Chapter 139

Equivalence Tests for the Ratio of Two Variances

Introduction

This procedure calculates power and sample size of *equivalence* tests of the ratio of two (total = between + within) variances from a two-group, parallel design.

Technical Details

This procedure uses the formulation given in Chow, Shao, Wang, and Lokhnygina (2018), pages 217 - 220.

Suppose x_{ij} is the response of the *i*th group (*i* = 1, 2) and *j*th subject (*j* = 1, ..., *Ni*). The model analyzed in this procedure is

$$x_{ijk} = \mu_i + e_{ij}$$

where μ_i is the treatment effect and e_{ij} is the between-subject error term which is normally distributed with mean 0 and variance $V_i = \sigma_{Bi}^2$. Unbiased estimators of these variances are given by

$$\hat{V}_i = \frac{1}{N_i - 1} \sum_{j=1}^{N_i} \left(x_{ij} - \bar{x}_i\right)^2$$

$$\bar{x}_i = \frac{1}{N_i} \sum_{j=1}^{N_i} x_{ij}$$

A common test statistic to compare variabilities in the two groups is $T = \hat{V}_1/\hat{V}_2$. Under the usual normality assumptions, *T* is distributed as an *F* distribution with degrees of freedom $N_1 - 1$ and $N_2 - 1$.

Testing Equivalence

The following hypotheses are usually used to test for equivalence

$$H_0: \sigma_1^2/\sigma_2^2 \geq RU \text{ or } \sigma_1^2/\sigma_2^2 \leq RL \quad \text{versus} \quad H_1: RL < \sigma_1^2/\sigma_2^2 < RU,$$

where RL and RU are the equivalence limits.

These hypotheses can be tested using the two one-sided hypotheses

$$H_{01}: \sigma_1^2/\sigma_2^2 \geq RU \quad \text{versus} \quad H_{11}: \sigma_1^2/\sigma_2^2 < RU$$

and

$$H_{02}: \sigma_1^2/\sigma_2^2 \leq RL \quad \text{versus} \quad H_{12}: \sigma_1^2/\sigma_2^2 > RL$$

The corresponding test statistics are $T_1 = RU\ (\hat{V}_1/\hat{V}_2)$ and $T_2 = RL\ (\hat{V}_1/\hat{V}_2)$.

Power

The power of this combination of tests is given by

$$\text{Power} = \text{P}\left(\left(\frac{RL}{R1}\right) F_{1-\alpha, N_1-1, N_2-1)} < F < \left(\frac{RU}{R1}\right) F_{\alpha, N_1-1, N_2-1)}\right)$$

where *F* is the common F distribution with the indicated degrees of freedom, α is the significance level, and *R1* is the value of the variance ratio stated by the alternative hypothesis. Lower quantiles of F are used in the equation.

A simple binary search algorithm can be applied to this power function to obtain an estimate of the necessary sample size.

Example 1 – Finding Sample Size

A company has developed a generic drug for treating rheumatism and wants to show that it is equivalent to the standard drug with respect to the variance. A parallel-group design will be used to test the equivalence of the two drugs.

Company researchers set the upper limit of equivalence to 1.5, the lower limit to 1/1.5, the significance level to 0.05, the power to 0.90, and the actual variance ratio values between 0.8 and 1.3. They want to investigate the range of required sample size values assuming that the two group sample sizes are equal.

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 .... **Sample Size**
Power.. **0.90**
Alpha... **0.05**
Group Allocation .... **Equal (N1 = N2)**
RU (Upper Equivalence Limit) **1.5**
RL (Lower Equivalence Limit)........................ **1/RU**
R1 (Actual Variance Ratio) **0.8 0.9 1 1.1 1.2 1.3**

Output

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

Numeric Reports

Numeric Results

Solve For: Sample Size
Hypotheses: H0: $\sigma^2 1/\sigma^2 2 \leq RL$ or $\sigma^2 1/\sigma^2 2 \geq RU$ vs. H1: $RL < \sigma^2 1/\sigma^2 2 < RU$

Power		Sample Size			Variance Ratio			
					Equivalence Limits			
Target	Actual	N1	N2	N	Lower RL	Upper RU	Actual R1	Alpha
0.9	0.9002	1033	1033	2066	0.667	1.5	0.8	0.05
0.9	0.9001	383	383	766	0.667	1.5	0.9	0.05
0.9	0.9009	266	266	532	0.667	1.5	1.0	0.05
0.9	0.9004	360	360	720	0.667	1.5	1.1	0.05
0.9	0.9001	690	690	1380	0.667	1.5	1.2	0.05
0.9	0.9000	1675	1675	3350	0.667	1.5	1.3	0.05

Target Power The desired power value entered in the procedure. Power is the probability of rejecting a false null hypothesis.
Actual Power The actual power achieved. Because N1 and N2 are discrete, this value is usually slightly larger than the target power.
N1 The number of subjects from group 1.
N2 The number of subjects from group 2.
N The total number of subjects. N = N1 + N2.
RL The lower equivalence limit for the variance ratio.
RU The upper equivalence limit for the variance ratio.
R1 The value of the variance ratio at which the power is calculated.
Alpha The probability of rejecting a true null hypothesis.

Summary Statements

A parallel two-group design will be used to test whether the treatment variance is equivalent to the control variance, by testing whether the variance ratio ($\sigma^2 1 / \sigma^2 2 = \sigma^2 Trt / \sigma^2 Ctrl$) is between 0.667 and 1.5 (H0: $\sigma^2 1 / \sigma^2 2 \leq 0.667$ or $\sigma^2 1 / \sigma^2 2 \geq 1.5$ versus H1: $0.667 < \sigma^2 1 / \sigma^2 2 < 1.5$). The comparison will be made using two one-sided, two-sample, variance-ratio F-tests, with an overall Type I error rate (α) of 0.05. To detect a variance ratio of 0.8 with 90% power, the number of subjects needed will be 1033 in Group 1 (treatment), and 1033 in Group 2 (control).

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%	1033	1033	2066	1292	1292	2584	259	259	518
20%	383	383	766	479	479	958	96	96	192
20%	266	266	532	333	333	666	67	67	134
20%	360	360	720	450	450	900	90	90	180
20%	690	690	1380	863	863	1726	173	173	346
20%	1675	1675	3350	2094	2094	4188	419	419	838

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. 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. After solving for N1 and N2, 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, 1292 subjects should be enrolled in Group 1, and 1292 in Group 2, to obtain final group sample sizes of 1033 and 1033, respectively.

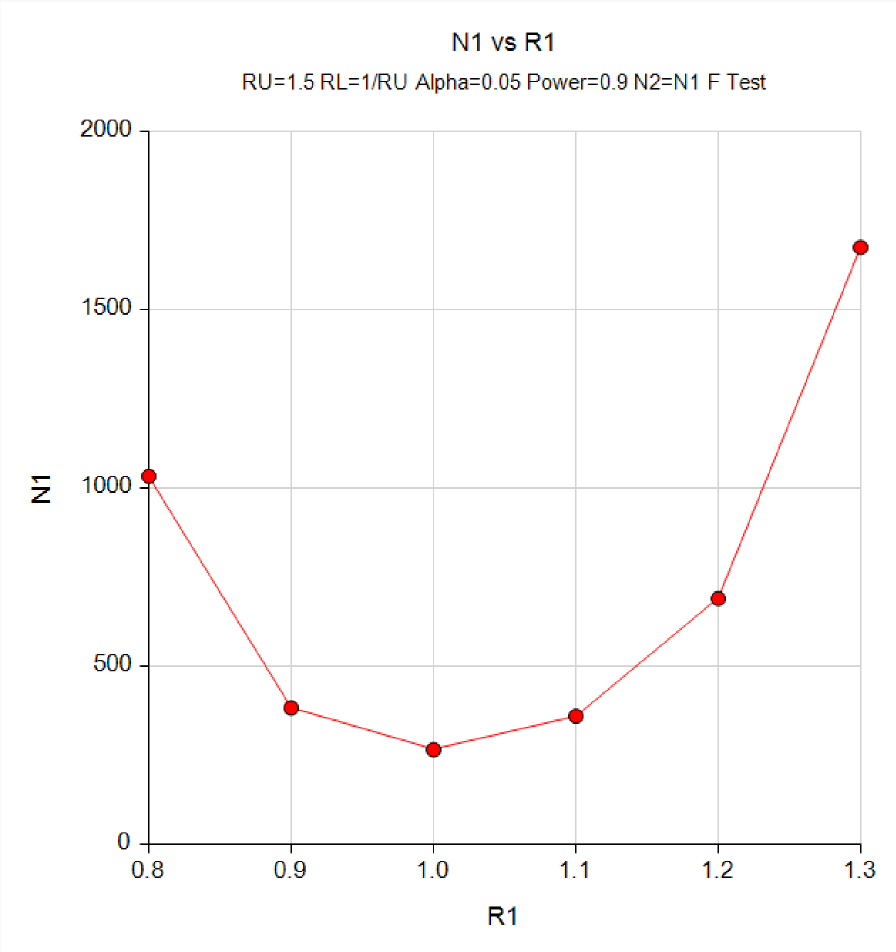
References

Chow, S.C., Shao, J., Wang, H., and Lokhnygina, Y. 2018. Sample Size Calculations in Clinical Research, Third Edition. Taylor & Francis/CRC. Boca Raton, Florida.
Chow, S.C. 2014. Biosimilars Design and Analysis of Follow-on Biologics, Third Edition. Taylor & Francis/CRC. Boca Raton, Florida.
Chow, S.C., and Liu, J.P. 2014. Design and Analysis of Clinical Trials, Third Edition. John Wiley & Sons. Hoboken, New Jersey.

This report gives the sample sizes for the indicated scenarios.

Plots Section

Plots



These plots show the relationship between sample size and R1.

Example 2 – Validation using Hand Calculations

We could not find an example in the literature, so we will present hand calculations to validate this procedure.

Set N1 to 266, the upper limit of equivalence to 1.5, the lower limit to 1/1.5, the significance level to 0.05, and the actual variance ratio values 1.0. Compute the power.

The calculations proceed as follows.

$$\text{Power} = \text{P}\left(\left(\frac{RL}{R1}\right) F_{1-\alpha,N_1-1,N_2-1} < F < \left(\frac{RU}{R1}\right) F_{\alpha,N_1-1,N_2-1}\right)$$

$$= \text{P}\left(0.666667/1 \left(F_{0.95,265,265}\right) < F < 1.5/1 \left(F_{0.05,265,265}\right)\right)$$

$$= \text{P}\big(0.666667(1.22439660) < F < 1.5(0.81672883)\big)$$

$$= \text{P}(0.81626440 < F < 1.22509325)$$

$$= 0.95047403 - 0.049525978$$

$$= 0.90094805$$

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 .... **Power**
Alpha.. **0.05**
Group Allocation .... **Equal (N1 = N2)**
Sample Size Per Group **265**
RU (Upper Equivalence Limit) **1.5**
RL (Lower Equivalence Limit)........................ **1/RU**
R1 (Actual Variance Ratio) **1**

Output

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

Numeric Results

Solve For: Power
Hypotheses: H0: $\sigma^2 1/\sigma^2 2 \leq RL$ or $\sigma^2 1/\sigma^2 2 \geq RU$ vs. H1: $RL < \sigma^2 1/\sigma^2 2 < RU$

	Sample Size			Variance Ratio Equivalence Limits			
Power	N1	N2	N	Lower RL	Upper RU	Actual R1	Alpha
0.9009	266	266	532	0.667	1.5	1	0.05

The power matches the value calculated by hand.