

## Chapter 442

# Confidence Intervals for One-Way Repeated Measures Contrasts

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## Introduction

This module calculates the expected width of a confidence interval for a contrast (linear combination) of the means in a one-way repeated measures design using either the multivariate test or the univariate test as described by Maxwell and Delaney (2003) and Davis (2002).

A repeated measures design is one in which subjects are observed at a fixed set of time points. These time points do not have to be equally spaced, but they must be identical for all subjects. A confidence interval about a contrast of the means can be calculated using the Student's  $t$  distribution.

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## Why Do We Promote the Multivariate Approach Instead of the Univariate Approach?

As we researched this procedure, we found that there were two possible methods to construct the confidence interval: multivariate and univariate. The univariate procedure was at first attractive because it gives more denominator degrees of freedom. Unfortunately, the univariate approach can only be used when all correlations among the measurements at the different time points are equal (compound symmetry). This assumption is seldom met in practice in repeated measures data. It is often met in a split plot design.

Therefore, Maxwell and Delaney (2003) recommend the multivariate approach because it makes no special assumption about the correlation pattern, and it forms a specific error term that depends only on the time points used in the contrast.

For a very comprehensive discussion of when to use each statistic, we refer you to Maxwell and Delaney (2003).

## Technical Details

The confidence interval details are presented in Rencher (1998). We refer you to that reference for more details.

### Technical Details for the Multivariate Approach

In one-factor case, a sample of  $N$  subjects are measured at  $M$  time points. We assume that all  $N$  subjects have the same multivariate normal distribution with mean vector  $\mu$  and variance covariance matrix  $\Sigma$ . Rencher (1998) shows that a 100  $(1 - \alpha)\%$  confidence interval for  $\sum c_i \mu_i$  may be computed using

$$C' \bar{y} - t_{1-\frac{\alpha}{2}, N-1} \sqrt{\frac{C' S C}{N}} \leq C' \mu \leq C' \bar{y} + t_{1-\frac{\alpha}{2}, N-1} \sqrt{\frac{C' S C}{N}}$$

where  $\bar{y}$  is the  $M$ -dimensional vector of sample means,  $C$  is  $M$ -dimensional vector of contrast coefficients, and  $S$  is the sample variance-covariance matrix.

The distance from the contrast to either of the limits is thus

$$D = t_{1-\frac{\alpha}{2}, N-1} \sqrt{\frac{C' S C}{N}}$$

This formula can be used to calculate an appropriate sample size.

### Technical Details for the Univariate Approach

The univariate (or mixed-models) approach may be used to calculate a 100  $(1 - \alpha)\%$  confidence interval for  $\sum c_i \mu_i$  if we are willing to adopt the very restrictive assumption of compound symmetry in the covariance matrix. If we are willing to adopt this assumption, the confidence interval is calculated using

$$C' \bar{y} - t_{1-\frac{\alpha}{2}, (M-1)(N-1)} \sqrt{\frac{MS_{ST} C' C}{N}} \leq C' \mu \leq C' \bar{y} + t_{1-\frac{\alpha}{2}, (M-1)(N-1)} \sqrt{\frac{MS_{ST} C' C}{N}}$$

where  $MS_{TS}$  is time period-by-subject interaction mean square.

The distance from the contrast to either of the limits is thus

$$D = t_{1-\frac{\alpha}{2}, N-1} \sqrt{\frac{MS_{ST} C' C}{N}}$$

This formula can be used to calculate an appropriate sample size.

## Confidence Intervals for One-Way Repeated Measures Contrasts

**PASS** requires the input of  $\sigma_Y$  and  $\rho$ . These can be estimated from a repeated measures ANOVA table which provides values for  $MS_S$  (mean square of subjects) and  $MS_{ST}$  (mean square of subject-time interaction). The parameters can then be calculated as follows

$$\hat{\rho} = \frac{F - 1}{F - 1 + M}, \quad F = \frac{MS_{ST}}{MS_S}, \quad \hat{\sigma}_Y^2 = \frac{MS_{ST}}{1 - \hat{\rho}}$$

It is useful to note the following expectations

$$E(MS_{ST}) = \sigma_Y^2(1 - \rho)$$

$$E(MS_S) = \sigma_Y^2(1 + (M - 1)\rho)$$

## Covariance Patterns

In a repeated measures design with  $N$  subjects, each measured  $M$  times, observations within a single subject may be correlated, and a pattern for their covariance must be specified. In this case, the overall covariance matrix will have the block-diagonal form:

$$V = \begin{pmatrix} V_1 & \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} \\ \mathbf{0} & V_2 & \mathbf{0} & \cdots & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & V_3 & \cdots & \mathbf{0} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \cdots & V_N \end{pmatrix},$$

where  $V_i$  is the  $M \times M$  covariance submatrices corresponding to the  $i^{\text{th}}$  subject. The  $\mathbf{0}$ 's represent  $M \times M$  matrices of zeros giving zero covariances for observations on different subjects. This routine allows the specification of four different covariance matrix types: All  $\rho$ 's Equal, AR(1), Banded(1), and Banded(2).

### All $\rho$ 's Equal (Compound Symmetry)

A compound symmetry covariance model assumes that all covariances are equal, and all variances on the diagonal are equal. That is

$$\Sigma = \sigma^2 \begin{pmatrix} 1 & \rho & \rho & \rho & \cdots & \rho \\ \rho & 1 & \rho & \rho & \cdots & \rho \\ \rho & \rho & 1 & \rho & \cdots & \rho \\ \rho & \rho & \rho & 1 & \cdots & \rho \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ \rho & \rho & \rho & \rho & \cdots & 1 \end{pmatrix}_{M \times M}$$

where  $\sigma^2$  is the subject variance and  $\rho$  is the correlation between observations on the same subject.

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## AR(1)

An AR(1) (autoregressive order 1) covariance model assumes that all variances on the diagonal are equal and that covariances  $t$  time periods apart are equal to  $\rho^t\sigma^2$ . **This choice is recommended.** That is

$$\Sigma = \sigma^2 \begin{pmatrix} 1 & \rho & \rho^2 & \rho^3 & \dots & \rho^{M-1} \\ \rho & 1 & \rho & \rho^2 & \dots & \rho^{M-2} \\ \rho^2 & \rho & 1 & \rho & \dots & \rho^{M-3} \\ \rho^3 & \rho^2 & \rho & 1 & \dots & \rho^{M-4} \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ \rho^{M-1} & \rho^{M-2} & \rho^{M-3} & \rho^{M-4} & \dots & 1 \end{pmatrix}_{M \times M}$$

where  $\sigma^2$  is the residual variance and  $\rho$  is the correlation between observations on the same subject.

## Banded(1)

A Banded(1) (banded order 1) covariance model assumes that all variances on the diagonal are equal, covariances for observations one time period apart are equal to  $\rho\sigma^2$ , and covariances for measurements greater than one time period apart are equal to zero. That is

$$\Sigma = \sigma^2 \begin{pmatrix} 1 & \rho & 0 & 0 & \dots & 0 \\ \rho & 1 & \rho & 0 & \dots & 0 \\ 0 & \rho & 1 & \rho & \dots & 0 \\ 0 & 0 & \rho & 1 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \dots & 1 \end{pmatrix}_{M \times M}$$

where  $\sigma^2$  is the residual variance and  $\rho$  is the correlation between observations on the same subject.

## Banded(2)

A Banded(2) (banded order 2) covariance model assumes that all variances on the diagonal are equal, covariances for observations one or two time periods apart are equal to  $\rho\sigma^2$ , and covariances for measurements greater than two time period apart are equal to zero. That is

$$\Sigma = \sigma^2 \begin{pmatrix} 1 & \rho & \rho & 0 & \dots & 0 \\ \rho & 1 & \rho & \rho & \dots & 0 \\ \rho & \rho & 1 & \rho & \dots & 0 \\ 0 & \rho & \rho & 1 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \dots & 1 \end{pmatrix}_{M \times M}$$

where  $\sigma^2$  is the residual variance and  $\rho$  is the correlation between observations on the same subject.

## Example 1 – Determining Sample Size

Researchers are planning a study of the impact of a new drug on heart rate. They want to evaluate the difference in heart rate between subjects that have taken the specific drug 30 minutes before exercise and the same subjects, two days later, who exercise without the drug.

Their experimental protocol calls for a baseline heart rate measurement, followed by exercise, followed by three additional measurements 5 minutes apart. They expect a quadratic pattern in the means and want to be able to detect a 10% difference in heart rate between the two treatments.

Similar studies have found a standard deviation of the difference between scores at each time point to be between 7 and 9, and a correlation between adjacent differences on the same individual to be 0.6. The researchers assume that a first-order autocorrelation pattern adequately models the data. Since the covariances will not be equal, they decide to use the multivariate test statistic.

They decide to find the sample size needed for a half-width of 3, 4, or 5.

The two-sided confidence interval will have a confidence level of 0.95. What sample size is necessary over a range of possible means and standard deviations?

### 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>
Statistic Type .....	<b>Multivariate</b>
Interval Type .....	<b>Two-Sided</b>
Confidence Level (1 – Alpha).....	<b>0.95</b>
M (Measurements).....	<b>4</b>
Contrast Coefficients.....	<b>Quadratic</b>
D (Distance from Contrast to Limit).....	<b>3 4 5</b>
Pattern of $\sigma$ 's Across Time.....	<b>Equal</b>
$\sigma$ (Standard Deviation).....	<b>7 9</b>
Pattern of $\rho$ 's Across Time.....	<b>AR(1)</b>
$\rho$ (Correlation).....	<b>0.6</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](#)  
 Type of C.I.: Two-Sided Multivariate  
 Contrast: Quadratic {1 -1 -1 1}  
 $\sigma$ 's: All Equal  
 $\rho$ 's: AR(1)

Distance D	Subjects N	Time Points M	Standard Deviation $\sigma$	Correlation $\rho$	Confidence Level CL	Contrast Standard Deviation $\sqrt{(C'VC)}$
2.9969	40	4	7	0.6	0.95	9.371
2.9853	65	4	9	0.6	0.95	12.048
3.9569	24	4	7	0.6	0.95	9.371
3.9600	38	4	9	0.6	0.95	12.048
4.9932	16	4	7	0.6	0.95	9.371
4.9731	25	4	9	0.6	0.95	12.048

D The distance from the contrast value to the limit(s).  
 N The number of subjects. Each subject is measured at two or more time points.  
 M The number of measurements obtained on each subject.  
 $\sigma$  The standard deviation across subjects at a given time point. It is assumed to be identical for all time points.  
 $\rho$  The (auto)correlation between observations made on a subject at the first and second time points.  
 CL The confidence level of the confidence interval.  
 $\sqrt{(C'VC)}$  The standard deviation of the contrast value.

### Summary Statements

A one-way repeated measures design, with 4 repeated measurements (time points) for each subject, will be used to obtain a two-sided 95% confidence interval for a contrast (linear combination) of the 4 means. The contrast is Quadratic {1 -1 -1 1}. The t-distribution-based multivariate approach will be used to calculate the confidence interval. The standard deviation across subjects at the same time point is assumed to be 7. The assumed pattern of the covariance matrix is AR(1) with a correlation of 0.6 between adjacent time point measurements. To produce a confidence interval with a distance of no more than 3 from the sample contrast value to either limit, 40 subjects 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%	40	50	10
20%	65	82	17
20%	24	30	6
20%	38	48	10
20%	16	20	4
20%	25	32	7

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, 50 subjects should be enrolled to obtain a final sample size of 40 subjects.

**References**

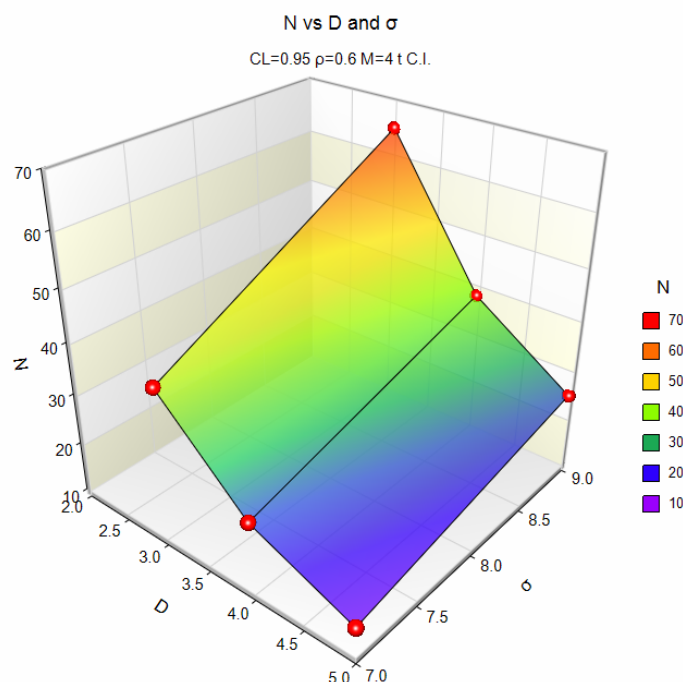
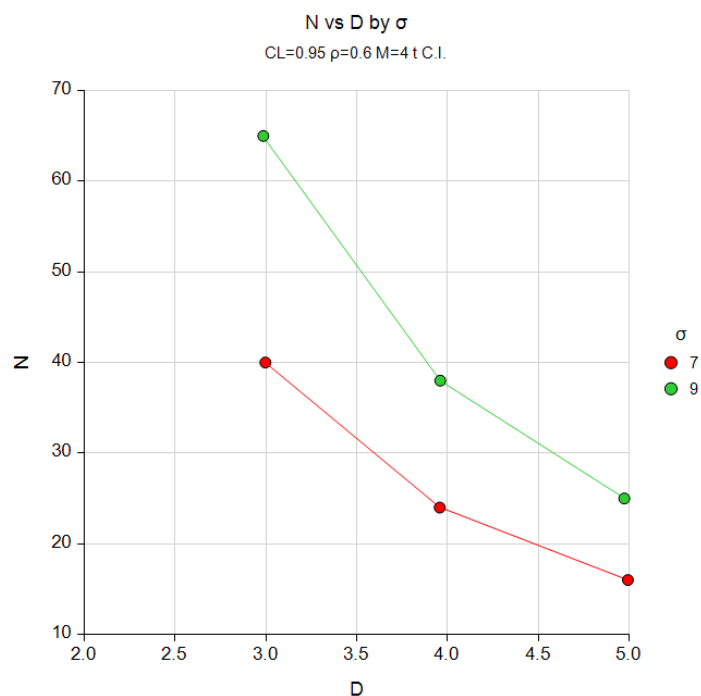
Rencher, Alvin C. 1998. Multivariate Statistical Inference and Applications. John Wiley. New York, New York.  
 Maxwell, S.E. and Delaney, H.D. 2003. Designing Experiments and Analyzing Data, Second Edition. Psychology Press. New York.

This report gives the half-width (distance) for each value of the other parameters. The definitions are shown in the report.

## Confidence Intervals for One-Way Repeated Measures Contrasts

## Plots Section

## Plots



The first chart shows the relationship between N, D, and  $\sigma$  when the other parameters in the design are held constant. The second chart shows a 3D view of the relationship between N, D, and  $\sigma$  when the other parameters in the design are held constant.



## Example 2 – Validation using Hand Calculations

We will compute the following example by hand and then compare that with the results that **PASS** obtains. Here are the settings:

<b>Statistics Type</b>	<b>Multivariable</b>
<b>Interval Type</b>	<b>Two-Sided</b>
<b>Confidence Level</b>	<b>0.95</b>
<b>N</b>	<b>20</b>
<b>M</b>	<b>3</b>
<b>Coefficients</b>	<b>-1, 0.5, 0.5</b>
<b><math>\sigma</math></b>	<b>2</b>
<b><math>\rho</math></b>	<b>0.2</b>
<b>Covariance Type</b>	<b>All <math>\rho</math>'s Equal</b>

Using these values, we find the following

<b>C'<math>\mu</math></b>	<b>3</b>
<b>C'VC</b>	<b>4.8</b>
<b><math>\Delta</math></b>	<b>0.3</b>
<b>t<sub>0.975,19</sub></b>	<b>2.09302</b>

The above results in

**D = 1.0254.**

## 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 .....	<b>Distance from Contrast to Limit</b>
Statistic Type .....	<b>Multivariate</b>
Interval Type .....	<b>Two-Sided</b>
Confidence Level (1 – Alpha).....	<b>0.95</b>
N (Subjects) .....	<b>20</b>
M (Measurements).....	<b>3</b>
Contrast Coefficients.....	<b>List</b>
List of Coefficients .....	<b>-1 0.5 0.5</b>
Pattern of $\sigma$ 's Across Time.....	<b>Equal</b>
$\sigma$ (Standard Deviation).....	<b>2</b>
Pattern of $\rho$ 's Across Time.....	<b>All <math>\rho</math>'s Equal</b>
$\rho$ (Correlation).....	<b>0.2</b>

## Output

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

### Numeric Results

Solve For: [Distance from Contrast to Limit](#)  
 Type of C.I.: Two-Sided Multivariate  
 Contrast: -1 0.5 0.5  
 $\sigma$ 's: All Equal  
 $\rho$ 's: All Equal

Distance D	Subjects N	Time Points M	Standard Deviation $\sigma$	Correlation $\rho$	Confidence Level CL	Contrast Standard Deviation $\sqrt{(C'VC)}$
1.0254	20	3	2	0.2	0.95	2.191

The distance of 1.0254 matches our hand calculations.