Chapter 238

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

Introduction

This module provides power analysis and sample size calculation for superiority by a margin tests of the ratio in two-sample, cluster-randomized designs in which the outcome is binary.

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, …, K_g is a cluster within group g, and m = 1, 2, …, 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

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

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

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

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The factor $\left[1+\left(m_g-1\right)\rho\right]$ is called the *inflation factor*. The Greek letter ρ 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 ρ 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 196, "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.

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.

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.

Design Tab

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

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.

Test

Higher Proportions Are

Use this option to specify the direction of the test.

If Higher Proportions are "Better", the alternative hypothesis is H1: P1/P2 > R0.

If Higher Proportions are "Worse", the alternative hypothesis is H1: P1/P2 < R0.

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*.

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*.

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*.

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 (Superiority Ratio)

This option specifies the trivial ratio (also called the Relative Margin of Superiority) between P1 and P2. The power calculations assume that P1.0 is the value of the P1 under the null hypothesis. This value is used with P2 to calculate the value of P1.0 using the formula: P1.0 = R0 x P2.

When *Higher Proportions Are* is set to *Better*, the trivial ratio is the relative amount by which P1 must be greater than P2 to have the treatment group declared superior to the reference group. R0 should be greater than one for superiority by a margin tests. The reverse is the case when *Higher Proportions Are* is set to *Worse*.

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 to .99 by .02*.

R1 (Actual Ratio)

This option specifies the ratio of P1.1 and P2, where P1.1 is the actual proportion in the treatment group. The power calculations assume that P1.1 is the actual value of the proportion in group 1. This difference is used with P2 to calculate the value of P1 using the formula: P1.1 = R1 x P2.

Ratios must be positive. You may enter a range of values such as *0.95 1 1.05* or *0.9 to 1.9 by 0.02*.

Effect Size – Group 2 (Reference)

P2 (Reference Group Proportion)

Specify the value of p_2 , the reference, baseline, or control group's proportion. The null hypothesis is that the two proportions differ by no more than a specified amount. Since P2 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 to 0.9 by 0.1*.

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.

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Example 1 – Finding Power

A study is being designed to establish the superiority of a new treatment compared to the current treatment. Historically, the current treatment has enjoyed a 60% cure rate. The new treatment is hoped to perform better than the current treatment. Thus, the new treatment will be adopted if it is more effective than the current treatment by a clinically significant amount. The researchers will recommend adoption of the new treatment if it has a cure rate of at least 72%.

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 when the superiority ratio is 1.2 and the actual ratio ranges from 1.25 to 1.4. 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**.

Option	Value
Design Tab	
Solve For	**Power**
Higher Proportions Are	**Better (H1: P1/P2 > R0)**
Alpha	**0.05**
K1 (Clusters in Group 1)	**2 4 6 8 10**
M1 (Items per Cluster in Group 1)	**100**
K2 (Clusters in Group 2)	**K1**
M2 (Items per Cluster in Group 2)	**M1**
R0 (Superiority Ratio)	**1.2**
R1 (Actual Ratio)	**1.25 to 1.4 by 0.05**
P2 (Group 2 Proportion)	**0.6**
ICC (Intracluster Correlation)	**0.002**

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Output

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

Numeric Results

Numeric Results
Test Statistic: Likelihood Score Test (Farrington & Manning)
Hypotheses: H0: P1/P2 ≤ R0 vs. H1: P1/P2 > R0

Power	Group 1 Clusters/ Items K1/M1	Group 2 Clusters/ Items K2/M2	Group 2 Prop P2	Group 1 Superior. Prop P1.0	Group 1 Actual Prop P1.1	Superior. Ratio R0	Actual Ratio R1	Intra-Cluster Corr. ICC	Alpha
0.13253	2/100	2/100	0.6000	0.7200	0.7500	1.200	1.250	0.0020	0.050
0.18550	4/100	4/100	0.6000	0.7200	0.7500	1.200	1.250	0.0020	0.050
0.23397	6/100	6/100	0.6000	0.7200	0.7500	1.200	1.250	0.0020	0.050
0.27974	8/100	8/100	0.6000	0.7200	0.7500	1.200	1.250	0.0020	0.050
0.32338	10/100	10/100	0.6000	0.7200	0.7500	1.200	1.250	0.0020	0.050
0.28507	2/100	2/100	0.6000	0.7200	0.7800	1.200	1.300	0.0020	0.050
0.45171	4/100	4/100	0.6000	0.7200	0.7800	1.200	1.300	0.0020	0.050
0.58756	6/100	6/100	0.6000	0.7200	0.7800	1.200	1.300	0.0020	0.050
0.69502	8/100	8/100	0.6000	0.7200	0.7800	1.200	1.300	0.0020	0.050
0.77774	10/100	10/100	0.6000	0.7200	0.7800	1.200	1.300	0.0020	0.050
0.49981	2/100	2/100	0.6000	0.7200	0.8100	1.200	1.350	0.0020	0.050
0.75208	4/100	4/100	0.6000	0.7200	0.8100	1.200	1.350	0.0020	0.050
0.88571	6/100	6/100	0.6000	0.7200	0.8100	1.200	1.350	0.0020	0.050
0.95000	8/100	8/100	0.6000	0.7200	0.8100	1.200	1.350	0.0020	0.050
0.97899	10/100	10/100	0.6000	0.7200	0.8100	1.200	1.350	0.0020	0.050
0.72344	2/100	2/100	0.6000	0.7200	0.8400	1.200	1.400	0.0020	0.050
0.93575	4/100	4/100	0.6000	0.7200	0.8400	1.200	1.400	0.0020	0.050
0.98717	6/100	6/100	0.6000	0.7200	0.8400	1.200	1.400	0.0020	0.050
0.99768	8/100	8/100	0.6000	0.7200	0.8400	1.200	1.400	0.0020	0.050
0.99961	10/100	10/100	0.6000	0.7200	0.8400	1.200	1.400	0.0020	0.050

Report Definitions
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, the standard, reference, baseline, or control group.
P1.0 is the proportion for group 1 (the treatment group) assuming the null hypothesis (H0).
P1.1 is the proportion for group 1 (the treatment group) assuming the alternative hypothesis (H1).
R0 = P1.0/P2 is the superiority ratio. 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 13.253% power to detect a ratio of 1.250 when the superiority ratio is 1.200. The proportion in group 1 (the treatment group) is assumed to be 0.7200 under the null hypothesis and 0.7500 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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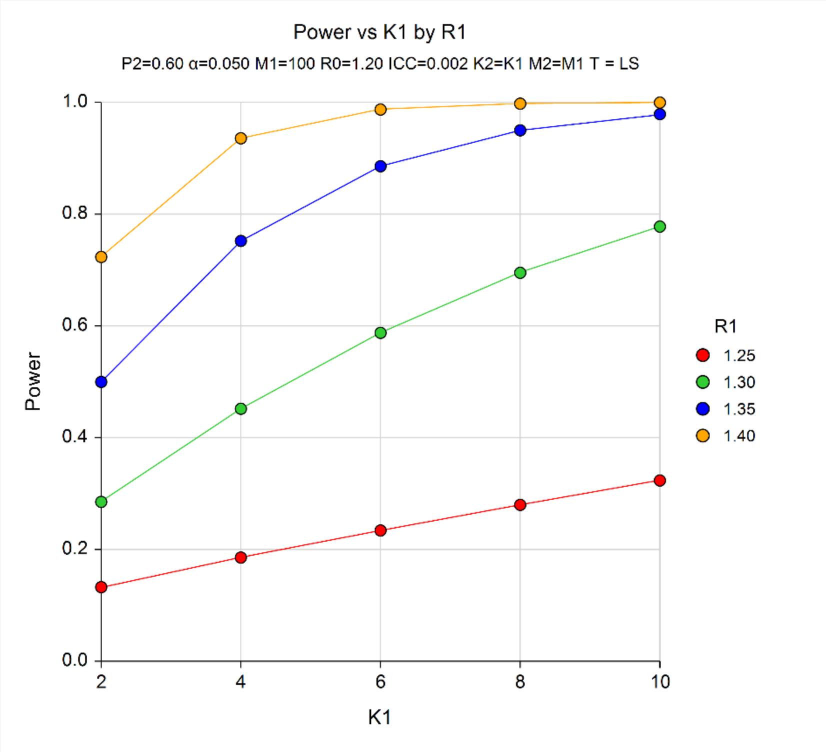
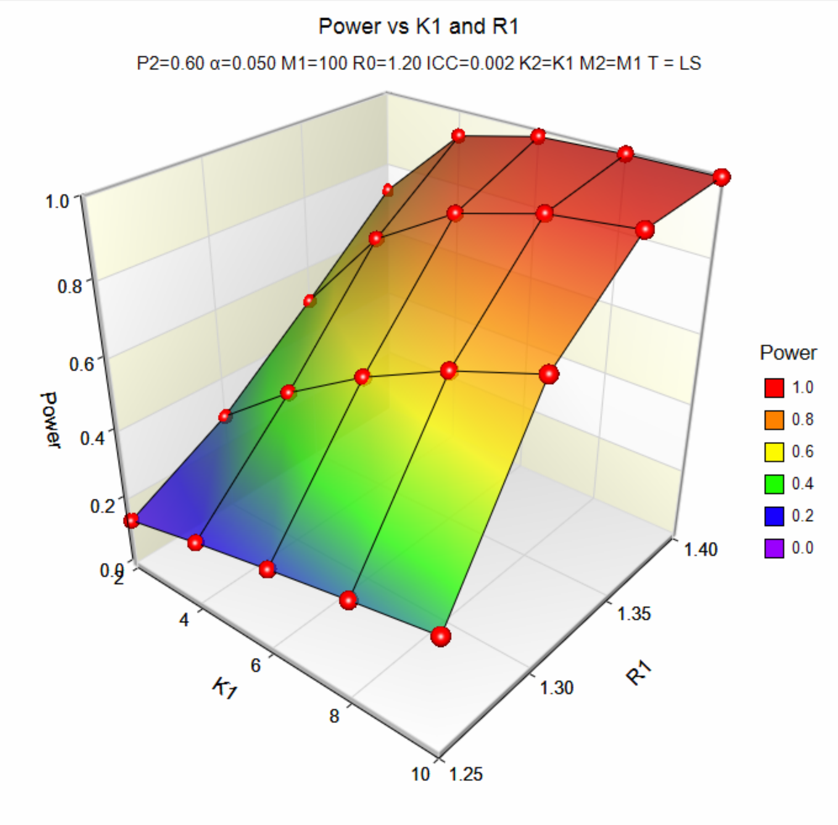
Plots Section





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

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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**.

Option	Value
Design Tab	
Solve For	**Sample Size (K1)**
Higher Proportions Are	**Better (H1: P1/P2 > R0)**
Power	**0.80**
Alpha	**0.05**
M1 (Items per Cluster in Group 1)	**100**
K2 (Clusters in Group 2)	**K1**
M2 (Items per Cluster in Group 2)	**M1**
R0 (Superiority Ratio)	**1.2**
R1 (Actual Ratio)	**1.25 to 1.4 by 0.05**
P2 (Group 2 Proportion)	**0.6**
ICC (Intracluster Correlation)	**0.002**

Output

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

Numeric Results

Numeric Results
Test Statistic: Likelihood Score Test (Farrington & Manning)
Hypotheses: H0: P1/P2 ≤ R0 vs. H1: P1/P2 > R0

Power	Group 1 Clusters/ Items K1/M1	Group 2 Clusters/ Items K2/M2	Group 2 Prop P2	Group 1 Superior. Prop P1.0	Group 1 Actual Prop P1.1	Superior. Ratio R0	Actual Ratio R1	Intra-Cluster Corr. ICC	Alpha
0.80086	44/100	44/100	0.6000	0.7200	0.7500	1.200	1.250	0.0020	0.050
0.81118	11/100	11/100	0.6000	0.7200	0.7800	1.200	1.300	0.0020	0.050
0.83039	5/100	5/100	0.6000	0.7200	0.8100	1.200	1.350	0.0020	0.050
0.86347	3/100	3/100	0.6000	0.7200	0.8400	1.200	1.400	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.

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Example 3 – Finding the Sample Size (Individuals within Clusters)

An agency would like to show the proportion of success of a new treatment greater that of the current treatment. Thirty doctors are available for the study. Fifteen will be randomly chosen to be trained to administer the new treatment. The remaining fifteen will continue to administer the current treatment. The new treatment will be considered superior if the proportion of success is at least 1.1 times that of the current treatment success. The agency would like to know the number of patients that need to be treated by each doctor to achieve 80% power for the superiority by a margin test if the actual ratio is 1.2. Various values for the intracluster correlation coefficient will be use since its true value is unknown. The current treatment has a success rate near 0.65. Alpha is set at 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 3** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Sample Size (M1)**
Higher Proportions Are	**Better (H1: P1/P2 > R0)**
Power	**0.80**
Alpha	**0.05**
K1 (Clusters in Group 1)	**15**
K2 (Clusters in Group 2)	**K1**
M2 (Items per Cluster in Group 2)	**M1**
R0 (Superiority Ratio)	**1.1**
R1 (Actual Ratio)	**1.2**
P2 (Group 2 Proportion)	**0.65**
ICC (Intracluster Correlation)	**0.001 to 0.01 by 0.001**

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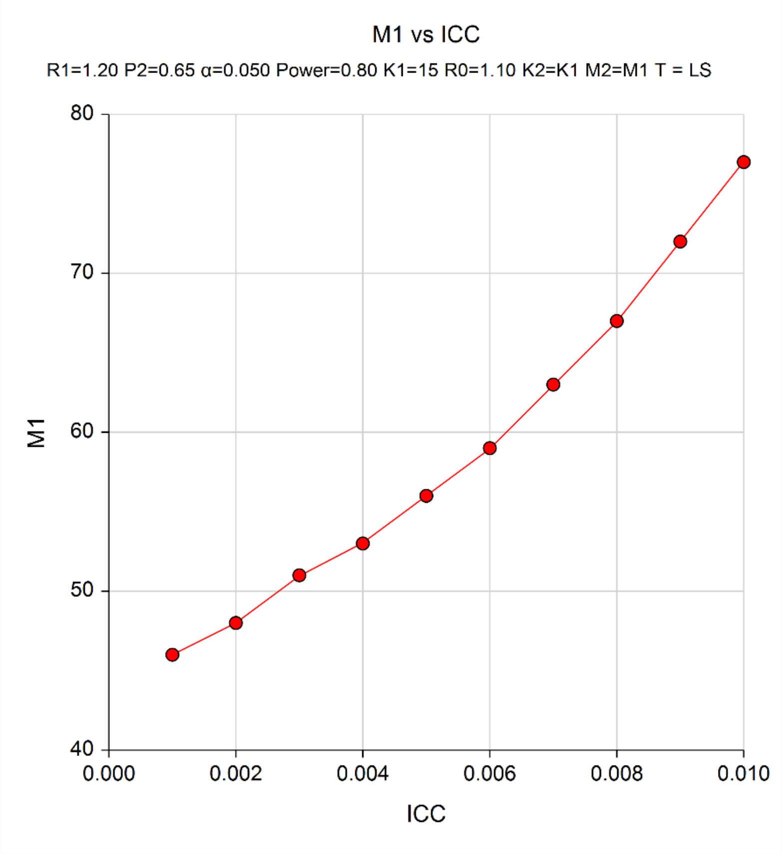
Output

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

Numeric Results

Numeric Results
Test Statistic: Likelihood Score Test (Farrington & Manning)
Hypotheses: H0: P1/P2 ≤ R0 vs. H1: P1/P2 > R0

Power	Group 1 Clusters/ Items K1/M1	Group 2 Clusters/ Items K2/M2	Group 2 Prop P2	Group 1 Superior. Prop P1.0	Group 1 Actual Prop P1.1	Superior. Ratio R0	Actual Ratio R1	Intra-Cluster Corr. ICC	Alpha
0.80314	15/46	15/46	0.6500	0.7150	0.7800	1.100	1.200	0.0010	0.050
0.80201	15/48	15/48	0.6500	0.7150	0.7800	1.100	1.200	0.0020	0.050
0.80571	15/51	15/51	0.6500	0.7150	0.7800	1.100	1.200	0.0030	0.050
0.80200	15/53	15/53	0.6500	0.7150	0.7800	1.100	1.200	0.0040	0.050
0.80237	15/56	15/56	0.6500	0.7150	0.7800	1.100	1.200	0.0050	0.050
0.80116	15/59	15/59	0.6500	0.7150	0.7800	1.100	1.200	0.0060	0.050
0.80246	15/63	15/63	0.6500	0.7150	0.7800	1.100	1.200	0.0070	0.050
0.80179	15/67	15/67	0.6500	0.7150	0.7800	1.100	1.200	0.0080	0.050
0.80243	15/72	15/72	0.6500	0.7150	0.7800	1.100	1.200	0.0090	0.050
0.80101	15/77	15/77	0.6500	0.7150	0.7800	1.100	1.200	0.0100	0.050



The number of patients that should be seen by each doctor ranges from 46 to 77, depending on the intracluster correlation coefficient.

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Example 4 – 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.

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