

## Chapter 396

# GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

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## Introduction

This module calculates the power for testing the time-averaged difference (TAD) between two means from continuous, correlated data that are analyzed using the GEE method. Such data occur in two design types: clustered and longitudinal.

GEE is different from MM in that it does not require the full specification of the joint distribution of the repeated measurements, as long as the marginal mean model is correctly specified. Estimation consistency is achieved even if the correlation matrix is incorrect. Also, the correlation matrix of the responses is specified directly, rather than using an intermediate, random effects model as is the case in MM. For clustered designs, GEE often uses a *compound symmetric* (CS) correlation structure. For longitudinal data, an *autoregressive* (AR(1)) correlation structure is often used.

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 the means of a certain outcome such as blood pressure. It is known that a person's blood pressure depends on several instantaneous factors such as amount of sleep, excitement level, mood, exercise, etc. If only a single measurement is taken from each patient, then the comparison of mean values from the two groups may be invalid because of the large degree of variation in blood pressure levels among patients. The precision of the experiment is increased by taking multiple measurements from each individual and comparing the time-averaged difference 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 correlation structure may take on several forms depending on the nature of the experiment and the subjects involved.

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## Missing Values

This procedure allows you to specify various patterns of incomplete (or missing) data. Subjects may miss some appointments but attend others. This phenomenon of incomplete data can be accounted for in the sample size calculation which can greatly reduce the overall sample size from that calculated by just omitting subjects with incomplete observations.

## Technical Details

### Theory and Notation

Technical details are given in Ahn, Heo, and Zhang (2015), chapter 4, section 4.4.1, pages 110-116.

Suppose we have  $n_1$  subjects in group 1 (treatment) and  $n_2$  subjects in group 2 (control) for a total of  $N$  subjects, each measured on  $M$  occasions at times  $t_j$  ( $j = 1, \dots, M$ ). For convenience, we normalize these time points to the proportion of total time so that  $t_1 = 0$  and  $t_M = 1$ . The mean of  $y_{ij}$  is modeled by

$$\mu_{ij} = \beta_1 + \beta_2 r_i$$

where

- $y_{ij}$  is the  $j^{\text{th}}$  response from subject  $i$ , with variance given by  $\sigma^2$ .
- $\mu_{ij}$  is expectation of  $y_{ij}$ ,
- $r_i$  is the subject treatment indicator with 0 for control and 1 for treatment,
- $\beta_1$  is the regression coefficient giving intercept of the control group,
- $\beta_2$  is the regression coefficient giving the TAD between the two groups,

In this procedure, the primary interest is on  $\beta_2$ .

This mean model is reparametrized as

$$\mu_{ij} = b_1 + b_2(r_i - \bar{r})$$

where

$$\begin{aligned} b_1 &= \beta_1 + \bar{r}\beta_2 \\ b_2 &= \beta_2 \end{aligned}$$

The vector of covariates is given by  $x_{ij} = (1, r_i - \bar{r})'$ .

GEE is used to estimate and test hypotheses about  $\mathbf{b}$  with  $\hat{\mathbf{b}}$ .

## Correlation Patterns

In a longitudinal design with  $N$  subjects, each measured  $M$  times, observations from a single subject are correlated, and a pattern of those correlations through time needs to be specified. Several choices are available.

### Compound Symmetry

A compound symmetry correlation model assumes that all correlations are equal. That is

$$[\rho_{jj'}] = \begin{bmatrix} 1 & \rho & \rho & \rho & \cdots & \rho \\ \rho & 1 & \rho & \rho & \cdots & \rho \\ \rho & \rho & 1 & \rho & \cdots & \rho \\ \rho & \rho & \rho & 1 & \cdots & \rho \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ \rho & \rho & \rho & \rho & \cdots & 1 \end{bmatrix}_{M \times M}$$

where  $\rho$  is the baseline correlation.

### Banded(1)

A Banded(1) (banded order 1) correlation model assumes that correlations for observations one time period apart are equal to  $\rho$ , and correlations for measurements greater than one time period apart are equal to zero. That is

$$[\rho_{jj'}] = \begin{bmatrix} 1 & \rho & 0 & 0 & \cdots & 0 \\ \rho & 1 & \rho & 0 & \cdots & 0 \\ 0 & \rho & 1 & \rho & \cdots & 0 \\ 0 & 0 & \rho & 1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & 1 \end{bmatrix}_{M \times M}$$

where  $\rho$  is the baseline correlation.

### Banded(2)

A Banded(2) (banded order 2) correlation model assumes that correlations for observations one time period or two periods apart are equal to  $\rho$ , and correlations for measurements greater than one time period apart are equal to zero. That is

$$[\rho_{jj'}] = \begin{bmatrix} 1 & \rho & \rho & 0 & \cdots & 0 \\ \rho & 1 & \rho & \rho & \cdots & 0 \\ \rho & \rho & 1 & \rho & \cdots & 0 \\ 0 & \rho & \rho & 1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & 1 \end{bmatrix}_{M \times M}$$

where  $\rho$  is the baseline correlation.

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**AR1 (Traditional)**

This version of AR1 (autoregressive order 1) correlation model assumes that correlations  $t$  time periods apart are equal to  $\rho^t$ . That is

$$[\rho_{jj'}] = \begin{bmatrix} 1 & \rho & \rho^2 & \rho^3 & \dots & \rho^{M-1} \\ \rho & 1 & \rho & \rho^2 & \dots & \rho^{M-2} \\ \rho^2 & \rho & 1 & \rho & \dots & \rho^{M-3} \\ \rho^3 & \rho^2 & \rho & 1 & \dots & \rho^{M-4} \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ \rho^{M-1} & \rho^{M-2} & \rho^{M-3} & \rho^{M-4} & \dots & 1 \end{bmatrix}_{M \times M}$$

where  $\rho$  is the baseline correlation.

**AR1 (Proportional)**

This version of AR1 (autoregressive order 1) correlation model is described in the book by Ahn et al. (2015). It assumes that correlations  $|t_j - t_k|$  time periods apart are equal to  $\rho^{|t_j - t_k|}$ . That is

$$[\rho_{jk}] = [\rho^{|t_j - t_k|}]_{M \times M}$$

where  $\rho$  is the baseline correlation. Note that in this pattern, the value of  $\rho$  is shown in the final column since in this case  $t_j = 0$  and  $t_k = 1$ , so  $|t_j - t_k| = 1$ .

**Damped Exponential**

A damped exponential is an extension of the AR(1) correlation model in which the exponents are raised to the power  $Dexp$  ( $\theta = Dexp$  in the diagram below). This causes the resulting correlations to be reduced (dampened). Here is an example

$$[\rho_{jj'}] = \begin{bmatrix} 1 & \rho & \rho^{2\theta} & \rho^{3\theta} & \dots & \rho^{(M-1)\theta} \\ \rho & 1 & \rho & \rho^{2\theta} & \dots & \rho^{(M-2)\theta} \\ \rho^{2\theta} & \rho & 1 & \rho & \dots & \rho^{(M-3)\theta} \\ \rho^{3\theta} & \rho^{2\theta} & \rho & 1 & \dots & \rho^{(M-4)\theta} \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ \rho^{(M-1)\theta} & \rho^{(M-2)\theta} & \rho^{(M-3)\theta} & \rho^{(M-4)\theta} & \dots & 1 \end{bmatrix}_{M \times M}$$

where  $\rho$  is the baseline correlation.

## Damped Exponential (Proportional)

This version of the damped exponential correlation model is described in the book by Ahn et al. (2015). It assumes that correlations  $|t_j - t_k|$  time periods apart are equal to  $\rho^{|t_j - t_k|^\theta}$ . That is

$$[\rho_{jk}] = \left[ \rho^{|t_j - t_k|^\theta} \right]_{M \times M}$$

where  $\rho$  is the baseline correlation. Note that in this pattern, the value of  $\rho^{|t_j - t_k|^\theta}$  turns up in the final column since in this case  $t_j = 0$  and  $t_k = 1$ , so  $|t_j - t_k| = 1$ .

## Linear Exponential Decay

A linear exponential decay correlation model is one in which the exponent of the correlation decays according to a linear equation from 1 at the *Base Time Proportion* to a final value, *Emax*. The resulting pattern looks similar to the damped exponential. Note that the exponents are applied to the absolute difference between the Measurement Time Proportions. This method allows you to easily construct comparable correlation matrices of different dimensions. Otherwise, differences in the resulting power would be more strongly due to differences in the correlation matrices.

Here is an example. Suppose  $m$  is 6,  $\rho = 0.5$ ,  $Emax = 3$ , the *Base Time Proportion* is 0.20, and the Measurement Time Proportions are (0, 0.2, 0.4, 0.6, 0.8, 1). The following correlation matrix would be obtained

$$[\rho_{jj'}] = \begin{bmatrix} 1 & 0.5 & 0.3536 & 0.25 & 0.1768 & 0.125 \\ 0.5 & 1 & 0.5 & 0.3536 & 0.25 & 0.1768 \\ 0.3536 & 0.5 & 1 & 0.5 & 0.3536 & 0.25 \\ 0.25 & 0.3536 & 0.5 & 1 & 0.5 & 0.3536 \\ 0.1768 & 0.25 & 0.3536 & 0.5 & 0.3536 & 0.5 \\ 0.125 & 0.1768 & 0.25 & 0.3536 & 0.5 & 1 \end{bmatrix}_{M \times M}$$

Note that in the top row, the correlation is 0.5 for the second (0.2 - 0) time point and 0.125 ( $0.5^3$ ) at the last (1 - 0) time points. The correlations are obtained by raising 0.5 to the appropriate exponent. The linear equation from 1 to 3 results in the exponents 1, 1.5, 2, 2.5, 3 correspondent to the time proportions 0, 0.2, 0.4, 0.6, 0.8, and 1.

As a further example, note that the correlation for the 0.4 time point is,  $0.5^{1.5} = 0.35355339 \approx 0.3536$ .

This method allows you to compare various values of  $M$  while keeping the correlation matrix similar. To see what we mean, consider what the correlation matrix looks like when  $M$  is reduced to 4 and the measurement time proportions are set to (0, 0.2, 0.6, 1). It becomes

$$[\rho_{jj'}] = \begin{bmatrix} 1 & 0.5 & 0.25 & 0.125 \\ 0.5 & 1 & 0.5 & 0.25 \\ 0.25 & 0.5 & 1 & 0.5 \\ 0.125 & 0.25 & 0.5 & 1 \end{bmatrix}_{M \times M}$$

Note that the correlation at a measurement time difference of 0.6 is equal to 0.25 in both matrices.

## Missing Data Patterns

The problem of missing data occurs for several reasons. In longitudinal studies in which a subject is measured multiple times, missing data becomes more complicated to model because it is possible that a subject is measured only some of the time. In fact, it is probably more common for data to be incomplete than complete. The approach of omitting subjects with incomplete data during the planning phase is very inaccurate. Certainly, subjects with partial measurements are included in the analysis. This procedure provides several missing data patterns to choose from so that your sample size calculations are more realistic.

In the presentation to follow, we denote the percent of subjects with a missing response at time point  $t_j$  as  $\kappa_j$ . The proportion non-missing at a particular time point is  $\phi_j = 1 - \kappa_j$ . We will refer to  $\phi_j$  as the *marginal observant probability* at time  $t_j$  and  $\phi_{jj'}$  as a *joint observant probability* at times  $t_j$  and  $t_{j'}$ .

### Pairwise Missing Pattern

The program provides three options for how the pairwise (joint) observant probabilities  $\phi_{jj'}$  are calculated. These are

**Independent (Ind):**  $\phi_{jj'} = \phi_j \phi_{j'}$ ,  $\phi_{jj} = \phi_j$

**Monotonic (Mon):**  $\phi_{jj'} = \phi_k$  where  $k = \max(j, j')$

**Mixture:**  $\phi_{jj'} = W(\text{Ind}) + (1 - W)(\text{Mon})$  for weighting factor  $W$ .

### Missing Input Type

There are several ways in which the missing value pattern can be specified. Each missing value pattern is a list of missing proportions at each of the  $M$  time points. Each value in the list must be non-negative and less than 1. Possible input choices are

- **Constant = 0**

All missing proportions are set to 0. That is, there are no missing values.

- **Constant**

All missing proportions are set to constant value.

- **Piecewise Constant on Spreadsheet**

A set of missing proportions are defined for several time intervals using the spreadsheet. One column contains the missing proportions for the interval, going down the rows. Another column defines the corresponding upper limit of time proportion of the interval. The lower limit is implied by the limit given immediately above. The program assumes that the first-time interval starts at 0 percent.

- **Linear (Steady Change)**

The missing proportions fall along a straight-line between 0 and 1 elapsed time. Only the first and last proportions are entered.

- **Piecewise Linear on Spreadsheet**

The missing proportions fall along a set of connected straight-lines that are defined by two columns on the spreadsheet.

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- **List**

Enter a list of M missing proportions, one for each time point.

- **Multiple Lists on Spreadsheet**

Select multiple columns containing vertical lists of missing proportions. Each column contains a set of missing proportions in rows, one for each time point.

- **Pairwise Observed Proportions on Spreadsheet**

Enter an  $M \times M$  matrix of observant probabilities by selecting M columns. These observant probabilities are the proportion of the responses for both the row and column time points that are observed.

## Sample Size Calculations

The details of the calculation of sample size and power is given in Ahn, Heo, and Zhang (2015), Chapter 4. These are summarized here.

As explained above, GEE is used to estimate the regression coefficients  $\mathbf{b}$  with  $\widehat{\mathbf{b}}$ . The significance of  $b_4$ , the coefficient associated with the difference between the control and treatment slopes, is tested using a Wald statistic from which the following sample size formula is derived

$$n = \frac{\sigma^2 \eta_0 \left( z_{1-\frac{\alpha}{h}} + z_{1-\gamma} \right)^2}{\delta^2 \mu_0^2 \sigma_r^2}$$

where

$h = 1$  (one-sided test) or  $2$  (two-sided test)

$\gamma = 1 - \text{power}$

$\alpha = \text{significance level}$

$\delta = \beta_2$

$$\mu_0 = \sum_{j=1}^M \phi_j$$

$$\eta_0 = \sum_{j=1}^M \sum_{j'=1}^M \phi_{jj'} \rho_{jj'}$$

$$\sigma_r^2 = \bar{r}(1 - \bar{r})$$

$\phi_j = 1 - \kappa_j$ , where  $\kappa_j$  = proportion missing at the  $j^{\text{th}}$  time point

$\rho_{jj'}$  is the corresponding element from within-subject correlation matrix

$\phi_{jj'}$  is the joint observant probability of observing both  $y_{ij}$  and  $y_{ij'}$  for every subject  $i$

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

Three possible choices are available to calculate  $\phi_{jj'}$ . These are

*Independent:*  $\phi_{jj'} = \phi_j \phi_{j'}$ ,  $\phi_{jj} = \phi_j$

*Monotonic:*  $\phi_{jj'} = \phi_k$  where  $k = \max(j, j')$

*Mixture:*  $\phi_{jj'} = W(\text{Independent}) + (1 - W)(\text{Monotonic})$  for weighting factor  $W$ .

The above formula is easily rearranged to obtain a formula for power.

## 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 change in heart rate between subjects who take the new drug, and subjects who take the standard drug. Their experimental protocol calls for the administration of a certain level of the drug, followed by three measurements 2 days apart. They want to be able to detect a TAD of 5 between the two groups. They want a sensitivity analysis by considering a range of differences from 3 to 8.

Similar studies have found a standard deviation of 9.2 of the residuals within a subject across time. These studies also showed an autocorrelation between adjacent measurements on the same individual of 0.7, so they want to try values of 0.6, 0.7, and 0.8. The researchers assume that first-order autocorrelation adequately represents the autocorrelation pattern. The two-sided test will be conducted at the 0.05 significance level and at 90% power. They are planning on dividing the subjects equally between the treatment and control groups.

The researchers anticipate that the missing pattern across time will begin at 0% missing and increase steadily to 30% at the third measurement. They assume that the pairwise missing is *independent*.

What are the sample size requirements for this study?

### 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>
Alternative Hypothesis .....	<b>Two-Sided</b>
Power.....	<b>0.90</b>
Alpha.....	<b>0.05</b>
R (Group 1 Allocation %) .....	<b>50</b>
Measurement Time Input Type .....	<b>Equally Spaced Measurement Times</b>
M (Number of Measurement Times) .....	<b>3</b>
$\delta$ (Time-Averaged Difference).....	<b>3 4 5 6 7 8</b>
$\sigma$ (Standard Deviation).....	<b>9.2</b>
Pattern of $p$ 's Across Time.....	<b>AR1 (Traditional)</b>
$\rho$ (Base Correlation).....	<b>0.6, 0.7, 0.8</b>
Missing Input Type.....	<b>Linear (Steady Change)</b>
Pairwise Missing Pattern.....	<b>Independent (Ind)</b>
First Missing Proportion (Ind).....	<b>0</b>
Last Missing Proportion (Ind) .....	<b>0.30</b>

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

## Output

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

### Numeric Reports

#### Numeric Results for a Time-Averaged Difference Test using GEE

Solve For: **Sample Size**  
 Measurement Times: Equally spaced  
 Correlation: AR1:  $\rho_{(j,k)} = \rho^{|j-k|}$   
 Missing Pattern: Range of missing proportions  
 Observant Proportions: Assume independence

Power	Total Sample Size N	Group 1 Allocation Percent R	Number of Measurement Times M	Time-Averaged Difference $\delta$	Standard Deviation $\sigma$	Base Correlation $\rho$	First Row of Correlation Matrix	Missing Data Proportions	Measurement Times	Alpha
0.9009	292	50	3	3	9.2	0.6	$\rho_1(1)$	0.05	Ms1(1)	T(1)
0.9003	320	50	3	3	9.2	0.7	$\rho_2(1)$	0.05	Ms1(1)	T(1)
0.9008	351	50	3	3	9.2	0.8	$\rho_3(1)$	0.05	Ms1(1)	T(1)
0.9005	164	50	3	4	9.2	0.6	$\rho_1(1)$	0.05	Ms1(1)	T(1)
0.9003	180	50	3	4	9.2	0.7	$\rho_2(1)$	0.05	Ms1(1)	T(1)
0.9002	197	50	3	4	9.2	0.8	$\rho_3(1)$	0.05	Ms1(1)	T(1)
0.9006	105	50	3	5	9.2	0.6	$\rho_1(1)$	0.05	Ms1(1)	T(1)
0.9022	116	50	3	5	9.2	0.7	$\rho_2(1)$	0.05	Ms1(1)	T(1)
0.9022	127	50	3	5	9.2	0.8	$\rho_3(1)$	0.05	Ms1(1)	T(1)
0.9009	73	50	3	6	9.2	0.6	$\rho_1(1)$	0.05	Ms1(1)	T(1)
0.9003	80	50	3	6	9.2	0.7	$\rho_2(1)$	0.05	Ms1(1)	T(1)
0.9016	88	50	3	6	9.2	0.8	$\rho_3(1)$	0.05	Ms1(1)	T(1)
0.9028	54	50	3	7	9.2	0.6	$\rho_1(1)$	0.05	Ms1(1)	T(1)
0.9014	59	50	3	7	9.2	0.7	$\rho_2(1)$	0.05	Ms1(1)	T(1)
0.9031	65	50	3	7	9.2	0.8	$\rho_3(1)$	0.05	Ms1(1)	T(1)
0.9005	41	50	3	8	9.2	0.6	$\rho_1(1)$	0.05	Ms1(1)	T(1)
0.9003	45	50	3	8	9.2	0.7	$\rho_2(1)$	0.05	Ms1(1)	T(1)
0.9044	50	50	3	8	9.2	0.8	$\rho_3(1)$	0.05	Ms1(1)	T(1)

Item	Values
$\rho_1(1)$	1, 0.6, 0.36
$\rho_2(1)$	1, 0.7, 0.49
$\rho_3(1)$	1, 0.8, 0.64
Ms1(1)	0, 0.15, 0.3
T(1)	0, 0.5, 1

Power	The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N	The total number of subjects in the study.
R	The treatment group allocation proportion. It is the proportion of subjects that are in the treatment group.
M	The number of time points at which each subject is measured.
$\delta$	The time-averaged difference (TAD) at which the power is calculated. It is in the same scale as $\sigma$ .
$\sigma$	The standard deviation of a response.
$\rho$	The base correlation between two responses on the same subject. It may be transformed based on the correlation pattern.
First Row of Correlation Matrix	Presents the top row of the correlation matrix.
Missing Data Proportions	Gives the name of the set containing the missing data proportions across time.
Measurement Times	Gives the name of the set containing the measurement time proportions. These measurement times represent the proportion of the total study time that has elapsed just before the measurement.
Alpha	The probability of rejecting a true null hypothesis.

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

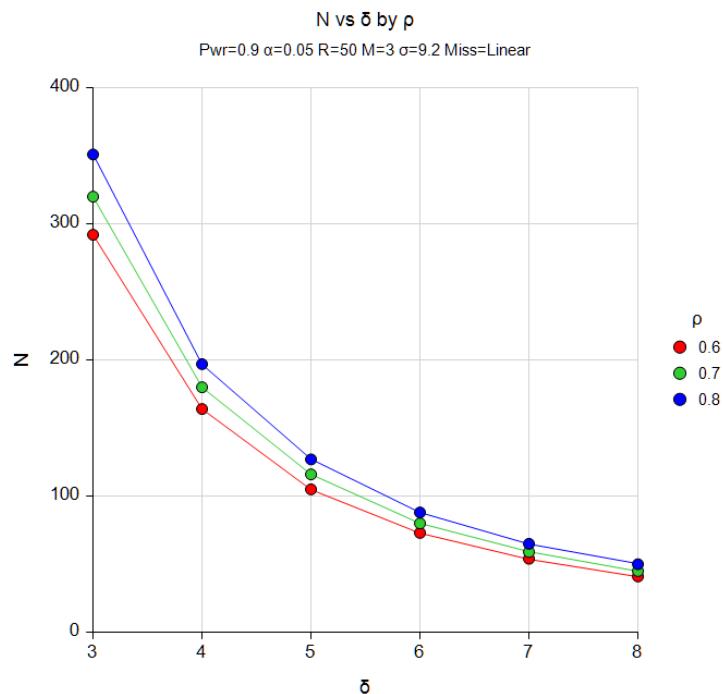
**Summary Statements**

A two-group repeated measures design (with a continuous response and with 3 measurements for each subject) will be used to test whether there is a group difference in time-averaged response. The comparison will be made using a two-sided Wald test using GEE methods, with a Type I error rate ( $\alpha$ ) of 0.05. The (repeated) measurements of each subject will be made at the following 3 times, expressed as proportions of the total study time: 0, 0.5, 1. Missing values are assumed to occur completely at random (MCAR). The missing value proportions will be combined to form the pairwise observant probabilities using an independent pairwise missing pattern. The anticipated proportions missing at each measurement time are 0, 0.15, 0.3. The first row of the autocorrelation matrix of the responses within a subject is assumed to be 1, 0.6, 0.36, with subsequent rows following the same pattern (AR1:  $\rho(j,k) = \rho^{|j-k|}$ ). The residual (zero-mean) standard deviation for both groups is assumed to be 9.2. To detect a time-averaged group mean difference of 3 with 90% power, the total number of needed subjects is 292 (with 50% of the subjects in the treatment group (Group 1)).

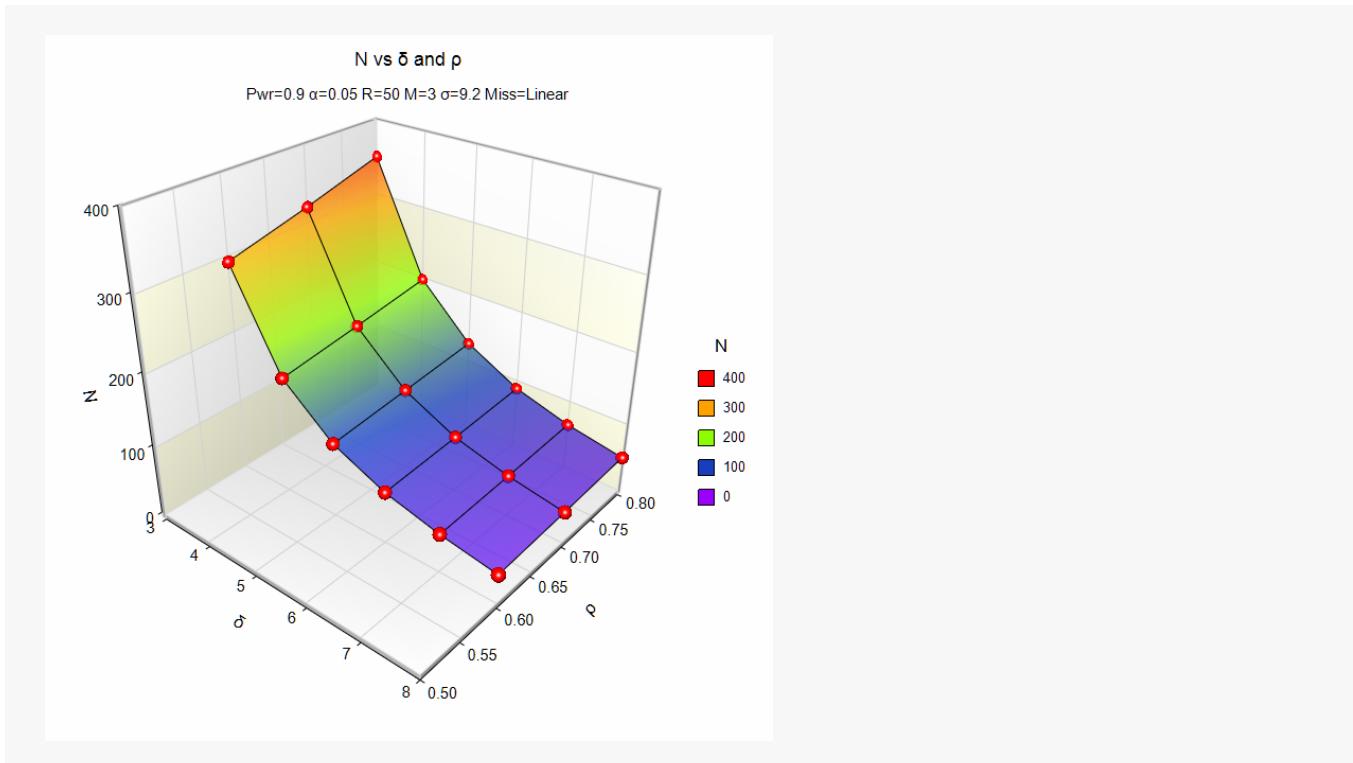
**References**

Ahn, C., Heo, M., and Zhang, S. 2015. Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research. CRC Press. New York.

This report gives the sample size for each value of the other parameters.

**Plots Section****Plots**

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)



These charts show the relationship between sample size,  $\delta$ , and  $\rho$  when the other parameters in the design are held constant.

## Autocorrelation Matrices

## Autocorrelation Matrix for Report Row 1

Time	T(0)	T(0.5)	T(1)
T(0)	1.00	0.6	0.36
T(0.5)	0.60	1.0	0.60
T(1)	0.36	0.6	1.00

## Autocorrelation Matrix for Report Row 2

Time	T(0)	T(0.5)	T(1)
T(0)	1.00	0.7	0.49
T(0.5)	0.70	1.0	0.70
T(1)	0.49	0.7	1.00

(More Reports Follow)

These reports show the autocorrelation matrix for the indicated row of the report.

## Example 2 – Finding the Power

Continuing with Example 1, the researchers want to determine the power corresponding to sample sizes ranging from 50 to 250 for the main cases of the other parameters.

### 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>Sample Size</b>
Alternative Hypothesis .....	<b>Two-Sided (<math>H_1: \sigma^2_{BT}/\sigma^2_{BC} \neq 1</math>)</b>
Power.....	<b>0.80</b>
Alpha.....	<b>0.05</b>
Sequence Allocation .....	<b>Equal (<math>N_1 = N_2</math>)</b>
M (Number of Replicates).....	<b>2</b>
R1 (Actual Variance Ratio) .....	<b>0.5625</b>
$\sigma^2_{BC}$ (Control Variance).....	<b>0.16</b>
$\sigma^2_{WT}$ (Treatment Variance) .....	<b>0.04</b>
$\sigma^2_{WC}$ (Control Variance).....	<b>0.09</b>
$\rho$ (Treatment, Control Correlation).....	<b>0.75</b>

### Output

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

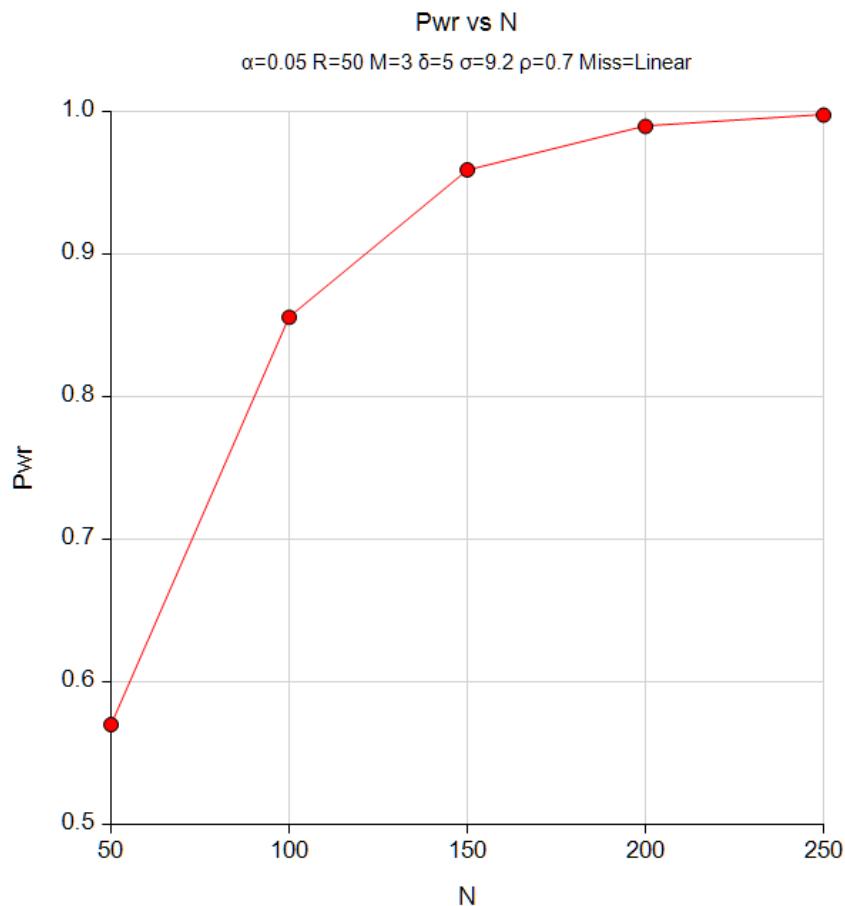
#### Numeric Results for a Time-Averaged Difference Test using GEE

Solve For: **Power**  
 Measurement Times: Equally spaced  
 Correlation: AR1:  $\rho_{(j,k)} = \rho^{|j-k|}$   
 Missing Pattern: Range of missing proportions  
 Observant Proportions: Assume independence

Power	Total Sample Size N	Group 1 Allocation Percent R	Number of Measurement Times M	Time-Averaged Difference $\delta$	Standard Deviation $\sigma$	Base Correlation $\rho$	First Row of Correlation Matrix	Missing Data Proportions	Measurement Times	Alpha
0.5701	50	50	3	5	9.2	0.7	$\rho_{1(1)}$	0.05	Ms1(1)	T(1)
0.8558	100	50	3	5	9.2	0.7	$\rho_{1(1)}$	0.05	Ms1(1)	T(1)
0.9591	150	50	3	5	9.2	0.7	$\rho_{1(1)}$	0.05	Ms1(1)	T(1)
0.9896	200	50	3	5	9.2	0.7	$\rho_{1(1)}$	0.05	Ms1(1)	T(1)
0.9976	250	50	3	5	9.2	0.7	$\rho_{1(1)}$	0.05	Ms1(1)	T(1)

Item	Values
$\rho_{1(1)}$	1, 0.7, 0.49
Ms1(1)	0, 0.15, 0.3
T(1)	0, 0.5, 1

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

**Plots**

The reports and plot indicate the power for each value of N.

## Example 3 – Impact of the Number of Repeated Measurements

Continuing with Examples 1 and 2, the researchers want to study the impact on the sample size of changing the number of measurements made on each individual. Their experimental protocol calls for 3 measurements that are 2 days apart. They want to see the impact on sample size of taking measurements daily. To do this, they will need to increase the number of measurements to 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 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 .....	<b>Power</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Alpha.....	<b>0.05</b>
N (Subjects).....	<b>50 to 250 by 50</b>
R (Group 1 Allocation %) .....	<b>50</b>
Measurement Time Input Type .....	<b>Equally Spaced Measurement Times</b>
M (Number of Measurement Times) .....	<b>3 5</b>
$\delta$ (Time-Averaged Difference).....	<b>5</b>
$\sigma$ (Standard Deviation).....	<b>9.2</b>
Pattern of p's Across Time.....	<b>AR1 (Traditional)</b>
$\rho$ (Base Correlation).....	<b>0.7</b>
Missing Input Type.....	<b>Linear (Steady Change)</b>
Pairwise Missing Pattern.....	<b>Independent</b>
First Missing Proportion (Ind).....	<b>0</b>
Last Missing Proportion (Ind) .....	<b>0.30</b>

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

## Output

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

**Numeric Results for a Time-Averaged Difference Test using GEE**

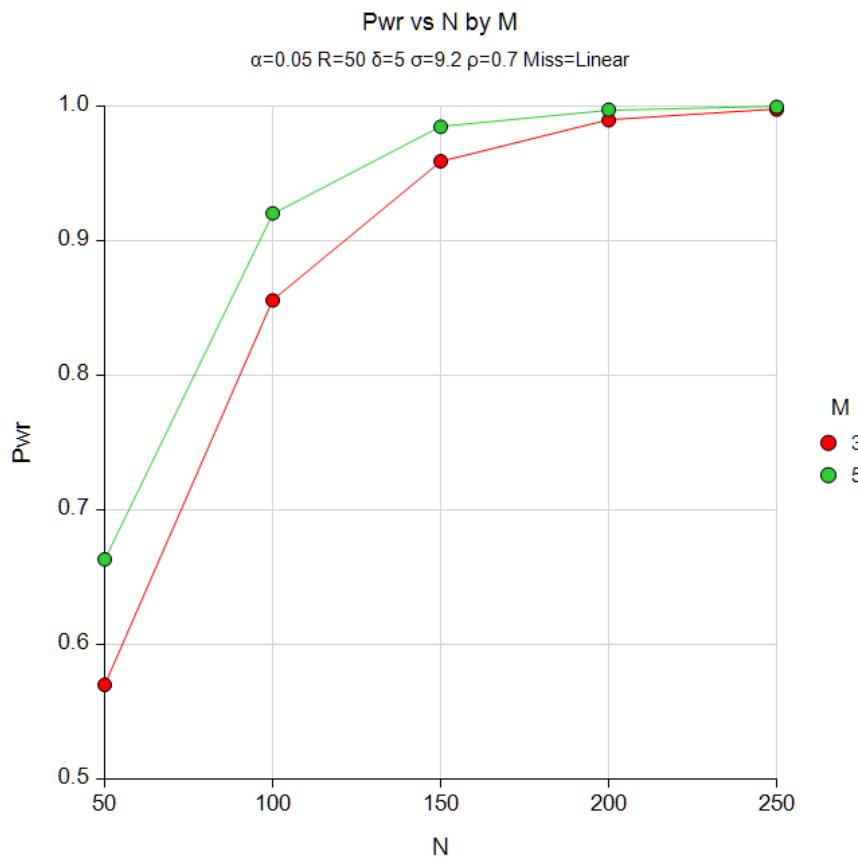
Solve For: **Power**  
 Measurement Times: Equally spaced  
 Correlation: AR1:  $p(j,k) = \rho^{|j-k|}$   
 Missing Pattern: Range of missing proportions  
 Observant Proportions: Assume independence

Power	Total Sample Size	Group 1 Allocation Percent	Number of Measurement Times	Time-Averaged Difference $\delta$	Standard Deviation $\sigma$	Base Correlation $\rho$	First Row of Correlation Matrix	Missing Data Proportions	Measurement Times	Alpha
N	R	M	δ	σ	ρ	ρ(1)	0.05	Ms1(1)	T(1)	
0.5701	50	50	3	5	9.2	0.7	ρ(1)	0.05	Ms1(1)	T(1)
0.6633	50	50	5	5	9.2	0.7	ρ(2)	0.05	Ms1(2)	T(2)
0.8558	100	50	3	5	9.2	0.7	ρ(1)	0.05	Ms1(1)	T(1)
0.9204	100	50	5	5	9.2	0.7	ρ(2)	0.05	Ms1(2)	T(2)
0.9591	150	50	3	5	9.2	0.7	ρ(1)	0.05	Ms1(1)	T(1)
0.9848	150	50	5	5	9.2	0.7	ρ(2)	0.05	Ms1(2)	T(2)
0.9896	200	50	3	5	9.2	0.7	ρ(1)	0.05	Ms1(1)	T(1)
0.9975	200	50	5	5	9.2	0.7	ρ(2)	0.05	Ms1(2)	T(2)
0.9976	250	50	3	5	9.2	0.7	ρ(1)	0.05	Ms1(1)	T(1)
0.9996	250	50	5	5	9.2	0.7	ρ(2)	0.05	Ms1(2)	T(2)

Item	Values
ρ(1)	1, 0.7, 0.49
ρ(2)	1, 0.7, 0.49, 0.343, 0.2401
Ms1(1)	0, 0.15, 0.3
Ms1(2)	0, 0.08, 0.15, 0.23, 0.3
T(1)	0, 0.5, 1
T(2)	0, 0.25, 0.5, 0.75, 1

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

## Plots



Note that increasing the number of measurements has had the result of increasing power.

## Example 4 – Validation of Sample Size Calculation using Ahn, Heo, and Zhang (2015)

Ahn, Heo, and Zhang (2015) do not present any numerical examples for this procedure. However, on page 115 they give a simplified formula for the compound symmetry case. We will calculate a result by hand using this formula and then calculate with the program to validate this procedure.

The simplified sample size formula is

$$n = \frac{4\sigma^2[1 + (m - 1)\rho]\left(z_{1-\frac{\alpha}{2}} + z_{1-\gamma}\right)^2}{\delta^2 m}$$

Using  $m = 5$ ,  $\sigma = 3$ ,  $\rho = 0.5$ ,  $\delta = 1.5$ ,  $\alpha = 0.05$ , and power = 0.9, we obtain

$$\begin{aligned} n &= \text{ceiling}\left(\frac{4(3^2)[1 + (5 - 1)0.5](1.96 + 1.28)^2}{1.5^2(5)}\right) \\ &= \text{ceiling}(100.78) \\ &= 101 \end{aligned}$$

### 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 .....	<b>Sample Size</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Power.....	<b>0.90</b>
Alpha.....	<b>0.05</b>
R (Group 1 Allocation %).....	<b>50</b>
Measurement Time Input Type .....	<b>Equally Spaced Measurement Times</b>
M (Number of Measurement Times) .....	<b>5</b>
$\delta$ (Time-Averaged Difference).....	<b>1.5</b>
$\sigma$ (Standard Deviation).....	<b>3</b>
Pattern of $\rho$ 's Across Time.....	<b>Compound Symmetry</b>
$\rho$ (Base Correlation).....	<b>0.5</b>
Missing Input Type.....	<b>Constant = 0</b>

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

## Output

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

### Numeric Results for a Time-Averaged Difference Test using GEE

Solve For: **Sample Size**  
Measurement Times: Equally spaced  
Correlation: Compound symmetry (all p's equal)  
Missing Pattern: No missing data

Power	Total Sample Size N	Group 1 Allocation Percent R	Number of Measurement Times M	Time-Averaged Difference $\delta$	Standard Deviation $\sigma$	Base Correlation $\rho$	First Row of Correlation Matrix	Missing Data Proportion	Measurement Times	Alpha
0.9004	101	50	5	1.5	3	0.5	$\rho_1(1)$	0.05	0	T(1)

Item	Values
$\rho_1(1)$	1, 0.5, 0.5, 0.5, 0.5
T(1)	0, 0.25, 0.5, 0.75, 1

The sample size is 101, which matches Ahn, Heo, and Zhang (2015) exactly.

## Example 5 – Impact of Measurement Time Distribution

This example will investigate the impact of measurement time on power. It will compare the power of studies that are evenly spaced with those that take more measurements at the beginning of the study, near the middle of the study, and at the end of the study.

In this example the standard deviation is 28, the TAD is 10, the significance level is 0.05, the sample size ranges from 70 to 150, and R is 50%. The correlation pattern will be Linear Exponential Decay with a base correlation of 0.8, Base Time Proportion of 0.20, and Emax set to 4. The missing input type will be set to Linear from 0 to 30% and the pairwise missing assumption will be independent.

The measurement times for five scenarios are given in the following table.

**Table of Measurement Times in Proportion of Total Study Time**

Tm1	Tm2	Tm3	Tm4	Tm5
0	0	0	0	0
0.20	0.60	0.10	0.10	0.45
0.40	0.70	0.20	0.20	0.50
0.60	0.80	0.30	0.80	0.55
0.80	0.90	0.40	0.90	0.60
1.00	1.00	1.00	1.00	1.00

Note that the measurements in Tm1 are evenly spaced, those in Tm2 are loaded near the end, those of Tm3 occur at the beginning, those of Tm4 occur only at the beginning and the end, and those of Tm5 occur mostly near the middle.

### 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 .....	<b>Power</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Alpha.....	<b>0.05</b>
N (Subjects) .....	<b>70, 100, 150</b>
R (Group 1 Allocation %) .....	<b>50</b>
Measurement Time Input Type .....	<b>Columns of Measurement Time Proportions</b>
Column(s) of Time Proportions .....	<b>Tm1-Tm5</b>
$\delta$ (Time-Averaged Difference).....	<b>10</b>
$\sigma$ (Standard Deviation).....	<b>28</b>
Pattern of $p$ 's Across Time.....	<b>Linear Exponential Decay</b>
$\rho$ (Base Correlation).....	<b>0.8</b>
Base Time Proportion .....	<b>0.2</b>
Emax (Max Decay Exponent) .....	<b>4</b>
Missing Input Type.....	<b>Linear (Steady Change)</b>

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

Pairwise Missing Pattern.....**Independent (Ind)**  
 First Missing Proportion (Ind).....**0**  
 Last Missing Proportion (Ind).....**0.3**

**Input Spreadsheet Data**

Row	Tm1	Tm2	Tm3	Tm4	Tm5
1	0.0	0.0	0.0	0.0	0.00
2	0.2	0.6	0.1	0.1	0.45
3	0.4	0.7	0.2	0.2	0.50
4	0.6	0.8	0.3	0.8	0.55
5	0.8	0.9	0.4	0.9	0.60
6	1.0	1.0	1.0	1.0	1.00

**Output**

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

**Numeric Results for a Time-Averaged Difference Test using GEE**

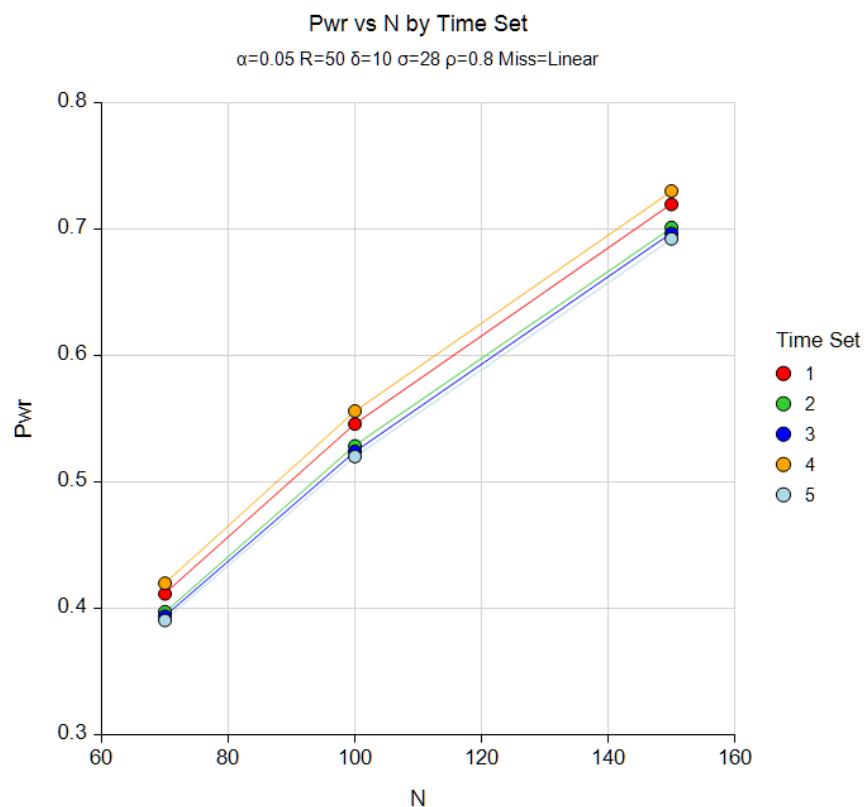
Solve For: **Power**  
 Measurement Times: Lists in spreadsheet columns: {TM1-TM5}  
 Correlation: Linear exponential decay, with Emax = 4 and Base Time Prop = 0.2  
 Missing Pattern: Range of missing proportions  
 Observant Proportions: Assume independence

Total Power	Sample Size N	Group 1 Allocation Percent R	Number of Measurement Times M	Time-Averaged Difference $\delta$	Standard Deviation $\sigma$	Base Correlation $\rho$	First Row of Correlation Matrix	Missing Data Proportions	Measurement Times	Alpha
0.4116	70	50	6	10	28	0.8	$\rho_1(Tm1)$	0.05	Ms1(Tm1)	Tm1(1)
0.3974	70	50	6	10	28	0.8	$\rho_1(Tm2)$	0.05	Ms1(Tm2)	Tm2(2)
0.3938	70	50	6	10	28	0.8	$\rho_1(Tm3)$	0.05	Ms1(Tm3)	Tm3(3)
0.4199	70	50	6	10	28	0.8	$\rho_1(Tm4)$	0.05	Ms1(Tm4)	Tm4(4)
0.3906	70	50	6	10	28	0.8	$\rho_1(Tm5)$	0.05	Ms1(Tm5)	Tm5(5)
0.5460	100	50	6	10	28	0.8	$\rho_1(Tm1)$	0.05	Ms1(Tm1)	Tm1(1)
0.5286	100	50	6	10	28	0.8	$\rho_1(Tm2)$	0.05	Ms1(Tm2)	Tm2(2)
0.5242	100	50	6	10	28	0.8	$\rho_1(Tm3)$	0.05	Ms1(Tm3)	Tm3(3)
0.5561	100	50	6	10	28	0.8	$\rho_1(Tm4)$	0.05	Ms1(Tm4)	Tm4(4)
0.5202	100	50	6	10	28	0.8	$\rho_1(Tm5)$	0.05	Ms1(Tm5)	Tm5(5)
0.7197	150	50	6	10	28	0.8	$\rho_1(Tm1)$	0.05	Ms1(Tm1)	Tm1(1)
0.7014	150	50	6	10	28	0.8	$\rho_1(Tm2)$	0.05	Ms1(Tm2)	Tm2(2)
0.6967	150	50	6	10	28	0.8	$\rho_1(Tm3)$	0.05	Ms1(Tm3)	Tm3(3)
0.7302	150	50	6	10	28	0.8	$\rho_1(Tm4)$	0.05	Ms1(Tm4)	Tm4(4)
0.6924	150	50	6	10	28	0.8	$\rho_1(Tm5)$	0.05	Ms1(Tm5)	Tm5(5)

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

Item	Values
p1(Tm1)	1, 0.8, 0.6767, 0.5724, 0.4842, 0.4096
p1(Tm2)	1, 0.5724, 0.5265, 0.4842, 0.4453, 0.4096
p1(Tm3)	1, 0.8698, 0.8, 0.7358, 0.6767, 0.4096
p1(Tm4)	1, 0.8698, 0.8, 0.4842, 0.4453, 0.4096
p1(Tm5)	1, 0.649, 0.6224, 0.5969, 0.5724, 0.4096
Ms1(Tm1)	0, 0.06, 0.12, 0.18, 0.24, 0.3
Ms1(Tm2)	0, 0.18, 0.21, 0.24, 0.27, 0.3
Ms1(Tm3)	0, 0.03, 0.06, 0.09, 0.12, 0.3
Ms1(Tm4)	0, 0.03, 0.06, 0.24, 0.27, 0.3
Ms1(Tm5)	0, 0.14, 0.15, 0.17, 0.18, 0.3
Tm1(1)	0, 0.2, 0.4, 0.6, 0.8, 1
Tm2(2)	0, 0.6, 0.7, 0.8, 0.9, 1
Tm3(3)	0, 0.1, 0.2, 0.3, 0.4, 1
Tm4(4)	0, 0.1, 0.2, 0.8, 0.9, 1
Tm5(5)	0, 0.45, 0.5, 0.55, 0.6, 1

## Plots



The legend, *Time Set*, gives the sequence number of the measurement columns. Thus, 1.0 is Tm1, 2.0 is Tm2, and so on.

The pattern Tm4 consistently produces the highest power across all sample sizes. Remember that Tm4 put the measurements at the beginning and the end, but none in the middle.

Patterns Tm3 and Tm5 are nearly tied for achieving the lowest powers. Tm3 put most of the measurements at the beginning of the study. Tm5 put most of the measurements during the middle of the study.

Note that Tm1, the equally spaced times, is in the middle of the pack.

## Example 6 – Entering a Correlation Matrix

This example will show how a correlation matrix can be loaded directly.

In this example, M is 4, the standard deviation is 9.2, the TAD is 5, the significance level is 0.05, the sample size ranges from 50 to 500, and R is 50%. A correlation matrix (shown below) is available from a previous study. The missing input type will be set to Linear from 0 to 30% and the pairwise missing assumption is independent.

**Table of Correlations**

C1	C2	C3	C4
1.0000	0.7000	0.4900	0.3430
0.7000	1.0000	0.7000	0.4900
0.4900	0.7000	1.0000	0.7000
0.3430	0.4900	0.7000	1.0000

## 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 .....	<b>Power</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Alpha.....	<b>0.05</b>
N (Subjects).....	<b>50 80 110 140</b>
R (Group 1 Allocation %).....	<b>50</b>
Measurement Time Input Type .....	<b>Equally Spaced Measurement Times</b>
M (Number of Measurement Times).....	<b>4</b>
$\delta$ (Time-Averaged Difference).....	<b>5</b>
$\sigma$ (Standard Deviation).....	<b>9.2</b>
Pattern of p's Across Time.....	<b>Matrix on Spreadsheet</b>
Columns Containing the pjk's .....	<b>C1-C4</b>
Missing Input Type.....	<b>Linear (Steady Change)</b>
Pairwise Missing Pattern.....	<b>Independent (Ind)</b>
First Missing Proportion (Ind).....	<b>0</b>
Last Missing Proportion (Ind) .....	<b>0.30</b>

### Input Spreadsheet Data

Row	C1	C2	C3	C4
1	1.000	0.70	0.49	0.343
2	0.700	1.00	0.70	0.490
3	0.490	0.70	1.00	0.700
4	0.343	0.49	0.70	1.000

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

## Output

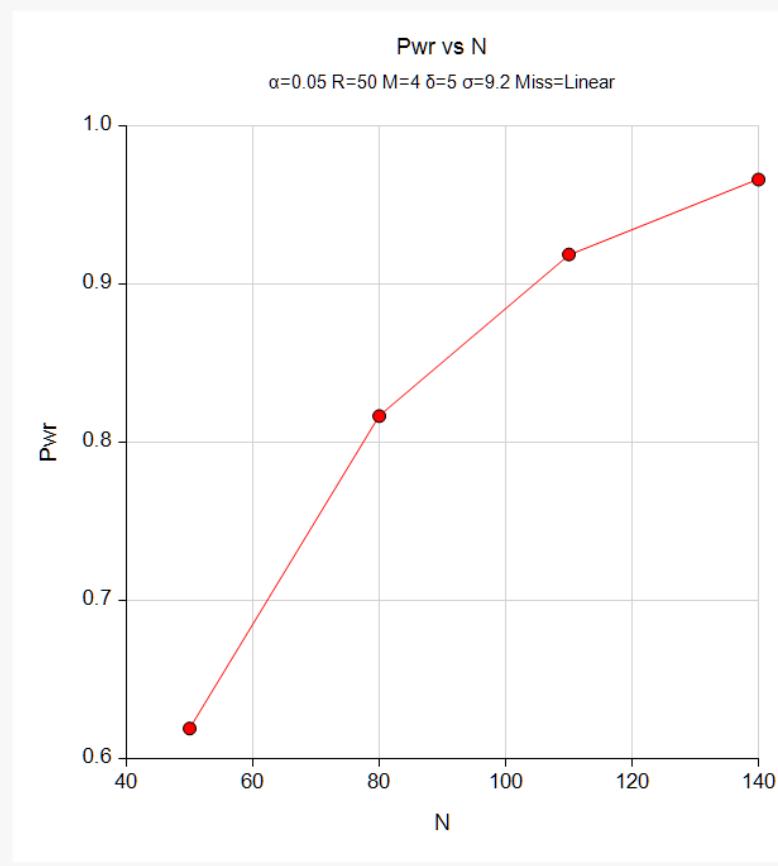
Click the Calculate button to perform the calculations and generate the following output.

**Numeric Results for a Time-Averaged Difference Test using GEE**

Solve For: Power  
 Measurement Times: Equally spaced  
 Correlation: Matrix stored on spreadsheet in columns C1-C4  
 Missing Pattern: Range of missing proportions  
 Observant Proportions: Assume independence

Power	Total Sample Size	Group 1 Allocation Percent	Number of Measurement Times	Time-Averaged Difference $\delta$	Standard Deviation $\sigma$	Base Correlation $\rho$	First Row of Correlation Matrix	Missing Data Proportions	Measurement Times	Alpha
	N	R	M	$\delta$	$\sigma$	$\rho$	$\rho_{1(1)}$	0.05	Ms1(1)	T(1)
0.6191	50	50	4	5	9.2	N/A	$\rho_{1(1)}$	0.05	Ms1(1)	T(1)
0.8166	80	50	4	5	9.2	N/A	$\rho_{1(1)}$	0.05	Ms1(1)	T(1)
0.9188	110	50	4	5	9.2	N/A	$\rho_{1(1)}$	0.05	Ms1(1)	T(1)
0.9661	140	50	4	5	9.2	N/A	$\rho_{1(1)}$	0.05	Ms1(1)	T(1)

Item	Values
$\rho_{1(1)}$	1, 0.7, 0.49, 0.343
Ms1(1)	0, 0.1, 0.2, 0.3
T(1)	0, 0.33, 0.67, 1

**Plots**

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

**Autocorrelation Matrix for Report Row 1**

Time	T(0)	T(0.33)	T(0.67)	T(1)
T(0)	1.000	0.70	0.49	0.343
T(0.33)	0.700	1.00	0.70	0.490
T(0.67)	0.490	0.70	1.00	0.700
T(1)	0.343	0.49	0.70	1.000

**Autocorrelation Matrix for Report Row 2**

Time	T(0)	T(0.33)	T(0.67)	T(1)
T(0)	1.000	0.70	0.49	0.343
T(0.33)	0.700	1.00	0.70	0.490
T(0.67)	0.490	0.70	1.00	0.700
T(1)	0.343	0.49	0.70	1.000

**Autocorrelation Matrix for Report Row 3**

Time	T(0)	T(0.33)	T(0.67)	T(1)
T(0)	1.000	0.70	0.49	0.343
T(0.33)	0.700	1.00	0.70	0.490
T(0.67)	0.490	0.70	1.00	0.700
T(1)	0.343	0.49	0.70	1.000

**Autocorrelation Matrix for Report Row 4**

Time	T(0)	T(0.33)	T(0.67)	T(1)
T(0)	1.000	0.70	0.49	0.343
T(0.33)	0.700	1.00	0.70	0.490
T(0.67)	0.490	0.70	1.00	0.700
T(1)	0.343	0.49	0.70	1.000

The standard reports are displayed.

## Example 7 – Entering an Observant Probabilities Matrix

This example will show how an observant probabilities matrix can be loaded directly.

In this example, M is 4, the standard deviation is 9.2, the TAD is 5, the significance level is 0.05, the sample size ranges from 50 to 140, and R is 50%. The correlation pattern will be Linear Exponential Decay with a base correlation of 0.8, Base Time Proportion of 0.1, and Emax set to 4. The missing input type will be set to Matrix of Pairwise Missing.

**Table of Observant Probabilities**

Row	C1	C2	C3	C4
1	1.00	0.90	0.80	0.70
2	0.90	0.90	0.72	0.63
3	0.80	0.72	0.80	0.56
4	0.70	0.63	0.56	0.70

This table gives the pairwise observant probabilities. That is, each entry gives the probability of obtaining a response for both the row and column time points. For example, 0.63 is the probability of observing both the second response and the fourth response.

## 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 .....	<b>Power</b>
Alternative Hypothesis .....	<b>Two-Sided</b>
Alpha.....	<b>0.05</b>
N (Subjects) .....	<b>50 80 110 140</b>
R (Group 1 Allocation %) .....	<b>50</b>
Measurement Time Input Type .....	<b>Equally Spaced Measurement Times</b>
M (Number of Measurement Times) .....	<b>4</b>
$\delta$ (Time-Averaged Difference).....	<b>5</b>
$\sigma$ (Standard Deviation).....	<b>9.2</b>
Pattern of $p$ 's Across Time.....	<b>Linear Exponential Decay</b>
$\rho$ (Base Correlation).....	<b>0.8</b>
Base Time Proportion .....	<b>0.1</b>
Emax (Max Decay Exponent) .....	<b>4</b>
Missing Input Type.....	<b>Pairwise Observed Proportions on Spreadsheet</b>
Columns of Pairwise Observed.....	<b>C1-C4</b>

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

**Input Spreadsheet Data**

Row	C1	C2	C3	C4
1	1.0	0.90	0.80	0.70
2	0.9	0.90	0.72	0.63
3	0.8	0.72	0.80	0.56
4	0.7	0.63	0.56	0.70

**Output**

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

**Numeric Results for a Time-Averaged Difference Test using GEE**

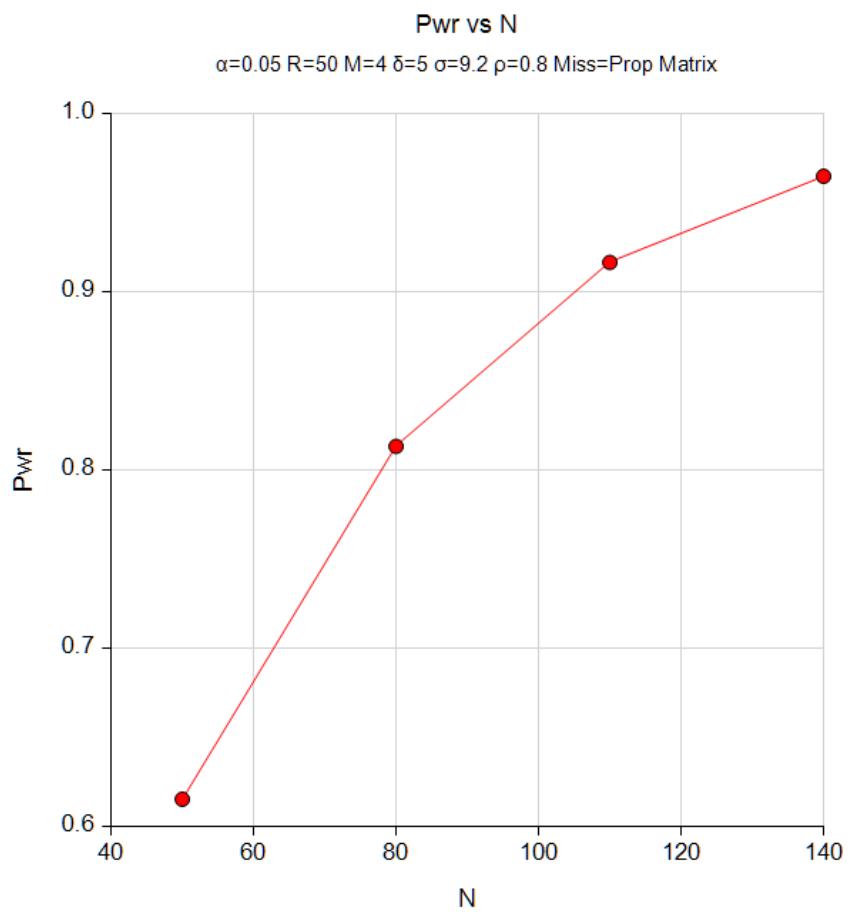
Solve For: Power  
Measurement Times: Equally spaced  
Correlation: Linear exponential decay, with Emax = 4 and Base Time Prop = 0.1  
Missing Pattern: N/A. Matrix of observant probabilities entered in columns C1-C4.

Power	Total Sample Size	Group 1 Allocation Percent	Number of Measurement Times	Time-Averaged Difference $\delta$	Standard Deviation $\sigma$	Base Correlation $\rho$	First Row of Correlation Matrix	Missing Data Proportions	Measurement Times	Alpha
0.6153	50	50	4	5	9.2	0.8	p1(1)	0.05	N/A	T(1)
0.8133	80	50	4	5	9.2	0.8	p1(1)	0.05	N/A	T(1)
0.9165	110	50	4	5	9.2	0.8	p1(1)	0.05	N/A	T(1)
0.9649	140	50	4	5	9.2	0.8	p1(1)	0.05	N/A	T(1)

**Item Values**

p1(1)	1, 0.6725, 0.5249, 0.4096
T(1)	0, 0.33, 0.67, 1

## GEE Tests for the TAD of Two Groups in a Repeated Measures Design (Continuous Outcome)

**Plots**

The standard reports are displayed.