Chapter 201

Tests for Two Proportions in a Repeated Measures Design

Introduction

This module calculates the power for testing the time-averaged difference (TAD) between two proportions in a *repeated measures* design. A repeated measures design is one in which subjects are observed repeatedly over time. Measurements may be taken at pre-determined intervals (e.g., weekly or at specified time points following the administration of a particular treatment), or at random times with variable intervals between repeated measurements.

This type of time-averaged difference analysis is often used when the outcome to be measured varies with time. For example, suppose that you want to compare two treatment groups based on a certain binary response variable such as the presence (or absence) of a disease. The disease status may change over time, depending on various factors unrelated to the treatment. The precision of the experiment is increased by taking multiple measurements from each individual and comparing the time-averaged difference in proportions between the two groups. Care must be taken in the analysis because of the correlation that is introduced when several measurements are taken from the same individual. The covariance structure may take on several forms depending on the nature of the experiment and the subjects involved. This procedure allows you to calculate sample sizes and power using four different covariance patterns: Compound Symmetry, AR(1), Banded(1), and Simple.

This procedure can be used to calculate sample size and power for tests of pairwise contrasts in a mixed models analysis of repeated measures data. Mixed models analysis of repeated measures data is also employed to provide more flexibility in covariance specification and a greater degree of robustness in the presence of missing data, provided that the data can be assumed to be missing at random.

Technical Details

Two Test Statistics

This routine has the capability of calculating power and sample size for testing time-averaged difference in proportions based on two different test statistics. The first test statistic is presented in Liu and Wu (2005) and Diggle et al. (1994). The test statistic is based on the difference in proportions:

$$d = p_1 - p_2,$$

and has the form

$$z = \frac{\hat{p}_1 - \hat{p}_2}{\sqrt{\mathrm{var}(\hat{p}_1 - \hat{p}_2)}}.$$

The second type of test statistic, presented in Brown and Prescott (2006), has application to mixed models analysis of repeated measures data where there aren't any random effects other than the subjects themselves, and is based on the difference in proportions defined on the logit link scale:

$$d = \log(OR) = \log\left(\frac{p_1}{1 - p_1}\right) - \log\left(\frac{p_2}{1 - p_2}\right) = \text{logit}(p_1) - \text{logit}(p_2),$$

and has the form

$$z = \frac{\text{logit}(\hat{p}_j) - \text{logit}(\hat{p}_h)}{\sqrt{\text{var}(\text{logit}(\hat{p}_j) - \text{logit}(\hat{p}_h))}}.$$

Testing the Time-Averaged Difference between Two Proportions

Theory and Notation

The following derivation is based on the results in Liu and Wu (2005). For a study with n_1 subjects in group 1, having success proportion p_1, and n_2 subjects in group 2, having success proportion p_2 (for a total of N subjects), each measured m times, the time-averaged difference ($d = p_1 - p_2$) in proportions between the two groups can be estimated using the following model:

$$E(y_{ij}|x_{ij}) = \Pr(y_{ij} = 1|x_{ij}) = \beta_0 + \beta_1 x_{ij}, \quad i = 1, \cdots, N; j = 1, \cdots, m,$$

where

y_{ij} is the jth binary response from subject i,

β_0 is the model intercept,

β_1 is the treatment effect or the time-averaged difference in proportions between groups 1 and 2 (i.e., $\beta_1 = d$),

x_{ij} is a binary group assignment variable, which is equal to 1 if the ith subject is in group 1 and equal to 0 if the ith subject is in group 2.

The proportions used to find the difference might be expressed directly as p_1 and p_2, or indirectly as p_2 and an odds ratio

$$\psi = \frac{p_1(1 - p_1)}{p_2(1 - p_2)} = \frac{p_1 q_2}{p_2 q_1}.$$

The proportion from group 1 can then be computed as

$$p_1 = \frac{\psi p_2}{1 - p_2 + \psi p_2}.$$

Accounting for the relationship between repeated measurements, the model presented above can be written in matrix form as

$$E(\boldsymbol{y}_i|x_i) = \boldsymbol{X}_i'\boldsymbol{\beta} \,,$$

where

$\boldsymbol{y}_i = (y_{i1} \quad y_{i2} \quad \cdots \quad y_{im})'$ is an $m \times 1$ vector of responses from subject i,

$$\boldsymbol{X}_i = \begin{pmatrix} 1 & 1 \\ 1 & 1 \\ \vdots & \vdots \\ 1 & 1 \end{pmatrix}_{m \times 2} \quad \text{if the } i^{\text{th}} \text{ subject is in group 1,}$$

$$\boldsymbol{X}_i = \begin{pmatrix} 1 & 0 \\ 1 & 0 \\ \vdots & \vdots \\ 1 & 0 \end{pmatrix}_{m \times 2} \quad \text{if the } i^{\text{th}} \text{ subject is in group 2, and}$$

$\boldsymbol{\beta} = \begin{pmatrix} \beta_0 \\ \beta_1 \end{pmatrix}$ is the vector of model parameters.

We can stack the data in a single vector and matrix form as follows:

$$\boldsymbol{y} = (\boldsymbol{y}_1', \boldsymbol{y}_2', \dots, \boldsymbol{y}_N')'$$

$$\mathbf{X} = (\mathbf{X}_1', \mathbf{X}_2', \cdots, X_N')'$$

and the model for the N equations can be compressed into one as

$$E(\boldsymbol{y}|\boldsymbol{x}) = \boldsymbol{X}'\boldsymbol{\beta} \,,$$

with

$$\mathbf{V} = \text{var}(\boldsymbol{y})$$

$$= \sigma^2 \begin{pmatrix} \mathbf{R}_1 & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \ddots & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{R}_N \end{pmatrix}$$

$$= \sigma^2 \mathbf{R}$$

as the covariance (or variance-covariance) matrix.

Model Estimation

With $\widehat{\boldsymbol{V}} = \hat{\sigma}^2 \widehat{\boldsymbol{R}}$, then estimates of the regression coefficients from the above regression model are given as

$$\widehat{\boldsymbol{\beta}} = \begin{pmatrix} \hat{\beta}_0 \\ \hat{\beta}_1 \end{pmatrix}$$

$$= \left(\mathbf{X}'\widehat{\mathbf{V}}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}'\widehat{\mathbf{V}}^{-1}\mathbf{y},$$

and the variance of $\widehat{\boldsymbol{\beta}}$ is estimated as

$$\text{var}(\widehat{\boldsymbol{\beta}}) = \begin{pmatrix} \text{var}(\hat{\beta}_0) & \text{cov}(\hat{\beta}_0, \hat{\beta}_1) \\ \text{cov}(\hat{\beta}_0, \hat{\beta}_1) & \text{var}(\hat{\beta}_1) \end{pmatrix}$$

$$= \left(\mathbf{X}'\widehat{\mathbf{V}}^{-1}\mathbf{X}\right)^{-1}$$

$$= \hat{\sigma}^2 \left(\mathbf{X}'\widehat{\mathbf{R}}^{-1}\mathbf{X}\right)^{-1}.$$

Since the data are binary, the variance term σ^2 depends on the proportions p_1 and p_2. Under the null hypothesis, H_0, the estimate of σ^2 is

$$\hat{\sigma}_0^2 = \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}\left(1 - \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}\right)$$

$$= \frac{(n_1 p_1 + n_2 p_2)(n_1 q_1 + n_2 q_2)}{(n_1 + n_2)^2}$$

where $q_1 = 1 - p_1$ and $q_2 = 1 - p_2$. Under the alternative hypothesis, H_1, the estimate of σ^2 is

$$\hat{\sigma}_1^2 = \frac{n_1}{n_1 + n_2}p_1 q_1 + \frac{n_2}{n_1 + n_2}p_2 q_2$$

$$= \frac{n_1 p_1 q_1 + n_2 p_2 q_2}{n_1 + n_2}.$$

The estimated variance of $\hat{\beta}_1$ under the null hypothesis is

$$\text{var}(\hat{\beta}_1 | H_0) = \hat{\sigma}_{\beta_1, H_0}^2 = \hat{\sigma}_0^2 \left[(\mathbf{X}'\widehat{\mathbf{R}}^{-1}\mathbf{X})^{-1}\right]_{11},$$

and the estimated variance of $\hat{\beta}_1$ under the alternative hypothesis is

$$\text{var}(\hat{\beta}_1 | H_1) = \hat{\sigma}_{\beta_1, H_1}^2 = \hat{\sigma}_1^2 \left[(\mathbf{X}'\widehat{\mathbf{R}}^{-1}\mathbf{X})^{-1}\right]_{11},$$

where $[A]_{11}$ denotes the lower right-hand element of a 2 × 2 matrix, A.

Hypothesis Test

A two-sided test of the null hypothesis that the time-averaged difference in proportions is equal to zero is equivalent to the test of $H_0: \beta_1 = 0$ vs. $H_1: \beta_1 \neq 0$. Similarly, the upper and lower one-sided tests are $H_0: \beta_1 \leq 0$ vs. $H_1: \beta_1 > 0$ and $H_0: \beta_1 \geq 0$ vs. $H_1: \beta_1 < 0$, respectively. The test can be carried out using the test statistic

$$z = \frac{\hat{\beta}_1}{\sqrt{\text{var}(\hat{\beta}_1)}} = \frac{\hat{p}_1 - \hat{p}_2}{\sqrt{\text{var}(\hat{p}_1 - \hat{p}_2)}} \rightarrow N(0,1).$$

Power Calculations

Sample sizes for repeated measures studies are often calculated as if a simple trial with no repeated measures was planned, which results in a higher calculated sample size than would be found if the correlation between repeated measures were taken into consideration. With an idea of the correct covariance structure, and an estimate of the within-patient correlation, you can get a better estimate of the power and sample size necessary to achieve your objectives. If you have no indication of the correct covariance structure for the experiment, then the compound symmetry (program default) is likely to be adequate. If you have no previous estimate of the within-patient correlation, then Brown and Prescott (2006) suggest using a conservative prediction of the correlation, i.e., a higher correlation than anticipated.

For a two-sided test where it is assumed that d > 0 (without loss of generality),

$$\text{Power} = 1 - \beta = \Pr(\text{rejecting } H_0 | H_1)$$

$$= \Pr\left(\left| \frac{\hat{\beta}_1}{\sqrt{\text{var}(\hat{\beta}_1)}} \right| > z_{1-\alpha/2} | H_1 \right)$$

$$\approx \Pr\left(\frac{\hat{\beta}_1}{\sqrt{\text{var}(\hat{\beta}_1)}} > z_{1-\alpha/2} | H_1 \right) \quad \text{since it is assumed that } d > 0$$

$$= \Pr\left(\frac{\hat{\beta}_1 - d}{\hat{\sigma}_{\overline{\beta}_1, H_0}} > z_{1-\alpha/2} - \frac{d}{\hat{\sigma}_{\overline{\beta}_1, H_0}} | H_1 \right)$$

$$= \Pr\left(\frac{\hat{\beta}_1 - d}{\hat{\sigma}_{\overline{\beta}_1, H_1}} \cdot \frac{\hat{\sigma}_{\overline{\beta}_1, H_1}}{\hat{\sigma}_{\overline{\beta}_1, H_0}} > z_{1-\alpha/2} - \frac{d}{\hat{\sigma}_{\overline{\beta}_1, H_0}} | H_1 \right)$$

$$= \Pr\left(\frac{\hat{\beta}_1 - d}{\hat{\sigma}_{\overline{\beta}_1, H_1}} > \frac{\hat{\sigma}_{\overline{\beta}_1, H_0}}{\hat{\sigma}_{\overline{\beta}_1, H_1}} \cdot z_{1-\alpha/2} - \frac{d}{\hat{\sigma}_{\overline{\beta}_1, H_1}} | H_1 \right)$$

$$= 1 - \Phi\left(\frac{\hat{\sigma}_{\overline{\beta}_1, H_0}}{\hat{\sigma}_{\overline{\beta}_1, H_1}} \cdot z_{1-\alpha/2} - \frac{d}{\hat{\sigma}_{\overline{\beta}_1, H_1}} \right),$$

where $\Phi()$ is the standard normal density function, and α and β are the probabilities of type I and type II error, respectively. For a one-sided test, α is used in place of $\alpha/2$.

Testing Two Proportions using the Time-Averaged Difference defined on the Logit Link Scale (Testing Pairwise Contrasts of Fixed Effects in Mixed Models)

Mixed Models Theory and Notation

The following derivation is based on the results in Brown and Prescott (2006) and Liu and Wu (2005). A generalized linear mixed model incorporates both fixed and random effects. Fixed effects are those effects in the model whose values are assumed constant, or unchanging. Random effects are those effects in the model that are assumed to have arisen from a distribution, resulting in another source of random variation other than residual variation. For an experiment with N subjects, p fixed effect parameters, and q random effect parameters, the generalized linear mixed model can be expressed using matrix notation as

$$\boldsymbol{y}_i = \boldsymbol{\mu}_i + \boldsymbol{\varepsilon}_i, \quad i = 1, \cdots, N$$

where

$\boldsymbol{y}_i$ is an $n_i \times 1$ vector of responses for subject i,

$\boldsymbol{\mu}_i$ is an $n_i \times 1$ vector of expected means for subject i, and is linked to the model parameters by a link function, g:

$$g(\boldsymbol{\mu}_i) = \operatorname{logit}(\boldsymbol{\mu}_i) = \begin{pmatrix} \log(\pi_i/(1-\pi_i)) \\ \log(\pi_i/(1-\pi_i)) \\ \vdots \\ \log(\pi_i/(1-\pi_i)) \end{pmatrix}_{n_i \times 1} = \boldsymbol{X}_i\boldsymbol{\beta} + \boldsymbol{Z}_i\boldsymbol{u}_i, \quad i = 1, \cdots, N$$

where

π_i is the probability of success from a bernoulli distribution for individual i,

$\boldsymbol{X}_i$ is an $n_i \times p$, full-rank design matrix of fixed effects for subject i,

$\boldsymbol{\beta}$ is a $p \times 1$ vector of fixed effects parameters,

$\boldsymbol{Z}_i$ is an $n_i \times q$ design matrix of the random effects for subject i,

$\boldsymbol{u}_i$ is a $q \times 1$ vector of random effects for subject i which has means of zero and scaled covariance matrix **G**,

$\boldsymbol{\varepsilon}_i$ is an $n_i \times 1$ vector of errors for subject i with zero mean and scaled covariance $\boldsymbol{\Sigma}_i$.

We can stack the data in a single vector and matrix form as follows:

$$\mathbf{y} = (\mathbf{y}_1, \mathbf{y}_2, \ldots, \mathbf{y}_N)'$$

$$\boldsymbol{\mu} = (\boldsymbol{\mu}_1, \boldsymbol{\mu}_2, \ldots, \boldsymbol{\mu}_N)'$$

$$\mathbf{X} = (\mathbf{X}_1, \mathbf{X}_2, \cdots, \mathbf{X}_N)'$$

$$\mathbf{Z} = \begin{pmatrix} \mathbf{Z}_1 & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \ddots & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{Z}_N \end{pmatrix}$$

$$\mathbf{u} = (\mathbf{u}_1, \mathbf{u}_2, \ldots, \mathbf{u}_N)'$$

$$\boldsymbol{\varepsilon} = (\boldsymbol{\varepsilon}_1, \boldsymbol{\varepsilon}_2, \ldots, \boldsymbol{\varepsilon}_N)'$$

and the mixed model for the *N* equations can be compressed into one as

$$y = \mu + \varepsilon$$

with

$$g(\boldsymbol{\mu}) = \operatorname{logit}(\boldsymbol{\mu}) = \boldsymbol{X\beta} + \boldsymbol{Zu} \, .$$

The covariance of $\mathbf{y}$, $\operatorname{var}(\mathbf{y}) = \boldsymbol{V}$, can then be written as

$$\mathbf{V} = \begin{pmatrix} \mathbf{V}_1 & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \ddots & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{V}_N \end{pmatrix}$$

$$= \operatorname{var}(\boldsymbol{\mu} + \boldsymbol{\varepsilon})$$

$$= \operatorname{var}(\boldsymbol{\mu}) + \boldsymbol{\Sigma}$$

$$\approx \mathbf{BZGZ'B} + \mathbf{B}^{1/2}\mathbf{RB}^{1/2},$$

where

$$\boldsymbol{B} = \begin{pmatrix} \pi_1(1-\pi_1) & 0 & 0 & 0 \\ 0 & \pi_2(1-\pi_2) & 0 & 0 \\ 0 & 0 & \ddots & \vdots \\ 0 & 0 & \cdots & \pi_N(1-\pi_N) \end{pmatrix}$$

R is the correlation matrix defined on the linear scale.

Mixed Models Estimation

In order to fit the generalized linear mixed model, a pseudo-variable **z** must be introduced to transform **y** onto the linear scale. More specifically,

$$\mathbf{z} = g(\mathbf{\mu}) + (\mathbf{y} - \mathbf{\mu})\mathbf{B}^{-1}$$

$$= \mathbf{X\beta} + \mathbf{Zu} + (\mathbf{y} - \mathbf{\mu})\mathbf{B}^{-1}$$

and **z** has variance

$$\mathbf{V_z} = \text{var}(\mathbf{X\beta} + \mathbf{Zu}) + \mathbf{B}^{-1}\text{var}(\mathbf{y} - \mathbf{\mu})\mathbf{B}^{-1}$$

$$= \mathbf{ZGZ'} + \mathbf{B}^{-1/2}\mathbf{R}\mathbf{B}^{-1/2}$$

If $\mathbf{ZGZ'} = \mathbf{0}$ (which is the case when no random effects are included in the model), then

$$\mathbf{V_z} = \mathbf{B}^{-1/2}\mathbf{R}\mathbf{B}^{-1/2}.$$

Estimates of the variance components are found using maximum likelihood (ML) or restricted/residual maximum likelihood (REML) methods. The fixed effects are then estimated as

$$\widehat{\mathbf{\beta}} = (\mathbf{X'}\widehat{\mathbf{V}}_\mathbf{z}^{-1}\mathbf{X})^{-1}\mathbf{X'}\widehat{\mathbf{V}}_\mathbf{z}^{-1}\mathbf{y}$$

with the variance estimated as

$$\text{var}(\widehat{\mathbf{\beta}}) = (\mathbf{X'}\widehat{\mathbf{V}}_\mathbf{z}^{-1}\mathbf{X})^{-1}$$

These estimation equations are nearly identical to the TAD estimation equations presented earlier, except for the fact that **β** may contain more than two parameters, i.e., a parameter for each fixed effect being modeled. In the TAD model presented above, β_1 represents the difference between two treatment proportions. In the generalized mixed model formulation presented here, β_1, β_2, etc. represent individual proportions defined on the logit link scale.

Testing Fixed Effects

Significance tests for fixed or random effects can be done using tests based on the *t* distribution. We can define tests of fixed and random effects as contrasts

$$\mathbf{C} = \mathbf{L'}\widehat{\mathbf{\beta}} = \mathbf{0},$$

respectively. For example, in a trial containing three treatments A, B, and C, a pairwise comparison of treatments A and C is given by the contrast

$$\mathbf{C}_{AC} = \mathbf{L'}\widehat{\mathbf{\beta}} = (0 \quad 1 \quad 0 \quad -1)\widehat{\mathbf{\beta}} = \hat{\beta}_A - \hat{\beta}_C,$$

where the first term in **β** is the intercept term, and the other three terms are the treatment effects.

For a single comparison, the Wald test statistic is given by

$$z = \frac{\mathbf{L'}\hat{\boldsymbol{\beta}}}{\sqrt{\text{var}(\mathbf{L'}\hat{\boldsymbol{\beta}})}}$$

$$= \frac{\hat{\beta}_j - \hat{\beta}_h}{\sqrt{\text{var}(\hat{\beta}_j - \hat{\beta}_h)}}$$

$$= \frac{\text{logit}(\hat{p}_j) - \text{logit}(\hat{p}_h)}{\sqrt{\text{var}\left(\text{logit}(\hat{p}_j) - \text{logit}(\hat{p}_h)\right)}} \rightarrow N(0,1),$$

where $\hat{\beta}_j$ and $\hat{\beta}_h$ ($j \neq h$) are estimated treatment effects defined on the logit link scale and p_j and p_h are the proportions from groups j and h, respectively.

Since the data are binary, $\text{var}(\hat{\beta}_j - \hat{\beta}_h)$ depends on the proportions p_j and p_h. Under the null hypothesis, H_0, the estimate of $\text{var}(\hat{\beta}_j - \hat{\beta}_h)$ is

$$\text{var}(\hat{\beta}_j - \hat{\beta}_h | H_0) = \hat{\sigma}^2_{\hat{\beta}_j - \hat{\beta}_h, H_0}$$

$$= \mathbf{L'}\left(\mathbf{X'}\hat{\mathbf{V}}_{\mathbf{z}}^{-1}\mathbf{X}\right)^{-1}\mathbf{L}$$

$$= \frac{\left(n_j + n_h\right)^2}{\left(n_j p_j + n_h p_h\right)\left(n_j q_j + n_h q_h\right)}\mathbf{L'}(\mathbf{X'}\hat{\mathbf{R}}^{-1}\mathbf{X})^{-1}\mathbf{L},$$

where $q_k = 1 - p_k$. Under the alternative hypothesis, H_1, the estimate of $\text{var}(\hat{\beta}_j - \hat{\beta}_h)$ is

$$\text{var}(\hat{\beta}_j - \hat{\beta}_h | H_1) = \hat{\sigma}^2_{\hat{\beta}_j - \hat{\beta}_h, H_1}$$

$$= \mathbf{L'}\left(\mathbf{X'}\hat{\mathbf{V}}_{\mathbf{z}}^{-1}\mathbf{X}\right)^{-1}\mathbf{L}$$

$$= \frac{n_j + n_h}{n_j p_j q_j + n_h p_h q_h}\mathbf{L'}(\mathbf{X'}\hat{\mathbf{R}}^{-1}\mathbf{X})^{-1}\mathbf{L},$$

In practice, the test is often performed using software containing generalized linear models capability, such as SAS® `PROC GLIMMIX` or SAS® `PROC GENMOD` with a `REPEATED` statement. The test of the difference in proportions is generated with an estimation statement such as

```
ESTIMATE 'A-C' treat 1 0 -1;   or   LSMEANS treat/ PDIFF;
```

The latter statement would produce tests of all pairwise comparisons of the levels of the treatment variable, defined on the logit link scale. The former would only test the difference between groups A and C. Of course, these comparison statements must be used in conjunction with appropriate model and class statements.

Power Calculations

Sample sizes for repeated measures studies are often calculated as if a simple trial with no repeated measures was planned, which results in a higher calculated sample size than would be found if the correlation between repeated measures were taken into consideration. With an idea of the correct covariance structure, and an estimate of the within-patient correlation, you can get a better estimate of the power and sample size necessary to achieve your objectives. If you have no indication of the correct covariance structure for the experiment, then the compound symmetry (program default) is likely to be adequate. If you have no previous estimate of the within-patient correlation, then Brown and Prescott (2006) suggest using a conservative prediction of the correlation, i.e., a higher correlation than anticipated.

For a two-sided test where it is assumed that $\hat{\beta}_j - \hat{\beta}_h > 0$ (without loss of generality),

$$\text{Power} = 1 - \beta = \Pr(\text{rejecting } H_0 | H_1)$$

$$= \Pr\left(\left|\frac{\hat{\beta}_j - \hat{\beta}_h}{\sqrt{\text{var}(\hat{\beta}_j - \hat{\beta}_h)}}\right| > z_{1-\alpha/2} | H_1\right)$$

$$\approx \Pr\left(\frac{\hat{\beta}_j - \hat{\beta}_h}{\sqrt{\text{var}(\hat{\beta}_j - \hat{\beta}_h)}} > z_{1-\alpha/2} | H_1\right) \text{ since it is assumed that } d > 0$$

$$= \Pr\left(\frac{\hat{\beta}_1 - d}{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_0}} > z_{1-\alpha/2} - \frac{d}{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_0}} | H_1\right)$$

$$= \Pr\left(\frac{\hat{\beta}_j - \hat{\beta}_h - d}{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_1}} \cdot \frac{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_1}}{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_0}} > z_{1-\alpha/2} - \frac{d}{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_0}} | H_1\right)$$

$$= \Pr\left(\frac{\hat{\beta}_1 - d}{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_1}} > \frac{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_0}}{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_1}} \cdot z_{1-\alpha/2} - \frac{d}{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_1}} | H_1\right)$$

$$= 1 - \Phi\left(\frac{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_0}}{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_1}} \cdot z_{1-\alpha/2} - \frac{d}{\hat{\sigma}_{\hat{\beta}_j - \hat{\beta}_h, H_1}}\right),$$

where $\Phi()$ is the standard normal density function, and α and β are the probabilities of type I and type II error, respectively. For a one-sided test, α is used in place of $\alpha/2$.

Covariance Patterns

In a repeated measures design with N subjects, each measured m times, observations from a single subject may be correlated and a pattern for their covariance is specified. In this case, **V** will have a block-diagonal form and can be written as

$$V = \sigma^2 R = \begin{pmatrix} V_1 & 0 & 0 & \cdots & 0 \\ 0 & V_2 & 0 & \cdots & 0 \\ 0 & 0 & V_3 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & \cdots & V_N \end{pmatrix}$$

where $\mathbf{V}_i$ are $m \times m$ covariance matrices corresponding to the ith subject. The **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: Compound Symmetry, AR(1), Banded(1), and Simple.

Compound Symmetry

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

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

where $\sigma^2 = \text{var}(y_{ij})$ 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 $\sigma^2 \rho^t$. That is

$$\mathbf{V}_i = \sigma^2 \begin{pmatrix} 1 & \rho & \rho^2 & \rho^3 & \cdots & \rho^{m-1} \\ \rho & 1 & \rho & \rho^2 & \cdots & \rho^{m-2} \\ \rho^2 & \rho & 1 & \rho & \cdots & \rho^{m-3} \\ \rho^3 & \rho^2 & \rho & 1 & \cdots & \rho^{m-4} \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ \rho^{m-1} & \rho^{m-2} & \rho^{m-3} & \rho^{m-4} & \cdots & 1 \end{pmatrix}_{m \times m}$$

where $\sigma^2 = \text{var}(y_{ij})$ 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 $\sigma^2\rho$, and covariances for measurements greater than one time period apart are equal to zero. That is

$$\boldsymbol{V}_i = \sigma^2 \begin{pmatrix} 1 & \rho & 0 & 0 & \cdots & 0 \\ \rho & 1 & \rho & 0 & \cdots & 0 \\ 0 & \rho & 1 & \rho & \cdots & 0 \\ 0 & 0 & \rho & 1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & 1 \end{pmatrix}_{m \times m}$$

where $\sigma^2 = \text{var}(y_{ij})$ and ρ is the correlation between observations on the same subject.

Simple

A simple covariance model assumes that all variances on the diagonal are equal and that all covariances are equal to zero. That is

$$\boldsymbol{V}_i = \sigma^2 \begin{pmatrix} 1 & 0 & 0 & 0 & \cdots & 0 \\ 0 & 1 & 0 & 0 & \cdots & 0 \\ 0 & 0 & 1 & 0 & \cdots & 0 \\ 0 & 0 & 0 & 1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & 1 \end{pmatrix}_{m \times m}$$

where $\sigma^2 = \text{var}(y_{ij})$.

Example 1 – Determining Power

A study is being planned to determine the efficacy of a prophylactic treatment for the common cold. The study will follow a treatment group and placebo control group through the winter to determine if there is an overall difference between the two treatment groups in the proportion of patients who get sick. Subjects will take the treatment (or placebo) once daily throughout the duration of the study. The study will be conducted from September to April with scheduled, monthly visits (beginning in October) to determine the patient's disease status (present or absent). Therefore, a total of seven responses will be observed for each patient. Previous studies have indicated a baseline disease rate of 60% for the common cold. The researchers want to be able to detect a treatment to control odds ratio of 0.5 (an odds ratio of 0.5 corresponds to a treatment group proportion of 0.4285714). A compound-symmetry covariance pattern with autocorrelation of 0.5 is assumed to be adequate. The test will be conducted using a mixed models analysis with an alpha level of 0.05.

What power does the study achieve over a range of possible sample sizes?

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 ....**Power**
Test Statistic Based on ....**Log(OR): logit(P1)-logit(P2)**
Alternative Hypothesis ....**Two-Sided**
Alpha...**0.05**
Group Allocation ....**Equal (N1 = N2)**
Sample Size Per Group ....**10 to 100 by 10**
Input Type..**Proportions or Odds Ratios**
P1 (*If using Proportions*) **0.4285714**
OR1 (*If using Odds Ratios*)...........................**0.5**
P2 ....**0.6**
M...**7**
Covariance Type..**Compound Symmetry**
Rho **0.5**

Output

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

Numeric Reports

Numeric Results

Solve For: Power
Test Statistic: Based on Log(OR): logit(P1) - logit(P2)
Hypotheses: Two-Sided. H0: OR = 1   vs.   H1: OR ≠ 1
Covariance Type: Compound Symmetry

| | Sample Size | | | Number of Time Points | Proportion | | Odds Ratio | Autocorrelation | |
Power	N1	N2	N	M	P1	P2	OR1	Rho	Alpha
0.17843	10	10	20	7	0.429	0.6	0.5	0.5	0.05
0.30742	20	20	40	7	0.429	0.6	0.5	0.5	0.05
0.42768	30	30	60	7	0.429	0.6	0.5	0.5	0.05
0.53515	40	40	80	7	0.429	0.6	0.5	0.5	0.05
0.62800	50	50	100	7	0.429	0.6	0.5	0.5	0.05
0.70610	60	60	120	7	0.429	0.6	0.5	0.5	0.05
0.77040	70	70	140	7	0.429	0.6	0.5	0.5	0.05
0.82241	80	80	160	7	0.429	0.6	0.5	0.5	0.05
0.86386	90	90	180	7	0.429	0.6	0.5	0.5	0.05
0.89646	100	100	200	7	0.429	0.6	0.5	0.5	0.05

Power   The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N1 and N2   The number of items sampled from each population.
N   The total sample size. N = N1 + N2.
M   The number of time points (repeated measurements) at which each subject is observed.
P1 and P2   The proportions from groups 1 and 2, respectively.
OR1   The odds ratio ((P1/(1 - P1))/(P2/(1 - P2))) to be detected.
Rho   The correlation between observations on the same subject.
Alpha   The probability of rejecting a true null hypothesis.

Summary Statements

A parallel two-group repeated-measures design with 7 measurements on each subject will be used to test whether the Group 1 (treatment) proportion (P1) is different from the Group 2 (control) proportion (P2). The comparison will be made using a two-sided, two-sample time-averaged difference in logit proportions test (from a generalized linear mixed model formulation) as in Brown and Prescott (2006) and Liu and Wu (2005). The Type I error rate (α) is to be 0.05. The control group proportion (P2) is assumed to be 0.6. The covariance structure for repeated observations on the same subject is Compound Symmetry, with a correlation between observations on the same subject (autocorrelation) of 0.5. To detect a Group 1 (treatment) proportion (P1) of 0.429 (or odds ratio of 0.5), with sample sizes of 10 for Group 1 (treatment) and 10 for Group 2 (control), the power is 0.17843.

Dropout-Inflated Sample Size

Dropout Rate	Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
	N1	N2	N	N1'	N2'	N'	D1	D2	D
20%	10	10	20	13	13	26	3	3	6
20%	20	20	40	25	25	50	5	5	10
20%	30	30	60	38	38	76	8	8	16
20%	40	40	80	50	50	100	10	10	20
20%	50	50	100	63	63	126	13	13	26
20%	60	60	120	75	75	150	15	15	30
20%	70	70	140	88	88	176	18	18	36
20%	80	80	160	100	100	200	20	20	40
20%	90	90	180	113	113	226	23	23	46
20%	100	100	200	125	125	250	25	25	50

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 power is computed (as entered by the user). 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 power.
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. 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, 13 subjects should be enrolled in Group 1, and 13 in Group 2, to obtain final group
sample sizes of 10 and 10, respectively.

References

Brown, H., Prescott, R., 2006. Applied Mixed Models in Medicine. 2nd ed. John Wiley & Sons Ltd. Chichester,
   West Sussex, England.
Liu, H. and Wu, T., 2005. 'Sample Size Calculation and Power Analysis of Time-Averaged Difference.' Journal of
   Modern Applied Statistical Methods, Vol. 4, No. 2, pages 434-445.
Diggle, P.J., Liang, K.Y., and Zeger, S.L., 1994. Analysis of Longitudinal Data. Oxford University Press. New York,
   New York. Chapter 2.

This report gives the power for each value of the other parameters.

Power

This is the computed power for detecting the time-averaged difference between the two group means.

Group 1 Sample Size (N1)

The value of *N1* is the number of subjects in group 1.

Group 2 Sample Size (N2)

The value of *N2* is the number of subjects in group 2.

Time Points (M)

This is the number of repeated measurements taken.

Proportion: Group 1 (P1) and Group 2 (P2)

These are the proportions of successes in groups 1 and 2, respectively.

Odds Ratio (OR1)

This is the value of the odds ratio under the alternative hypothesis.

Autocorrelation (Rho)

This is the correlation between observations from the same subject.

Alpha

Alpha is the significance level of the test.

Plots Section

Plots
_____
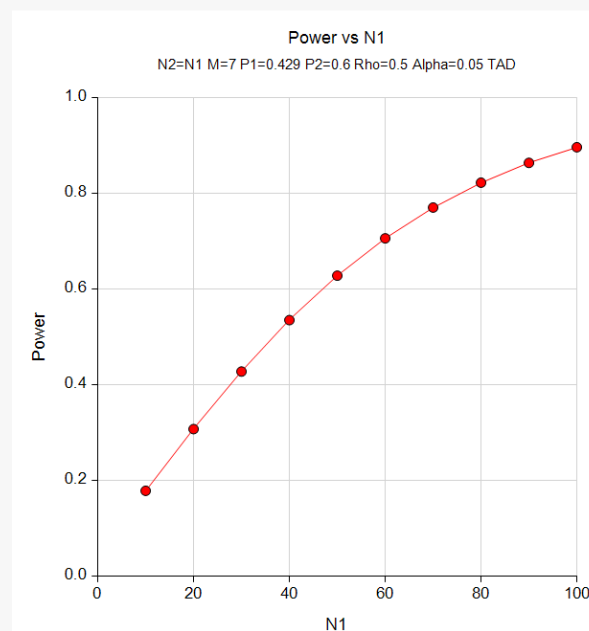
Using Proportions   **Using Odds Ratios**
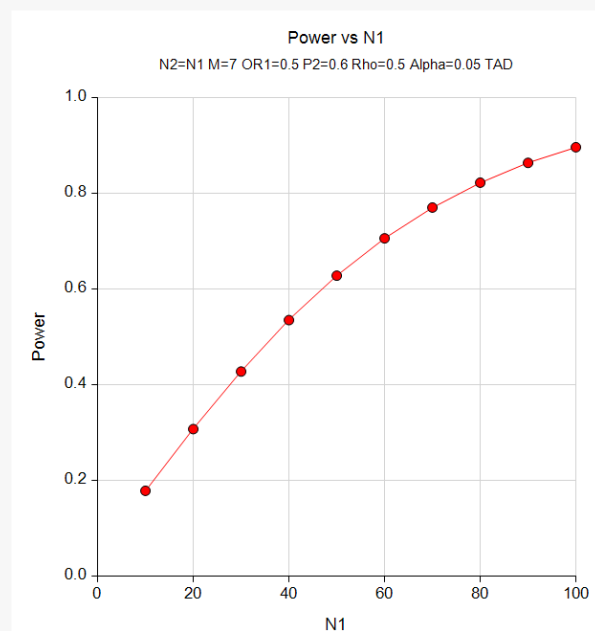
The chart shows the relationship between power and *N1* when the other parameters in the design are held constant.

Example 2 – Finding the Sample Size

Continuing with Example 1, the researchers want to determine the exact sample size necessary to achieve at least 80% power.

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**
Test Statistic Based on ....**Log(OR): logit(P1)-logit(P2)**
Alternative Hypothesis ....**Two-Sided**
Power...**0.80**
Alpha..**0.05**
Group Allocation ....**Equal (N1 = N2)**
Input Type..**Proportions or Odds Ratios**
P1 (If using Proportions) **0.4285714**
OR1 (If using Odds Ratios)...........................**0.5**
P2 ....**0.6**
M...**7**
Covariance Type...**Compound Symmetry**
Rho **0.5**

Output

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

Numeric Results
_____
Solve For: Sample Size
Test Statistic: Based on Log(OR): logit(P1) - logit(P2)
Hypotheses: Two-Sided. H0: OR = 1   vs.   H1: OR ≠ 1
Covariance Type: Compound Symmetry
_____

Power		Sample Size			Number of Time Points	Proportion		Odds Ratio	Autocorrelation		
Target	Actual	N1	N2	N	M	P1	P2	OR1	Rho	Alpha	
0.8	0.80297	76	76	152	7	0.429	0.6	0.5	0.5	0.05	

A group sample size of 76 is required to achieve at least 80% power.

Example 3 – Varying the Odds Ratio

Continuing with Examples 1 and 2, the researchers want to evaluate the impact on power of varying the odds ratio from 0.4 to 0.8.

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 ....**Power**
Test Statistic Based on ....**Log(OR): logit(P1)-logit(P2)**
Alternative Hypothesis ....**Two-Sided**
Alpha..**0.05**
Group Allocation ....**Equal (N1 = N2)**
Sample Size Per Group ....**10 to 100 by 10**
Input Type...**Odds Ratios**
OR1 ....**0.4 to 0.8 by 0.1**
P2 ....**0.6**
M..**7**
Covariance Type..**Compound Symmetry**
Rho **0.5**

Output

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

Numeric Results
───
Solve For: Power
Test Statistic: Based on Log(OR): logit(P1) - logit(P2)
Hypotheses: Two-Sided. H0: OR = 1   vs.   H1: OR ≠ 1
Covariance Type: Compound Symmetry
───

	Sample Size			Number of Time Points	Proportion		Odds Ratio	Autocorrelation	
Power	N1	N2	N	M	P1	P2	OR1	Rho	Alpha
0.27771	10	10	20	7	0.375	0.6	0.4	0.5	0.05
0.17843	10	10	20	7	0.429	0.6	0.5	0.5	0.05
0.11570	10	10	20	7	0.474	0.6	0.6	0.5	0.05
0.07634	10	10	20	7	0.512	0.6	0.7	0.5	0.05
0.05145	10	10	20	7	0.545	0.6	0.8	0.5	0.05
0.48290	20	20	40	7	0.375	0.6	0.4	0.5	0.05
0.30742	20	20	40	7	0.429	0.6	0.5	0.5	0.05
0.18749	20	20	40	7	0.474	0.6	0.6	0.5	0.05
0.11240	20	20	40	7	0.512	0.6	0.7	0.5	0.05
0.06734	20	20	40	7	0.545	0.6	0.8	0.5	0.05
0.64679	30	30	60	7	0.375	0.6	0.4	0.5	0.05
0.42768	30	30	60	7	0.429	0.6	0.5	0.5	0.05
0.25796	30	30	60	7	0.474	0.6	0.6	0.5	0.05
.	.	.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.	.	.
───

Plots

These charts show how the power depends on the odds ratio, OR1, as well as the group sample size N1.

Example 4 – Varying the Proportions

Continuing with Examples 1 and 2, the researchers want to evaluate the impact on power of varying the group 1 proportion from 0.2 to 0.5.

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 4** 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 Based on ....**Log(OR): logit(P1)-logit(P2)**
Alternative Hypothesis ....**Two-Sided**
Alpha..**0.05**
Group Allocation ....**Equal (N1 = N2)**
Sample Size Per Group ....**10 to 100 by 10**
Input Type...**Proportions**
P1 ....**0.2 to 0.5 by 0.1**
P2 ....**0.6**
M..**7**
Covariance Type..**Compound Symmetry**
Rho **0.5**

Output

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

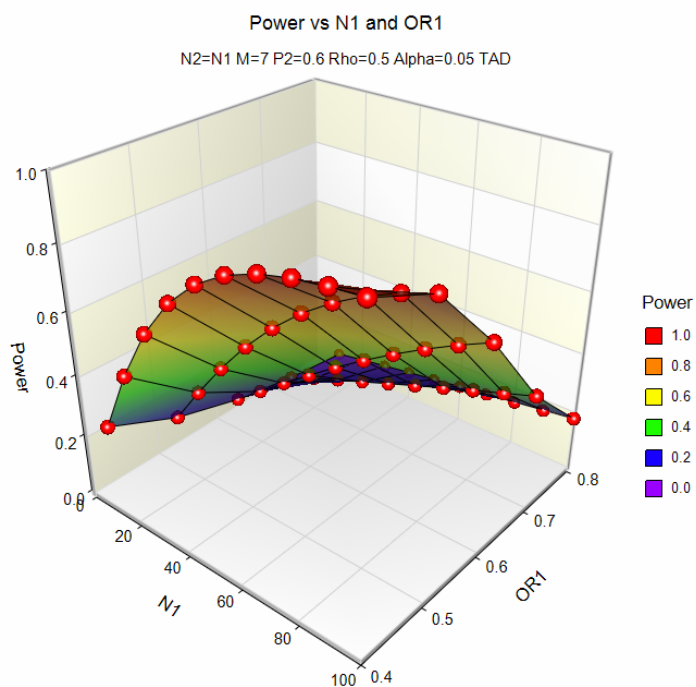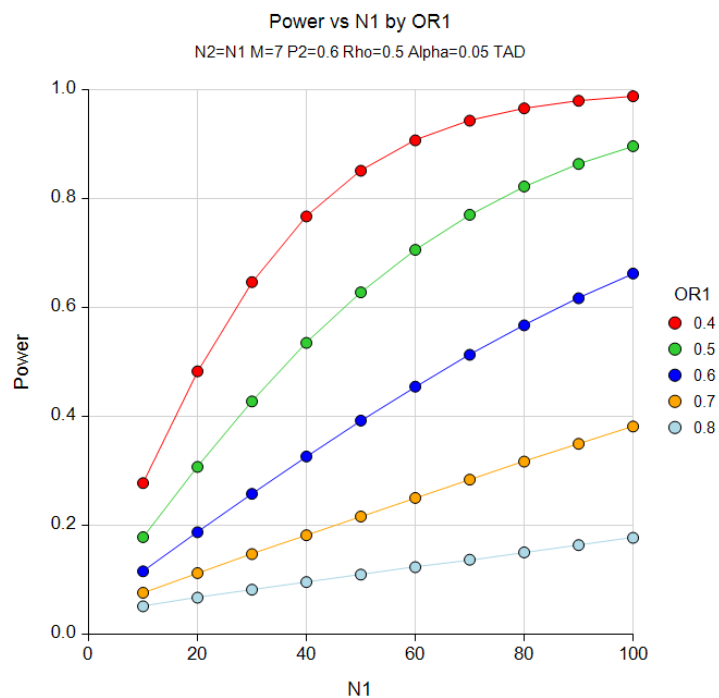**Numeric Results**
_____

Solve For: Power
Test Statistic: Based on Log(OR): logit(P1) - logit(P2)
Hypotheses: Two-Sided. H0: OR = 1   vs.   H1: OR ≠ 1
Covariance Type: Compound Symmetry
_____

| | Sample Size | | | Number of Time Points | Proportion | | Odds Ratio | Autocorrelation | |
Power	N1	N2	N	M	P1	P2	OR1	Rho	Alpha
0.71941	10	10	20	7	0.2	0.6	0.167	0.5	0.05
0.45582	10	10	20	7	0.3	0.6	0.286	0.5	0.05
0.22807	10	10	20	7	0.4	0.6	0.444	0.5	0.05
0.08749	10	10	20	7	0.5	0.6	0.667	0.5	0.05
0.94096	20	20	40	7	0.2	0.6	0.167	0.5	0.05
0.73142	20	20	40	7	0.3	0.6	0.286	0.5	0.05
0.39803	20	20	40	7	0.4	0.6	0.444	0.5	0.05
0.13340	20	20	40	7	0.5	0.6	0.667	0.5	0.05
0.98973	30	30	60	7	0.2	0.6	0.167	0.5	0.05
0.88016	30	30	60	7	0.3	0.6	0.286	0.5	0.05
0.54580	30	30	60	7	0.4	0.6	0.444	0.5	0.05
0.17832	30	30	60	7	0.5	0.6	0.667	0.5	0.05
0.99842	40	40	80	7	0.2	0.6	0.167	0.5	0.05
0.95020	40	40	80	7	0.3	0.6	0.286	0.5	0.05
0.66638	40	40	80	7	0.4	0.6	0.444	0.5	0.05
0.22282	40	40	80	7	0.5	0.6	0.667	0.5	0.05
0.99978	50	50	100	7	0.2	0.6	0.167	0.5	0.05
0.98038	50	50	100	7	0.3	0.6	0.286	0.5	0.05
0.76033	50	50	100	7	0.4	0.6	0.444	0.5	0.05
0.26678	50	50	100	7	0.5	0.6	0.667	0.5	0.05
0.99997	60	60	120	7	0.2	0.6	0.167	0.5	0.05
0.99259	60	60	120	7	0.3	0.6	0.286	0.5	0.05
0.83101	60	60	120	7	0.4	0.6	0.444	0.5	0.05
0.30999	60	60	120	7	0.5	0.6	0.667	0.5	0.05
1.00000	70	70	140	7	0.2	0.6	0.167	0.5	0.05
0.99730	70	70	140	7	0.3	0.6	0.286	0.5	0.05
0.88274	70	70	140	7	0.4	0.6	0.444	0.5	0.05
0.35221	70	70	140	7	0.5	0.6	0.667	0.5	0.05
1.00000	80	80	160	7	0.2	0.6	0.167	0.5	0.05
0.99904	80	80	160	7	0.3	0.6	0.286	0.5	0.05
0.91976	80	80	160	7	0.4	0.6	0.444	0.5	0.05
0.39323	80	80	160	7	0.5	0.6	0.667	0.5	0.05
1.00000	90	90	180	7	0.2	0.6	0.167	0.5	0.05
0.99967	90	90	180	7	0.3	0.6	0.286	0.5	0.05
0.94576	90	90	180	7	0.4	0.6	0.444	0.5	0.05
0.43288	90	90	180	7	0.5	0.6	0.667	0.5	0.05
1.00000	100	100	200	7	0.2	0.6	0.167	0.5	0.05
0.99989	100	100	200	7	0.3	0.6	0.286	0.5	0.05
0.96374	100	100	200	7	0.4	0.6	0.444	0.5	0.05
0.47102	100	100	200	7	0.5	0.6	0.667	0.5	0.05

Plots
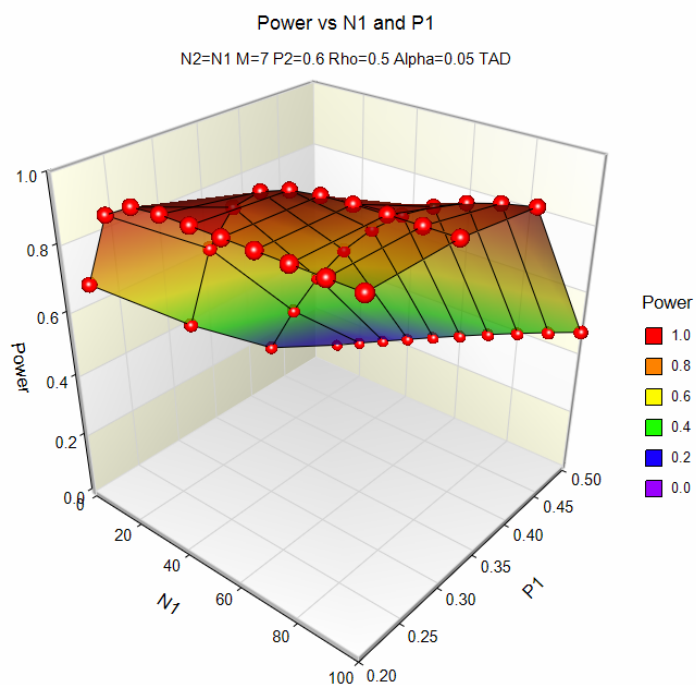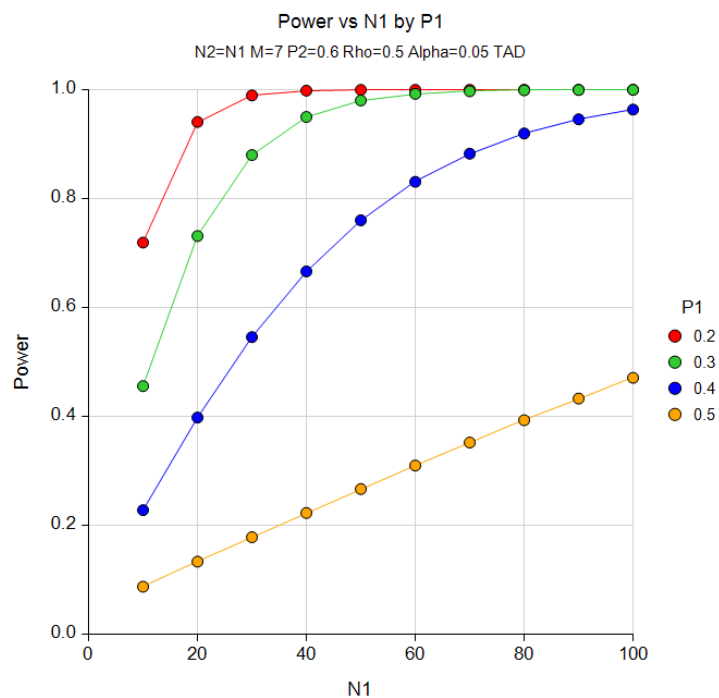
These charts show how the power depends on the proportion, P1, as well as the group sample size N1.

Example 5 – Impact of the Number of Repeated Measurements

Continuing with Example 2, the researchers want to study the impact on the sample size if they change the number of measurements made on each individual. Their experimental protocol calls for seven measurements. They want to see the impact of taking twice that many measurements.

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 5** 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 Based on ....**Log(OR): logit(P1)-logit(P2)**
Alternative Hypothesis ....**Two-Sided**
Power...**0.80**
Alpha...**0.05**
Group Allocation ....**Equal (N1 = N2)**
Input Type..**Proportions or Odds Ratios**
P1 (*If using Proportions*) **0.4285714**
OR1 (*If using Odds Ratios*)...........................**0.5**
P2 ....**0.6**
M..**7 14**
Covariance Type...**Compound Symmetry**
Rho **0.5**

Output

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

Numeric Results

Solve For: Sample Size
Test Statistic: Based on Log(OR): logit(P1) - logit(P2)
Hypotheses: Two-Sided. H0: OR = 1   vs.   H1: OR ≠ 1
Covariance Type: Compound Symmetry

Power		Sample Size			Number of Time Points	Proportion		Odds Ratio	Autocorrelation	
Target	Actual	N1	N2	N	M	P1	P2	OR1	Rho	Alpha
0.8	0.80297	76	76	152	7	0.429	0.6	0.5	0.5	0.05
0.8	0.80161	71	71	142	14	0.429	0.6	0.5	0.5	0.05

Doubling the number of repeated measurements per individual decreases the group sample size by only 5 individuals. This reduction in sample size may not justify the additional seven trips to the clinic for each subject.

Example 6 – Validation using Diggle et al. (1994)

Diggle et al. (1994) pages 31 and 32 present an example of calculating the sample size for a TAD study. They calculate the group sample sizes for the cases where the difference in proportions (P1-P2) ranges from 0.1 to 0.3, ρ ranges from 0.2 to 0.8, alpha = 0.05, p_2 = 0.5, M = 3, and power = 0.8. Note that Diggle et al (1994) uses a one-sided test and the test statistic based on the difference in proportions.

To calculate the sample sizes using the odds ratio specification, we must first convert the differences to odds ratios using the formula:

$$OR = \frac{p_1/(1-p_1)}{p_2/(1-p_2)}$$

Differences of 0.1, 0.2, and 0.3 with P2 = 0.5 correspond to odds ratios of 1.5, 2.333, and 4.0, respectively.

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 6** 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 Based on ....**Difference: P1-P2**
Alternative Hypothesis ....**One-Sided**
Power...**0.80**
Alpha..**0.05**
Group Allocation ....**Equal (N1 = N2)**
Input Type...**Proportions or Odds Ratios**
P1 (*If using Proportions*) **0.6 0.7 0.8**
OR1 (*If using Odds Ratios*)............................**1.5 2.333 4**
P2 ....**0.5**
M...**3**
Covariance Type...**Compound Symmetry**
Rho **0.2 0.5 0.8**

Output

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

Numeric Results

Solve For: Sample Size
Test Statistic: Based on Difference: P1 - P2
Hypotheses: One-Sided. H0: OR = 1   vs.   H1: OR > 1 (or OR < 1)
Covariance Type: Compound Symmetry

Power		Sample Size			Number of Time Points	Proportion		Odds Ratio	Autocorrelation	
Target	Actual	N1	N2	N	M	P1	P2	OR1	Rho	Alpha
0.8	0.80164	143	143	286	3	0.6	0.5	1.500	0.2	0.05
0.8	0.80116	204	204	408	3	0.6	0.5	1.500	0.5	0.05
0.8	0.80089	265	265	530	3	0.6	0.5	1.500	0.8	0.05
0.8	0.80882	35	35	70	3	0.7	0.5	2.333	0.2	0.05
0.8	0.80175	49	49	98	3	0.7	0.5	2.333	0.5	0.05
0.8	0.80340	64	64	128	3	0.7	0.5	2.333	0.8	0.05
0.8	0.82213	15	15	30	3	0.8	0.5	4.000	0.2	0.05
0.8	0.81509	21	21	42	3	0.8	0.5	4.000	0.5	0.05
0.8	0.81120	27	27	54	3	0.8	0.5	4.000	0.8	0.05

The sample sizes calculated by **PASS** match the results of Diggle et al. (1994) exactly.

Example 7 – Validation using Brown and Prescott (2006)

Brown and Prescott (2006) page 270 presents an example of calculating the sample size for a future study. They calculate the group sample size to be 85 for a future study involving four post-treatment visits to detect a doubling of the odds ratio (i.e., OR1 = 2) at the 5% significance level with 80% power. They assume an autocorrelation of 0.5, and an expected rate of positives ((P1+P2)/2) of 0.4. We can calculate the corresponding values of P1, P2, and OR for use in **PASS** by solving the following system of equations for P1 and P2:

$$\frac{P1 + P2}{2} = 0.4 \quad and \quad \frac{P1/(1 - P1)}{P2/(1 - P2)} = OR = 2.0$$

The solution to these equations occurs when P1 = 0.482255312124 and P2 = 0.317744687876. The decimal places are kept to make the solution exact.

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 7** 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 Based on ....**Log(OR): logit(P1)-logit(P2)**
Alternative Hypothesis ....**Two-Sided**
Power..**0.80**
Alpha..**0.05**
Group Allocation ....**Equal (N1 = N2)**
Input Type..**Proportions or Odds Ratios**
P1 (*If using Proportions*) **0.482255312124**
OR1 (*If using Odds Ratios*)............................**2.0**
P2 ....**0.317744687876**
M...**4**
Covariance Type..**Compound Symmetry**
Rho **0.5**

Output

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

Numeric Results

Solve For: Sample Size
Test Statistic: Based on Log(OR): logit(P1) - logit(P2)
Hypotheses: Two-Sided. H0: OR = 1   vs.   H1: OR ≠ 1
Covariance Type: Compound Symmetry

| Power | | Sample Size | | | Number of Time Points | Proportion | | Odds Ratio | Autocorrelation | |
Target	Actual	N1	N2	N	M	P1	P2	OR1	Rho	Alpha
0.8	0.8008	86	86	172	4	0.482	0.318	2	0.5	0.05

The sample size of 86 calculated by **PASS** matches the results of Brown and Prescott (2006). The slight difference is due to rounding. Calculation of the sample size presented by Brown and Prescott (2006) on page 270 results in a value of 85.025337, which they round down to 85. Note that the numerical formula has a typographical error: the denominator term should be $(4 \times .693^2)$, not $(4 \times .693)^2$ (see the formula on page 269 of Brown and Prescott (2006)).