Chapter 511

One Proportion – Non-Inferiority Tests

Introduction

This procedure computes confidence limits and non-inferiority hypothesis tests for a single proportion. For example, you might want confidence limits for the proportion of individuals with the common cold who took ascorbic acid (vitamin C) and recovered within twenty-four hours. You might want to test the non-inferiority hypothesis that at least 50% of individuals with the common cold recovered immediately after taking a new treatment when compared to a standard proportion of 55%.

Exact results, based on the binomial distribution, are calculated. Approximate results based on the normal approximation to the binomial distribution are also given. In the case of a single proportion, the exact results are preferable to the approximate results and should always be used. The approximate results are available in the software because they are commonly presented in elementary statistical texts.

This procedure accepts data entered as summary counts (number of “successes” and sample size) but can also tabulate data from columns in the database.

The Binomial Model

Binomial data must exhibit the following four conditions:

1. The response can take on only one of two possible values. This is a binary response variable.
2. The response is observed a known number of times. Each replication is called a Bernoulli trial. The number of replications is labeled \( n \). The number of responses out of the \( n \) total that exhibit the outcome of interest is labeled \( X \). Thus, \( X \) takes on the possible values 0, 1, 2, ..., \( n \).
3. The probability that a particular outcome (a success) occurs is constant for each trial. This probability is labeled \( P \).
4. The trials are independent. The outcome of one trial does not influence the outcome of the any other trial.

The binomial probability, \( b(X; n, P) \), is calculated using:

\[
b(X; n, P) = \binom{n}{X} P^X (1 - P)^{n-X}
\]

where

\[
\binom{n}{X} = \frac{n!}{X! (n-X)!}
\]
The estimate of \( P \) from a sample is labeled \( p \) and is estimated using:

\[ p = \frac{X}{n} \]

The label \( \hat{p} \) is often used in place of \( p \) in practice.

## Confidence Limits

Using a mathematical relationship (see Ostle(1988), page 110) between the \( F \) distribution and the cumulative binomial distribution, the lower and upper confidence limits of a 100(1 – \( \alpha \))% confidence interval are given by:

\[
LCL = \frac{XF_{[\alpha/2],[2X,2(n-X+1)]}}{(n-X) + XF_{[\alpha/2],[2X,2(n-X+1)]}}
\]

\[
UCL = \frac{(X+1)F_{[1-\alpha/2],[2(X+1),2(n-X)]}}{(n-X) + (X+1)F_{[1-\alpha/2],[2(X+1),2(n-X)]}}
\]

Note that although these limits are based on direct calculation of the binomial distribution, they are only “exact” for a few values of alpha. Otherwise, these limits are conservative (wider than necessary). These limits may be approximated using the normal approximation to the binomial as

\[
CI = p \pm z_{\alpha/2} \sqrt{\frac{p(1-p)}{n}}
\]

If a correction for continuity is added, the above formula becomes

\[
CI_{cc} = p \pm \left( z_{\alpha/2} \sqrt{\frac{p(1-p)}{n}} + \frac{1}{2n} \right)
\]

Although these two approximate confidence intervals are found in many elementary statistics books, they are not recommended in general. For example, Newcombe (1998) made a comparative study of seven confidence interval techniques and these methods came in last. Instead, Newcombe (1998) recommended the Wilson Score confidence interval method because of its performance. The Wilson Score confidence interval is calculated using

\[
CI_{\text{Wilson Score}} = \frac{(2np + z_{\alpha/2}^2) \pm z_{\alpha/2} \sqrt{z_{\alpha/2}^2 + 4np(1-p)}}{2(n + z_{\alpha/2}^2)}
\]
Non-Inferiority Hypothesis Tests

Assume that **lower proportions are worse**, \( P \) represents the population proportion of the response, \( S \) is a standard reference proportion, and that \( M \) is the positive non-inferiority margin. The null and alternative hypotheses are

\[
H_0 : P \leq S - M \\
H_1 : P > S - M
\]

If, on the other hand, we assume that **lower proportions are better**, then null and alternative hypotheses are

\[
H_0 : P \geq S + M \\
H_1 : P < S + M
\]

The non-inferiority test compares the proportion to a non-zero quantity \( S - M \) or \( S + M \). This test can also be computed using the One Proportion procedure.

The exact \( p \)-values for each of these situations may be computed as follows:

1. \( P(|\bar{p} - P_0| \geq |p - P_0|) \), where \( \bar{p} \) represents all possible values of \( p \). This probability is calculated using the binomial distribution.
2. \( \sum_{r=0}^{X} b(r; n, p) \)
3. \( \sum_{r=X}^{n} b(r; n, p) \)

The simple large-sample \( z \)-test is based on the test statistic

\[
z = \frac{p - P_0}{\sqrt{P_0(1 - P_0)/n}}
\]

Two approximations to the exact \( p \)-values are also available. One uses \( P_0 \) and the other uses \( p \) in the calculation of the standard error. The first approximation uses \( P_0 \) in the calculation of the standard error:

\[
z_c = \frac{X + 0.5 - nP_0}{\sqrt{nP_0(1 - P_0)}}
\]

if \( X < nP_0 \), or

\[
z_c = \frac{X - 0.5 - nP_0}{\sqrt{nP_0(1 - P_0)}}
\]

if \( X > nP_0 \).
The second approximation uses $p$ in the calculation of the standard error:

$$z_c = \frac{X + 0.5 - nP_0}{\sqrt{np(1-p)}}$$

if $X < nP_0$, or

$$z_c = \frac{X - 0.5 - nP_0}{\sqrt{np(1-p)}}$$

if $X > nP_0$.

These $z$-values are used to calculate probabilities using the standard normal probability distribution.

**Data Structure**

The procedure accepts data entered as summary counts (number of “successes” ($X$) and sample size ($n$)), but can also tabulate data from columns in the database. A separate report is generated for each outcome variable entered.
Example 1 – Non-Inferiority Test of One Proportion using Summary Data

This section presents an example of how to run a non-inferiority test of summary data in which \( n \) is 100, \( X \) is 55, the standard proportion, \( S \), is 0.50, and the non-inferiority margin, \( M \), is set to 0.10.

Setup

To run this example, complete the following steps:

1. **Specify the One Proportion – Non-Inferiority Tests procedure options**
   - Find and open the One Proportion – Non-Inferiority Tests 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.

<table>
<thead>
<tr>
<th>Data Tab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Data Input</td>
</tr>
<tr>
<td>Enter the Number of &quot;Successes&quot; (X) and the Sample Size (n)</td>
</tr>
<tr>
<td>Number of &quot;Successes&quot; (X)</td>
</tr>
<tr>
<td>Sample Size (n)</td>
</tr>
<tr>
<td>Lower Proportions Are</td>
</tr>
<tr>
<td>Standard Proportion</td>
</tr>
<tr>
<td>Non-Inferiority Margin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reports Tab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exact (Binomial)</td>
</tr>
<tr>
<td>Simple Z</td>
</tr>
<tr>
<td>Simple Z with Continuity Correction</td>
</tr>
<tr>
<td>Wilson Score</td>
</tr>
<tr>
<td>Exact (Binomial) Test</td>
</tr>
<tr>
<td>Simple Z-Test</td>
</tr>
<tr>
<td>Z Approximation Test using P0</td>
</tr>
<tr>
<td>Z Approximation Test using p</td>
</tr>
</tbody>
</table>

2. **Run the procedure**
   - Click the Run button to perform the calculations and generate the output.
Data Report

This report documents the values that were entered.

Confidence Limits Section

**Exact Confidence Interval of P**

<table>
<thead>
<tr>
<th>Number of &quot;Successes&quot; (X)</th>
<th>Sample Size (n)</th>
<th>Sample Proportion (p)</th>
<th>Z*</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>100</td>
<td>0.55</td>
<td>1.95996</td>
<td>0.4472802</td>
<td>0.6496798</td>
</tr>
</tbody>
</table>

**Simple Z Confidence Interval of P**

<table>
<thead>
<tr>
<th>Number of &quot;Successes&quot; (X)</th>
<th>Sample Size (n)</th>
<th>Sample Proportion (p)</th>
<th>Z*</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>100</td>
<td>0.55</td>
<td>1.95996</td>
<td>0.452493</td>
<td>0.647507</td>
</tr>
</tbody>
</table>

**Simple Z Confidence Interval of P with Continuity Correction**

<table>
<thead>
<tr>
<th>Number of &quot;Successes&quot; (X)</th>
<th>Sample Size (n)</th>
<th>Sample Proportion (p)</th>
<th>Z*</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>100</td>
<td>0.55</td>
<td>1.95996</td>
<td>0.447493</td>
<td>0.6525069</td>
</tr>
</tbody>
</table>

**Wilson Score Confidence Interval of P**

<table>
<thead>
<tr>
<th>Number of &quot;Successes&quot; (X)</th>
<th>Sample Size (n)</th>
<th>Sample Proportion (p)</th>
<th>Z*</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>100</td>
<td>0.55</td>
<td>1.95996</td>
<td>0.452446</td>
<td>0.6438546</td>
</tr>
</tbody>
</table>

The Wilson score interval is the interval recommended in Newcombe (1998). The limits are based on the formulas that were presented earlier.
### Exact Test for Non-Inferiority

Lower Proportions are Worse  
Non-Inferiority Hypothesis: \( P > 0.5 - 0.1 \)

<table>
<thead>
<tr>
<th>Alternative Hypothesis</th>
<th>Sample Proportion</th>
<th>Prob Level</th>
<th>Conclude Non-Inferiority at ( \alpha = 0.05 )?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ha: ( P &gt; 0.4 )</td>
<td>0.55</td>
<td>0.00171</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Simple Z-Test for Non-Inferiority

Lower Proportions are Worse  
Non-Inferiority Hypothesis: \( P > 0.5 - 0.1 \)

<table>
<thead>
<tr>
<th>Alternative Hypothesis</th>
<th>Sample Proportion</th>
<th>Z-Statistic</th>
<th>Prob Level</th>
<th>Conclude Non-Inferiority at ( \alpha = 0.05 )?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ha: ( P &gt; 0.4 )</td>
<td>0.55</td>
<td>3.06190</td>
<td>0.00110</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Z Approximation Test using \( P_0 \) for Non-Inferiority

Lower Proportions are Worse  
Non-Inferiority Hypothesis: \( P > 0.5 - 0.1 \)

<table>
<thead>
<tr>
<th>Alternative Hypothesis</th>
<th>Sample Proportion</th>
<th>Z-Statistic</th>
<th>Prob Level</th>
<th>Conclude Non-Inferiority at ( \alpha = 0.05 )?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ha: ( P &gt; 0.4 )</td>
<td>0.55</td>
<td>2.95980</td>
<td>0.00154</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Z Approximation Test using \( p \) for Non-Inferiority

Lower Proportions are Worse  
Non-Inferiority Hypothesis: \( P > 0.5 - 0.1 \)

<table>
<thead>
<tr>
<th>Alternative Hypothesis</th>
<th>Sample Proportion</th>
<th>Z-Statistic</th>
<th>Prob Level</th>
<th>Conclude Non-Inferiority at ( \alpha = 0.05 )?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ha: ( P &gt; 0.4 )</td>
<td>0.55</td>
<td>2.91460</td>
<td>0.00178</td>
<td>Yes</td>
</tr>
</tbody>
</table>

The formulas for these tests were shown earlier.
Example 2 – Non-Inferiority Test of One Proportion using Raw Data

This section presents an example of how to run an analysis of raw data that may have been used to generate the summary data in example 1. The data for this example are found in the Prop1 dataset.

Setup

To run this example, complete the following steps:

1. **Open the Prop1 example dataset**
   - From the File menu of the NCSS Data window, select Open Example Data.
   - Select Prop1 and click OK.

2. **Specify the One Proportion – Non-Inferiority Tests procedure options**
   - Find and open the One Proportion – Non-Inferiority Tests procedure using the menus or the Procedure Navigator.
   - The settings 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.

   **Variables Tab**
   - Type of Data Input: Tabulate "Successes" from a Categorical Outcome Variable in the Database
   - Outcome Variable(s): Response
   - "Success" Value: 1
   - Lower Proportions Are: Worse
   - Standard Proportion: 0.50
   - Non-Inferiority Margin: 0.10

   **Reports Tab**
   - Exact (Binomial): Checked
   - Simple Z: Checked
   - Simple Z with Continuity Correction: Checked
   - Wilson Score: Checked
   - Exact (Binomial) Test: Checked
   - Simple Z-Test: Checked
   - Z Approximation Test using P0: Checked
   - Z Approximation Test using p: Checked

3. **Run the procedure**
   - Click the Run button to perform the calculations and generate the output.
### Output

Data Report for Response

<table>
<thead>
<tr>
<th>Number of &quot;Successes&quot; (X)</th>
<th>Sample Size (n)</th>
<th>Sample Proportion (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>100</td>
<td>0.55</td>
</tr>
</tbody>
</table>

The results are exactly the same as they were in example 1.