

Chapter 298

Assurance for Superiority by a Margin Tests for the Ratio of Two Proportions

Introduction

This procedure calculates the assurance of superiority by a margin tests of the ratio of two independent proportions. 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).

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).

Test Procedure

Suppose you have two populations from which dichotomous (binary) responses will be recorded. The probability (or risk) of obtaining the event of interest in population 1 (the treatment group) is P_1 and in population 2 (the control group) is P_2 . The corresponding failure proportions are given by $Q_1 = 1 - P_1$ and $Q_2 = 1 - P_2$.

The assumption is made that the responses from each group follow a binomial distribution. This means that the event probability, P_i , is the same for all subjects within the group and that the response from one subject is independent of that of any other subject.

Random samples of N_1 and N_2 individuals are obtained from these two populations. The data from these samples can be displayed in a 2-by-2 contingency table as follows

Group	Success	Failure	Total
Treatment	x_{11}	x_{12}	N_1
Control	x_{21}	x_{22}	N_2
Total	M_1	M_2	N

The binomial proportions P_1 and P_2 are estimated from these data using the formulae

$$\hat{P}_1 = \frac{x_{11}}{N_1}$$

$$\hat{P}_2 = \frac{x_{21}}{N_2}$$

In the following discussion, let $P_{1.0} = P_1|H_0$ and $P_{1.1} = P_1|H_1$. The value of P_2 remains the same for both hypotheses, so $P_2 = P_2|H_0 = P_2|H_1$.

Superiority by a Margin Z-Test

A *superiority by a margin test* tests that the treatment proportion is better than the reference proportion by more than a small, superiority margin. The actual direction of the hypothesis depends on the response variable being studied. We let $\delta_0 = P_{1.0} - P_2$ refer to the superiority difference (or margin).

Case 1: High Proportions Good

In this case, higher proportions are better. The null and alternative hypotheses are arranged so that rejecting the null hypothesis implies that the treatment proportion is more than a small amount above the reference proportion. The statistical hypotheses are

$$H_0: \frac{P_1}{P_2} \leq R_0 \text{ versus } H_1: \frac{P_1}{P_2} > R_0 .$$

Case 2: High Proportions Bad

In this case, lower proportions are better. The hypotheses are arranged so that rejecting the null hypothesis implies that the treatment proportion is more than a small amount below the reference proportion. The statistical hypotheses are

$$H_0: \frac{P_1}{P_2} \geq R_0 \text{ versus } H_1: \frac{P_1}{P_2} < R_0 .$$

Test Statistics

Several test statistics have been proposed for testing whether the difference, ratio, or odds ratio are different from a specified value. The main difference among the several test statistics is in the formula used to compute the standard error used in the denominator.

Following is a list of the test statistics available in **PASS**. The availability of several test statistics begs the question of which test statistic you should use. The answer is simple: you should use the test statistic that you will use to analyze your data. You may choose a method because it is a standard in your industry, because it seems to have better statistical properties, or because your statistical package calculates it. Whatever your reasons for selecting a certain test statistic, you should use the same test statistic during power or sample calculations.

Miettinen and Nurminen's Likelihood Score Test

Miettinen and Nurminen (1985) proposed a test statistic for testing whether the ratio is equal to a specified value, R_0 . The regular MLE's, \hat{p}_1 and \hat{p}_2 , are used in the numerator of the score statistic while MLE's \tilde{p}_1 and \tilde{p}_2 , constrained so that $\tilde{p}_1/\tilde{p}_2 = R_0$, are used in the denominator. A correction factor of $N/(N-1)$ is applied to make the variance estimate less biased. The significance level of the test statistic is based on the asymptotic normality of the score statistic.

The formula for computing this test statistic is

$$z_{MNR} = \frac{\hat{p}_1 / \hat{p}_2 - R_0}{\hat{\sigma}_{MNR}}$$

where

$$\hat{\sigma}_{MNR} = \sqrt{\left(\frac{\tilde{p}_1 \tilde{q}_1}{N_1} + R_0^2 \frac{\tilde{p}_2 \tilde{q}_2}{N_2}\right) \left(\frac{N}{N-1}\right)}$$

$$\tilde{p}_1 = \tilde{p}_2 R_0$$

$$\tilde{p}_2 = \frac{-B - \sqrt{B^2 - 4AC}}{2A}$$

$$A = NR_0$$

$$B = -[N_1 R_0 + x_{11} + N_2 + x_{21} R_0]$$

$$C = M_1$$

Farrington and Manning's Likelihood Score Test

Farrington and Manning (1990) proposed a test statistic for testing whether the ratio is equal to a specified value, R_0 . The regular MLE's, \hat{p}_1 and \hat{p}_2 , are used in the numerator of the score statistic while MLE's \tilde{p}_1 and \tilde{p}_2 , constrained so that $\tilde{p}_1/\tilde{p}_2 = R_0$, are used in the denominator. The significance level of the test statistic is based on the asymptotic normality of the score statistic.

The formula for computing the test statistic is

$$z_{FMR} = \frac{\hat{p}_1 / \hat{p}_2 - R_0}{\sqrt{\left(\frac{\tilde{p}_1 \tilde{q}_1}{N_1} + R_0^2 \frac{\tilde{p}_2 \tilde{q}_2}{N_2}\right)}}$$

where the estimates, \tilde{p}_1 and \tilde{p}_2 , are computed as in the corresponding test of Miettinen and Nurminen (1985) given above.

Gart and Nam's Likelihood Score Test

Gart and Nam (1988), page 329, proposed a modification to the Farrington and Manning (1988) ratio test that corrected for skewness. Let $z_{FMR}(R_0)$ stand for the Farrington and Manning ratio test statistic described above. The skewness corrected test statistic, z_{GNR} , is the appropriate solution to the quadratic equation

$$(-\tilde{\psi})z_{GNR}^2 + (-1)z_{GNR} + (z_{FMR}(R_0) + \tilde{\psi}) = 0$$

where

$$\tilde{\psi} = \frac{1}{6\tilde{u}^{3/2}} \left(\frac{\tilde{q}_1(\tilde{q}_1 - \tilde{p}_1)}{N_1^2 \tilde{p}_1^2} - \frac{\tilde{q}_2(\tilde{q}_2 - \tilde{p}_2)}{N_2^2 \tilde{p}_2^2} \right)$$

$$\tilde{u} = \frac{\tilde{q}_1}{N_1 \tilde{p}_1} + \frac{\tilde{q}_2}{N_2 \tilde{p}_2}$$

Power Calculations

The power is calculated using the standard formulas for the z-test. The differences in the results of the above tests occur because of the different formulas that are used for the standard error. To compute the power, the values of \hat{p}_1 and \hat{p}_2 in the test statistic are replaced by the corresponding values of P_1 and P_2 . The power is then computed using the normal approximation to the binomial as presented in Chow et al. (2008).

Assurance Calculation

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

Let $P'(H|P_1, P_2)$ be the power function described above where H is the event that null hypothesis is rejected conditional on the parameter values. The specification of P_1 and P_2 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 P_1 and P_2 . Hence, the definition of assurance is

$$Assurance = E_{P_1, P_2}(P'(H|P_1, P_2)) = \iint P'(H|P_1, P_2) f(P_1, P_2) dP_1 dP_2$$

where $f(P_1, P_2)$ is the joint prior distribution of P_1 and P_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 $f(P_1, P_2)$. 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 univariate distributions as follows

$$f(P_1, P_2) = f_1(P_1)f_2(P_2)$$

where $f_1(P_1)$ is the prior distribution of P_1 and $f_2(P_2)$ is the prior distribution of P_2 . This method is also available in **PASS**. In this case, the definition of assurance becomes

$$Assurance = E_{P_1, P_2}(P'(H|P_1, P_2)) = \iint P'(H|P_1, P_2)f_1(P_1)f_2(P_2)dP_1 dP_2$$

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.

List of Available Univariate Prior Distributions

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

No Prior

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

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

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

The probability density function of the beta distribution is

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

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

The mean of X is

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

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

Symmetric and Unimodal

$$\alpha = \beta > 1$$

U Shaped

$$\alpha = \beta < 1$$

Bimodal

$$\alpha, \beta < 1$$

Uniform

$$\alpha = \beta = 1$$

Parabolic

$$\alpha = \beta = 2$$

Bell-Shaped

$$\alpha = \beta > 2$$

Gamma (Shape, Scale)

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

The probability density function of the gamma distribution is

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

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

The mean of X is

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

A truncated version of the distribution is constructed by dividing the density by $1 - \text{Prob}(Min \leq X \leq Max)$ 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

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

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.

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

Suppose a new drug has been developed to replace the drug currently used for the treatment of a particular disease because it performs better.

Researchers conducted a power analysis using the PASS procedure *Superiority by a Margin Tests for the Ratio of Two Proportions* and determined that a sample size of 523 per group were needed to achieve the 90% power that is required at the 0.025 significance level when using the Farrington and Manning score test. The baseline cure rate during the first year using with the control drug is 0.63. The cure rate of the new drug under the alternative hypothesis is anticipated to be 0.81. The superiority ratio is set to 1.1.

To complete their sample size study, the researchers want to run an assurance analysis for a range of group sample sizes from 300 to 900. An elicitation exercise determined that the prior distribution of the P1 should be normal with mean 0.81 and standard deviation 0.04. The elicitation also concluded that the prior distribution of P2 should be normal with mean 0.63 and standard deviation 0.02.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 1** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For	Assurance
Prior Entry Method	Individual (Enter a prior distribution for each applicable parameter)
Higher Proportions Are	Better (H1: $P1/P2 > R0$)
Test Type	Likelihood Score (Farrington & Manning)
Alpha	0.025
Group Allocation	Equal (N1 = N2)
Sample Size Per Group	100 300 500 700 900
R0 (Superiority Ratio)	1.1
Prior Distribution of P1	Normal (Mean, SD)
Mean	0.81
SD	0.04
Truncation Boundaries	None
Prior Distribution of P2	Normal (Mean, SD)
Mean	0.63
SD	0.02
Truncation Boundaries	None

Options Tab

Number of Computation Points for each	30
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](#)
 Hypotheses: $H_0: P_1 / P_2 \leq R_0$ vs. $H_1: P_1 / P_2 > R_0$
 Test Statistic: Farrington & Manning Likelihood Score Test
 Prior Type: Independent Univariate Distributions

Prior Distributions

P1: Normal (Mean = 0.81, SD = 0.04).

P2: Normal (Mean = 0.63, SD = 0.02).

Assurance*	Power‡	Sample Size			Expected Group 1 Proportion E(P1)	Expected Group 2 Proportion E(P2)	Ratio of Proportions		
		N1	N2	N			Superiority R0	H1 R1	Alpha
0.44171	0.42256	100	100	200	0.81	0.63	1.1	1.28571	0.025
0.75839	0.86474	300	300	600	0.81	0.63	1.1	1.28571	0.025
0.85784	0.97698	500	500	1000	0.81	0.63	1.1	1.28571	0.025
0.90146	0.99675	700	700	1400	0.81	0.63	1.1	1.28571	0.025
0.92488	0.99959	900	900	1800	0.81	0.63	1.1	1.28571	0.025

* The number of points used for computation of the prior(s) was 30.

‡ Power was calculated using $P_1 = E(P_1) = 0.81$ and $P_2 = E(P_2) = 0.63$.

Assurance The expected power where the expectation is with respect to the prior distribution(s).
 Power The power calculated using the parameter values shown in the footnote. Note that these parameter values may be different from those shown in the report.
 N1 The number of subjects in group 1.
 N2 The number of subjects in group 2.
 N The total sample size. $N = N_1 + N_2$.
 E(P1) The expected value over its prior distribution of the group 1 response proportion.
 E(P2) The expected value over its prior distribution of the group 2 response proportion.
 R0 The superiority ratio (margin) between the two proportions.
 R1 The proportion ratio (P_1 / P_2) between the two proportions assuming the alternative hypothesis.
 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) proportion (P_1) is superior to the Group 2 (control) proportion (P_2) by a margin, with a superiority ratio of 1.1 ($H_0: P_1 / P_2 \leq 1.1$ versus $H_1: P_1 / P_2 > 1.1$). The comparison will be made using a one-sided, two-sample Farrington & Manning Likelihood Score test of the ratio, with a Type I error rate (α) of 0.025. The prior distribution used for the Group 1 proportion is Normal (Mean = 0.81, SD = 0.04). The prior distribution used for the Group 2 proportion is Normal (Mean = 0.63, SD = 0.02). With sample sizes of 100 for Group 1 (treatment) and 100 for Group 2 (control), the assurance (average power) is 0.44171.

Assurance for Superiority by a Margin Tests for the Ratio of Two Proportions

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%	300	300	600	375	375	750	75	75	150
20%	500	500	1000	625	625	1250	125	125	250
20%	700	700	1400	875	875	1750	175	175	350
20%	900	900	1800	1125	1125	2250	225	225	450

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.

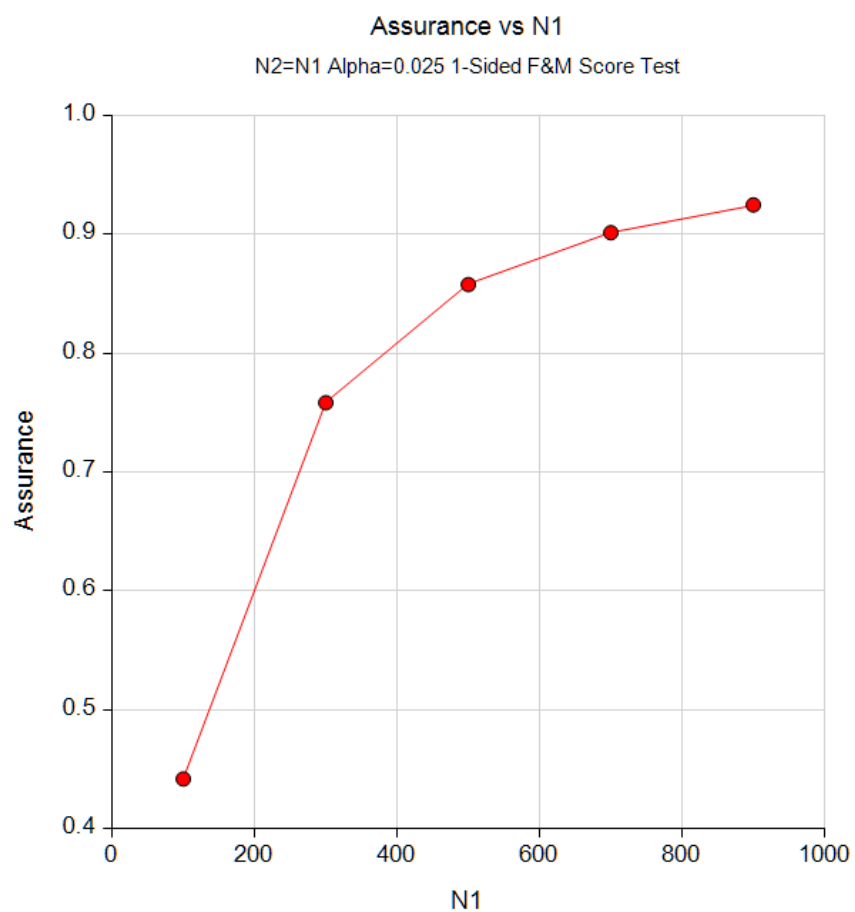
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This report shows the assurance values obtained by the various sample sizes.

Plots Section

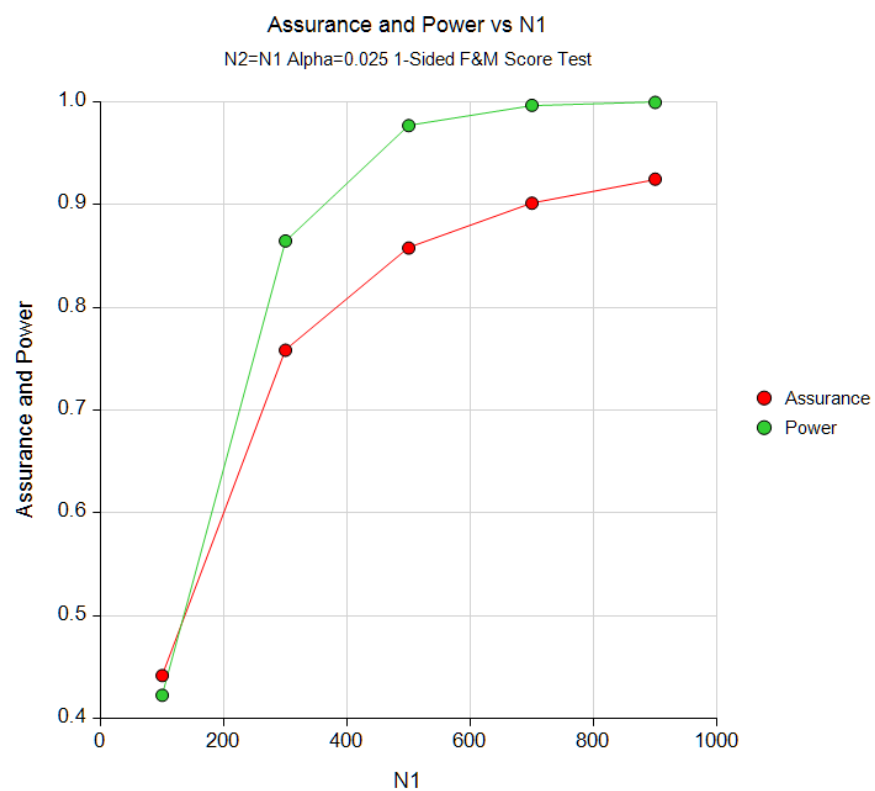
Plots



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

Comparison Plots Section

Comparison Plots



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

Example 2 – Validation using Hand Computation

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

Suppose a one-sided, Farrington and Manning Likelihood Score Test is used where $N1 = N2 = 500$ and the significance level is 0.025. Further suppose that the superiority ratio is 1.05.

The prior distribution of P1.1 is approximated by the following table.

P1.1	Prob
0.48	0.3
0.54	0.4
0.60	0.3

The prior distribution of P2 is approximated by the following table.

P2	Prob
0.41	0.2
0.44	0.6
0.47	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 here.

The *Superiority by a Margin Tests for the Ratio of Two Proportions* procedure is used to compute the power for each of the nine combinations of P1 and P2. The results of these calculations are shown next.

Numeric Results

Solve For: [Power](#)
 Groups: 1 = Treatment, 2 = Reference
 Test Statistic: Farrington & Manning Likelihood Score Test
 Hypotheses: $H0: P1 / P2 \leq R0$ vs. $H1: P1 / P2 > R0$

Power*	Sample Size			Proportions			Ratio		Alpha
	N1	N2	N	Superiority P1.0	Actual P1.1	Reference P2	Superiority R0	Actual R1	
0.33554	500	500	1000	0.4305	0.48	0.41	1.05	1.170732	0.025
0.08020	500	500	1000	0.4620	0.48	0.44	1.05	1.090909	0.025
0.00874	500	500	1000	0.4935	0.48	0.47	1.05	1.021277	0.025
0.92430	500	500	1000	0.4305	0.54	0.41	1.05	1.317073	0.025
0.67330	500	500	1000	0.4620	0.54	0.44	1.05	1.227273	0.025
0.29930	500	500	1000	0.4935	0.54	0.47	1.05	1.148936	0.025
0.99956	500	500	1000	0.4305	0.60	0.41	1.05	1.463415	0.025
0.99009	500	500	1000	0.4620	0.60	0.44	1.05	1.363636	0.025
0.91062	500	500	1000	0.4935	0.60	0.47	1.05	1.276596	0.025

* Power was computed using the normal approximation method.

The assurance calculation is made by summing the quantities $\left[(power_{i,j})(p(P1_i)) (p(P2_j)) \right]$ as follows

$$Assurance = (0.33554 \times 0.3 \times 0.2) + (0.08020 \times 0.3 \times 0.6) + \dots + (0.91062 \times 0.3 \times 0.2) = 0.5874.$$

Assurance for Superiority by a Margin Tests for the Ratio of Two Proportions

To run this example, the spreadsheet will need to be loaded with the following four columns in which the first two are for P1 and the second two are for P2.

C1	C2	C3	C4
0.48	0.3	0.41	0.2
0.54	0.4	0.44	0.6
0.60	0.3	0.47	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)
Higher Proportions Are	Better (H1: $P1/P2 > R0$)
Test Type	Likelihood Score (Farrington & Manning)
Alpha	0.025
Group Allocation	Equal ($N1 = N2$)
Sample Size Per Group	500
R0 (Superiority Ratio)	1.05
Prior Distribution of P1	Custom (Values and Probabilities in Spreadsheet)
Column of Values	C1
Column of Pr(Values)	C2
Prior Distribution of P2	Custom (Values and Probabilities in Spreadsheet)
Column of Values	C3
Column of Pr(Values)	C4

Options Tab

Number of Computation Points for each	30
Prior Distribution	
Maximum N1 in Sample Size Search	5000

Input Spreadsheet Data

Row	C1	C2	C3	C4
1	0.48	0.3	0.41	0.2
2	0.54	0.4	0.44	0.6
3	0.60	0.3	0.47	0.2

Output

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

Numeric Results

Solve For: [Assurance](#)
 Hypotheses: $H_0: P_1 / P_2 \leq R_0$ vs. $H_1: P_1 / P_2 > R_0$
 Test Statistic: Farrington & Manning Likelihood Score Test
 Prior Type: Independent Univariate Distributions

Prior Distributions

P1: Point List (Values = C1, Probs = C2).
 C1: 0.48 0.54 0.6
 C2: 0.3 0.4 0.3
 P2: Point List (Values = C3, Probs = C4).
 C3: 0.41 0.44 0.47
 C4: 0.2 0.6 0.2

Assurance	Power‡	Sample Size			Expected Group 1 Proportion E(P1)	Expected Group 2 Proportion E(P2)	Ratio of Proportions		
		N1	N2	N			Superiority R0	H1 R1	Alpha
0.5874	0.6733	500	500	1000	0.54	0.44	1.05	1.22727	0.025

‡ Power was calculated using $P_1 = E(P_1) = 0.54$ and $P_2 = E(P_2) = 0.44$.

PASS has also calculated the assurance as 0.5874 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, 0.5, 0.6, 0.7, 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 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 3** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For	Sample Size
Prior Entry Method	Individual (Enter a prior distribution for each applicable parameter)
Higher Proportions Are	Better ($H_1: P_1/P_2 > R_0$)
Test Type	Likelihood Score (Farrington & Manning)
Assurance	0.4 0.5 0.6 0.7 0.8
Alpha	0.025
Group Allocation	Equal ($N_1 = N_2$)
R_0 (Superiority Ratio)	1.1
Prior Distribution of P_1	Normal (Mean, SD)
Mean	0.81
SD	0.04
Truncation Boundaries	None
Prior Distribution of P_2	Normal (Mean, SD)
Mean	0.63
SD	0.02
Truncation Boundaries	None

Options Tab

Number of Computation Points for each	20
Prior Distribution	
Maximum N_1 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: [Sample Size](#)
Hypotheses: $H_0: P_1 / P_2 \leq R_0$ vs. $H_1: P_1 / P_2 > R_0$
Test Statistic: Farrington & Manning Likelihood Score Test
Prior Type: Independent Univariate Distributions

Prior Distributions

P1: Normal (Mean = 0.81, SD = 0.04).

P2: Normal (Mean = 0.63, SD = 0.02).

Assurance*			Sample Size			Expected Group 1 Proportion E(P1)	Expected Group 2 Proportion E(P2)	Ratio of Proportions		
Actual	Target	Power‡	N1	N2	N			Superiority R0	H1 R1	Alpha
0.40171	0.4	0.37656	87	87	174	0.81	0.63	1.1	1.28571	0.025
0.50142	0.5	0.49597	122	122	244	0.81	0.63	1.1	1.28571	0.025
0.60108	0.6	0.63166	169	169	338	0.81	0.63	1.1	1.28571	0.025
0.70076	0.7	0.77997	239	239	478	0.81	0.63	1.1	1.28571	0.025
0.80037	0.8	0.92055	363	363	726	0.81	0.63	1.1	1.28571	0.025

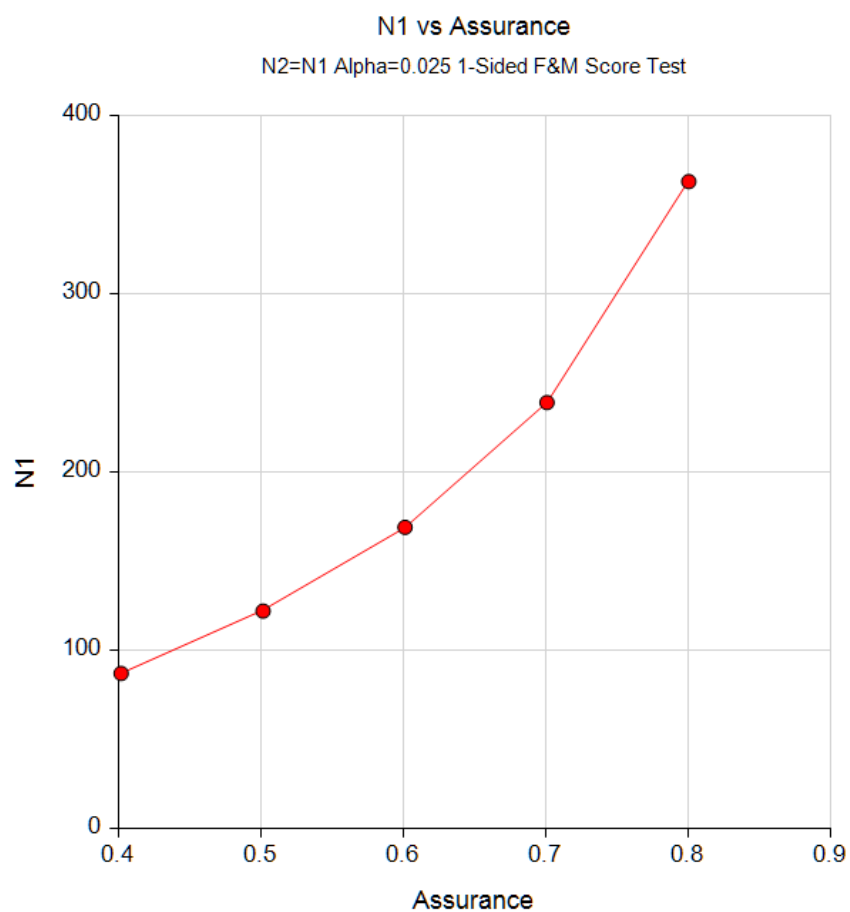
* The number of points used for computation of the prior(s) was 20.

‡ Power was calculated using $P_1 = E(P_1) = 0.81$ and $P_2 = E(P_2) = 0.63$.

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 two parameters.

Suppose a one-sided, superiority by a margin Farrington and Manning Likelihood Score Test will be used for a study in which higher values of the response proportion are better. In this study, $N_1 = N_2 = 3000$, the significance level is 0.025, and the superiority ratio is 1.02.

Further suppose that the joint prior distribution of the P1 (treatment) and P2 (control) 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>P1</u>	<u>P2</u>	<u>Prob</u>
0.32	0.34	0.05
0.36	0.34	0.10
0.44	0.34	0.25
0.34	0.35	0.20
0.37	0.35	0.25
0.45	0.35	0.40
0.34	0.36	0.50
0.38	0.36	0.55
0.46	0.36	0.70
0.35	0.37	0.50
0.39	0.37	0.55
0.47	0.37	0.70
0.36	0.38	0.20
0.40	0.38	0.25
0.48	0.38	0.40
0.37	0.39	0.05
0.41	0.39	0.10
0.49	0.39	0.25

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>
0.32	0.34	0.05
0.36	0.34	0.10
0.44	0.34	0.25
0.34	0.35	0.20
0.37	0.35	0.25
0.45	0.35	0.40
0.34	0.36	0.50
0.38	0.36	0.55
0.46	0.36	0.70
0.35	0.37	0.50
0.39	0.37	0.55
0.47	0.37	0.70
0.36	0.38	0.20
0.40	0.38	0.25

Assurance for Superiority by a Margin Tests for the Ratio of Two Proportions

0.48 0.38 0.40
 0.37 0.39 0.05
 0.41 0.39 0.10
 0.49 0.39 0.25

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 Proportions Are **Better (H1: $P1/P2 > R0$)**
 Test Type **Likelihood Score (Farrington & Manning)**
 Alpha **0.025**
 Group Allocation **Equal ($N1 = N2$)**
 Sample Size Per Group **3000**
 R0 (Superiority Ratio) **1.02**
 Column of P1 Values **C1**
 Column of P2 Values **C2**
 Column of Pr(Values) **C3**

Options Tab

Number of Computation Points for each **30**
 Prior Distribution
 Maximum N1 in Sample Size Search **5000**

Input Spreadsheet Data

Row	C1	C2	C3
1	0.32	0.34	0.05
2	0.36	0.34	0.10
3	0.44	0.34	0.25
4	0.34	0.35	0.20
5	0.37	0.35	0.25
6	0.45	0.35	0.40
7	0.34	0.36	0.50
8	0.38	0.36	0.55
9	0.46	0.36	0.70
10	0.35	0.37	0.50
11	0.39	0.37	0.55
12	0.47	0.37	0.70
13	0.36	0.38	0.20
14	0.40	0.38	0.25
15	0.48	0.38	0.40
16	0.37	0.39	0.05
17	0.41	0.39	0.10
18	0.49	0.39	0.25

Output

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

Numeric Results

Solve For: [Assurance](#)
 Hypotheses: $H_0: P_1 / P_2 \leq R_0$ vs. $H_1: P_1 / P_2 > R_0$
 Test Statistic: Farrington & Manning Likelihood Score Test
 Prior Type: Joint Multivariate Distribution

Prior Distribution

Point Lists

P1: C1: 0.32 0.36 0.44 0.34 0.37 0.45 0.34 0.38 0.46 0.35 0.39 0.47 0.36 0.4 0.48 0.37 0.41 0.49

P2: C2: 0.34 0.34 0.34 0.35 0.35 0.35 0.36 0.36 0.36 0.37 0.37 0.37 0.38 0.38 0.38 0.39 0.39 0.39

Prob: C3: 0.05 0.1 0.25 0.2 0.25 0.4 0.5 0.55 0.7 0.5 0.55 0.7 0.2 0.25 0.4 0.05 0.1 0.25

Assurance	Power‡	Sample Size			Expected Group 1 Proportion E(P1)	Expected Group 2 Proportion E(P2)	Ratio of Proportions		
		N1	N2	N			Superiority R0	H1 R1	Alpha
0.50107	0.8671	3000	3000	6000	0.41133	0.365	1.02	1.12694	0.025

‡ Power was calculated using $P_1 = E(P_1) = 0.41133$ and $P_2 = E(P_2) = 0.365$.

PASS has calculated the assurance as 0.50107.

Example 5 – Joint Prior Validation

The settings 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 P1 and P2 are

<u>P1</u>	<u>Prob</u>
0.48	0.3
0.54	0.4
0.60	0.3

<u>P2</u>	<u>Prob</u>
0.41	0.2
0.44	0.6
0.47	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.

<u>P1</u>	<u>P2</u>	<u>P(P1)</u>	<u>P(P2)</u>	<u>Prob</u>
0.48	0.41	0.3	0.2	0.06
0.48	0.44	0.3	0.6	0.18
0.48	0.47	0.3	0.2	0.06
0.54	0.41	0.4	0.2	0.08
0.54	0.44	0.4	0.6	0.24
0.54	0.47	0.4	0.2	0.08
0.60	0.41	0.3	0.2	0.06
0.60	0.44	0.3	0.6	0.18
0.60	0.47	0.3	0.2	0.06

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

<u>C1</u>	<u>C2</u>	<u>C3</u>	<u>C4</u>	<u>C5</u>
0.48	0.41	0.3	0.2	0.06
0.48	0.44	0.3	0.6	0.18
0.48	0.47	0.3	0.2	0.06
0.54	0.41	0.4	0.2	0.08
0.54	0.44	0.4	0.6	0.24
0.54	0.47	0.4	0.2	0.08
0.60	0.41	0.3	0.2	0.06
0.60	0.44	0.3	0.6	0.18
0.60	0.47	0.3	0.2	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 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 Proportions Are **Better (H1: $P1/P2 > R0$)**
 Test Type **Likelihood Score (Farrington & Manning)**
 Alpha **0.025**
 Group Allocation **Equal (N1 = N2)**
 Sample Size Per Group **500**
 R0 (Superiority Ratio) **1.05**
 Column of P1 Values **C1**
 Column of P2 Values **C2**
 Column of Pr(Values) **C5**

Options Tab

Number of Computation Points for each **30**
 Prior Distribution
 Maximum N1 in Sample Size Search **5000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5
1	0.48	0.41	0.3	0.2	0.06
2	0.48	0.44	0.3	0.6	0.18
3	0.48	0.47	0.3	0.2	0.06
4	0.54	0.41	0.4	0.2	0.08
5	0.54	0.44	0.4	0.6	0.24
6	0.54	0.47	0.4	0.2	0.08
7	0.60	0.41	0.3	0.2	0.06
8	0.60	0.44	0.3	0.6	0.18
9	0.60	0.47	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: $H_0: P_1 / P_2 \leq R_0$ vs. $H_1: P_1 / P_2 > R_0$
Test Statistic: Farrington & Manning Likelihood Score Test
Prior Type: Joint Multivariate Distribution

Prior Distribution

Point Lists

P1: C1: 0.48 0.48 0.48 0.54 0.54 0.54 0.6 0.6 0.6

P2: C2: 0.41 0.44 0.47 0.41 0.44 0.47 0.41 0.44 0.47

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 Group 1 Proportion E(P1)	Expected Group 2 Proportion E(P2)	Ratio of Proportions		
		N1	N2	N			Superiority R0	H1 R1	Alpha
0.5874	0.6733	500	500	1000	0.54	0.44	1.05	1.22727	0.025

‡ Power was calculated using $P_1 = E(P_1) = 0.54$ and $P_2 = E(P_2) = 0.44$.

PASS has also calculated the assurance as 0.5874 which matches Example 2 and thus validates the procedure.