Chapter 518

Equivalence Tests for One Mean

Introduction

This procedure allows you to study the power and sample size of tests of equivalence of one mean with a value (e.g. a historical control or gold standard). Schuirmann's (1987) two one-sided tests (TOST) approach is used to test equivalence. The one-sample t-test is commonly used in this situation.

Outline of an Equivalence Test

PASS follows the *two one-sided tests* approach described by Schuirmann (1987) and Phillips (1990). It will be convenient to adopt the following specialize notation for the discussion of these tests.

Parameter	PASS Input/Output	Interpretation
EL, EU	EL, EU	*Lower* and *Upper Equivalence Limits*. If the true population mean of the treatment group is between these two limits, the new mean is said to be *equivalent*.
μ	μ	*True mean*. This is the actual value of μ, the mean of the new group.

The null hypothesis of non-equivalence is

$$H_0: \mu \leq EL \text{ or } \mu \geq EU \text{ where } EL < E.$$

The alternative hypothesis of equivalence is

$$H_0: EL < \mu < EU.$$

Test Statistics

This section describes the test statistic that is used to perform the hypothesis test.

One-Sample T-Test

A one-sample t-test is used to analyze the data. The test assumes that the data are a simple random sample from a population of normally-distributed values that have the same variance. This assumption implies that the observations are continuous and normal. The calculation of the two, one-sided t-tests proceeds as follow

$$t_L = \frac{\bar{x} - E_L}{s_x/\sqrt{N}}$$

$$t_U = \frac{\bar{x} - E_U}{s_x/\sqrt{N}}$$

where s_x is the sample standard deviation of the measurements. The test is usually calculated using a 100 (1 - 2α) % confidence interval of the mean. If the both limits of this confidence interval are between EL and EU, equivalence is concluded.

Power Calculation

The power of this test is

$$\Pr\left(t_L \geq t_{1-\alpha,N-1} \text{ and } t_U \leq t_{\alpha,N-1}\right)$$

where t_L and t_U are distributed as the bivariate, noncentral *t* distribution with noncentrality parameters Δ_L and Δ_U given by

$$\Delta_L = \frac{\mu - E_L}{\sigma\sqrt{1/N}}$$

$$\Delta_U = \frac{\mu - E_U}{\sigma\sqrt{1/N}}$$

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. Under most situations, you will select either *Power* for a power analysis or *Sample Size* for sample size determination.

Select *Sample Size* when you want to calculate the sample size needed to achieve a given power and alpha level.

Select *Power* when you want to calculate the power of an experiment that has already been run.

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. 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. 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

N (Sample Size)

This option specifies one or more values of the sample size, the number of individuals in the study (total subjects). This value must be an integer greater than one.

You may enter a list of values using the syntax *50,100,150,200,250* or *50 to 250 by 50*.

Effect Size – Equivalence Limits

EU (Upper Equivalence Limit)

Enter the upper limit on equivalence. Mean differences outside EL and EU are not considered equivalent. Differences between them are considered equivalent.

Note that you must have EL < μ < EU.

EL (Lower Equivalence Limit)

Enter the lower limit on equivalence. Differences outside EL and EU are not considered equivalent. Differences between them are.

If you want symmetric limits about zero, enter -UPPER LIMIT for EL to force EL = -|EU|. Of course, μ must be close to zero.

Note that you must have EL < μ < EU. Finally, the scale of these numbers must match the scale of σ.

Effect Size – True Mean

μ (True Mean)

This is the mean at which the power is to be computed. Often this value is set to zero, but it can be non-zero as long as it is between the equivalence limits EL and EU.

Effect Size – Standard Deviation

σ (Std Dev)

Enter one or more values for the standard deviation σ of the data values. You can press the σ button to load the Standard Deviation Estimator window.

Example 1 – Finding Power

A one-group design is to be used to compare the impact on diastolic blood pressure of a new drug with the known standard drug. The average diastolic blood pressure after administration of the reference drug is 96 mmHg. Researchers believe this average may drop to 92 mmHg with the use of a new drug. An estimate of σ is 25.

Following FDA guidelines, the researchers want to show that the diastolic blood pressure with the new drug is within 20% of the diastolic blood pressure with the standard drug. Thus, the equivalence limits of the mean difference of the two drugs are 96 - 19.2 = 76.8 and 96 + 19.2 = 115.2. They decide to calculate the power for a range of sample sizes between 5 and 50. The significance level is 0.05.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Equivalence Tests for One Mean** procedure window by expanding **Means**, then **One Mean**, selecting **Equivalence**, and then clicking on **Equivalence Tests for One Mean**. 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**
Alpha	**0.05**
N (Sample Size)	**5 10 15 20 30 40 50**
EU (Upper Equivalence Limit)	**115.2**
EL (Lower Equivalence Limit)	**76.8**
μ (True Mean)	**92**
σ (Standard Deviation)	**25**

Annotated Output

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

Numeric Results

Numeric Results of an Equivalence Test for One Mean

Power	Sample Size N	Lower Equiv Limit EL	Upper Equiv Limit EU	True Mean μ	Standard Deviation σ	Alpha
0.1133	5	76.800	115.200	92.000	25.000	0.050
0.4178	10	76.800	115.200	92.000	25.000	0.050
0.6852	15	76.800	115.200	92.000	25.000	0.050
0.8260	20	76.800	115.200	92.000	25.000	0.050
0.9454	30	76.800	115.200	92.000	25.000	0.050
0.9835	40	76.800	115.200	92.000	25.000	0.050
0.9953	50	76.800	115.200	92.000	25.000	0.050

References

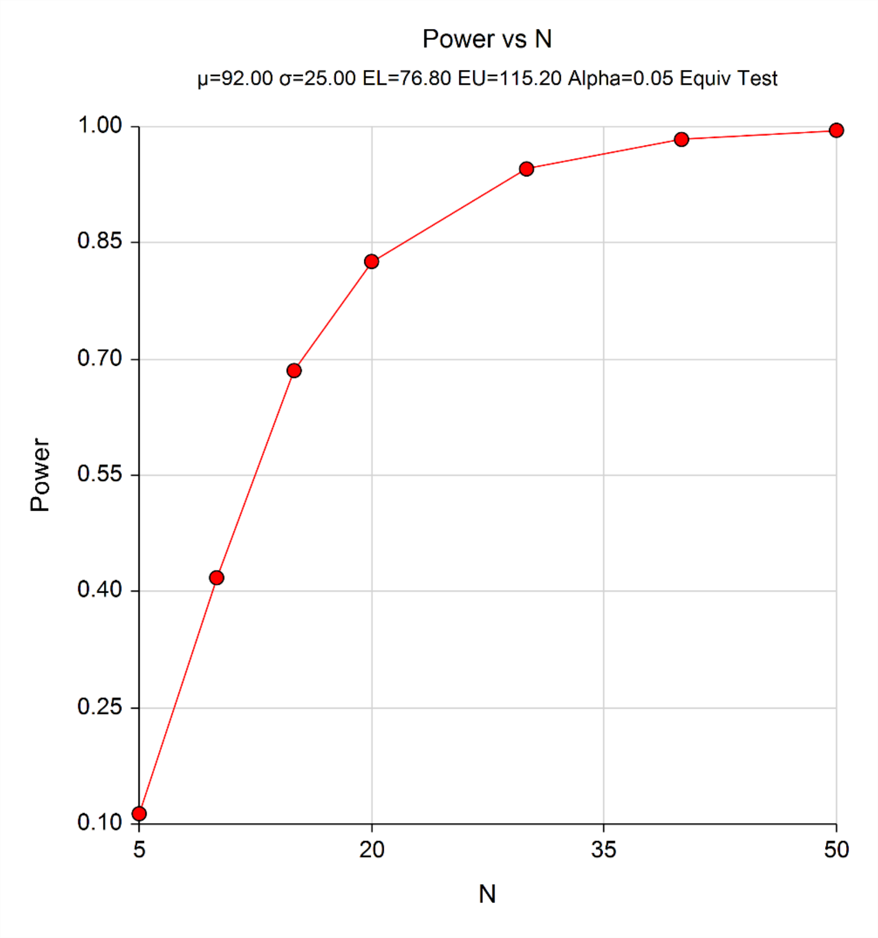
Chow, S.C.; Shao, J.; Wang, H. 2008. Sample Size Calculations in Clinical Research, 2nd Edition. Chapman & Hall/CRC. Boca Raton, FL.
Mathews, Paul. 2010. Sample Size Calculations - Practical Methods for Engineers and Scientists. Mathews Malnar and Bailey. Fairport Harbor, OH.
Blackwelder, W.C. 1998. 'Equivalence Trials.' In Encyclopedia of Biostatistics, John Wiley and Sons. New York. Volume 2, 1367-1372.

Report Definitions
Power is the probability of rejecting non-equivalence when equivalence is true.
N is the number of subjects.
EL is the minimum allowable mean that still results in equivalence.
EU is the maximum allowable mean that still result in equivalence.
μ is the true value of the mean under the alternative hypothesis.
σ is the standard deviation of the individual subject data values.
Alpha is the probability of rejecting non-equivalence when non-equivalence is true.

Summary Statements
In an equivalence test of one mean using two one-sided tests, a sample size of 5 achieves 11% power at a 5% significance level when the true mean is 92.000, the standard deviation is 25.000, and the equivalence limits are 76.800 and 115.200.

This report shows the power for the indicated scenarios. Note that if they want 90% power, they will require a sample of around 30 subjects.

Plots Section



This plot shows the power versus the sample size.

Example 2 – Validation using Phillips (1990)

Phillips (1990) page 142 presents a table of sample sizes for various parameter values. In this table, the treatment mean, standard deviation, and equivalence limits are all specified as percentages of the reference mean. We will reproduce the second line of the table in which the square root of the within mean square error is 20% (σ of 28.284%); the equivalence limits are 80% and 120%; the treatment mean is 100%, 95%, 90%, and 85%; the power is 70%; and the significance level is 0.05.

Phillips reports total sample size as 16, 20, 40, and 152 corresponding to the four treatment mean percentages. We will now setup this example in **PASS**.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Equivalence Tests for One Mean** procedure window by expanding **Means**, then **One Mean**, selecting **Equivalence**, and then clicking on **Equivalence Tests for One Mean**. You may then make the appropriate entries as listed below, or open **Example 2** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Sample Size**
Power	**0.70**
Alpha	**0.05**
EU (Upper Equivalence Limit)	**120**
EL (Lower Equivalence Limit)	**80**
μ (True Mean)	**85 90 95 100**
σ (Standard Deviation)	**28.284**

Output

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

Numeric Results

Numeric Results of an Equivalence Test for One Mean

Power	Sample Size N	Lower Equiv Limit EL	Upper Equiv Limit EU	True Mean μ	Standard Deviation σ	Alpha
0.7002	152	80.000	120.000	85.000	28.284	0.050
0.7096	40	80.000	120.000	90.000	28.284	0.050
0.7240	20	80.000	120.000	95.000	28.284	0.050
0.7075	16	80.000	120.000	100.000	28.284	0.050

Note that **PASS** obtains the same samples sizes as Phillips (1990).