Chapter 198

Two-Sample T-Test for Non-Inferiority

Introduction

This procedure provides reports for making inference about the non-inferiority of a treatment mean compared to a control mean from data taken from independent groups. The question of interest is whether the treatment mean is better than or, at least, no worse than the control mean. Another way of saying this is that if the treatment mean is actually worse than the control mean, it is only worse by a small, acceptable value called the *margin*.

Three different test statistics may be used: two-sample t-test, the Aspin-Welch unequal-variance t-test, and the nonparametric Mann-Whitney U (or Wilcoxon Rank-Sum) test.

Technical Details

Suppose you want to evaluate the non-inferiority of a continuous random variable X_T as compared to a second random variable X_C using data on each variable taken on the different subjects. Assume that n_T observations (X_{Tk}), k = 1, 2, …, n_T are available from the treatment group and that n_C observations (X_{Ck}), k = 1, 2, …, n_C are available from the control group.

Non-Inferiority Test

This discussion is based on the book by Rothmann, Wiens, and Chan (2012) which discusses the two-independent sample case. Assume that higher values are better, that μ_T and μ_C represent the means of the two variables, and that M is the positive *non-inferiority margin.* The null and alternative hypotheses when the **higher values are better** are

$$\text{H0}: (\mu_T - \mu_C) \leq -M$$
$$\text{H1}: (\mu_T - \mu_C) > -M$$

or

$$\text{H0}: \mu_T \leq \mu_C - M$$
$$\text{H1}: \mu_T > \mu_C - M$$

If, on the other hand, we assume that **higher values are worse**, then null and alternative hypotheses are

$$\text{H0}: (\mu_T - \mu_C) \geq M$$
$$\text{H1}: (\mu_T - \mu_C) < M$$

or

$$H0: \mu_T \geq \mu_C + M$$
$$H1: \mu_T < \mu_C + M$$

The two-sample t-test is usually employed to test that the mean difference is zero. The non-inferiority test is a one-sided two-sample t-test that compares the difference to a non-zero quantity, *M*. One-sided editions of the Aspin-Welch unequal-variance t-test, and the Mann-Whitney U (or Wilcoxon Rank-Sum) nonparametric test are also optionally available.

Data Structure

The data may be entered in two formats, as shown in the two examples below. The examples give the yield of corn for two types of fertilizer. The first format, shown in the first table, is the case in which the responses for each group are entered in separate columns. That is, each variable contains all responses for a single group. In the second format the data are arranged so that all responses are entered in a single column. A second column, referred to as the *grouping variable,* contains an index that gives the group (A or B) to which the row of data belongs.

In most cases, the second format is more flexible. Unless there is some special reason to use the first format, we recommend that you use the second.

Two Response Variables

Yield A	Yield B
452	546
874	547
554	774
447	465
356	459
754	665
558	467
574	365
664	589
682	534
547	456
435	651
245	654
	665
	546
	537

Grouping and Response Variables

Fertilizer	Yield
A	452
A	874
A	554
A	447
A	356
.	.
.	.
.	.
B	546
B	547
B	774
B	465
B	459
.	.
.	.
.	.

Example 1 – Non-Inferiority Test for Two Independent Samples

This section presents an example of how to test non-inferiority. Suppose the current (control) fertilizer has an undesirable impact on the ground water so a replacement (treatment) fertilizer has been developed that does not have this negative impact. The researchers of the new fertilizer want to show that the new fertilizer is not less than a small margin below the current fertilizer. Further suppose that the average corn yield of the current fertilizer is about 550. The researchers want to show that the yield of the new fertilizer is not less than 20% below the current type. That is, the non-inferiority margin is 20% of 550 which is 110.

Setup

To run this example, complete the following steps:

1 Open the Corn Yield example dataset

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Select **Corn Yield** and click **OK**.

2 Specify the Two-Sample T-Test for Non-Inferiority procedure options

- Find and open the **Two-Sample T-Test for Non-Inferiority** procedure using the menus or the Procedure Navigator.
- The settings 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.

Variables Tab

Data Input Type .... **Two Variables with Response Data in each Variable**
Treatment Variable .... **YldA**
Control Variable .... **YldB**
Higher Values Are... **Better**
Non-Inferiority Margin **110**

Report Options (*in the Toolbar*)

Variable Labels .... **Column Names**

3 Run the procedure

- Click the **Run** button to perform the calculations and generate the output.

Descriptive Statistics and Confidence Intervals for the Group Means (μ's)

Descriptive Statistics and Confidence Intervals for the Group Means (μ's)

						95% Confidence Interval Limits for the Mean (μ)	
Variable	N	Mean	Standard Deviation of the Data	Standard Error of the Mean	T*	Lower	Upper
YldA	13	549.3846	168.7629	46.80641	2.1788	447.4022	651.367
YldB	16	557.5	104.6219	26.15546	2.1314	501.7509	613.249

This report provides basic descriptive statistics and confidence intervals for the two variables.

Variable

These are the names of the variables or groups.

N

This gives the number of non-missing values. This value is often referred to as the group sample size or count.

Mean

This is the average for each group.

Standard Deviation of the Data

The sample standard deviation is the square root of the sample variance. It is a measure of spread.

Standard Error of the Mean

This is the estimated standard deviation for the distribution of sample means for an infinite population. It is the sample standard deviation divided by the square root of sample size.

T*

This is the t-value used to construct the confidence interval. If you were constructing the interval manually, you would obtain this value from a table of the Student's t distribution with *n* - 1 degrees of freedom.

95% Confidence Interval Limits for the Mean (μ) (Lower and Upper)

These are the lower and upper limits of an interval estimate of the mean based on a Student's t distribution with *n* - 1 degrees of freedom. This interval estimate assumes that the population standard deviation is not known and that the data are normally distributed.

Descriptive Statistics and Confidence Intervals for the Mean Difference (μ1 - μ2)

Descriptive Statistics and Confidence Intervals for the Mean Difference (μ1 - μ2)

Variance Assumption	DF	Mean Difference	Standard Error	T*	95% Confidence Interval Limits for the Mean Difference (μ1 - μ2) Lower	Upper
Equal	27	-8.115385	51.11428	2.0518	-112.9932	96.76247
Unequal	19.17	-8.115385	53.61855	2.0918	-120.2734	104.0426

Given that the assumptions of independent samples and normality are valid, this section provides an interval estimate (confidence limits) of the difference between the two means. Results are given for both the equal and unequal variance cases.

DF

The degrees of freedom are used to determine the T distribution from which T* is generated.

For the equal variance case:

$$df = n_T + n_C - 2$$

For the unequal variance case:

$$df = \frac{\left(\frac{s_T^2}{n_T} + \frac{s_C^2}{n_C}\right)^2}{\frac{\left(\frac{s_T^2}{n_T}\right)^2}{n_T - 1} + \frac{\left(\frac{s_C^2}{n_C}\right)^2}{n_C - 1}}$$

Mean Difference

This is the difference between the sample means, $\overline{X}_T - \overline{X}_C$.

Standard Error

This is the estimated standard deviation of the distribution of differences between independent sample means.

For the equal variance case:

$$SE_{\overline{X}_T - \overline{X}_C} = \sqrt{\left(\frac{(n_T - 1)s_T^2 + (n_C - 1)s_C^2}{n_T + n_C - 2}\right)\left(\frac{1}{n_T} + \frac{1}{n_C}\right)}$$

For the unequal variance case:

$$SE_{\overline{X}_T-\overline{X}_C} = \sqrt{\frac{s_T^2}{n_T} + \frac{s_C^2}{n_C}}$$

T*

This is the t-value used to construct the confidence limits. It is based on the degrees of freedom and the confidence level.

95% Confidence Interval Limits for the Mean Difference (Lower and Upper)

These are the confidence limits of the confidence interval for $\mu_T - \mu_C$. The confidence interval formula is

$$\overline{X}_T - \overline{X}_C \pm T_{df}^* SE_{\overline{X}_T-\overline{X}_C}$$

The equal-variance and unequal-variance assumption formulas differ by the values of T* and the standard error.

Descriptive Statistics and Confidence Intervals for the Group Medians

Descriptive Statistics and Confidence Intervals for the Group Medians

			95% Confidence Interval Limits for the Median	
Variable	**N**	**Median**	**Lower**	**Upper**
YldA	13	554	435	682
YldB	16	546	465	651

This report provides the medians and corresponding confidence intervals for the medians of each group.

Variable

These are the names of the variables or groups.

N

This gives the number of non-missing values. This value is often referred to as the group sample size or count.

Median

The median is the 50th percentile of the group data, using the AveXp(n+1) method. The details of this method are described in the Descriptive Statistics chapter under Percentile Type.

95% Confidence Interval Limits for the Median (Lower and Upper)

These are the lower and upper confidence limits for the median. These limits are exact and make no distributional assumptions other than a continuous distribution. No limits are reported if the algorithm for this interval is not able to find a solution. This may occur if the number of unique values is small.

Equal-Variance T-Test for Non-Inferiority

Equal-Variance T-Test for Non-Inferiority

Higher Values Are:	Better
Null Hypothesis (H0):	(YldA) ≤ (YldB) - 110
Non-Inferiority Hypothesis (H1):	(YldA) > (YldB) - 110

Alternative Hypothesis	Mean Difference	Standard Error	T-Statistic	DF	P-Value	Reject H0 and Conclude Non-Inferiority at α = 0.05?
μT > μC - 110	-8.115385	51.11428	1.9933	27	0.02821	Yes

This report shows the non-inferiority test for the equal-variance assumption. Since the Prob Level is less than the designated value of alpha (0.05), the null hypothesis of inferiority is rejected and the alternative hypothesis of non-inferiority is concluded.

Aspin-Welch Unequal-Variance T-Test for Non-Inferiority

Aspin-Welch Unequal-Variance T-Test for Non-Inferiority

Higher Values Are:	Better
Null Hypothesis (H0):	(YldA) ≤ (YldB) - 110
Non-Inferiority Hypothesis (H1):	(YldA) > (YldB) - 110

Alternative Hypothesis	Mean Difference	Standard Error	T-Statistic	DF	P-Value	Reject H0 and Conclude Non-Inferiority at α = 0.05?
μT > μC - 110	-8.115385	53.61855	1.9002	19.17	0.03628	Yes

This report shows the non-inferiority test for the unequal-variance assumption. Since the Prob Level is again less than the designated value of alpha (0.05), the null hypothesis of inferiority is rejected, and the alternative hypothesis of non-inferiority is concluded.

Mann-Whitney U or Wilcoxon Rank-Sum Location Difference Test for Non-Inferiority

Mann-Whitney U or Wilcoxon Rank-Sum Location Difference Test for Non-Inferiority

Higher Values Are:	Better
Null Hypothesis (H0):	(YldA) ≤ (YldB) - 110
Non-Inferiority Hypothesis (H1):	(YldA) > (YldB) - 110

Variable Details

Variable	Mann-Whitney U	Sum of Ranks (W)	Mean of W	Standard Deviation of W
YldA	150.5	241.5	195	22.79508
YldB	57.5	193.5	240	22.79508

Number of Sets of Ties = 3, Multiplicity Factor = 18

Test Results

Test Type	Alternative Hypothesis†	Z-Value	P-Value	Reject H0 and Conclude Non-Inferiority at α = 0.05?
Exact*	LocT > LocC - 110			
Normal Approximation	LocT > LocC - 110	2.0399	0.02068	Yes
Normal Approx. with C.C.	LocT > LocC - 110	2.0180	0.02180	Yes

† "LocT" and "LocC" refer to the location parameters of the treatment and control distributions, respectively.
* The Exact Test is provided only when there are no ties and the sample size is ≤ 20 in both groups.

This report shows the non-inferiority test based on the Mann-Whitney U statistic. This test is documented in the Two-Sample T-Test chapter.

Tests of Assumptions

Tests of the Normality Assumption for YldA

Normality Test	Test Statistic	P-Value	Reject the Assumption of Normality at α = 0.05?
Shapiro-Wilk	0.9843	0.99420	No
Skewness	0.2691	0.78785	No
Kurtosis	0.3081	0.75803	No
Omnibus (Skewness or Kurtosis)	0.1673	0.91974	No

Tests of the Normality Assumption for YldB

Normality Test	Test Statistic	P-Value	Reject the Assumption of Normality at α = 0.05?
Shapiro-Wilk	0.9593	0.64856	No
Skewness	0.4587	0.64644	No
Kurtosis	0.1291	0.89726	No
Omnibus (Skewness or Kurtosis)	0.2271	0.89267	No

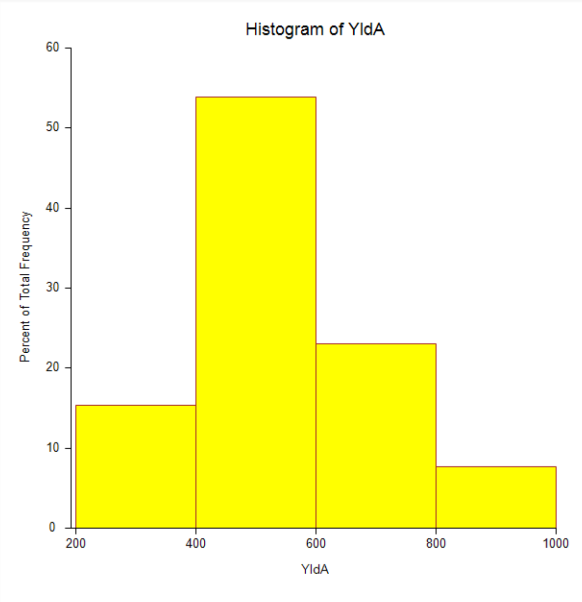
Tests of the Equal-Variance Assumption

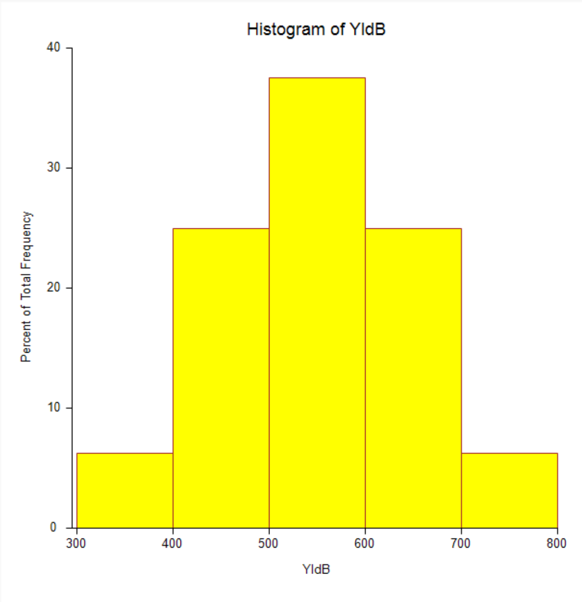
Equal-Variance Test	Test Statistic	P-Value	Reject the Assumption of Equal Variances at α = 0.05?
Variance-Ratio	2.6020	0.08315	No
Modified-Levene	1.9940	0.16935	No

This section reports the results of diagnostic tests to determine if the data are normal and the variances are close to being equal. The details of these tests are given in the Descriptive Statistics chapter.

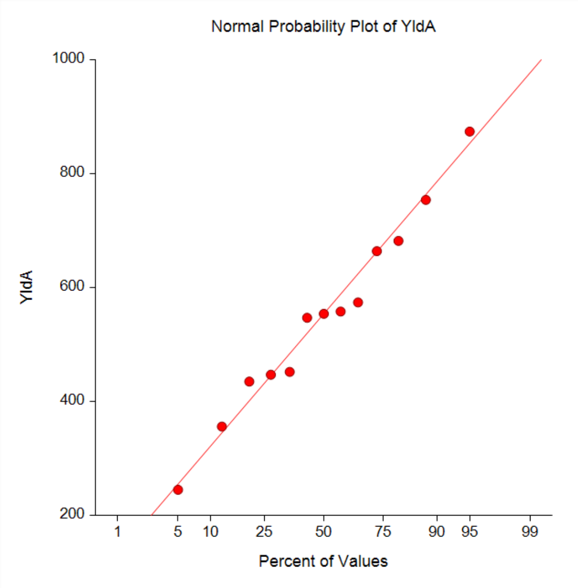
Evaluation of Assumptions Plots

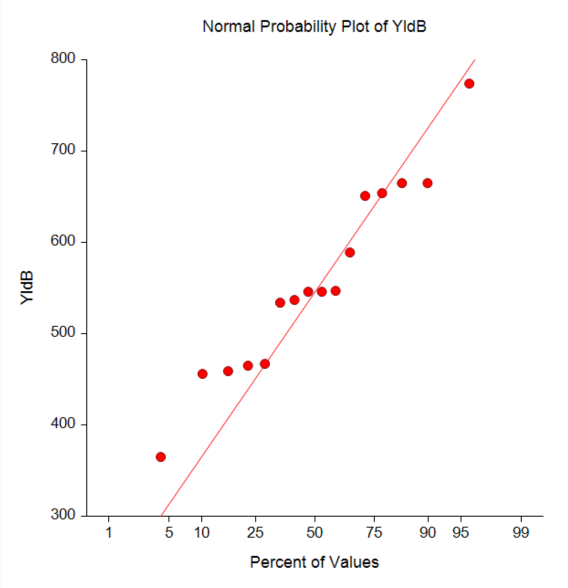
Histograms



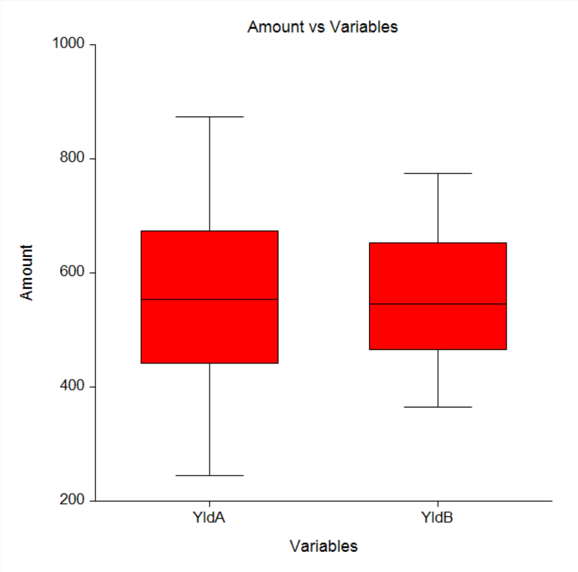


Probability Plots





Box Plots



These plots let you visually evaluate the assumptions of normality and equal variance. The probability plots also let you see if outliers are present in the data.