

## Chapter 497

# Confidence Intervals for Paired Means with Tolerance Probability

## Introduction

This routine calculates the sample size necessary to achieve a specified distance from the paired sample mean difference to the confidence limit(s) with a given tolerance probability at a stated confidence level for a confidence interval about a single mean difference when the underlying data distribution is normal.

## Technical Details

For a paired sample mean difference from a normal distribution with unknown variance, a two-sided,  $100(1 - \alpha)\%$  confidence interval is calculated by

$$\bar{X}_{Diff} \pm \frac{t_{1-\alpha/2, n-1} \hat{\sigma}_{Diff}}{\sqrt{n}}$$

where  $\bar{X}_{Diff}$  is the mean of the paired differences of the sample, and  $\hat{\sigma}_{Diff}$  is the estimated standard deviation of paired sample differences.

A one-sided  $100(1 - \alpha)\%$  upper confidence limit is calculated by

$$\bar{X}_{Diff} + \frac{t_{1-\alpha, n-1} \hat{\sigma}_{Diff}}{\sqrt{n}}$$

Similarly, the one-sided  $100(1 - \alpha)\%$  lower confidence limit is

$$\bar{X}_{Diff} - \frac{t_{1-\alpha, n-1} \hat{\sigma}_{Diff}}{\sqrt{n}}$$

Each confidence interval is calculated using an estimate of the mean difference plus and/or minus a quantity that represents the distance from the mean difference to the edge of the interval. For two-sided confidence intervals, this distance is sometimes called the precision, margin of error, or half-width. We will label this distance,  $D$ .

The basic equation for determining sample size when  $D$  has been specified is

$$D = \frac{t_{1-\alpha/2, n-1} \hat{\sigma}_{Diff}}{\sqrt{n}}$$

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Solving for  $n$ , we obtain

$$n = \left( \frac{t_{1-\alpha/2, n-1} \hat{\sigma}_{Diff}}{D} \right)^2$$

This equation can be solved for any of the unknown quantities in terms of the others. The value  $\alpha/2$  is replaced by  $\alpha$  when a one-sided interval is used.

There is an additional subtlety that arises when the standard deviation is to be chosen for estimating sample size. The sample sizes determined from the formula above produce confidence intervals with the specified widths only when the future sample has a sample standard deviation of differences that is no greater than the value specified.

As an example, suppose that 15 pairs of individuals are sampled in a pilot study, and a standard deviation estimate of 3.5 is obtained from the sample. The purpose of a later study is to estimate the mean difference within 10 units. Suppose further that the sample size needed is calculated to be 57 pairs using the formula above with 3.5 as the estimate for the standard deviation. The sample of size 57 pairs is then obtained from the population, but the standard deviation of the 57 paired differences turns out to be 3.9 rather than 3.5. The confidence interval is computed and the distance from the mean difference to the confidence limits is greater than 10 units.

This example illustrates the need for an adjustment to adjust the sample size such that the distance from the mean difference to the confidence limits will be below the specified value with known probability.

Such an adjustment for situations where a previous sample is used to estimate the standard deviation is derived by Harris, Horvitz, and Mood (1948) and discussed in Zar (1984) and Hahn and Meeker (1991). The adjustment is

$$n = \left( \frac{t_{1-\alpha/2, n-1} \hat{\sigma}_{Diff}}{D} \right)^2 F_{1-\gamma; n-1, m-1}$$

where  $1 - \gamma$  is the probability that the distance from the mean difference to the confidence limit(s) will be below the specified value, and  $m$  is the sample size in the previous paired sample that was used to estimate the standard deviation.

The corresponding adjustment when no previous sample is available is discussed in Kupper and Hafner (1989) and Hahn and Meeker (1991). The adjustment in this case is

$$n = \left( \frac{t_{1-\alpha/2, n-1} \hat{\sigma}_{Diff}}{D} \right)^2 \left( \frac{\chi^2_{1-\gamma, n-1}}{n-1} \right)$$

where, again,  $1 - \gamma$  is the probability that the distance from the mean difference to the confidence limit(s) will be below the specified value.

Each of these adjustments accounts for the variability in a future estimate of the standard deviation. In the first adjustment formula (Harris, Horvitz, and Mood, 1948), the distribution of the standard deviation is based on the estimate from a previous paired sample. In the second adjustment formula, the distribution of the standard deviation is based on a specified value that is assumed to be the population standard deviation of differences.

## Finite Population Size

The above calculations assume that samples are being drawn from a large (infinite) population. When the population is of finite size ( $N$ ), an adjustment must be made. The adjustment reduces the standard deviation as follows:

$$\sigma_{finite} = \sigma \sqrt{1 - \frac{n}{N}}$$

This new standard deviation replaces the regular standard deviation in the above formulas.

## The Standard Deviation of Paired Differences ( $\sigma_{Diff}$ ) for the Population

If you have an estimate of the standard deviation of paired differences for the population,  $\sigma_{Diff}$ , you may enter it directly. Another reasonable (but somewhat rough) estimate of  $\sigma_{Diff}$  may be obtained using the range of paired differences as

$$\sigma_{Diff} = \frac{Range}{4}$$

If you have estimates of the expected standard deviations of the paired variables ( $\sigma_1$  and  $\sigma_2$ ) and the Pearson correlation between the paired variables ( $\rho$ ), the standard deviation of paired differences ( $\sigma_{Diff}$ ) may be calculated using the equation

$$\sigma_{Diff}^2 = \sigma_1^2 + \sigma_2^2 - 2\rho\sigma_1\sigma_2$$

such that

$$\sigma_{Diff} = \sqrt{\sigma_1^2 + \sigma_2^2 - 2\rho\sigma_1\sigma_2}.$$

If  $\sigma_1 = \sigma_2 = \sigma_x$ , then this formula reduces to

$$\sigma_{Diff}^2 = 2\sigma_x^2(1 - \rho)$$

such that

$$\sigma_{Diff} = \sqrt{2\sigma_x^2(1 - \rho)}.$$

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If you have an estimate of the within-subject population standard deviation ( $\sigma_w$ ), then  $\sigma_{Diff}$  may be calculated using the equation

$$\sigma_{Diff}^2 = 2\sigma_w^2$$

such that

$$\sigma_{Diff} = \sqrt{2\sigma_w^2}.$$

$\sigma_w$  is often estimated by the square root of the within mean square error (WMSE) from a repeated measures ANOVA.

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## Confidence Level

The confidence level,  $1 - \alpha$ , has the following interpretation. If thousands of samples of  $n$  items are drawn from a population using simple random sampling and a confidence interval is calculated for each sample, the proportion of those intervals that will include the true population mean difference is  $1 - \alpha$ .

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## Example 1 – Calculating Sample Size

A researcher would like to estimate the mean difference in weight following a specific diet with 95% confidence. It is very important that the mean difference is estimated within 5 lbs. Data available from a previous study are used to provide an estimate of the standard deviation. The estimate of the standard deviation of before/after differences is 16.7 lbs, from a sample of size 17 individuals.

The goal is to determine the sample size necessary to obtain a two-sided confidence interval such that the mean weight is estimated within 5 lbs. Tolerance probabilities of 0.70 to 0.95 will be examined.

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### 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 .....	<b>Sample Size</b>
Interval Type .....	<b>Two-Sided</b>
Population Size .....	<b>Infinite</b>
Confidence Level (1 - Alpha) .....	<b>0.95</b>
Tolerance Probability .....	<b>0.70 to 0.95 by 0.05</b>
Distance from Mean Difference to Limit(s) .....	<b>5</b>
Standard Deviation Source .....	<b>S from a Previous Sample</b>
S (SD Estimated from a Previous Sample) .....	<b>16.7</b>
Sample Size (# of Pairs) of Previous Sample .....	<b>17</b>

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## Output

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

## Numeric Reports

### Numeric Results

Solve For: **Sample Size**

Interval Type: Two-Sided

Confidence Level	Sample Size N	Distance from Mean Difference to Limits		Standard Deviation of Paired Differences S*	Tolerance Probability
		Target	Actual		
0.95	58	5	4.97001	16.7	0.70
0.95	61	5	4.99638	16.7	0.75
0.95	66	5	4.96749	16.7	0.80
0.95	71	5	4.98549	16.7	0.85
0.95	79	5	4.97308	16.7	0.90
0.95	92	5	4.98078	16.7	0.95

\* Sample size of the previous paired sample for the estimate of S = 17

Confidence Level	The proportion of confidence intervals (constructed with this same confidence level, sample size, etc.) that would contain the population mean difference.
N	The size of the sample (or number of pairs) drawn from the population.
Distance from Mean Difference to Limits	The distance from the confidence limit(s) to the mean paired difference. For two-sided intervals, it is also known as the precision, half-width, or margin of error.
Target Distance	The value of the distance that is entered into the procedure.
Actual Distance	The value of the distance that is obtained from the procedure.
S	The standard deviation of paired differences for the population that was estimated from a previous paired sample of the indicated size.
Tolerance Probability	The probability that a future interval with sample size N and corresponding confidence level will have a distance from the mean difference to the limit(s) that is less than or equal to the specified distance.

### Summary Statements

A paired design will be used to obtain a two-sided 95% confidence interval for the paired mean difference. The standard t-distribution-based formula for the paired differences will be used to calculate the confidence interval. The population standard deviation of paired differences is estimated to be 16.7 by a previous paired sample of size 17. To produce a confidence interval with 0.7 probability that the distance from the paired sample mean difference to either limit will be no more than 5, 58 pairs will be needed.

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## Dropout-Inflated Sample Size

Dropout Rate	Sample Size N	Dropout- Inflated Enrollment Sample Size N'	Expected Number of Dropouts D
20%	58	73	15
20%	61	77	16
20%	66	83	17
20%	71	89	18
20%	79	99	20
20%	92	115	23

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.
N	The evaluable sample size at which the confidence interval is computed. If N subjects are evaluated out of the N' subjects that are enrolled in the study, the design will achieve the stated confidence interval.
N'	The total number of subjects that should be enrolled in the study in order to obtain N evaluable subjects, based on the assumed dropout rate. After solving for N, N' is calculated by inflating N using the formula $N' = N / (1 - DR)$ , with N' 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.)
D	The expected number of dropouts. $D = N' - N$ .

## Dropout Summary Statements

Anticipating a 20% dropout rate, 73 subjects should be enrolled to obtain a final sample size of 58 subjects.

## References

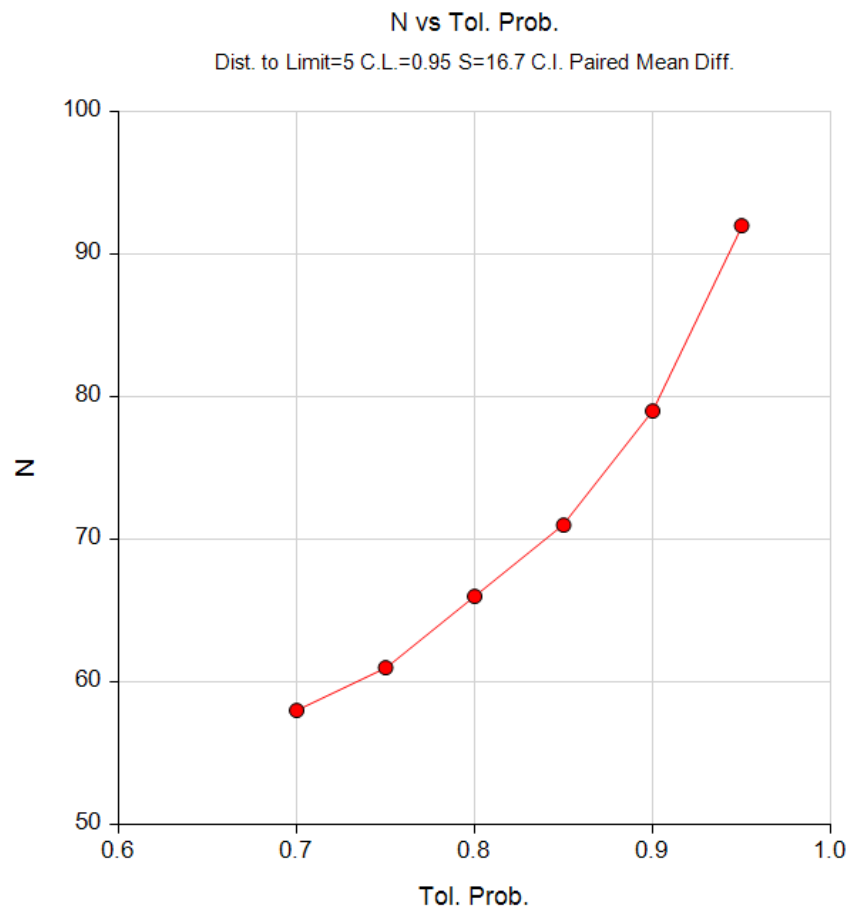
Hahn, G. J. and Meeker, W.Q. 1991. Statistical Intervals. John Wiley & Sons. New York.  
 Zar, J. H. 1984. Biostatistical Analysis. Second Edition. Prentice-Hall. Englewood Cliffs, New Jersey.  
 Harris, M., Horvitz, D. J., and Mood, A. M. 1948. 'On the Determination of Sample Sizes in Designing Experiments', Journal of the American Statistical Association, Volume 43, No. 243, pp. 391-402.

This report shows the calculated sample size for each of the scenarios.

## Confidence Intervals for Paired Means with Tolerance Probability

## Plots Section

## Plots



This plot shows the sample size versus the tolerance probability.



## Example 2 – Validation

This procedure uses the same mechanics as the *Confidence Intervals for One Mean with Tolerance Probability* procedure. The validation of this procedure is given in Examples 2, 3, and 4 of the *Confidence Intervals for One Mean with Tolerance Probability* procedure.