Chapter 445

Tests for the Ratio of Two Means (Log-Normal Data)

Introduction

This procedure calculates power and sample size for t-tests from a parallel-groups design in which the logarithm of the outcome is a continuous normal random variable. This routine deals with the case in which the statistical hypotheses are expressed in terms of mean ratios instead of mean differences.

The details of testing two treatments using data from a two-group design are given in another chapter, and they will not be repeated here. If the logarithms of the responses can be assumed to follow a normal distribution, hypotheses stated in terms of the ratio can be transformed into hypotheses about the difference. The details of this analysis are given in Julious (2004). They will only be summarized here.

Testing Using Ratios

It will be convenient to adopt the following specialized notation for the discussion of these tests.

Parameter	PASS Input/Output	Interpretation
μ_T	Not used	*Treatment mean*. This is the treatment (group 1) mean.
μ_R	Not used	*Reference mean*. This is the reference (group 2) mean.
ϕ_0	R0	*Null ratio*. This is the value of $\phi = \mu_T/\mu_R$ under the null hypothesis, H_0.
ϕ	R1	*Actual ratio*. This is the value of $\phi = \mu_T/\mu_R$ at which the power is calculated.

Note that the actual values of μ_T and μ_R are not needed. Only the ratio of these values is needed for power and sample size calculations.

In the two-sided case, the null and alternative hypotheses are

$$H_0: \phi = \phi_0 \quad \text{versus} \quad H_1: \phi \neq \phi_0.$$

The one-sided hypotheses are

$$H_0: \phi \leq \phi_0 \quad \text{versus} \quad H_1: \phi > \phi_0$$

and

$$H_0: \phi \geq \phi_0 \quad \text{versus} \quad H_1: \phi < \phi_0.$$

Log-Transformation

In many cases, hypotheses stated in terms of ratios are more convenient than hypotheses stated in terms of differences. This is because ratios can be interpreted as percentages, but differences must be interpreted as actual amounts in their original scale. Hence, it has become a common practice to take the following steps in hypothesis testing.

1. State the statistical hypotheses in terms of the ratio of the means.
2. Transform this into hypotheses about a difference by taking logarithms.
3. Analyze the logged data—that is, do the analysis in terms of the difference.
4. Draw the conclusion in terms of the ratio.

The details of step 2 for the two-sided null hypothesis are as follows:

$$H_0: \phi = \phi_0 \quad \Rightarrow \quad H_0: \frac{\mu_T}{\mu_R} = \phi_0 \quad \Rightarrow \quad H_0: \ln(\mu_T) - \ln(\mu_R) = \ln(\phi_0)$$

Thus, a hypothesis about the ratio of the means on the original scale can be translated into a hypothesis about the difference of two means on the logged scale.

Coefficient of Variation

The coefficient of variation (COV) is the ratio of the standard deviation to the mean. This parameter can be used to represent the variation in the data because of a unique relationship that it has in the case of log-normal data.

Suppose the variable *X* is the logarithm of the original variable *Y*. That is, *X* = ln(*Y*) and *Y* = exp(*X*). Label the mean and variance of *X* as μ_X and σ_X^2, respectively. Similarly, label the mean and variance of *Y* as μ_Y and σ_Y^2, respectively. If *X* is normally distributed, then *Y* is log-normally distributed. Julious (2004) presents the following well-known relationships between these two variables

$$\mu_Y = e^{\mu_X + \frac{\sigma_X^2}{2}}$$

$$\sigma_Y^2 = \mu_Y^2 \left(e^{\sigma_X^2} - 1\right)$$

From this relationship, the coefficient of variation of *Y* can be found to be

$$COV_Y = \frac{\sqrt{\mu_Y^2 \left(e^{\sigma_X^2} - 1\right)}}{\mu_Y}$$

$$= \sqrt{e^{\sigma_X^2} - 1}$$

Solving this relationship for σ_X^2, the standard deviation of *X* can be stated in terms of the coefficient of variation of *Y* as

$$\sigma_X = \sqrt{\ln(COV_Y^2 + 1)}$$

Similarly, the mean of *X* is

$$\mu_X = \ln\left(\frac{\mu_Y}{\sqrt{COV_Y^2 + 1}}\right)$$

Thus, the hypotheses can be stated in the original (Y) scale and then the power can be analyzed in the transformed (X) scale. For parallel-group designs, $\sigma_X^2 = \sigma_d^2$, the average variance used in the t-test of the logged data.

Power Calculation

As is shown above, the hypotheses can be stated in the original (Y) scale using ratios or the logged (X) scale using differences. In either case, the power and sample size calculations are made using the formulas for testing the difference in two means. These formulas are presented in another chapter and are not duplicated here.

Example 1 – Finding Power

A company has developed a generic drug for treating rheumatism and wants to show that it is better than the standard drug. From previous studies, responses for either treatment are known to follow a lognormal distribution. A parallel-group design will be used and the logged data will be analyzed with a one-sided, two-sample t-test.

Past experience leads the researchers to set the COV to 1.20. The significance level is 0.025. The power will be computed for R1 equal 1.10 and 1.20. Sample sizes between 100 and 900 will be examined in the analysis.

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	**One-Sided (H1: R > R0)**
Alpha	**0.025**
Group Allocation	**Equal (N1 = N2)**
Sample Size Per Group	**100 to 900 by 200**
R0 (Ratio | H0)	**1.0**
R1 (Actual Ratio)	**1.1 1.2**
COV (Coefficient of Variation)	**1.2**

Output

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

Numeric Reports

Numeric Results

Solve For: Power
Test Type: Two-Sample T-Test
Groups: 1 = Treatment, 2 = Reference
Ratio: R = μ1 / μ2 = Treatment Mean / Reference Mean
Hypotheses: H0: R1 ≤ R0 vs. H1: R1 > R0

	Sample Size			Ratio		Coefficient	Effect	
				Null	Actual	of Variation	Effect	
Power	N1	N2	N	R0	R1	COV	Size	Alpha
0.10568	100	100	200	1	1.1	1.2	0.101	0.025
0.23392	300	300	600	1	1.1	1.2	0.101	0.025
0.35811	500	500	1000	1	1.1	1.2	0.101	0.025
0.47146	700	700	1400	1	1.1	1.2	0.101	0.025
0.57180	900	900	1800	1	1.1	1.2	0.101	0.025
0.27374	100	100	200	1	1.2	1.2	0.193	0.025
0.65562	300	300	600	1	1.2	1.2	0.193	0.025
0.86253	500	500	1000	1	1.2	1.2	0.193	0.025
0.95061	700	700	1400	1	1.2	1.2	0.193	0.025
0.98359	900	900	1800	1	1.2	1.2	0.193	0.025

Power The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N1 and N2 The number of items sampled from each population.
N The total sample size. N = N1 + N2.
R0 The ratio of the means (μ1/μ2) under the null hypothesis, H0.
R1 The ratio of the means (μ1/μ2) under the alternative hypothesis, H1. This is the ratio at which the power is calculated.
COV The coefficient of variation on the original scale. The value of σ is calculated from this.
Effect Size The effect size = |Ln(R0) - Ln(R1)|/σ.
Alpha The probability of rejecting a true null hypothesis.

Summary Statements

A parallel two-group design will be used to test whether the ratio of means (μ1 / μ2) is greater than 1 (H0: μ1 / μ2 ≤ 1 versus Ha: μ1 / μ2 > 1). The comparison will be made using a one-sided, two-sample t-test using a log-transformation, with a Type I error rate (α) of 0.025. The coefficient of variation on the original scale is assumed to be 1.2. To detect a ratio of means (μ1 / μ2) of 1.1, with a sample size of 100 in Group 1 and 100 in Group 2, the power is 0.10568.

Dropout-Inflated Sample Size

	Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
Dropout Rate	N1	N2	N	N1'	N2'	N'	D1	D2	D
20%	100	100	200	125	125	250	25	25	50
20%	300	300	600	375	375	750	75	75	150
20%	500	500	1000	625	625	1250	125	125	250
20%	700	700	1400	875	875	1750	175	175	350
20%	900	900	1800	1125	1125	2250	225	225	450

Dropout Rate The percentage of subjects (or items) that are expected to be lost at random during the course of the study and for whom no response data will be collected (i.e., will be treated as "missing"). Abbreviated as DR.
N1, N2, and N The evaluable sample sizes at which power is computed (as entered by the user). If N1 and N2 subjects are evaluated out of the N1' and N2' subjects that are enrolled in the study, the design will achieve the stated power.
N1', N2', and N' The number of subjects that should be enrolled in the study in order to obtain N1, N2, and N evaluable subjects, based on the assumed dropout rate. N1' and N2' are calculated by inflating N1 and N2 using the formulas N1' = N1 / (1 - DR) and N2' = N2 / (1 - DR), with N1' and N2' always rounded up. (See Julious, S.A. (2010) pages 52-53, or Chow, S.C., Shao, J., Wang, H., and Lokhnygina, Y. (2018) pages 32-33.)
D1, D2, and D The expected number of dropouts. D1 = N1' - N1, D2 = N2' - N2, and D = D1 + D2.

Dropout Summary Statements

Anticipating a 20% dropout rate, 125 subjects should be enrolled in Group 1, and 125 in Group 2, to obtain final group sample sizes of 100 and 100, respectively.

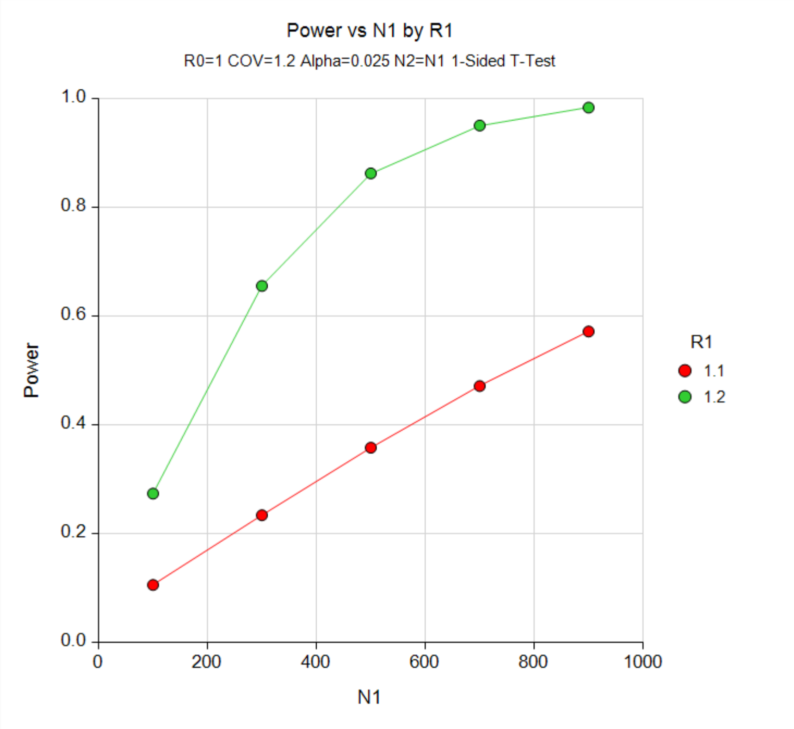
References

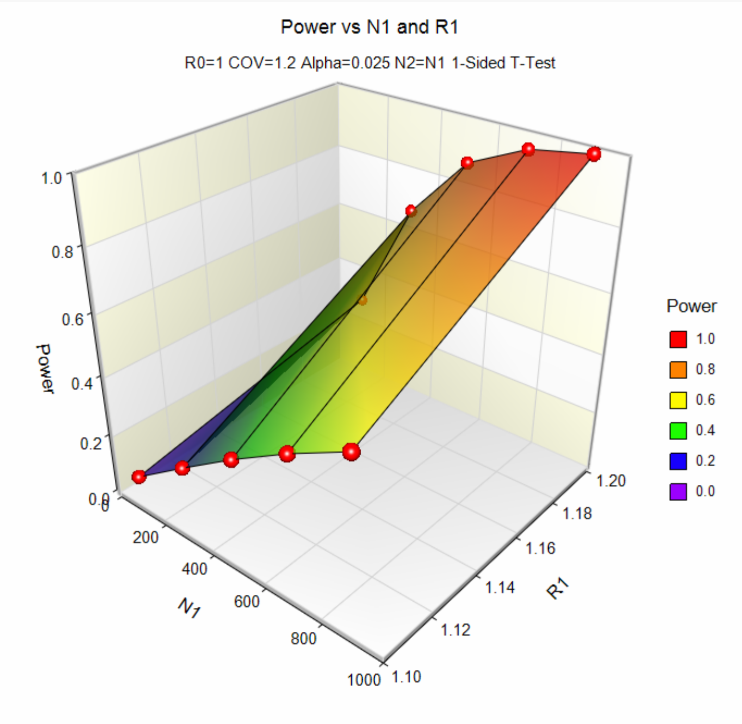
Chow, S.C., Shao, J., Wang, H., and Lokhnygina, Y. 2018. Sample Size Calculations in Clinical Research, Third Edition. Taylor & Francis/CRC. Boca Raton, Florida.
Julious, Steven A. 2004. 'Tutorial in Biostatistics. Sample sizes for clinical trials with Normal data.' Statistics in Medicine, 23:1921-1986.

This report shows the power for the indicated scenarios.

Plots Section

Plots





These plots show the relationship of power to sample size for the two values of R1.

Example 2 – Validation

We will validate this procedure by showing that it gives the identical results to the regular test on differences—a procedure that has been validated. We will use the same settings as those given in Example 1. Since the output for this example is shown above, only the output from the procedure that uses differences (Two-Sample T-Tests Assuming Equal Variance) is shown below.

To run the power analysis of a *t-test* on differences, we need the values of δ and σ.

$$\delta = \ln(R1)$$
$$= \ln(1.1)$$
$$= 0.095310$$

$$\delta = \ln(R1)$$
$$= \ln(1.2)$$
$$= 0.182322$$

$$\sigma = \sqrt{\ln(COV_Y^2 + 1)}$$
$$= \ln(1.2^2 + 1)$$
$$= 0.944456$$

Setup

If the procedure window (Two-Sample T-Tests Assuming Equal Variance) 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 2b** 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	**One-Sided**
Alpha	**0.025**
Group Allocation	**Equal (N1 = N2)**
Sample Size Per Group	**100 to 900 by 200**
Input Type	**Difference**
δ	**0.095310 0.182322**
σ	**0.944456**

Reports Tab

Means, Difference Decimals **6**
Standard Deviation Decimals......................... **4**

Plot Text Tab

Means, Difference Decimals **6**
Standard Deviation Decimals......................... **4**

Output

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

Numeric Results

Solve For: Power
Test Type: Two-Sample Equal-Variance T-Test
Difference: δ = μ1 - μ2
Hypotheses: H0: δ ≤ 0 vs. H1: δ > 0

	Sample Size			Mean Difference	Standard Deviation	
Power	**N1**	**N2**	**N**	**δ**	**σ**	**Alpha**
0.10568	100	100	200	0.095310	0.9445	0.025
0.23392	300	300	600	0.095310	0.9445	0.025
0.35811	500	500	1000	0.095310	0.9445	0.025
0.47145	700	700	1400	0.095310	0.9445	0.025
0.57180	900	900	1800	0.095310	0.9445	0.025
0.27374	100	100	200	0.182322	0.9445	0.025
0.65562	300	300	600	0.182322	0.9445	0.025
0.86253	500	500	1000	0.182322	0.9445	0.025
0.95061	700	700	1400	0.182322	0.9445	0.025
0.98359	900	900	1800	0.182322	0.9445	0.025

You can compare these power values with those shown above in Example 1 to validate the procedure. You will find that the power values are identical.