

Chapter 283

Assurance for Tests for Two Proportions

Introduction

This procedure calculates the assurance of one- or two-sided tests of the difference between two independent proportions. The four test statistics analyzed by this procedure assume that the difference between the two proportions is zero under the null hypothesis. The *non-null (offset) case* is discussed in another procedure. 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.

Assurance for Tests for Two Proportions

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

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

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

Comparing Two Proportions

When analyzing studies such as this, one usually wants to compare the two binomial probabilities. A common measure for comparing these quantities is their difference.

The tests analyzed by this routine are for the *null case*. This refers to the values of the above parameters under the null hypothesis. In the *null case*, the difference is zero under the null hypothesis. In the *non-null case*, discussed in another chapter, the difference is some value other than zero. The non-null case appears in equivalence and non-inferiority testing.

Hypothesis Tests

Several statistical tests have been developed for testing the inequality of two proportions. For large samples, the powers of the various tests are about the same. However, for small samples, the differences in the powers can be quite large. Hence, it is important to base the assurance analysis on the test statistic that will be used to analyze the data. If you have not selected a test statistic, you may wish to determine which one offers the best power in your situation. No single test is the champion in every situation, so you must compare the powers of the various tests to determine which to use.

Difference

The (risk) difference, $\delta = P_1 - P_2$, is perhaps the most direct measure for comparing two proportions. Three sets of statistical hypotheses can be formulated:

1. $H_0: P_1 - P_2 = 0$ versus $H_1: P_1 - P_2 \neq 0$; this is often called the *two-tailed test*.
2. $H_0: P_1 - P_2 \leq 0$ versus $H_1: P_1 - P_2 > 0$; this is often called the *upper-tailed test*.
3. $H_0: P_1 - P_2 \geq 0$ versus $H_1: P_1 - P_2 < 0$; this is often called the *lower-tailed test*.

The traditional approach for testing these hypotheses has been to use the Pearson chi-square test for large samples, the Yates chi-square for intermediate sample sizes, and the Fisher Exact test for small samples. Recently, some authors have begun questioning this solution. For example, based on exact enumeration, Upton (1982) and D'Agostino (1988) conclude that the Fisher Exact test and Yates test should never be used.

Power Calculation

The power for a test statistic is often based on a normal approximation, especially for large samples. The various test statistics that are available in this routine are listed next.

Z-Test (or Chi-Square Test) (Pooled and Unpooled)

This test statistic was first proposed by Karl Pearson in 1900. Although this test is usually expressed directly as a chi-square statistic, it is expressed here as a z statistic so that it can be more easily used for one-sided hypothesis testing.

Both *pooled* and *unpooled* versions of this test have been discussed in the statistical literature. The pooling refers to the way in which the standard error is estimated. In the pooled version, the two proportions are averaged, and only one proportion is used to estimate the standard error. In the unpooled version, the two proportions are used separately.

The formula for the test statistic is

$$z = \frac{\hat{p}_1 - \hat{p}_2}{\hat{\sigma}_D}$$

Assurance for Tests for Two Proportions

Pooled Version

$$\hat{\sigma}_D = \sqrt{\hat{p}(1 - \hat{p}) \left(\frac{1}{N_1} + \frac{1}{N_2} \right)}$$

$$\hat{p} = \frac{N_1 \hat{p}_1 + N_2 \hat{p}_2}{N_1 + N_2}$$

Unpooled Version

$$\hat{\sigma}_D = \sqrt{\frac{\hat{p}_1(1 - \hat{p}_1)}{N_1} + \frac{\hat{p}_2(1 - \hat{p}_2)}{N_2}}$$

Power

The power of this test uses the normal approximation as presented in Chow et al. (2008).

1. Find the critical value (or values in the case of a two-sided test) using the standard normal distribution. The critical value is that value of z that leaves exactly the target value of α in the tail.
2. Use the normal approximation to binomial distribution to compute binomial probabilities, compute the power for the pooled and unpooled tests, respectively, using

$$\textbf{Pooled: } 1 - \beta = \Pr \left(Z < \frac{z_\alpha \sigma_{D,p} + (P_1 - P_2)}{\sigma_{D,u}} \right) \quad \textbf{Unpooled: } 1 - \beta = \Pr \left(Z < \frac{z_\alpha \sigma_{D,u} + (P_1 - P_2)}{\sigma_{D,u}} \right)$$

where

$$\sigma_{D,u} = \sqrt{\frac{P_1 Q_1}{N_1} + \frac{P_2 Q_2}{N_2}} \quad (\text{unpooled standard error})$$

$$\sigma_{D,p} = \sqrt{\bar{P} \bar{Q} \left(\frac{1}{N_1} + \frac{1}{N_2} \right)} \quad (\text{pooled standard error})$$

$$\bar{P} = \frac{N_1 P_1 + N_2 P_2}{N_1 + N_2} \quad \text{and} \quad \bar{Q} = 1 - \bar{P}$$

Z-Test (or Chi-Square Test) with Continuity Correction (Pooled and Unpooled)

Frank Yates is credited with proposing a correction to the Pearson Chi-Square test for the lack of continuity in the binomial distribution. However, the correction was in common use when he proposed it in 1922.

Although this test is often expressed directly as a chi-square statistic, it is expressed here as a z statistic so that it can be used for one-sided hypothesis testing.

Both *pooled* and *unpooled* versions of this test have been discussed in the statistical literature. The pooling refers to the way in which the standard error is estimated. In the pooled version, the two proportions are averaged, and only one proportion is used to estimate the standard error. In the unpooled version, the two proportions are used separately.

The continuity corrected z-test is

$$z = \frac{\hat{p}_1 - \hat{p}_2 + \frac{F}{2} \left(\frac{1}{N_1} + \frac{1}{N_2} \right)}{\hat{\sigma}_D}$$

where F is -1 for lower-tailed, 1 for upper-tailed, and both -1 and 1 for two-sided hypotheses.

Pooled Version

$$\hat{\sigma}_D = \sqrt{\hat{p}(1 - \hat{p}) \left(\frac{1}{N_1} + \frac{1}{N_2} \right)}$$

$$\hat{p} = \frac{N_1 \hat{p}_1 + N_2 \hat{p}_2}{N_1 + N_2}$$

Unpooled Version

$$\hat{\sigma}_D = \sqrt{\frac{\hat{p}_1(1 - \hat{p}_1)}{N_1} + \frac{\hat{p}_2(1 - \hat{p}_2)}{N_2}}$$

Power

The power of this test is computed using approximate results based on the normal approximation to the binomial.

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

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

Assurance for Tests for Two Proportions

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

Assurance for Tests for Two Proportions

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

The probability density function of the logT distribution is

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

The mean of X is not defined.

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

Assurance for Tests for Two Proportions

Normal (Mean, SD)

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

The probability density function of the normal distribution is

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

The mean of X is

$$\mu_X = \mu$$

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

T (Mean, SD, DF)

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

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

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

The mean of X is μ if $\nu > 1$.

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

Assurance for Tests for Two Proportions

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 positive response rate. A sample size analysis assuming that a two-sample, pooled z-test would be used to analyze the experimental data found that 524 subjects per group were needed to achieve 90% power at a 0.05 level of significance. The difference under the alternative hypothesis was set to 0.1. The baseline cure rate during the first year was 0.44. (See Example 2 of the *Tests for Two Proportions* procedure).

To complete their sample size study, the researchers want to run an assurance analysis for a range of group sample sizes from 100 to 2000. An elicitation exercise determined that the prior distribution of the P1 should be normal with mean 0.54 and standard deviation 0.1. The elicitation also concluded that prior distribution of P2 should be normal with mean 0.44 and standard deviation 0.1. To avoid proportion values that are not between zero and one, the range of both priors is set as 0.0001 to 0.9999.

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 ($H_1: P_1 \neq P_2$)
Test Type	Z-Test (Pooled)
Alpha	0.05
Group Allocation	Equal ($N_1 = N_2$)
Sample Size Per Group	100 500 1000 1500 2000
Prior Distribution of P1	Normal (Mean, SD)
Mean	0.54
SD	0.1
Truncation Boundaries	Left and Right
Left Boundary	0.0001
Right Boundary	0.9999
Prior Distribution of P2	Normal (Mean, SD)
Mean	0.44
SD	0.1
Truncation Boundaries	Left and Right
Left Boundary	0.0001
Right Boundary	0.9999

Options Tab

Number of Computation Points for each	50
Prior Distribution	
Maximum N1 in Sample Size Search	5000

Assurance for Tests for Two Proportions

Output

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

Numeric Reports

Numeric Results

Solve For: [Assurance](#)
 Hypotheses: $H_0: P_1 = P_2$ vs. $H_1: P_1 \neq P_2$
 Test Statistic: Z-Test with Pooled Variance
 Prior Type: Independent Univariate Distributions

Prior Distributions

P1: Normal (Mean = 0.54, SD = 0.1), Left Boundary = 0.0001, Right Boundary = 0.9999.

P2: Normal (Mean = 0.44, SD = 0.1), Left Boundary = 0.0001, Right Boundary = 0.9999.

Assurance*	Power‡	Sample Size			Expected Group 1 Proportion E(P1)	Expected Group 2 Proportion E(P2)	Alpha
		N1	N2	N			
0.47312	0.29212	100	100	200	0.54	0.44	0.05
0.73735	0.88667	500	500	1000	0.54	0.44	0.05
0.81159	0.99423	1000	1000	2000	0.54	0.44	0.05
0.84542	0.99980	1500	1500	3000	0.54	0.44	0.05
0.86581	0.99999	2000	2000	4000	0.54	0.44	0.05

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

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

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.
 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 (P1) is different from the Group 2 (control) proportion (P2) ($H_0: P_1 = P_2$ versus $H_1: P_1 \neq P_2$). The comparison will be made using a two-sided, two-sample Z-test with pooled variance, with a Type I error rate (α) of 0.05. The prior distribution used for the Group 1 proportion is Normal (Mean = 0.54, SD = 0.1), Left Boundary = 0.0001, Right Boundary = 0.9999. The prior distribution used for the Group 2 proportion is Normal (Mean = 0.44, SD = 0.1), Left Boundary = 0.0001, Right Boundary = 0.9999. With sample sizes of 100 for Group 1 (treatment) and 100 for Group 2 (control), the assurance (average power) is 0.47312.

Assurance for Tests for 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%	500	500	1000	625	625	1250	125	125	250
20%	1000	1000	2000	1250	1250	2500	250	250	500
20%	1500	1500	3000	1875	1875	3750	375	375	750
20%	2000	2000	4000	2500	2500	5000	500	500	1000

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

Dropout Summary Statements

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

References

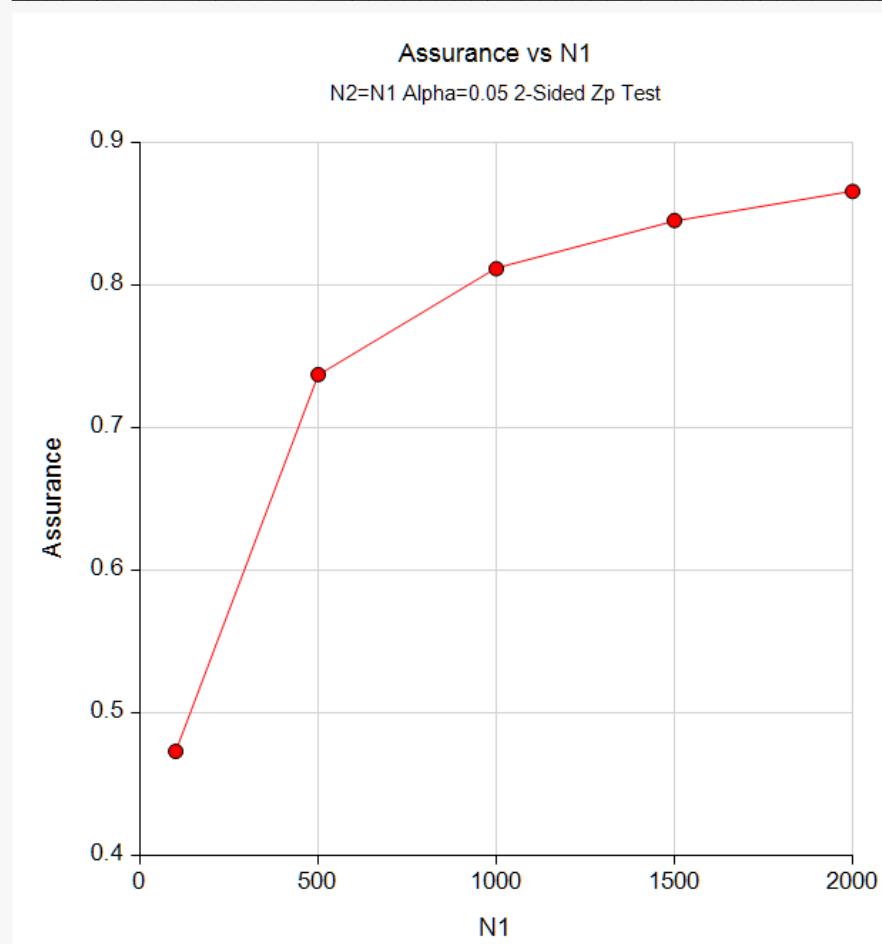
- O'Hagan, A., Stevens, J.W., and Campbell, M.J. 2005. 'Assurance in clinical trial design'. Pharmaceutical Statistics, Volume 4, Pages 187-201.
- Ciarleglio, M.M., Arendt, C.D., and Peduzzi, P.N. 2016. 'Selection of the effect size for sample size determination for a continuous response in a superiority clinical trial using a hybrid classical and Bayesian procedure'. Clinical Trials, Volume 13(3), pages 275-285.
- Dias, L.C., Morton, A., and Quigley, J. 2018. Elicitation, The Science and Art of Structuring Judgement. Springer.
- Chow, S.C., Shao, J., Wang, H., and Lohknygina, Y. 2018. Sample Size Calculations in Clinical Research, Third Edition. Taylor & Francis/CRC. Boca Raton, Florida.
- D'Agostino, R.B., Chase, W., and Belanger, A. 1988. 'The Appropriateness of Some Common Procedures for Testing the Equality of Two Independent Binomial Populations', The American Statistician, August 1988, Volume 42 Number 3, pages 198-202.
- Fleiss, J. L., Levin, B., and Paik, M.C. 2003. Statistical Methods for Rates and Proportions. Third Edition. John Wiley & Sons. New York.
- Lachin, John M. 2000. Biostatistical Methods. John Wiley & Sons. New York.
- Machin, D., Campbell, M., Fayers, P., and Pinol, A. 1997. Sample Size Tables for Clinical Studies, 2nd Edition. Blackwell Science. Malden, Mass.
- Ryan, Thomas P. 2013. Sample Size Determination and Power. John Wiley & Sons. Hoboken, New Jersey.

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

Assurance for Tests for Two Proportions

Plots Section

Plots

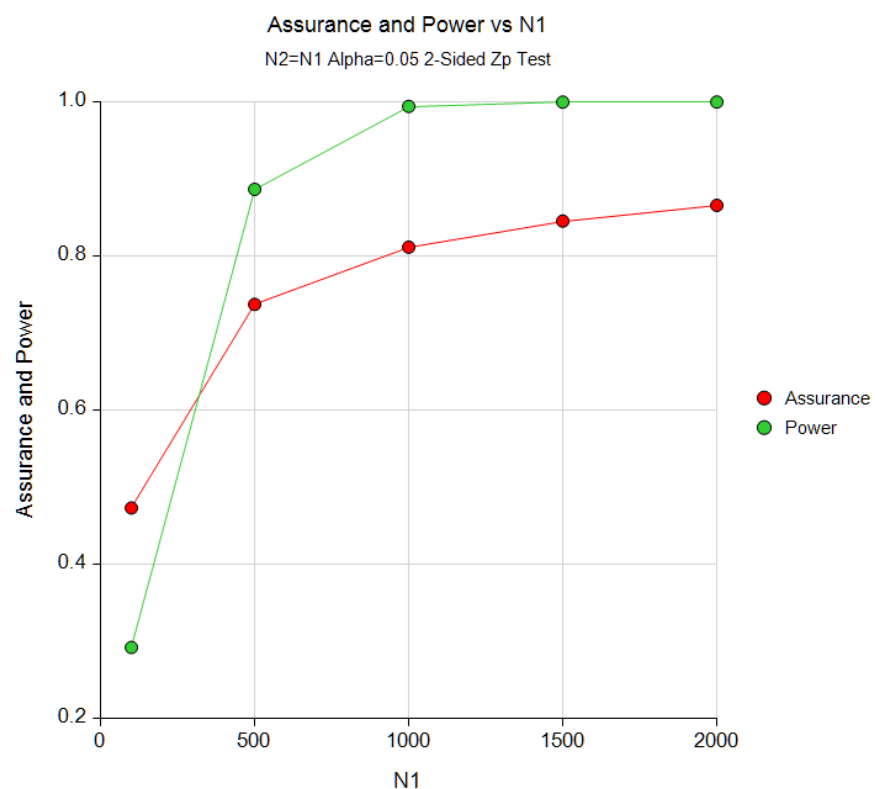


This plot shows the relationship between the assurance and sample size. Note the diminishing impact on assurance of each increase in the number of subjects.

Assurance for Tests for Two Proportions

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, so we have developed a validation example of our own.

Suppose a two-sided, two-sample pooled z-test is used in which $N_1 = N_2 = 500$ and the significance level is 0.05.

The prior distribution of P_1 is approximated by the following table.

P1	Prob
0.48	0.3
0.54	0.4
0.60	0.3

The prior distribution of P_2 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 *Tests for Two Proportions* procedure is used to compute the power for each of the nine combinations of P_1 and P_2 . The results of these calculations are shown next.

Numeric Results

Solve For: [Power](#)
 Groups: 1 = Treatment, 2 = Control
 Test Type: Z-Test with Pooled Variance
 Hypotheses: $H_0: P_1 - P_2 = 0$ vs. $H_1: P_1 - P_2 \neq 0$

Power*	Sample Size			Proportions		Difference δ_1	Alpha
	N1	N2	N	P1	P2		
0.60559	500	500	1000	0.48	0.41	0.07	0.05
0.24523	500	500	1000	0.48	0.44	0.04	0.05
0.06155	500	500	1000	0.48	0.47	0.01	0.05
0.98517	500	500	1000	0.54	0.41	0.13	0.05
0.88667	500	500	1000	0.54	0.44	0.10	0.05
0.60041	500	500	1000	0.54	0.47	0.07	0.05
0.99998	500	500	1000	0.60	0.41	0.19	0.05
0.99917	500	500	1000	0.60	0.44	0.16	0.05
0.98536	500	500	1000	0.60	0.47	0.13	0.05

* Power was computed using the normal approximation method.

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

$$Assurance = (0.60559 \times 0.3 \times 0.2) + (0.24523 \times 0.3 \times 0.6) + \cdots + (0.98536 \times 0.3 \times 0.2) = 0.72279.$$

Assurance for Tests for 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)
Alternative Hypothesis	Two-Sided ($H_1: P_1 \neq P_2$)
Test Type	Z-Test (Pooled)
Alpha	0.05
Group Allocation	Equal ($N_1 = N_2$)
Sample Size Per Group	500
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	50
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

Assurance for Tests for Two Proportions

Output

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

Numeric Results

Solve For: [Assurance](#)
Hypotheses: $H_0: P_1 = P_2$ vs. $H_1: P_1 \neq P_2$
Test Statistic: Z-Test with Pooled Variance
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)	Alpha
		N1	N2	N			
0.72279	0.88667	500	500	1000	0.54	0.44	0.05

‡ 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 0.72279 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)
Alternative Hypothesis	Two-Sided ($H_1: P_1 \neq P_2$)
Test Type	Z-Test (Pooled)
Assurance	0.4 0.5 0.6 0.7 0.8
Alpha	0.05
Group Allocation	Equal ($N_1 = N_2$)
Prior Distribution of P1	Normal (Mean, SD)
Mean	0.54
SD	0.1
Truncation Boundaries	Left and Right
Left Boundary	0.0001
Right Boundary	0.9999
Prior Distribution of P2	Normal (Mean, SD)
Mean	0.44
SD	0.1
Truncation Boundaries	Left and Right
Left Boundary	0.0001
Right Boundary	0.9999

Options Tab

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

Assurance for Tests for Two Proportions

Output

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

Numeric Reports

Numeric Results

Solve For: [Sample Size](#)
Hypotheses: $H_0: P_1 = P_2$ vs. $H_1: P_1 \neq P_2$
Test Statistic: Z-Test with Pooled Variance
Prior Type: Independent Univariate Distributions

Prior Distributions

P1: Normal (Mean = 0.54, SD = 0.1), Left Boundary = 0.0001, Right Boundary = 0.9999.

P2: Normal (Mean = 0.44, SD = 0.1), Left Boundary = 0.0001, Right Boundary = 0.9999.

Assurance*			Sample Size			Expected Group 1 Proportion E(P1)	Expected Group 2 Proportion E(P2)	Alpha
Actual	Target	Power‡	N1	N2	N			
0.40010	0.4	0.21588	69	69	138	0.54	0.44	0.05
0.50078	0.5	0.32828	115	115	230	0.54	0.44	0.05
0.60050	0.6	0.51223	198	198	396	0.54	0.44	0.05
0.70023	0.7	0.78430	376	376	752	0.54	0.44	0.05
0.80006	0.8	0.98792	883	883	1766	0.54	0.44	0.05

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

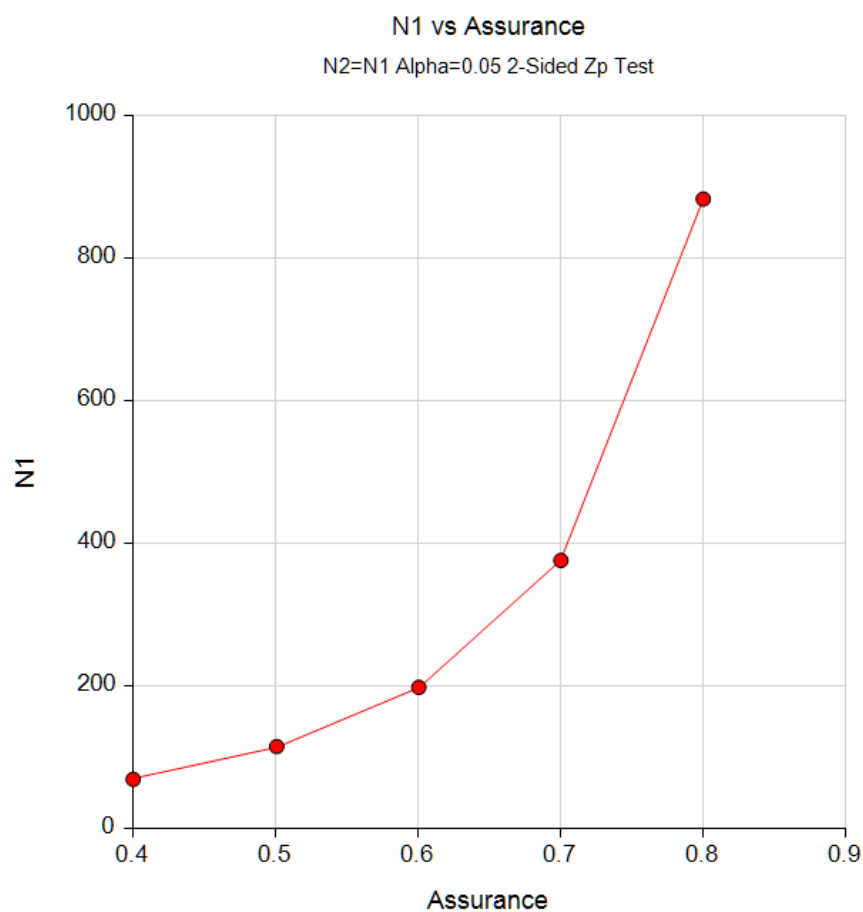
‡ Power was calculated using $P_1 = E(P_1) = 0.54$ and $P_2 = E(P_2) = 0.44$.

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

Assurance for Tests for Two Proportions

Plots Section

Plots



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

Example 4 – Joint Prior Distribution

The following example shows the complexity required to specify a joint distribution for two parameters.

Suppose a two-sided, unpooled-variance z-test will be used in which $N1 = N2 = 2000$ and the significance level is 0.05.

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.

P1	P2	Prob
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 three columns.

C1	C2	C3
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

Assurance for Tests for Two Proportions

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)**
 Alternative Hypothesis **Two-Sided ($H_1: P_1 \neq P_2$)**
 Test Type **Z-Test (Unpooled)**
 Alpha **0.05**
 Group Allocation **Equal ($N_1 = N_2$)**
 Sample Size Per Group **2000**
 Column of P1 Values **C1**
 Column of P2 Values **C2**
 Column of Pr(Values) **C3**

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
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

Assurance for Tests for Two Proportions

Output

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

Numeric Results

Solve For: [Assurance](#)
 Hypotheses: $H_0: P_1 = P_2$ vs. $H_1: P_1 \neq P_2$
 Test Statistic: Z-Test with Unpooled Variance
 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)	Alpha
		N1	N2	N			
0.58736	0.85314	2000	2000	4000	0.41133	0.365	0.05

‡ 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 0.58736.

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 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)**
 Alternative Hypothesis **Two-Sided ($H_1: P_1 \neq P_2$)**
 Test Type **Z-Test (Pooled)**
 Alpha **0.05**
 Group Allocation **Equal ($N_1 = N_2$)**
 Sample Size Per Group **500**
 Column of P1 Values **C1**
 Column of P2 Values **C2**
 Column of Pr(Values) **C5**

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
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: $H_0: P_1 = P_2$ vs. $H_1: P_1 \neq P_2$
 Test Statistic: Z-Test with Pooled Variance
 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)	Alpha
		N1	N2	N			
0.72279	0.88667	500	500	1000	0.54	0.44	0.05

‡ 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 0.72279 which matches Example 2 and thus validates the procedure.