Chapter 241

Equivalence Tests for the Ratio of Two Proportions in a Cluster-Randomized Design

Introduction

This module provides power analysis and sample size calculation for equivalence 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

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

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

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

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 214, "Equivalence 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

Test Type

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

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 this group. 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*.

Effect Size – Equivalence Ratios (P1.0/P2)

R0.U & R0.L (Upper & Lower Equivalence Ratio)

Specify the *margin of equivalence* by specifying the largest ratio (P1/P2) above (R0.U), and below (R0.L), which will still result in the conclusion of equivalence. As long as the actual ratio is between these two values, the difference between the proportions is not said to be large enough to be of practical importance.

The values of R0.U must be greater than 1 and the values of R0.L must be less than 1. R0.L can be set to '1/R0.U', which is most often desired.

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: P1.0U = R0.U x P2.

You may enter a range of values for R0.U such as *1.1 1.5 1.8* or *1.1 to 2.1 by 0.2*.

Note that if you enter values for R0.L (other than '1/R0.U'), they are used in pairs with the values of R0.U. Thus, the first values of R0.U and R0.L are used together, then the second values of each are used, and so on.

R0.L must be between 0 and 1. R0.U must be greater than 1. Neither can take on the value 1.

Effect Size – Actual Ratio (P1.1/P2)

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. In equivalence trials, this ratio is often set to 1.

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 (Group 2 Proportion)

Specify the value of P2, the control, baseline, or standard group's proportion. The null hypothesis is that the two proportions differ by a specified amount (See *Specify Group 1 Proportion using* below).

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 from 0 to 1, typical values range from 0.002 to 0.05.

Example 1 – Finding Power

A study is being designed to establish the equivalence of a new treatment compared to the current treatment. Historically, the standard treatment has enjoyed a 60% cure rate. The new treatment reduces the seriousness of certain side effects that occur with the standard treatment. Thus, the new treatment will be adopted even if it is slightly less effective than the standard treatment. The researchers will recommend adoption of the new treatment if the rate ratio of treatment to control is between 0.75 and 1.25.

The researchers will recruit patients from various hospitals. All patients at a particular hospital will receive the same treatment. They anticipate enlisting an average of 50 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 two, one-sided tests proposed by Farrington and Manning when the number of clusters per groups ranges from 2 to 10. They want to investigate the behavior of this test when the actual cure rate of the new treatment ranges from 60% to 66% (rate ratio = 1.0 to 1.1). 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 **Equivalence 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 **Equivalence**, and then clicking on **Equivalence 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**
Test Type	**Likelihood Score (Farr. & Mann.)**
Alpha	**0.05**
K1 (Clusters in Group 1)	**2 4 6 8 10**
M1 (Items per Cluster in Group 1)	**50**
K2 (Clusters in Group 2)	**K1**
M2 (Items per Cluster in Group 2)	**M1**
R0.U (Upper Equivalence Ratio)	**1.25**
R0.L (Lower Equivalence Ratio)	**0.75**
R1 (Actual Ratio)	**1.0 1.05 1.1**
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 for Equivalence Tests for the Ratio of Two Proportions (Cluster-Randomized)
Test Statistic: Likelihood Score Test (Farrington & Manning)
H0: P1/P2 ≤ R0.L or P1/P2 ≥ R0.U.   H1: R0.L < P1/P2 = R1 < R0.U.

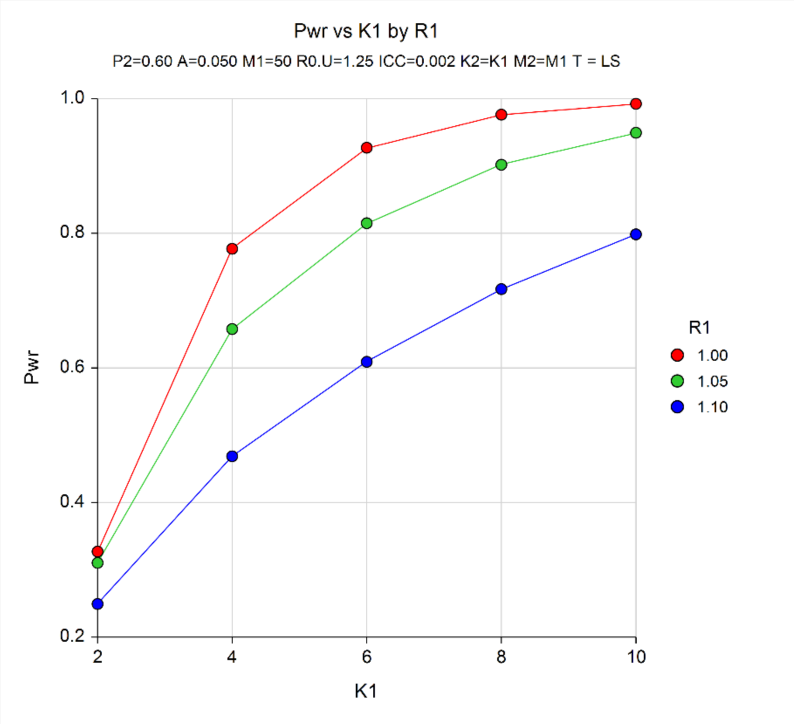
Power	Group 1 Clusters/ Items K1/M1	Group 2 Clusters/ Items K2/M2	Grp 2 Prop P2	Grp 1 Lower Equiv. Prop P1.0L	Grp 1 Upper Equiv. Prop P1.0U	Grp 1 Actual Prop P1.1	Lower Equiv. Ratio R0.L	Upper Equiv. Ratio R0.U	Actual Ratio R1	Intra-Cluster Corr. ICC	Alpha
0.32704	2/50	2/50	0.6000	0.4500	0.7500	0.6000	0.750	1.250	1.000	0.0020	0.050
0.77694	4/50	4/50	0.6000	0.4500	0.7500	0.6000	0.750	1.250	1.000	0.0020	0.050
0.92712	6/50	6/50	0.6000	0.4500	0.7500	0.6000	0.750	1.250	1.000	0.0020	0.050
0.97630	8/50	8/50	0.6000	0.4500	0.7500	0.6000	0.750	1.250	1.000	0.0020	0.050
0.99240	10/50	10/50	0.6000	0.4500	0.7500	0.6000	0.750	1.250	1.000	0.0020	0.050
0.31030	2/50	2/50	0.6000	0.4500	0.7500	0.6300	0.750	1.250	1.050	0.0020	0.050
0.65767	4/50	4/50	0.6000	0.4500	0.7500	0.6300	0.750	1.250	1.050	0.0020	0.050
0.81499	6/50	6/50	0.6000	0.4500	0.7500	0.6300	0.750	1.250	1.050	0.0020	0.050
0.90181	8/50	8/50	0.6000	0.4500	0.7500	0.6300	0.750	1.250	1.050	0.0020	0.050
0.94937	10/50	10/50	0.6000	0.4500	0.7500	0.6300	0.750	1.250	1.050	0.0020	0.050
0.24921	2/50	2/50	0.6000	0.4500	0.7500	0.6600	0.750	1.250	1.100	0.0020	0.050
0.46869	4/50	4/50	0.6000	0.4500	0.7500	0.6600	0.750	1.250	1.100	0.0020	0.050
0.60903	6/50	6/50	0.6000	0.4500	0.7500	0.6600	0.750	1.250	1.100	0.0020	0.050
0.71705	8/50	8/50	0.6000	0.4500	0.7500	0.6600	0.750	1.250	1.100	0.0020	0.050
0.79842	10/50	10/50	0.6000	0.4500	0.7500	0.6600	0.750	1.250	1.100	0.0020	0.050

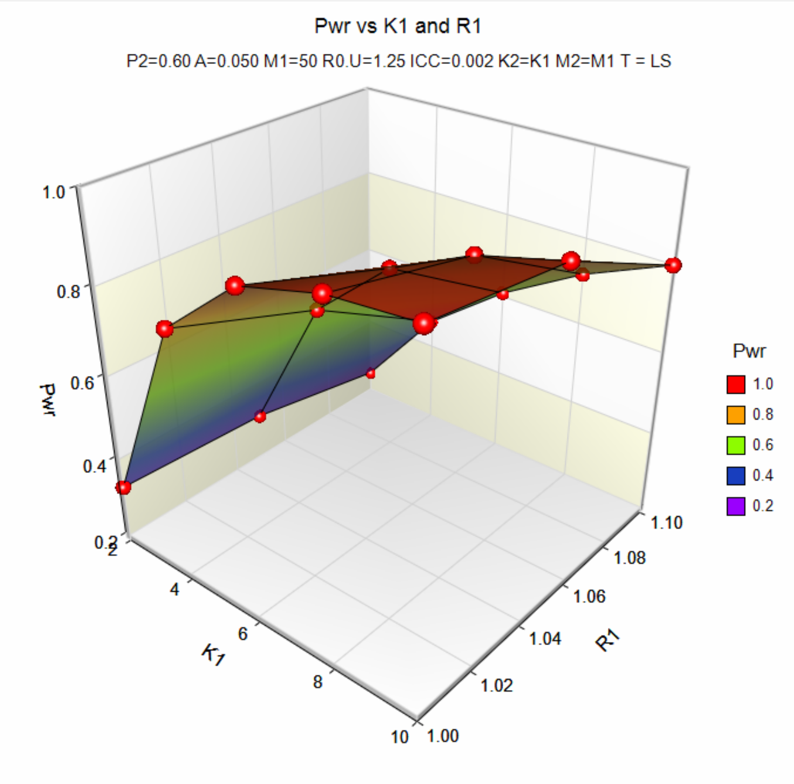
Report Definitions
Power is the probability of rejecting a false null hypothesis. It should be close to one.
K1 and K2 are the number of clusters in groups 1 and 2, respectively.
M1 and M2 are the average number of items (subjects) per cluster in groups 1 and 2, respectively.
P2 is the proportion for group 2. This is the standard, reference, baseline, or control group.
P1.0L is the smallest proportion for group 1 (treatment group) that still results in the conclusion of equivalence.
P1.0U is the largest proportion for group 1 (treatment group) that still results in the conclusion of equivalence.
R0.L = P1.0L/P2 is the smallest ratio that still results in the conclusion of equivalence.
R0.U = P1.0U/P2 is the largest ratio that still results in the conclusion of equivalence.
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 100 in group 1 and 100 in group 2, which were obtained by sampling 2 clusters with 50 subjects each in group 1 and 2 clusters with 50 subjects each in group 2, achieve 32.704% power to detect equivalence. The margin of equivalence, given in terms of the ratio of the proportions, extends from 0.750 to 1.250. The actual ratio of the proportions is 1.000. The group 2 proportion is 0.6000. The calculations assume that two, one-sided Likelihood Score Tests (Farrington & Manning) were used. 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.

Plots Section





The values from the table are displayed on the above charts. These charts give a quick look at the sample size 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 **Equivalence 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 **Equivalence**, and then clicking on **Equivalence 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)**
Test Type	**Likelihood Score (Farr. & Mann.)**
Power	**0.80**
Alpha	**0.05**
M1 (Items per Cluster in Group 1)	**50**
K2 (Clusters in Group 2)	**K1**
M2 (Items per Cluster in Group 2)	**M1**
R0.U (Upper Equivalence Ratio)	**1.25**
R0.L (Lower Equivalence Ratio)	**0.75**
R1 (Actual Ratio)	**1.0 1.05 1.1**
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 for Equivalence Tests for the Ratio of Two Proportions (Cluster-Randomized)
Test Statistic: Likelihood Score Test (Farrington & Manning)
H0: P1/P2 ≤ R0.L or P1/P2 ≥ R0.U. H1: R0.L < P1/P2 = R1 < R0.U.

Power	Group 1 Clusters/ Items K1/M1	Group 2 Clusters/ Items K2/M2	Grp 2 Prop P2	Grp 1 Lower Equiv. Prop P1.0L	Grp 1 Upper Equiv. Prop P1.0U	Grp 1 Actual Prop P1.1	Lower Equiv. Ratio R0.L	Upper Equiv. Ratio R0.U	Actual Ratio R1	Intra-Cluster Corr. ICC	Alpha
0.87247	5/50	5/50	0.6000	0.4500	0.7500	0.6000	0.750	1.250	1.000	0.0020	0.050
0.81499	6/50	6/50	0.6000	0.4500	0.7500	0.6300	0.750	1.250	1.050	0.0020	0.050
0.83073	11/50	11/50	0.6000	0.4500	0.7500	0.6600	0.750	1.250	1.100	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 – Finding Sample Size (Individuals within Clusters)

Continuing with the scenario given in Example 2, the researchers want to determine the number of individuals that they'll need to recruit in each hospital if they can enroll only 5 hospitals vs 10 in each group 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 **Equivalence 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 **Equivalence**, and then clicking on **Equivalence 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)**
Test Type	**Likelihood Score (Farr. & Mann.)**
Power	**0.80**
Alpha	**0.05**
K1 (Clusters in Group 1)	**5 10**
K2 (Clusters in Group 2)	**K1**
M2 (Items per Cluster in Group 2)	**M1**
R0.U (Upper Equivalence Ratio)	**1.25**
R0.L (Lower Equivalence Ratio)	**0.75**
R1 (Actual Ratio)	**1.0 1.05 1.1**
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 for Equivalence Tests for the Ratio of Two Proportions (Cluster-Randomized)
Test Statistic: Likelihood Score Test (Farrington & Manning)
H0: P1/P2 ≤ R0.L or P1/P2 ≥ R0.U. H1: R0.L < P1/P2 = R1 < R0.U.

Power	Group 1 Clusters/ Items K1/M1	Group 2 Clusters/ Items K2/M2	Grp 2 Prop P2	Grp 1 Lower Equiv. Prop P1.0L	Grp 1 Upper Equiv. Prop P1.0U	Grp 1 Actual Prop P1.1	Lower Equiv. Ratio R0.L	Upper Equiv. Ratio R0.U	Actual Ratio R1	Intra-Cluster Corr. ICC	Alpha
0.80732	5/42	5/42	0.6000	0.4500	0.7500	0.6000	0.750	1.250	1.000	0.0020	0.050
0.80397	10/20	10/20	0.6000	0.4500	0.7500	0.6000	0.750	1.250	1.000	0.0020	0.050
0.80349	5/59	5/59	0.6000	0.4500	0.7500	0.6300	0.750	1.250	1.050	0.0020	0.050
0.80523	10/28	10/28	0.6000	0.4500	0.7500	0.6300	0.750	1.250	1.050	0.0020	0.050
0.80063	5/112	5/112	0.6000	0.4500	0.7500	0.6600	0.750	1.250	1.100	0.0020	0.050
0.80466	10/51	10/51	0.6000	0.4500	0.7500	0.6600	0.750	1.250	1.100	0.0020	0.050

If they can enroll 10 hospitals, then they need to recruit between 20 and 51 patients at each, depending on the actual cure rate ratio. If they can only enroll 5 hospitals, then they'll need to recruit many more patients… between 42 and 112.

Example 4 – Validation

We could not find an example of this type of analysis in the literature. Therefore, we will validate the procedure by comparing the results to those computed by the “Equivalence Tests for the Ratio of Two Proportions” procedure since both should give identical results for the same sample sizes when the ICC is set to zero. We ran the case when N1 = N2 = 200, P2 = 0.6, R0.U = 1.2, R0.L = 1/R0.U, R1 = 1, and Alpha = 0.05. In this procedure, set M1 = 1 and set K1 = 200. The Equivalence Tests for the Ratio of Two Proportions procedure calculates the power to be 0.43259 for the Likelihood Score (Farrington & Manning) test.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Equivalence 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 **Equivalence**, and then clicking on **Equivalence 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 4** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	Power
Test Type	Likelihood Score (Farr. & Mann.)
Alpha	0.05
K1 (Clusters in Group 1)	200
M1 (Items per Cluster in Group 1)	1
K2 (Clusters in Group 2)	K1
M2 (Items per Cluster in Group 2)	M1
R0.U (Upper Equivalence Ratio)	1.2
R0.L (Lower Equivalence Ratio)	1/R0.U
R1 (Actual Ratio)	1.0
P2 (Group 2 Proportion)	0.6
ICC (Intracluster Correlation)	0.0

Output

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

Numeric Results

Numeric Results for Equivalence Tests for the Ratio of Two Proportions (Cluster-Randomized)
Test Statistic: Likelihood Score Test (Farrington & Manning)
H0: P1/P2 ≤ R0.L or P1/P2 ≥ R0.U.   H1: R0.L < P1/P2 = R1 < R0.U.

Power	Group 1 Clusters/ Items K1/M1	Group 2 Clusters/ Items K2/M2	Grp 2 Prop P2	Grp 1 Lower Equiv. Prop P1.0L	Grp 1 Upper Equiv. Prop P1.0U	Grp 1 Actual Prop P1.1	Lower Equiv. Ratio R0.L	Upper Equiv. Ratio R0.U	Actual Ratio R1	Intra-Cluster Corr. ICC	Alpha
0.43259	200/1	200/1	0.6000	0.5000	0.7200	0.6000	0.833	1.200	1.000	0.0000	0.050

The power computed by this procedure is also 0.43259 when ICC = 0.