Chapter 434

One-Way Repeated Measures Contrasts

Introduction

This module calculates the power of a test of a contrast among the means in a one-way repeated measures design using either the multivariate test or the univariate, repeated-measures F-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 hypothesis about a contrast of the means can be tested using Hotelling's T^2 test or the univariate F test.

Why Do We Promote the Multivariate Test Instead of the Univariate Test?

As we researched this procedure, we found that there were two possible methods to test the contrast: multivariate and univariate. The univariate test was at first attractive because it gives more denominator degrees of freedom. Unfortunately, the univariate approach can only by used when all correlations among the measurements at the different time points are equal (called sphericity or compound symmetry). This assumption is seldom met in practice.

Therefore, Maxwell and Delaney (2003) recommend the multivariate approach because it makes no special assumption about the correlation pattern, it forms a specific error term that depends only on the time points used in the contrast, and its type-1 error rate is exact.

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

Technical Details

The formulas used to perform a Hotelling's T^2 power analysis provide exact answers if the above assumptions are met. These formulas can be found in many places. We use the results in Davis (2002). We refer you to that reference for more details.

Technical Details for the Multivariate Test

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 μ and variance covariance matrix Σ, and that Hotelling's T^2 is used for testing the null hypothesis that $\sum c_i \mu_i = 0$ versus the alternative that $\sum c_i \mu_i = A \neq 0$. The value of T^2 is computed using the formula

$$F_{1,N-1} = T^2_{1,N-1} = N\frac{\left(C^{\bar{}}y\right)^2}{C'SC}$$

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. Rather than use the T^2 distribution, we use the well-known relationship between it and the F-distribution with $df_1 = 1$ and $df_2 = (N - 1)$.

To calculate power, we need the non-centrality parameter for this distribution. This non-centrality parameter is defined as follows

$$\lambda = N \frac{(C'\mu)^2}{C'\Sigma C} = N\Delta^2$$

We define Δ as the *effect size* because it provides an expression for the magnitude of the contrast of the means under the alternative hypothesis.

Using this non-centrality parameter, the power of the Hotelling's T^2 may be calculated for any value of the means and standard deviations. Since there is a simple relationship between the non-central T^2 and the non-central F, calculations are based on the non-central F using the formula

$$Power = 1 - P\left(F' > F_{1-\alpha,1,(N-1),0} \middle| F' \sim F_{1,(N-1),\lambda}\right)$$

Technical Details for the Univariate Test

The univariate approach calculates an F-test for testing the hypothesis using

$$F_{1,(M-1)(N-1)} = \frac{MS_C}{MS_{TxS}}$$

where MS_C is the mean square for the contrast (including an adjustment for the sum of squared contrast coefficients) and MS_{TxS} is time period-by-subject interaction mean square.

To calculate power, we need the non-centrality parameter. This is defined as

$$\lambda = N \frac{(C'\mu)^2}{C'\Sigma C} = N\Delta^2$$

where Σ meets the compound symmetry requirement defined below. We define Δ as the *effect size* because it provides an expression for the magnitude of the contrast of the means under the alternative hypothesis.

PASS requires the input of σ_Y and ρ. 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

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

It is useful to note the following expectations

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

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

The power is calculated using a formula similar to the one above based on the non-central F distribution

$$Power = 1 - P\left(F' > F_{1-\alpha,1,(M-1)(N-1),0}|F'{\sim}F_{1,(M-1)(N-1),\lambda}\right)$$

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:

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

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

All ρ'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 σ^2 is the subject variance and ρ is the correlation between observations on the same subject.

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

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

where σ^2 is the residual variance and ρ 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

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

where σ^2 is the residual variance and ρ 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

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

where σ^2 is the residual variance and ρ 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 decided to use a mean pattern of 0, -4, -3, and 0 to represent the differences at the four time points. They decide to look at three values of K: 1, 2, and 3.

The test will be conducted at the 0.05 significance level. What sample size is necessary to achieve 90% power 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 ....**Sample Size**
Test Statistic Type ....**Multivariate**
Power..**0.90**
Alpha...**0.05**
M (Measurements)..**4**
Means..**List**
Means – List Values......................................**0 -4 -3 0**
K (Mean Multipliers)......................................**1 2 3**
Contrast Coefficients.....................................**Quadratic**
Pattern of σ's Across Time............................**Equal**
σ (Standard Deviation)...................................**7 9**
Pattern of ρ's Across Time............................**AR(1)**
ρ (Correlation)..**0.6**

Output

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

Numeric Reports

Numeric Results
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Solve For: Sample Size
Test Type: Multivariate T² Test
Means: 0 -4 -3 0
Contrast: Quadratic {1 -1 -1 1}
ρ's: AR(1)
σᵢ's: All Equal
_____

| | | | Means | | | Within- | | |
| | Sample | Number of | Multiplier | Contrast | Standard Deviation | Subject Correlation | | |
Power	Size N	Measurements M	K	Σcμ	σ	ρ	Alpha
0.9023	21	4	1	7	7	0.6	0.05
0.9079	34	4	1	7	9	0.6	0.05
0.9055	7	4	2	14	7	0.6	0.05
0.9036	10	4	2	14	9	0.6	0.05
0.9556	5	4	3	21	7	0.6	0.05
0.9216	6	4	3	21	9	0.6	0.05
_____

Power   The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N   The number of subjects. Each subject is measured at two or more time points.
M   The number of time points at which each subject is measured.
K   The effect size multiplier. The original means are all multiplied by this value, resulting in a corresponding change in
         the effect size.
Σcμ   The linear combination of the means and the contrast coefficients. This represents the difference among the means
         that is being tested.
σ   The standard deviation across subjects at a given time point. It is assumed to be identical for all time points.
ρ   The (auto)correlation between observations made on a subject at the first and second time points.
Alpha   The probability of rejecting a true null hypothesis.

Summary Statements
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A one-way repeated measures design, with 4 repeated measurements (time points) for each subject, will be used
to test a contrast (linear combination) of the 4 means against zero. The comparison will be made using a
multivariate T² test, with a Type I error rate (α) of 0.05. The means at each time point, before applying the multiplier
(1), are assumed to be 0 -4 -3 0. The contrast is Quadratic {1 -1 -1 1}. The value of the contrast applied to the
assumed means is 7. 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 obtain a power of 90%, 21 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%	21	27	6
20%	34	43	9
20%	7	9	2
20%	10	13	3
20%	5	7	2
20%	6	8	2

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 power is computed. If N subjects are evaluated out of the N' subjects that are enrolled in the study, the design will achieve the stated power.
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, 27 subjects should be enrolled to obtain a final sample size of 21 subjects.

References

Maxwell, S.E. and Delaney, H.D. 2003. Designing Experiments and Analyzing Data, 2nd Edition. Psychology Press. New York.

Davis, Charles S. 2002. Statistical Methods for the Analysis of Repeated Measurements. Springer. New York, New York.

Rencher, Alvin C. 1998. Multivariate Statistical Inference and Applications. John Wiley. New York, New York.

Vonesh, E.F. and Schork, M.A. 1986. 'Sample Sizes in the Multivariate Analysis of Repeated Measurements.' Biometrics, Volume 42, pages 601-610.

Overall, J.E. and Doyle, S.R. 1994. 'Estimating Sample Sizes for Repeated Measurement Designs.' Controlled Clinical Trials, Volume 15, pages 100-123.

This report gives the power for each value of the other parameters. The definitions are shown in the report.

Plots Section
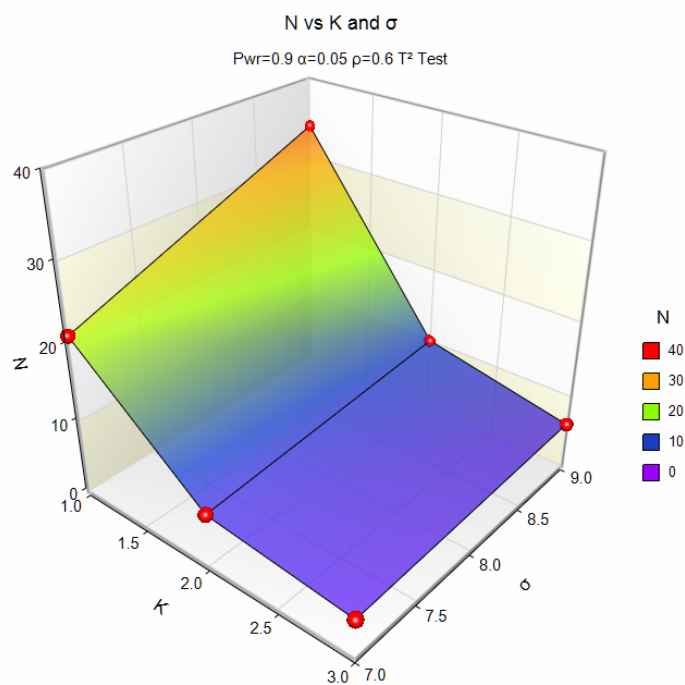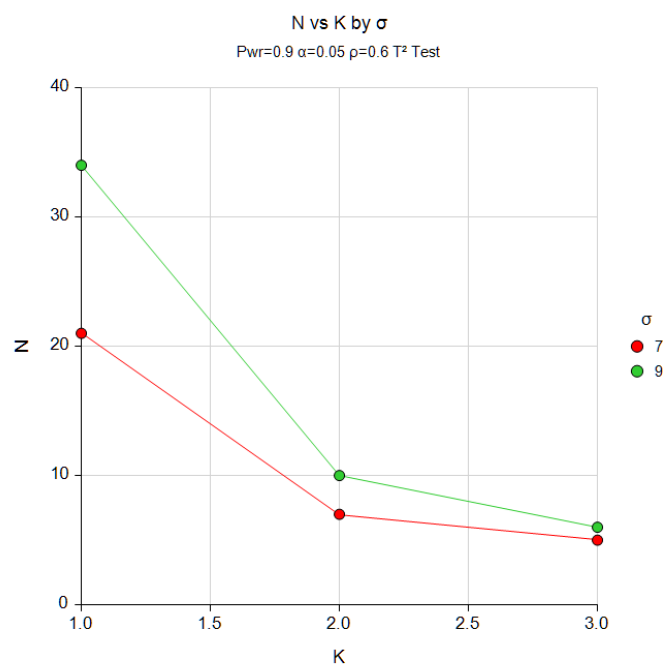
Plots
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The plots show the relationship between N, K, and σ when the other parameters in the design are held constant.

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:

Test Statistic	**Multivariable**
M	**3**
Means	**1, 2, 3**
K	**1**
Coefficients	**-2, 1, 1**
σ	**5**
ρ	**0.5**
Covariance Type	**AR(1)**
Alpha	**0.05**
N	**100**

Using these values, we find the following

C'μ	**3**
C'ΣC	**100**
Δ	**0.3**
F 0.95,1,99	**3.9371169**
Non-Centrality	**9**

The above results in

Power = 0.8439

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 ....**Power**
Test Statistic Type ....**Multivariate**
Alpha...**0.05**
N (Subjects) **100**
M (Measurements)..**3**
Means ....**List**
Means – List Values......................................**1 2 3**
K (Mean Multipliers)......................................**1**
Contrast Coefficients....................................**List**
Contrast – Custom List ....**-2 1 1**
Pattern of σ's Across Time............................**Equal**
σ (Standard Deviation)..................................**5**
Pattern of ρ's Across Time............................**AR(1)**
ρ (Correlation)...**0.5**

Output

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

Numeric Results
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Solve For: Power
Test Type: Multivariate T² Test
Means: 1 2 3
Contrast: -2 1 1
ρ's: AR(1)
σi's: All Equal
───

			Means			Within-		
	Sample	Number of	───────────────		Standard	Subject		
	Size	Measurements	Multiplier	Contrast	Deviation	Correlation		
Power	N	M	K	$\Sigma c\mu$	σ	ρ	Alpha	
0.8439	100	3	1	3	5	0.5	0.05	

PASS's power of 0.8439 matches what we obtained above by hand.