Chapter 739

Assurance for Equivalence Tests for the Ratio of Two Negative Binomial Rates

Introduction

This procedure calculates the assurance of equivalence tests of the ratio of two independent negative binomial event rates. A negative binomial regression model gives the probability distribution of the number of events occurring in a specified interval of time or space. The negative binomial distribution is often used to fit count data when over dispersion disqualifies the Poisson model.

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).

Technical Details

Definition of Terms

The following table presents the various terms that are used.

Group	**1 (Control)**	**2 (Treatment)**
Sample size	N_1	N_2
Individual event rates	λ_1	λ_2

Dispersion parameter: κ

Average exposure time: μ_t

Equivalence ratios: RR_L (where $RR_L < 1$); RR_U (where $RR_U > 1$)

Sample size ratio: $\theta = N_2/N_1$

Hypotheses

The equivalence test hypotheses are

$$H_0: \frac{\lambda_2}{\lambda_1} \leq RR_L \text{ or } \frac{\lambda_2}{\lambda_1} \geq RR_U \quad \text{vs.} \quad H_1: RR_L < \frac{\lambda_2}{\lambda_1} < RR_U$$

where $RR_L < 1$ and $RR_U > 1$.

For a given equivalence test with significance level α, a two-sided confidence interval with 100(1 – 2α)% confidence is typically used. H_0 is rejected if the confidence interval falls completely between R_L and R_U.

Sample Size and Power Calculations

Sample Size Calculation

Zhu (2017) bases the power calculation on an equivalence test derived from a Poisson regression model. The power calculation is

$$Power = \Phi\left(\frac{\sqrt{N_1}\left(\log(\lambda_2/\lambda_1) - \log(RR_L)\right) - z_\alpha\sqrt{V_0^-}}{\sqrt{V_1}}\right) + \Phi\left(\frac{\sqrt{N_1}\left(\log(RR_U) - \log(\lambda_2/\lambda_1)\right) - z_\alpha\sqrt{V_0^+}}{\sqrt{V_1}}\right) - 1$$

where

$$V_1 = \frac{1}{\mu_t}\left(\frac{1}{\lambda_1} + \frac{1}{\theta\lambda_2}\right) + \frac{(1+\theta)\kappa}{\theta}$$

and V_0^- and V_0^+ may be calculated in either of two ways.

V_0 Calculation Method 1 (using assumed true rates)

$$V_{01}^- = V_{01}^+ = \frac{1}{\mu_t}\left(\frac{1}{\lambda_1} + \frac{1}{\theta\lambda_2}\right) + \frac{(1+\theta)\kappa}{\theta}$$

Using Method 1, V_0^-, V_0^+, and V_1 are equal.

V_0 Calculation Method 2 (fixed marginal total)

$$V_{02}^- = \frac{\left(1 + (RR_L)\theta\right)^2}{\mu_t (RR_L)\theta(\lambda_1 + \theta\lambda_2)} + \frac{(1+\theta)\kappa}{\theta}$$

$$V_{02}^+ = \frac{\left(1 + (RR_U)\theta\right)^2}{\mu_t (RR_U)\theta(\lambda_1 + \theta\lambda_2)} + \frac{(1+\theta)\kappa}{\theta}$$

V_0 Calculation Method 3 (restricted maximum likelihood estimation)

$$V_{03}^- = \frac{2a}{\mu_t\left(-b - \sqrt{b^2 - 4ac}\right)}\left(1 + \frac{1}{\theta(RR_L)}\right) + \frac{(1+\theta)\kappa}{\theta}$$

where

$$a = -\kappa\mu_t(RR_L)(1+\theta),$$

$$b = \kappa\mu_t\left((RR_L) + \theta\lambda_2\right) - \left(1 + \theta(RR_L)\right),$$

$$c = \lambda_1 + \theta\lambda_2$$

V_{03}^+ is calculated in the same way, replacing RR_L with RR_U.

Zhu (2017) did not give a recommendation regarding whether Method 1, 2, or 3 should be used, except to say that "in summary, based on scenarios simulated, all of the sample size methods derived in this paper calculated reasonably accurate sample sizes for the intended power. Although some methods seemed slightly better than the others for some scenarios, the sample size differences were very small relative to the actual sample sizes."

Assurance Calculation

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

Let $P'(H|\lambda_1, \lambda_2, \mu_t, \kappa)$ be the power function described above where *H* is the event that null hypothesis is rejected conditional on the parameter values. The specification of $\lambda_1, \lambda_2, \mu_t,$ and κ 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 $\lambda_1, \lambda_2, \mu_t,$ and κ. Hence, the definition of assurance is

$$Assurance = E_{\lambda_1,\lambda_2,\mu_t,\kappa}\big(P'(H|\lambda_1, \lambda_2, \mu_t, \kappa)\big) = \int\int\int\int P'(H|\lambda_1, \lambda_2, \mu_t, \kappa) f(\lambda_1, \lambda_2, \mu_t, \kappa) d\lambda_1\, d\lambda_2\, d\mu_t\, d\kappa$$

where $f(\lambda_1, \lambda_2, \mu_t, \kappa)$ is the joint prior distribution using the four parameters.

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 $f(\lambda_1, \lambda_2, \mu_t, \kappa)$. This provides flexibility in specifying the joint prior distribution. In the four-parameter case, five columns are entered on the spreadsheet: four for the parameters and a fifth 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

$$f(\lambda_1, \lambda_2, \mu_t, \kappa) = f_1(\lambda_1) f_2(\lambda_2) f_3(\mu_t) f_4(\kappa)$$

where $f_1(\lambda_1)$ is the prior distribution of λ_1, $f_2(\lambda_2)$ is the prior distribution of λ_2, and so on. This method is also available in **PASS**. In this case, the definition of assurance becomes

$$Assurance = E_{\lambda_1,\lambda_2,\mu_t,\kappa}\left(P'\left(H\middle|\lambda_1, \lambda_2, \mu_t, \kappa\right)\right) = \int\int\int\int P'\left(H\middle|\lambda_1, \lambda_2, \mu_t, \kappa\right) f_1(\lambda_1) f_2(\lambda_2) f_3(\mu_t) f_4(\kappa) d\lambda_1\, d\lambda_2\, d\mu_t\, d\kappa$$

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* ~ gamma, then *X* = 1 / *Y* ~ 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

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

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

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

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

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

The probability density function of the logT distribution is

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

The mean of *X* is not defined.

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

Normal (Mean, SD)

A random variable *X* that follows the normal distribution is defined on the interval $(-\infty, \infty)$. A location parameter, 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.

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

$$f(x|a,b,c) = \begin{cases} \frac{2(x-a)}{(b-a)(c-a)} & \text{for } a \le x < c \\ \frac{2}{b-a} & \text{for } x = c \\ \frac{2(b-x)}{(b-a)(b-c)} & \text{for } c < x \le b \end{cases}$$

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

$$f(x|a,b) = \begin{cases} \frac{1}{b-a} & \text{for } a \le x \le b \end{cases}$$

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 $1 - \text{Prob}(Min \le X \le Max)$ 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 their event rates are equivalent. They will analyze the data using a negative binomial regression model. The equivalence test will use a confidence interval of the regression coefficient associated with a variable that identifies the treatment group. The significance level of the test is 0.05. The equivalence limits are set at 0.8 and 1.25.

To complete their sample size study, the researchers want to run an assurance analysis for a range of group sample sizes from 500 to 2000. An elicitation exercise determined that $\lambda_1 \sim N(1.4, 0.05^2)$, $\lambda_2 \sim N(1.4, 0.15^2)$, $\mu_t \sim N(1.0, 0.03^2)$, and $\kappa \sim N(1.8, 0.04^2)$.

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 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)**
Variance Calculation Method	**Using Assumed True Rates**
Alpha	**0.05**
Prior Distribution of μ(t)	**Normal (Mean, SD)**
Mean	**1**
SD	**0.03**
Truncation Boundaries	**None**
Group Allocation	**Equal (N1 = N2)**
Sample Size Per Group	**500 1000 1500 2000**
RRU (Upper Equivalence Limit)	**1.25**
RRL (Lower Equivalence Limit)	**0.80**
Prior Distribution of λ1	**Normal (Mean, SD)**
Mean	**1.4**
SD	**0.05**
Truncation Boundaries	**None**
Prior Distribution of λ2	**Normal (Mean, SD)**
Mean	**1.4**
SD	**0.15**
Truncation Boundaries	**None**
Prior Distribution of κ	**Normal (Mean, SD)**
Mean	**1.8**
SD	**0.04**
Truncation Boundaries	**None**

Options Tab

Number of Computation Points for each Prior Distribution	**10**
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: H0: λ2 / λ1 ≤ RRL or λ2 / λ1 ≥ RRU vs. H1: RRL < λ2 / λ1 < RRU
Variance Calculation Method: Using Assumed True Rates
Prior Type: Independent Univariate Distributions

Prior Distributions
μ(t): Normal (Mean = 1, SD = 0.03).
λ1: Normal (Mean = 1.4, SD = 0.05).
λ2: Normal (Mean = 1.4, SD = 0.15).
κ: Normal (Mean = 1.8, SD = 0.04).

					Average Exposure	Event Rate		Event Rate Ratio				
Assurance*	Power‡	N1	N2	N	Time E(μ(t))	Group 1 E(λ1)	Group 2 E(λ2)	Actual RR	Lower RRL	Upper RRU	Dispersion E(κ)	Alpha
0.29953	0.43824	500	500	1000	1	1.4	1.4	1	0.8	1.25	1.8	0.05
0.57498	0.86688	1000	1000	2000	1	1.4	1.4	1	0.8	1.25	1.8	0.05
0.68579	0.97283	1500	1500	3000	1	1.4	1.4	1	0.8	1.25	1.8	0.05
0.74423	0.99497	2000	2000	4000	1	1.4	1.4	1	0.8	1.25	1.8	0.05

* The number of points used for computation of the prior(s) was 10.
‡ Power was calculated using λ1 = E(λ1) = 1.4, λ2 = E(λ2) = 1.4, μ(t) = E(μ(t)) = 1, and κ = E(κ) = 1.8.

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 = N1 + N2.
E(μ(t)) The expected value over its prior distribution of the average exposure time across subjects in both groups.
E(λ1) The expected value over its prior distribution of the group 1 mean event rate.
E(λ2) The expected value over its prior distribution of the group 2 mean event rate.
RR The ratio of the average event rates (λ2 / λ1).
RR0 The superiority margin ratio is the smallest (or largest) the ratio can be and still be called superior.
E(κ) The expected value over its prior distribution of the dispersion parameter.
Alpha The probability of rejecting a true null hypothesis.

Summary Statements

Group sample sizes of 500 in group 1 and 500 in group 2 achieve 0.29953 assurance using an equivalence test of the ratio of two negative binomial event rates. The lower equivalence limit of the event rate ratio is 0.8. The upper equivalence limit of the event rate ratio is 1.25. This test is based on a negative binomial regression model. The average group 2 (treatment) event rate is 1.4 and the average group 1 (control) event rate is 1.4. The variance of the negative binomial regression coefficient being tested is calculated using the assumed true rates method. The significance level (alpha) of the test is 0.05. The prior distribution used for the group 1 event rate is Normal (Mean = 1.4, SD = 0.05). The prior distribution used for the group 2 event rate is Normal (Mean = 1.4, SD = 0.15). The prior distribution used for the average exposure time is Normal (Mean = 1, SD = 0.03). The prior distribution used for the dispersion factor is Normal (Mean = 1.8, SD = 0.04).

Dropout-Inflated Sample Size

	Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
Dropout Rate	**N1**	**N2**	**N**	**N1'**	**N2'**	**N'**	**D1**	**D2**	**D**
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 Lokhnygina, Y. (2018) pages 32-33.)
D1, D2, and D The expected number of dropouts. D1 = N1' - N1, D2 = N2' - N2, and D = D1 + D2.

Dropout Summary Statements

Anticipating a 20% dropout rate, 625 subjects should be enrolled in Group 1, and 625 in Group 2, to obtain final group sample sizes of 500 and 500, respectively.

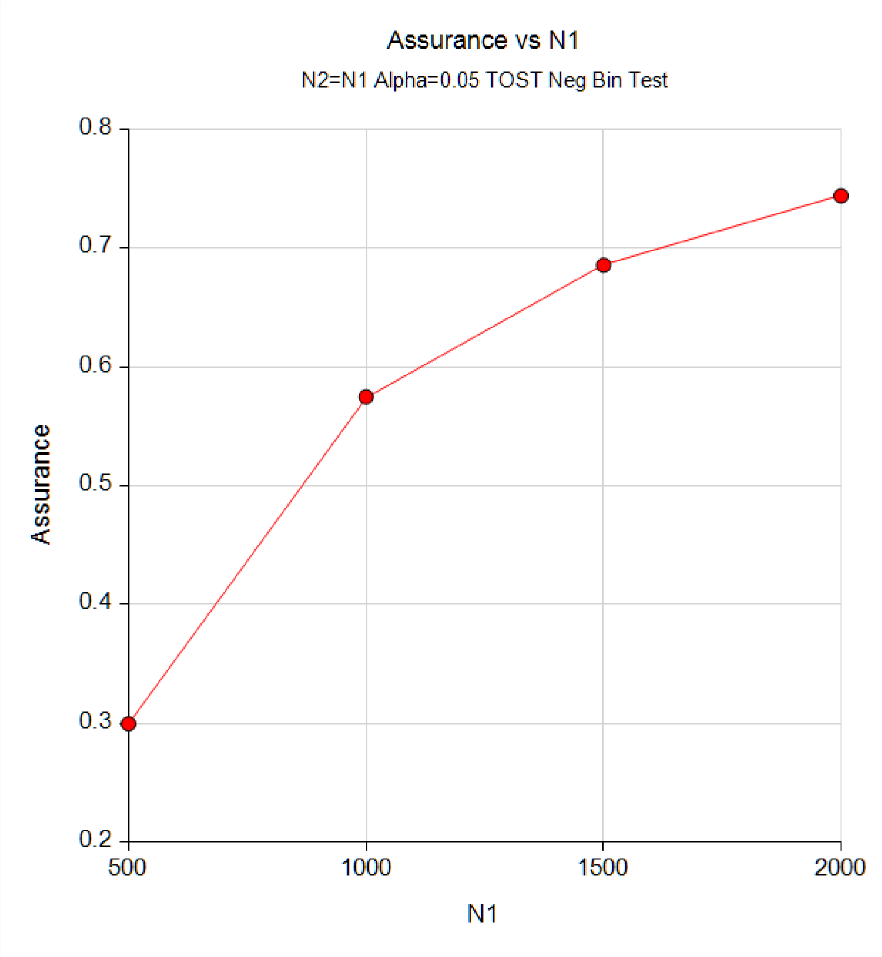
References

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.
Mathews, Paul. 2010. Sample Size Calculations: Practical Methods for Engineers and Scientists. Mathews Malnar and Bailey. Fairport Harbor, OH. www.mmbstatical.com
Zhu, H. 2017. 'Sample Size Calculation for Comparing Two Poisson or Negative Binomial Rates in Non-Inferiority or Equivalence Trials.' Statistics in Biopharmaceutical Research, 9(1), 107-115, doi:10.1080/19466315.2016.1225594.

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

Plots Section

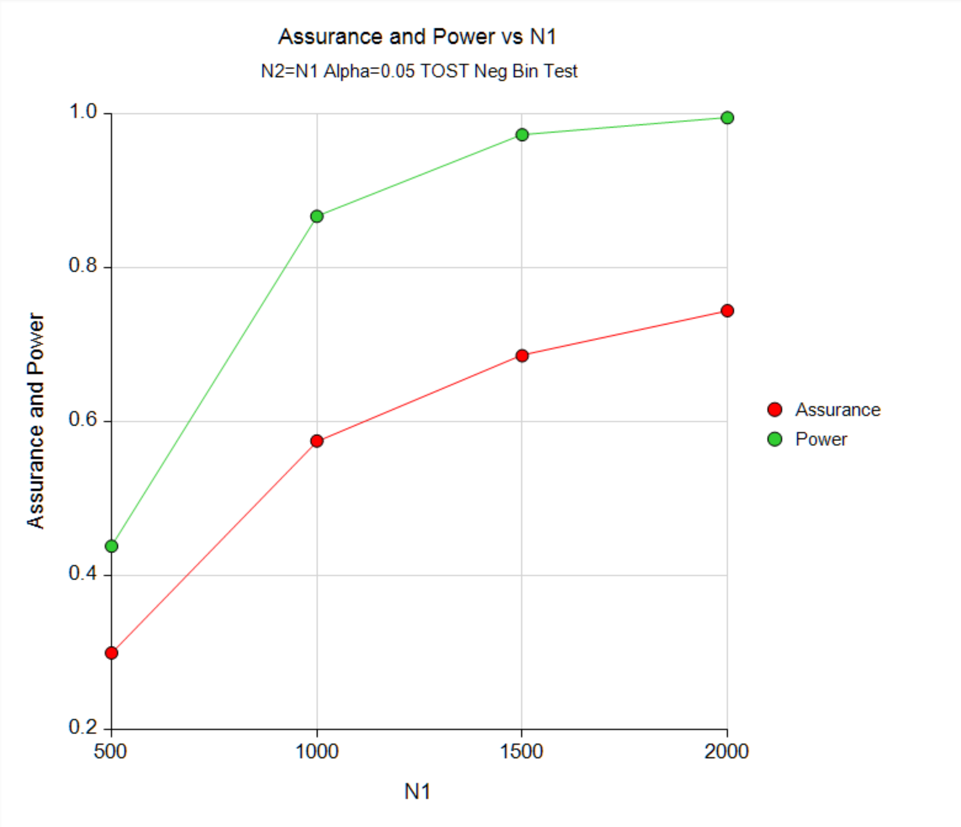
Plots



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

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 does 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 an equivalence test is used in which N1 = N2 = 2000, the significance level is 0.05, RRL = 0.8, and RRU = 1.25.

The prior distribution of λ1 is approximated by the following table.

λ1	Prob
1.2	0.4
1.6	0.6

The prior distribution of λ2 is approximated by the following table.

λ2	Prob
1.3	0.4
1.7	0.6

The prior distribution of μ(t) is approximated by the following table.

μ(t)	Prob
0.95	0.5
1.05	0.5

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

κ	Prob
1.7	0.5
1.9	0.5

The *Equivalence Tests for the Ratio of Two Negative Binomial Rates* procedure is used to compute the power for each of the 16 combinations of the four parameters. The results of these calculations are shown next.

Numeric Results

Solve For: Power
Hypotheses: H0: λ2 / λ1 ≤ RL or λ2 / λ1 ≥ RU vs. H1: RL < λ2 / λ1 < RU
Variance Calculation Method: Using Assumed True Rates

Power	N1	N2	N	Average Exposure Time μ(t)	Grp 1 Cntrl Event Rate λ1	Grp 2 Trt Event Rate λ2	Event Rate Ratio λ2 / λ1	Lower Equiv. Limit RL	Upper Equiv. Limit RU	Dispersion φ	Alpha
0.88348	2000	2000	4000	0.95	1.2	1.3	1.08333	0.8	1.25	1.7	0.05
0.00001	2000	2000	4000	0.95	1.2	1.7	1.41667	0.8	1.25	1.7	0.05
0.09166	2000	2000	4000	0.95	1.6	1.3	0.81250	0.8	1.25	1.7	0.05
0.95689	2000	2000	4000	0.95	1.6	1.7	1.06250	0.8	1.25	1.7	0.05
0.86151	2000	2000	4000	0.95	1.2	1.3	1.08333	0.8	1.25	1.9	0.05
0.00002	2000	2000	4000	0.95	1.2	1.7	1.41667	0.8	1.25	1.9	0.05
0.08968	2000	2000	4000	0.95	1.6	1.3	0.81250	0.8	1.25	1.9	0.05
0.94300	2000	2000	4000	0.95	1.6	1.7	1.06250	0.8	1.25	1.9	0.05
0.89223	2000	2000	4000	1.05	1.2	1.3	1.08333	0.8	1.25	1.7	0.05
0.00001	2000	2000	4000	1.05	1.2	1.7	1.41667	0.8	1.25	1.7	0.05
0.09242	2000	2000	4000	1.05	1.6	1.3	0.81250	0.8	1.25	1.7	0.05
0.96082	2000	2000	4000	1.05	1.6	1.7	1.06250	0.8	1.25	1.7	0.05

0.87035	2000	2000	4000	1.05	1.2	1.3	1.08333	0.8	1.25	1.9	0.05
0.00002	2000	2000	4000	1.05	1.2	1.7	1.41667	0.8	1.25	1.9	0.05
0.09034	2000	2000	4000	1.05	1.6	1.3	0.81250	0.8	1.25	1.9	0.05
0.94737	2000	2000	4000	1.05	1.6	1.7	1.06250	0.8	1.25	1.9	0.05

The assurance calculation is made by summing the quantities $\left[(power_{i,j,k,l})(p(\lambda1_i))\left(p(\lambda2_j)\right)(p(\mu_k))(p(\kappa_l))\right]$ as follows

$$\begin{aligned} Assurance &= (0.88348 \times 0.4 \times 0.4 \times 0.5 \times 0.5) + (0.00001 \times 0.4 \times 0.6 \times 0.5 \times 0.5) + \cdots \\ &\quad + (0.94737 \times 0.6 \times 0.6 \times 0.5 \times 0.5) \\ &= 0.50488. \end{aligned}$$

To run this example, the spreadsheet will need to be loaded with the following eight columns in which the first two are for λ1, the second two are for λ2, and so on.

C1	C2	C3	C4	C5	C6	C7	C8
1.2	**0.4**	**1.3**	**0.4**	**0.95**	**0.5**	**1.7**	**0.5**
1.6	**0.6**	**1.7**	**0.6**	**1.05**	**0.5**	**1.9**	**0.5**

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)**
Variance Calculation Method .... **Using Assumed True Rates**
Alpha.. **0.05**
Prior Distribution of μ(t)................................. **Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C5**
Column of Pr(Values).................................... **C6**
Group Allocation .... **Equal (N1 = N2)**
Sample Size Per Group **2000**
RRU (Upper Equivalence Limit)..................... **1.25**
RRL (Lower Equivalence Limit) **0.80**
Prior Distribution of λ1.................................. **Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C1**
Column of Pr(Values).................................... **C2**
Prior Distribution of λ2.................................. **Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C3**
Column of Pr(Values).................................... **C4**
Prior Distribution of κ.................................... **Custom (Values and Probabilities in Spreadsheet)**
Column of Values **C7**
Column of Pr(Values).................................... **C8**

Options Tab

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

Maximum N1 in Sample Size Search **5000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5	C6	C7	C8
1	1.2	0.4	1.3	0.4	0.95	0.5	1.7	0.5
2	1.6	0.6	1.7	0.6	1.05	0.5	1.9	0.5

Output

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

Numeric Results

Solve For: Assurance
Hypotheses: H0: λ2 / λ1 ≤ RRL or λ2 / λ1 ≥ RRU vs. H1: RRL < λ2 / λ1 < RRU
Variance Calculation Method: Using Assumed True Rates
Prior Type: Independent Univariate Distributions

Prior Distributions

μ(t): Point List (Values = C5, Probs = C6).
C5: 0.95 1.05
C6: 0.5 0.5
λ1: Point List (Values = C1, Probs = C2).
C1: 1.2 1.6
C2: 0.4 0.6
λ2: Point List (Values = C3, Probs = C4).
C3: 1.3 1.7
C4: 0.4 0.6
κ: Point List (Values = C7, Probs = C8).
C7: 1.7 1.9
C8: 0.5 0.5

					Average	Event Rate		Event Rate Ratio				
					Exposure Time	Group 1	Group 2	Actual	Lower	Upper	Dispersion	
Assurance	Power‡	N1	N2	N	E(μ(t))	E(λ1)	E(λ2)	RR	RRL	RRU	E(κ)	Alpha
0.50488	0.93226	2000	2000	4000	1	1.44	1.54	1.06944	0.8	1.25	1.8	0.05

‡ Power was calculated using λ1 = E(λ1) = 1.44, λ2 = E(λ2) = 1.54, μ(t) = E(μ(t)) = 1, and κ = E(κ) = 1.8.

PASS has also calculated the assurance as 0.50488 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.

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)**
Variance Calculation Method .... **Using Assumed True Rates**
Assurance **0.4 0.5 0.6 0.7 0.8**
Alpha... **0.05**
Prior Distribution of μ(t)................................. **Normal (Mean, SD)**
Mean... **1**
SD... **0.03**
Truncation Boundaries.................................. **None**
Group Allocation .... **Equal (N1 = N2)**
RRU (Upper Equivalence Limit)..................... **1.25**
RRL (Lower Equivalence Limit) **0.80**
Prior Distribution of λ1................................... **Normal (Mean, SD)**
Mean... **1.4**
SD... **0.05**
Truncation Boundaries.................................. **None**
Prior Distribution of λ2................................... **Normal (Mean, SD)**
Mean... **1.4**
SD... **0.15**
Truncation Boundaries.................................. **None**
Prior Distribution of κ..................................... **Normal (Mean, SD)**
Mean... **1.8**
SD... **0.04**
Truncation Boundaries.................................. **None**

Options Tab

Number of Computation Points for each Prior Distribution **10**
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: Sample Size
Hypotheses: H0: λ2 / λ1 ≤ RRL or λ2 / λ1 ≥ RRU vs. H1: RRL < λ2 / λ1 < RRU
Variance Calculation Method: Using Assumed True Rates
Prior Type: Independent Univariate Distributions

Prior Distributions
μ(t): Normal (Mean = 1, SD = 0.03).
λ1: Normal (Mean = 1.4, SD = 0.05).
λ2: Normal (Mean = 1.4, SD = 0.15).
κ: Normal (Mean = 1.8, SD = 0.04).

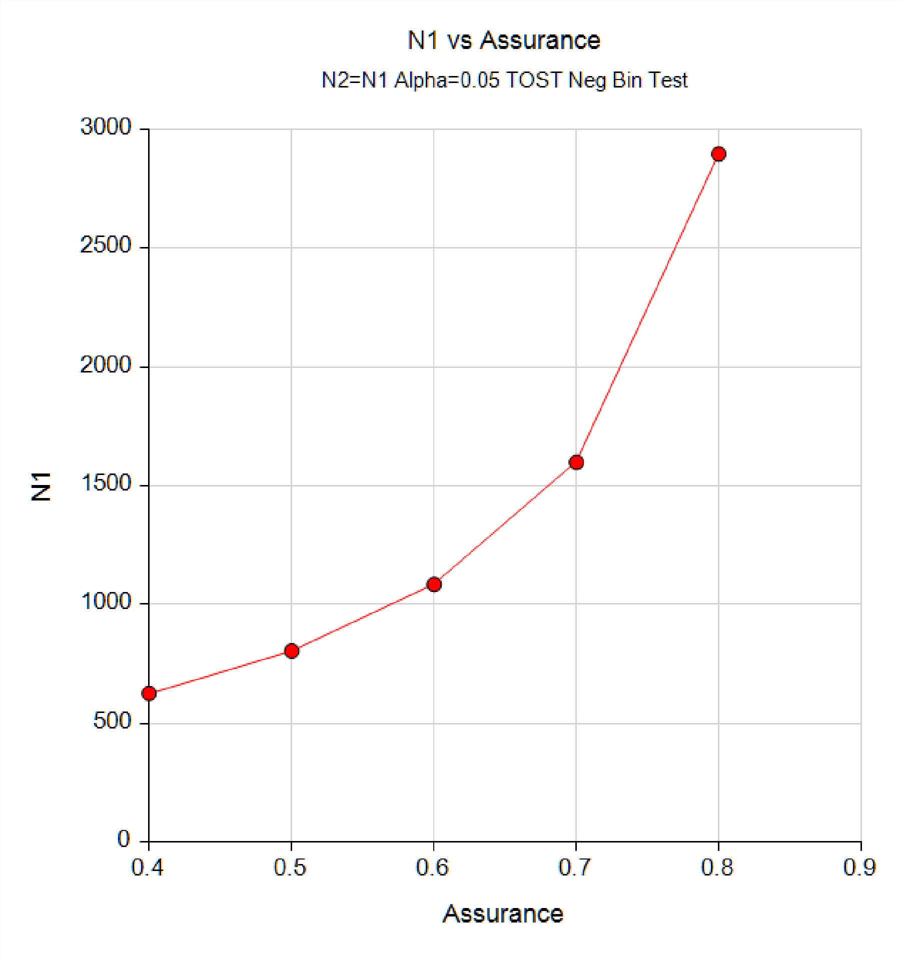
					Average Exposure	Event Rate		Event Rate Ratio				
Assurance	Power‡	N1	N2	N	Time E(μ(t))	Group 1 E(λ1)	Group 2 E(λ2)	Actual RR	Lower RRL	Upper RRU	Dispersion E(κ)	Alpha
0.40010	0.60181	626	626	1252	1	1.4	1.4	1	0.8	1.25	1.8	0.05
0.50028	0.76139	805	805	1610	1	1.4	1.4	1	0.8	1.25	1.8	0.05
0.60022	0.89751	1085	1085	2170	1	1.4	1.4	1	0.8	1.25	1.8	0.05
0.70010	0.98042	1599	1599	3198	1	1.4	1.4	1	0.8	1.25	1.8	0.05
0.80002	0.99979	2897	2897	5794	1	1.4	1.4	1	0.8	1.25	1.8	0.05

* The number of points used for computation of the prior(s) was 10.
‡ Power was calculated using λ1 = E(λ1) = 1.4, λ2 = E(λ2) = 1.4, μ(t) = E(μ(t)) = 1, and κ = E(κ) = 1.8.

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 four parameters.

Suppose an equivalence test will be used in which N1 = N2 = 2000, RRL = 0.8, RRU = 1.25, and the significance level is 0.05.

Further suppose that the joint prior distribution of the λ1 (control), λ2 (treatment), μ(t), and κ 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.

λ1	λ2	μ(t)	κ	Prob
1.2	1.3	0.95	1.7	0.03
1.2	1.7	0.95	1.7	0.06
1.6	1.3	0.95	1.7	0.08
1.6	1.7	0.95	1.7	0.09
1.2	1.3	0.95	1.9	0.13
1.2	1.7	0.95	1.9	0.06
1.6	1.3	0.95	1.9	0.08
1.6	1.7	0.95	1.9	0.09
1.2	1.3	1.05	1.7	0.12
1.2	1.7	1.05	1.7	0.06
1.6	1.3	1.05	1.7	0.08
1.6	1.7	1.05	1.7	0.09
1.2	1.3	1.05	1.9	0.14
1.2	1.7	1.05	1.9	0.06
1.6	1.3	1.05	1.9	0.08
1.6	1.7	1.05	1.9	0.09

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

C1	C2	C3	C4	C5
1.2	1.3	0.95	1.7	0.03
1.2	1.7	0.95	1.7	0.06
1.6	1.3	0.95	1.7	0.08
1.6	1.7	0.95	1.7	0.09
1.2	1.3	0.95	1.9	0.13
1.2	1.7	0.95	1.9	0.06
1.6	1.3	0.95	1.9	0.08
1.6	1.7	0.95	1.9	0.09
1.2	1.3	1.05	1.7	0.12
1.2	1.7	1.05	1.7	0.06
1.6	1.3	1.05	1.7	0.08
1.6	1.7	1.05	1.7	0.09
1.2	1.3	1.05	1.9	0.14
1.2	1.7	1.05	1.9	0.06
1.6	1.3	1.05	1.9	0.08
1.6	1.7	1.05	1.9	0.09

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)**
Variance Calculation Method.........................**Using Assumed True Rates**
Alpha...**0.05**
Column of μ(t) Values...................................**C3**
Group Allocation ....**Equal (N1 = N2)**
Sample Size Per Group.................................**2000**
RRU (Upper Equivalence Limit).....................**1.25**
RRL (Lower Equivalence Limit) **0.80**
Column of λ1 Values.....................................**C1**
Column of λ2 Values.....................................**C2**
Column of κ Values.......................................**C4**
Column of Pr(Values)....................................**C5**

Options Tab

Number of Computation Points for each Prior Distribution........**10**
Maximum N1 in Sample Size Search **5000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5
1	1.2	1.3	0.95	1.7	0.03
2	1.2	1.7	0.95	1.7	0.06
3	1.6	1.3	0.95	1.7	0.08
4	1.6	1.7	0.95	1.7	0.09
5	1.2	1.3	0.95	1.9	0.13
6	1.2	1.7	0.95	1.9	0.06
7	1.6	1.3	0.95	1.9	0.08
8	1.6	1.7	0.95	1.9	0.09
9	1.2	1.3	1.05	1.7	0.12
10	1.2	1.7	1.05	1.7	0.06
11	1.6	1.3	1.05	1.7	0.08
12	1.6	1.7	1.05	1.7	0.09
13	1.2	1.3	1.05	1.9	0.14
14	1.2	1.7	1.05	1.9	0.06
15	1.6	1.3	1.05	1.9	0.08
16	1.6	1.7	1.05	1.9	0.09

Output

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

Numeric Results

Solve For:	Assurance
Hypotheses:	H0: λ2 / λ1 ≤ RRL or λ2 / λ1 ≥ RRU vs. H1: RRL < λ2 / λ1 < RRU
Variance Calculation Method:	Using Assumed True Rates
Prior Type:	Joint Multivariate Distribution

Prior Distribution
Point Lists

λ1:	C1:	1.2 1.2 1.6 1.6 1.2 1.2 1.6 1.6 1.2 1.2 1.6 1.6 1.2 1.2 1.6 1.6
λ2:	C2:	1.3 1.7 1.3 1.7 1.3 1.7 1.3 1.7 1.3 1.7 1.3 1.7 1.3 1.7 1.3 1.7
μ(t):	C3:	0.95 0.95 0.95 0.95 0.95 0.95 0.95 0.95 1.05 1.05 1.05 1.05 1.05 1.05 1.05 1.05
κ:	C4:	1.7 1.7 1.7 1.7 1.9 1.9 1.9 1.9 1.7 1.7 1.7 1.7 1.9 1.9 1.9 1.9
Prob:	C5:	0.03 0.06 0.08 0.09 0.13 0.06 0.08 0.09 0.12 0.06 0.08 0.09 0.14 0.06 0.08 0.09

					Average Exposure	Event Rate		Event Rate Ratio				
Assurance	Power‡	N1	N2	N	Time E(μ(t))	Group 1 E(λ1)	Group 2 E(λ2)	Actual RR	Lower RRL	Upper RRU	Dispersion E(κ)	Alpha
0.5517	0.96081	2000	2000	4000	1.00373	1.40299	1.4791	1.05426	0.8	1.25	1.80896	0.05

‡ Power was calculated using λ1 = E(λ1) = 1.40299, λ2 = E(λ2) = 1.4791, μ(t) = E(μ(t)) = 1.00373, and κ = E(κ) = 1.80896.

PASS has calculated the assurance as 0.5517.

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.

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

λ1	λ2	μ(t)	κ	Prob
1.2	1.3	0.95	1.7	0.04
1.2	1.7	0.95	1.7	0.06
1.6	1.3	0.95	1.7	0.06
1.6	1.7	0.95	1.7	0.09
1.2	1.3	0.95	1.9	0.04
1.2	1.7	0.95	1.9	0.06
1.6	1.3	0.95	1.9	0.06
1.6	1.7	0.95	1.9	0.09
1.2	1.3	1.05	1.7	0.04
1.2	1.7	1.05	1.7	0.06
1.6	1.3	1.05	1.7	0.06
1.6	1.7	1.05	1.7	0.09
1.2	1.3	1.05	1.9	0.04
1.2	1.7	1.05	1.9	0.06
1.6	1.3	1.05	1.9	0.06
1.6	1.7	1.05	1.9	0.09

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

C1	C2	C3	C4	C5
1.2	1.3	0.95	1.7	0.04
1.2	1.7	0.95	1.7	0.06
1.6	1.3	0.95	1.7	0.06
1.6	1.7	0.95	1.7	0.09
1.2	1.3	0.95	1.9	0.04
1.2	1.7	0.95	1.9	0.06
1.6	1.3	0.95	1.9	0.06
1.6	1.7	0.95	1.9	0.09
1.2	1.3	1.05	1.7	0.04
1.2	1.7	1.05	1.7	0.06
1.6	1.3	1.05	1.7	0.06
1.6	1.7	1.05	1.7	0.09
1.2	1.3	1.05	1.9	0.04
1.2	1.7	1.05	1.9	0.06
1.6	1.3	1.05	1.9	0.06
1.6	1.7	1.05	1.9	0.09

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)**
Variance Calculation Method .... **Using Assumed True Rates**
Alpha.. **0.05**
Column of μ(t) Values **C3**
Group Allocation .... **Equal (N1 = N2)**
Sample Size Per Group **2000**
RRU (Upper Equivalence Limit)..................... **1.25**
RRL (Lower Equivalence Limit) **0.80**
Column of λ1 Values..................................... **C1**
Column of λ2 Values..................................... **C2**
Column of κ Values....................................... **C4**
Column of Pr(Values).................................... **C5**

Options Tab

Number of Computation Points for each Prior Distribution **10**
Maximum N1 in Sample Size Search **5000**

Input Spreadsheet Data

Row	C1	C2	C3	C4	C5
1	1.2	1.3	0.95	1.7	0.04
2	1.2	1.7	0.95	1.7	0.06
3	1.6	1.3	0.95	1.7	0.06
4	1.6	1.7	0.95	1.7	0.09
5	1.2	1.3	0.95	1.9	0.04
6	1.2	1.7	0.95	1.9	0.06
7	1.6	1.3	0.95	1.9	0.06
8	1.6	1.7	0.95	1.9	0.09
9	1.2	1.3	1.05	1.7	0.04
10	1.2	1.7	1.05	1.7	0.06
11	1.6	1.3	1.05	1.7	0.06
12	1.6	1.7	1.05	1.7	0.09
13	1.2	1.3	1.05	1.9	0.04
14	1.2	1.7	1.05	1.9	0.06
15	1.6	1.3	1.05	1.9	0.06
16	1.6	1.7	1.05	1.9	0.09

Output

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

Numeric Results

Solve For: Assurance
Hypotheses: H0: λ2 / λ1 ≤ RRL or λ2 / λ1 ≥ RRU vs. H1: RRL < λ2 / λ1 < RRU
Variance Calculation Method: Using Assumed True Rates
Prior Type: Joint Multivariate Distribution

Prior Distribution
Point Lists
λ1: C1: 1.2 1.2 1.6 1.6 1.2 1.2 1.6 1.6 1.2 1.2 1.6 1.6 1.2 1.2 1.6 1.6
λ2: C2: 1.3 1.7 1.3 1.7 1.3 1.7 1.3 1.7 1.3 1.7 1.3 1.7 1.3 1.7 1.3 1.7
μ(t): C3: 0.95 0.95 0.95 0.95 0.95 0.95 0.95 0.95 1.05 1.05 1.05 1.05 1.05 1.05 1.05 1.05
κ: C4: 1.7 1.7 1.7 1.7 1.9 1.9 1.9 1.9 1.7 1.7 1.7 1.7 1.9 1.9 1.9 1.9
Prob: C5: 0.04 0.06 0.06 0.09 0.04 0.06 0.06 0.09 0.04 0.06 0.06 0.09 0.04 0.06 0.06 0.09

					Average Exposure	Event Rate		Event Rate Ratio				
Assurance	Power‡	N1	N2	N	Time E(μ(t))	Group 1 E(λ1)	Group 2 E(λ2)	Actual RR	Lower RRL	Upper RRU	Dispersion E(κ)	Alpha
0.50488	0.93226	2000	2000	4000	1	1.44	1.54	1.06944	0.8	1.25	1.8	0.05

‡ Power was calculated using λ1 = E(λ1) = 1.44, λ2 = E(λ2) = 1.54, μ(t) = E(μ(t)) = 1, and κ = E(κ) = 1.8.

PASS has also calculated the assurance as 0.50488 which matches Example 2 and thus validates the procedure.