

## Chapter 902

# Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

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## Introduction

This procedure computes the sample size and power of a logrank test for equality of survival distributions. Time-period weights, accrual time, follow-up time, loss during follow up, noncompliance, and time-dependent hazard rates are parameters that can be set.

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. The use of these weights allows models to be power analyzed with *non-proportional hazards*, including *delayed-onset event rates*.

Power and sample size calculations for the logrank test have been studied by several authors. This module uses the method of Lakatos (1988) as presented in Wu (2018). This method is based on a Markov model that yields the asymptotic mean and variance of the logrank statistic under very general conditions.

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## 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 reasonably 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,  $T_0$  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,  $T_0$  is taken to be the time period number.

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## Technical Details

The logrank statistic is defined as

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

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 Lakatos (1988) and Wu (2018), the trial is partitioned into  $K$  equal time intervals. Actually, the user specifies the number of intervals,  $B$ , per time period. The value of  $K$  is then determined using  $K = BM$ , where  $M$  is the number of time periods.

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

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

where  $P_{1,k} = \{p_{1,k,j}\}$  is a vector giving the occupancy probabilities in the control group (group 1) where the index  $j$  runs from 1 to 4 and designates a state of the process: 1 = lost, 2 = event (dead), 3 = active complier,

## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

and 4 = active non-complier.  $T_{k-1,k}$  is the transition matrix constructed so that each element gives the probability of transferring from state  $j_1$  to state  $j_2$ .

A similar formulation is defined for the treatment group by replacing the value of the first subscript with a "2".

At each iteration

$$P_{1,k} = \begin{bmatrix} p_{1,k,1} \\ p_{1,k,2} \\ p_{1,k,3} \\ p_{1,k,4} \end{bmatrix}, \quad P_{2,k} = \begin{bmatrix} p_{2,k,1} \\ p_{2,k,2} \\ p_{2,k,3} \\ p_{2,k,4} \end{bmatrix}$$

Iterations begin using

$$P_{1,0} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 1 \end{bmatrix}, \quad P_{2,0} = \begin{bmatrix} 0 \\ 0 \\ 1 \\ 0 \end{bmatrix}$$

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 contain labels which are not part of the actual matrix).

$$T_{k,k-1} = \begin{bmatrix} \text{States} & \text{Lost} & \text{Event} & \text{Complier} & \text{Non-complier} \\ \text{Lost} & 1 & 0 & p_{\text{loss},k} & p_{\text{loss},k} \\ \text{Event} & 0 & 1 & p_{\text{event}1,k} & p_{\text{event}2,k} \\ \text{Complier} & 0 & 0 & 1 - \text{sum}_c & p_{\text{drop-in},k} \\ \text{Non-complier} & 0 & 0 & p_{\text{noncomp},k} & 1 - \text{sum}_n \end{bmatrix}$$

where  $\text{sum}_c$  and  $\text{sum}_n$  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.

Let  $r_1:r_2$  represent the allocation ratio of control to treatment. We substitute the group sample sizes to represent these values.

The parameters  $\rho_k$ ,  $\phi_k$ ,  $\theta_k$ ,  $\gamma_k$ , and  $\eta_k$  are estimated from the occupancy probabilities using the following formulas (see Wu (2018) page 120):

### Events (deaths)

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

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

### At Risk

$$a_{1,k} = (p_{1,k-1,3} + p_{1,k-1,4})$$

$$a_{2,k} = (p_{2,k-1,3} + p_{2,k-1,4})$$

Define the interval parameters as follows (see Wu (2018) page 120):

$$\rho_k = \frac{r_1 d_{1,k} + r_2 d_{2,k}}{r_1 p_{1,K,2} + r_2 p_{2,K,2}}$$

$$\phi_k = \frac{r_1 a_{1,k}}{r_2 a_{2,k}}$$

$$\theta_k = \frac{\ln\left(1 - \frac{d_{1,k}}{a_{1,k}}\right)}{\ln\left(1 - \frac{d_{2,k}}{a_{2,k}}\right)}$$

$$\gamma_k = \frac{\phi_k \theta_k}{1 + \phi_k \theta_k} - \frac{\phi_k}{1 + \phi_k}$$

$$\eta_k = \frac{\phi_k}{(1 + \phi_k)^2}$$

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## Power

The distribution of  $L$  is assumed to be asymptotically normal which leads to the following definition of the power of a two-sided test.

$$Power = \left[ \left( \sum_{k=1}^K \rho_k \gamma_k \right) \sqrt{\frac{N_1 P_C + N_2 P_E}{\sum_{k=1}^K \rho_k \eta_k}} - z_{1-\alpha/2} \right]$$

where

$$P_C = p_{1,K,2} \text{ and } P_E = p_{2,K,2}.$$

## Example 1 – Finding the Sample Size 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 sample size 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, when power is 80% or 90%, and when the significance level is 0.05.

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.

### 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 .....	<b>Sample Size</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Power.....	<b>0.8 0.9</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Input Type.....	<b>Proportion Surviving</b>
S1 (Proportion Surviving - Control) .....	<b>0.50</b>
Treatment Group Parameter.....	<b>S2 (Proportion Surviving - Treatment)</b>
S2 (Proportion Surviving - Treatment) .....	<b>0.65 0.70 0.75</b>
T0 (Survival Time) .....	<b>1</b>
Accrual Time (Integers Only) .....	<b>1</b>
Accrual Pattern .....	<b>Uniform or Equal</b>
Total Time (Integers Only) .....	<b>3</b>
Controls Lost.....	<b>0.05</b>
Treatments Lost.....	<b>0.05</b>
Controls Switch to Treatments.....	<b>0.03</b>
Treatments Switch to Controls.....	<b>0.04</b>

#### Options Tab

Number of Intervals per Time Period .....	<b>100</b>
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## Output

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

## Numeric Reports

### Numeric Results (Sample Size)

Solve For: [Sample Size](#)  
 Test Type: Two-Sample, Logrank Test  
 Groups: 1 = Control, 2 = Treatment  
 Alternative Hypothesis: Two-Sided  
 Accrual Pattern: Uniform or Equal  
 T0 (Survival Time): 1

Power	Sample Size			Hazard Ratio HR	Proportion Surviving		Accrual Pattern	Time		Proportions*				Alpha
										Lost		Switching Groups		
	N1	N2	N		S1	S2		Accrual	Total	C   T		C to T   T to C		
0.8000	113	113	226	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9005	151	152	303	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8020	61	62	123	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9019	82	83	165	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8010	37	38	75	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9022	50	51	101	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.

Note: All calculations were made using 100 intervals per time period.

Power	The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N1, N2, and N	The sample sizes in the control group, the treatment group, and their total, respectively. $N = N1 + N2$ .
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.
T0	The length of time on which S1 and S2 are based.
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).
C	Controls Lost. The proportion of the control group that is lost (drop out) during a single time period (e.g., year or month).
T	Treatments Lost. The proportion of the treatment group that is lost (drop out) during a single time period (e.g., year or month).
C to T	Controls to Treatments or Drop In. The proportion of the control group that switch to a group with a hazard rate equal to the treatment group.
T to C	Treatments to Controls or 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.

## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

## Numeric Results (Events)

Solve For: [Sample Size](#)  
 Test Type: Two-Sample, Logrank Test  
 Groups: 1 = Control, 2 = Treatment  
 Alternative Hypothesis: Two-Sided  
 Accrual Pattern: Uniform or Equal  
 T0 (Survival Time): 1

Power	Number of Events			Hazard Ratio HR	Proportion Surviving		Accrual Pattern	Time		Proportions*				Alpha
										Lost		Switching Groups		
	E1	E2	E		S1	S2		Accrual	Total	C   T		C to T   T to C		
0.8000	88.0	71.4	159.4	0.6215	0.5	0.65	Equal	1	3	0.05   0.05	0.03   0.04		0.05	
0.9005	117.6	96.1	213.6	0.6215	0.5	0.65	Equal	1	3	0.05   0.05	0.03   0.04		0.05	
0.8020	47.4	35.3	82.7	0.5146	0.5	0.70	Equal	1	3	0.05   0.05	0.03   0.04		0.05	
0.9019	63.7	47.3	110.9	0.5146	0.5	0.70	Equal	1	3	0.05   0.05	0.03   0.04		0.05	
0.8010	28.7	19.0	47.7	0.4150	0.5	0.75	Equal	1	3	0.05   0.05	0.03   0.04		0.05	
0.9022	38.7	25.5	64.2	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.

Note: All calculations were made using 100 intervals per time period.

Power	The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
E1, E2, and E	The required number of events (failures) in the control group, the treatment group, and their total, respectively. $E = E1 + E2$ .
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.
T0	The length of time on which S1 and S2 are based.
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).
C	Controls Lost. The proportion of the control group that is lost (drop out) during a single time period (e.g., year or month).
T	Treatments Lost. The proportion of the treatment group that is lost (drop out) during a single time period (e.g., year or month).
C to T	Controls to Treatments or Drop In. The proportion of the control group that switch to a group with a hazard rate equal to the treatment group.
T to C	Treatments to Controls or 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.

## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

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

**Detailed Input when Power = 0.8, N1 = 113, N2 = 113, N = 226, Accrual Time = 1, Total Time = 3, Alpha = 0.05**

T0 = 1

Accrual Pattern: Uniform or Equal

Time Period	Proportion Surviving		Hazard Ratio HR (0.6215)	Percent Accrual (Equal)	Percent Administrative Censored (Calculated)	Proportion Lost		Proportion Switching Groups	
	Control (0.5)	Treatment (0.65)				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 (month). It becomes very useful when you want to document a study in which these parameters vary from month to month.

### Percent Administrative Censored

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

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 ( $\alpha$ ) 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  $[h_2 / h_1]$  of 0.6215) when the proportion surviving (in a time of 1) in the control group is 0.5, with 80% power, the number of needed subjects will be 113 in Group 1 and 113 in Group 2 (totaling 226 subjects). The corresponding required number of events are 88 in Group 1 and 71.4 in Group 2 (totaling 159.4 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.
- Wu, Jianrong. 2018. Statistical Methods for Survival Trial Design. CRC Press. Boca Raton.
- Chen, H. and He, J. 2023. 'Sample size calculation for the combination test under nonproportional hazards', Biometrical Journal. <https://doi.org/10.1002/bimj.202100403>

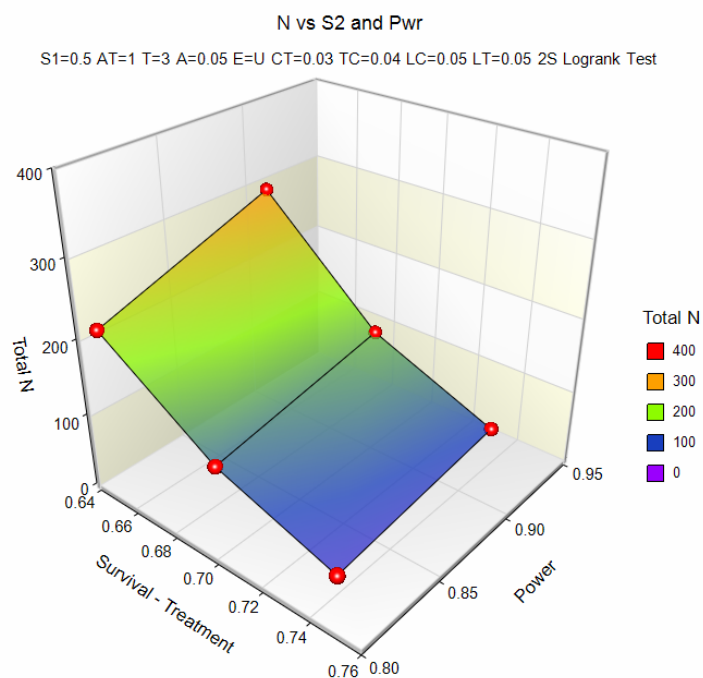
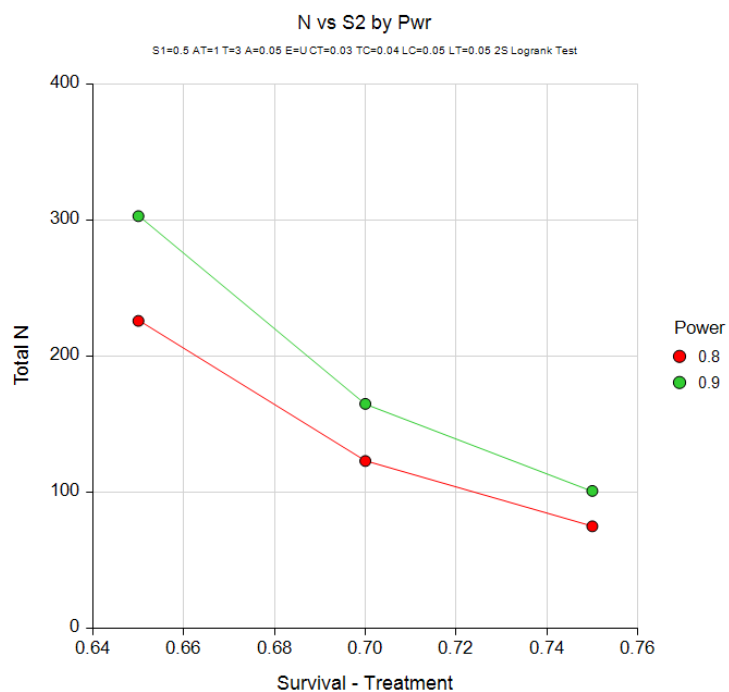
Finally, scatter plots of the results are displayed.



## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

## Plots Section

## Plots



These plots show the relationship between sample size and power for the three values of S2.

## Example 2 – Validation using Wu (2018)

Wu (2018) pages 120-122 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. Wu obtains a sample size of 139, with the number of events needed as 101.7.

### 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 .....	<b>Sample Size</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Power.....	<b>0.90</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Input Type.....	<b>Hazard Rate</b>
h1 (Hazard Rate of Control Group) .....	<b>1.0</b>
Treatment Group Parameter .....	<b>h2 (Hazard of Treatment Group)</b>
h2 (Hazard Rate of Treatment Group) .....	<b>0.5</b>
Accrual Time (Integers Only) .....	<b>0</b>
Accrual Pattern .....	<b>Uniform or Equal</b>
Total Time (Integers Only) .....	<b>2</b>
Controls Lost.....	<b>0.03</b>
Treatments Lost.....	<b>0.03</b>
Controls Switch to Treatments.....	<b>0.05</b>
Treatments Switch to Controls.....	<b>0.04</b>

#### Options Tab

Number of Intervals per Time Period .....	<b>100</b>
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## 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  
 Accrual Pattern: Uniform or Equal

										Proportions*			
Power	Sample Size			Hazard Ratio HR	Hazard Rate		Accrual Pattern	Time		Lost	Switching Groups	Alpha	
	N1	N2	N		h1	h2		Accrual	Total	C   T	C to T   T to C		
0.90181	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.

Note: All calculations were made using 100 intervals per time period.

### Numeric Results (Events)

Solve For: [Sample Size](#)  
 Test Type: Two-Sample, Logrank Test  
 Groups: 1 = Control, 2 = Treatment  
 Alternative Hypothesis: Two-Sided  
 Accrual Pattern: Uniform or Equal

Power	Number of Events			Hazard Ratio HR	Hazard Rate		Accrual Pattern	Time		Proportions*		
	E1	E2	E		h1	h2		Lost	Switching Groups		Alpha	
									C   T	C to T   T to C		
0.90181	57.8	43.9	101.7	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.

Note: All calculations were made using 100 intervals per time period.

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

## Example 3 – 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.

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 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 (Hazard Rate of Control Group) ..... **=H1**  
 Treatment Group Parameter..... **HR (Hazard Ratio = h2/h1)**  
 HR (Hazard Ratio = h2/h1) ..... **0.50**  
 Accrual Time (Integers Only) ..... **3**  
 Accrual Pattern ..... **Non-Uniform (Spreadsheet Entry)**  
 Accrual Values in Columns ..... **=Acc**  
 Total Time (Integers Only) ..... **5**  
 Controls Lost..... **=Ls1**  
 Treatments Lost..... **=Ls2**  
 Controls Switch to Treatments..... **0.02**  
 Treatments Switch to Controls..... **=NCom**

### Options Tab

Number of Intervals per Time Period ..... **100**

### 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  
 Accrual Pattern: Non-Uniform

										Proportions*			
Power	Sample Size			Hazard Ratio HR	Hazard Rate		Accrual Pattern	Time		Lost	Switching Groups	Alpha	
	N1	N2	N		h1	h2		Accrual	Total	C   T	C to T   T to C		
0.9002	432	433	865	0.5	H1	Calc.	Acc	3	5	Ls1   Ls2	0.02   NCom	0.05	

\* The reported proportions are during a single time period.

Note: All calculations were made using 100 intervals per time period.

### Numeric Results (Events)

Solve For: [Sample Size](#)  
 Test Type: Two-Sample, Logrank Test  
 Groups: 1 = Control, 2 = Treatment  
 Alternative Hypothesis: Two-Sided  
 Accrual Pattern: Non-Uniform

										Proportions*		
Power	Number of Events			Hazard Ratio HR	Hazard Rate		Accrual Pattern	Time		Lost	Switching Groups	Alpha
	E1	E2	E		h1	h2		Accrual	Total	C   T	C to T   T to C	
0.9002	76.9	42.6	119.5	0.5	H1	Calc.	Acc	3	5	Ls1   Ls2	0.02   NCom	0.05

\* The reported proportions are during a single time period.

Note: All calculations were made using 100 intervals per time period.

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 865 subjects.

## Example 4 – 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 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 .....	<b>Power</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Enter total sample size and percentage in Group 1</b>
Total Sample Size (N).....	<b>50 to 250 by 50</b>
Percent in Group 1 .....	<b>50</b>
Input Type.....	<b>Proportion Surviving</b>
S1 (Proportion Surviving - Control) .....	<b>0.50</b>
Treatment Group Parameter.....	<b>S2 (Proportion Surviving - Treatment)</b>
S2 (Proportion Surviving - Treatment) .....	<b>0.65 0.70 0.75</b>
T0 (Survival Time) .....	<b>1</b>
Accrual Time (Integers Only) .....	<b>1</b>
Accrual Pattern .....	<b>Uniform or Equal</b>
Total Time (Integers Only) .....	<b>3</b>
Controls Lost.....	<b>0.05</b>
Treatments Lost.....	<b>0.05</b>
Controls Switch to Treatments.....	<b>0.03</b>
Treatments Switch to Controls.....	<b>0.04</b>

#### Options Tab

Number of Intervals per Time Period .....	<b>100</b>
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## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

## 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  
 Accrual Pattern: Uniform or Equal  
 T0 (Survival Time): 1

Power	Sample Size			Percent in Group 1 %N1	Hazard Ratio HR	Proportion Surviving		Accrual Pattern	Time		Proportions*					
											Lost		Switching Groups		Alpha	
	N1	N2	N			S1	S2		Accrual	Total						C   T
0.2604	25	25	50	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.4616	50	50	100	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.6265	75	75	150	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.7504	100	100	200	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.8381	125	125	250	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.4324	25	25	50	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.7160	50	50	100	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.8728	75	75	150	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.9473	100	100	200	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.9794	125	125	250	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.6283	25	25	50	50	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.8988	50	50	100	50	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.9773	75	75	150	50	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.9955	100	100	200	50	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05	
0.9992	125	125	250	50	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.

Note: All calculations were made using 100 intervals per time period.

## Numeric Results (Events)

Solve For: [Power](#)  
 Test Type: Two-Sample, Logrank Test  
 Groups: 1 = Control, 2 = Treatment  
 Alternative Hypothesis: Two-Sided  
 Accrual Pattern: Uniform or Equal  
 T0 (Survival Time): 1

Power	Number of Events			Percent in Group 1 %N1	Hazard Ratio HR	Proportion Surviving		Accrual Pattern	Time		Proportions*				Alpha
											Lost		Switching Groups		
	E1	E2	E			S1	S2		Accrual	Total	C   T		C to T   T to C		
0.2604	19.5	15.8	35.3	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.4616	38.9	31.6	70.5	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.6265	58.4	47.4	105.8	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.7504	77.9	63.2	141.1	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8381	97.3	79.0	176.3	50	0.6215	0.5	0.65	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.4324	19.4	14.2	33.7	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.7160	38.8	28.5	67.3	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8728	58.3	42.7	101.0	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9473	77.7	56.9	134.6	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9794	97.1	71.2	168.3	50	0.5146	0.5	0.70	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.6283	19.4	12.5	31.9	50	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.8988	38.7	25.0	63.7	50	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9773	58.1	37.5	95.6	50	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9955	77.5	50.0	127.5	50	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05
0.9992	96.9	62.5	159.4	50	0.4150	0.5	0.75	Equal	1	3	0.05	0.05	0.03	0.04	0.05

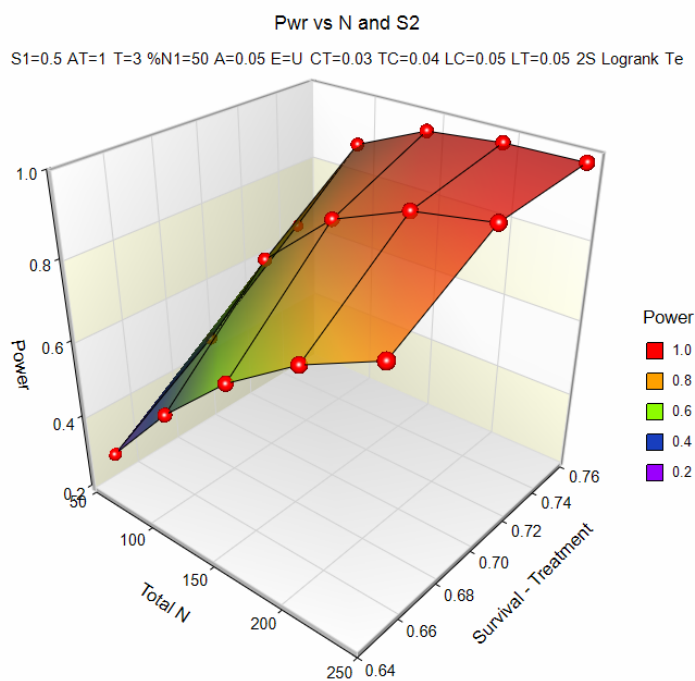
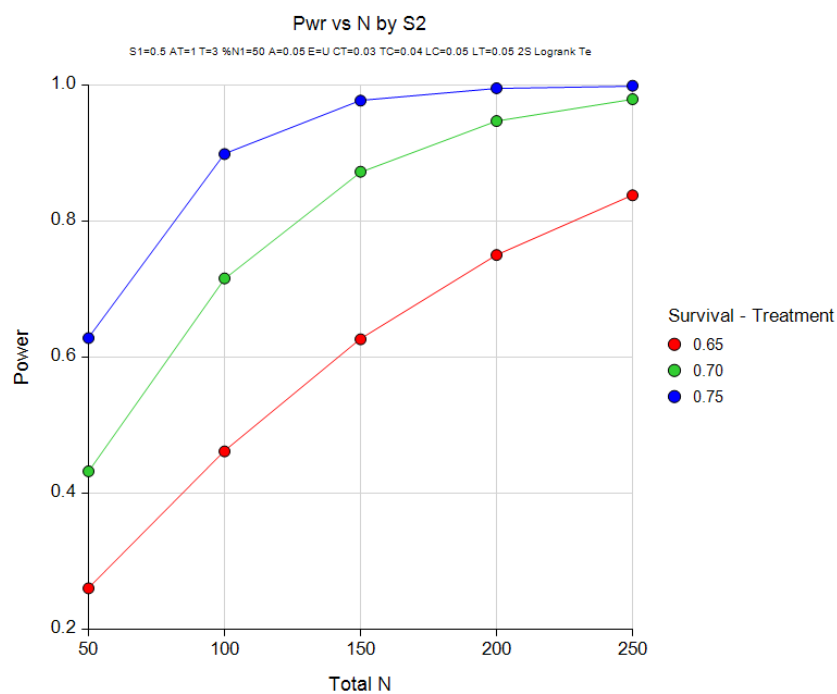
\* The reported proportions are during a single time period.

Note: All calculations were made using 100 intervals per time period.



## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

## Plots



These reports and plots show the relationship between sample size and power for the three treatment survival proportions.

## 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 .....	<b>Power</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Enter total sample size and percentage in Group 1</b>
Total Sample Size (N).....	<b>50 to 200 by 50</b>
Percent in Group 1 .....	<b>50</b>
Input Type.....	<b>Median Survival Time</b>
T1 (Median Survival Time - Control) .....	<b>1.6</b>
Treatment Group Parameter.....	<b>T2 (Med. Survival Time - Treatment)</b>
T2 (Median Survival Time - Treatment) .....	<b>2.0 2.5 3.0</b>
Accrual Time (Integers Only) .....	<b>1</b>
Accrual Pattern .....	<b>Uniform or Equal</b>
Total Time (Integers Only) .....	<b>3</b>
Controls Lost.....	<b>0.04</b>
Treatments Lost.....	<b>0.04</b>
Controls Switch to Treatments.....	<b>0.05</b>
Treatments Switch to Controls.....	<b>0.06</b>

#### Options Tab

Number of Intervals per Time Period .....	<b>100</b>
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## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

## 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  
 Accrual Pattern: Uniform or Equal

Power	Sample Size			Percent in Group 1 %N1	Hazard Ratio HR	Median Survival Time		Accrual Pattern	Time		Proportions*					
											Lost		Switching Groups		Alpha	
	N1	N2	N			T1	T2		Accrual	Total	C   T	C to T	T to C			
0.0781	25	25	50	50	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.1163	50	50	100	50	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.1535	75	75	150	50	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.1904	100	100	200	50	0.8000	1.6	2.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.1794	25	25	50	50	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.3135	50	50	100	50	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.4386	75	75	150	50	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.5496	100	100	200	50	0.6400	1.6	2.5	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.2945	25	25	50	50	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.5190	50	50	100	50	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.6910	75	75	150	50	0.5333	1.6	3.0	Equal	1	3	0.04	0.04	0.05	0.06	0.05	
0.8103	100	100	200	50	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.

Note: All calculations were made using 100 intervals per time period.

## Numeric Results (Events)

Solve For: [Power](#)  
 Test Type: Two-Sample, Logrank Test  
 Groups: 1 = Control, 2 = Treatment  
 Alternative Hypothesis: Two-Sided  
 Accrual Pattern: Uniform or Equal

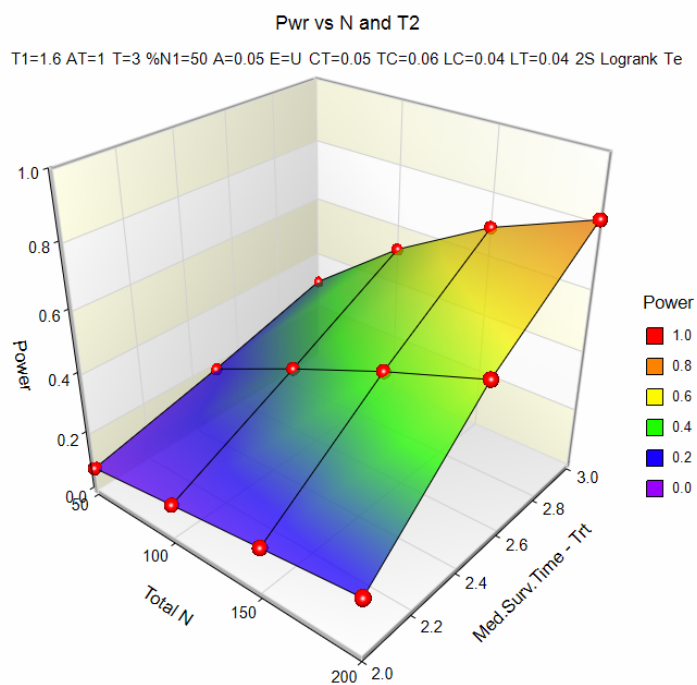
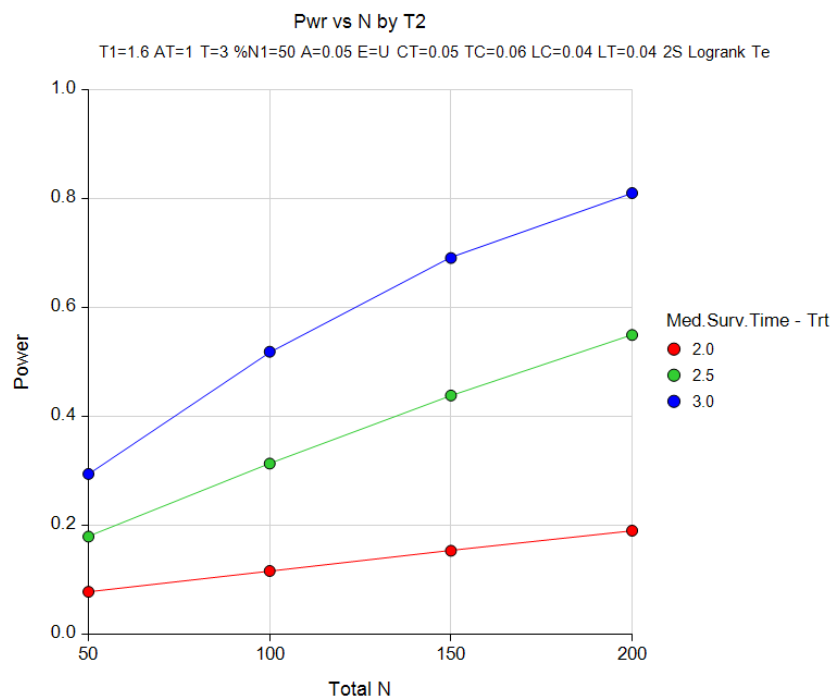
Power	Number of Events			Percent in Group 1 %N1	Hazard Ratio HR	Median Survival Time		Accrual Pattern	Time		Proportions*				Alpha
											Lost		Switching Groups		
	E1	E2	E			T1	T2		Accrual	Total	C   T		C to T   T to C		
0.0781	15.7	14.0	29.7	50	0.8000	1.6	2.0	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.1163	31.4	28.0	59.4	50	0.8000	1.6	2.0	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.1535	47.1	41.9	89.1	50	0.8000	1.6	2.0	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.1904	62.8	55.9	118.7	50	0.8000	1.6	2.0	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.1794	15.6	12.2	27.8	50	0.6400	1.6	2.5	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.3135	31.2	24.4	55.6	50	0.6400	1.6	2.5	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.4386	46.8	36.6	83.5	50	0.6400	1.6	2.5	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.5496	62.4	48.9	111.3	50	0.6400	1.6	2.5	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.2945	15.5	10.9	26.4	50	0.5333	1.6	3.0	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.5190	31.1	21.7	52.8	50	0.5333	1.6	3.0	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.6910	46.6	32.6	79.2	50	0.5333	1.6	3.0	Equal	1	3	0.04   0.04	0.05   0.06	0.05		
0.8103	62.1	43.4	105.6	50	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.

Note: All calculations were made using 100 intervals per time period.

## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

## Plots



These reports and 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 .....	<b>Power</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Enter total sample size and percentage in Group 1</b>
Total Sample Size (N).....	<b>50 to 200 by 50</b>
Percent in Group 1 .....	<b>50</b>
Input Type.....	<b>Mortality</b>
M1 (Mortality - Control) .....	<b>0.4</b>
Treatment Group Parameter.....	<b>M2 (Mortality - Treatment)</b>
M2 (Mortality - Treatment) .....	<b>0.20 0.25 0.30</b>
T0 (Survival Time) .....	<b>1</b>
Accrual Time (Integers Only) .....	<b>1</b>
Accrual Pattern .....	<b>Uniform or Equal</b>
Total Time (Integers Only) .....	<b>3</b>
Controls Lost.....	<b>0.05</b>
Treatments Lost.....	<b>0.05</b>
Controls Switch to Treatments.....	<b>0.04</b>
Treatments Switch to Controls.....	<b>0.03</b>

#### Options Tab

Number of Intervals per Time Period .....	<b>100</b>
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## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

## 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  
 Accrual Pattern: Uniform or Equal  
 T0 (Survival Time): 1

Power	Sample Size			Percent in Group 1 %N1	Mortality Ratio MR	Mortality		Accrual Pattern	Time		Proportions*					Alpha
											Lost	Switching Groups				
	C   T	C to T	T to C			C to T	T to C									
0.5080	25	25	50	50	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.7996	50	50	100	50	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.9292	75	75	150	50	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.9773	100	100	200	50	0.500	0.4	0.20	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.3002	25	25	50	50	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.5283	50	50	100	50	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.7010	75	75	150	50	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.8192	100	100	200	50	0.625	0.4	0.25	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.1517	25	25	50	50	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.2599	50	50	100	50	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.3639	75	75	150	50	0.750	0.4	0.30	Equal	1	3	0.05	0.05	0.04	0.03	0.05	
0.4607	100	100	200	50	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.

Note: All calculations were made using 100 intervals per time period.

## Numeric Results (Events)

Solve For: [Power](#)  
 Test Type: Two-Sample, Logrank Test  
 Groups: 1 = Control, 2 = Treatment  
 Alternative Hypothesis: Two-Sided  
 Accrual Pattern: Uniform or Equal  
 T0 (Survival Time): 1

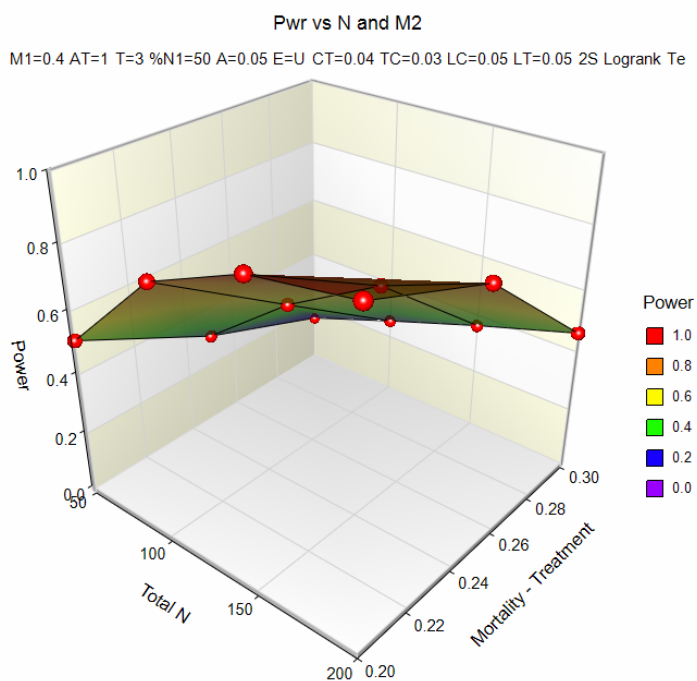
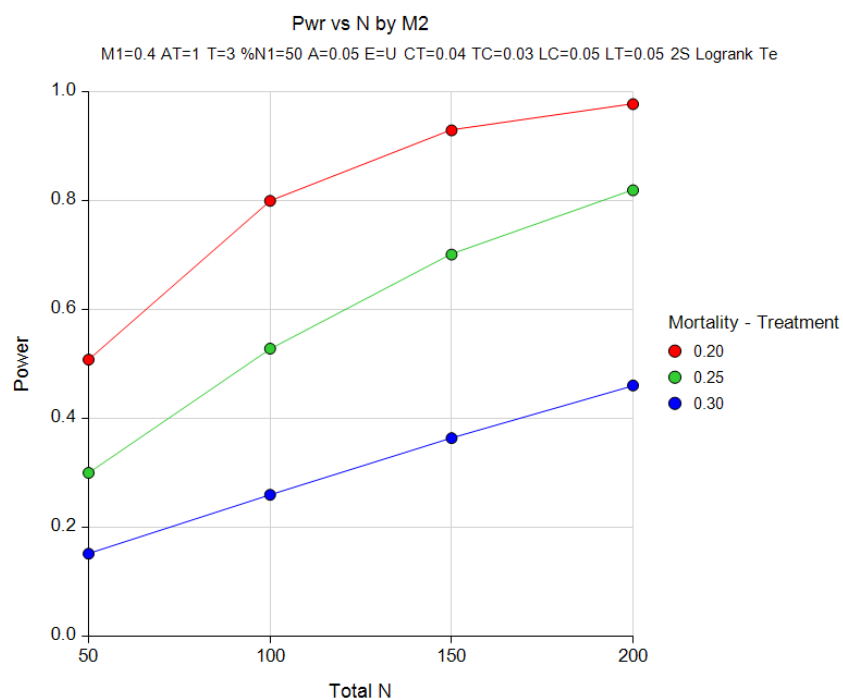
											Proportions*				
	Number of Events			Percent in Group 1 %N1	Mortality Ratio MR	Mortality		Accrual Pattern	Time		Lost		Switching Groups		Alpha
	E1	E2	E			M1	M2		Accrual	Total	C   T	C to T   T to C			
Power															
0.5080	16.8	10.3	27.1	50	0.500	0.4	0.20	Equal	1	3	0.05   0.05	0.04   0.03	0.04   0.03	0.05	
0.7996	33.6	20.7	54.3	50	0.500	0.4	0.20	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	
0.9292	50.4	31.0	81.4	50	0.500	0.4	0.20	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	
0.9773	67.2	41.4	108.6	50	0.500	0.4	0.20	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	
0.3002	16.9	12.3	29.2	50	0.625	0.4	0.25	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	
0.5283	33.8	24.6	58.3	50	0.625	0.4	0.25	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	
0.7010	50.6	36.9	87.5	50	0.625	0.4	0.25	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	
0.8192	67.5	49.2	116.7	50	0.625	0.4	0.25	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	
0.1517	17.0	14.1	31.0	50	0.750	0.4	0.30	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	
0.2599	33.9	28.1	62.0	50	0.750	0.4	0.30	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	
0.3639	50.9	42.2	93.0	50	0.750	0.4	0.30	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	
0.4607	67.8	56.2	124.0	50	0.750	0.4	0.30	Equal	1	3	0.05   0.05	0.04   0.05	0.04   0.03	0.05	

\* The reported proportions are during a single time period.

Note: All calculations were made using 100 intervals per time period.

## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

## Plots



These reports and 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  $P(\text{annual}) = 1 - (1 - P(\text{monthly}))^{12}$ . 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  $R(\text{monthly}) = R(\text{annual})/12$ .

### 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 .....	<b>Power</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Enter total sample size and percentage in Group 1</b>
Total Sample Size (N).....	<b>50 to 350 by 50</b>
Percent in Group 1 .....	<b>50</b>
Input Type.....	<b>Hazard Rate</b>
h1 (Hazard Rate of Control Group) .....	<b>0.01166666666667</b>
Treatment Group Parameter.....	<b>HR (Hazard Ratio = h2/h1)</b>
HR (Hazard Ratio = h2/h1) .....	<b>0.4 0.5 0.6</b>
Accrual Time (Integers Only) .....	<b>4</b>
Accrual Pattern .....	<b>Uniform or Equal</b>
Total Time (Integers Only) .....	<b>24</b>



## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

Controls Lost.....**0.00339605319892**  
 Treatments Lost.....**0.00339605319892**  
 Controls Switch to Treatments.....**0.00253504861384**  
 Treatments Switch to Controls.....**0.00253504861384**

## Options Tab

Number of Intervals per Time Period ..... **100**

## 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  
 Accrual Pattern: Uniform or Equal

											Proportions*					
Power	Sample Size			Percent in Group 1 %N1	Hazard Ratio HR	Hazard Rate		Accrual Pattern	Time		Lost		Switching Groups		Alpha	
	N1	N2	N			h1	h2		Accrual	Total	C   T	C to T   T to C				
0.2098	25	25	50	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.3708	50	50	100	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.5147	75	75	150	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.6352	100	100	200	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.7316	125	125	250	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.8062	150	150	300	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.8622	175	175	350	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.1499	25	25	50	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.2563	50	50	100	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.3589	75	75	150	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.4546	100	100	200	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.5414	125	125	250	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.6182	150	150	300	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.6851	175	175	350	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.1059	25	25	50	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.1701	50	50	100	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.2334	75	75	150	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.2956	100	100	200	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.3561	125	125	250	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.4140	150	150	300	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.4691	175	175	350	50	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.

Note: All calculations were made using 100 intervals per time period.

## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)

## Numeric Results (Events)

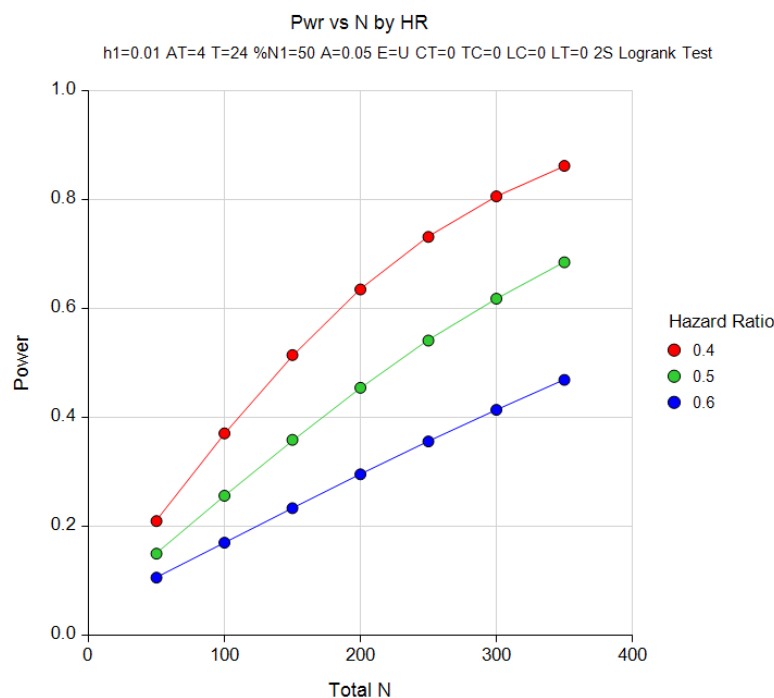
Solve For: [Power](#)  
 Test Type: Two-Sample, Logrank Test  
 Groups: 1 = Control, 2 = Treatment  
 Alternative Hypothesis: Two-Sided  
 Accrual Pattern: Uniform or Equal

Power	Number of Events			Percent in Group 1 %N1	Hazard Ratio HR	Hazard Rate		Accrual Pattern	Time		Proportions*					Alpha
											Lost		Switching Groups			
	E1	E2	E			h1	h2		Accrual	Total	C   T		C to T	T to C		
0.2098	5.4	2.4	7.8	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.3708	10.8	4.9	15.6	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.5147	16.1	7.3	23.4	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.6352	21.5	9.7	31.3	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.7316	26.9	12.2	39.1	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.8062	32.3	14.6	46.9	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.8622	37.7	17.1	54.7	50	0.4	0.0117	0.0047	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.1499	5.4	3.0	8.4	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.2563	10.8	5.9	16.7	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.3589	16.2	8.9	25.1	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.4546	21.6	11.9	33.5	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.5414	27.0	14.9	41.8	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.6182	32.4	17.8	50.2	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.6851	37.8	20.8	58.6	50	0.5	0.0117	0.0058	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.1059	5.4	3.5	8.9	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.1701	10.8	7.0	17.8	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.2334	16.2	10.5	26.7	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.2956	21.6	14.0	35.6	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.3561	27.0	17.5	44.5	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.4140	32.4	21.0	53.4	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	
0.4691	37.9	24.5	62.3	50	0.6	0.0117	0.0070	Equal	4	24	0.0034	0.0034	0.0025	0.0025	0.05	

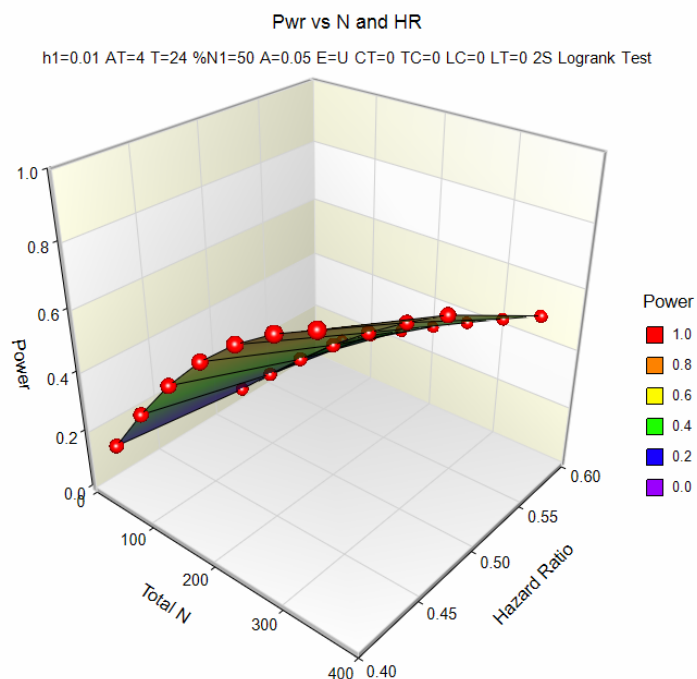
\* The reported proportions are during a single time period.

Note: All calculations were made using 100 intervals per time period.

## Plots



## Logrank Tests with Non-Proportional Hazards (Lakatos and Wu)



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