Chapter 714

One-Sample Logrank Tests Assuming a Weibull Model (Wu)

Introduction

This module computes the sample size and power of the one-sample logrank test which is used to compare the survival curve of a single treatment group to that of a historic control. Such is often the case in clinical phase-II trials with survival endpoints. Accrual time, follow-up time, and hazard rates are parameters that can be set.

Several authors have presented sample size formulas for this situation. We have adopted those of Wu (2015) because his paper included an extensive simulation study that showed that his formulation is the most accurate.

Technical Details

One-Sample Logrank Test Statistic

The following details follow closely the results in Wu (2015).

Suppose N subjects are enrolled in a study during the accrual period of length t_a and then observed during a follow-up period of length t_f. Let t_i and C_i denote the failure time and censoring time of the i^{th} subject. The observed failure time is $X_i = t_i \wedge C_i$ and the observed failure indicator is $\Delta_i = I(t_i \leq C_i)$. The one-sample logrank test L is defined in terms of the number of observed events O and the number of expected events E, as follows.

$$L = \frac{O - E}{\sqrt{E}}$$

where

$$O = \sum_{i=1}^{N} \Delta_i$$

$$E = \sum_{i=1}^{N} \Lambda_0(X_i)$$

Here $\Lambda_0(X_i)$ represents the cumulative hazard function $\Lambda_0(t)$ under the null hypothesis evaluated at X_i. The test statistic L is asymptotically distributed as the standard normal distribution under the null hypothesis.

The cumulative survival function is taken to be the Weibull distribution because of the many different shapes that it can take depending on its shape parameter.

Power Calculation

Wu (2015) gives the following power and sample size formulas for a one-sided hypothesis test based on *L*. Note that we use the subscript 0 to represent the historic control and the subscript 1 to represent the new treatment group.

$$Power \cong \Phi\left(-\frac{\sigma_0}{\sigma} z_{1-\alpha} - \frac{\omega\sqrt{n}}{\sigma}\right)$$

$$n = \frac{(\sigma_0 z_{1-\alpha} + \sigma z_{Power})^2}{\omega^2}$$

where

$$\omega = \sigma_1^2 - \sigma_0^2$$

$$\sigma^2 = p_1 - p_1^2 + 2p_{00} - p_0^2 - 2p_{01} + 2p_0 p_1$$

$$\sigma_0^2 = p_0$$

$$\sigma_1^2 = p_1$$

$$p_0 = \int_0^\infty G(t) S_1(t) \lambda_0(t) dt$$

$$p_1 = \int_0^\infty G(t) S_1(t) \lambda_1(t) dt$$

$$p_{00} = \int_0^\infty G(t) S_1(t) \Lambda_0(t) \lambda_0(t) dt$$

$$p_{01} = \int_0^\infty G(t) S_1(t) \Lambda_0(t) \lambda_1(t) dt$$

Note that p_1 gives the probability that a subject experiences a failure during the study.

Assuming a uniform accrual, the censoring distribution function *G*(*t*) is given by

$$G(t) = \begin{cases} 1 & \text{if } t \le t_f \\ \dfrac{t_a + t_f - t}{t_a} & \text{if } t_f \le t \le t_a + t_f \\ 0 & \text{otherwise} \end{cases}$$

Note that t_a represents the accrual time and t_f represents the follow-up time.

Assuming that failure times follow a two-parameter Weibull distribution, the cumulative survival function $S(t)$ under null and alternative is given by

$$S_0(t) = \exp\left(-\lambda_0 t^k\right)$$

$$S_1(t) = \exp\left(-\lambda_1 t^k\right)$$

The hazard and cumulative hazard functions are given as

$$\lambda_0(t) = k\lambda_0 t^{k-1}$$

$$\lambda_1(t) = k\lambda_1 t^{k-1}$$

$$\Lambda_0(\mathrm{t}) = \lambda_0 t^k$$

The values of the p_0, p_1, p_{00}, and p_{01} can be calculated by numeric integration.

The hazard rates λ_0 and λ_1 can be given in terms of the hazard ratio HR, the median survival times M_0 and M_1, or the survival proportions S_0 and S_1 at time t_0. These parameters are defined as

$$HR = \frac{\lambda_1}{\lambda_0}$$

$$\lambda_0 = \frac{\log 2}{M_0^k} = \frac{-\log S_0(t_0)}{t_0^k} = \theta_0^{-k}$$

$$\lambda_1 = \frac{\log 2}{M_1^k} = \frac{-\log S_1(t_0)}{t_0^k} = \theta_1^{-k}$$

Example 1 – Finding the Sample Size

A researcher is planning a clinical trial to compare the response of a new treatment to that of the current treatment. The median survival time in the current population is 1.54. The current population of responses exhibits a Weibull distribution with a shape parameter of 1.67. The researcher wants a sample size large enough to detect hazard ratios of 0.7 and 0.8 or less at a 5% significance level for a two-sided, one-sample logrank test. The accrual period will be 1 year. The researcher would like to compare the sample requirements if the follow-up period is 1, 2, or 3 years.

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 .... **Sample Size**
Alternative Hypothesis .... **Two-Sided**
Power.. **0.90**
Alpha... **0.05**
Ta (Accrual Time) **1**
Tf (Follow-Up Time) **1 2 3**
Input Type.. **M0, HR (Median Survival, Hazard Ratio)**
M0 (Median Survival - Control) **1.54**
HR (Hazard Ratio - λ1/λ0)............................. **0.7 0.8**
k (Weibull Shape Parameter)......................... **1.67**

Output

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

Numeric Reports

Numeric Results

Solve For: Sample Size
Groups: 0 = Historic Control, 1 = New or Treatment
Alternative Hypothesis: Two-Sided

Power	Sample Size N	Number of Events E	Time: Accrual Ta	Time: Follow-Up Tf	Hazard Ratio HR	Median Survival Time: M0	Median Survival Time: M1	Weibull Shape k	Probability of Event in New Group P1	Alpha
0.9011	208	77	1	1	0.7	1.54	1.91	1.67	0.3706	0.05
0.9004	495	203	1	1	0.8	1.54	1.76	1.67	0.4098	0.05
0.9017	125	82	1	2	0.7	1.54	1.91	1.67	0.6591	0.05
0.9007	300	212	1	2	0.8	1.54	1.76	1.67	0.7066	0.05
0.9014	103	87	1	3	0.7	1.54	1.91	1.67	0.8481	0.05
0.9003	249	220	1	3	0.8	1.54	1.76	1.67	0.8833	0.05

Power The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N The sample size of the new group, assuming no subject lost to dropout or follow-up during the study.
E The expected number of events (failures) in the new group during the study.
Ta The length of the accrual time during which subjects are added to the study. Subjects are added uniformly.
Tf The length of the follow-up time after the last subject is added to the study.
HR The hazard ratio is the new group's hazard rate divided by the hazard rate of the historic control. HR = λ1/λ0.
M0 The median survival time of the historic control group.
M1 The median survival time of the new (treatment) group.
k The shape parameter of the Weibull distribution used for both groups.
P1 The probability that a subject in the new group experiences an event (failure) during the study.
Alpha The probability of rejecting a true null hypothesis.

Summary Statements

A single-group design will be used to test whether a new treatment (Weibull) hazard rate is different from that of a historical control. The comparison will be made using a two-sided, one-sample logrank test, with a Type I error rate (α) of 0.05. It is assumed that the survival time distribution is approximated reasonably well by the Weibull distribution with a shape parameter value of 1.67. The accrual time will be 1 and the follow-up time (time after complete accrual) will be 1. To detect a hazard ratio of 0.7 when the median survival time of the historical control group is 1.54, with 90% power, the number of needed subjects will be 208. The probability that an individual subject experiences an event during the study is 0.3706, and the expected number of events during the study is 77.

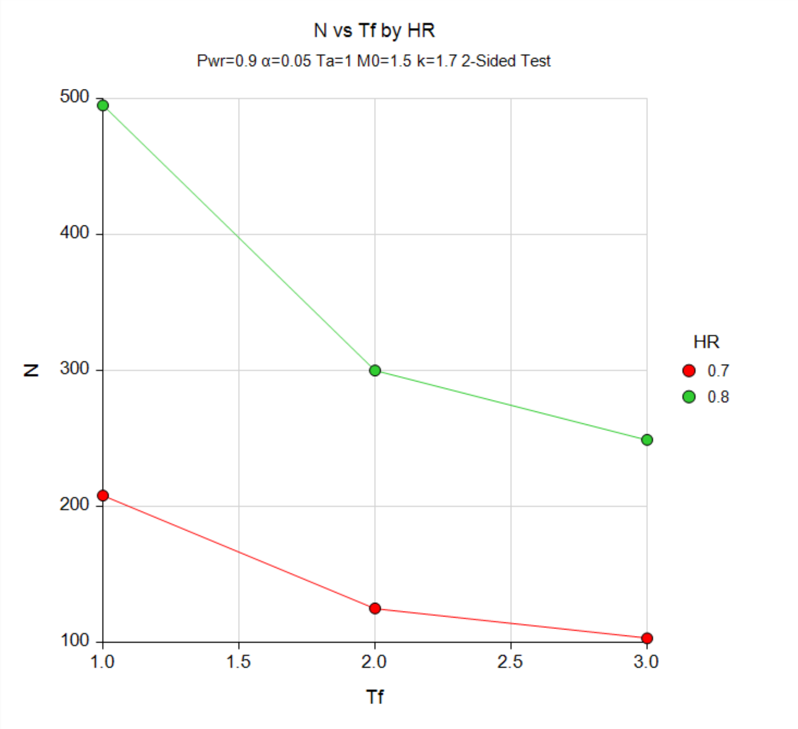
References

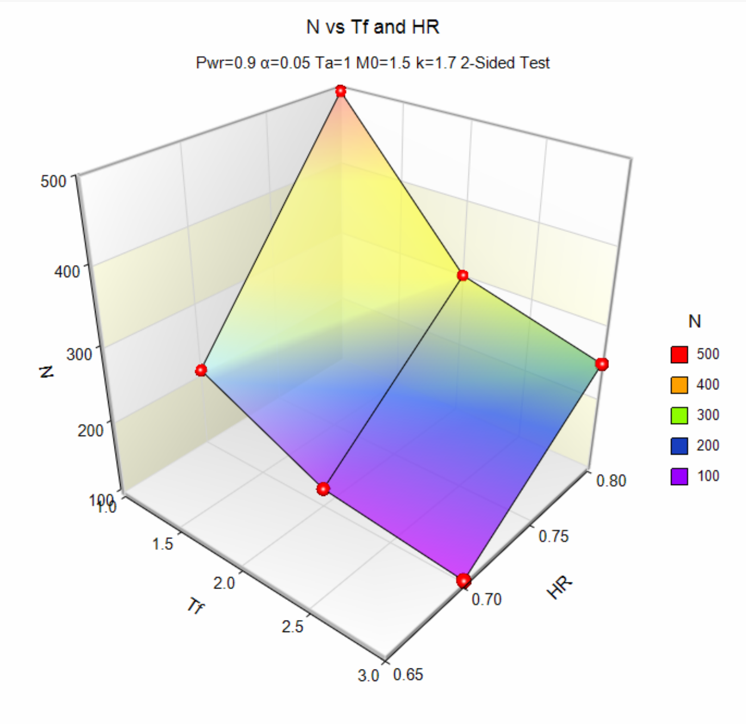
Wu, Jianrong. 2015. 'Sample size calculation for the one-sample log-rank test', Pharmaceutical Statistics, Volume 14, pages 26-33.
Wu, Jianrong. 2014. 'A New One-Sample Log-Rank Test', J Biomet Biostat 5; 210.
Finkelstein D, Muzikansky A, Schoenfeld D. 2003. 'Comparing Survival of a Sample to That of a Standard Population', Journal of the National Cancer Institute, 95, pages 1434-1439.
Sun X, Peng P, Tu D. 2011. 'Phase II cancer clinical trials with a one-sample log-rank test and its corrections based on the Edgeworth expansion', Contemporary Clinical Trials, 32, pages 108-113.
Schmidt R., Kwiecien R, Faldum A, Berthold F, Hero B, Ligges S. 2015. 'Sample size calculation for the one-sample log-rank test', Stat Med, 34(6), pages 1031-40.

This report presents the calculated sample sizes for each scenario as well as the values of the other parameters.

Plots Section

Plots





These plots show the relationship between sample size, follow-up time, and HR.

Example 2 – Validation using Wu (2015)

Wu (2015) gives an example in which the power is 0.80, alpha = 0.05 for a one-sided test, k = 1.22, Ta = 5 and Tf = 3, HR = 0.57143, and M0 = 9. Wu calculates N to be 88.

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 .... **One-Sided**
Power.. **0.80**
Alpha... **0.05**
Ta (Accrual Time) **5**
Tf (Follow-Up Time) **3**
Input Type.. **M0, HR (Median Survival, Hazard Ratio)**
M0 (Median Survival - Control) **9**
HR (Hazard Ratio - λ1/λ0)............................. **0.5714**
k (Weibull Shape Parameter)......................... **1.22**

Output

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

Numeric Results

Solve For: Sample Size
Groups: 0 = Historic Control, 1 = New or Treatment
Alternative Hypothesis: One-Sided

			Time			Median Survival Time				
Power	Sample Size N	Number of Events E	Accrual Ta	Follow-Up Tf	Hazard Ratio HR	M0	M1	Weibull Shape k	Probability of Event in New Group P1	Alpha
0.8032	88	17	5	3	0.571	9	14.24	1.22	0.1949	0.05

PASS has also calculated N as 88.