

## Chapter 268

# Assurance for Two-Sample Z-Tests Assuming Equal Variance

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## Introduction

This procedure calculates the assurance of one- or two-sided two-sample z-tests when the variances of the two groups (populations) are assumed to be equal and known. 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 procedure is based on O'Hagan, Stevens, and Campbell (2005).

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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.

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## 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.

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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).

## Two-Sample Z-Test Procedure

If we assume that  $\mu_1$  and  $\mu_2$  represent the means of the two populations of interest, and that  $\delta = \mu_1 - \mu_2$ , the null hypothesis for comparing the two means is  $H_0: \mu_1 = \mu_2$  (or  $H_0: \delta = 0$ ). The alternative hypothesis can be any one of

Two-Sided:  $H_1: \mu_1 \neq \mu_2$  (or  $H_1: \delta \neq 0$ )

Upper One-Sided:  $H_1: \mu_1 > \mu_2$  (or  $H_1: \delta > 0$ )

Lower One-Sided:  $H_1: \mu_1 < \mu_2$  (or  $H_1: \delta < 0$ )

depending upon the desire of the researcher or the protocol instructions. A suitable Type I error probability ( $\alpha$ ) is chosen for the test, the data is collected, and a z-statistic is generated using the formula:

$$z = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\sigma^2 \left( \frac{1}{N_1} + \frac{1}{N_2} \right)}}$$

This z-statistic follows a standard normal distribution. The null hypothesis is rejected in favor of the alternative if,

for  $H_1: \mu_1 \neq \mu_2$  (or  $H_1: \delta \neq 0$ ),

$$z < z_{\alpha/2} \text{ or } z > z_{1-\alpha/2},$$

for  $H_1: \mu_1 > \mu_2$  (or  $H_1: \delta > 0$ ),

$$z > z_{1-\alpha},$$

or, for  $H_1: \mu_1 < \mu_2$  (or  $H_1: \delta < 0$ ),

$$z < z_{\alpha}.$$

Comparing the z-statistic to the cut-off z-value (as shown here) is equivalent to comparing the p-value to  $\alpha$ .

## Power Calculation

The power is calculated from  $N_1$  and  $N_2$ ,  $\alpha$ , the assumed  $\mu_1$  and  $\mu_2$ , and the assumed common standard deviation,  $\sigma_1 = \sigma_2 = \sigma$ . Two good references for these methods are Julious (2010) and Chow, Shao, Wang, and Lokhnygina (2018).

If we call the assumed difference between the means,  $\delta = \mu_1 - \mu_2$ , the steps for calculating the power are as follows:

1. Find  $z_{1-\alpha}$  based on the standard normal distribution.
2. Calculate the power as the probability that the test statistic  $z$  is greater than  $z_{1-\alpha}$  under the normal distribution with mean difference  $\delta$ .

$$\text{Power} = \Pr(z > z_{1-\alpha} | \delta).$$

The algorithms for calculating power for the opposite direction and the two-sided hypotheses are analogous to this method.

## Assurance Calculation

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

Let  $P_1(H|\delta, \sigma)$  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  $\delta$  and  $\sigma$  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  $\delta$  and  $\sigma$ . Hence, the definition of assurance is

$$\text{Assurance} = E_{\delta, \sigma}(P_1(H|\delta, \sigma)) = \iint P_1(H|\delta, \sigma) f(\delta, \sigma) d\delta d\sigma$$

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

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  $f(\delta, \sigma)$ . This provides flexibility in specifying the joint prior distribution. In the two-parameter case, three columns are entered on the spreadsheet: two for the parameters and a third 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

$$f(\delta, \sigma) = f_1(\delta)f_2(\sigma)$$

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

$$Assurance = E_{\delta, \sigma}(P_1(H|\delta, \sigma)) = \iint P_1(H|\delta, \sigma)f_1(\delta)f_2(\sigma)d\delta d\sigma$$

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 ( $\alpha$  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

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

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

$$\alpha = \beta = 1$$

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**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  $1 - \text{Prob}(\text{Min} \leq X \leq \text{Max})$  where  $\text{Min}$  and  $\text{Max}$  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  $Z \sim$  standard normal, then  $X = e^{\mu + \sigma Z} \sim$  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  $1 - \text{Prob}(\text{Min} \leq X \leq \text{Max})$  where  $\text{Min}$  and  $\text{Max}$  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  $t \sim \text{Student's } t$ , then  $X = e^{\mu + \sigma t} \sim \text{logT}$ .

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  $1 - \text{Prob}(\text{Min} \leq X \leq \text{Max})$  where  $\text{Min}$  and  $\text{Max}$  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  $1 - \text{Prob}(\text{Min} \leq X \leq \text{Max})$  where  $\text{Min}$  and  $\text{Max}$  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  $1 - \text{Prob}(\text{Min} \leq X \leq \text{Max})$  where  $\text{Min}$  and  $\text{Max}$  are two truncation bounds.



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**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  $1 - \text{Prob}(\text{Min} \leq X \leq \text{Max})$  where  $\text{Min}$  and  $\text{Max}$  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

Researchers wish to compare two drugs to determine whether there is a meaningful difference in the response. A sample size analysis assuming that a two-sample z-test would be used to analyze the experimental data found that 62 subjects per group were needed to achieve 90% power for a two-sided test at a 0.05 level of significance. The mean difference under the alternative hypothesis was set to 10.2. The common standard deviation was 17.5.

To complete their sample size study, the researchers want to run an assurance analysis for a range of group sample sizes from 40 to 200. An elicitation exercise determined that the prior distribution of the mean difference should be normal with mean 10.2 and standard deviation 8. The elicitation concluded that a known standard deviation of 17.5 should be used.

### 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>
Alternative Hypothesis .....	<b>Two-Sided (<math>H_1: \delta \neq 0</math>)</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Equal (<math>N_1 = N_2</math>)</b>
Sample Size Per Group .....	<b>40 62 80 120 160 200</b>
Prior Distribution of $\delta$ .....	<b>Normal (Mean, SD)</b>
Mean.....	<b>10.2</b>
SD.....	<b>8</b>
Truncation Boundaries.....	<b>None</b>
Prior Distribution of $\sigma$ .....	<b>No Prior (Fixed Value)</b>
Fixed Value of $\sigma$ .....	<b>17.5</b>

#### Options Tab

Number of Computation Points for each.....	<b>50</b>
Prior Distribution	
Maximum $N_1$ 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: [Assurance](#)

Hypotheses:  $H_0: \delta = 0$  vs.  $H_1: \delta \neq 0$

Prior Type: Independent Univariate Distributions

### Prior Distributions

$\delta$ : Normal (Mean = 10.2, SD = 8).

$\sigma$ : No Prior

Assurance*	Power‡	Sample Size			Expected Mean Difference E( $\delta$ )	Standard Deviation $\sigma$	Alpha
		N1	N2	N			
<a href="#">0.63367</a>	0.74107	40	40	80	10.2	17.5	0.05
<a href="#">0.70884</a>	0.90065	62	62	124	10.2	17.5	0.05
<a href="#">0.74579</a>	0.95786	80	80	160	10.2	17.5	0.05
<a href="#">0.79517</a>	0.99469	120	120	240	10.2	17.5	0.05
<a href="#">0.82410</a>	0.99943	160	160	320	10.2	17.5	0.05
<a href="#">0.84357</a>	0.99995	200	200	400	10.2	17.5	0.05

\* The number of points used for computation of the prior(s) was 50.

‡ Power was calculated using  $\delta = E(\delta) = 10.2$  and  $\sigma = 17.5$ .

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.
N1	The number of subjects in group 1.
N2	The number of subjects in group 2.
N	The total sample size. $N = N1 + N2$ .
E( $\delta$ )	The expected value over its prior distribution of the difference in the group means assumed by the alternative hypothesis. Note that $\delta = \mu_1 - \mu_2$ .
$\sigma$	The value of the standard deviation used for both groups.
Alpha	The probability of rejecting a true null hypothesis.

### Summary Statements

A parallel two-group design will be used to test whether the Group 1 (treatment) mean ( $\mu_1$ ) is different from the Group 2 (control) mean ( $\mu_2$ ) ( $H_0: \delta = 0$  versus  $H_1: \delta \neq 0$ ,  $\delta = \mu_1 - \mu_2$ ). The comparison will be made using a two-sided, two-sample, equal-variance Z-test, with a Type I error rate ( $\alpha$ ) of 0.05. The prior distribution used for the mean difference is Normal (Mean = 10.2, SD = 8). A prior distribution is not used for the standard deviation. The standard deviation is assumed to be the fixed value 17.5. With sample sizes of 40 for Group 1 (treatment) and 40 for Group 2 (control), the assurance (average power) is 0.63367.

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## 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%	40	40	80	50	50	100	10	10	20
20%	62	62	124	78	78	156	16	16	32
20%	80	80	160	100	100	200	20	20	40
20%	120	120	240	150	150	300	30	30	60
20%	160	160	320	200	200	400	40	40	80
20%	200	200	400	250	250	500	50	50	100

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

## Dropout Summary Statements

Anticipating a 20% dropout rate, 50 subjects should be enrolled in Group 1, and 50 in Group 2, to obtain final group sample sizes of 40 and 40, respectively.

## References

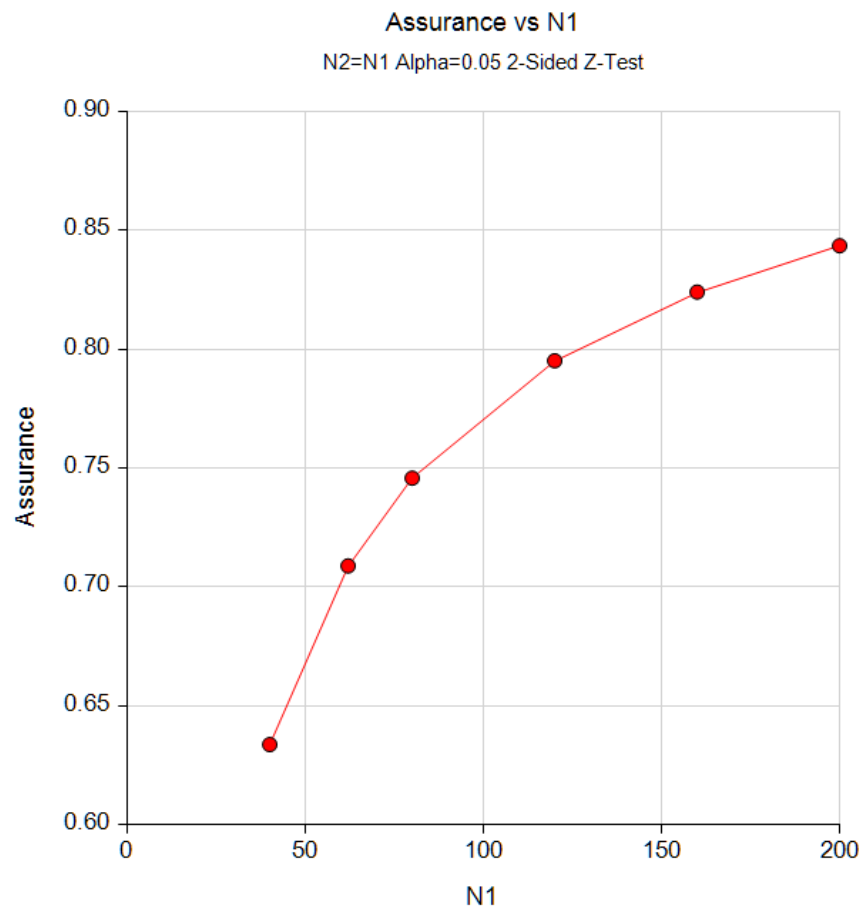
- O'Hagan, A., Stevens, J.W., and Campbell, M.J. 2005. 'Assurance in clinical trial design'. Pharmaceutical Statistics, Volume 4, Pages 187-201.
- Ciarleglio, M.M., Arendt, C.D., and Peduzzi, P.N. 2016. 'Selection of the effect size for sample size determination for a continuous response in a superiority 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.

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

## Assurance for Two-Sample Z-Tests Assuming Equal Variance

## Plots Section

## Plots

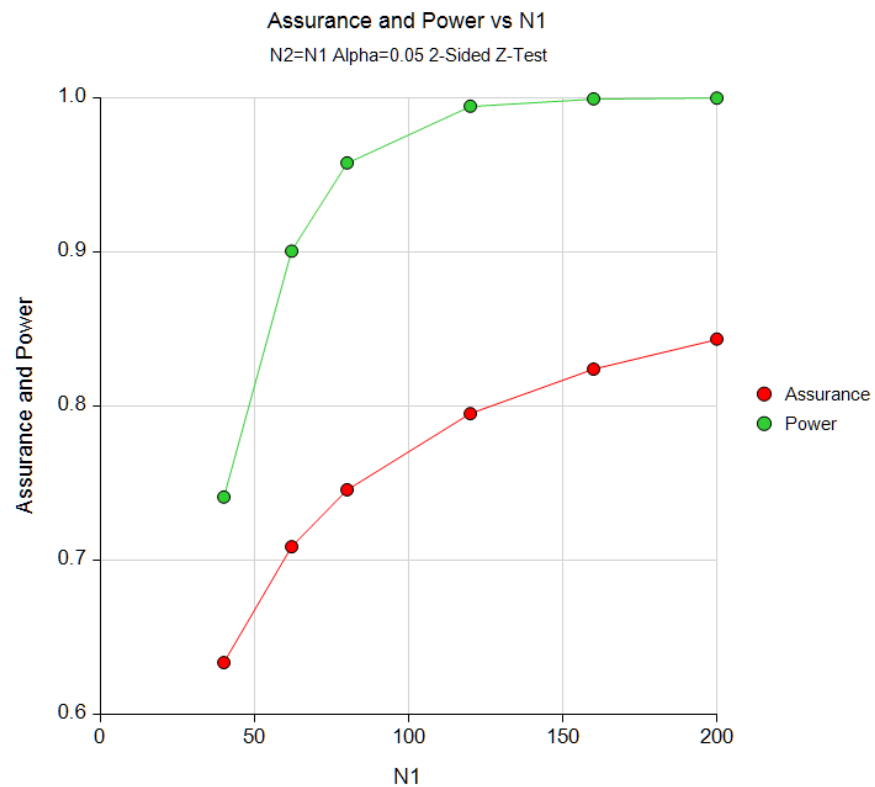


This plot shows the relationship between the assurance and sample size. Note the diminishing impact on assurance of each increase in the number of subjects.

## Assurance for Two-Sample Z-Tests Assuming Equal Variance

## Comparison Plots Section

## Comparison Plots



This plot compares the assurance and power across values of sample size. Note that assurance does not increase nearly as fast as power.

## Example 2 – Validation using Hand Computation

We could not find a validation example in the literature for the case in which both the difference and the standard deviation had prior distributions, so we have developed a validation example of our own.

Suppose a one-sided, two-sample t-test will be used in which  $N_1 = N_2 = 70$  and the significance level is 0.025.

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

$\delta$	Prob
5	0.3
7	0.4
9	0.3

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

$\sigma$	Prob
12	0.2
16	0.6
20	0.2

The *Two-Sample Z-Tests Assuming Equal Variance* procedure is used to compute the power for each of the nine combinations of  $\delta$  and  $\sigma$ . The results of these calculations are shown next.

### Numeric Results

Solve For: [Power](#)  
 Test Type: Two-Sample Equal-Variance Z-Test  
 Difference:  $\delta = \mu_1 - \mu_2$   
 Hypotheses:  $H_0: \delta \leq 0$  vs.  $H_1: \delta > 0$

Power	Sample Size			Mean Difference $\delta$	Standard Deviation $\sigma$	Alpha
	N1	N2	N			
0.69324	70	70	140	5	12	0.025
0.45573	70	70	140	5	16	0.025
0.31528	70	70	140	5	20	0.025
0.93203	70	70	140	7	12	0.025
0.73510	70	70	140	7	16	0.025
0.54406	70	70	140	7	20	0.025
0.99338	70	70	140	9	12	0.025
0.91432	70	70	140	9	16	0.025
0.75875	70	70	140	9	20	0.025

The assurance calculation is made by summing the quantities  $\left[ (power_{i,j})(p(\delta_i))(p(\sigma_j)) \right]$  as follows

$$Assurance = (0.69324 \times 0.3 \times 0.2) + (0.45573 \times 0.3 \times 0.6) + \cdots + (0.75875 \times 0.3 \times 0.2) = 0.70676.$$



## Assurance for Two-Sample Z-Tests Assuming Equal Variance

To run this example, the spreadsheet will need to be loaded with the following four columns in which the first two are for the difference,  $\delta$ , and the second two are for the standard deviation,  $\sigma$ .

<b>C1</b>	<b>C2</b>	<b>C3</b>	<b>C4</b>
<b>5</b>	<b>0.3</b>	<b>12</b>	<b>0.2</b>
<b>7</b>	<b>0.4</b>	<b>16</b>	<b>0.6</b>
<b>9</b>	<b>0.3</b>	<b>20</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 .....	<b>Assurance</b>
Prior Entry Method .....	<b>Individual (Enter a prior distribution for each applicable parameter)</b>
Alternative Hypothesis .....	<b>One-Sided (H1: <math>\delta &gt; 0</math>)</b>
Alpha.....	<b>0.025</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Sample Size Per Group .....	<b>70</b>
Prior Distribution of $\delta$ .....	<b>Custom (Values and Probabilities in Spreadsheet)</b>
Column of Values .....	<b>C1</b>
Column of Pr(Values).....	<b>C2</b>
Prior Distribution of $\sigma$ .....	<b>Custom (Values and Probabilities in Spreadsheet)</b>
Column of Values .....	<b>C3</b>
Column of Pr(Values).....	<b>C4</b>

### Options Tab

Number of Computation Points for each.....	<b>50</b>
Prior Distribution	
Maximum N1 in Sample Size Search .....	<b>5000</b>

### Input Spreadsheet Data

<b>Row</b>	<b>C1</b>	<b>C2</b>	<b>C3</b>	<b>C4</b>
1	5	0.3	12	0.2
2	7	0.4	16	0.6
3	9	0.3	20	0.2

## Output

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

### Numeric Results

Solve For: [Assurance](#)

Hypotheses:  $H_0: \delta \leq 0$  vs.  $H_1: \delta > 0$

Prior Type: Independent Univariate Distributions

### Prior Distributions

$\delta$ : Point List (Values = C1, Probs = C2).

C1: 5 7 9

C2: 0.3 0.4 0.3

$\sigma$ : Point List (Values = C3, Probs = C4).

C3: 12 16 20

C4: 0.2 0.6 0.2

Assurance	Power‡	Sample Size			Expected Mean Difference E( $\delta$ )	Expected Standard Deviation E( $\sigma$ )	Alpha
		N1	N2	N			
0.70676	0.7351	70	70	140	7	16	0.025

‡ Power was calculated using  $\delta = E(\delta) = 7$  and  $\sigma = E(\sigma) = 16$ .

**PASS** calculated the assurance as 0.70676, which validates this procedure.

## Example 3 – Validation using O’Hagan et al. (2005)

O’Hagan *et al.* (2005) pages 192 - 193 present an example for a one-sided z-test in which  $N1 = N2 = 25$  and the significance level is 0.025. The prior distribution of the mean difference is normal with mean 0.2 and standard deviation  $\sqrt{0.06} = 0.244949$ . The standard deviation is set to 0.25. O’Hagan gives the assurance as 0.595.

### 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>Assurance</b>
Prior Entry Method .....	<b>Individual (Enter a prior distribution for each applicable parameter)</b>
Alternative Hypothesis .....	<b>One-Sided (<math>H1: \delta &gt; 0</math>)</b>
Alpha .....	<b>0.025</b>
Group Allocation .....	<b>Equal (<math>N1 = N2</math>)</b>
Sample Size Per Group .....	<b>25</b>
Prior Distribution of $\delta$ .....	<b>Normal (Mean, SD)</b>
Mean .....	<b>0.2</b>
SD .....	<b>0.244929</b>
Truncation Boundaries .....	<b>None</b>
Prior Distribution of $\sigma$ .....	<b>No Prior (Fixed Value)</b>
Fixed Value of $\sigma$ .....	<b>0.25</b>

#### Options Tab

Number of Computation Points for each .....	<b>50</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 Results

Solve For: [Assurance](#)

Hypotheses:  $H_0: \delta \leq 0$  vs.  $H_1: \delta > 0$

Prior Type: Independent Univariate Distributions

### Prior Distributions

$\delta$ : Normal (Mean = 0.2, SD = 0.244929).

$\sigma$ : No Prior

Assurance*	Power‡	Sample Size			Expected Mean Difference $E(\delta)$	Standard Deviation $\sigma$	Alpha
		N1	N2	N			
0.59533	0.80743	25	25	50	0.2	0.25	0.025

\* The number of points used for computation of the prior(s) was 50.

‡ Power was calculated using  $\delta = E(\delta) = 0.2$  and  $\sigma = 0.25$ .

PASS has also calculated the assurance as 0.595 which validates the procedure.

## Example 4 – 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, 0.5, 0.6, 0.7, and 0.8.

### Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 4** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

#### Design Tab

Solve For .....	<b>Sample Size</b>
Prior Entry Method .....	<b>Individual (Enter a prior distribution for each applicable parameter)</b>
Alternative Hypothesis .....	<b>Two-Sided (<math>H_1: \delta \neq 0</math>)</b>
Assurance .....	<b>0.4 0.5 0.6 0.7 0.8</b>
Alpha .....	<b>0.05</b>
Group Allocation .....	<b>Equal (<math>N_1 = N_2</math>)</b>
Prior Distribution of $\delta$ .....	<b>Normal (Mean, SD)</b>
Mean .....	<b>10.2</b>
SD .....	<b>8</b>
Truncation Boundaries .....	<b>None</b>
Prior Distribution of $\sigma$ .....	<b>No Prior (Fixed Value)</b>
Fixed Value of $\sigma$ .....	<b>17.5</b>

#### Options Tab

Number of Computation Points for each .....	<b>50</b>
Prior Distribution	
Maximum $N_1$ 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](#)

Hypotheses:  $H_0: \delta = 0$  vs.  $H_1: \delta \neq 0$

Prior Type: Independent Univariate Distributions

### Prior Distributions

$\delta$ : Normal (Mean = 10.2, SD = 8).

$\sigma$ : No Prior

Assurance*			Sample Size			Expected Mean Difference E( $\delta$ )	Standard Deviation $\sigma$	Alpha
Actual	Target	Power†	N1	N2	N			
0.40710	0.4	0.33825	14	14	28	10.2	17.5	0.05
0.50944	0.5	0.48934	22	22	44	10.2	17.5	0.05
0.60209	0.6	0.67120	34	34	68	10.2	17.5	0.05
0.70108	0.7	0.88605	59	59	118	10.2	17.5	0.05
0.80040	0.8	0.99617	126	126	252	10.2	17.5	0.05

\* The number of points used for computation of the prior(s) was 50.

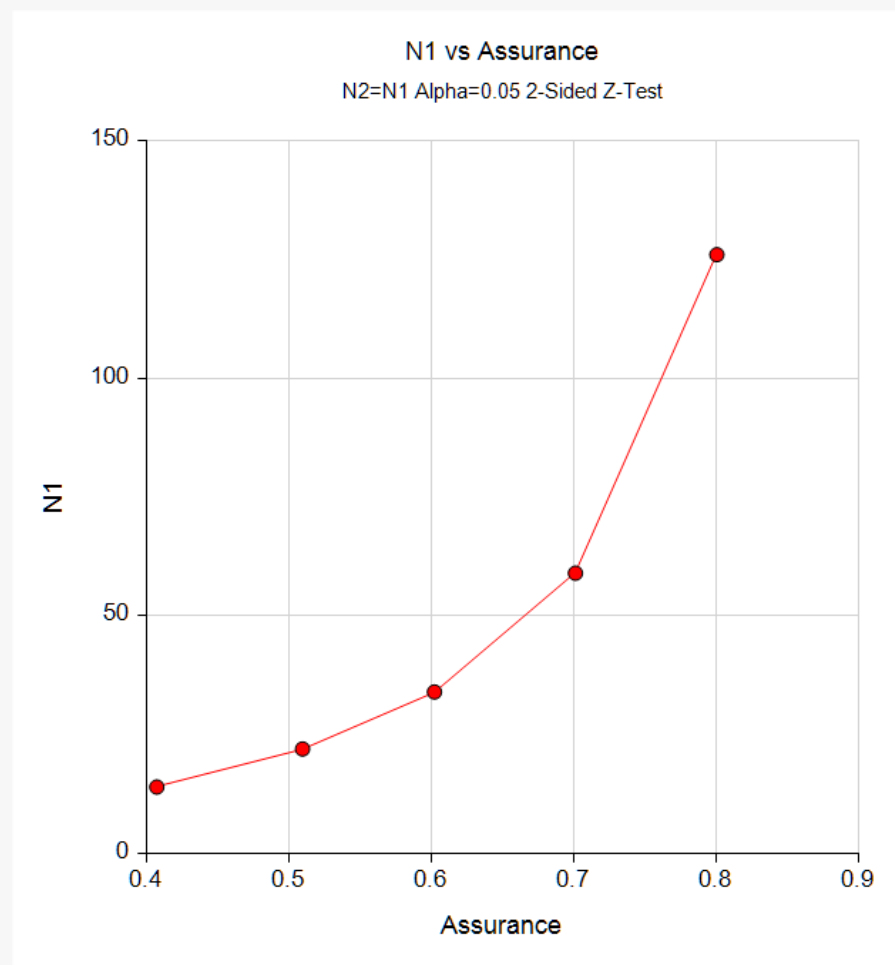
† Power was calculated using  $\delta = E(\delta) = 10.2$  and  $\sigma = 17.5$ .

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

## Assurance for Two-Sample Z-Tests Assuming Equal Variance

## Plots Section

## Plots



This plot shows the relationship between the sample size and assurance. Note the large increase in assurance when the assurance is increased from 0.7 to 0.8.

## Example 5 – Joint Prior Distribution

Suppose a one-sided, two-sample z-test will be used in which  $N_1 = N_2 = 70$  and the significance level is 0.025.

The joint prior distribution of the difference and standard deviation is approximated by the following table. Note the relationship between the difference and the standard deviation.

$\delta$	$\sigma$	Prob
4	11	0.1
5	12	0.2
6	13	0.1
6	15	0.3
7	16	0.4
8	17	0.3
11	19	0.1
13	20	0.2
15	21	0.1

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

<u>C1</u>	<u>C2</u>	<u>C3</u>
4	11	0.1
5	12	0.2
6	13	0.1
6	15	0.3
7	16	0.4
8	17	0.3
11	19	0.1
13	20	0.2
15	21	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 5** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

### Design Tab

Solve For .....	<b>Assurance</b>
Prior Entry Method .....	<b>Combined (Enter parameter values and probabilities on spreadsheet)</b>
Alternative Hypothesis .....	<b>One-Sided (<math>H_1: \delta &gt; 0</math>)</b>
Alpha .....	<b>0.025</b>
Group Allocation .....	<b>Equal (<math>N_1 = N_2</math>)</b>
Sample Size Per Group .....	<b>70</b>
Column of $\delta$ Values .....	<b>C1</b>
Column of $\sigma$ Values .....	<b>C2</b>
Column of Probabilities .....	<b>C3</b>



## Assurance for Two-Sample Z-Tests Assuming Equal Variance

## Options Tab

Number of Computation Points for each.....50

Prior Distribution

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

## Input Spreadsheet Data

Row	C1	C2	C3
1	4	11	0.1
2	5	12	0.2
3	6	13	0.1
4	6	15	0.3
5	7	16	0.4
6	8	17	0.3
7	11	19	0.1
8	13	20	0.2
9	15	21	0.1

## Output

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

## Numeric Results

Solve For: Assurance

Hypotheses:  $H_0: \delta \leq 0$  vs.  $H_1: \delta > 0$ 

Prior Type: Joint Multivariate Distribution

## Prior Distribution

Point Lists

 $\delta$ : C1: 4 5 6 6 7 8 11 13 15 $\sigma$ : C2: 11 12 13 15 16 17 19 20 21

Prob: C3: 0.1 0.2 0.1 0.3 0.4 0.3 0.1 0.2 0.1

Assurance	Power‡	Sample Size			Expected Mean Difference $E(\delta)$	Expected Standard Deviation $E(\sigma)$	Alpha
		N1	N2	N			
0.77213	0.83071	70	70	140	7.88889	16	0.025

‡ Power was calculated using  $\delta = E(\delta) = 7.88889$  and  $\sigma = E(\sigma) = 16$ .

PASS has calculated the assurance as 0.77213.

## Example 6 – Joint Prior Distribution Validation

The validation example 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 distribution of the difference is given as follows.

<u><math>\delta</math></u>	<u>Prob</u>
5	0.3
7	0.4
9	0.3

Similarly, the prior distribution of the standard deviation is given as follows.

<u><math>\sigma</math></u>	<u>Prob</u>
12	0.2
16	0.6
20	0.2

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

<u><math>\delta</math></u>	<u><math>\sigma</math></u>	<u><math>P(\delta)</math></u>	<u><math>P(\sigma)</math></u>	<u><math>P(\delta)P(\sigma)</math></u>
5	12	0.3	0.2	0.06
5	16	0.3	0.6	0.18
5	20	0.3	0.2	0.06
7	12	0.4	0.2	0.08
7	16	0.4	0.6	0.24
7	20	0.4	0.2	0.08
9	12	0.3	0.2	0.06
9	16	0.3	0.6	0.18
9	20	0.3	0.2	0.06

To run this example, the spreadsheet is loaded with the following three columns. (Note that columns C3 and C4 are used to hold intermediate values which are not referenced in this example. C3 holds  $P(\delta)$  and C4 holds  $P(\sigma)$ .)

<u>C1</u>	<u>C2</u>	<u>C5</u>
5	12	0.06
5	16	0.18
5	20	0.06
7	12	0.08
7	16	0.24
7	20	0.08
9	12	0.06
9	16	0.18
9	20	0.06

## Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 6** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

### Design Tab

Solve For ..... **Assurance**  
 Prior Entry Method ..... **Combined (Enter parameter values and probabilities on spreadsheet)**  
 Alternative Hypothesis ..... **One-Sided ( $H_1: \delta > 0$ )**  
 Alpha ..... **0.025**  
 Group Allocation ..... **Equal ( $N_1 = N_2$ )**  
 Sample Size Per Group ..... **70**  
 Column of  $\delta$  Values ..... **C1**  
 Column of  $\sigma$  Values ..... **C2**  
 Column of Probabilities ..... **C5**

### Options Tab

Number of Computation Points for each ..... **50**  
 Prior Distribution  
 Maximum  $N_1$  in Sample Size Search ..... **5000**

### Input Spreadsheet Data

Row	C1	C2	C3	C4	C5
1	5	12	0.3	0.2	0.06
2	5	16	0.3	0.6	0.18
3	5	20	0.3	0.2	0.06
4	7	12	0.4	0.2	0.08
5	7	16	0.4	0.6	0.24
6	7	20	0.4	0.2	0.08
7	9	12	0.3	0.2	0.06
8	9	16	0.3	0.6	0.18
9	9	20	0.3	0.2	0.06

## Output

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

### Numeric Results

Solve For: [Assurance](#)

Hypotheses:  $H_0: \delta \leq 0$  vs.  $H_1: \delta > 0$

Prior Type: Joint Multivariate Distribution

### Prior Distribution

Point Lists

$\delta$ : C1: 5 5 5 7 7 7 9 9 9

$\sigma$ : C2: 12 16 20 12 16 20 12 16 20

Prob: C5: 0.06 0.18 0.06 0.08 0.24 0.08 0.06 0.18 0.06

Assurance	Power‡	Sample Size			Expected Mean Difference $E(\delta)$	Expected Standard Deviation $E(\sigma)$	Alpha
		N1	N2	N			
0.70676	0.7351	70	70	140	7	16	0.025

‡ Power was calculated using  $\delta = E(\delta) = 7$  and  $\sigma = E(\sigma) = 16$ .

PASS has calculated the assurance as 0.70676, which matches the result in Example 2. This validates the joint prior method.