Chapter 454

Mixed Models Tests for Two Means in a Cluster-Randomized Design

Introduction

This procedure calculates power and sample size for a two-level hierarchical mixed model in which clusters (groups, classes, hospitals, etc.) of subjects are measured one time (cross-sectional) on a continuous variable. The goal of the study is to compare the two group means.

In this design, the subjects are the level one units and the clusters are the level two units. All subjects in a particular cluster (level two unit) receive one of two possible interventions. This intervention is selected at random. Note that a companion procedure power analyzes the other case in which the randomization occurs for the level one units (the subjects).

Note that this procedure provides results for fixed cluster sizes. Another procedure provides results for variable cluster sizes.

Technical Details

Our formulation comes from Ahn, Heo, and Zhang (2015), chapter 5, section 5.3.1, pages 151-154. The hierarchical mixed model that is adopted is

$$Y_{ij} = \beta_0 + \delta X_{ij} + u_i + e_{ij}$$

where

Y_{ij}	is the continuous response of the j^{th} subject in the i^{th} cluster.
β_0	is the fixed intercept.
δ	is the treatment effect of interest. It is the difference between the two treatment means.
X_{ij}	is an indicator variable that is = 1 if cluster i is assigned to group 1, and 0 otherwise.
u_i	is a random effect (subject-specific intercept) term for the i^{th} cluster the is distributed as $N(0, \sigma_u^2)$.
e_{ij}	is a random effect for the j^{th} subject in the i^{th} cluster that is distributed as $N(0, \sigma_e^2)$.
σ_u^2	is variance of the level two (cluster) random effects.
σ_e^2	is variance of the level one (subject) random effects.
σ^2	is the variance of Y, where $\sigma^2 = \sigma_u^2 + \sigma_e^2$.
ρ	is the intraclass correlation (ICC), where $\rho = Corr\left(Y_{ij}, Y_{ij'}\right) = (\sigma_u^2/\sigma^2) = \sigma_u^2/(\sigma_u^2 + \sigma_e^2)$.

The test of significance of the X_{ij} term in the mixed model analysis is the test statistic of interest. It tests the difference of the two treatment means. Since these are asymptotic results, the specific type of mixed model is not stated.

Assume that $\delta = \mu_1 - \mu_2$ is to be tested using a z-test (large sample). The statistical hypotheses are $H_0: \delta = 0$ vs. $H_a: \delta \neq 0$. When $K_1 = K_2$, the test statistic, given by

$$z = \frac{(\bar{Y}_1 - \bar{Y}_2)\sqrt{K_1 M}}{\sigma\sqrt{2(1 + (M-1)\rho)}}$$

where

$$\bar{Y}_g = \frac{1}{K_1 M}\sum_{i=1}^{K_1}\sum_{j=1}^{M} Y_{ij}\,, g = 1,2$$

has an approximate normal distribution.

When $K_1 = K_2$, the power can be calculated using

$$Power = \Phi\left\{\frac{\delta}{\sigma}\sqrt{K_1 M/[2(1+(M-1)\rho]} - \Phi(1-\alpha/2)\right\}$$

Procedure Options

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

Design Tab

The Design tab contains most of the parameters and options that you will be concerned with.

Solve For

Solve For

This option specifies the parameter to be solved for from the other parameters. The parameters that may be selected are *δ*, *Power*, *K1*, and *M*.

Under most situations, you will select either *Power* to calculate power or *K1* to calculate the number of clusters. Occasionally, you may want to fix the number of clusters and find the necessary cluster size.

Note that the value selected here always appears as the vertical axis on the charts.

The program is set up to calculate power directly. To find appropriate values of the other parameters, a binary search is made using an iterative procedure until an appropriate value is found. This search considers integer values of M only.

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

If your only interest is in determining the appropriate sample size for a confidence interval, set power to 0.5.

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. Usually, the value of 0.05 is used for alpha and this has become a standard. 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 – Number of Clusters and Subjects – Number of Clusters

K1 (Number of Group 1 Clusters)

This is the number of clusters in group 1, which we have designated as the treatment group. The sample size for this group is equal to the number of clusters times the number of subjects per cluster.

Range

This value must be a positive number.

It can be a decimal (fractional) number such as '12.7'. The resulting value of N1 will be rounded to an integer.

List

You can enter a list of values such as "10 20 30". A separate analysis will be run for each element in the list.

K2 (Number of Group 2 Clusters)

This is the number of clusters in group 2, which we have designated as the control group. The sample size for this group is equal to the number of clusters times the number of subjects per cluster.

Range

This value must be a positive number.

It can be a decimal (fractional) number such as '12.7'. The resulting value of N2 will be rounded to an integer.

Using Multiples of K1

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 enter the leading "1". For example, all of the following are valid entries:

10K1 2K1 0.5K1 K1.

List

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

Sample Size – Number of Clusters and Subjects – Number of Subjects Per Cluster

M (Number of Subjects Per Cluster)

This is the average number of items (subjects) per cluster in both groups.

Range

This value must be a positive number that is at least 1.

It can be a decimal (fractional) number such as '2.7'. The resulting values of N1 and N2 will be rounded to integers.

List

You can use a list of values such as "100 150 200". A separate analysis will be run for each element in the list.

Effect Size

δ (Mean Difference = μ1 – μ2)

Enter a value for the difference between the means of groups 1 and 2 at which the design is powered. That is, the power is the probability of detecting a difference of at least this amount. This value is not necessarily the true mean difference. Rather, it is the difference you want to be able to detect.

Range

δ can be any non-zero value (positive or negative). Since this procedure uses a is a two-sided test statistic, you will get the same result with either positive or negative values.

The difference has the same scale as the standard deviation.

Notes

You can enter a single value such as 10 or a series of values such as 10 20 30 or 5 to 50 by 5.

When a series of values is entered, PASS will generate a separate calculation result for each value of the series.

σ (Standard Deviation)

Enter the subject-to-subject standard deviation. This standard deviation applies for both groups.

Note that σ must be a positive number. You can enter a single value such as *5* or a series of values such as *1 3 5 7 9* or *1 to 9 by 2*.

Press the small 'σ' button to the right to obtain calculation options for estimating the standard deviation.

ρ (Intracluster Correlation, ICC)

This is the value of the intracluster (or intraclass) correlation coefficient. It may be interpreted as the correlation between any two observations in the same cluster. It may also be thought of as the proportion of the variation in response that can be accounted for by the between-cluster variation.

Possible values are from 0 to just below 1. Typical values are between 0.0001 and 0.05.

You may enter a single value or a list of values.

Example 1 – Calculating Power

Suppose that a two-level hierarchical design is planned in which there will be only one measurement per subject and treatments will be applied to clusters (level-two units). The analysis will be a mixed model of continuous data. The following parameter settings are to be used for the power analysis: δ = 0.5; σ = 1; ρ = 0.01; M = 5 or 10; ICC = 0.01; α = 0.05; and $K1$ and $K2$ = 5 to 20 by 5.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. 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**
Alpha	**0.05**
K1 (Number of Group 1 Clusters)	**5 10 15 20**
K2 (Number of Group 2 Clusters)	**K1**
M (Number of Subjects Per Cluster)	**5 10**
δ (Mean Difference = μ1 - μ2)	**0.5**
σ (Standard Deviation)	**1**
ρ (Intracluster Correlation, ICC)	**0.01**

Annotated Output

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

Numeric Results

Numeric Results

Power	Total Subject Count N	Subject Count Grp 1 N1	Subject Count Grp 2 N2	Cluster Count Grp 1 K1	Cluster Count Grp 2 K2	Cluster Size M	Diff μ1-μ2 δ	Std Dev σ	ICC ρ	Alpha
0.4104	50	25	25	5	5	5	0.50	1.00	0.010	0.050
0.6681	100	50	50	5	5	10	0.50	1.00	0.010	0.050
0.6885	100	50	50	10	10	5	0.50	1.00	0.010	0.050
0.9231	200	100	100	10	10	10	0.50	1.00	0.010	0.050
0.8514	150	75	75	15	15	5	0.50	1.00	0.010	0.050
0.9856	300	150	150	15	15	10	0.50	1.00	0.010	0.050
0.9341	200	100	100	20	20	5	0.50	1.00	0.010	0.050
0.9977	400	200	200	20	20	10	0.50	1.00	0.010	0.050

References

Ahn, C., Heo, M., and Zhang, S. 2015. Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research. CRC Press. New York.

Report Definitions

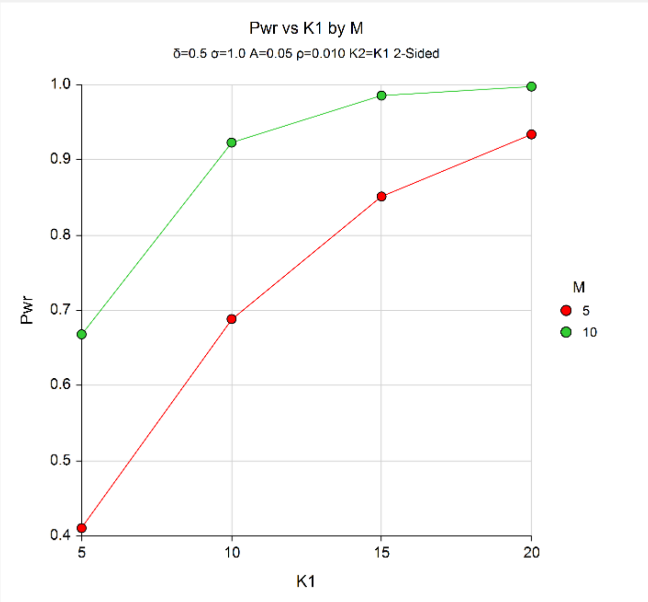
Power is the probability of rejecting a false null hypothesis. It should be close to one.
N, N1, and N2 are the total number of subjects and the number in groups 1 and 2, respectively.
K1 and K2 are the number of clusters in groups 1 and 2, respectively.
M is the average number of items (subjects) per cluster.
δ is the mean difference (μ1 - μ2) in the response at which the power is calculated.
σ is the standard deviation of the subject responses.
ρ (ICC) is the intracluster correlation.
Alpha is the probability of rejecting a true null hypothesis, that is, rejecting when the means are actually equal.

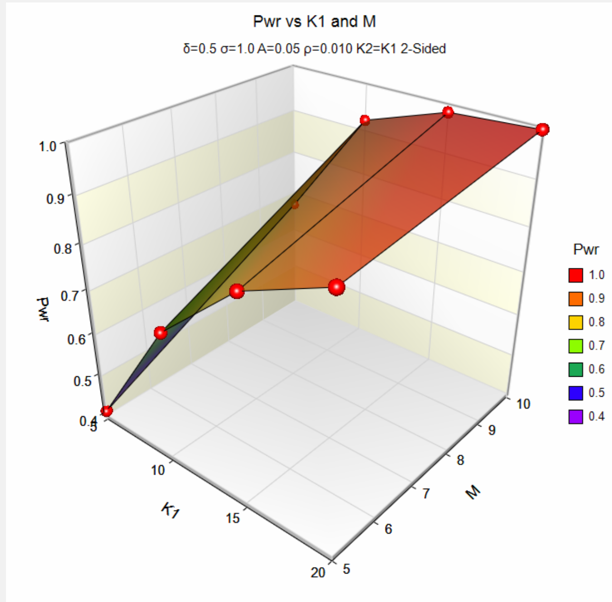
Summary Statements

Sample sizes of 25 in group one and 25 in group two, which were obtained from a cluster-randomized design with 5 clusters in group one and 5 clusters in group two with an average of 5 subjects per cluster, achieve 41% power to detect a difference between the group means of at least 1. The standard deviation of subjects is 1.00. The intracluster correlation coefficient is 0.010. A test based on a mixed-model analysis is anticipated at a significance level of 0.050.

This report shows the power for each of the scenarios.

Plots Section





These plots show the power versus the number of clusters for the two cluster size values.

Example 2 – Calculating Sample Size (Number of Clusters)

Continuing with the last example, suppose the researchers want to determine the number of clusters needed to achieve 90% power for both values of M.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. 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	**K1 (Number of Clusters)**
Power	**0.90**
Alpha	**0.05**
K2 (Number of Group 2 Clusters)	**K1**
M (Number of Subjects Per Cluster)	**5 10**
δ (Mean Difference = μ1 - μ2)	**0.5**
σ (Standard Deviation)	**1**
ρ (Intracluster Correlation, ICC)	**0.01**

Output

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

Numeric Results

Numeric Results

Power	Total Subject Count N	Subject Count Grp 1 N1	Subject Count Grp 2 N2	Cluster Count Grp 1 K1	Cluster Count Grp 2 K2	Cluster Size M	Diff μ1-μ2 δ	Std Dev σ	ICC ρ	Alpha
0.9081	180	90	90	18	18	5	0.50	1.00	0.010	0.050
0.9231	200	100	100	10	10	10	0.50	1.00	0.010	0.050

This report shows the power for each of the scenarios.

Example 3 – Calculating Sample Size (Number of Subjects)

Continuing with the last example, suppose the researchers want to determine the number of subjects needed to achieve 90% power for all values of K1.

Note that this calculation is sensitive to the value of ICC in that if ICC is too large, no value of M is possible.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. 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	**M (Number of Subjects Per Cluster)**
Power	**0.90**
Alpha	**0.05**
K1 (Number of Group 1 Clusters)	**5 10 15 20**
K2 (Number of Group 2 Clusters)	**K1**
δ (Mean Difference = μ1 - μ2)	**0.5**
σ (Standard Deviation)	**1**
ρ (Intracluster Correlation, ICC)	**0.01**

Output

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

Numeric Results

Numeric Results

Power	Total Subject Count N	Subject Count Grp 1 N1	Subject Count Grp 2 N2	Cluster Count Grp 1 K1	Cluster Count Grp 2 K2	Cluster Size M	Diff μ1-μ2 δ	Std Dev σ	ICC ρ	Alpha
0.9110	210	105	105	5	5	21	0.50	1.00	0.010	0.050
0.9231	200	100	100	10	10	10	0.50	1.00	0.010	0.050
0.9055	180	90	90	15	15	6	0.50	1.00	0.010	0.050
0.9341	200	100	100	20	20	5	0.50	1.00	0.010	0.050

This report shows the values of M needed for each scenario.

Example 4 – Validation using Ahn, Heo, and Zhang (2015)

Ahn, Heo, and Zhang (2015) page 154 provide a table in which several scenarios are reported. We will validate this procedure by duplicating two of the table entries. The following parameter settings are used for the power analysis: Power = 0.80; δ = 0.4; σ = 1; ρ = 0.01; M = 10 or 20; ICC = 0.1; and α = 0.05. The reported values of $K1$ and $K2$ are 19 and 15.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. 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**.

Design Tab

Solve For .... **K1 (Number of Clusters)**
Power... **0.8**
Alpha.. **0.05**
K2 (Number of Group 2 Clusters)........... **K1**
M (Number of Subjects Per Cluster)....... **10 20**
δ (Mean Difference = μ1 - μ2) **0.4**
σ (Standard Deviation) **1**
ρ (Intracluster Correlation, ICC)............. **0.1**

Output

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

Numeric Results

Numeric Results

Power	Total Subject Count N	Subject Count Grp 1 N1	Subject Count Grp 2 N2	Cluster Count Grp 1 K1	Cluster Count Grp 2 K2	Cluster Size M	Diff μ1-μ2 δ	Std Dev σ	ICC ρ	Alpha
0.8074	380	190	190	19	19	10	0.40	1.00	0.100	0.050
0.8204	600	300	300	15	15	20	0.40	1.00	0.100	0.050

PASS calculates the same values of K1: 19 and 15.