Chapter 467

Tests for the Ratio of Two Within-Subject Variances in a Parallel Design

Introduction

This procedure calculates power and sample size of inequality tests of within-subject variabilities from a two-group, parallel design with replicates (repeated measurements). This routine deals with the case in which the statistical hypotheses are expressed in terms of the ratio of the within-subject variances.

Technical Details

This procedure uses the formulation given in Chow, Shao, Wang, and Lokhnygina (2018), pages 192-193.

Suppose x_{ijk} is the response of the i^{th} treatment (i = 1,2), j^{th} subject (j = 1, ..., Ni), and k^{th} replicate (k = 1, ..., M). The model analyzed in this procedure is

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

where μ_i is the treatment effect, S_{ij} is the random effect of the j^{th} subject in the i^{th} treatment, and e_{ijk} is the within-subject error term which is normally distributed with mean 0 and variance $V_i = \sigma_{Wi}^2$.

Unbiased estimates of these variances are given by

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

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 $N_1(M-1)$ and $N_2(M-1)$.

Testing Inequality

The following hypotheses are usually used to test for inequality

$$H_0: \frac{\sigma_{W1}^2}{\sigma_{W2}^2} = 1 \quad \text{versus} \quad H_A: \frac{\sigma_{W1}^2}{\sigma_{W2}^2} \neq 1.$$

The corresponding test statistics are $T = (\hat{V}_1/\hat{V}_2)$.

Power

The power of this combination of tests is given by

$$\text{Power} = \Pr\left(R1\left(F_{\alpha/2,N_1(M-1),N_2(M-1)}\right)\right) + 1 - \Pr\left(F < R1\left(F_{1-\alpha/2,N_1(M-1),N_2(M-1)}\right)\right)$$

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 actual variance ratio. 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 has a different within-subject variance from the standard drug. A parallel-group design with replicates will be used.

Company researchers set the significance level to 0.05, the power to 0.90, M to 2 or 3, and the alternative variance ratio values between 0.5 and 2.0. 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)**
M (Measurements Per Subject) **2 3**
R1 (Actual Variance Ratio) **0.5 0.66667 0.8 1.25 1.5 2**

Output

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

Numeric Reports

Numeric Results

Solve For: Sample Size
Groups: 1 = Treatment, 2 = Control
Variance Ratio: σ^2w1 / σ^2w2 or σ^2w_T / σ^2wc
Hypotheses: H0: $\sigma^2w_T / \sigma^2wc = 1$ vs. H1: $\sigma^2w_T / \sigma^2wc \neq 1$

Power		Sample Size			Measurements per Subject	Actual Variance Ratio	
Target	Actual	N1	N2	N	M	R1	Alpha
0.9	0.9017	89	89	178	2	0.500	0.05
0.9	0.9049	45	45	90	3	0.500	0.05
0.9	0.9004	257	257	514	2	0.667	0.05
0.9	0.9015	129	129	258	3	0.667	0.05
0.9	0.9003	846	846	1692	2	0.800	0.05
0.9	0.9003	423	423	846	3	0.800	0.05
0.9	0.9003	846	846	1692	2	1.250	0.05
0.9	0.9003	423	423	846	3	1.250	0.05
0.9	0.9004	257	257	514	2	1.500	0.05
0.9	0.9015	129	129	258	3	1.500	0.05
0.9	0.9017	89	89	178	2	2.000	0.05
0.9	0.9049	45	45	90	3	2.000	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. Each subject is measured M times.
N2 The number of subjects from group 2. Each subject is measured M times.
N The total number of subjects. N = N1 + N2.
M The number of times each subject is measured.
R1 The value of the within-subject variance ratio at which the power is calculated.
Alpha The probability of rejecting a true null hypothesis.

Summary Statements

A parallel, two-group, repeated measurement design (with 2 measurements per subject) will be used to test whether the Group 1 (treatment) within-subject variance (σ^2w_T) is different from the Group 2 (control) within-subject variance (σ^2wc), by testing whether the within-subject variance ratio (σ^2w_T / σ^2wc) is different from 1 (H0: $\sigma^2w_T / \sigma^2wc = 1$ versus H1: $\sigma^2w_T / \sigma^2wc \neq 1$). The comparison will be made using a two-sided, variance-ratio F-test (with the treatment within-subject variance in the numerator), with a Type I error rate (α) of 0.05. To detect a within-subject variance ratio (σ^2w_T / σ^2wc) of 0.5 with 90% power, the number of subjects needed will be 89 in Group 1 (treatment), and 89 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%	89	89	178	112	112	224	23	23	46
20%	45	45	90	57	57	114	12	12	24
20%	257	257	514	322	322	644	65	65	130
20%	129	129	258	162	162	324	33	33	66
20%	846	846	1692	1058	1058	2116	212	212	424
20%	423	423	846	529	529	1058	106	106	212
20%	846	846	1692	1058	1058	2116	212	212	424
20%	423	423	846	529	529	1058	106	106	212
20%	257	257	514	322	322	644	65	65	130
20%	129	129	258	162	162	324	33	33	66
20%	89	89	178	112	112	224	23	23	46
20%	45	45	90	57	57	114	12	12	24

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, 112 subjects should be enrolled in Group 1, and 112 in Group 2, to obtain final group sample sizes of 89 and 89, respectively.

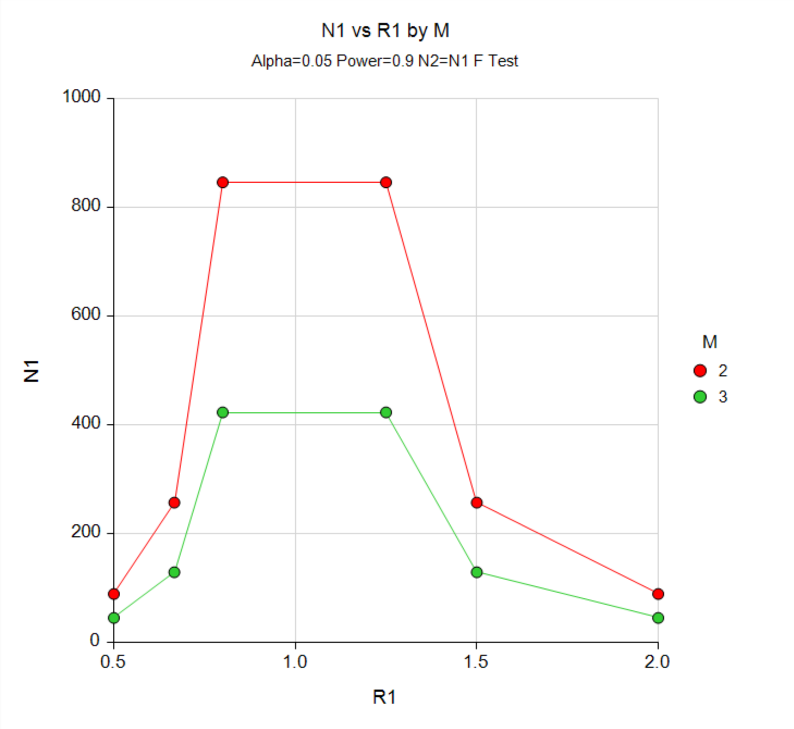
References

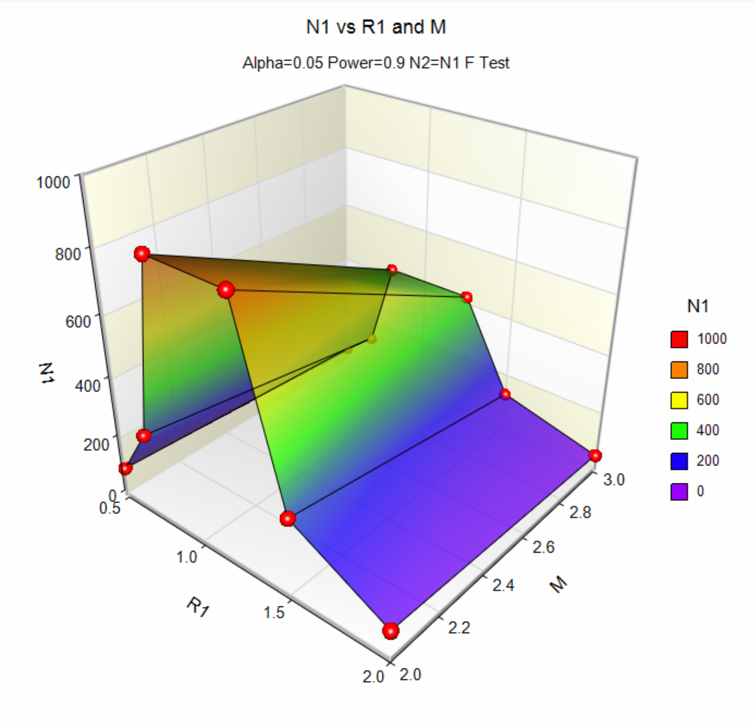
Chow, S.C., Shao, J., Wang, H., and Lokhnygina, Y. 2018. Sample Size Calculations in Clinical Research, Third Edition. Taylor & Francis/CRC. Boca Raton, Florida.
Chow, S.C., and Liu, J.P. 2014. Design and Analysis of Clinical Trials, Third Edition. John Wiley & Sons. Hoboken, New Jersey.

This report gives the sample sizes for the indicated scenarios.

Plots Section

Plots





These plots show the relationship between sample size, R1, and M.

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 257, the significance level to 0.05, M to 2, and the actual variance ratio value 0.66667. Compute the power.

The calculations proceed as follows.

$$\text{Power} = \text{P}\left(R1\left(F_{\alpha/2,N_1(M-1),N_2(M-1)}\right)\right) + 1 - \text{P}\left(F < R1\left(F_{1-\alpha/2,N_1(M-1),N_2(M-1)}\right)\right)$$

$$= \text{P}\left(F < 0.66667F_{0.025,257,257}\right) + 1 - \text{P}\left(0.66667F_{0.975,257,257}\right)$$

$$= \text{P}(F < 0.66667(0.78265629)) + 1 - \text{P}(F < 0.66667(1.27770007))$$

$$= \text{P}(F < 0.52177347) + 1 - \text{P}(F < 0.85180431)$$

$$= 0.00000012 + 1 - 0.099613912$$

$$= 0.9003862$$

Hence, the power is 0.9004 to four decimal places.

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 **257**
M (Measurements Per Subject) **2**
RA (Alternative Variance Ratio) **0.66667**

Output

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

Numeric Results

Solve For: Power
Groups: 1 = Treatment, 2 = Control
Variance Ratio: $\sigma^2 w1 / \sigma^2 w2$ or $\sigma^2 wT / \sigma^2 wC$
Hypotheses: H0: $\sigma^2 wT / \sigma^2 wC = 1$ vs. H1: $\sigma^2 wT / \sigma^2 wC \neq 1$

	Sample Size			Measurements per Subject	Actual Variance Ratio	
Power	N1	N2	N	M	R1	Alpha
0.9004	257	257	514	2	0.667	0.05

The power matches the hand-calculated result.