Chapter 747

Assurance for Superiority by a Margin Tests for Two Means in a Cluster-Randomized Design

Introduction

This procedure computes assurance and sample size for a *superiority by a margin* test in cluster-randomized designs in which the outcome is a continuous normal random variable. The calculation is based on a user-specified prior distribution of the effect size parameters. This procedure may also be used to determine the needed sample size to obtain a specified assurance.

The methods for assurance calculation in this procedure are based on O'Hagan, Stevens, and Campbell (2005).

Cluster-randomized designs are those in which whole clusters of subjects (classes, hospitals, communities, etc.) are put into the treatment group or the control group. In this case, the means of two groups, made up of K_i clusters of M_{ij} individuals each, are to be tested using a t-test. The t-test can be calculated on the cluster means or the individual subject responses. Generally speaking, the larger the cluster sizes and the higher the correlation among subjects within the same cluster, the larger will be the overall sample size necessary to detect an effect with the same power.

For more details on this test, please refer to the *Superiority by a Margin Tests for Two Means in a Cluster-Randomized Design* chapter.

Assurance

The assurance of a design is the expected value of the power with respect to one or more prior distributions of the design parameters. Assurance is also referred to as *Bayesian assurance*, *expected power*, *average power*, *statistical assurance*, *hybrid classical-Bayesian procedure,* or *probability of success*.

The power of a design is the probability of rejecting the null hypothesis, conditional on a given set of design attributes, such as the test statistic, the significance level, the sample size, and the effect size to be detected. As the effect size parameters are typically unknown quantities, the stated power may be very different from the true power if the specified parameter values are inaccurate.

While power is conditional on individual design parameter values, and is highly sensitive to those values, assurance is the average power across a presumed prior distribution of the effect size parameters. Thus, assurance adds a Bayesian element to the frequentist framework, resulting in a hybrid approach to the probability of trial or study success. It should be noted that when it comes time to perform the statistical test on the resulting data, these methods for calculating assurance assume that the traditional (frequentist) tests will be used.

The next section describes some of the ways in which the prior distributions for effect size parameters may be determined.

Elicitation

In order to calculate assurance, a suitable prior distribution for the effect size parameters must be determined. This process is called the *elicitation* of the prior distribution.

The elicitation may be as simple as choosing a distribution that seems plausible for the parameter(s) of interest, or as complex as combining the informed advice of several experts based on experience in the field, available pilot data, or previous studies. The accuracy of the assurance value depends on the accuracy of the elicited prior distribution. The assumption (or hope) is that an informed prior distribution will produce a more accurate estimate of the probability of trial success than a single value estimate. Because clinical trials and other studies are often costly, many institutions now routinely require an elicitation step.

Two reference texts that focus on elicitation are O'Hagan, Buck, Daneshkhah, Eiser, Garthwaite, Jenkinson, Oakley, and Rakow (2006) and Dias, Morton, and Quigley (2018).

The Statistical Hypotheses

Superiority by a margin tests are examples of directional (one-sided) tests. This program module provides the input and output in formats that are convenient for these types of tests. This section will review the specifics of superiority by a margin testing.

Remember that in the usual t-test setting, the null (H_0) and alternative (H_1) hypotheses for one-sided tests are defined as follows, assuming that $\delta = \mu_1 - \mu_2$ is to be tested.

$$H_0: \delta \leq 0 \quad \text{versus} \quad H_1: \delta > 0$$

Rejecting this test implies that the mean difference is larger than the value δ. This test is called an *upper-tailed test* because it is rejected in samples in which the difference between the sample means is larger than *D.*

Following is an example of a *lower-tailed test*.

$$H_0: \delta \geq 0 \quad \text{versus} \quad H_1: \delta < 0$$

Superiority by a margin tests are special cases of the above directional tests. It will be convenient to adopt the following specialized notation for the discussion of these tests.

Parameter	PASS Input/Output	Interpretation
μ_1	Not used	*Mean* of population 1. Population 1 is assumed to consist of those who have received the new treatment.
μ_2	Not used	*Mean* of population 2. Population 2 is assumed to consist of those who have received the reference treatment.
SM	SM	*Margin of superiority.* This is a tolerance value that defines the magnitude of the amount that is not of practical importance. This may be thought of as the smallest change from the baseline that is not considered to be trivial.
δ	δ	*True difference*. This is the value of $\mu_1 - \mu_2$, the difference between the means.

Note that the actual values of μ_1 and μ_2 are not needed. Only their difference is needed for power and sample size calculations.

Superiority by a Margin Hypotheses

A *superiority by a margin test* tests that the treatment mean is better than the reference mean by more than a superiority margin. The actual direction of the hypothesis depends on the response variable being studied. The word *SM* refers to the superiority margin.

Case 1: High Values Good

In this case, higher values are better. The hypotheses are arranged so that rejecting the null hypothesis implies that the treatment mean is greater than the reference mean by at least the margin of superiority. The value of δ at which power is calculated must be greater than $|SM|$. The null and alternative hypotheses with $\delta_0 = |SM|$ are

$H_0: \mu_1 \leq \mu_2 + |SM|$ versus $H_1: \mu_1 > \mu_2 + |SM|$

$H_0: \mu_1 - \mu_2 \leq |SM|$ versus $H_1: \mu_1 - \mu_2 > |SM|$

$H_0: \delta \leq |SM|$ versus $H_1: \delta > |SM|$

Case 2: High Values Bad

In this case, higher values are worse. The hypotheses are arranged so that rejecting the null hypothesis implies that the treatment mean is less than the reference mean by at least the margin of superiority. The value of δ at which power is calculated must be less than $-|SM|$. The null and alternative hypotheses with $\delta_0 = -|SM|$ are

$H_0: \mu_1 \geq \mu_2 - |SM|$ versus $H_1: \mu_1 < \mu_2 - |SM|$

$H_0: \mu_1 - \mu_2 \geq -|SM|$ versus $H_1: \mu_1 - \mu_2 < -|SM|$

$H_0: \delta \geq -|SM|$ versus $H_1: \delta < -|SM|$

Superiority by a Margin Test Statistic

Our formulation comes from Campbell and Walters (2014) and Ahn, Heo, and Zhang (2015). Denote an observation by Y_{ijk} where i = 1, 2 gives the group, j = 1,2, ..., K_i gives the cluster within group i, and k = 1, 2, ..., m_{ij} denotes an individual in cluster j of group i.

We let σ^2 denote the variance of Y_{ijk}, which is $\sigma_{Between}^2 + \sigma_{Within}^2$, where $\sigma_{Between}^2$ is the variation between clusters and σ_{Within}^2 is the variation within clusters. Also, let ρ denote the intracluster correlation coefficient (ICC) which is $\sigma_{Between}^2 / \left(\sigma_{Between}^2 + \sigma_{Within}^2\right)$. This correlation is simply the correlation between any two observations in the same cluster.

For sample size calculation, we assume that the m_{ij} are distributed with a mean cluster size of M_i and a coefficient of variation cluster sizes of *COV*. The variances of the two group means, $\bar{Y}_i$, are approximated by

$$V_i = \frac{\sigma^2 (DE_i)(RE_i)}{K_i M_i}$$

$$DE_i = 1 + (M_i - 1)\rho$$

$$RE_i = \frac{1}{1 - (COV)^2 \lambda_i (1 - \lambda_i)}$$

$$\lambda_i = M_i \rho / (M_i \rho + 1 - \rho)$$

DE is called the *Design Effect* and RE is the *Relative Efficiency* of unequal to equal cluster sizes. Both are greater than or equal to one, so both inflate the variance.

Assume that $\delta = \mu_1 - \mu_2$ is to be tested using a modified two-sample t-test. Assuming that higher values are better, the superiority test statistic is

$$t = \frac{\bar{Y}_1 - \bar{Y}_2 - SM}{\sqrt{\hat{V}_1 + \hat{V}_2}}$$

has an approximate t distribution with degrees of freedom $DF = K_1 M_1 + K_2 M_2 - 2$ for a *subject-level* analysis or $K_1 + K_2 - 2$ for a *cluster-level* analysis.

Let the noncentrality parameter $\Delta = (\delta - SM)/\sigma_d$, where $\sigma_d = \sqrt{V_1 + V_2}$. We can define the critical value based on a central t-distribution with DF degrees of freedom as follows.

$$X = t_{\alpha, DF}$$

The power can be found from the following to probabilities

$$Power = 1 - H_{X, DF, \Delta}$$

where $H_{X, DF, \Delta}$ is the cumulative probability distribution of the noncentral-t distribution.

Assurance Calculation

The assurance computation described here is based on O'Hagan, Stevens, and Campbell (2005).

Let $P_1(H|\delta,\sigma,\rho,M_1,M_2,COV)$ be the power function described above where *H* is the event that null hypothesis is rejected conditional on the values of the parameters. The specification of the parameters is critical to the power calculation, but the actual values are seldom known. Assurance is defined as the expected power where the expectation is with respect to a joint prior distribution for the parameters. Hence, the definition of assurance is

$$Assurance = E_{\delta,\sigma,\rho,M_1,M_2,COV}\left(P_1(H|\delta,\sigma,\rho,M_1,M_2,COV)\right)$$

$$= \int\int\int\int\int\int P_1(H|\delta,\sigma,\rho,M_1,M_2,COV) f(\delta,\sigma,\rho,M_1,M_2,COV) d\delta \ldots dCOV$$

where $f(\delta,\sigma,\rho,M_1,M_2,COV)$ is the joint prior distribution of the parameters.

In **PASS**, the joint prior distribution can be specified as either a discrete approximation to the joint prior distribution, or as individual prior distributions, one for each parameter.

Specifying a Joint Prior Distribution

If the joint prior distribution is to be specified directly, the distribution is specified in **PASS** using a discrete approximation to the function $f(\delta,\sigma,\rho,M_1,M_2,COV)$. This provides flexibility in specifying the joint prior distribution. In the six-parameter case, seven columns are entered on the spreadsheet: six for the parameters and one more for the probability. Each row gives a value for each parameter and the corresponding parameter-combination probability. The accuracy of the distribution approximation is controlled by the number of points (spreadsheet rows) that are used.

An example of entering a joint prior distribution is included at the end of the chapter.

Specifying Individual Prior Distributions

Ciarleglio, Arendt, and Peduzzi (2016) suggest that more flexibility is available if the joint prior distribution is separated into two independent distributions as follows:

$$f(\delta,\sigma,\rho,M_1,M_2,COV) = f_1(\delta)f_2(\sigma)f_3(\rho)f_4(M_1)f_5(M_2)f_6(COV)$$

where $f_1(\delta)$ is the prior distribution of δ and so forth. This method is also available in **PASS**. In this case, the definition of assurance becomes

$$Assurance = E_{\delta,\sigma,\rho,M_1,M_2,COV}\left(P_1(H|\delta,\sigma,\rho,M_1,M_2,COV)\right)$$

$$= \int\int\int\int\int\int P_1(H|\delta,\sigma,\rho,M_1,M_2,COV) f_1(\delta)f_2(\sigma)f_3(\rho)f_4(M_1)f_5(M_2)f_6(COV) d\delta \ldots dCOV$$

Using this definition, the assurance can be calculated using numerical integration. There are a variety of pre-programmed, univariate prior distributions available in **PASS**.

Fixed Values (No Prior) and Custom Values

For any given parameter, **PASS** also provides the option of entering a single fixed value for the prior distribution, or a series of values and corresponding probabilities (using the spreadsheet), rather than one of the pre-programmed distributions.

Numerical Integration in PASS (and Notes on Computation Speed)

When the prior distribution is specified as independent univariate distributions, **PASS** uses a numerical integration algorithm to compute the assurance value as follows:

The domain of each prior distribution is divided into *M* intervals. Since many of the available prior distributions are unbounded on one (e.g., Gamma) or both (e.g., Normal) ends, an approximation is made to make the domain finite. This is accomplished by truncating the distribution to a domain between the two quantiles: $q_{0.001}$ and $q_{0.999}$.

The value of *M* controls the accuracy and speed of the algorithm. If only one parameter is to be given a prior distribution, then a value of *M* between 50 and 100 usually gives an accurate result in a timely manner. However, if two parameters are given priors, the number of iterations needed increases from M to M^2. For example, if *M* is 100, 10000 iterations are needed. Reducing *M* from 100 to 50 reduces the number of iterations from 10000 to 2500.

The algorithm runtime increases when searching for sample size rather than solving for assurance, as a search algorithm is employed in this case. When solving for sample size, we recommend reducing *M* to 20 or less while exploring various scenarios, and then increasing *M* to 50 or more for a final, more accurate, result.

List of Available Univariate Prior Distributions

This section lists the univariate prior distributions that may be used for any of the applicable parameters when the Prior Entry Method is set to Individual.

No Prior

If 'No Prior' is chosen for a parameter, the parameter is assumed to take on a single, fixed value with probability one.

Beta (Shape 1, Shape 2, a, c)

A random variable *X* that follows the beta distribution is defined on a finite interval [a, c]. Two shape parameters (α and β) control the shape of this distribution. Two location parameters *a* and *c* give the minimum and maximum of *X*.

The probability density function of the beta distribution is

$$f(x|\alpha,\beta,a,c) = \frac{\left(\frac{x-a}{c-a}\right)^{\alpha-1}\left(\frac{c-x}{c-a}\right)^{\beta-1}}{(c-a)B(\alpha,\beta)}$$

where $B(\alpha,\beta) = \Gamma(\alpha)\,\Gamma(\beta)/\,\Gamma(\alpha+\beta)$ and $\Gamma(z)$ is the gamma function.

The mean of *X* is

$$\mu_X = \frac{\alpha c + \beta a}{\alpha + \beta}$$

Various distribution shapes are controlled by the values of α and β. These include

Symmetric and Unimodal

$$\alpha = \beta > 1$$

U Shaped

$$\alpha = \beta < 1$$

Bimodal

$$\alpha, \beta < 1$$

Uniform

$$\alpha = \beta = 1$$

Parabolic

$$\alpha = \beta = 2$$

Bell-Shaped

$$\alpha = \beta > 2$$

Gamma (Shape, Scale)

A random variable *X* that follows the gamma distribution is defined on the interval $(0, \infty)$. A shape parameter, κ, and a scale parameter, θ, control the distribution.

The probability density function of the gamma distribution is

$$f(x|\kappa,\theta) = \frac{x^{\kappa-1}e^{-\frac{x}{\theta}}}{\theta^{\kappa}\Gamma(\kappa)}$$

where $\Gamma(z)$ is the gamma function.

The mean of *X* is

$$\mu_X = \frac{\kappa}{\theta}$$

A truncated version of the distribution is constructed by dividing the density by $1 - \mathrm{Prob}(Min \le X \le Max)$ where *Min* and *Max* are two truncation bounds.

Inverse-Gamma (Shape, Scale)

A random variable *X* that follows the inverse-gamma distribution is defined on the interval $(0, \infty)$. If *Y* ~ gamma, then *X* = 1 / *Y* ~ inverse-gamma. A shape parameter, α, and a scale parameter, β, control the distribution.

The probability density function of the inverse-gamma distribution is

$$f(x|\alpha,\beta) = \frac{\beta^{\alpha}x^{\alpha-1}e^{-\frac{\beta}{x}}}{\Gamma(\alpha)}$$

where $\Gamma(z)$ is the gamma function.

The mean of *X* is

$$\mu_X = \frac{\beta}{\alpha - 1} \text{ for } \alpha > 1$$

A truncated version of the distribution is constructed by dividing the density by $1 - \mathrm{Prob}(Min \le X \le Max)$ where *Min* and *Max* are two truncation bounds.

Logistic (Location, Scale)

A random variable *X* that follows the logistic distribution is defined on the interval $(-\infty, \infty)$. A location parameter, μ, and a scale parameter, s, control the distribution.

The probability density function of the logistic distribution is

$$f(x|\mu, s) = \frac{e^{-\frac{x-\mu}{s}}}{\mathrm{s}\left(1 + e^{-\frac{x-\mu}{s}}\right)^2}$$

The mean of *X* is

$$\mu_X = \mu$$

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

Lognormal (Mean, SD)

A random variable *X* that follows the lognormal distribution is defined on the interval $(0, \infty)$. A location parameter, $\mu_{\log(X)}$, and a scale parameter, $\sigma_{\log(X)}$, control the distribution. If Z ~ standard normal, then $X = e^{\mu+\sigma Z} \sim$ lognormal. Note that $\mu_{\log(X)} = E(\log(X))$ and $\sigma_{\log(X)} = Standard\ Deviation(\log(X))$.

The probability density function of the lognormal distribution is

$$f(x|\mu, \sigma) = \frac{e^{-\frac{1}{2}\left(\frac{\log x - \mu}{\sigma}\right)^2}}{x\sigma\sqrt{2\pi}}$$

The mean of *X* is

$$\mu_X = e^{\mu + \frac{\sigma^2}{2}}$$

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

LogT (Mean, SD)

A random variable *X* that follows the logT distribution is defined on the interval $(0, \infty)$. A location parameter, $\mu_{\log(X)}$, a scale parameter, $\sigma_{\log(X)}$, and a shape parameter, ν, control the distribution. Note that ν is referred to as the *degrees of freedom*.

If t ~ Student's t, then $X = e^{\mu+\sigma t} \sim$ logT.

The probability density function of the logT distribution is

$$f(x|\mu,\sigma,\nu) = \frac{\Gamma\left(\frac{\nu+1}{2}\right)}{x\Gamma\left(\frac{\nu}{2}\right)\sigma\sqrt{\nu\pi}}\left(1+\frac{1}{\nu}\left(\frac{\log x-\mu}{\sigma}\right)^2\right)^{\left(\frac{-\nu-1}{2}\right)}$$

The mean of *X* is not defined.

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

Normal (Mean, SD)

A random variable *X* that follows the normal distribution is defined on the interval $(-\infty, \infty)$. A location parameter, μ, and a scale parameter, σ, control the distribution.

The probability density function of the normal distribution is

$$f(x|\mu,\sigma) = \frac{e^{-\frac{1}{2}\left(\frac{x-\mu}{\sigma}\right)^2}}{\sigma\sqrt{2\pi}}$$

The mean of *X* is

$$\mu_X = \mu$$

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

T (Mean, SD, DF)

A random variable *X* that follows Student's t distribution is defined on the interval $(-\infty, \infty)$. A location parameter, μ, a scale parameter, σ, and a shape parameter, ν, control the distribution. Note that ν is referred to as the *degrees of freedom* or *DF*.

The probability density function of the Student's t distribution is

$$f(x|\mu,\sigma,\nu) = \frac{\Gamma\left(\frac{\nu+1}{2}\right)}{\Gamma\left(\frac{\nu}{2}\right)\sigma\sqrt{\nu\pi}}\left(1+\frac{1}{\nu}\left(\frac{x-\mu}{\sigma}\right)^2\right)^{\left(\frac{-\nu-1}{2}\right)}$$

The mean of *X* is μ if $\nu > 1$.

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

Triangle (Mode, Min, Max)

Let *a* = minimum, *b* = maximum, and *c* = mode. A random variable *X* that follows a triangle distribution is defined on the interval (a, b).

The probability density function of the triangle distribution is

$$f(x|a,b,c) = \begin{cases} \frac{2(x-a)}{(b-a)(c-a)} & \text{for } a \leq x < c \\ \frac{2}{b-a} & \text{for } x = c \\ \frac{2(b-x)}{(b-a)(b-c)} & \text{for } c < x \leq b \end{cases}$$

The mean of *X* is

$$\frac{a+b+c}{3}$$

Uniform (Min, Max)

Let *a* = minimum and *b* = maximum. A random variable *X* that follows a uniform distribution is defined on the interval $[a, b]$.

The probability density function of the uniform distribution is

$$f(x|a,b) = \begin{cases} \frac{1}{b-a} & \text{for } a \leq x \leq b \end{cases}$$

The mean of *X* is

$$\frac{a+b}{2}$$

Weibull (Shape, Scale)

A random variable *X* that follows the Weibull distribution is defined on the interval $(0, \infty)$. A shape parameter, κ, and a scale parameter, λ, control the distribution.

The probability density function of the Weibull distribution is

$$f(x|\kappa,\lambda) = \frac{\kappa}{\lambda}\left(\frac{x}{\lambda}\right)^{\kappa-1} e^{-\left(\frac{x}{\lambda}\right)^{\kappa}}$$

The mean of *X* is

$$\mu_X = \kappa\Gamma\left(1 + \frac{1}{\kappa}\right)$$

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ where *Min* and *Max* are two truncation bounds.

Custom (Values and Probabilities in Spreadsheet)

This custom prior distribution is represented by a set of user-specified points and associated probabilities, entered in two columns of the spreadsheet. The points make up the entire set of values that are used for this parameter in the calculation of assurance. The associated probabilities should sum to one. Note that custom values and probabilities can be used to approximate any continuous distribution.

For example, a prior distribution of X might be

$\boldsymbol{X_i}$	$\boldsymbol{P_i}$
10	0.2
20	0.2
30	0.3
40	0.2
50	0.1

In this example, the mean of X is

$$\mu_X = \sum_{i=1}^{5} X_i P_i$$

Example 1 – Assurance Over a Range of Sample Sizes

Suppose that a cluster randomized study that uses a superiority by a margin test is being planned in which *SM = 0.05;* δ = 1; σ = 2; ρ = 0.01; *M1* and *M2* = 10; *COV* = 0.65; *alpha* = 0.025; and *K1* and *K2* = 5, 10, 15, 20. Power is to be calculated for a subject-level test.

To complete their sample size study, the researchers want to run an assurance analysis for a range of group sample sizes from 5 to 20. An elicitation exercise determined that the prior distribution of the mean difference should be normal with mean 0.8 and standard deviation 0.2, the prior distribution of the common group standard deviation should be a normal with mean 2 and standard deviation 0.2, the prior distribution of the ICC should be a normal with mean 0.01 and standard deviation 0.002, the prior distribution of the cluster size of group 1 should be a normal with mean 7.5 and standard deviation 1.5, the prior distribution of the cluster size of group 2 should be a normal with mean 7.5 and standard deviation 1.5, and the prior distribution of the coefficient of variation of cluster sizes should be a normal with mean 0.65 and standard deviation 0.05.

To reduce the runtime of this example, the number of computation points is set to 4. In practice, we recommend setting this value to 10 or more for the most accurate results.

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 .... **Assurance**
Prior Entry Method.. **Individual (Enter a prior distribution for each applicable parameter)**
Higher Means Are... **Better (H1: δ > SM)**
Test Statistic .... **T-Test Based on Number of Subjects**
Alpha... **0.025**
K1 (Number of Clusters) **5 10 15 20**
Prior Distribution of M1 .... **Normal (Mean, SD)**
Mean... **7.5**
SD... **1.5**
Truncation Boundaries.................................. **None**
K2 (Number of Clusters) **K1**
Prior Distribution of M2 .... **Normal (Mean, SD)**
Mean... **7.5**
SD... **1.5**
Truncation Boundaries.................................. **None**
Prior Distribution of COV............................... **Normal (Mean, SD)**
Mean... **0.65**
SD... **0.05**
Truncation Boundaries.................................. **None**
SM (Superiority Margin)................................ **0.05**

Prior Distribution of δ ....**Normal (Mean, SD)**
Mean..**0.8**
SD..**0.2**
Truncation Boundaries.................................**None**
Prior Distribution of σ ....**Normal (Mean, SD)**
Mean..**2**
SD..**0.2**
Truncation Boundaries.................................**None**
Prior Distribution of ρ ....**Normal (Mean, SD)**
Mean..**0.01**
SD..**0.002**
Truncation Boundaries.................................**None**

Options Tab

Number of Computation Points for each Prior Distribution........**4**
Maximum K1 in Sample Size Search............**1000**

Output

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

Numeric Reports

Numeric Results

Solve For: Assurance
Groups: 1 = Treatment, 2 = Control
Test Statistic: T-Test with DF based on number of subjects
Higher Means Are: Better
Superiority Margin (SM): 0.05
Hypotheses: H0: δ ≤ SM vs. H1: δ > SM
Prior Type: Individual Univariate Distributions

Prior Distributions
M1: Normal (Mean = 7.5, SD = 1.5).
M2: Normal (Mean = 7.5, SD = 1.5).
COV: Normal (Mean = 0.65, SD = 0.05).
δ: Normal (Mean = 0.8, SD = 0.2).
σ: Normal (Mean = 2, SD = 0.2).
ρ: Normal (Mean = 0.01, SD = 0.002).

		Sample Size			Number of Clusters			Cluster Size			Mean Difference	Standard Deviation	Intracluster Correlation	
Assurance*	Power‡	N1	N2	N	K1	K2	K	E(M1)	E(M2)	E(COV)	E(δ)	E(σ)	E(ρ)	Alpha
0.35120	0.33784	38	38	76	5	5	10	7.5	7.5	0.65	0.8	2	0.01	0.025
0.56646	0.59277	76	76	152	10	10	20	7.5	7.5	0.65	0.8	2	0.01	0.025
0.69719	0.76479	113	113	226	15	15	30	7.5	7.5	0.65	0.8	2	0.01	0.025
0.78028	0.87358	151	151	302	20	20	40	7.5	7.5	0.65	0.8	2	0.01	0.025

* The number of points used for computation of the prior(s) was 4.
‡ Power was calculated using M1 = E(M1) = 7.5, M2 = E(M2) = 7.5, COV = E(COV) = 0.65, δ = E(δ) = 0.8, σ = E(σ) = 2, and ρ = E(ρ) = 0.01.

SM	The magnitude and direction of the margin of superiority. Since higher means are better, this value is positive and is the distance above the reference mean that is considered superior.
Assurance	The expected power where the expectation is with respect to the prior distribution(s).
Power	The power calculated using the means of the prior distributions as the values of the corresponding parameters.
N1	The number of subjects in group 1.
N2	The number of subjects in group 2.
N	The total sample size. N = N1 + N2.
K1	The number of clusters in group 1.
K2	The number of clusters in group 2.
K	The total number of clusters.
E(M1)	The expected average number of items (subjects) per cluster in group 1.
E(M2)	The expected average number of items (subjects) per cluster in group 2.
E(COV)	The expected coefficient of variation of the cluster sizes.
E(δ)	The expected mean difference in the response assumed by H1. $\delta = \mu1 - \mu2$.
E(σ)	The expected standard deviation of the subject responses.
E(ρ)	The expected intracluster correlation (ICC).
Alpha	The probability of rejecting a true null hypothesis.

Summary Statements

A parallel two-group cluster-randomized design will be used to test whether the Group 1 (treatment) mean (μ1) is superior to the Group 2 (control) mean (μ2) by a margin, with a superiority margin of 0.05 (H0: $\delta \leq 0.05$ versus H1: $\delta > 0.05$, $\delta = \mu1 - \mu2$). The comparison will be made using a one-sided t-test with degrees of freedom based on the number of subjects (as in a subject-level analysis), and with a Type I error rate (α) of 0.025. The prior distribution used for the average cluster size in Group 1 is Normal (Mean = 7.5, SD = 1.5). The prior distribution used for the average cluster size in Group 2 is Normal (Mean = 7.5, SD = 1.5). The prior distribution used for the coefficient of variation of cluster sizes is Normal (Mean = 0.65, SD = 0.05). The prior distribution used for the difference between the group means is Normal (Mean = 0.8, SD = 0.2). The prior distribution used for the standard deviation of subjects is Normal (Mean = 2, SD = 0.2). The prior distribution used for the intracluster correlation coefficient is Normal (Mean = 0.01, SD = 0.002). With 5 clusters (38 total subjects) in Group 1 (treatment) and 5 clusters (38 total subjects) in Group 2 (control), the assurance (average power) is 0.3512.

References

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Campbell, M.J. and Walters, S.J. 2014. How to Design, Analyse and Report Cluster Randomised Trials in Medicine and Health Related Research. Wiley. New York.
Ahn, C., Heo, M., and Zhang, S. 2015. Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research. CRC Press. New York.
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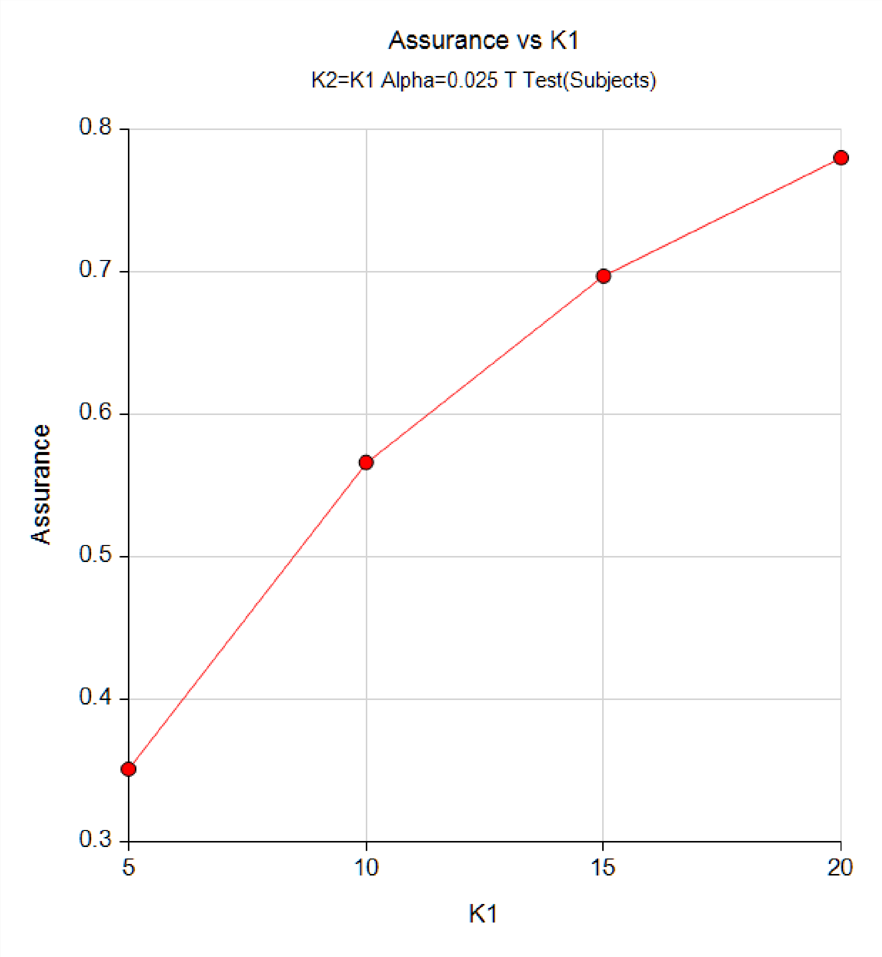
Donner, A. and Klar, N. 2000. Design and Analysis of Cluster Randomization Trials in Health Research. Arnold. London.
Chow, S.C., Shao, J., Wang, H., and Lokhnygina, Y. 2018. Sample Size Calculations in Clinical Research, Third Edition. Taylor & Francis/CRC. Boca Raton, Florida.

This report shows the assurance values obtained by the various sample sizes.

Plots Section

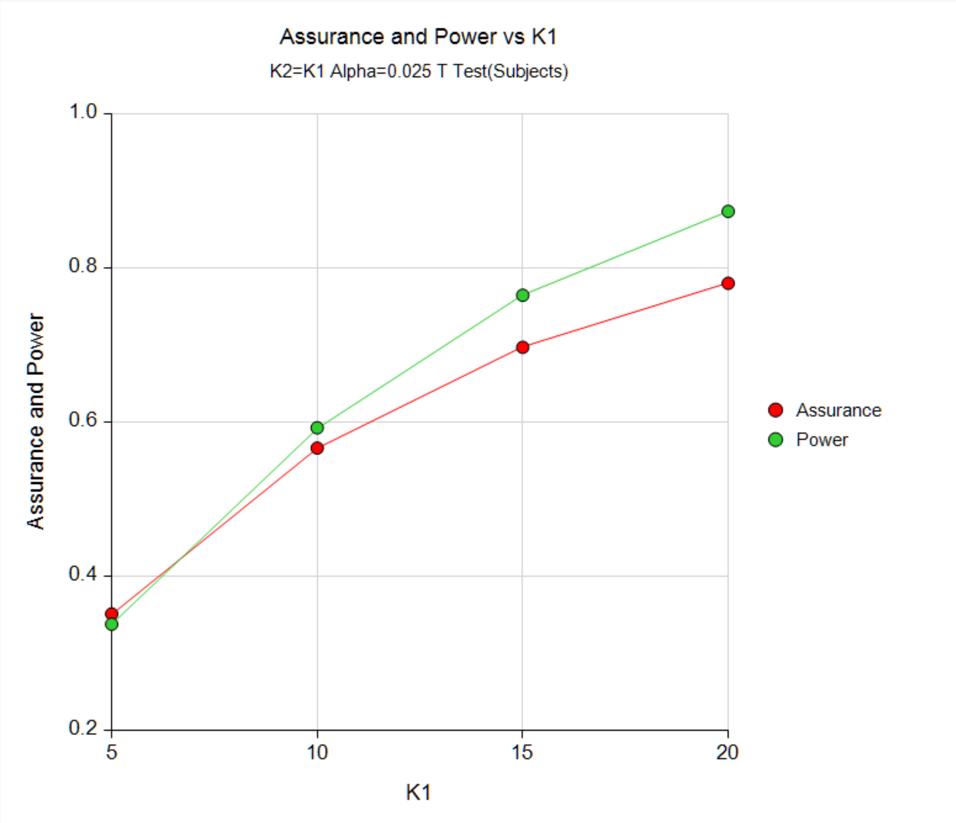
Plots



This plot shows the relationship between the assurance and sample size.

Comparison Plots Section

Comparison Plots



This plot compares the assurance and power across values of sample size.

Example 2 – Validation using Hand Computation

We could not find a validation example in the literature for procedure, so we have developed a validation example of our own.

Suppose a superiority by a margin t-test will be used in which the superiority margin is 0.05, K1 = K2 = 100, and the significance level is 0.025.

The prior distribution of δ is approximated by the following table. These are loaded into C1 and C2.

δ	Prob
-0.3	0.4
0.7	0.6

The prior distribution of the σ is approximated by the following table. These are loaded into C3 and C4.

σ	Prob
1.5	0.4
2.5	0.6

The prior distribution of the ρ is approximated by the following table. These are loaded into C5 and C6.

ρ	Prob
0.01	0.5
0.02	0.5

The prior distribution of the M1 is approximated by the following table. These are loaded into C7 and C8.

M1	Prob
7	0.5
9	0.5

The prior distribution of the M2 is approximated by the following table. These are loaded into C9 and C10.

M2	Prob
7	0.5
9	0.5

The prior distribution of the COV is approximated by the following table. These are loaded into C11 and 12.

COV	Prob
0.6	0.3
0.7	0.7

To run this example, the spreadsheet will need to be loaded with the following 12 columns corresponding to the values listed above.

C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12
-0.3	0.4	1.5	0.4	0.01	0.5	7	0.5	7	0.5	0.6	0.3
0.7	0.6	2.5	0.6	0.02	0.5	9	0.5	9	0.5	0.7	0.7

The *Superiority by a Margin Tests for Two Means in a Cluster-Randomized Design* procedure is used to compute the power for each of the 64 combinations the parameters. The results of these calculations are shown next.

Numeric Results for a Test of Mean Difference

Solve For: Power
Groups: 1 = Treatment, 2 = Control
Test Statistic: T-Test with DF based on number of subjects
Higher Means Are: Better
Hypotheses: H0: δ ≤ SM vs. H1: δ > SM

	Number of Clusters			Cluster Size			Sample Size			Mean Difference	Superiority Margin	Standard Deviation	ICC	
Power	K1	K2	K	M1	M2	COV	N1	N2	N	δ	SM	σ	ρ	Alpha
0.00000	100	100	200	7	7	0.3	700	700	1400	-0.3	0.05	1.5	0.01	0.025
0.00000	100	100	200	7	7	0.7	700	700	1400	-0.3	0.05	1.5	0.01	0.025
0.00000	100	100	200	7	9	0.3	700	900	1600	-0.3	0.05	1.5	0.01	0.025
0.00000	100	100	200	7	9	0.7	700	900	1600	-0.3	0.05	1.5	0.01	0.025
0.00000	100	100	200	9	7	0.3	900	700	1600	-0.3	0.05	1.5	0.01	0.025
0.00000	100	100	200	9	7	0.7	900	700	1600	-0.3	0.05	1.5	0.01	0.025
0.00000	100	100	200	9	9	0.3	900	900	1800	-0.3	0.05	1.5	0.01	0.025
0.00000	100	100	200	9	9	0.7	900	900	1800	-0.3	0.05	1.5	0.01	0.025
0.00000	100	100	200	7	7	0.3	700	700	1400	-0.3	0.05	1.5	0.02	0.025
0.00000	100	100	200	7	7	0.7	700	700	1400	-0.3	0.05	1.5	0.02	0.025
0.00000	100	100	200	7	9	0.3	700	900	1600	-0.3	0.05	1.5	0.02	0.025
0.00000	100	100	200	7	9	0.7	700	900	1600	-0.3	0.05	1.5	0.02	0.025
0.00000	100	100	200	9	7	0.3	900	700	1600	-0.3	0.05	1.5	0.02	0.025
0.00000	100	100	200	9	7	0.7	900	700	1600	-0.3	0.05	1.5	0.02	0.025
0.00000	100	100	200	9	9	0.3	900	900	1800	-0.3	0.05	1.5	0.02	0.025
0.00000	100	100	200	9	9	0.7	900	900	1800	-0.3	0.05	1.5	0.02	0.025
0.00000	100	100	200	7	7	0.3	700	700	1400	-0.3	0.05	2.5	0.01	0.025
0.00000	100	100	200	7	7	0.7	700	700	1400	-0.3	0.05	2.5	0.01	0.025
0.00000	100	100	200	7	9	0.3	700	900	1600	-0.3	0.05	2.5	0.01	0.025
0.00000	100	100	200	7	9	0.7	700	900	1600	-0.3	0.05	2.5	0.01	0.025
0.00000	100	100	200	9	7	0.3	900	700	1600	-0.3	0.05	2.5	0.01	0.025
0.00000	100	100	200	9	7	0.7	900	700	1600	-0.3	0.05	2.5	0.01	0.025
0.00000	100	100	200	9	9	0.3	900	900	1800	-0.3	0.05	2.5	0.01	0.025
0.00000	100	100	200	9	9	0.7	900	900	1800	-0.3	0.05	2.5	0.01	0.025
0.00000	100	100	200	7	7	0.3	700	700	1400	-0.3	0.05	2.5	0.02	0.025
0.00001	100	100	200	7	7	0.7	700	700	1400	-0.3	0.05	2.5	0.02	0.025
0.00000	100	100	200	7	9	0.3	700	900	1600	-0.3	0.05	2.5	0.02	0.025
0.00000	100	100	200	7	9	0.7	700	900	1600	-0.3	0.05	2.5	0.02	0.025
0.00000	100	100	200	9	7	0.3	900	700	1600	-0.3	0.05	2.5	0.02	0.025
0.00000	100	100	200	9	7	0.7	900	700	1600	-0.3	0.05	2.5	0.02	0.025
0.00000	100	100	200	9	9	0.3	900	900	1800	-0.3	0.05	2.5	0.02	0.025
0.00000	100	100	200	9	9	0.7	900	900	1800	-0.3	0.05	2.5	0.02	0.025
1.00000	100	100	200	7	7	0.3	700	700	1400	0.7	0.05	1.5	0.01	0.025
1.00000	100	100	200	7	7	0.7	700	700	1400	0.7	0.05	1.5	0.01	0.025
1.00000	100	100	200	7	9	0.3	700	900	1600	0.7	0.05	1.5	0.01	0.025
1.00000	100	100	200	7	9	0.7	700	900	1600	0.7	0.05	1.5	0.01	0.025
1.00000	100	100	200	9	7	0.3	900	700	1600	0.7	0.05	1.5	0.01	0.025
1.00000	100	100	200	9	7	0.7	900	700	1600	0.7	0.05	1.5	0.01	0.025
1.00000	100	100	200	9	9	0.3	900	900	1800	0.7	0.05	1.5	0.01	0.025
1.00000	100	100	200	9	9	0.7	900	900	1800	0.7	0.05	1.5	0.01	0.025
1.00000	100	100	200	7	7	0.3	700	700	1400	0.7	0.05	1.5	0.02	0.025
1.00000	100	100	200	7	7	0.7	700	700	1400	0.7	0.05	1.5	0.02	0.025
1.00000	100	100	200	7	9	0.3	700	900	1600	0.7	0.05	1.5	0.02	0.025
1.00000	100	100	200	7	9	0.7	700	900	1600	0.7	0.05	1.5	0.02	0.025
1.00000	100	100	200	9	7	0.3	900	700	1600	0.7	0.05	1.5	0.02	0.025
1.00000	100	100	200	9	7	0.7	900	700	1600	0.7	0.05	1.5	0.02	0.025
1.00000	100	100	200	9	9	0.3	900	900	1800	0.7	0.05	1.5	0.02	0.025
1.00000	100	100	200	9	9	0.7	900	900	1800	0.7	0.05	1.5	0.02	0.025
0.99702	100	100	200	7	7	0.3	700	700	1400	0.7	0.05	2.5	0.01	0.025
0.99644	100	100	200	7	7	0.7	700	700	1400	0.7	0.05	2.5	0.01	0.025
0.99871	100	100	200	7	9	0.3	700	900	1600	0.7	0.05	2.5	0.01	0.025
0.99839	100	100	200	7	9	0.7	700	900	1600	0.7	0.05	2.5	0.01	0.025
0.99871	100	100	200	9	7	0.3	900	700	1600	0.7	0.05	2.5	0.01	0.025
0.99839	100	100	200	9	7	0.7	900	700	1600	0.7	0.05	2.5	0.01	0.025
0.99956	100	100	200	9	9	0.3	900	900	1800	0.7	0.05	2.5	0.01	0.025
0.99941	100	100	200	9	9	0.7	900	900	1800	0.7	0.05	2.5	0.01	0.025

0.99550	100	100	200	7	7	0.3	700	700	1400	0.7	0.05	2.5	0.02	0.025
0.99396	100	100	200	7	7	0.7	700	700	1400	0.7	0.05	2.5	0.02	0.025
0.99781	100	100	200	7	9	0.3	700	900	1600	0.7	0.05	2.5	0.02	0.025
0.99686	100	100	200	7	9	0.7	700	900	1600	0.7	0.05	2.5	0.02	0.025
0.99781	100	100	200	9	7	0.3	900	700	1600	0.7	0.05	2.5	0.02	0.025
0.99686	100	100	200	9	7	0.7	900	700	1600	0.7	0.05	2.5	0.02	0.025
0.99912	100	100	200	9	9	0.3	900	900	1800	0.7	0.05	2.5	0.02	0.025
0.99862	100	100	200	9	9	0.7	900	900	1800	0.7	0.05	2.5	0.02	0.025

The assurance calculation is made by summing the quantities

$$\left[\left(power_{i,j,k,l,m,n}\right)p(\delta_i)p\left(\sigma_j\right)p(\rho_k)p(M1_l)p(M2_m)p(COV_n)\right]$$

as follows

$$Assurance = (0.00000 \times 0.4 \times 0.4 \times 0.5 \times 0.5 \times 0.5 \times 0.3) + (0.00000 \times 0.4 \times 0.4 \times 0.5 \times 0.5 \times 0.5 \times 0.7) + \cdots + (0.99862 \times 0.6 \times 0.6 \times 0.5 \times 0.5 \times 0.5 \times 0.7) = 0.59908.$$

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 ....**Assurance**
Prior Entry Method.......................................**Individual (Enter a prior distribution for each applicable parameter)**
Higher Means Are..**Better (H1: δ > SM)**
Test Statistic ....**T-Test Based on Number of Subjects**
Alpha...**0.025**
K1 (Number of Clusters) **100**
Prior Distribution of M1 ....**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C7**
Column of Pr(Values)....................................**C8**
K2 (Number of Clusters) **K1**
Prior Distribution of M2 ....**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C9**
Column of Pr(Values)....................................**C10**

Prior Distribution of COV................................**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C11**
Column of Pr(Values)....................................**C12**
SM (Superiority Margin).................................**0.05**
Prior Distribution of δ ....**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C1**
Column of Pr(Values)....................................**C2**
Prior Distribution of σ ....**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C3**
Column of Pr(Values)....................................**C4**
Prior Distribution of ρ ....**Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C5**
Column of Pr(Values)....................................**C6**

Options Tab

Number of Computation Points for each Prior Distribution........**4**
Maximum K1 in Sample Size Search.............**1000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12
1	-0.3	0.4	1.5	0.4	0.01	0.5	7	0.5	7	0.5	0.6	0.3
2	0.7	0.6	2.5	0.6	0.02	0.5	9	0.5	9	0.5	0.7	0.7

Output

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

Numeric Results

Solve For:	Assurance
Groups:	1 = Treatment, 2 = Control
Test Statistic:	T-Test with DF based on number of subjects
Higher Means Are:	Better
Superiority Margin (SM):	0.05
Hypotheses:	H0: δ ≤ SM vs. H1: δ > SM
Prior Type:	Individual Univariate Distributions

Prior Distributions

M1:	Point List (Values = C7, Probs = C8).
C7:	7 9
C8:	0.5 0.5
M2:	Point List (Values = C9, Probs = C10).
C9:	7 9
C10:	0.5 0.5
COV:	Point List (Values = C11, Probs = C12).
C11:	0.6 0.7
C12:	0.3 0.7
δ:	Point List (Values = C1, Probs = C2).
C1:	-0.3 0.7
C2:	0.4 0.6
σ:	Point List (Values = C3, Probs = C4).
C3:	1.5 2.5
C4:	0.4 0.6
ρ:	Point List (Values = C5, Probs = C6).
C5:	0.01 0.02
C6:	0.5 0.5

		Sample Size			Number of Clusters			Cluster Size			Mean Difference	Standard Deviation	Intracluster Correlation	
Assurance	Power‡	N1	N2	N	K1	K2	K	E(M1)	E(M2)	E(COV)	E(δ)	E(σ)	E(ρ)	Alpha
0.59908	0.60081	800	800	1600	100	100	200	8	8	0.67	0.3	2.1	0.015	0.025

‡ Power was calculated using M1 = E(M1) = 8, M2 = E(M2) = 8, COV = E(COV) = 0.67, δ = E(δ) = 0.3, σ = E(σ) = 2.1, and ρ = E(ρ) = 0.015.

PASS has also calculated the assurance as 0.59908 which validates the procedure.

Example 3 – Finding the Sample Size Needed to Achieve a Specified Assurance

Continuing with Example 1, the researchers want to investigate the sample sizes necessary to achieve assurances of 0.5, 0.6, and 0.7.

In order to reduce the runtime during this exploratory phase of the analysis, the number of points in the prior computation is reduced to 4. This slightly reduces the accuracy, but greatly reduces the runtime.

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	**Sample Size**
Prior Entry Method	**Individual (Enter a prior distribution for each applicable parameter)**
Higher Means Are	**Better (H1: δ > SM)**
Test Statistic	**T-Test Based on Number of Subjects**
Assurance	**0.5 0.6 0.7**
Alpha	**0.025**
Prior Distribution of M1	**Normal (Mean, SD)**
Mean	**7.5**
SD	**1.5**
Truncation Boundaries	**None**
K2 (Number of Clusters)	**K1**
Prior Distribution of M2	**Normal (Mean, SD)**
Mean	**7.5**
SD	**1.5**
Truncation Boundaries	**None**
Prior Distribution of COV	**Normal (Mean, SD)**
Mean	**0.65**
SD	**0.05**
Truncation Boundaries	**None**
SM (Superiority Margin)	**0.05**
Prior Distribution of δ	**Normal (Mean, SD)**
Mean	**0.8**
SD	**0.2**
Truncation Boundaries	**None**
Prior Distribution of σ	**Normal (Mean, SD)**
Mean	**2**
SD	**0.2**
Truncation Boundaries	**None**

Prior Distribution of ρ ....**Normal (Mean, SD)**
Mean...**0.01**
SD...**0.002**
Truncation Boundaries..................................**None**

Options Tab

Number of Computation Points for each Prior Distribution........**4**
Maximum K1 in Sample Size Search............**1000**

Output

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

Numeric Reports

Numeric Results

Solve For:	Sample Size
Groups:	1 = Treatment, 2 = Control
Test Statistic:	T-Test with DF based on number of subjects
Higher Means Are:	Better
Superiority Margin (SM):	0.05
Hypotheses:	H0: δ ≤ SM vs. H1: δ > SM
Prior Type:	Individual Univariate Distributions

Prior Distributions

M1:	Normal (Mean = 7.5, SD = 1.5).
M2:	Normal (Mean = 7.5, SD = 1.5).
COV:	Normal (Mean = 0.65, SD = 0.05).
δ:	Normal (Mean = 0.8, SD = 0.2).
σ:	Normal (Mean = 2, SD = 0.2).
ρ:	Normal (Mean = 0.01, SD = 0.002).

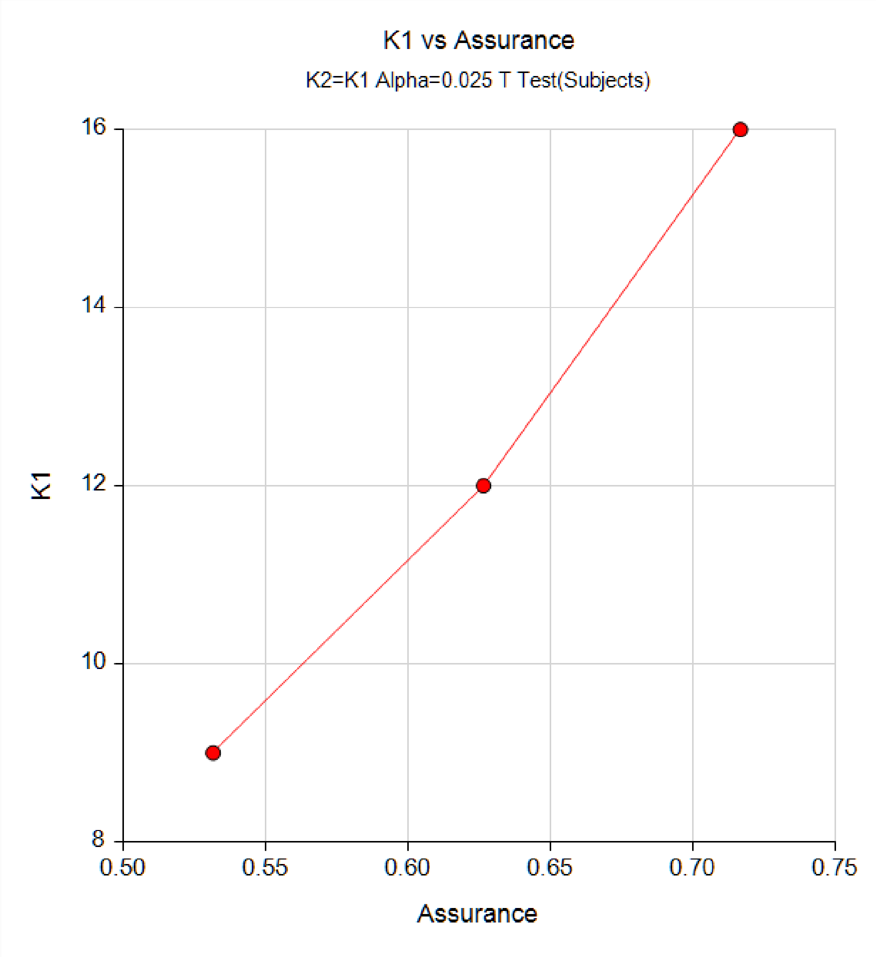
		Sample Size			Number of Clusters			Cluster Size			Mean Difference	Standard Deviation	Intracluster Correlation	
Assurance*	Power‡	N1	N2	N	K1	K2	K	E(M1)	E(M2)	E(COV)	E(δ)	E(σ)	E(ρ)	Alpha
0.53154	0.54553	68	68	136	9	9	18	7.5	7.5	0.65	0.8	2	0.01	0.025
0.62653	0.67151	91	91	182	12	12	24	7.5	7.5	0.65	0.8	2	0.01	0.025
0.71673	0.79272	121	121	242	16	16	32	7.5	7.5	0.65	0.8	2	0.01	0.025

* The number of points used for computation of the prior(s) was 4.
‡ Power was calculated using M1 = E(M1) = 7.5, M2 = E(M2) = 7.5, COV = E(COV) = 0.65, δ = E(δ) = 0.8, σ = E(σ) = 2, and ρ = E(ρ) = 0.01.

This report shows the required sample size for each assurance target.

Plots Section

Plots



This plot shows the relationship between the sample size and assurance.

Example 4 – Joint Prior Distribution

Suppose a superiority by a margin t-test will be used in which K1 = K2 = (10, 20, 30) and the significance level is 0.025. The superiority margin is 0.05.

The joint prior distribution of the parameters is approximated by the following table. Note that the labels in parentheses identify the corresponding column of the spreadsheet. Also note that the prior probabilities in C7 will be automatically rescaled so that they sum to one.

δ (C1)	σ (C2)	ρ (C3)	M1 (C4)	M2 (C5)	COV (C6)	Prob (C7)
1.00	2.00	0.01	5	5	0.65	0.25
1.00	2.00	0.01	10	10	0.65	0.20
1.00	2.00	0.01	5	5	0.55	0.25
1.00	2.00	0.01	10	10	0.55	0.20
0.75	1.70	0.01	5	5	0.65	0.65
0.75	1.70	0.01	10	10	0.65	0.60
0.75	1.70	0.01	5	5	0.55	0.65
0.75	1.70	0.01	10	10	0.55	0.60
0.50	1.50	0.01	5	5	0.65	0.45
0.50	1.50	0.01	10	10	0.65	0.40
0.50	1.50	0.01	5	5	0.55	0.45
0.50	1.50	0.01	10	10	0.55	0.40
0.25	1.25	0.01	5	5	0.65	0.25
0.25	1.25	0.01	10	10	0.65	0.20
0.25	1.25	0.01	5	5	0.55	0.25
0.25	1.25	0.01	10	10	0.55	0.20
1.00	2.00	0.02	5	5	0.65	0.15
1.00	2.00	0.02	10	10	0.65	0.10
1.00	2.00	0.02	5	5	0.55	0.15
1.00	2.00	0.02	10	10	0.55	0.10
0.75	1.70	0.02	5	5	0.65	0.35
0.75	1.70	0.02	10	10	0.65	0.30
0.75	1.70	0.02	5	5	0.55	0.35
0.75	1.70	0.02	10	10	0.55	0.30
0.50	1.50	0.02	5	5	0.65	0.25
0.50	1.50	0.02	10	10	0.65	0.20
0.50	1.50	0.02	5	5	0.55	0.25
0.50	1.50	0.02	10	10	0.55	0.20
0.25	1.25	0.02	5	5	0.65	0.15
0.25	1.25	0.02	10	10	0.65	0.10
0.25	1.25	0.02	5	5	0.55	0.15
0.25	1.25	0.02	10	10	0.55	0.10

To run this example, the spreadsheet will need to be loaded with the above data.

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 .... **Assurance**
Prior Entry Method .... **Combined (Enter parameter values and probabilities on spreadsheet)**
Higher Means Are .... **Better (H1: δ > SM)**
Test Statistic .... **T-Test Based on Number of Subjects**
Alpha... **0.025**
K1 (Number of Clusters) **10 20 30**
Column of M1 Values.................................... **C1**
K2 (Number of Clusters) **K1**
Column of M2 Values.................................... **C2**
Column of COV Values................................. **C3**
SM (Superiority Margin)................................ **0.05**
Column of δ Values **C4**
Column of σ Values **C5**
Column of ρ Values **C6**
Column of Pr(Values).................................... **C7**

Options Tab

Number of Computation Points for each Prior Distribution **4**
Maximum K1 in Sample Size Search............ **1000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5	C6	C7
1	1.00	2.00	0.01	5	5	0.65	0.25
2	1.00	2.00	0.01	10	10	0.65	0.20
3	1.00	2.00	0.01	5	5	0.55	0.25
4	1.00	2.00	0.01	10	10	0.55	0.20
5	0.75	1.70	0.01	5	5	0.65	0.65
6	0.75	1.70	0.01	10	10	0.65	0.60
7	0.75	1.70	0.01	5	5	0.55	0.65
8	0.75	1.70	0.01	10	10	0.55	0.60
9	0.50	1.50	0.01	5	5	0.65	0.45
10	0.50	1.50	0.01	10	10	0.65	0.40
11	0.50	1.50	0.01	5	5	0.55	0.45
12	0.50	1.50	0.01	10	10	0.55	0.40
13	0.25	1.25	0.01	5	5	0.65	0.25
14	0.25	1.25	0.01	10	10	0.65	0.20
15	0.25	1.25	0.01	5	5	0.55	0.25
16	0.25	1.25	0.01	10	10	0.55	0.20
17	1.00	2.00	0.02	5	5	0.65	0.15
18	1.00	2.00	0.02	10	10	0.65	0.10
19	1.00	2.00	0.02	5	5	0.55	0.15
20	1.00	2.00	0.02	10	10	0.55	0.10
21	0.75	1.70	0.02	5	5	0.65	0.35

22	0.75	1.70	0.02	10	10	0.65	0.30
23	0.75	1.70	0.02	5	5	0.55	0.35
24	0.75	1.70	0.02	10	10	0.55	0.30
25	0.50	1.50	0.02	5	5	0.65	0.25
26	0.50	1.50	0.02	10	10	0.65	0.20
27	0.50	1.50	0.02	5	5	0.55	0.25
28	0.50	1.50	0.02	10	10	0.55	0.20
29	0.25	1.25	0.02	5	5	0.65	0.15
30	0.25	1.25	0.02	10	10	0.65	0.10
31	0.25	1.25	0.02	5	5	0.55	0.15
32	0.25	1.25	0.02	10	10	0.55	0.10

Output

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

Numeric Results

Solve For: Assurance
Groups: 1 = Treatment, 2 = Control
Test Statistic: T-Test with DF based on number of subjects
Higher Means Are: Better
Superiority Margin (SM): 0.05
Hypotheses: H0: δ ≤ SM vs. H1: δ > SM
Prior Type: Joint Multivariate Distribution

Prior Distribution
Point Lists
M1: C1: 1 1 1 1 0.75 0.75 0.75 0.75 0.5 0.5 0.5 0.5 0.25 0.25 0.25 0.25 1 1 1 1 0.75 0.75 0.75 0.75 0.5 0.5 0.5 0.5 0.25 0.25 0.25 0.25
M2: C2: 2 2 2 2 1.7 1.7 1.7 1.7 1.5 1.5 1.5 1.5 1.25 1.25 1.25 1.25 2 2 2 2 1.7 1.7 1.7 1.7 1.5 1.5 1.5 1.5 1.25 1.25 1.25 1.25
COV: C3: 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02
δ: C4: 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10
σ: C5: 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10 5 10
ρ: C6: 0.65 0.65 0.55 0.55 0.65 0.65 0.55 0.55 0.65 0.65 0.55 0.55 0.65 0.65 0.55 0.55 0.65 0.65 0.55 0.55 0.65 0.65 0.55 0.55 0.65 0.65 0.55 0.55 0.65 0.65 0.55 0.55
Prob: C7: 0.25 0.2 0.25 0.2 0.65 0.6 0.65 0.6 0.45 0.4 0.45 0.4 0.25 0.2 0.25 0.2 0.15 0.1 0.15 0.1 0.35 0.3 0.35 0.3 0.25 0.2 0.25 0.2 0.15 0.1 0.15 0.1

		Sample Size			Number of Clusters			Cluster Size			Mean Difference	Standard Deviation	Intracluster Correlation	
Assurance	Power‡	N1	N2	N	K1	K2	K	E(M1)	E(M2)	E(COV)	E(δ)	E(σ)	E(ρ)	Alpha
0.54434	0.58012	7	17	24	10	10	20	0.6	1.6	0.01348	7.28261	7.28261	0.6	0.025
0.83247	0.86031	13	33	46	20	20	40	0.6	1.6	0.01348	7.28261	7.28261	0.6	0.025
0.94893	0.96518	20	49	69	30	30	60	0.6	1.6	0.01348	7.28261	7.28261	0.6	0.025

‡ Power was calculated using M1 = E(M1) = 0.6, M2 = E(M2) = 1.6, COV = E(COV) = 0.01348, δ = E(δ) = 7.28261, σ = E(σ) = 7.28261, and ρ = E(ρ) = 0.6.

PASS has calculated the required number of clusters to achieve each assurance goal.

Example 5 – Joint Prior Distribution Validation

The problem given in Example 2 will be used to validate the joint prior distribution method. This will be done by running the individual-prior scenario used in that example through the joint-prior method and checking that the assurance values match.

In Example 2, the prior distribution of δ is given as follows.

δ	Prob
-0.3	0.4
0.7	0.6

The prior distribution of the σ is approximated by the following table.

σ	Prob
1.5	0.4
2.5	0.6

The prior distribution of the ρ is approximated by the following table.

ρ	Prob
0.01	0.5
0.02	0.5

The prior distribution of the M1 is approximated by the following table.

M1	Prob
7	0.5
9	0.5

The prior distribution of the M2 is approximated by the following table.

M2	Prob
7	0.5
9	0.5

The prior distribution of the COV is approximated by the following table.

COV	Prob
0.6	0.3
0.7	0.7

The joint prior distribution can be found by multiplying the independent probabilities. This results in the following discrete probability distribution.

M1 (C1)	M2 (C2)	COV(C3)	δ (C4)	σ (C5)	ρ (C6)	Prob (C7)
7	7	0.6	-0.3	1.5	0.01	0.006
7	7	0.7	-0.3	1.5	0.01	0.014
7	9	0.6	-0.3	1.5	0.01	0.006
7	9	0.7	-0.3	1.5	0.01	0.014
9	7	0.6	-0.3	1.5	0.01	0.006
9	7	0.7	-0.3	1.5	0.01	0.014
9	9	0.6	-0.3	1.5	0.01	0.006
9	9	0.7	-0.3	1.5	0.01	0.014
7	7	0.6	-0.3	1.5	0.02	0.006
7	7	0.7	-0.3	1.5	0.02	0.014

7	9	0.6	-0.3	1.5	0.02	0.006
7	9	0.7	-0.3	1.5	0.02	0.014
9	7	0.6	-0.3	1.5	0.02	0.006
9	7	0.7	-0.3	1.5	0.02	0.014
9	9	0.6	-0.3	1.5	0.02	0.006
9	9	0.7	-0.3	1.5	0.02	0.014
7	7	0.6	-0.3	2.5	0.01	0.009
7	7	0.7	-0.3	2.5	0.01	0.021
7	9	0.6	-0.3	2.5	0.01	0.009
7	9	0.7	-0.3	2.5	0.01	0.021
9	7	0.6	-0.3	2.5	0.01	0.009
9	7	0.7	-0.3	2.5	0.01	0.021
9	9	0.6	-0.3	2.5	0.01	0.009
9	9	0.7	-0.3	2.5	0.01	0.021
7	7	0.6	-0.3	2.5	0.02	0.009
7	7	0.7	-0.3	2.5	0.02	0.021
7	9	0.6	-0.3	2.5	0.02	0.009
7	9	0.7	-0.3	2.5	0.02	0.021
9	7	0.6	-0.3	2.5	0.02	0.009
9	7	0.7	-0.3	2.5	0.02	0.021
9	9	0.6	-0.3	2.5	0.02	0.009
9	9	0.7	-0.3	2.5	0.02	0.021
7	7	0.6	0.7	1.5	0.01	0.009
7	7	0.7	0.7	1.5	0.01	0.021
7	9	0.6	0.7	1.5	0.01	0.009
7	9	0.7	0.7	1.5	0.01	0.021
9	7	0.6	0.7	1.5	0.01	0.009
9	7	0.7	0.7	1.5	0.01	0.021
9	9	0.6	0.7	1.5	0.01	0.009
9	9	0.7	0.7	1.5	0.01	0.021
7	7	0.6	0.7	1.5	0.02	0.009
7	7	0.7	0.7	1.5	0.02	0.021
7	9	0.6	0.7	1.5	0.02	0.009
7	9	0.7	0.7	1.5	0.02	0.021
9	7	0.6	0.7	1.5	0.02	0.009
9	7	0.7	0.7	1.5	0.02	0.021
9	9	0.6	0.7	1.5	0.02	0.009
9	9	0.7	0.7	1.5	0.02	0.021
7	7	0.6	0.7	2.5	0.01	0.0135
7	7	0.7	0.7	2.5	0.01	0.0315
7	9	0.6	0.7	2.5	0.01	0.0135
7	9	0.7	0.7	2.5	0.01	0.0315
9	7	0.6	0.7	2.5	0.01	0.0135
9	7	0.7	0.7	2.5	0.01	0.0315
9	9	0.6	0.7	2.5	0.01	0.0135
9	9	0.7	0.7	2.5	0.01	0.0315
7	7	0.6	0.7	2.5	0.02	0.0135
7	7	0.7	0.7	2.5	0.02	0.0315
7	9	0.6	0.7	2.5	0.02	0.0135

7	**9**	**0.7**	**0.7**	**2.5**	**0.02**	**0.0315**
9	**7**	**0.6**	**0.7**	**2.5**	**0.02**	**0.0135**
9	**7**	**0.7**	**0.7**	**2.5**	**0.02**	**0.0315**
9	**9**	**0.6**	**0.7**	**2.5**	**0.02**	**0.0135**
9	**9**	**0.7**	**0.7**	**2.5**	**0.02**	**0.0315**

To run this example, the spreadsheet is loaded with the above data.

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 .... **Assurance**
Prior Entry Method .... **Combined (Enter parameter values and probabilities on spreadsheet)**
Higher Means Are .... **Better (H1: δ > SM)**
Test Statistic .... **T-Test Based on Number of Subjects**
Alpha.. **0.025**
K1 (Number of Clusters) **100**
Column of M1 Values.................................... **C1**
K2 (Number of Clusters) **K1**
Column of M2 Values.................................... **C2**
Column of COV Values................................. **C3**
SM (Superiority Margin)................................ **0.05**
Column of δ Values **C4**
Column of σ Values **C5**
Column of ρ Values **C6**
Column of Pr(Values).................................... **C7**

Options Tab

Number of Computation Points for each Prior Distribution **4**
Maximum K1 in Sample Size Search............ **1000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5	C6	C7
1	7	7	0.6	-0.3	1.5	0.01	0.0060
2	7	7	0.7	-0.3	1.5	0.01	0.0140
3	7	9	0.6	-0.3	1.5	0.01	0.0060
4	7	9	0.7	-0.3	1.5	0.01	0.0140
5	9	7	0.6	-0.3	1.5	0.01	0.0060
6	9	7	0.7	-0.3	1.5	0.01	0.0140
7	9	9	0.6	-0.3	1.5	0.01	0.0060
8	9	9	0.7	-0.3	1.5	0.01	0.0140
9	7	7	0.6	-0.3	1.5	0.02	0.0060
10	7	7	0.7	-0.3	1.5	0.02	0.0140
11	7	9	0.6	-0.3	1.5	0.02	0.0060

12	7	9	0.7	-0.3	1.5	0.02	0.0140
13	9	7	0.6	-0.3	1.5	0.02	0.0060
14	9	7	0.7	-0.3	1.5	0.02	0.0140
15	9	9	0.6	-0.3	1.5	0.02	0.0060
16	9	9	0.7	-0.3	1.5	0.02	0.0140
17	7	7	0.6	-0.3	2.5	0.01	0.0090
18	7	7	0.7	-0.3	2.5	0.01	0.0210
19	7	9	0.6	-0.3	2.5	0.01	0.0090
20	7	9	0.7	-0.3	2.5	0.01	0.0210
21	9	7	0.6	-0.3	2.5	0.01	0.0090
22	9	7	0.7	-0.3	2.5	0.01	0.0210
23	9	9	0.6	-0.3	2.5	0.01	0.0090
24	9	9	0.7	-0.3	2.5	0.01	0.0210
25	7	7	0.6	-0.3	2.5	0.02	0.0090
26	7	7	0.7	-0.3	2.5	0.02	0.0210
27	7	9	0.6	-0.3	2.5	0.02	0.0090
28	7	9	0.7	-0.3	2.5	0.02	0.0210
29	9	7	0.6	-0.3	2.5	0.02	0.0090
30	9	7	0.7	-0.3	2.5	0.02	0.0210
31	9	9	0.6	-0.3	2.5	0.02	0.0090
32	9	9	0.7	-0.3	2.5	0.02	0.0210
33	7	7	0.6	0.7	1.5	0.01	0.0090
34	7	7	0.7	0.7	1.5	0.01	0.0210
35	7	9	0.6	0.7	1.5	0.01	0.0090
36	7	9	0.7	0.7	1.5	0.01	0.0210
37	9	7	0.6	0.7	1.5	0.01	0.0090
38	9	7	0.7	0.7	1.5	0.01	0.0210
39	9	9	0.6	0.7	1.5	0.01	0.0090
40	9	9	0.7	0.7	1.5	0.01	0.0210
41	7	7	0.6	0.7	1.5	0.02	0.0090
42	7	7	0.7	0.7	1.5	0.02	0.0210
43	7	9	0.6	0.7	1.5	0.02	0.0090
44	7	9	0.7	0.7	1.5	0.02	0.0210
45	9	7	0.6	0.7	1.5	0.02	0.0090
46	9	7	0.7	0.7	1.5	0.02	0.0210
47	9	9	0.6	0.7	1.5	0.02	0.0090
48	9	9	0.7	0.7	1.5	0.02	0.0210
49	7	7	0.6	0.7	2.5	0.01	0.0135
50	7	7	0.7	0.7	2.5	0.01	0.0315
51	7	9	0.6	0.7	2.5	0.01	0.0135
52	7	9	0.7	0.7	2.5	0.01	0.0315
53	9	7	0.6	0.7	2.5	0.01	0.0135
54	9	7	0.7	0.7	2.5	0.01	0.0315
55	9	9	0.6	0.7	2.5	0.01	0.0135
56	9	9	0.7	0.7	2.5	0.01	0.0315
57	7	7	0.6	0.7	2.5	0.02	0.0135
58	7	7	0.7	0.7	2.5	0.02	0.0315
59	7	9	0.6	0.7	2.5	0.02	0.0135
60	7	9	0.7	0.7	2.5	0.02	0.0315
61	9	7	0.6	0.7	2.5	0.02	0.0135
62	9	7	0.7	0.7	2.5	0.02	0.0315
63	9	9	0.6	0.7	2.5	0.02	0.0135
64	9	9	0.7	0.7	2.5	0.02	0.0315

Output

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

Numeric Results

Solve For:	Assurance
Groups:	1 = Treatment, 2 = Control
Test Statistic:	T-Test with DF based on number of subjects
Higher Means Are:	Better
Superiority Margin (SM):	0.05
Hypotheses:	H0: δ ≤ SM vs. H1: δ > SM
Prior Type:	Joint Multivariate Distribution

Prior Distribution

Point Lists

M1:	C1:	7 7 7 7 9 9 9 9 7 7 7 7 9 9 9 9 7 7 7 7 9 9 9 9 7 7 7 7 9 9 9 9 7 7 7 7 9 9 9 9 7 7 7 7 9 9 9 9 7 7 7 7 9 9 9 9 7 7 7 7 9 9 9 9
M2:	C2:	7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9 7 7 9 9
COV:	C3:	0.6 0.7 0.6 0.7
δ:	C4:	-0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 -0.3 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7
σ:	C5:	1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5
ρ:	C6:	0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.02 0.02 0.02 0.02 0.02 0.02 0.02 0.02
Prob:	C7:	0.006 0.014 0.006 0.014 0.006 0.014 0.006 0.014 0.006 0.014 0.006 0.014 0.006 0.014 0.006 0.014 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.009 0.021 0.0135 0.0315 0.0135 0.0315 0.0135 0.0315 0.0135 0.0315 0.0135 0.0315 0.0135 0.0315 0.0135 0.0315 0.0135 0.0315

		Sample Size			Number of Clusters			Cluster Size			Mean Difference	Standard Deviation	Intracluster Correlation	
Assurance	Power‡	N1	N2	N	K1	K2	K	E(M1)	E(M2)	E(COV)	E(δ)	E(σ)	E(ρ)	Alpha
0.59908	0.60134	801	801	1602	100	100	200	8	8	0.67	0.3	2.1	0.015	0.025

‡ Power was calculated using M1 = E(M1) = 8, M2 = E(M2) = 8, COV = E(COV) = 0.67, δ = E(δ) = 0.3, σ = E(σ) = 2.1, and ρ = E(ρ) = 0.015.

PASS has calculated the assurance as 0.59908 which matches the result in Example 2. This validates the joint prior method.