Chapter 453

Superiority by a Margin Tests for the Ratio of Two Means (Log-Normal Data)

Introduction

This procedure calculates power and sample size for *superiority by a margin* 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 the superiority (or non-unity null) hypothesis of two treatments using data from a two-group design are given in another chapter and they will not be repeated here. If the logarithm of the response can be assumed to follow a normal distribution, non-unity null 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.

Superiority 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 mean.
μ_R	Not used	*Reference mean*. This is the mean of a reference population.
M_S	SM	*Margin of superiority*. This is a tolerance value that defines the magnitude of difference that is required for practical importance. This may be thought of as the smallest difference from the reference that is considered to be practically significant.
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.

When higher means are better, the hypotheses are arranged so that rejecting the null hypothesis implies that the ratio of the treatment mean to the reference mean is greater than one by at least the margin of superiority. The value of ϕ at which power is calculated must be greater than $\phi_0 = 1 + |M_S|$.

$H_0: \phi \leq 1 + |M_S|$ versus $H_1: \phi > 1 + |M_S|$

$H_0: \phi \leq \phi_0$ versus $H_1: \phi > \phi_0$

When higher means are worse, the hypotheses are arranged so that rejecting the null hypothesis implies that the ratio of the treatment mean to the reference mean is less than one by at least the margin of superiority. The value of ϕ at which power is calculated must be less than $\phi_0 = 1 - |M_S|$.

$H_0: \phi \geq 1 - |M_S|$ versus $H_1: \phi < 1 - |M_S|$

$H_0: \phi \geq \phi_0$ versus $H_1: \phi < \phi_0$

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 scale-less 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 ratios.
2. Transform these into hypotheses about differences 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 null hypothesis when higher means are better are as follows:

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

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.

Procedure Options

This section describes the options that are specific to this procedure. These are located on the Design tab. For more information about the options of other tabs, go to the Procedure Window chapter.

Design Tab

The Design tab contains the parameters associated with this test such as the means, sample sizes, alpha, and power.

Solve For

Solve For

This option specifies the parameter to be solved for from the other parameters. In most situations, you will select either *Power* or *Sample Size (N1)*.

Test

Higher Means Are

This option defines whether higher values of the response variable are to be considered better or worse. The choice here determines the direction of the superiority test.

If Higher Means Are Better the null hypothesis is H0: R ≤ 1+SM and the alternative hypothesis is H1: R > 1+SM. If Higher Means Are Worse the null hypothesis is H0: R ≥ 1-SM and the alternative hypothesis is H1: R < 1-SM.

Power and Alpha

Power

This option specifies one or more values for power. Power is the probability of rejecting a false null hypothesis, and is equal to one minus Beta. Beta is the probability of a type-II error, which occurs when a false null hypothesis is not rejected. In this procedure, a type-II error occurs when you fail to reject the null hypothesis of non-superiority when in fact the treatment mean is superior.

Values must be between zero and one. Historically, the value of 0.80 (Beta = 0.20) was used for power. Now, 0.90 (Beta = 0.10) is also commonly used. A single value may be entered here or a range of values such as *0.8 to 0.95 by 0.05* may be entered.

Alpha

This option specifies one or more values for the probability of a type-I error. A type-I error occurs when a true null hypothesis is rejected. In this procedure, a type-I error occurs when rejecting the null hypothesis of non-superiority when in fact the treatment group is not superior to the reference group.

Values must be between zero and one. Historically, the value of 0.05 has been used for alpha. This means that about one test in twenty will falsely reject the null hypothesis. You should pick a value for alpha that represents the risk of a type-I error you are willing to take in your experimental situation.

You may enter a range of values such as *0.01 0.05 0.10* or *0.01 to 0.10 by 0.01*.

Sample Size (When Solving for Sample Size)

Group Allocation

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

The options are

- **Equal (N1 = N2)**

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

- **Enter N2, solve for N1**

  Select this option when you wish to fix *N2* at some value (or values), and then solve only for *N1*. Please note that for some values of *N2*, there may not be a value of *N1* that is large enough to obtain the desired power.

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

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

  $$N2 = R * N1.$$

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

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

N2 (Sample Size, Group 2)

This option is displayed if Group Allocation = "Enter N2, solve for N1"

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

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

R (Group Sample Size Ratio)

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

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

$$R = N2 / N1.$$

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

N2 is related to *N1* by the formula:

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

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

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

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

Percent in Group 1

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

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

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

Sample Size (When Not Solving for Sample Size)

Group Allocation

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

The options are

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

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

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

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

Sample Size Per Group

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

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

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

N1 (Sample Size, Group 1)

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

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

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

N2 (Sample Size, Group 2)

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

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

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

R (Group Sample Size Ratio)

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

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

$$R = N2/N1$$

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

N2 is calculated from *N1* using the formula:

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

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

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

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

Total Sample Size (N)

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

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

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

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

Percent in Group 1

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

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

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

Effect Size – Ratios

SM (Superiority Margin)

This is the magnitude of the margin of superiority. It must be entered as a positive number.

When higher means are better, this value is the distance above one that is required for the mean ratio (Treatment Mean / Reference Mean) to be considered superior. When higher means are worse, this value is the distance below one that is required for the mean ratio (Treatment Mean / Reference Mean) to be considered superior.

R1 (Actual Ratio)

This is the value of the ratio of the two means (Treatment Mean / Reference Mean) at which the power is to be calculated.

When higher means are better, this value should be greater than 1+SM. When higher means are worse, this value should be less than 1-SM.

Effect Size – Coefficient of Variation

COV (Coefficient of Variation)

The coefficient of variation is the ratio of the standard deviation and the mean (SD/Mean). It is used to specify the variability (standard deviation). Note that this COV is defined on the original (not logarithmic) scale. This value must be determined from past experience or from a pilot study.

To be clear, consider the following definition. Suppose data on a response variable Y are collected. This procedure assumes that the values of X = Ln(Y) are analyzed using a two-sample t-test. Thus, there are two sets of means and standard deviations: those of X labelled MX and SX and those of Y labelled MY and SY. The COV entered here is the COV of Y = SY/MY. For log-normal data, the following relationship exists: COV(Y) = SQR(Exp(SX*SX)-1) where SX is the standard deviation of the log-transformed values.

Example 1 – Finding Power

A company has developed a drug for treating rheumatism and wants to show that it is superior to the standard drug by a certain amount. Responses following either treatment are known to follow a log normal distribution. A parallel-group design will be used, and the logged data will be analyzed with a two-sample t-test.

Researchers have decided to set the margin of superiority at 0.20. Past experience leads the researchers to set the COV to 1.50. The significance level is 0.025. The power will be computed assuming that the true ratio is either 1.30 or 1.40. Sample sizes between 100 and 1000 will be included in the analysis.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. You may then make the appropriate entries as listed below, or open **Example 1** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Power**
Higher Means Are	**Better**
Alpha	**0.025**
Group Allocation	**Equal (N1 = N2)**
Sample Size Per Group	**100 to 1000 by 100**
SM (Superiority Margin)	**0.2**
R1 (Actual Ratio)	**1.3 1.4**
COV (Coefficient of Variation)	**1.5**

Annotated Output

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

Numeric Results

Numeric Results for a T-Test
R = Treatment Mean / Reference Mean
Higher Means are Better
Hypotheses: H0: R ≤ 1 + SM vs. H1: R > 1 + SM

Power	N1	N2	N	SM	Bound R0	R1	COV	Alpha
0.07477	100	100	200	0.200	1.200	1.3000	1.500	0.025
0.11039	200	200	400	0.200	1.200	1.3000	1.500	0.025
0.14493	300	300	600	0.200	1.200	1.3000	1.500	0.025
0.17994	400	400	800	0.200	1.200	1.3000	1.500	0.025
0.21389	500	500	1000	0.200	1.200	1.3000	1.500	0.025
0.24762	600	600	1200	0.200	1.200	1.3000	1.500	0.025
0.28099	700	700	1400	0.200	1.200	1.3000	1.500	0.025
0.31390	800	800	1600	0.200	1.200	1.3000	1.500	0.025
0.34624	900	900	1800	0.200	1.200	1.3000	1.500	0.025
0.37791	1000	1000	2000	0.200	1.200	1.3000	1.500	0.025
0.16832	100	100	200	0.200	1.200	1.4000	1.500	0.025
0.29339	200	200	400	0.200	1.200	1.4000	1.500	0.025

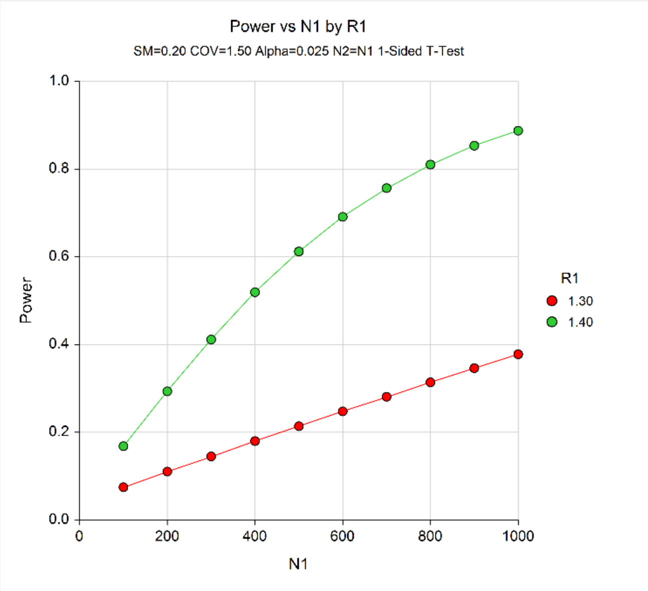
(report continues)

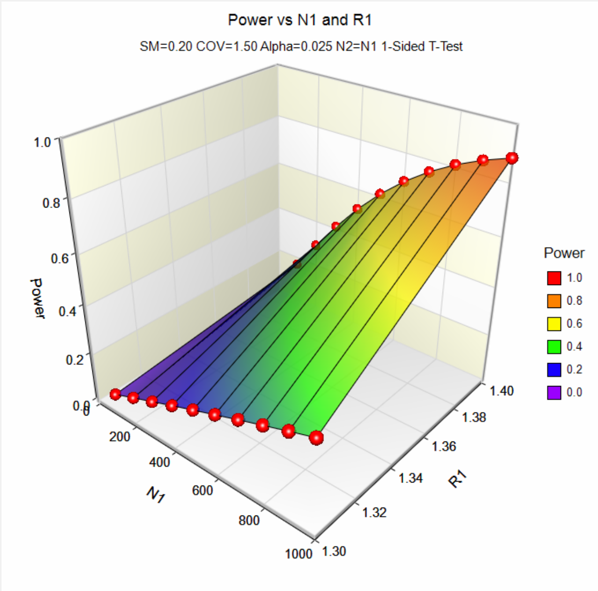
Report Definitions
Power is the probability of rejecting a false null hypothesis.
N1 and N2 are the number of items sampled from each population.
N is the total sample size, N1 + N2.
SM is the magnitude of the margin of superiority. Since higher means are better, this value is positive and is the distance above one that is required to be considered superior. R0 is the corresponding superiority margin bound and equals 1 + SM.
R1 is the mean ratio (treatment/reference) at which the power is computed.
COV is the coefficient of variation on the original scale.
Alpha is the probability of rejecting a true null hypothesis.

Summary Statements
Group sample sizes of 100 in the first group and 100 in the second group achieve 7% power to detect superiority using a one-sided, two-sample t-test. The margin of superiority is 0.200. The true ratio of the means at which the power is evaluated is 1.3000. The significance level (alpha) of the test is 0.025. The coefficients of variation of both groups are assumed to be 1.5..

This report shows the power for the indicated scenarios.

Plots Section





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

Example 2 – Validation using Another Procedure

We could not find a validation example for this procedure in the statistical literature. Therefore, we will show that this procedure gives the same results as the test on differences (Two-Sample T-Tests for Superiority by a Margin Assuming Equal Variance)—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, all that we need is the output from the procedure that uses differences.

To run the superiority test on differences, we need the values of SM, δ, and σ.

$$\begin{aligned} SM &= \ln(1+SM) \\ &= \ln(1.2) \\ &= 0.182322 \end{aligned}$$

$$\begin{aligned} \delta &= \ln(R1) \\ &= \ln(1.3) \\ &= 0.262364 \end{aligned}$$

$$\begin{aligned} \sigma &= \sqrt{\ln(COV_Y^2+1)} \\ &= \ln(1.5^2+1) \\ &= 1.085659 \end{aligned}$$

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Two-Sample T-Tests for Superiority by a Margin Assuming Equal Variance** procedure window. You may then make the appropriate entries as listed below, or open **Example 2b** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Power**
Higher Means Are	**Better (H1: δ > SM)**
Alpha	**0.025**
Group Allocation	**Equal (N1 = N2)**
Sample Size Per Group	**100 to 1000 by 100**
SM (Superiority Margin)	**0.182322**
δ (Actual Difference to Detect)	**0.262364**
σ (Standard Deviation)	**1.085659**

Output

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

Numeric Results

Numeric Results for an Equal-Variance T-Test
δ = μ1 - μ2 = μT - μR
Higher Means are Better
Hypotheses: H0: δ ≤ SM vs. H1: δ > SM

Power	N1	N2	N	SM	δ	σ	Alpha
0.07477	100	100	200	0.182322	0.262364	1.085659	0.025
0.11039	200	200	400	0.182322	0.262364	1.085659	0.025
0.14493	300	300	600	0.182322	0.262364	1.085659	0.025
0.17994	400	400	800	0.182322	0.262364	1.085659	0.025
0.21389	500	500	1000	0.182322	0.262364	1.085659	0.025
0.24761	600	600	1200	0.182322	0.262364	1.085659	0.025
0.28099	700	700	1400	0.182322	0.262364	1.085659	0.025
0.31390	800	800	1600	0.182322	0.262364	1.085659	0.025
0.34624	900	900	1800	0.182322	0.262364	1.085659	0.025
0.37790	1000	1000	2000	0.182322	0.262364	1.085659	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.