

## Chapter 280

# Assurance for Two-Sample T-Tests for Non-Inferiority Allowing Unequal Variance

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## Introduction

This procedure calculates the assurance of non-inferiority two-sample t-tests in which the outcome is a continuous normal random variable and the variances of the two groups (populations) are allowed to be unequal. 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). Sample size formulas for non-inferiority tests of two means are presented in Chow et al. (2018) pages 50-51.

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## 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).

## Non-Inferiority, Two-Sample T-Test

A *non-inferiority test* tests that the treatment mean is not worse than the reference mean by more than a non-inferiority margin. The actual direction of the hypothesis depends on the response variable being studied. The word *NIM* refers to the non-inferiority 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 no less than a small amount below the reference mean. The value of  $\delta$  at which power is calculated is often set to zero. The null and alternative hypotheses with  $\delta_0 = -|NIM|$  are

$$H_0: \mu_1 \leq \mu_2 - |NIM| \quad \text{versus} \quad H_1: \mu_1 > \mu_2 - |NIM|$$

$$H_0: \mu_1 - \mu_2 \leq -|NIM| \quad \text{versus} \quad H_1: \mu_1 - \mu_2 > -|NIM|$$

$$H_0: \delta \leq -|NIM| \quad \text{versus} \quad H_1: \delta > -|NIM|$$

### Case 2: High Values Bad

In this case, lower values are better. The hypotheses are arranged so that rejecting the null hypothesis implies that the treatment mean is no more than a small amount above the reference mean. The value of  $\delta$  at which power is calculated is often set to zero. The null and alternative hypotheses with  $\delta_0 = |NIM|$  are

$$H_0: \mu_1 \geq \mu_2 + |NIM| \quad \text{versus} \quad H_1: \mu_1 < \mu_2 + |NIM|$$

$$H_0: \mu_1 - \mu_2 \geq |NIM| \quad \text{versus} \quad H_1: \mu_1 - \mu_2 < |NIM|$$

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

## Test Statistic

Welch (1938) proposed the following test when the two variances are not assumed to be equal.

$$t_{df}^* = \frac{(\bar{X}_1 - \bar{X}_2) - \delta_0}{S_{\bar{X}_1 - \bar{X}_2}^*}$$

where

$$\bar{X}_k = \frac{\sum_{i=1}^{n_k} X_{ki}}{N_k},$$

$$s_k = \sqrt{\left( \frac{\sum_{i=1}^{N_k} (X_{ki} - \bar{X}_k)^2}{(N_k - 1)} \right)},$$

$$S_{\bar{X}_1 - \bar{X}_2}^* = \sqrt{\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}},$$

$$df = \frac{S_{\bar{X}_1 - \bar{X}_2}^{*4}}{\frac{s_1^4}{N_1^2(N_1 - 1)} + \frac{s_2^4}{N_2^2(N_2 - 1)}}$$

and  $\delta_0$  is the value of the difference hypothesized by the null hypothesis which depends on the magnitude and sign of  $NIM$ .

The null hypothesis is rejected if the computed p-value is less than a specified level (usually 0.05). Otherwise, no conclusion can be reached.

## Power Calculation

When  $\sigma_1 \neq \sigma_2$ , the power for Welch's unequal-variance  $t$ -test is calculated as follows.

1. Calculate:  $\sigma_{\bar{X}} = \sqrt{\frac{\sigma_1^2}{N_1} + \frac{\sigma_2^2}{N_2}}$ .

2. Calculate:  $df = \frac{\sigma_{\bar{X}}^4}{\frac{\sigma_1^4}{N_1^2(N_1-1)} + \frac{\sigma_2^4}{N_2^2(N_2-1)}}$

which is the adjusted degrees of freedom.

3. Find  $t_\alpha$  such that  $1 - T_{df}(t_\alpha) = \alpha$ , where  $T_{df}(x)$  is the area to the left of  $x$  under a central- $t$  distribution with degrees of freedom,  $df$ .

4. Calculate the noncentrality parameter:  $\lambda = \frac{\delta - \delta_0}{\sigma_{\bar{X}}}$ .

5. Calculate:  $Power = 1 - T'_{df,\lambda}(t_\alpha)$ , where  $T'_{df,\lambda}(x)$  is the area to the left of  $x$  under a noncentral- $t$  distribution with degrees of freedom,  $df$ , and noncentrality parameter,  $\lambda$ .

When solving for sample size, **PASS** uses this same power calculation formulation, but performs a binary search to determine that parameter.

## Assurance Calculation

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

Let  $P_1(H|\delta, \sigma_1, \sigma_2)$  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  $\delta, \sigma_1,$  and  $\sigma_2$  is critical to the power calculation, but their actual values are seldom known. This uncertainty has led to the development of another quantity that is useful in sample size determination: *assurance*. Assurance is defined as the expected power where the expectation is with respect to a joint prior distribution for  $\delta, \sigma_1,$  and  $\sigma_2$ . Hence, assurance is

$$Assurance = E_{\delta, \sigma_1, \sigma_2}(P_1(H|\delta, \sigma_1, \sigma_2)) = \iiint P_1(H|\delta, \sigma_1, \sigma_2) f(\delta, \sigma_1, \sigma_2) d\delta d\sigma_1 d\sigma_2$$

where  $f(\delta, \sigma_1, \sigma_2)$  is the joint prior distribution of  $\delta, \sigma_1,$  and  $\sigma_2$ .

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  $f(\delta, \sigma_1, \sigma_2)$ . This provides flexibility in specifying the joint prior distribution. In the three-parameter case, four columns are entered on the spreadsheet: three for the parameters and a fourth 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 three independent univariate distributions as follows:

$$f(\delta, \sigma_1, \sigma_2) = f_1(\delta)f_2(\sigma_1)f_3(\sigma_2)$$

where  $f_1(\delta)$  is the prior distribution of  $\delta$ ,  $f_2(\sigma_1)$  is the prior distribution of  $\sigma_1$ , and  $f_3(\sigma_2)$  is the prior distribution of  $\sigma_2$ . This method is also available in **PASS**. In this case, the definition of assurance becomes

$$Assurance = E_{\delta, \sigma_1, \sigma_2}(P_1(H|\delta, \sigma_1, \sigma_2)) = \iiint P_1(H|\delta, \sigma_1, \sigma_2) f_1(\delta) f_2(\sigma_1) f_3(\sigma_2) d\delta d\sigma_1 d\sigma_2$$

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.

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## 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 ( $\alpha$  and  $\beta$ ) 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

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

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Various distribution shapes are controlled by the values of  $\alpha$  and  $\beta$ . 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,  $\kappa$ , and a scale parameter,  $\theta$ , 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  $1 - \text{Prob}(Min \leq X \leq Max)$  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  $Y \sim \text{gamma}$ , then  $X = 1 / Y \sim \text{inverse-gamma}$ . A shape parameter,  $\alpha$ , and a scale parameter,  $\beta$ , 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  $1 - \text{Prob}(Min \leq X \leq Max)$  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,  $\mu$ , and a scale parameter,  $s$ , control the distribution.

The probability density function of the logistic distribution is

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

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  $Z \sim \text{standard normal}$ , then  $X = e^{\mu + \sigma Z} \sim \text{lognormal}$ . Note that  $\mu_{\log(X)} = E(\log(X))$  and  $\sigma_{\log(X)} = \text{Standard Deviation}(\log(X))$ .

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,  $\nu$ , control the distribution. Note that  $\nu$  is referred to as the *degrees of freedom*.

If  $t \sim$  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,  $\mu$ , and a scale parameter,  $\sigma$ , 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,  $\mu$ , a scale parameter,  $\sigma$ , and a shape parameter,  $\nu$ , control the distribution. Note that  $\nu$  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  $\mu$  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,  $\kappa$ , and a scale parameter,  $\lambda$ , 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

$X_i$	$P_i$
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 a test is to be conducted to determine if a new cancer treatment adversely affects bone density. The adjusted mean bone density (AMBD) in the population of interest is 0.002300 gm/cm with a standard deviation of 0.000300 gm/cm. Clinicians decide that if the treatment reduces AMBD by more than 5% (0.000115 gm/cm), it poses a significant health threat. Note that all AMBD amounts have been multiplied by 10000 to make the reports and plots easier to read.

The analysis will be a non-inferiority test using the Welch's t-test at the 0.025 significance level. Power is to be calculated assuming that the new treatment has no effect on AMBD. The researchers found that the required group sample sizes to achieve 70%, 80%, and 90% power are 160, 203, and 272.

To complete their sample size study, the researchers want to run an assurance analysis for a range of group sample sizes from 100 to 400. An elicitation exercise determined that a reasonable prior distribution of the mean difference should be normal with mean 0.0 and standard deviation 0.5. The elicitation also concluded that the prior distribution of the group 1 standard deviation should be normal with mean 3 and standard deviation 0.5. The prior distribution of the group 2 standard deviation should be normal with mean 5 and standard deviation 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 20. 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 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>Assurance</b>
Prior Entry Method.....	<b>Individual (Enter a prior distribution for each applicable parameter)</b>
Higher Means Are.....	<b>Better (H1: <math>\delta &gt; -NIM</math>)</b>
Alpha.....	<b>0.025</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Sample Size Per Group .....	<b>100 200 300 400</b>
NIM (Non-Inferiority Margin) .....	<b>1.15</b>
Prior Distribution of $\delta$ .....	<b>Normal (Mean, SD)</b>
Mean.....	<b>0</b>
SD.....	<b>0.5</b>
Truncation Boundaries.....	<b>None</b>
Prior Distribution of $\sigma_1$ .....	<b>Normal (Mean, SD)</b>
Mean.....	<b>3</b>
SD.....	<b>0.5</b>
Truncation Boundaries.....	<b>None</b>

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Prior Distribution of  $\sigma_2$  ..... **Normal (Mean, SD)**  
 Mean..... **5**  
 SD..... **0.7**  
 Truncation Boundaries..... **None**

Options Tab

Number of Computation Points for each..... **20**  
 Prior Distribution  
 Maximum N1 in Sample Size Search ..... **5000**

## Output

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

## Numeric Reports

### Numeric Results

Solve For: [Assurance](#)  
 Higher Means Are: Better  
 Hypotheses: H0:  $\delta \leq -NIM$  vs. H1:  $\delta > -NIM$   
 Prior Type: Independent Univariate Distributions

### Prior Distributions

$\delta$ : Normal (Mean = 0, SD = 0.5).  
 $\sigma_1$ : Normal (Mean = 3, SD = 0.5).  
 $\sigma_2$ : Normal (Mean = 5, SD = 0.7).

<b>Assurance*</b>	<b>Power‡</b>	<b>N1</b>	<b>N2</b>	<b>N</b>	<b>-NIM</b>	<b>Expected Mean Diff E(<math>\delta</math>)</b>	<b>Group 1 Std Dev E(<math>\sigma_1</math>)</b>	<b>Group 2 Std Dev E(<math>\sigma_2</math>)</b>	<b>Alpha</b>
0.50149	0.50023	100	100	200	-1.15	0	3	5	0.025
0.69733	0.79417	200	200	400	-1.15	0	3	5	0.025
0.78833	0.92638	300	300	600	-1.15	0	3	5	0.025
0.83850	0.97628	400	400	800	-1.15	0	3	5	0.025

\* The number of points used for computation of the prior(s) was 20.  
 ‡ Power was calculated using  $\delta = E(\delta) = 0$ ,  $\sigma_1 = E(\sigma_1) = 3$ , and  $\sigma_2 = E(\sigma_2) = 5$ .

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.  
 E( $\delta$ ) The expected value over its prior distribution of the difference in the group means assumed by the alternative hypothesis. Note that  $\delta = \mu_1 - \mu_2$ .  
 E( $\sigma_1$ ) The expected value over its prior distribution of the group 1 standard deviation.  
 E( $\sigma_2$ ) The expected value over its prior distribution of the group 2 standard deviation.  
 Alpha The probability of rejecting a true null hypothesis.

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**Summary Statements**

Group sample sizes of 100 in group 1 and 100 in group 2 achieve 0.50149 assurance using a one-sided, unequal variances t-test. The margin of non-inferiority is -1.15. The significance level (alpha) of the test is 0.025. The prior distribution used for the mean difference is Normal (Mean = 0, SD = 0.5). The prior distribution used for the group 1 standard deviation is Normal (Mean = 3, SD = 0.5). The prior distribution used for the group 2 standard deviation is Normal (Mean = 5, SD = 0.7).

**Dropout-Inflated Sample Size**

Dropout Rate	Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
	N1	N2	N	N1'	N2'	N'	D1	D2	D
20%	100	100	200	125	125	250	25	25	50
20%	200	200	400	250	250	500	50	50	100
20%	300	300	600	375	375	750	75	75	150
20%	400	400	800	500	500	1000	100	100	200

- Dropout Rate The percentage of subjects (or items) that are expected to be lost at random during the course of the study and for whom no response data will be collected (i.e., will be treated as "missing"). Abbreviated as DR.
- N1, N2, and N The evaluable sample sizes at which power is computed (as entered by the user). If N1 and N2 subjects are evaluated out of the N1' and N2' subjects that are enrolled in the study, the design will achieve the stated power.
- N1', N2', and N' The number of subjects that should be enrolled in the study in order to obtain N1, N2, and N evaluable subjects, based on the assumed dropout rate. N1' and N2' are calculated by inflating N1 and N2 using the formulas  $N1' = N1 / (1 - DR)$  and  $N2' = N2 / (1 - DR)$ , with N1' and N2' always rounded up. (See Julious, S.A. (2010) pages 52-53, or Chow, S.C., Shao, J., Wang, H., and Lohknygina, Y. (2018) pages 32-33.)
- D1, D2, and D The expected number of dropouts.  $D1 = N1' - N1$ ,  $D2 = N2' - N2$ , and  $D = D1 + D2$ .

**Dropout Summary Statements**

Anticipating a 20% dropout rate, 125 subjects should be enrolled in Group 1, and 125 in Group 2, to obtain final group sample sizes of 100 and 100, respectively.

**References**

O'Hagan, A., Stevens, J.W., and Campbell, M.J. 2005. 'Assurance in clinical trial design'. Pharmaceutical Statistics, Volume 4, Pages 187-201.

Ciarleglio, M.M., Arendt, C.D., and Peduzzi, P.N. 2016. 'Selection of the effect size for sample size determination for a continuous response in a superiority clinical trial using a hybrid classical and Bayesian procedure'. Clinical Trials, Volume 13(3), pages 275-285.

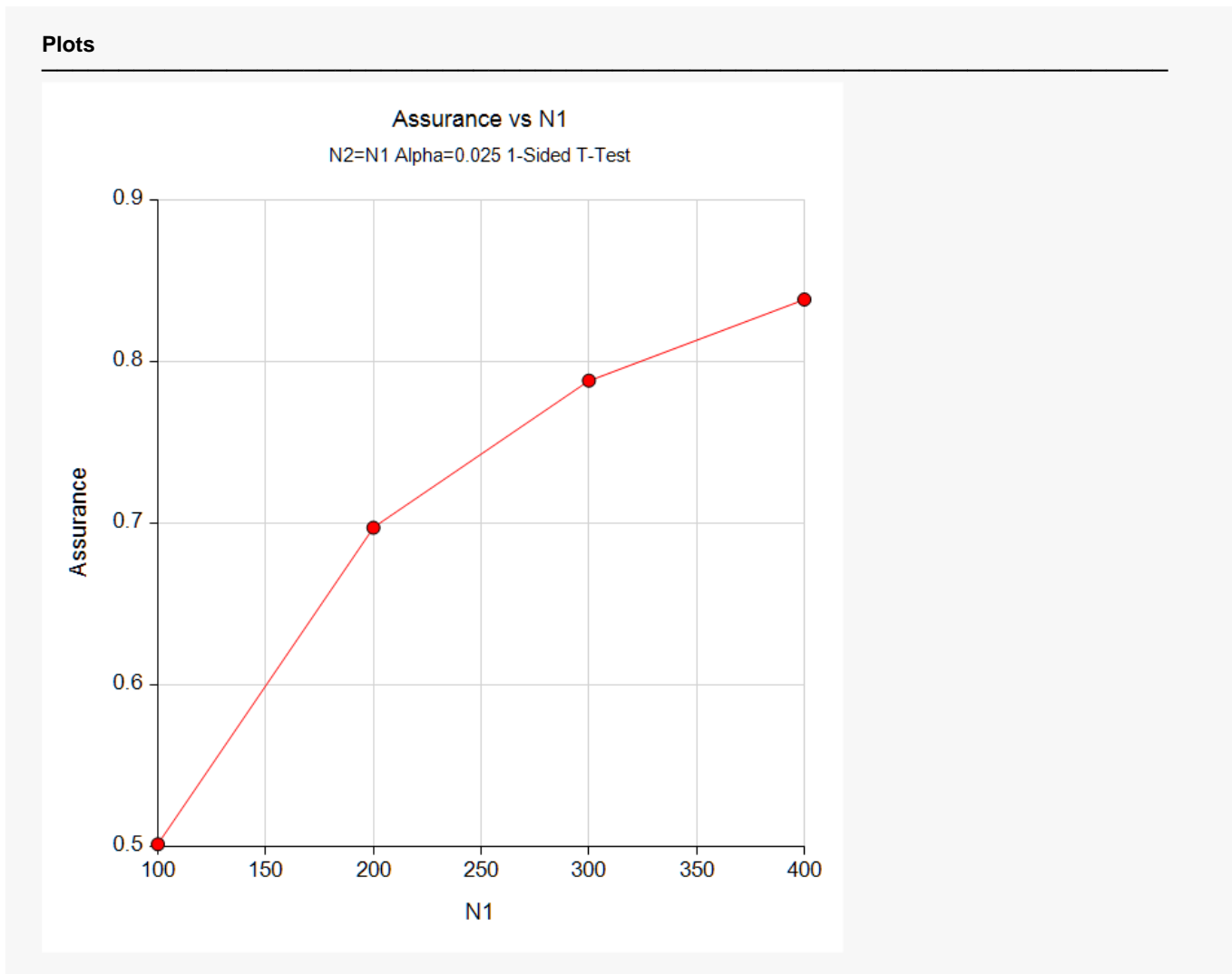
Dias, L.C., Morton, A., and Quigley, J. 2018. Elicitation, The Science and Art of Structuring Judgement. Springer.

Chow, S.C., Shao, J., Wang, H., and Lohknygina, Y. 2018. Sample Size Calculations in Clinical Research, Third Edition. Taylor & Francis/CRC. Boca Raton, Florida.

Julious, S. A. 2010. Sample Sizes for Clinical Trials. Chapman & Hall/CRC. Boca Raton, FL.

This report shows the assurance values obtained by each sample size.

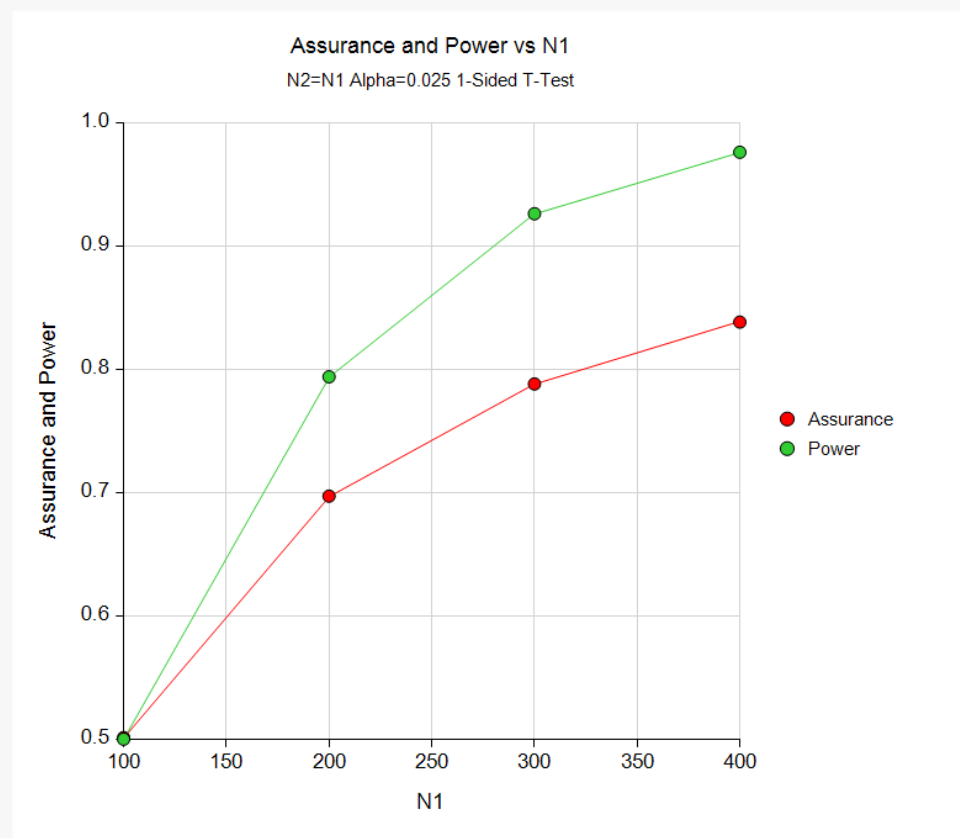
## Plots Section



This plot shows the relationship between the assurance and sample size. Note the diminishing impact on assurance of each increase in the number of subjects.

## Comparison Plots Section

### Comparison Plots



This plot shows the relationship of assurance, power, and sample size.

## Example 2 – Validation using Hand Computation

We could not find a validation example in the literature, so we have developed a validation example of our own. Suppose a non-inferiority, two-sample t-test will be used in which  $N1 = N2 = 150$  and the significance level is 0.025. The non-inferiority margin is set to 6.0. Higher means are better.

The prior distribution of the difference will be approximated by the following table.

$\delta$	Prob
-4	0.3
0	0.4
4	0.3

The prior distribution of the group 1 standard deviation will be approximated by the following table.

$\sigma_1$	Prob
12	0.2
16	0.6
20	0.2

The prior distribution of the group 2 standard deviation will be approximated by the following table.

$\sigma_2$	Prob
15	0.2
19	0.6
23	0.2

Note that in both of these tables, the parameter values are equi-spaced. This is important when using a discrete approximation such as we have done here.

The *Two-Sample T-Tests for Non-Inferiority Allowing Unequal Variance* procedure is used to compute the power for each of the 27 combinations of  $\delta$ ,  $\sigma_1$ , and  $\sigma_2$ . The results of these calculations were as follows.

### Numeric Results for an Unequal-Variance T-Test

Solve For: Power  
 Difference:  $\delta = \mu_1 - \mu_2 = \mu_T - \mu_R$   
 Higher Means Are: Better  
 Hypotheses:  $H_0: \delta \leq -NIM$  vs.  $H_1: \delta > -NIM$

Power	N1	N2	N	-NIM	$\delta$	$\sigma_1$	$\sigma_2$	Alpha
0.24538	150	150	300	-6	-4	12	15	0.025
0.19103	150	150	300	-6	-4	12	19	0.025
0.15391	150	150	300	-6	-4	12	23	0.025
0.19858	150	150	300	-6	-4	16	15	0.025
0.16426	150	150	300	-6	-4	16	19	0.025
0.13811	150	150	300	-6	-4	16	23	0.025
0.16266	150	150	300	-6	-4	20	15	0.025
0.14121	150	150	300	-6	-4	20	19	0.025
0.12324	150	150	300	-6	-4	20	23	0.025
0.96803	150	150	300	-6	0	12	15	0.025
0.90278	150	150	300	-6	0	12	19	0.025
0.80525	150	150	300	-6	0	12	23	0.025
0.91617	150	150	300	-6	0	16	15	0.025
0.83857	150	150	300	-6	0	16	19	0.025
0.74323	150	150	300	-6	0	16	23	0.025
0.83378	150	150	300	-6	0	20	15	0.025
0.75655	150	150	300	-6	0	20	19	0.025



Assurance for Two-Sample T-Tests for Non-Inferiority Allowing Unequal Variance

0.67114	150	150	300	-6	0	20	23	0.025
0.99999	150	150	300	-6	4	12	15	0.025
0.99974	150	150	300	-6	4	12	19	0.025
0.99694	150	150	300	-6	4	12	23	0.025
0.99984	150	150	300	-6	4	16	15	0.025
0.99843	150	150	300	-6	4	16	19	0.025
0.99170	150	150	300	-6	4	16	23	0.025
0.99826	150	150	300	-6	4	20	15	0.025
0.99316	150	150	300	-6	4	20	19	0.025
0.97958	150	150	300	-6	4	20	23	0.025

The assurance calculation is made by summing the quantities  $[(power_{i,j,k})(p(\delta_i))(p(\sigma_{1j}))(p(\sigma_{2k}))]$  as follows

$$Assurance = (0.24538 \times 0.3 \times 0.2 \times 0.2) + (0.19103 \times 0.3 \times 0.2 \times 0.6) + \dots + (0.97958 \times 0.3 \times 0.2 \times 0.2)$$

$$= 0.68152.$$

To run this example, the spreadsheet will need to be loaded with the following six columns in which the first two are for the difference,  $\delta$ , the second two are for the group 1 standard deviation,  $\sigma_1$ , and the third two are for the group 2 standard deviation,  $\sigma_2$ .

<b>C1</b>	<b>C2</b>	<b>C3</b>	<b>C4</b>	<b>C5</b>	<b>C6</b>
<b>-4</b>	<b>0.3</b>	<b>12</b>	<b>0.2</b>	<b>15</b>	<b>0.2</b>
<b>0</b>	<b>0.4</b>	<b>16</b>	<b>0.6</b>	<b>19</b>	<b>0.6</b>
<b>4</b>	<b>0.3</b>	<b>20</b>	<b>0.2</b>	<b>23</b>	<b>0.2</b>

## 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:  $\delta > -NIM$ )**
- Alpha ..... **0.025**
- Group Allocation ..... **Equal (N1 = N2)**
- Sample Size Per Group ..... **150**
- NIM (Non-Inferiority Margin) ..... **6**
- Prior Distribution of  $\delta$  ..... **Custom (Values and Probabilities in Spreadsheet)**
- Column of Values ..... **C1**
- Column of Pr(Values) ..... **C2**
- Prior Distribution of  $\sigma_1$  ..... **Custom (Values and Probabilities in Spreadsheet)**
- Column of Values ..... **C3**
- Column of Pr(Values) ..... **C4**
- Prior Distribution of  $\sigma_2$  ..... **Custom (Values and Probabilities in Spreadsheet)**
- Column of Values ..... **C5**
- Column of Pr(Values) ..... **C6**

Assurance for Two-Sample T-Tests for Non-Inferiority Allowing Unequal Variance

Options Tab

Number of Computation Points for each.....**20**

Prior Distribution

Maximum N1 in Sample Size Search .....**5000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5	C6
1	-4	0.3	12	0.2	15	0.2
2	0	0.4	16	0.6	19	0.6
3	4	0.3	20	0.2	23	0.2

## Output

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

**Numeric Results**

Solve For: [Assurance](#)  
 Higher Means Are: Better  
 Hypotheses: H0:  $\delta \leq -NIM$  vs. H1:  $\delta > -NIM$   
 Prior Type: Independent Univariate Distributions

**Prior Distributions**

$\delta$ : Point List (Values = C1, Probs = C2).  
 C1: -4 0 4  
 C2: 0.3 0.4 0.3  
 $\sigma_1$ : Point List (Values = C3, Probs = C4).  
 C3: 12 16 20  
 C4: 0.2 0.6 0.2  
 $\sigma_2$ : Point List (Values = C5, Probs = C6).  
 C5: 15 19 23  
 C6: 0.2 0.6 0.2

<a href="#">Assurance</a>	Power‡	N1	N2	N	-NIM	Expected Mean Diff E( $\delta$ )	Group 1 Std Dev E( $\sigma_1$ )	Group 2 Std Dev E( $\sigma_2$ )	Alpha
<a href="#">0.68152</a>	0.83857	150	150	300	-6	0	16	19	0.025

‡ Power was calculated using  $\delta = E(\delta) = 0$ ,  $\sigma_1 = E(\sigma_1) = 16$ , and  $\sigma_2 = E(\sigma_2) = 19$ .

**PASS** has also calculated the assurance as 0.68152 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 0.4, 0.6, and 0.8.

In order to reduce the runtime during this exploratory phase of the analysis, the number of points in the prior is set to 20.

### 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>Sample Size</b>
Prior Entry Method .....	<b>Individual (Enter a prior distribution for each applicable parameter)</b>
Higher Means Are .....	<b>Better (H1: <math>\delta &gt; -NIM</math>)</b>
Assurance .....	<b>0.4 0.6 0.8</b>
Alpha .....	<b>0.025</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
NIM (Non-Inferiority Margin) .....	<b>1.15</b>
Prior Distribution of $\delta$ .....	<b>Normal (Mean, SD)</b>
Mean .....	<b>0</b>
SD .....	<b>0.5</b>
Truncation Boundaries .....	<b>None</b>
Prior Distribution of $\sigma_1$ .....	<b>Normal (Mean, SD)</b>
Mean .....	<b>3</b>
SD .....	<b>0.5</b>
Truncation Boundaries .....	<b>None</b>
Prior Distribution of $\sigma_2$ .....	<b>Normal (Mean, SD)</b>
Mean .....	<b>5</b>
SD .....	<b>0.7</b>
Truncation Boundaries .....	<b>None</b>

#### Options Tab

Number of Computation Points for each .....	<b>10</b>
Prior Distribution	
Maximum N1 in Sample Size Search .....	<b>5000</b>

## Output

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

### Numeric Reports

#### Numeric Results

Solve For: [Sample Size](#)  
 Higher Means Are: Better  
 Hypotheses:  $H_0: \delta \leq -NIM$  vs.  $H_1: \delta > -NIM$   
 Prior Type: Independent Univariate Distributions

#### Prior Distributions

$\delta$ : Normal (Mean = 0, SD = 0.5).  
 $\sigma_1$ : Normal (Mean = 3, SD = 0.5).  
 $\sigma_2$ : Normal (Mean = 5, SD = 0.7).

Assurance*		Power‡	N1	N2	N	-NIM	Expected Mean Diff E( $\delta$ )	Group 1 Std Dev E( $\sigma_1$ )	Group 2 Std Dev E( $\sigma_2$ )	Alpha
Actual	Target									
0.40298	0.4	0.37750	71	71	142	-1.15	0	3	5	0.025
0.60025	0.6	0.64198	140	140	280	-1.15	0	3	5	0.025
0.80043	0.8	0.94081	320	320	640	-1.15	0	3	5	0.025

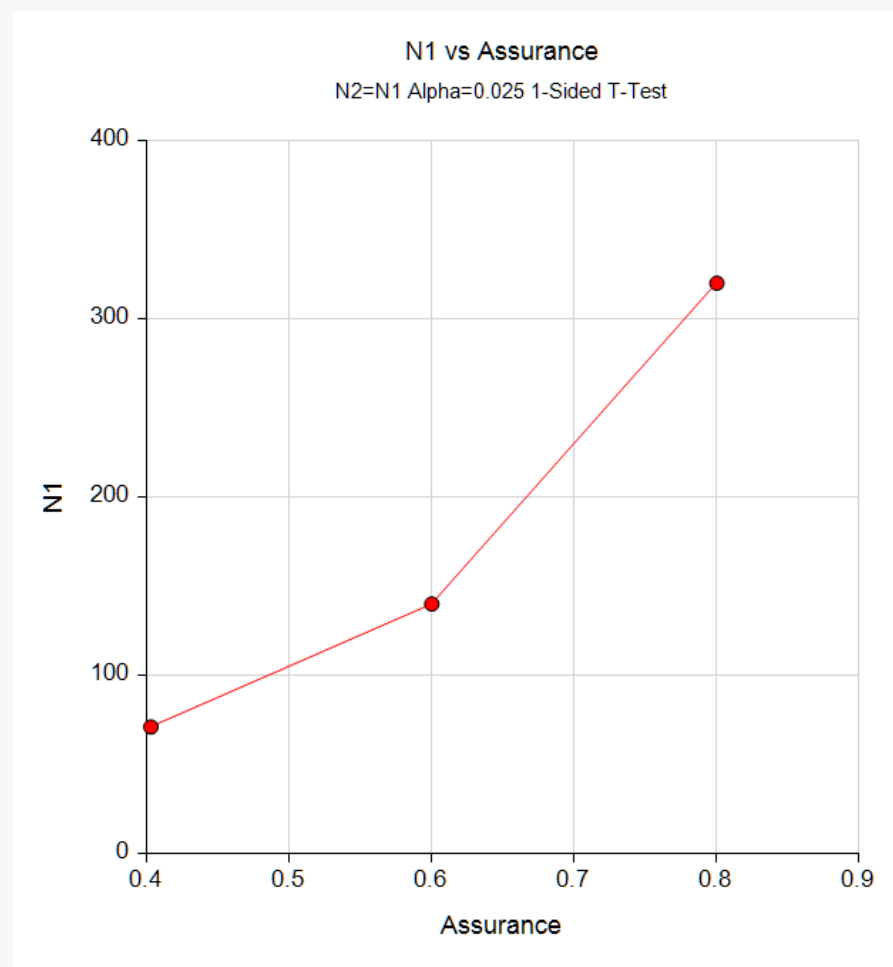
\* The number of points used for computation of the prior(s) was 10.

‡ Power was calculated using  $\delta = E(\delta) = 0$ ,  $\sigma_1 = E(\sigma_1) = 3$ , and  $\sigma_2 = E(\sigma_2) = 5$ .

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

The following example shows the complexity required to specify a joint distribution for three or more parameters.

Suppose a one-sided non-inferiority, two-sample Welch's unequal-variance test will be used in which  $N_1 = N_2 = 200$  and the significance level is 0.025. The non-inferiority margin is set to 2.0. Higher means are better.

Further suppose that the joint prior distribution of the difference and standard deviation is approximated by the following table. In a real study, the values in this table would be provided by an elicitation study.

Note that the program will rescale the probabilities so they sum to one.

<u><math>\delta</math></u>	<u><math>\sigma_1</math></u>	<u><math>\sigma_2</math></u>	<u>Prob</u>
-6	21	24	0.1
-4	20	23	0.1
-3	23	25	0.2
-2	22	24	0.2
-1	25	28	0.1
0	24	27	0.1
2	25	29	0.3
3	24	27	0.3
6	27	31	0.5
7	25	28	0.5
8	29	33	0.3
9	28	32	0.3
12	35	39	0.1
13	34	37	0.1
15	39	42	0.2
16	38	40	0.2
21	43	47	0.1
23	42	45	0.1

To run this example, the spreadsheet will need to be loaded with the following four columns.

<u>C1</u>	<u>C2</u>	<u>C3</u>	<u>C4</u>
-6	21	24	0.1
-4	20	23	0.1
-3	23	25	0.2
-2	22	24	0.2
-1	25	28	0.1
0	24	27	0.1
2	25	29	0.3
3	24	27	0.3
6	27	31	0.5
7	25	28	0.5
8	29	33	0.3
9	28	32	0.3
12	35	39	0.1
13	34	37	0.1
15	39	42	0.2

Assurance for Two-Sample T-Tests for Non-Inferiority Allowing Unequal Variance

16	38	40	0.2
21	43	47	0.1
23	42	45	0.1

## 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:  $\delta > -NIM$ )**
- Alpha ..... **0.025**
- Group Allocation ..... **Equal (N1 = N2)**
- Sample Size Per Group ..... **100**
- NIM (Non-Inferiority Margin) ..... **1**
- Column of  $\delta$  Values ..... **C1**
- Column of  $\sigma_1$  Values ..... **C2**
- Column of  $\sigma_2$  Values ..... **C3**
- Column of Pr(Values) ..... **C4**

Options Tab

---

- Number of Computation Points for each ..... **20**
- Prior Distribution
- Maximum N1 in Sample Size Search ..... **5000**

Input Spreadsheet Data

---

Row	C1	C2	C3	C4
1	-6	21	24	0.1
2	-4	20	23	0.1
3	-3	23	25	0.2
4	0	22	24	0.2
5	1	25	28	0.1
6	3	24	27	0.1
7	12	25	29	0.3
8	13	24	27	0.3
9	16	27	31	0.5
10	17	25	28	0.5
11	18	29	33	0.3
12	19	28	32	0.3
13	22	35	39	0.1
14	23	34	37	0.1
15	25	39	42	0.2
16	26	38	40	0.2
17	31	43	47	0.1
18	33	42	45	0.1

---

## Output

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

### Numeric Results

Solve For: Assurance  
 Higher Means Are: Better  
 Hypotheses:  $H_0: \delta \leq -NIM$  vs.  $H_1: \delta > -NIM$   
 Prior Type: Joint Multivariate Distribution

### Prior Distribution

Point Lists

$\delta$ : C1: -6 -4 -3 0 1 3 12 13 16 17 18 19 22 23 25 26 31 33  
 $\sigma_1$ : C2: 21 20 23 22 25 24 25 24 27 25 29 28 35 34 39 38 43 42  
 $\sigma_2$ : C3: 24 23 25 24 28 27 29 27 31 28 33 32 39 37 42 40 47 45  
 Prob: C4: 0.1 0.1 0.2 0.2 0.1 0.1 0.3 0.3 0.5 0.5 0.3 0.3 0.1 0.1 0.2 0.2 0.1 0.1

Assurance	Power‡	N1	N2	N	-NIM	Expected Mean Diff E( $\delta$ )	Group 1 Std Dev E( $\sigma_1$ )	Group 2 Std Dev E( $\sigma_2$ )	Alpha
0.78702	0.95565	100	100	200	-1	14.47368	28.05263	31.31579	0.025

‡ Power was calculated using  $\delta = E(\delta) = 14.47368$ ,  $\sigma_1 = E(\sigma_1) = 28.05263$ , and  $\sigma_2 = E(\sigma_2) = 31.31579$ .

PASS has calculated the assurance as 0.78702.



## Example 5 – Joint Prior Validation

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

In Example 2, the prior distributions of the difference, the group 1 standard deviation, and the group 2 standard deviation are

$\delta$	<u>Prob</u>
-4	0.3
0	0.4
4	0.3

$\sigma_1$	<u>Prob</u>
12	0.2
16	0.6
20	0.2

$\sigma_2$	<u>Prob</u>
15	0.2
19	0.6
23	0.2

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

$\delta$	$\sigma_1$	$\sigma_2$	<u>Prob</u>
-4	12	15	0.012
-4	12	19	0.036
-4	12	23	0.012
-4	16	15	0.036
-4	16	19	0.108
-4	16	23	0.036
-4	20	15	0.012
-4	20	19	0.036
-4	20	23	0.012
0	12	15	0.016
0	12	19	0.048
0	12	23	0.016
0	16	15	0.048
0	16	19	0.144
0	16	23	0.048
0	20	15	0.016
0	20	19	0.048
0	20	23	0.016
4	12	15	0.012
4	12	19	0.036
4	12	23	0.012
4	16	15	0.036
4	16	19	0.108
4	16	23	0.036

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<b>4</b>	<b>20</b>	<b>15</b>	<b>0.012</b>
<b>4</b>	<b>20</b>	<b>19</b>	<b>0.036</b>
<b>4</b>	<b>20</b>	<b>23</b>	<b>0.012</b>

To run this example, the spreadsheet is loaded with the following four columns.

<b><u>C1</u></b>	<b><u>C2</u></b>	<b><u>C3</u></b>	<b><u>C4</u></b>
-4	12	15	0.012
-4	12	19	0.036
-4	12	23	0.012
-4	16	15	0.036
-4	16	19	0.108
-4	16	23	0.036
-4	20	15	0.012
-4	20	19	0.036
-4	20	23	0.012
0	12	15	0.016
0	12	19	0.048
0	12	23	0.016
0	16	15	0.048
0	16	19	0.144
0	16	23	0.048
0	20	15	0.016
0	20	19	0.048
0	20	23	0.016
4	12	15	0.012
4	12	19	0.036
4	12	23	0.012
4	16	15	0.036
4	16	19	0.108
4	16	23	0.036
4	20	15	0.012
4	20	19	0.036
4	20	23	0.012

## 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:  $\delta > -NIM$ )**  
 Alpha ..... **0.025**  
 Group Allocation ..... **Equal (N1 = N2)**  
 Sample Size Per Group ..... **150**  
 NIM (Non-Inferiority Margin) ..... **6**  
 Column of  $\delta$  Values ..... **C1**  
 Column of  $\sigma_1$  Values ..... **C2**  
 Column of  $\sigma_2$  Values ..... **C3**  
 Column of Pr(Values) ..... **C4**

### Options Tab

---

Number of Computation Points for each ..... **20**  
 Prior Distribution  
 Maximum N1 in Sample Size Search ..... **5000**

### Input Spreadsheet Data

---

Row	C1	C2	C3	C4
1	-4	12	15	0.012
2	-4	12	19	0.036
3	-4	12	23	0.012
4	-4	16	15	0.036
5	-4	16	19	0.108
6	-4	16	23	0.036
7	-4	20	15	0.012
8	-4	20	19	0.036
9	-4	20	23	0.012
10	0	12	15	0.016
11	0	12	19	0.048
12	0	12	23	0.016
13	0	16	15	0.048
14	0	16	19	0.144
15	0	16	23	0.048
16	0	20	15	0.016
17	0	20	19	0.048
18	0	20	23	0.016
19	4	12	15	0.012
20	4	12	19	0.036
21	4	12	23	0.012
22	4	16	15	0.036
23	4	16	19	0.108
24	4	16	23	0.036

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25	4	20	15	0.012
26	4	20	19	0.036
27	4	20	23	0.012

## Output

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

### Numeric Results

Solve For: Assurance  
 Higher Means Are: Better  
 Hypotheses: H0:  $\delta \leq -NIM$  vs. H1:  $\delta > -NIM$   
 Prior Type: Joint Multivariate Distribution

### Prior Distribution

Point Lists

$\delta$ : C1: -4 -4 -4 -4 -4 -4 -4 -4 -4 0 0 0 0 0 0 0 0 0 4 4 4 4 4 4 4 4  
 $\sigma_1$ : C2: 12 12 12 16 16 16 20 20 20 12 12 12 16 16 16 20 20 20 12 12 12 16 16 16 20 20  
 $\sigma_2$ : C3: 15 19 23 15 19 23 15 19 23 15 19 23 15 19 23 15 19 23 15 19 23 15 19 23 15 19 23  
 Prob: C4: 0.012 0.036 0.012 0.036 0.108 0.036 0.012 0.036 0.012 0.016 0.048 0.016 0.048 0.144 0.048  
 0.016 0.048 0.016 0.012 0.036 0.012 0.036 0.108 0.036 0.012 0.036 0.012

Assurance	Power‡	N1	N2	N	-NIM	Expected Mean Diff E( $\delta$ )	Group 1 Std Dev E( $\sigma_1$ )	Group 2 Std Dev E( $\sigma_2$ )	Alpha
0.68152	0.83857	150	150	300	-6	0	16	19	0.025

‡ Power was calculated using  $\delta = E(\delta) = 0$ ,  $\sigma_1 = E(\sigma_1) = 16$ , and  $\sigma_2 = E(\sigma_2) = 19$ .

PASS has also calculated the assurance as 0.68152 which matches Example 2 and thus validates the procedure.