Chapter 471

# Confidence Intervals for the Difference Between Two Means

## Introduction

This procedure calculates the sample size necessary to achieve a specified distance from the difference in sample means to the confidence limit(s) at a stated confidence level for a confidence interval about the difference in means when the underlying data distribution is normal.

Caution: This procedure assumes that the standard deviations of the future samples will be the same as the standard deviations that are specified. If the standard deviation to be used in the procedure is estimated from a previous sample or represents the population standard deviation, the Confidence Intervals for the Difference between Two Means with Tolerance Probability procedure should be considered. That procedure controls the probability that the distance from the difference in means to the confidence limits will be less than or equal to the value specified.

## Technical Details

There are two formulas for calculating a confidence interval for the difference between two population means. The different formulas are based on whether the standard deviations are assumed to be equal or unequal.

For each of the cases below, let the means of the two populations be represented by $\mu_1$ and $\mu_2$, and let the standard deviations of the two populations be represented as $\sigma_1$ and $\sigma_2$.

### Case 1 – Standard Deviations Assumed Equal

When $\sigma_1 = \sigma_2 = \sigma$ are unknown, the appropriate two-sided confidence interval for $\mu_1 - \mu_2$ is

$$\bar{X}_1 - \bar{X}_2 \pm t_{1-\alpha/2, n_1+n_2-2} s_p \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}$$

where

$$s_p = \sqrt{\frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{n_1 + n_2 - 2}}$$

Upper and lower one-sided confidence intervals can be obtained by replacing $\alpha/2$ with $\alpha$.

The required sample size for a given precision, D, can be found by solving the following equation iteratively

$$D = t_{1-\alpha/2,n_1+n_2-2} s_p \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}$$

This equation can be used to solve for D or $n_1$ or $n_2$ based on the values of the remaining parameters.

## Case 2 – Standard Deviations Assumed Unequal

When $\sigma_1 \neq \sigma_2$ are unknown, the appropriate two-sided confidence interval for $\mu_1 - \mu_2$ is

$$\bar{X}_1 - \bar{X}_2 \pm t_{1-\alpha/2,\nu} \sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}$$

where

$$\nu = \frac{\left(\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}\right)^2}{\frac{s_1^4}{n_1^2(n_1 - 1)} + \frac{s_2^4}{n_2^2(n_2 - 1)}}$$

In this case t is an approximate t and the method is known as the Welch-Satterthwaite method. Upper and lower one-sided confidence intervals can be obtained by replacing $\alpha/2$ with $\alpha$.

The required sample size for a given precision, D, can be found by solving the following equation iteratively

$$D = t_{1-\alpha/2,\nu} \sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}$$

This equation can be used to solve for D or $n_1$ or $n_2$ based on the values of the remaining parameters.

## Confidence Level

The confidence level, 1 – $\alpha$, has the following interpretation. If thousands of samples of $n_1$ and $n_2$ items are drawn from populations 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 – $\alpha$.

Notice that is a long term statement about many, many samples.

# Example 1 – Calculating Sample Size

Suppose a study is planned in which the researcher wishes to construct a two-sided 95% confidence interval for the difference between two population means such that the width of the interval is no wider than 20 units. The confidence level is set at 0.95, but 0.99 is included for comparative purposes. The standard deviation estimates, based on the range of data values, are 32 for Population 1 and 38 for Population 2. Instead of examining only the interval half-width of 10, a series of half-widths from 5 to 15 will also be considered.

The goal is to determine the necessary sample size for each group.

## 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 ...................................................... **Sample Size**
Interval Type ................................................. **Two-Sided**
Confidence Level ........................................... **0.95 0.99**
Group Allocation ............................................ **Equal (N1 = N2)**
Distance from Mean Diff to Limit(s)................ **5 to 15 by 1**
S1 (Standard Deviation Group 1).................. **32**
S2 (Standard Deviation Group 2).................. **38**
Std. Dev. Equality Assumption....................... **Assume S1 and S2 are Unequal**

# 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
Standard Deviations: Unknown and Unequal

| | Sample Size | | | Distance from Mean Difference to Limits | | Standard Deviations | |
|---|---|---|---|---|---|---|---|
| Confidence Level | N1 | N2 | N | Target | Actual | S1 | S2 |
| 0.95 | 380 | 380 | 760 | 5 | 4.995 | 32 | 38 |
| 0.95 | 265 | 265 | 530 | 6 | 5.995 | 32 | 38 |
| 0.95 | 195 | 195 | 390 | 7 | 6.995 | 32 | 38 |
| 0.95 | 150 | 150 | 300 | 8 | 7.984 | 32 | 38 |
| 0.95 | 119 | 119 | 238 | 9 | 8.973 | 32 | 38 |
| 0.95 | 97 | 97 | 194 | 10 | 9.951 | 32 | 38 |
| 0.95 | 80 | 80 | 160 | 11 | 10.973 | 32 | 38 |
| 0.95 | 68 | 68 | 136 | 12 | 11.918 | 32 | 38 |
| 0.95 | 58 | 58 | 116 | 13 | 12.926 | 32 | 38 |
| 0.95 | 50 | 50 | 100 | 14 | 13.947 | 32 | 38 |
| 0.95 | 44 | 44 | 88 | 15 | 14.895 | 32 | 38 |
| 0.99 | 655 | 655 | 1310 | 5 | 5.000 | 32 | 38 |
| 0.99 | 455 | 455 | 910 | 6 | 5.999 | 32 | 38 |
| 0.99 | 335 | 335 | 670 | 7 | 6.991 | 32 | 38 |
| 0.99 | 258 | 258 | 516 | 8 | 7.997 | 32 | 38 |
| 0.99 | 205 | 205 | 410 | 9 | 8.981 | 32 | 38 |
| 0.99 | 166 | 166 | 332 | 10 | 9.991 | 32 | 38 |
| 0.99 | 138 | 138 | 276 | 11 | 10.972 | 32 | 38 |
| 0.99 | 116 | 116 | 232 | 12 | 11.983 | 32 | 38 |
| 0.99 | 99 | 99 | 198 | 13 | 12.991 | 32 | 38 |
| 0.99 | 86 | 86 | 172 | 14 | 13.960 | 32 | 38 |
| 0.99 | 75 | 75 | 150 | 15 | 14.975 | 32 | 38 |

| | |
|---|---|
| Confidence Level | The proportion of confidence intervals (constructed with this same confidence level, sample size, etc.) that would contain the true difference in population means. |
| N1 and N2 | The number of items sampled from each population. |
| N | The total sample size. N = N1 + N2. |
| Distance from Mean Difference to Limits | The distance from the confidence limit(s) to the difference in sample means. |
| 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. |
| S1 and S2 | The standard deviations upon which the distance from mean difference to limit calculations are based. |

### Summary Statements

A parallel two-group design will be used to obtain a two-sided 95% confidence interval for the difference between two means. The standard deviations of the two groups are assumed to be unequal and the individual-variance t-distribution formula (using the Welch-Satterthwaite method for degrees of freedom) will be used to calculate the confidence interval. The Group 1 sample standard deviation is assumed to be 32 and the Group 2 sample standard deviation is assumed to be 38. To produce a confidence interval with a distance of no more than 5 from the sample mean difference to either limit, the number of subjects needed will be 380 in Group 1 and 380 in Group 2.

**Dropout-Inflated Sample Size**

| | Sample Size | | | Dropout-Inflated Enrollment Sample Size | | | Expected Number of Dropouts | | |
|---|---|---|---|---|---|---|---|---|---|
| **Dropout Rate** | **N1** | **N2** | **N** | **N1'** | **N2'** | **N'** | **D1** | **D2** | **D** |
| 20% | 380 | 380 | 760 | 475 | 475 | 950 | 95 | 95 | 190 |
| 20% | 265 | 265 | 530 | 332 | 332 | 664 | 67 | 67 | 134 |
| 20% | 195 | 195 | 390 | 244 | 244 | 488 | 49 | 49 | 98 |
| 20% | 150 | 150 | 300 | 188 | 188 | 376 | 38 | 38 | 76 |
| 20% | 119 | 119 | 238 | 149 | 149 | 298 | 30 | 30 | 60 |
| 20% | 97 | 97 | 194 | 122 | 122 | 244 | 25 | 25 | 50 |
| 20% | 80 | 80 | 160 | 100 | 100 | 200 | 20 | 20 | 40 |
| 20% | 68 | 68 | 136 | 85 | 85 | 170 | 17 | 17 | 34 |
| 20% | 58 | 58 | 116 | 73 | 73 | 146 | 15 | 15 | 30 |
| 20% | 50 | 50 | 100 | 63 | 63 | 126 | 13 | 13 | 26 |
| 20% | 44 | 44 | 88 | 55 | 55 | 110 | 11 | 11 | 22 |
| 20% | 655 | 655 | 1310 | 819 | 819 | 1638 | 164 | 164 | 328 |
| 20% | 455 | 455 | 910 | 569 | 569 | 1138 | 114 | 114 | 228 |
| 20% | 335 | 335 | 670 | 419 | 419 | 838 | 84 | 84 | 168 |
| 20% | 258 | 258 | 516 | 323 | 323 | 646 | 65 | 65 | 130 |
| 20% | 205 | 205 | 410 | 257 | 257 | 514 | 52 | 52 | 104 |
| 20% | 166 | 166 | 332 | 208 | 208 | 416 | 42 | 42 | 84 |
| 20% | 138 | 138 | 276 | 173 | 173 | 346 | 35 | 35 | 70 |
| 20% | 116 | 116 | 232 | 145 | 145 | 290 | 29 | 29 | 58 |
| 20% | 99 | 99 | 198 | 124 | 124 | 248 | 25 | 25 | 50 |
| 20% | 86 | 86 | 172 | 108 | 108 | 216 | 22 | 22 | 44 |
| 20% | 75 | 75 | 150 | 94 | 94 | 188 | 19 | 19 | 38 |

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.
N1, N2, and N — The evaluable sample sizes at which the confidence interval is computed. If N1 and N2 subjects are evaluated out of the N1' and N2' subjects that are enrolled in the study, the design will achieve the stated confidence interval.
N1', N2', and N' — The number of subjects that should be enrolled in the study in order to obtain N1, N2, and N evaluable subjects, based on the assumed dropout rate. After solving for N1 and N2, N1' and N2' are calculated by inflating N1 and N2 using the formulas N1' = N1 / (1 - DR) and N2' = N2 / (1 - DR), with N1' and N2' 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.)
D1, D2, and D — The expected number of dropouts. D1 = N1' - N1, D2 = N2' - N2, and D = D1 + D2.

**Dropout Summary Statements**

Anticipating a 20% dropout rate, 475 subjects should be enrolled in Group 1, and 475 in Group 2, to obtain final group sample sizes of 380 and 380, respectively.

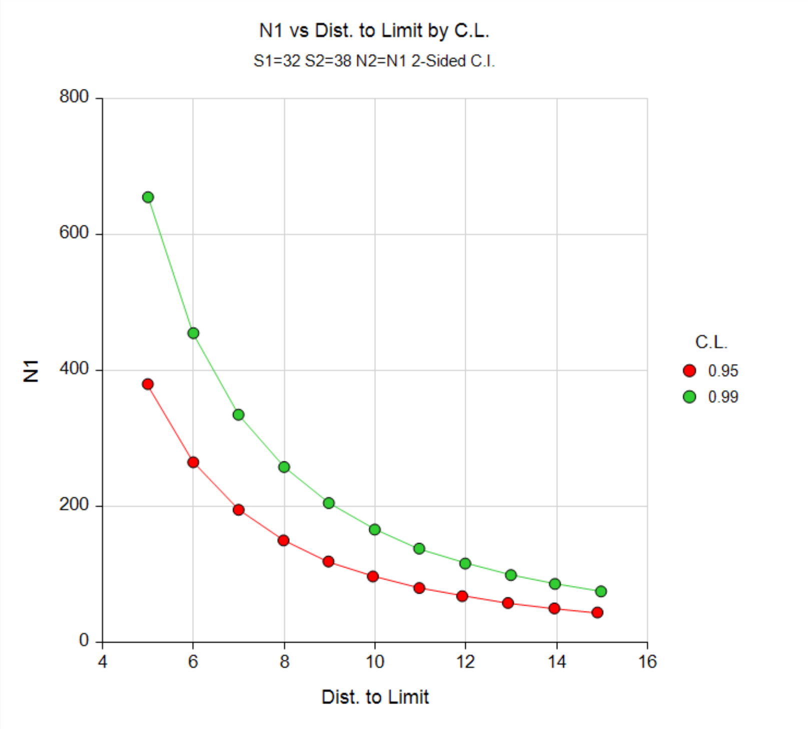
**References**

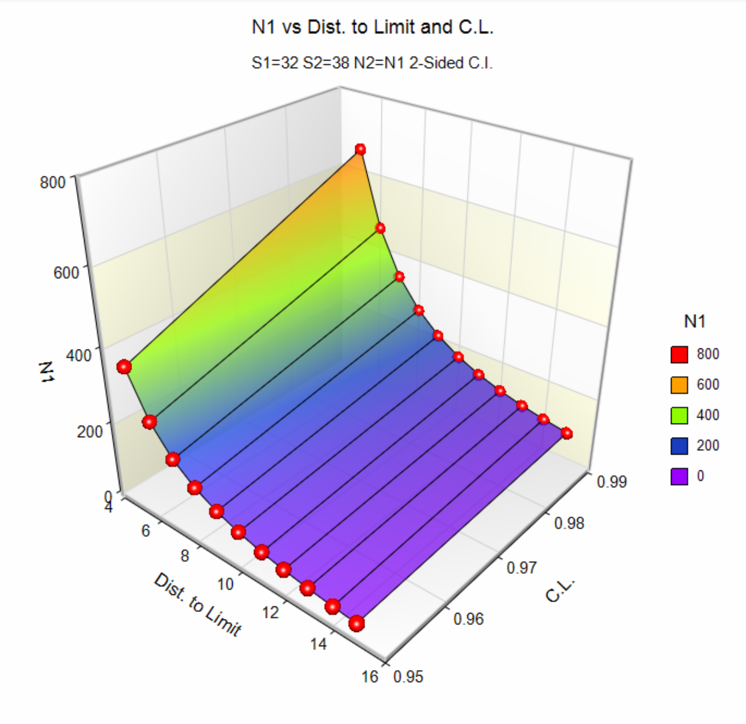
Ostle, B. and Malone, L.C. 1988. Statistics in Research. Iowa State University Press. Ames, Iowa.
Zar, Jerrold H. 1984. Biostatistical Analysis (Second Edition). Prentice-Hall. Englewood Cliffs, New Jersey.

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

## Plots Section

### Plots




These plots show the sample size of each group versus the precision for the two confidence levels.

# Example 2 – Validation using Ostle and Malone

Ostle and Malone (1988) page 150 give an example of a precision calculation for a confidence interval for the difference between two means when the confidence level is 95%, the two standard deviations are 6.2185 and 16.06767, and the sample sizes are 7 and 6. The precision is 13.433 (when df = 6.257, not 6).

## 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 2** 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 ...................................................... **Sample Size**
Interval Type ................................................ **Two-Sided**
Confidence Level .......................................... **0.90**
Group Allocation ........................................... **Enter N2, solve for N1**
N2 ................................................................. **6**
Distance from Mean Diff to Limit(s)............... **13.433**
S1 (Standard Deviation Group 1).................. **6.2185**
S2 (Standard Deviation Group 2).................. **16.06767**
Std. Dev. Equality Assumption...................... **Assume S1 and S2 are Unequal**

## Output

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

**Numeric Results**

Solve For: Sample Size
Interval Type: Two-Sided
Standard Deviations: Unknown and Unequal

| | Sample Size | | | Distance from Mean Difference to Limits | | Standard Deviations | |
|---|---|---|---|---|---|---|---|
| **Confidence Level** | **N1** | **N2** | **N** | **Target** | **Actual** | **S1** | **S2** |
| 0.9 | 7 | 6 | 13 | 13.433 | 13.433 | 6.22 | 16.07 |

**PASS** also calculated the sample size in Group 1 to be 7.

# Example 3 – Validation using Zar (1984)

Zar (1984) page 132 gives an example of a precision calculation for a confidence interval for the difference between two means when the confidence level is 95%, the pooled standard deviation estimate is 0.7206, and the sample sizes are 6 and 7. The precision is 0.88.

## 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 3** 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 ...................................................... **Distance from Mean Difference to Limit**
Interval Type ................................................. **Two-Sided**
Confidence Level .......................................... **0.95**
Group Allocation ........................................... **Enter N1 and N2 individually**
N1 (Sample Size Group 1)............................. **6**
N2 (Sample Size Group 2)............................. **7**
S1 (Standard Deviation Group 1)................... **0.7206**
S2 (Standard Deviation Group 2)................... **S1**
Std. Dev. Equality Assumption....................... **Assume S1 and S2 are Equal**

## Output

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

**Numeric Results**

Solve For: Distance from Mean Difference to Limit(s)
Interval Type: Two-Sided
Standard Deviations: Unknown and Equal

| | Sample Size | | | Distance | Standard Deviations | |
|---|---|---|---|---|---|---|
| Confidence Level | N1 | N2 | N | from Mean Difference to Limits | S1 | S2 |
| 0.95 | 6 | 7 | 13 | 0.882 | 0.72 | 0.72 |

**PASS** also calculates the precision to be 0.88.