

Chapter 269

Assurance for Two-Sample T-Tests Allowing Unequal Variance

Introduction

This procedure calculates the assurance of one- or two-sided two-sample t-tests when the variances of the two groups (populations) are allowed to be unequal (Welch, 1937).

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

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.

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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 T-Test Procedure

If we assume that μ_1 and μ_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 (α) is chosen for the test, the data is collected, and a t -statistic is generated using the formula:

$$t = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}}}$$

This t -statistic follows a t distribution approximately, with estimated degrees of freedom

$$df = \frac{\left(\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}\right)^2}{\frac{1}{N_1 - 1} \left(\frac{s_1^2}{N_1}\right)^2 + \frac{1}{N_2 - 1} \left(\frac{s_2^2}{N_2}\right)^2}$$

The null hypothesis is rejected in favor of the alternative if,

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

$$t < t_{\alpha/2} \text{ or } t > t_{1-\alpha/2},$$

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

$$t > t_{1-\alpha},$$

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

$$t < t_{\alpha}.$$

Comparing the t -statistic to the cut-off t -value (as shown here) is equivalent to comparing the p -value to α .

Power Calculation

The power is calculated from N_1 and N_2 , α , the assumed μ_1 and μ_2 , and the assumed standard deviations, σ_1 and σ_2 . Two good references for these methods are Julious (2010) and Chow, Shao, Wang, and Lokhnygina (2018), although these texts do not specifically cover the Aspin-Welch-Satterthwaite t-test methods.

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 $t_{1-\alpha}$ based on the central- t distribution with degrees of freedom,

$$df = \frac{\left(\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}\right)^2}{\frac{1}{N_1 - 1} \left(\frac{s_1^2}{N_1}\right)^2 + \frac{1}{N_2 - 1} \left(\frac{s_2^2}{N_2}\right)^2}$$

2. Calculate the non-centrality parameter:

$$\lambda = \frac{\delta}{\sqrt{\frac{\sigma_1^2}{N_1} + \frac{\sigma_2^2}{N_2}}}$$

3. Calculate the power as the probability that the test statistic t is greater than $t_{1-\alpha}$ under the non-central- t distribution with non-centrality parameter λ :

$$Power = Pr_{Non-central-t}(t > t_{1-\alpha} | df, \lambda).$$

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 $P_1(H|\delta, \sigma_1, \sigma_2)$ 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 δ , σ_1 , and σ_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 δ , σ_1 , and σ_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 δ , σ_1 , and σ_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 δ , $f_2(\sigma_1)$ is the prior distribution of σ_1 , and $f_3(\sigma_2)$ is the prior distribution of σ_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.

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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

$$\alpha, \beta < 1$$

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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 $1 - \text{Prob}(Min \leq X \leq Max)$ 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, 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

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

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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, μ , and a scale parameter, s , control the distribution.

The probability density function of the logistic distribution is

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

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 $Z \sim$ 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 $1 - \text{Prob}(Min \leq X \leq Max)$ 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 $t \sim \text{Student's } t$, 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 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 $1 - \text{Prob}(\text{Min} \leq X \leq \text{Max})$ 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 $1 - \text{Prob}(\text{Min} \leq X \leq \text{Max})$ where Min and 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, 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 $1 - \text{Prob}(\text{Min} \leq X \leq \text{Max})$ 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

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 t-test would be used to analyze the experimental data found that 64 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 also concluded that prior distribution of the two group standard deviations should be Normal (19, 3) truncated between 7 and 31 and Normal (16, 3) truncated between 4 and 28.

To shorten the runtime in this exploratory situation, the number of points in the prior computations was 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 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)
Alternative Hypothesis	Two-Sided ($H_1: \delta \neq 0$)
Alpha	0.05
Group Allocation	Equal ($N_1 = N_2$)
Sample Size Per Group	40 64 80 120 160 200
Prior Distribution of δ	Normal (Mean, SD)
Mean	10.2
SD	8
Truncation Boundaries	None
Prior Distribution of σ_1	Normal (Mean, SD)
Mean	19
SD	3
Truncation Boundaries	Left and Right
Left Boundary	7
Right Boundary	31
Prior Distribution of σ_2	Normal (Mean, SD)
Mean	16
SD	3
Truncation Boundaries	Left and Right
Left Boundary	4
Right Boundary	28

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Options Tab

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

Prior Distribution

Maximum N1 in Sample Size Search5000

Output

Click the Calculate button to perform the calculations and generate the following output. Note that because of the extensive calculations required, this example requires 5 to 10 minutes to run.

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

 δ : Normal (Mean = 10.2, SD = 8). σ_1 : Normal (Mean = 19, SD = 3), Left Boundary = 7, Right Boundary = 31. σ_2 : Normal (Mean = 16, SD = 3), Left Boundary = 4, Right Boundary = 28.

Assurance*	Power‡	Sample Size			Expected Mean Difference E(δ)	Expected Group 1 Standard Deviation E(σ_1)	Expected Group 2 Standard Deviation E(σ_2)	Alpha
		N1	N2	N				
0.62525	0.72712	40	40	80	10.2	19	16	0.05
0.70800	0.90307	64	64	128	10.2	19	16	0.05
0.74105	0.95447	80	80	160	10.2	19	16	0.05
0.79178	0.99413	120	120	240	10.2	19	16	0.05
0.82141	0.99935	160	160	320	10.2	19	16	0.05
0.84131	0.99994	200	200	400	10.2	19	16	0.05

* The number of points used for computation of the prior(s) was 20.

‡ Power was calculated using $\delta = E(\delta) = 10.2$, $\sigma_1 = E(\sigma_1) = 19$, and $\sigma_2 = E(\sigma_2) = 16$.

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(δ)	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(σ_1)	The expected value over its prior distribution of the group 1 standard deviation.
E(σ_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

A parallel two-group design will be used to test whether the Group 1 (treatment) mean (μ_1) is different from the Group 2 (control) mean (μ_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, unequal-variance t-test, with a Type I error rate (α) of 0.05. The prior distribution used for the mean difference is Normal (Mean = 10.2, SD = 8). The prior distribution used for the Group 1 standard deviation is Normal (Mean = 19, SD = 3), Left Boundary = 7, Right Boundary = 31. The prior distribution used for the Group 2 standard deviation is Normal (Mean = 16, SD = 3), Left Boundary = 4, Right Boundary = 28. With sample sizes of 40 for Group 1 (treatment) and 40 for Group 2 (control), the assurance (average power) is 0.62525.

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%	64	64	128	80	80	160	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 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, 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

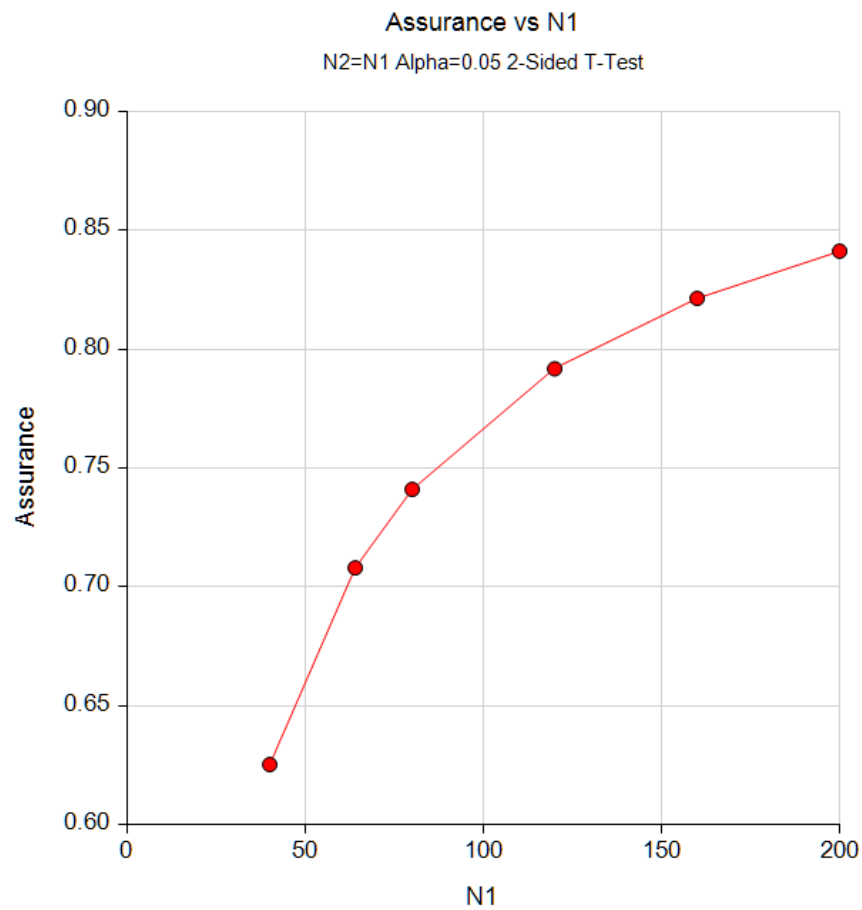
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These reports show the assurance values obtained by each sample size.

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Plots Section

Plots

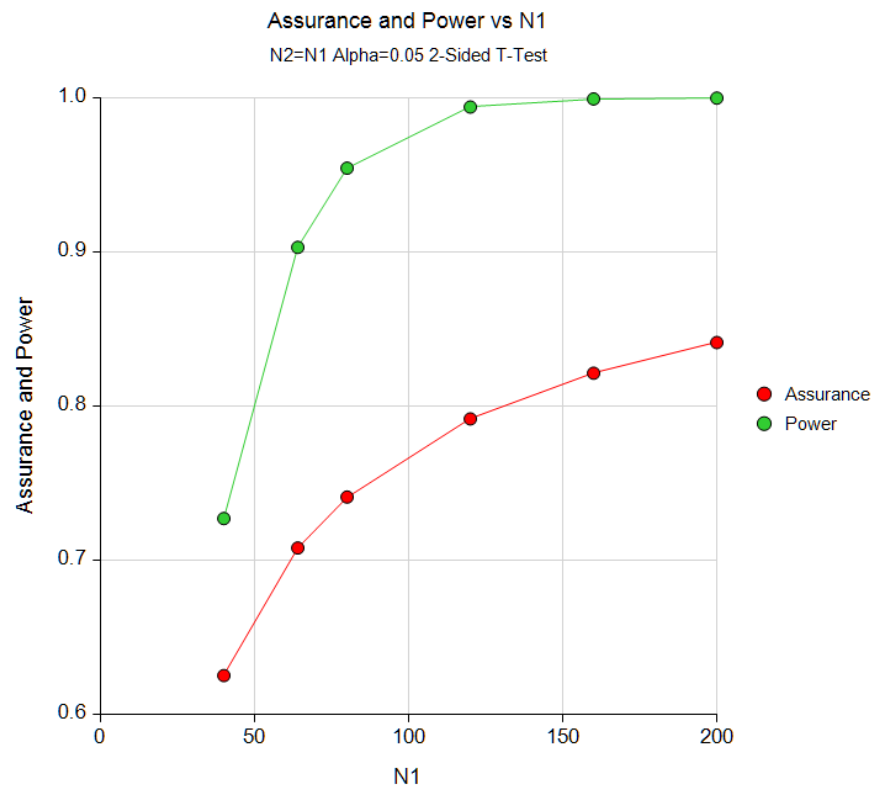


This plot shows the relationship between the assurance and sample size. Note the diminishing impact on assurance of each increase in the number of subjects.

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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.

δ	Prob
5	0.3
7	0.4
9	0.3

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

σ_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.

σ_2	Prob
15	0.2
19	0.6
23	0.2

The *Two-Sample T-Tests Allowing Unequal Variance* procedure is used to compute the power for each of the nine combinations of δ and σ . The results of these calculations are shown next.

Numeric Results

Solve For: [Power](#)
 Test Type: Two-Sample Welch's Unequal-Variance T-Test
 Difference: $\delta = \mu_1 - \mu_2$
 Hypotheses: $H_0: \delta \leq 0$ vs. $H_1: \delta > 0$

Power	Sample Size			Mean Difference δ	Standard Deviation		Alpha
	N1	N2	N		σ_1	σ_2	
0.57999	70	70	140	5	12	15	0.025
0.45471	70	70	140	5	12	19	0.025
0.35856	70	70	140	5	12	23	0.025
0.47374	70	70	140	5	16	15	0.025
0.38672	70	70	140	5	16	19	0.025
0.31614	70	70	140	5	16	23	0.025
0.38239	70	70	140	5	20	15	0.025
0.32488	70	70	140	5	20	19	0.025
0.27519	70	70	140	5	20	23	0.025
0.85691	70	70	140	7	12	15	0.025
0.73390	70	70	140	7	12	19	0.025
0.60900	70	70	140	7	12	23	0.025

Assurance for Two-Sample T-Tests Allowing Unequal Variance

0.75544	70	70	140	7	16	15	0.025
0.64837	70	70	140	7	16	19	0.025
0.54539	70	70	140	7	16	23	0.025
0.64247	70	70	140	7	20	15	0.025
0.55892	70	70	140	7	20	19	0.025
0.47922	70	70	140	7	20	23	0.025
0.97327	70	70	140	9	12	15	0.025
0.91357	70	70	140	9	12	19	0.025
0.82009	70	70	140	9	12	23	0.025
0.92637	70	70	140	9	16	15	0.025
0.85307	70	70	140	9	16	19	0.025
0.76008	70	70	140	9	16	23	0.025
0.84834	70	70	140	9	20	15	0.025
0.77354	70	70	140	9	20	19	0.025
0.68898	70	70	140	9	20	23	0.025

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

$$Assurance = (0.57999 \times 0.3 \times 0.2 \times 0.2) + (0.45471 \times 0.3 \times 0.2 \times 0.6) + \cdots + (0.68898 \times 0.3 \times 0.2 \times 0.2) = 0.63023.$$

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, δ , the second two are for the group 1 standard deviation, σ_1 , and the third two are for the group 2 standard deviation, σ_2 .

C1	C2	C3	C4	C5	C6
5	0.3	12	0.2	15	0.2
7	0.4	16	0.6	19	0.6
9	0.3	20	0.2	23	0.2

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)
Alternative Hypothesis	One-Sided (H1: $\delta > 0$)
Alpha.....	0.025
Group Allocation	Equal (N1 = N2)
Sample Size Per Group	70
Prior Distribution of δ	Custom (Values and Probabilities in Spreadsheet)
Column of Values	C1
Column of Pr(Values).....	C2

Assurance for Two-Sample T-Tests Allowing Unequal Variance

Prior Distribution of σ_1 **Custom (Values and Probabilities in Spreadsheet)**
 Column of Values **C3**
 Column of Pr(Values)..... **C4**
 Prior Distribution of σ_2 **Custom (Values and Probabilities in Spreadsheet)**
 Column of Values **C5**
 Column of Pr(Values)..... **C6**

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	C4	C5	C6
1	5	0.3	12	0.2	15	0.2
2	7	0.4	16	0.6	19	0.6
3	9	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](#)
 Hypotheses: $H_0: \delta \leq 0$ vs. $H_1: \delta > 0$
 Prior Type: Independent Univariate Distributions

Prior Distributions

δ : Point List (Values = C1, Probs = C2).
 C1: 5 7 9
 C2: 0.3 0.4 0.3
 σ_1 : Point List (Values = C3, Probs = C4).
 C3: 12 16 20
 C4: 0.2 0.6 0.2
 σ_2 : Point List (Values = C5, Probs = C6).
 C5: 15 19 23
 C6: 0.2 0.6 0.2

Assurance	Power‡	Sample Size			Expected Mean Difference E(δ)	Expected Group 1 Standard Deviation E(σ_1)	Expected Group 2 Standard Deviation E(σ_2)	Alpha
		N1	N2	N				
0.63023	0.64837	70	70	140	7	16	19	0.025

‡ Power was calculated using $\delta = E(\delta) = 7$, $\sigma_1 = E(\sigma_1) = 16$, and $\sigma_2 = E(\sigma_2) = 19$.

PASS has also calculated the assurance as 0.63023 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 computation is reduced to 10. 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)
Alternative Hypothesis	Two-Sided ($H_1: \delta \neq 0$)
Assurance	0.4 0.6 0.8
Alpha	0.05
Group Allocation	Equal ($N_1 = N_2$)
Prior Distribution of δ	Normal (Mean, SD)
Mean	10.2
SD	8
Truncation Boundaries	None
Prior Distribution of σ_1	Normal (Mean, SD)
Mean	19
SD	3
Truncation Boundaries	Left and Right
Left Boundary	7
Right Boundary	31
Prior Distribution of σ_2	Normal (Mean, SD)
Mean	16
SD	3
Truncation Boundaries	Left and Right
Left Boundary	4
Right Boundary	28

Options Tab

Number of Computation Points for each	10
Prior Distribution	
Maximum N_1 in Sample Size Search	5000

Assurance for Two-Sample T-Tests Allowing Unequal Variance

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

δ : Normal (Mean = 10.2, SD = 8).

σ_1 : Normal (Mean = 19, SD = 3), Left Boundary = 7, Right Boundary = 31.

σ_2 : Normal (Mean = 16, SD = 3), Left Boundary = 4, Right Boundary = 28.

Assurance*			Sample Size			Expected Mean Difference $E(\delta)$	Expected Group 1 Standard Deviation $E(\sigma_1)$	Expected Group 2 Standard Deviation $E(\sigma_2)$	Alpha
Actual	Target	Power†	N1	N2	N				
0.40505	0.4	0.33544	15	15	30	10.2	19	16	0.05
0.60446	0.6	0.68045	36	36	72	10.2	19	16	0.05
0.80053	0.8	0.99657	130	130	260	10.2	19	16	0.05

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

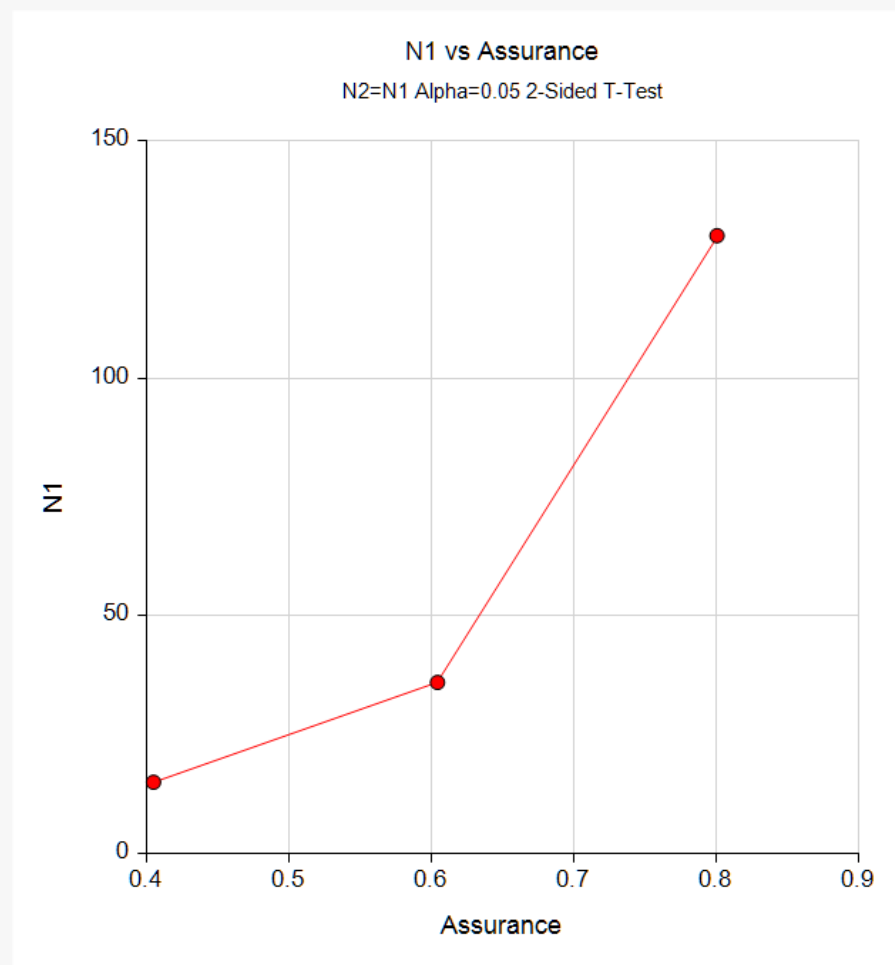
† Power was calculated using $\delta = E(\delta) = 10.2$, $\sigma_1 = E(\sigma_1) = 19$, and $\sigma_2 = E(\sigma_2) = 16$.

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

Assurance for Two-Sample T-Tests Allowing Unequal Variance

Plots Section

Plots



This plot shows the relationship between the assurance and sample size. Note the large increase in required sample size that occurs between an assurance of 0.6 and 0.8.

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, two-sample t-test will be used in which $N1 = N2 = 70$ and the significance level is 0.025. 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>δ</u>	<u>σ_1</u>	<u>σ_2</u>	<u>Prob</u>
-6	21	24	0.1
-4	20	23	0.1
-3	23	25	0.2
0	22	24	0.2
1	25	28	0.1
3	24	27	0.1
12	25	29	0.3
13	24	27	0.3
16	27	31	0.5
17	25	28	0.5
18	29	33	0.3
19	28	32	0.3
22	35	39	0.1
23	34	37	0.1
25	39	42	0.2
26	38	40	0.2
31	43	47	0.1
33	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
0	22	24	0.2
1	25	28	0.1
3	24	27	0.1
12	25	29	0.3
13	24	27	0.3
16	27	31	0.5
17	25	28	0.5
18	29	33	0.3
19	28	32	0.3
22	35	39	0.1
23	34	37	0.1

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25	39	42	0.2
26	38	40	0.2
31	43	47	0.1
33	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)
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 δ Values	C1
Column of σ_1 Values	C2
Column of σ_2 Values	C3
Column of Pr(Values).....	C4

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
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](#)

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

Prior Type: Joint Multivariate Distribution

Prior Distribution

Point Lists

δ : C1: -6 -4 -3 0 1 3 12 13 16 17 18 19 22 23 25 26 31 33

σ_1 : C2: 21 20 23 22 25 24 25 24 27 25 29 28 35 34 39 38 43 42

σ_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‡	Sample Size			Expected Mean Difference E(δ)	Expected Group 1 Standard Deviation E(σ_1)	Expected Group 2 Standard Deviation E(σ_2)	Alpha
		N1	N2	N				
0.72816	0.81593	70	70	140	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 0.72816.

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

δ	<u>Prob</u>
5	0.3
7	0.4
9	0.3

σ_1	<u>Prob</u>
12	0.2
16	0.6
20	0.2

σ_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.

δ	σ_1	σ_2	<u>Prob</u>
5	12	15	0.012
5	12	19	0.036
5	12	23	0.012
5	16	15	0.036
5	16	19	0.108
5	16	23	0.036
5	20	15	0.012
5	20	19	0.036
5	20	23	0.012
7	12	15	0.016
7	12	19	0.048
7	12	23	0.016
7	16	15	0.048
7	16	19	0.144
7	16	23	0.048
7	20	15	0.016
7	20	19	0.048
7	20	23	0.016
9	12	15	0.012
9	12	19	0.036
9	12	23	0.012
9	16	15	0.036

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9	16	19	0.108
9	16	23	0.036
9	20	15	0.012
9	20	19	0.036
9	20	23	0.012

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

<u>C1</u>	<u>C2</u>	<u>C3</u>	<u>C7</u>
5	12	15	0.012
5	12	19	0.036
5	12	23	0.012
5	16	15	0.036
5	16	19	0.108
5	16	23	0.036
5	20	15	0.012
5	20	19	0.036
5	20	23	0.012
7	12	15	0.016
7	12	19	0.048
7	12	23	0.016
7	16	15	0.048
7	16	19	0.144
7	16	23	0.048
7	20	15	0.016
7	20	19	0.048
7	20	23	0.016
9	12	15	0.012
9	12	19	0.036
9	12	23	0.012
9	16	15	0.036
9	16	19	0.108
9	16	23	0.036
9	20	15	0.012
9	20	19	0.036
9	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)**
 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 δ Values **C1**
 Column of σ_1 Values **C2**
 Column of σ_2 Values **C3**
 Column of $\Pr(\text{Values})$ **C7**

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	C6	C7
1	5	12	15	0.3	0.2	0.2	0.012
2	5	12	19	0.3	0.2	0.6	0.036
3	5	12	23	0.3	0.2	0.2	0.012
4	5	16	15	0.3	0.6	0.2	0.036
5	5	16	19	0.3	0.6	0.6	0.108
6	5	16	23	0.3	0.6	0.2	0.036
7	5	20	15	0.3	0.2	0.2	0.012
8	5	20	19	0.3	0.2	0.6	0.036
9	5	20	23	0.3	0.2	0.2	0.012
10	7	12	15	0.4	0.2	0.2	0.016
11	7	12	19	0.4	0.2	0.6	0.048
12	7	12	23	0.4	0.2	0.2	0.016
13	7	16	15	0.4	0.6	0.2	0.048
14	7	16	19	0.4	0.6	0.6	0.144
15	7	16	23	0.4	0.6	0.2	0.048
16	7	20	15	0.4	0.2	0.2	0.016
17	7	20	19	0.4	0.2	0.6	0.048
18	7	20	23	0.4	0.2	0.2	0.016
19	9	12	15	0.3	0.2	0.2	0.012
20	9	12	19	0.3	0.2	0.6	0.036
21	9	12	23	0.3	0.2	0.2	0.012
22	9	16	15	0.3	0.6	0.2	0.036
23	9	16	19	0.3	0.6	0.6	0.108
24	9	16	23	0.3	0.6	0.2	0.036
25	9	20	15	0.3	0.2	0.2	0.012
26	9	20	19	0.3	0.2	0.6	0.036
27	9	20	23	0.3	0.2	0.2	0.012

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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

δ : C1: 5 5 5 5 5 5 5 5 7 7 7 7 7 7 7 7 9 9 9 9 9 9 9 9

σ_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 20

σ_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: C7: 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‡	Sample Size			Expected Mean Difference $E(\delta)$	Expected Group 1 Standard Deviation $E(\sigma_1)$	Expected Group 2 Standard Deviation $E(\sigma_2)$	Alpha
		N1	N2	N				
0.63023	0.64837	70	70	140	7	16	19	0.025

‡ Power was calculated using $\delta = E(\delta) = 7$, $\sigma_1 = E(\sigma_1) = 16$, and $\sigma_2 = E(\sigma_2) = 19$.

PASS has also calculated the assurance as 0.63023 which matches Example 2 and thus validates the procedure.