Accrual (Acc)	Percent Admin. Censored (Calc.)	Control Loss (Ls1)	Treatment Loss (Ls2)	Control to Treatment (0.0200)	Treatment to Control (NCom)
1	0.0800	0.0400	0.5000	50.00	0.00	0.0400	0.0600	0.0200	0.0400
2	0.0400	0.0200	0.5000	25.00	0.00	0.0400	0.0600	0.0200	0.0400
3	0.0500	0.0250	0.5000	25.00	25.00	0.0500	0.0700	0.0200	0.0500
4	0.0600	0.0300	0.5000	0.00	33.33	0.0600	0.0700	0.0200	0.0600
5	0.0700	0.0350	0.5000	0.00	100.00	0.0700	0.0800	0.0200	0.0700

Summary Statements

A two-sided logrank test with an overall sample size of 837 subjects (418 in the control group and 419 in the treatment group) achieves 90.0% power at a 0.050 significance level to detect a hazard ratio of 0.5000 when the control group hazard rate is given in column H1. The study lasts for 5 time periods of which subject accrual (entry) occurs in the first 3 time periods. The accrual pattern across time periods is given in column Acc. The proportion dropping out of the control group is given in column Ls1. The proportion dropping out of the treatment group is given in column Ls2. The proportion switching from the control group to another group with a hazard rate equal to the treatment group is 0.0200. The proportion switching from the treatment group to another group with a hazard rate equal to the control group is given in column NCom.

For the 5-year study, the total sample size needed to detect a change in hazard rate, if the true hazard ratio is 0.5, is 837 subjects.

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Example 5 – Finding the Power using Median Survival Time

A researcher is planning a clinical trial using a parallel, two-group, equal sample allocation design to compare the survivability of a new treatment with that of the current treatment. The median survival time for the current treatment is 1.6 years. The new treatment will be adopted if the median survival time can be shown to be higher than the current treatment. Because the true median survival time is unknown, the researcher wishes to determine the power of the logrank test to detect a difference in survival when the true median survival time for the new treatment is 2.0, 2.5, or 3.0 years.

The trial will include a recruitment period of one year, after which participants will be followed for an additional two years. It is assumed that patients will enter the study uniformly over the accrual period. The researcher estimates a loss-to-follow rate of 4% per year in both the control and the experimental groups. Past experience has led to estimates of noncompliance and drop in of 6% and 5%, respectively.

The researcher decides to investigate various sample sizes between 50 and 200 at a 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 **Logrank Tests** procedure window by expanding **Survival**, then **Two Survival Curves**, then clicking on **Test (Inequality)**, and then clicking on **Logrank Tests**. You may then make the appropriate entries as listed below, or open **Example 5** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Power**
Alternative Hypothesis	**Two-Sided**
Alpha	**0.05**
Group Allocation	**Enter total sample size and percentage in Group 1**
Total Sample Size (N)	**50 to 200 by 50**
Percent in Group 1	**50**
Input Type	**Median Survival Time**
T1	**1.6**
Treatment Group Parameter	**T2**
T2	**2.0 2.5 3.0**
Accrual Time	**1**
Accrual Pattern	**Uniform or Equal**
Total Time	**3**
Controls Lost	**0.04**
Treatments Lost	**0.04**
Controls Switch to Treatments	**0.05**
Treatments Switch to Controls	**0.06**

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Output

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

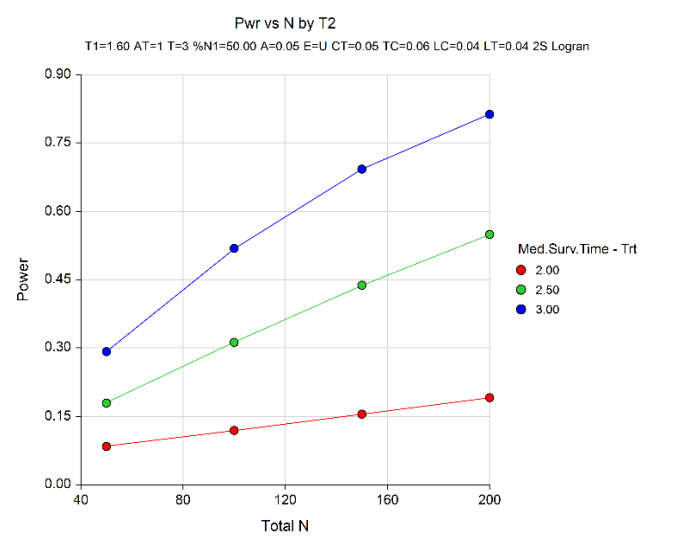
Numeric Results and Plots

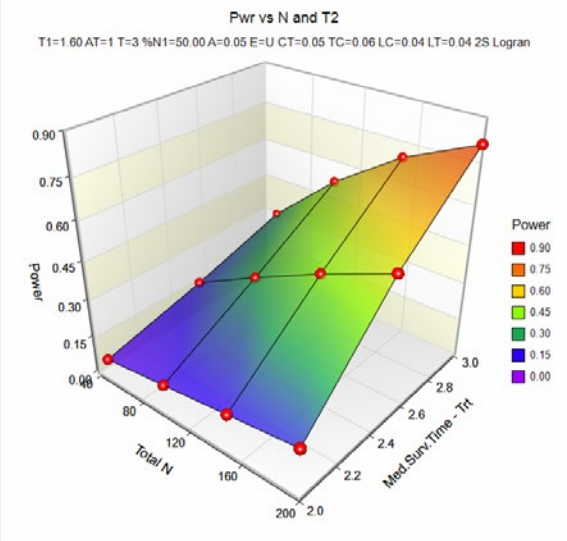
Numeric Results for the Logrank Test in Terms of Sample Size
Alternative Hypothesis: Two-Sided

Power	N1	N2	N	Haz Ratio (HR)	Ctrl Med Surv Time (M1)	Trt Med Surv Time (M2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.0839	25	25	50	0.8000	1.60	2.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.9161
0.1191	50	50	100	0.8000	1.60	2.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.8809
0.1549	75	75	150	0.8000	1.60	2.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.8451
0.1911	100	100	200	0.8000	1.60	2.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.8089
0.1792	25	25	50	0.6400	1.60	2.50	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.8208
0.3125	50	50	100	0.6400	1.60	2.50	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.6875
0.4379	75	75	150	0.6400	1.60	2.50	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.5621
0.5495	100	100	200	0.6400	1.60	2.50	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.4505
0.2921	25	25	50	0.5333	1.60	3.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.7079
0.5188	50	50	100	0.5333	1.60	3.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.4812
0.6928	75	75	150	0.5333	1.60	3.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.3072
0.8130	100	100	200	0.5333	1.60	3.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.1870

Numeric Results for the Logrank Test in Terms of Events
Alternative Hypothesis: Two-Sided

Power	Ctrl Evts (E1)	Trt Evts (E2)	Total Evts (E)	Haz Ratio (HR)	Ctrl Med Surv Time (T1)	Trt Med Surv Time (T2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.0839	15.7	14.0	29.7	0.8000	1.60	2.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.9161
0.1191	31.4	27.9	59.3	0.8000	1.60	2.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.8809
0.1549	47.1	41.9	89.0	0.8000	1.60	2.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.8451
0.1911	62.8	55.8	118.6	0.8000	1.60	2.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.8089
0.1792	15.6	12.2	27.8	0.6400	1.60	2.50	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.8208
0.3125	31.2	24.4	55.6	0.6400	1.60	2.50	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.6875
0.4379	46.8	36.6	83.4	0.6400	1.60	2.50	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.5621
0.5495	62.4	48.8	111.2	0.6400	1.60	2.50	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.4505
0.2921	15.5	10.8	26.4	0.5333	1.60	3.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.7079
0.5188	31.0	21.7	52.7	0.5333	1.60	3.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.4812
0.6928	46.6	32.5	79.1	0.5333	1.60	3.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.3072
0.8130	62.1	43.4	105.5	0.5333	1.60	3.00	Equal	1 / 3	0.0400	0.0400	0.0500	0.0600	0.0500	0.1870





These plots show the relationship between sample size and power for the three median survival times.

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Example 6 – Finding the Power using Mortality

A researcher is planning a clinical trial using a parallel, two-group, equal sample allocation design to compare the mortality rate of a new treatment with that of the current treatment. The mortality rate at one-year after the current treatment is 0.40. The new treatment will be adopted if the mortality rate after one year can be shown to be lower than the current treatment. The researcher wishes to determine the power of the logrank test to detect a difference in mortality when the true mortality rate in the new treatment group at one year is 0.20, 0.25, or 0.30.

The trial will include a recruitment period of one year, after which participants will be followed for an additional two 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 control and the experimental groups. Past experience has led to estimates of noncompliance and drop in of 3% and 4%, respectively.

The researcher decides to investigate various sample sizes between 50 and 200 at a 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 **Logrank Tests** procedure window by expanding **Survival**, then **Two Survival Curves**, then clicking on **Test (Inequality)**, and then clicking on **Logrank Tests**. You may then make the appropriate entries as listed below, or open **Example 6** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Power**
Alternative Hypothesis	**Two-Sided**
Alpha	**0.05**
Group Allocation	**Enter total sample size and percentage in Group 1**
Total Sample Size (N)	**50 to 200 by 50**
Percent in Group 1	**50**
Input Type	**Mortality**
M1	**0.4**
Treatment Group Parameter	**M2**
M2	**0.20 0.25 0.30**
T0 (Survival Time)	**1**
Accrual Time	**1**
Accrual Pattern	**Uniform or Equal**
Total Time	**3**
Controls Lost	**0.05**
Treatments Lost	**0.05**
Controls Switch to Treatments	**0.04**
Treatments Switch to Controls	**0.03**

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Output

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

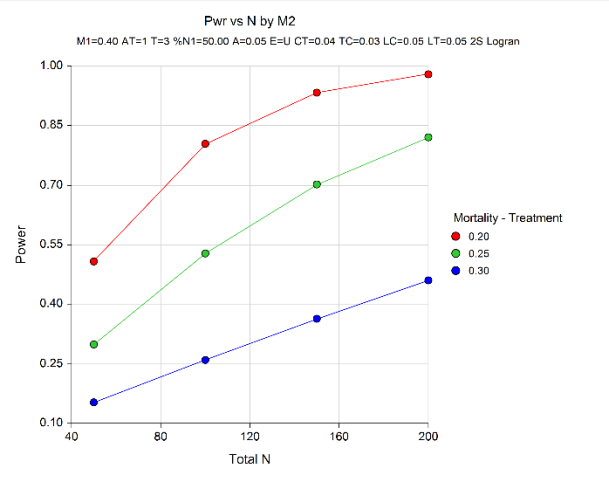
Numeric Results and Plots

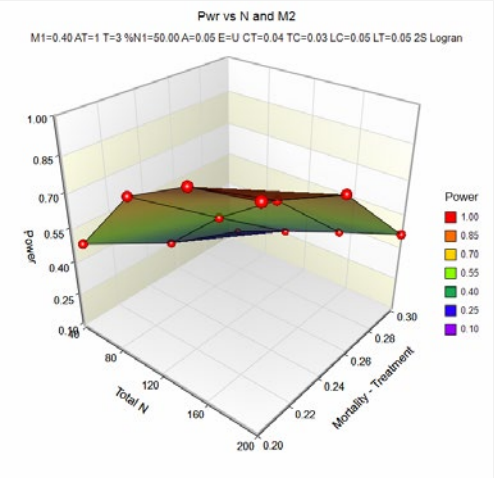
Numeric Results for the Logrank Test in Terms of Sample Size
Alternative Hypothesis: Two-Sided
T0 = 1

Power	N1	N2	N	Mort Ratio (MR)	Ctrl Mort (M1)	Trt Mort (M2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.5079	25	25	50	0.5000	0.4000	0.2000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.4921
0.8044	50	50	100	0.5000	0.4000	0.2000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.1956
0.9332	75	75	150	0.5000	0.4000	0.2000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.0668
0.9794	100	100	200	0.5000	0.4000	0.2000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.0206
0.2988	25	25	50	0.6250	0.4000	0.2500	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.7012
0.5281	50	50	100	0.6250	0.4000	0.2500	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.4719
0.7021	75	75	150	0.6250	0.4000	0.2500	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.2979
0.8207	100	100	200	0.6250	0.4000	0.2500	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.1793
0.1529	25	25	50	0.7500	0.4000	0.3000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.8471
0.2597	50	50	100	0.7500	0.4000	0.3000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.7403
0.3635	75	75	150	0.7500	0.4000	0.3000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.6365
0.4603	100	100	200	0.7500	0.4000	0.3000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.5397

Numeric Results for the Logrank Test in Terms of Events
Alternative Hypothesis: Two-Sided
T0 = 1

Power	Ctrl Evts (E1)	Trt Evts (E2)	Total Evts (E)	Mort Ratio (MR)	Ctrl Mort (M1)	Trt Mort (M2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.5079	16.8	10.3	27.1	0.5000	0.4000	0.2000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.4921
0.8044	33.6	20.7	54.2	0.5000	0.4000	0.2000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.1956
0.9332	50.4	31.0	81.4	0.5000	0.4000	0.2000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.0668
0.9794	67.1	41.3	108.5	0.5000	0.4000	0.2000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.0206
0.2988	16.9	12.3	29.1	0.6250	0.4000	0.2500	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.7012
0.5281	33.7	24.5	58.3	0.6250	0.4000	0.2500	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.4719
0.7021	50.6	36.8	87.4	0.6250	0.4000	0.2500	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.2979
0.8207	67.5	49.1	116.5	0.6250	0.4000	0.2500	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.1793
0.1529	16.9	14.0	31.0	0.7500	0.4000	0.3000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.8471
0.2597	33.9	28.1	61.9	0.7500	0.4000	0.3000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.7403
0.3635	50.8	42.1	92.9	0.7500	0.4000	0.3000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.6365
0.4603	67.7	56.1	123.9	0.7500	0.4000	0.3000	Equal	1 / 3	0.0500	0.0500	0.0400	0.0300	0.0500	0.5397





These plots show the relationship between sample size and power for the three mortality rates.

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Example 7 – Converting Years to Months

A researcher is planning a clinical trial using a parallel, two-group, equal sample allocation design to compare the hazard rate of a new treatment with that of the current treatment. The hazard rate for the current treatment is 0.14. The new treatment will be adopted if the hazard rate after can be shown to be lower than the current treatment. The researcher wishes to determine the power of the logrank test to detect true hazard ratios for the new treatment of 0.4, 0.5, and 0.6.

The trial will include a recruitment period of four months, after which participants will be followed for an additional year and 8 months. It is assumed that patients will enter the study uniformly over the accrual period. The researcher estimates a loss-to-follow proportion of 4% per year in both the control and the experimental groups. Past experience has led to estimates of noncompliance and drop in of 3% each.

The researcher decides to investigate various sample sizes between 50 and 350 at a significance level of 0.05.

Before entering the values into the Logrank Test (Hazard Ratio) window, the values stated above in terms of years must be converted to the corresponding monthly values. This can be done using the Proportions (Years to Months) tab of the Survival Parameter Conversion Tool.

The number of sub time units in one main time unit is 12, since there are 12 months in a year. The yearly proportion 0.04 corresponding to the loss-to-follow 4% is converted to the monthly value of 0.00339605319892 using the relationship $P(\text{annual}) = 1-(1-P(\text{monthly}))^{12}$. Similarly, the yearly noncompliance and drop in values of 3% are converted to the monthly value of 0.00253504861384. The annual hazard rate of 0.14 is converted to the monthly hazard rate of 0.01166666666667 using the relationship R(monthly) = R(annual)/12.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Logrank Tests** procedure window by expanding **Survival**, then **Two Survival Curves**, then clicking on **Test (Inequality)**, and then clicking on **Logrank Tests**. You may then make the appropriate entries as listed below, or open **Example 7** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Power**
Alternative Hypothesis	**Two-Sided**
Alpha	**0.05**
Group Allocation	**Enter total sample size and percentage in Group 1**
Total Sample Size (N)	**50 to 350 by 50**
Percent in Group 1	**50**
Input Type	**Hazard Rate**
h1	**0.01166666666667**
Treatment Group Parameter	**HR (Hazard Ratio = h2/h1)**
HR	**0.4 0.5 0.6**
Accrual Time	**4**
Accrual Pattern	**Uniform or Equal**
Total Time	**24**
Controls Lost	**0.00339605319892**
Treatment Lost	**0.00339605319892**
Controls Switch to Treatments	**0.00253504861384**
Treatments Switch to Controls	**0.00253504861384**

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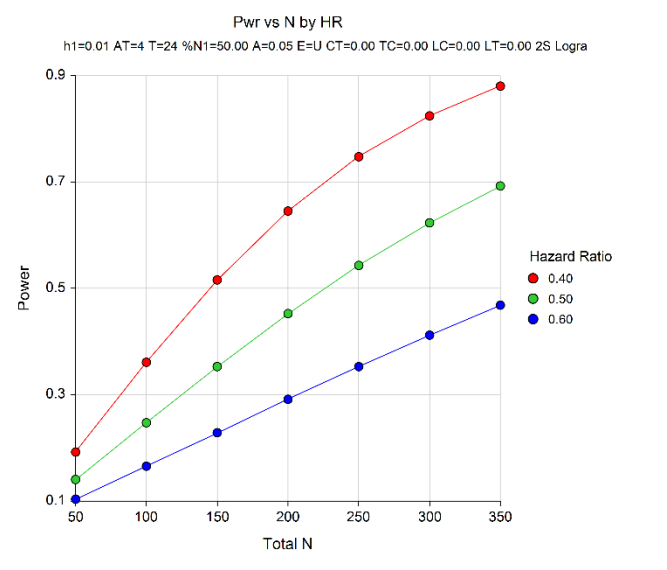
Output

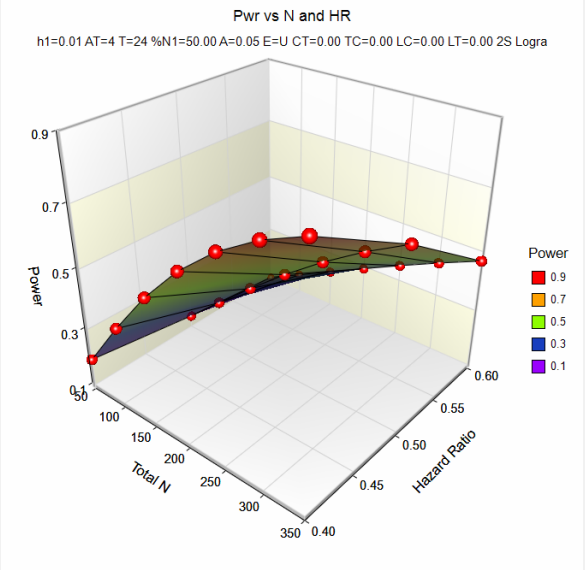
Click the Calculate button to perform the calculations and generate the following output.

Numeric Results and Plots

Numeric Results for the Logrank Test in Terms of Sample Size
Alternative Hypothesis: Two-Sided

Power	N1	N2	N	Haz Ratio (HR)	Ctrl Haz Rate (h1)	Trt Haz Rate (h2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.1922	25	25	50	0.4000	0.0117	0.0047	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.8078
0.3610	50	50	100	0.4000	0.0117	0.0047	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.6390
0.5157	75	75	150	0.4000	0.0117	0.0047	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.4843
0.6453	100	100	200	0.4000	0.0117	0.0047	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.3547
0.7474	125	125	250	0.4000	0.0117	0.0047	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.2526
0.8243	150	150	300	0.4000	0.0117	0.0047	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.1757
0.8802	175	175	350	0.4000	0.0117	0.0047	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.1198
0.1407	25	25	50	0.5000	0.0117	0.0058	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.8593
0.2473	50	50	100	0.5000	0.0117	0.0058	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.7527
0.3530	75	75	150	0.5000	0.0117	0.0058	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.6470
0.4526	100	100	200	0.5000	0.0117	0.0058	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.5474
0.5431	125	125	250	0.5000	0.0117	0.0058	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.4569
0.6232	150	150	300	0.5000	0.0117	0.0058	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.3768
0.6926	175	175	350	0.5000	0.0117	0.0058	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.3074
0.1037	25	25	50	0.6000	0.0117	0.0070	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.8963
0.1656	50	50	100	0.6000	0.0117	0.0070	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.8344
0.2287	75	75	150	0.6000	0.0117	0.0070	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.7713
0.2915	100	100	200	0.6000	0.0117	0.0070	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.7085
0.3529	125	125	250	0.6000	0.0117	0.0070	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.6471
0.4120	150	150	300	0.6000	0.0117	0.0070	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.5880
0.4683	175	175	350	0.6000	0.0117	0.0070	Equal	4 / 24	0.0034	0.0034	0.0025	0.0025	0.0500	0.5317





These plots show the relationship between sample size and power for the three hazard ratios.

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