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

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

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 *T*0 is specified. These are transformed to hazard rates using the relationship *h* = –ln(*S*(*T*0)) / *T*0. 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 *T*0 is specified. These are transformed to hazard rates using the relationship *h* = –ln(1 – M(*T*0)) / *T*0. 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

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.

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

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

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

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.

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

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

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

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

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: $z_\beta = \frac{X_\alpha - E_1}{V_1}$
5. Calculate beta and power: $\beta = \Phi\left(z_\beta\right)$.

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

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 1** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

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**

Output

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

Numeric Reports

Numeric Results (Sample Size)

Solve For:	Power
Test Type:	Two-Sample Logrank Test
Groups:	1 = Control, 2 = Treatment
Alternative Hypothesis:	Two-Sided
T0 (Survival Time):	1

	Sample Size			Hazard Ratio	Proportion Surviving			Time		Proportion Lost*		Proportion Switching Groups*		
Power	N1	N2	N	HR	S1	S2	Accrual Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.2608	25	25	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.4615	50	50	100	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.6262	75	75	150	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.7500	100	100	200	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8378	125	125	250	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.4320	25	25	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.7162	50	50	100	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8732	75	75	150	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9477	100	100	200	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9796	125	125	250	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.6293	25	25	50	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9010	50	50	100	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9784	75	75	150	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9959	100	100	200	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9993	125	125	250	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05

* The reported proportions are during a single time period.

Power	The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N1, N2, and N	The sample sizes of the control group, treatment group, and both groups, respectively.
HR	Hazard Ratio. The treatment group's hazard rate divided by the control group's hazard rate.
S1 and S2	The proportion surviving past time T0.
Accrual Pattern	The pattern of accrual times across individual time periods.
Accrual Time	The number of time periods (years or months) during which accrual takes place.
Total Time	The total number of time periods in the study. Follow-up time = (Total Time) - (Accrual Time).
Control Lost	The proportion of the control group that is lost (drop out) during a single time period (year or month).
Treatment Lost	The proportion of the treatment group that is lost (drop out) during a single time period (year or month).
Control to Treatment	Drop In. The proportion of the control group that switch to a group with a hazard rate equal to the treatment group.
Treatment to Control	Noncompliance. The proportion of the treatment group that switch to a group with a hazard rate equal to the control group.
Alpha	The probability of rejecting a true null hypothesis.

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.

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

Numeric Results (Events)

Solve For:	Power
Test Type:	Two-Sample Logrank Test
Groups:	1 = Control, 2 = Treatment
Alternative Hypothesis:	Two-Sided
T0 (Survival Time):	1

	Number of Events			Hazard Ratio	Proportion Surviving			Time		Proportion Lost*		Proportion Switching Groups*		
Power	E1	E2	E	HR	S1	S2	Accrual Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.2608	19.5	15.8	35.2	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.4615	38.9	31.6	70.5	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.6262	58.4	47.4	105.7	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.7500	77.8	63.1	140.9	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8378	97.3	78.9	176.2	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.4320	19.4	14.2	33.6	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.7162	38.8	28.4	67.2	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8732	58.2	42.7	100.9	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9477	77.6	56.9	134.5	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9796	97.0	71.1	168.1	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.6293	19.4	12.5	31.8	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9010	38.7	25.0	63.7	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9784	58.1	37.5	95.5	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9959	77.4	49.9	127.4	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9993	96.8	62.4	159.2	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05

* The reported proportions are during a single time period.

Power	The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
E1, E2, and E	The number of events in the control group, treatment group, and both groups, respectively.
HR	Hazard Ratio. The treatment group's hazard rate divided by the control group's hazard rate.
S1 and S2	The proportion surviving past time T0.
Accrual Pattern	The pattern of accrual times across individual time periods.
Accrual Time	The number of time periods (years or months) during which accrual takes place.
Total Time	The total number of time periods in the study. Follow-up time = (Total Time) - (Accrual Time).
Control Lost	The proportion of the control group that is lost (drop out) during a single time period (year or month).
Treatment Lost	The proportion of the treatment group that is lost (drop out) during a single time period (year or month).
Control to Treatment	Drop In. The proportion of the control group that switch to a group with a hazard rate equal to the treatment group.
Treatment to Control	Noncompliance. The proportion of the treatment group that switch to a group with a hazard rate equal to the control group.
Alpha	The probability of rejecting a true null hypothesis.

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, Accrual Time = 1, Total Time = 3, Alpha = 0.05

T0 = 1

	Proportion Surviving		Hazard Ratio		Percent Administrative	Proportion Lost		Proportion Switching Groups	
Time Period	Control (0.5)	Treatment (0.65)	HR (0.6215)	Percent Accrual (Equal)	Censored (Calculated)	Control (0.05)	Treatment (0.05)	Control to Treatment (0.03)	Treatment to Control (0.04)
1	0.500	0.6500	0.6215	100	0	0.05	0.05	0.03	0.04
2	0.250	0.4225	0.6215	0	0	0.05	0.05	0.03	0.04
3	0.125	0.2746	0.6215	0	100	0.05	0.05	0.03	0.04

(More Reports Follow)

These reports show 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

Next, summary statements and references are displayed, followed by the references.

Summary Statements

A parallel, two-group design will be used to test whether the Group 2 (treatment) hazard rate is different from the Group 1 (control) hazard rate. The comparison will be made using a two-sided, two-sample logrank test with a Type I error rate (α) of 0.05. The total duration of the study will be 3 time periods, with subject accrual (entry) occurring in the first time period. The proportion of subjects dropping out of the control group during each time period will be 0.05. The proportion of subjects dropping out of the treatment group during each time period will be 0.05. The proportion of subjects switching from the control group to another group with a survival proportion equal to that of the treatment group is 0.03 (per time period). The proportion of subjects switching from the treatment group to another group with a survival proportion equal to that of the control group is 0.04 (per time period). To detect a treatment group proportion surviving (in a time of 1) of 0.65 (or hazard ratio [h2 / h1] of 0.6215) when the proportion surviving (in a time of 1) in the control group is 0.5, with a sample size of 25 subjects in Group 1 and 25 subjects in Group 2 (totaling 50 subjects), the power is 0.2608. The corresponding number of events is 19.5 in Group 1 and 15.8 in Group 2 (totaling 35.2 events).

References

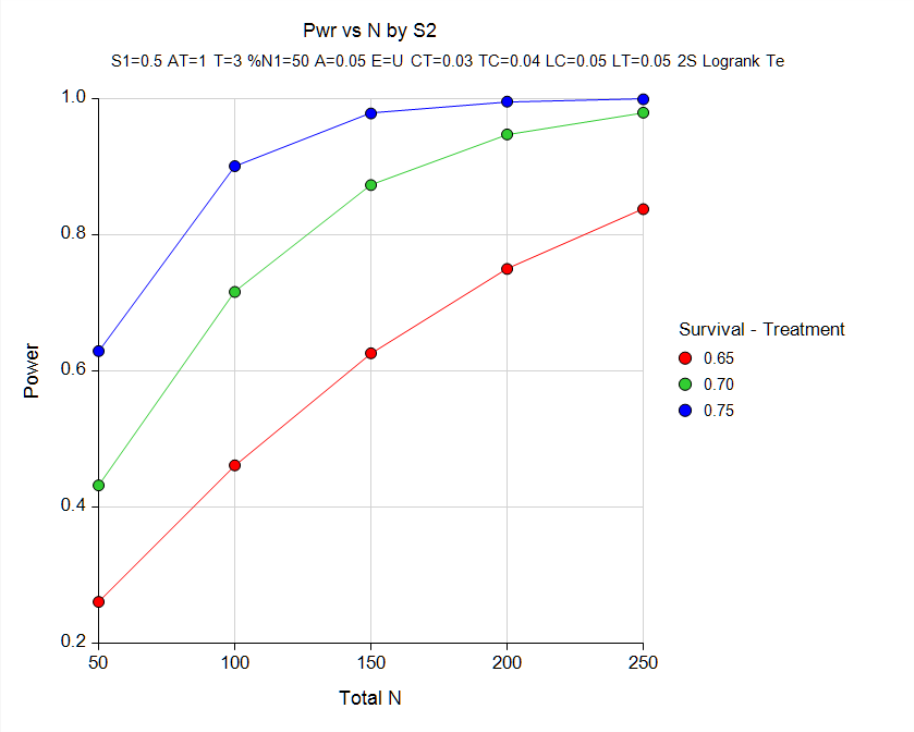
Lakatos, Edward. 1988. 'Sample Sizes Based on the Log-Rank Statistic in Complex Clinical Trials', Biometrics, Volume 44, March, pages 229-241.

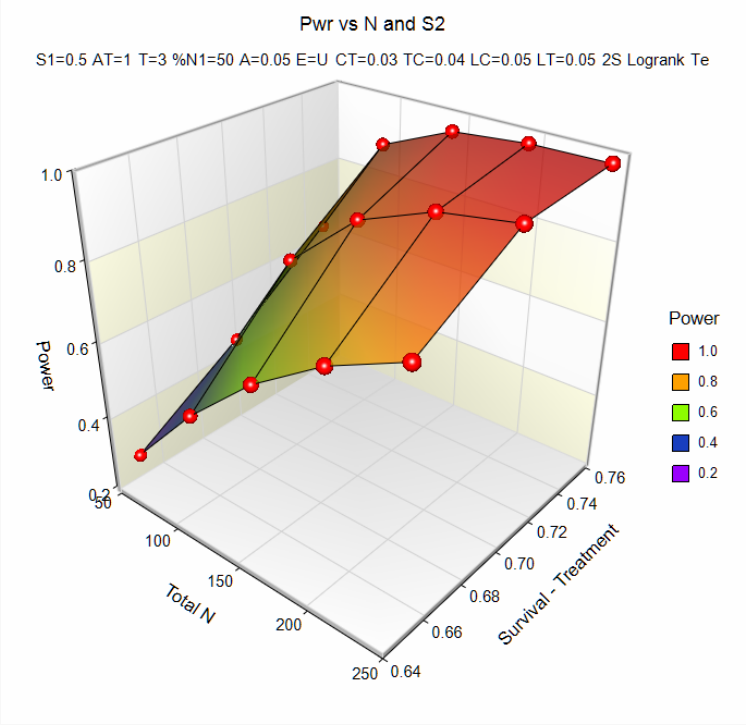
Lakatos, Edward. 2002. 'Designing Complex Group Sequential Survival Trials', Statistics in Medicine, Volume 21, pages 1969-1989.

Finally, a scatter plot of the results is displayed.

Plots Section

Plots





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.

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

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 2** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

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 (Sample Size)

Solve For: Sample Size
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided
T0 (Survival Time): 1

	Sample Size			Hazard	Proportion Surviving			Time		Proportion Lost*		Proportion Switching Groups*		
Power	N1	N2	N	Ratio HR	S1	S2	Accrual Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.8014	113	114	227	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9002	151	152	303	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8019	61	62	123	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9004	82	82	164	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8022	37	38	75	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9010	50	50	100	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05

* The reported proportions are during a single time period.

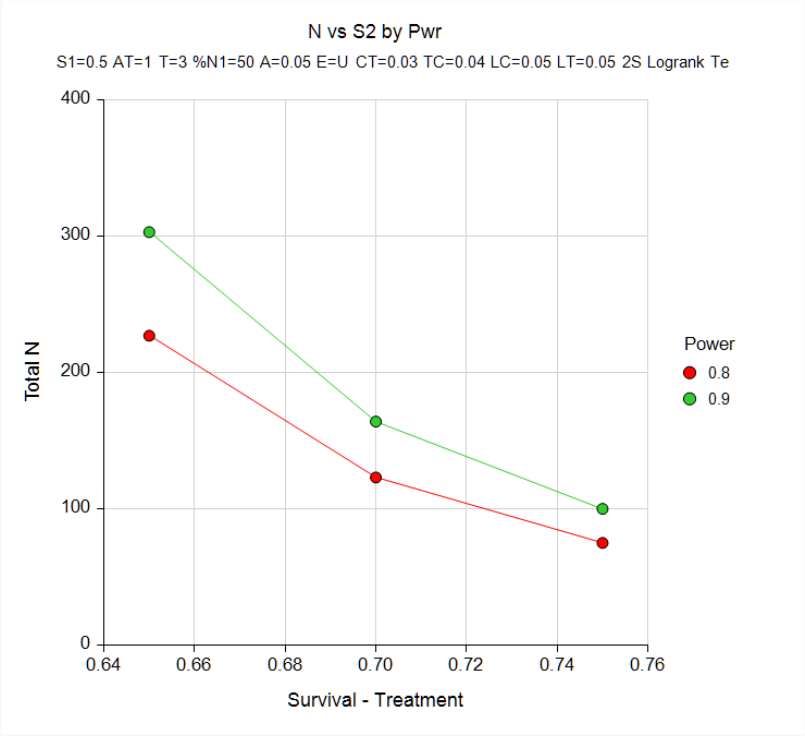
Numeric Results (Events)

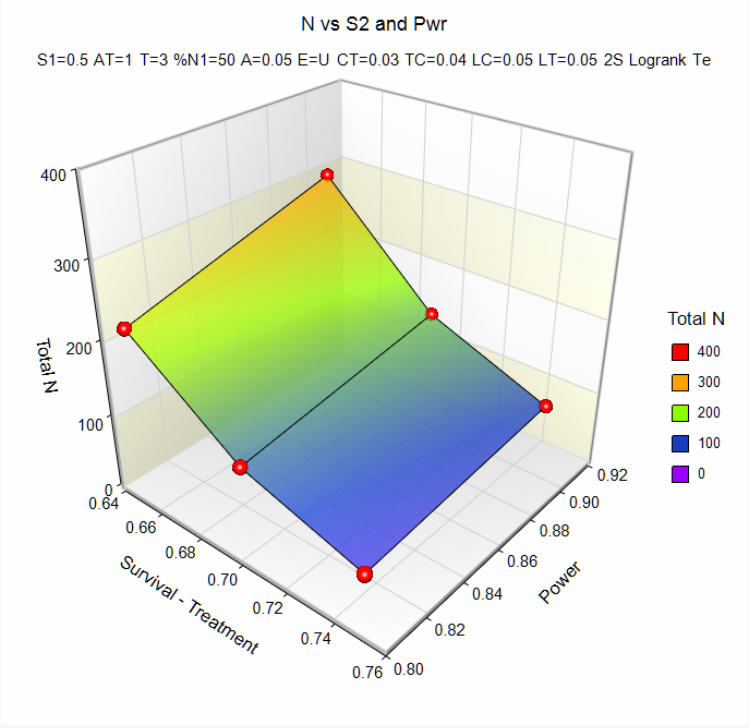
Solve For: Sample Size
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided
T0 (Survival Time): 1

	Number of Events			Hazard	Proportion Surviving			Time		Proportion Lost*		Proportion Switching Groups*		
Power	E1	E2	E	Ratio HR	S1	S2	Accrual Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.8014	88.3	71.7	160.0	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9002	117.9	95.7	213.5	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8019	47.7	35.0	82.7	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9004	63.7	46.6	110.3	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8022	29.0	18.7	47.8	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9010	38.7	25.0	63.7	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05

* The reported proportions are during a single time period.

Plots





The total sample size needed 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.

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

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 3** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

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	**0.05**
Treatments Switch to Controls	**0.04**

Output

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

Numeric Results (Sample Size)

Solve For: Sample Size
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided

	Sample Size			Hazard Ratio	Hazard Rate		Accrual	Time		Proportion Lost*		Proportion Switching Groups*		
Power	N1	N2	N	HR	h1	h2	Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.9012	69	70	139	0.5	1	0.5	Equal	0	2	0.03	0.03	0.05	0.04	0.05

* The reported proportions are during a single time period.

Numeric Results (Events)

Solve For: Sample Size
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided

	Number of Events			Hazard Ratio	Hazard Rate		Accrual	Time		Proportion Lost*		Proportion Switching Groups*		
Power	E1	E2	E	HR	h1	h2	Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.9012	58.2	43.5	101.8	0.5	1	0.5	Equal	0	2	0.03	0.03	0.05	0.04	0.05

* The reported proportions are during a single time period.

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

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 to 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

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 4** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

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**
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**

Input Spreadsheet Data

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

Output

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

Numeric Results (Sample Size)

Solve For: Sample Size
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided

	Sample Size			Hazard Ratio	Hazard Rate			Time		Proportion Lost*		Proportion Switching Groups*		
Power	N1	N2	N	HR	h1	h2	Accrual Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.9001	418	419	837	0.5	H1	Calc.	Acc	3	5	Ls1	Ls2	0.02	NCom	0.05

* The reported proportions are during a single time period.

Numeric Results (Events)

Solve For: Sample Size
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided

	Number of Events			Hazard Ratio	Hazard Rate			Time		Proportion Lost*		Proportion Switching Groups*		
Power	E1	E2	E	HR	h1	h2	Accrual Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.9001	74.4	41.2	115.6	0.5	H1	Calc.	Acc	3	5	Ls1	Ls2	0.02	NCom	0.05

* The reported proportions are during a single time period.

Detailed Input when Power = 0.9001, N1 = 418, N2 = 419, N = 837, Accrual Time = 3, Total Time = 5, Alpha = 0.05

	Hazard Rate		Hazard Ratio		Percent Administrative	Proportion Lost		Proportion Switching Groups	
Time Period	Control (H1)	Treatment (Calc.)	HR (0.5)	Percent Accrual (Acc)	Censored (Calculated)	Control (Ls1)	Treatment (Ls2)	Control to Treatment (0.02)	Treatment to Control (NCom)
1	0.08	0.040	0.5	50	0.00	0.04	0.06	0.02	0.04
2	0.04	0.020	0.5	25	0.00	0.04	0.06	0.02	0.04
3	0.05	0.025	0.5	25	25.00	0.05	0.07	0.02	0.05
4	0.06	0.030	0.5	0	33.33	0.06	0.07	0.02	0.06
5	0.07	0.035	0.5	0	100.00	0.07	0.08	0.02	0.07

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.

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

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 5** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

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**

Output

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

Numeric Results (Sample Size)

Solve For: Power
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided

	Sample Size			Hazard Ratio	Median Survival Time		Accrual	Time		Proportion Lost*		Proportion Switching Groups*		
Power	N1	N2	N	HR	T1	T2	Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.0839	25	25	50	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.1191	50	50	100	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.1549	75	75	150	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.1911	100	100	200	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.1792	25	25	50	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.3125	50	50	100	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.4379	75	75	150	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.5495	100	100	200	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.2921	25	25	50	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.5188	50	50	100	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.6928	75	75	150	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.8130	100	100	200	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05

* The reported proportions are during a single time period.

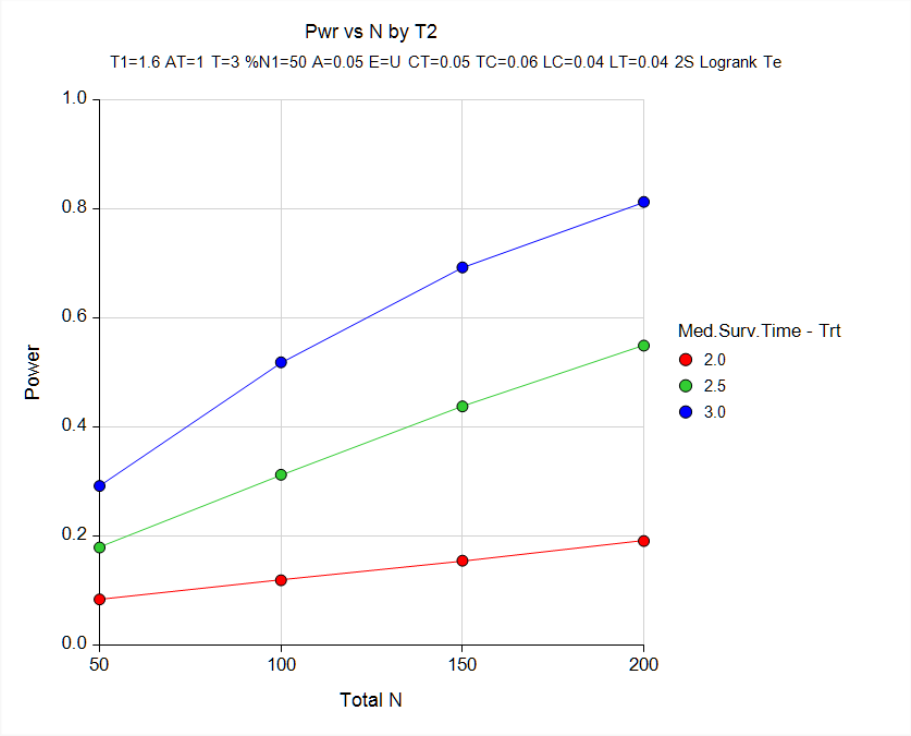
Numeric Results (Events)

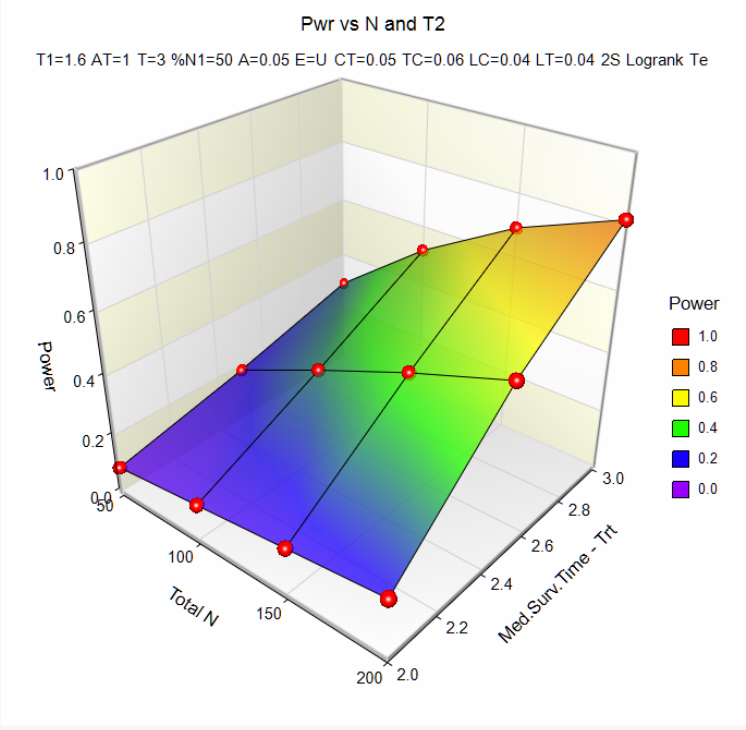
Solve For: Power
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided

	Number of Events			Hazard Ratio	Median Survival Time		Accrual	Time		Proportion Lost*		Proportion Switching Groups*		
Power	E1	E2	E	HR	T1	T2	Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.0839	15.7	14.0	29.7	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.1191	31.4	27.9	59.3	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.1549	47.1	41.9	89.0	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.1911	62.8	55.8	118.6	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.1792	15.6	12.2	27.8	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.3125	31.2	24.4	55.6	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.4379	46.8	36.6	83.4	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.5495	62.4	48.8	111.2	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.2921	15.5	10.8	26.4	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.5188	31.0	21.7	52.7	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.6928	46.6	32.5	79.1	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05
0.8130	62.1	43.4	105.5	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05

* The reported proportions are during a single time period.

Plots





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

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

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 6** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

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**

Output

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

Numeric Results (Sample Size)

Solve For: Power
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided
T0 (Survival Time): 1

	Sample Size			Mortality Ratio	Mortality			Time		Proportion Lost*		Proportion Switching Groups*		
Power	N1	N2	N	MR	M1	M2	Accrual Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.5079	25	25	50	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.8044	50	50	100	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.9332	75	75	150	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.9794	100	100	200	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.2988	25	25	50	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.5281	50	50	100	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.7021	75	75	150	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.8207	100	100	200	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.1529	25	25	50	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.2597	50	50	100	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.3635	75	75	150	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.4603	100	100	200	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05

* The reported proportions are during a single time period.

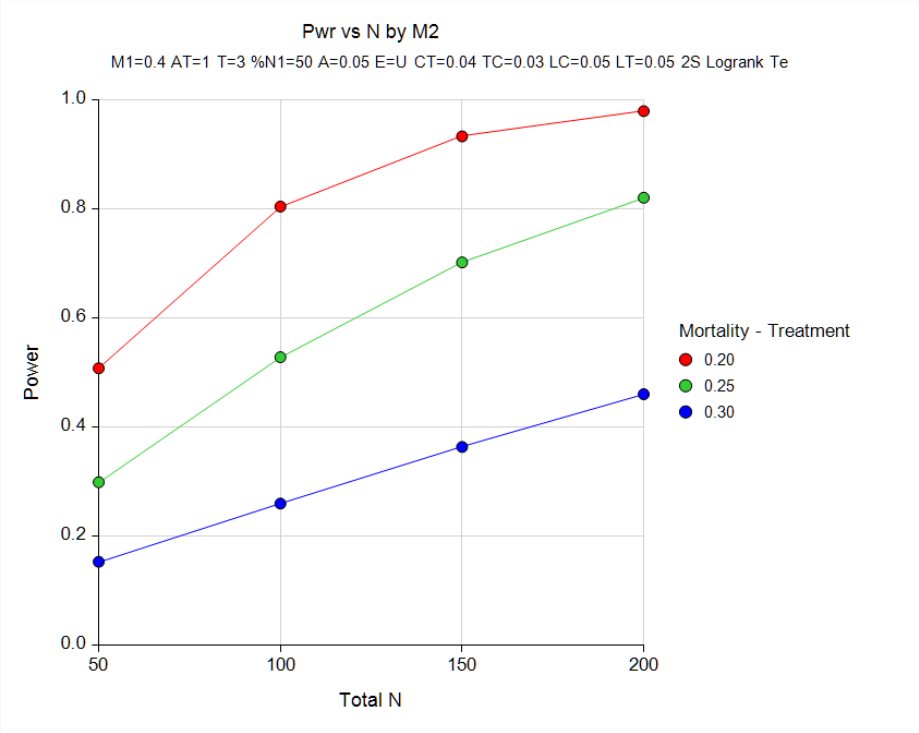
Numeric Results (Events)

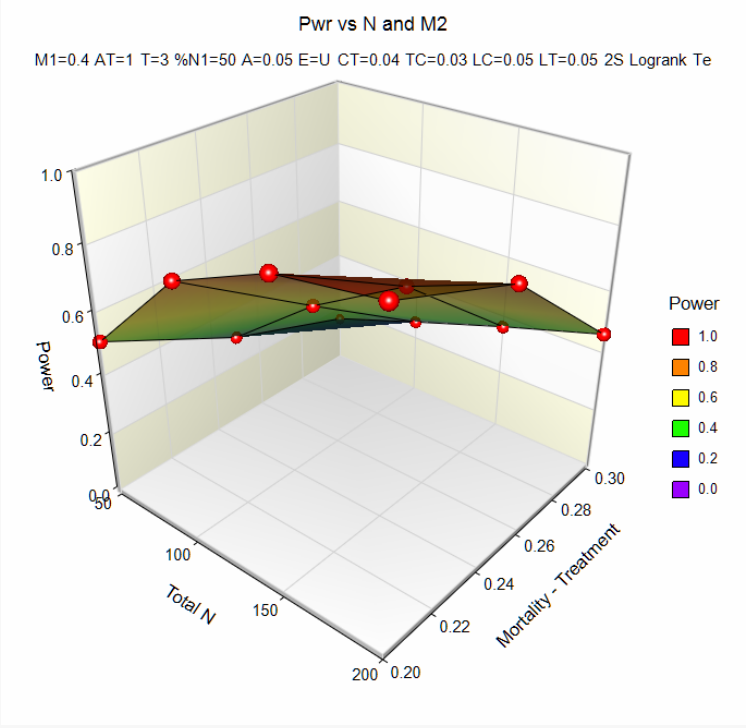
Solve For: Power
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided
T0 (Survival Time): 1

	Number of Events			Mortality Ratio	Mortality			Time		Proportion Lost*		Proportion Switching Groups*		
Power	E1	E2	E	MR	M1	M2	Accrual Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.5079	16.8	10.3	27.1	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.8044	33.6	20.7	54.2	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.9332	50.4	31.0	81.4	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.9794	67.1	41.3	108.5	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.2988	16.9	12.3	29.1	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.5281	33.7	24.5	58.3	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.7021	50.6	36.8	87.4	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.8207	67.5	49.1	116.5	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.1529	16.9	14.0	31.0	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.2597	33.9	28.1	61.9	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.3635	50.8	42.1	92.9	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05
0.4603	67.7	56.1	123.9	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05

* The reported proportions are during a single time period.

Plots





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

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(annual) = 1-(1-P(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

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 7** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

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**

Output

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

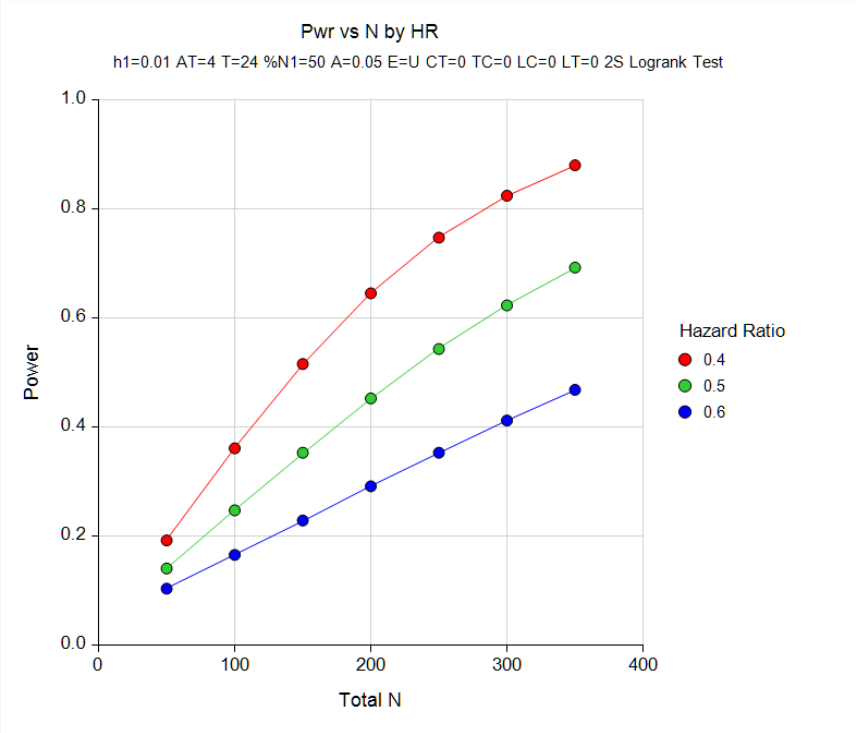
Numeric Results (Sample Size)

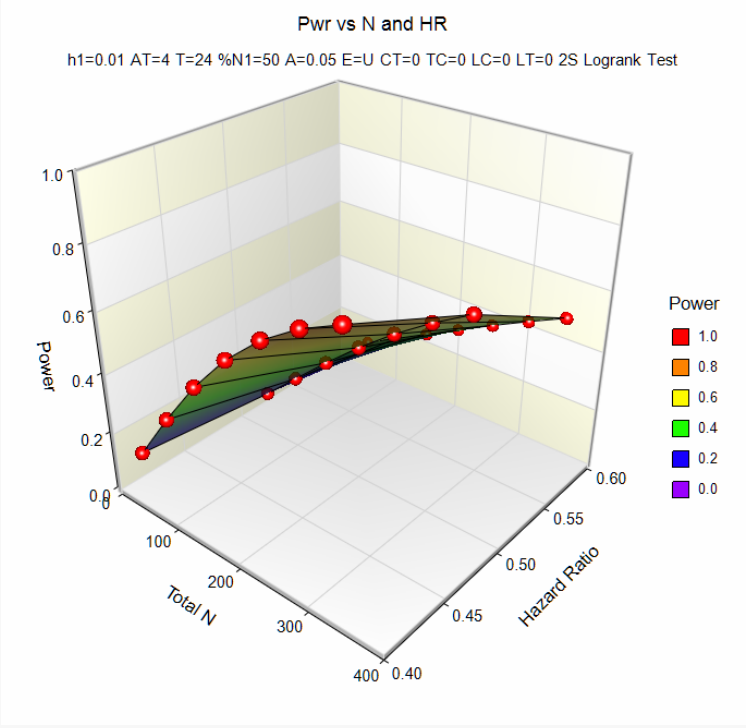
Solve For: Power
Test Type: Two-Sample Logrank Test
Groups: 1 = Control, 2 = Treatment
Alternative Hypothesis: Two-Sided

	Sample Size			Hazard Ratio	Hazard Rate		Accrual	Time		Proportion Lost*		Proportion Switching Groups*		
Power	N1	N2	N	HR	h1	h2	Pattern	Accrual	Total	Control	Treatment	Control to Treatment	Treatment to Control	Alpha
0.1922	25	25	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.3610	50	50	100	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.5157	75	75	150	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.6453	100	100	200	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.7474	125	125	250	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.8243	150	150	300	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.8802	175	175	350	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.1407	25	25	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.2473	50	50	100	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.3530	75	75	150	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.4526	100	100	200	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.5431	125	125	250	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.6232	150	150	300	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.6926	175	175	350	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.1037	25	25	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.1656	50	50	100	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.2287	75	75	150	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.2915	100	100	200	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.3529	125	125	250	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.4120	150	150	300	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05
0.4683	175	175	350	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05

* The reported proportions are during a single time period.

Plots





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