

## Chapter 234

# Superiority by a Margin Tests for the Ratio of Two Proportions in a Cluster- Randomized Design

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### Introduction

This module provides power analysis and sample size calculation for inequality tests of the ratio with a non-zero null hypothesis in two-sample, cluster-randomized designs in which the outcome is binary.

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### Technical Details

Our formulation comes from Donner and Klar (2000). Denote a binary observation by  $Y_{gkm}$  where  $g = 1$  or  $2$  is the group,  $k = 1, 2, \dots, K_g$  is a cluster within group  $g$ , and  $m = 1, 2, \dots, M_g$  is an individual in cluster  $k$  of group  $g$ . The results that follow assume an equal number of individuals per cluster. When the number of subjects from cluster to cluster are about the same, the power and sample size values should be fairly accurate. In these cases, the average number of subjects per cluster can be used.

The statistical hypothesis that is tested concerns the ratio of the two group proportions,  $p_1$  and  $p_2$ . When necessary, we assume that group 1 is the treatment group and group 2 is the control group. With a simple modification, all of the large-sample sample size formulas that are listed in the module for testing superiority by a margin with two proportions using the ratio can be used here.

When the individual subjects are randomly assigned to one of the two groups, the variance of the sample proportion is

$$\sigma_{S,g}^2 = \frac{p_g(1-p_g)}{n_g}$$

When the randomization is by clusters of subjects, the variance of the sample proportion is

$$\begin{aligned}\sigma_{C,g}^2 &= \frac{p_g(1-p_g)(1+(m_g-1)\rho)}{k_g m_g} \\ &= \sigma_{S,g}^2 [1+(m_g-1)\rho] \\ &= F_{g,\rho} \sigma_{S,g}^2\end{aligned}$$

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The factor  $\left[1 + (m_g - 1)\rho\right]$  is called the *inflation factor*. The Greek letter  $\rho$  is used to represent the *intracluster correlation coefficient (ICC)*. This correlation may be thought of as the simple correlation between any two subjects within the same cluster. If we stipulate that  $\rho$  is positive, it may also be interpreted as the proportion of total variability that is attributable to differences between clusters. This value is critical to the sample size calculation.

The asymptotic formula for the Farrington and Manning Likelihood Score Test that was used in comparing two proportions (see Chapter 206, “Superiority by a Margin Tests for the Ratio of Two Proportions”) may be used with cluster-randomized designs as well, as long as an adjustment is made for the inflation factor.

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## Power Calculations

A large sample approximation may be used that is most accurate when the values of  $n_1$  and  $n_2$  are large. The large approximation is made by replacing the values of  $\hat{p}_1$  and  $\hat{p}_2$  in the  $z$  statistic with the corresponding values of  $p_1$  and  $p_2$  under the alternative hypothesis, and then computing the results based on the normal distribution.

Note that in this case, exact calculations are not possible.

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## Procedure Options

This section describes the options that are specific to this procedure. These are located on the Design and Options tabs. For more information about the options of other tabs, go to the Procedure Window chapter.

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## Design Tab

The Design tab contains the parameters associated with this test such as the proportions, sample sizes, alpha, and power.

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### Solve For

#### Solve For

This option specifies the parameter to be solved for using the other parameters. The parameters that may be selected are *Power*, *Sample Size (K1)*, *Sample Size (M1)*, *Effect Size*, and *ICC*. Under most situations, you will select either *Power* or *Sample Size (K1)*.

Select *Sample Size (K1)* when you want to calculate the number of clusters per group needed to achieve a given power and alpha level.

Select *Power* when you want to calculate the power of an experiment.

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### Test

#### Alternative Hypothesis

Specify the direction of the alternative hypothesis.

- **One-Sided (H1: R1 > R0)**  
Refers to an upper-tailed, one-sided test in which H1 is of the type  $H1: P1/P2 = R1 > R0$ .
- **One-Sided (H1: R1 < R0)**  
Refers to a lower-tailed, one-sided test in which H1 is of the type  $H1: P1/P2 = R1 < R0$ .

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- **Two-Sided**

Refers to a two-sided test in which  $H_1$  is of the type  $H_1: P_1/P_2 = R_1 \neq R_0$ .

For one-sided tests, the direction you select must match the values entered for  $H_0$  and  $H_1$ . For example, if you select  $H_1: R_1 < R_0$ , then the value(s) for  $R_1$  must be less than the value(s) for  $R_0$ .

### Test Type

The Likelihood Score Test (Farrington & Manning) is the only test available for this procedure.

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## Power and Alpha

### Power

This option specifies one or more values for power. Power is the probability of rejecting a false null hypothesis, and is equal to one minus Beta. Beta is the probability of a type-II error, which occurs when a false null hypothesis is not rejected.

Values must be between zero and one. Historically, the value of 0.80 (Beta = 0.20) was used for power. Now, 0.90 (Beta = 0.10) is also commonly used.

A single value may be entered here or a range of values such as *0.8 to 0.95 by 0.05* may be entered.

### Alpha

This option specifies one or more values for the probability of a type-I error. A type-I error occurs when a true null hypothesis is rejected.

Values must be between zero and one. Historically, the value of 0.05 has been used for alpha. This means that about one test in twenty will falsely reject the null hypothesis. You should pick a value for alpha that represents the risk of a type-I error you are willing to take in your experimental situation.

You may enter a range of values such as *0.01 0.05 0.10* or *0.01 to 0.10 by 0.01*.

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## Sample Size – Group 1 (Treatment)

### K1 (Clusters in Group 1)

Enter a value (or range of values) for the number of clusters in group one. You may enter a range of values such as *10 to 20 by 2*. The sample size for this group is equal to the number of clusters times the number of subjects per cluster.

### M1 (Items per Cluster in Group 1)

This is the average number of items (subjects) per cluster in group one. This value must be a positive number that is at least 1. You can use a list of values such as *100 150 200*.

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## Sample Size – Group 2 (Reference)

### K2 (Clusters in Group 2)

This is the number of clusters in group two. The sample size for this group is equal to the number of clusters times the number of subjects per cluster. This value must be a positive number.

If you simply want a multiple of the value for group one, you would enter the multiple followed by *K1*, with no blanks. If you want to use *K1* directly, you do not have to pre-multiply by 1. For example, all of the following are valid entries: *10 K1 2K1 0.5K1*.

You can use a list of values such as *10 20 30* or *K1 2K1 3K1*.

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### M2 (Items per Cluster in Group 2)

This is the number of items (subjects) per cluster in group two. This value must be a positive number.

If you simply want a multiple of the value for group one, you would enter the multiple followed by  $M1$ , with no blanks. If you want to use  $M1$  directly, you do not have to pre-multiply by  $1$ . For example, all of the following are valid entries:  $10 M1$   $2M1$   $0.5M1$ .

You can use a list of values such as  $10 20 30$  or  $M1 2M1 3M1$ .

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### Effect Size – Ratios

#### R0 (Ratio|H0 = P1.0/P2)

Specify the ratio between P1.0 and P2 where P1.0 is the group one proportion under the null hypothesis.

This ratio is used with P2 to calculate the value of P1.0 using the formula:  $P1.0 = (\text{Ratio}) \times (P2)$ .

The power calculations assume that P1.0 is the value of the P1 under the null hypothesis. In this non-null case, the value of P1.0 is not equal to P2 as it is in the null case.

Ratios must be positive. R0 cannot take on the value of 1.

You may enter a range of values such as  $0.95 .97 .99$  or  $.91 \text{ to } .99 \text{ by } .02$ .

#### R1 (Ratio|H1 = P1.1/P2)

Specify the ratio between P1.1 and P2. P1.1 is the proportion in group 1 under the alternative hypothesis. This ratio is used with P2 to calculate the value of P1.1 using the formula:  $P1.1 = R1 \times P2$ .

The power calculations assume that P1.1 is the actual value of the proportion in group 1 (experimental or treatment group).

Ratios must be positive. You may enter a range of values such as  $0.95 1 1.05$  or  $0.9 \text{ to } 1.9 \text{ by } 0.02$ .

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### Effect Size – Group 2 (Reference)

#### P2 (Group 2 Proportion)

Specify the value of  $p_2$ , the control, baseline, or standard group's proportion. The null hypothesis is that the two proportions differ by a specified amount (See *Group 1 Proportion* below).

Since  $p_2$  is a proportion, these values must be between 0 and 1.

You may enter a range of values such as  $0.1 0.2 0.3$  or  $0.1 \text{ to } 0.9 \text{ by } 0.1$ .

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### Effect Size – Intracluster Correlation

#### ICC (Intracluster Correlation)

Enter a value (or range of values) for the intracluster correlation. This correlation may be thought of as the simple correlation between any two observations in the same cluster. It may also be thought of as the proportion of total variance in the observations that can be attributed to difference between clusters.

Although the actual range for this value is between 0 to 1, typical values range from 0.002 to 0.05.

## Example 1 – Finding Power

A study is being designed to study the effectiveness of a new treatment. Historically, the standard treatment has enjoyed a 60% cure rate. The new treatment is more expensive and has more side effects than the standard treatment. Thus, the new treatment will be adopted if the ratio of the new treatment to the old treatment is at least 1.1333.

The researchers will recruit patients from various hospitals. All patients at a particular hospital will receive the same treatment. They anticipate an average of 100 patients per hospital. Based on similar studies, they estimate the intracluster correlation to be 0.002.

The researchers plan to use the Farrington and Manning likelihood score test statistic to analyze the data. They want to study the power of the one-sided Farrington and Manning test at group cluster sizes ranging from 2 to 10 for detecting a ratio of 1.1333 when the actual cure rate ratio ranges from 1.1667 to 1.2667. The significance level will be 0.05.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Superiority by a Margin Tests for the Ratio of Two Proportions in a Cluster-Randomized Design** procedure window by expanding **Proportions**, then **Two Proportions – Cluster Randomized**, then clicking on **Superiority by a Margin**, and then clicking on **Superiority by a Margin Tests for the Ratio of Two Proportions in a Cluster-Randomized Design**. You may then make the appropriate entries as listed below, or open **Example 1** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Power</b>
Alternative Hypothesis .....	<b>One-Sided (H1: R1 &gt; R0)</b>
Test Type .....	<b>Likelihood Score (Farr. &amp; Mann.)</b>
Alpha .....	<b>0.05</b>
K1 (Clusters in Group 1) .....	<b>2 4 6 8 10</b>
M1 (Items per Cluster in Group 1) .....	<b>100</b>
K2 (Clusters in Group 2) .....	<b>K1</b>
M2 (Items per Cluster in Group 2) .....	<b>M1</b>
R0 (Ratio H0 = P1.0/P2) .....	<b>1.1333</b>
R1 (Ratio  H1 = P1.1/P2) .....	<b>1.1667 to 1.2667 by 0.02</b>
P2 (Group 2 Proportion) .....	<b>0.6</b>
ICC (Intracluster Correlation) .....	<b>0.002</b>

Superiority by a Margin Tests for the Ratio of Two Proportions in a Cluster-Randomized Design

Output

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

Numeric Results

Numeric Results for Superiority Tests for the Ratio of Two Proportions (Cluster-Randomized)

Test Statistic: Likelihood Score Test (Farrington & Manning)

H0: P1/P2 ≤ R0. H1: P1/P2 = R1 > R0.

Power	Group 1	Group 2	Group 2 Prop P2	Group 1 Prop H0 P1.0	Group 1 Prop H1 P1.1	Ratio H0 R0	Ratio H1 R1	Intra-Cluster	Alpha
	Clusters/ Items K1/M1	Clusters/ Items K2/M2						Corr. ICC	
0.09925	2/100	2/100	0.6000	0.6800	0.7000	1.133	1.167	0.0020	0.050
0.12780	4/100	4/100	0.6000	0.6800	0.7000	1.133	1.167	0.0020	0.050
0.15327	6/100	6/100	0.6000	0.6800	0.7000	1.133	1.167	0.0020	0.050
0.17719	8/100	8/100	0.6000	0.6800	0.7000	1.133	1.167	0.0020	0.050
0.20011	10/100	10/100	0.6000	0.6800	0.7000	1.133	1.167	0.0020	0.050
0.14271	2/100	2/100	0.6000	0.6800	0.7120	1.133	1.187	0.0020	0.050
0.20359	4/100	4/100	0.6000	0.6800	0.7120	1.133	1.187	0.0020	0.050
0.25939	6/100	6/100	0.6000	0.6800	0.7120	1.133	1.187	0.0020	0.050
0.31193	8/100	8/100	0.6000	0.6800	0.7120	1.133	1.187	0.0020	0.050
0.36167	10/100	10/100	0.6000	0.6800	0.7120	1.133	1.187	0.0020	0.050
0.19812	2/100	2/100	0.6000	0.6800	0.7240	1.133	1.207	0.0020	0.050
0.30234	4/100	4/100	0.6000	0.6800	0.7240	1.133	1.207	0.0020	0.050
0.39591	6/100	6/100	0.6000	0.6800	0.7240	1.133	1.207	0.0020	0.050
0.48004	8/100	8/100	0.6000	0.6800	0.7240	1.133	1.207	0.0020	0.050
0.55504	10/100	10/100	0.6000	0.6800	0.7240	1.133	1.207	0.0020	0.050
0.26566	2/100	2/100	0.6000	0.6800	0.7360	1.133	1.227	0.0020	0.050
0.41960	4/100	4/100	0.6000	0.6800	0.7360	1.133	1.227	0.0020	0.050
0.54844	6/100	6/100	0.6000	0.6800	0.7360	1.133	1.227	0.0020	0.050
0.65373	8/100	8/100	0.6000	0.6800	0.7360	1.133	1.227	0.0020	0.050
0.73779	10/100	10/100	0.6000	0.6800	0.7360	1.133	1.227	0.0020	0.050
0.34426	2/100	2/100	0.6000	0.6800	0.7480	1.133	1.247	0.0020	0.050
0.54610	4/100	4/100	0.6000	0.6800	0.7480	1.133	1.247	0.0020	0.050
0.69577	6/100	6/100	0.6000	0.6800	0.7480	1.133	1.247	0.0020	0.050
0.80136	8/100	8/100	0.6000	0.6800	0.7480	1.133	1.247	0.0020	0.050
0.87306	10/100	10/100	0.6000	0.6800	0.7480	1.133	1.247	0.0020	0.050
0.43146	2/100	2/100	0.6000	0.6800	0.7600	1.133	1.267	0.0020	0.050
0.66963	4/100	4/100	0.6000	0.6800	0.7600	1.133	1.267	0.0020	0.050
0.81810	6/100	6/100	0.6000	0.6800	0.7600	1.133	1.267	0.0020	0.050
0.90384	8/100	8/100	0.6000	0.6800	0.7600	1.133	1.267	0.0020	0.050
0.95076	10/100	10/100	0.6000	0.6800	0.7600	1.133	1.267	0.0020	0.050

Report Definitions

H0 is an abbreviation for the null hypothesis. This is the hypothesis being evaluated by the statistical test.

H1 is an abbreviation for the alternative hypothesis. This hypothesis gives the 'true' parameter values.

Power is the probability of rejecting a false null hypothesis. It should be close to one.

K1 and K2 are the number of clusters in groups 1 and 2, respectively.

M1 and M2 are the average number of items (subjects) per cluster in groups 1 and 2, respectively.

P2 is the proportion for group 2. This is the standard, reference, baseline, or control group.

P1.0 is the proportion for group 1 (treatment group) assuming the null hypothesis (H0).

P1.1 is the proportion for group 1 (treatment group) assuming the alternative hypothesis (H1).

R0 = P1.0/P2 is the superiority margin. It is the ratio assuming H0.

R1 = P1.1/P2 is the actual ratio at which the power is calculated.

ICC is the intracluster correlation.

Alpha is the probability of rejecting a true null hypothesis.

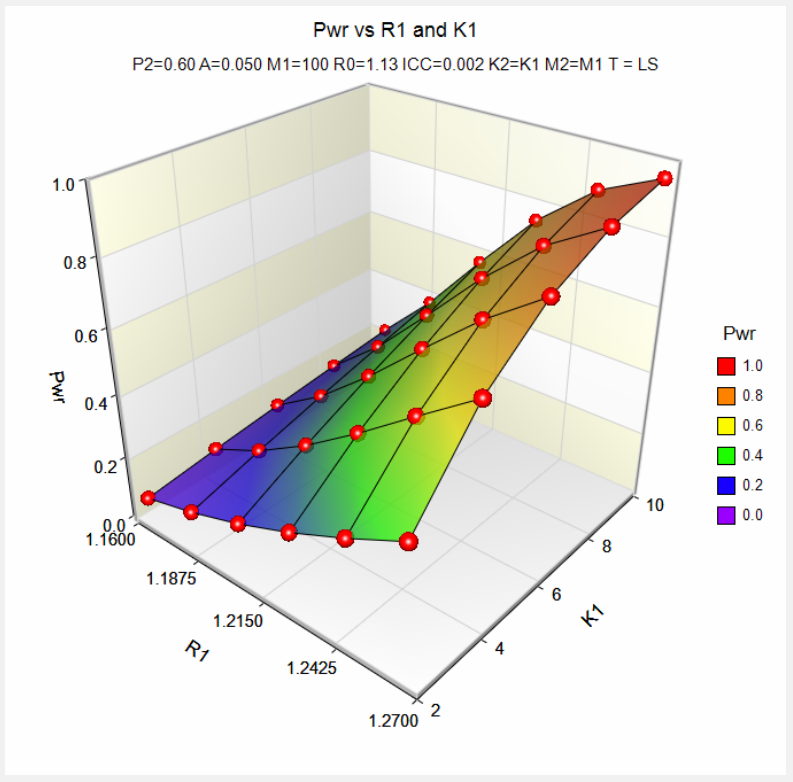
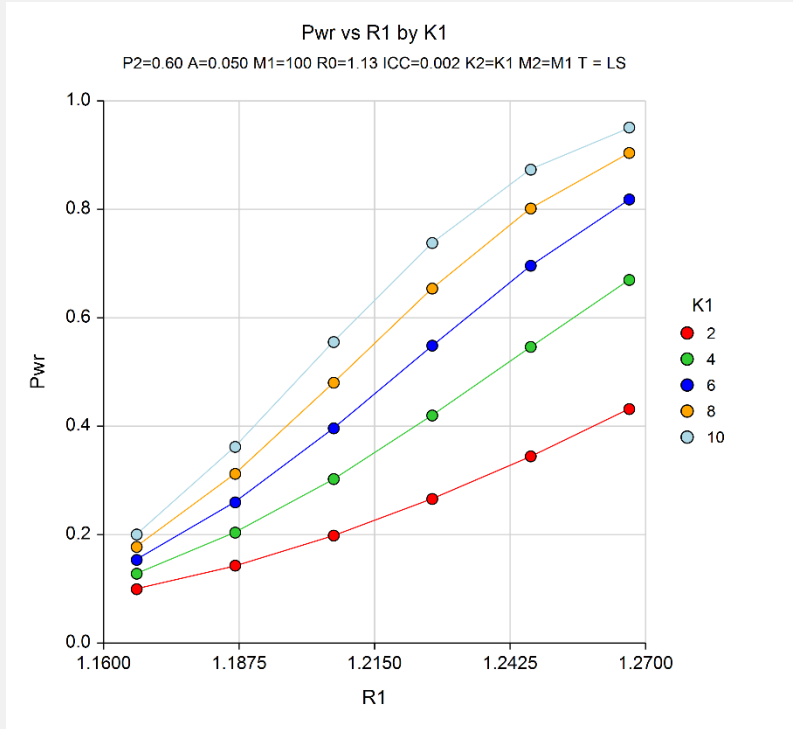
Summary Statements

Sample sizes of 200 in group 1 and 200 in group 2, which were obtained by sampling 2 clusters with 100 subjects each in group 1 and 2 clusters with 100 subjects each in group 2, achieve 9.925% power to detect a superiority margin ratio of the group proportions of 1.133. The proportion in group 1 (the treatment group) is assumed to be 0.6800 under the null hypothesis and 0.7000 under the alternative hypothesis. The proportion in group 2 (the control group) is 0.6000. The test statistic used is the one-sided Likelihood Score Test (Farrington & Manning). The intracluster correlation is 0.0020, and the significance level of the test is 0.050.

This report shows the values of each of the parameters, one scenario per row. The total number of items sampled in group 1 is N1 = K1 x M1. The total number of items sampled in group 2 is N2 = K2 x M2.

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Plots Section



The values from the table are displayed on the above charts. These charts give us a quick look at the sample sizes that will be required for various values of R1.

## Example 2 – Finding the Sample Size (Number of Clusters)

Continuing with the scenario given in Example 1, the researchers want to determine the number of clusters necessary for each value of R1 when the target power is set to 0.80.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Superiority by a Margin Tests for the Ratio of Two Proportions in a Cluster-Randomized Design** procedure window by expanding **Proportions**, then **Two Proportions – Cluster Randomized**, then clicking on **Superiority by a Margin**, and then clicking on **Superiority by a Margin Tests for the Ratio of Two Proportions in a Cluster-Randomized Design**. You may then make the appropriate entries as listed below, or open **Example 2** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Sample Size (K1)</b>
Alternative Hypothesis .....	<b>One-Sided (H1: R1 &gt; R0)</b>
Test Type .....	<b>Likelihood Score (Farr. &amp; Mann.)</b>
Power .....	<b>0.80</b>
Alpha .....	<b>0.05</b>
M1 (Items per Cluster in Group 1) .....	<b>100</b>
K2 (Clusters in Group 2) .....	<b>K1</b>
M2 (Items per Cluster in Group 2) .....	<b>M1</b>
R0 (Ratio H0 = P1.0/P2) .....	<b>1.1333</b>
R1 (Ratio  H1 = P1.1/P2) .....	<b>1.1667 to 1.2667 by 0.02</b>
P2 (Group 2 Proportion) .....	<b>0.6</b>
ICC (Intracluster Correlation) .....	<b>0.002</b>

### Output

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

### Numeric Results

#### Numeric Results for Superiority Tests for the Ratio of Two Proportions (Cluster-Randomized)

Test Statistic: Likelihood Score Test (Farrington & Manning)

H0: P1/P2 ≤ R0. H1: P1/P2 = R1 > R0.

Power	Group 1	Group 2	Group 2 Prop P2	Group 1	Group 1	Ratio H0 R0	Ratio H1 R1	Intra- Cluster Corr. ICC	Alpha
	Clusters/ Items K1/M1	Clusters/ Items K2/M2		Prop H0 P1.0	Prop H1 P1.1				
0.80135	96/100	96/100	0.6000	0.6800	0.7000	1.133	1.167	0.0020	0.050
0.80857	38/100	38/100	0.6000	0.6800	0.7120	1.133	1.187	0.0020	0.050
0.80998	20/100	20/100	0.6000	0.6800	0.7240	1.133	1.207	0.0020	0.050
0.80359	12/100	12/100	0.6000	0.6800	0.7360	1.133	1.227	0.0020	0.050
0.80136	8/100	8/100	0.6000	0.6800	0.7480	1.133	1.247	0.0020	0.050
0.81810	6/100	6/100	0.6000	0.6800	0.7600	1.133	1.267	0.0020	0.050

The required sample size depends a great deal on the value of R1. The researchers should spend time determining the most appropriate value for R1.



## Example 3 – Validation

This procedure uses the same mechanics as the Tests for Two Proportions in a Cluster-Randomized Design procedure. We refer the user to Example 4 of Chapter 230 for the validation.