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 that 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 $\rho = Corr(Y_{ij}, Y_{ij'}) = (\sigma_u^2/\sigma^2) = \sigma_u^2/(\sigma_u^2 + \sigma_e^2)$.

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

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

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

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	**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**

Output

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

Numeric Reports

Numeric Results

Solve For: Power
Groups: 1 = Treatment, 2 = Control
Difference: δ = μ1 - μ2

	Number of Subjects			Number of Clusters			Number of Subjects per Cluster	Mean Difference	Standard Deviation	Intracluster Correlation	
Power	Group 1 N1	Group 2 N2	Total N	Group 1 K1	Group 2 K2	Total K	M	δ	σ	ρ	Alpha
0.4104	25	25	50	5	5	10	5	0.5	1	0.01	0.05
0.6681	50	50	100	5	5	10	10	0.5	1	0.01	0.05
0.6885	50	50	100	10	10	20	5	0.5	1	0.01	0.05
0.9231	100	100	200	10	10	20	10	0.5	1	0.01	0.05
0.8514	75	75	150	15	15	30	5	0.5	1	0.01	0.05
0.9856	150	150	300	15	15	30	10	0.5	1	0.01	0.05
0.9341	100	100	200	20	20	40	5	0.5	1	0.01	0.05
0.9977	200	200	400	20	20	40	10	0.5	1	0.01	0.05

Power The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N1, N2, and N The number of subjects in groups 1, 2, and both, respectively.
K1, K2, and K The number of clusters in groups 1, 2, and both, respectively.
M The average number of items (subjects) per cluster.
δ The mean difference in the response at which the power is calculated. δ = μ1 - μ2.
σ The standard deviation of the subject responses.
ρ The intracluster correlation (ICC).
Alpha The probability of rejecting a true null hypothesis.

Summary Statements

A 2-group cluster-randomized design will have subjects in clusters with random assignment of clusters to each of the 2 groups. This design will be used to test the difference of two means (μ1 - μ2), using the appropriate term of the hierarchical mixed-effects model, with a Type I error rate (α) of 0.05. The standard deviation of subjects is assumed to be 1. The correlation of subjects within a cluster (intracluster correlation) is assumed to be 0.01. To detect a mean difference (μ1 - μ2) of 0.5, with 5 clusters in Group 1 and 5 clusters in Group 2, and with 5 subjects in each cluster (for a grand total of 50 subjects), the power is 0.4104.

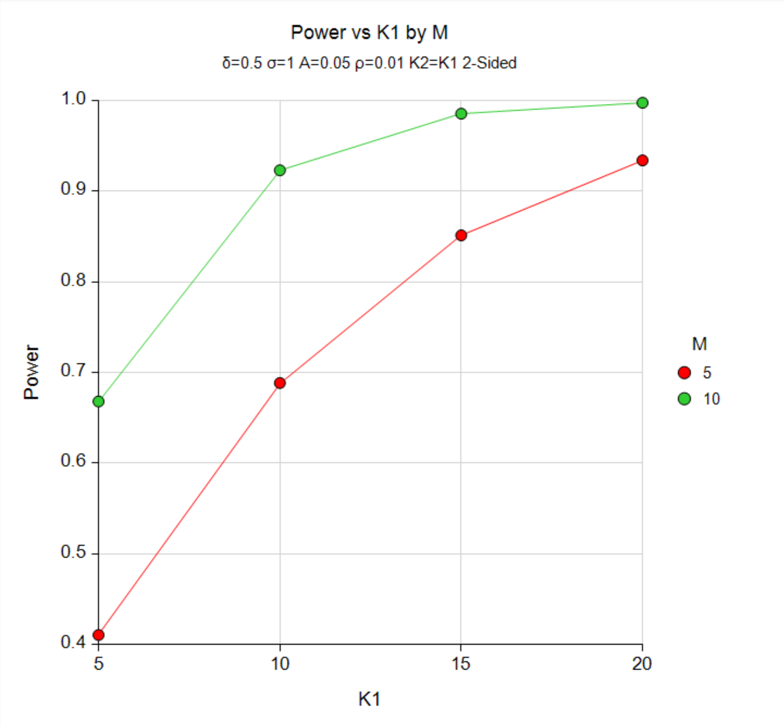
References

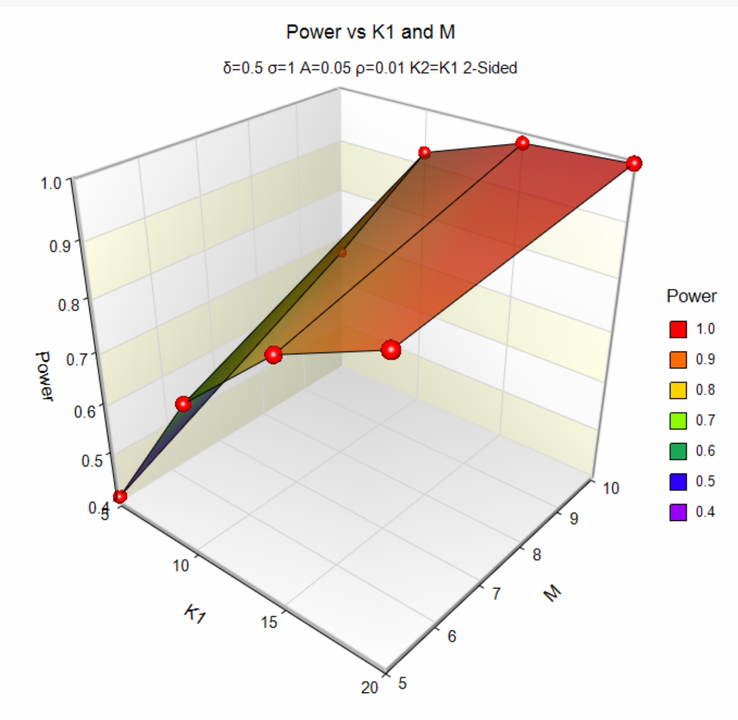
Ahn, C., Heo, M., and Zhang, S. 2015. Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research. CRC Press. New York.

This report shows the power for each of the scenarios.

Plots Section

Plots





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

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 .... **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

Solve For: K1 (Number of Clusters)
Groups: 1 = Treatment, 2 = Control
Difference: δ = μ1 - μ2

	Number of Subjects			Number of Clusters							
Power	Group 1 N1	Group 2 N2	Total N	Group 1 K1	Group 2 K2	Total K	Number of Subjects per Cluster M	Mean Difference δ	Standard Deviation σ	Intracluster Correlation ρ	Alpha
0.9081	90	90	180	18	18	36	5	0.5	1	0.01	0.05
0.9231	100	100	200	10	10	20	10	0.5	1	0.01	0.05

This report shows the power for each of the scenarios.

Example 3 – Calculating Sample Size (Number of Subjects per Cluster)

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

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 3** 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 .... **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

Solve For: M (Number of Subjects Per Cluster)
Groups: 1 = Treatment, 2 = Control
Difference: δ = μ1 - μ2

	Number of Subjects			Number of Clusters			Number of Subjects per Cluster	Mean Difference	Standard Deviation	Intracluster Correlation	
Power	Group 1 N1	Group 2 N2	Total N	Group 1 K1	Group 2 K2	Total K	M	δ	σ	ρ	Alpha
0.9110	105	105	210	5	5	10	21	0.5	1	0.01	0.05
0.9231	100	100	200	10	10	20	10	0.5	1	0.01	0.05
0.9055	90	90	180	15	15	30	6	0.5	1	0.01	0.05
0.9341	100	100	200	20	20	40	5	0.5	1	0.01	0.05

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

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 4** 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 .... **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

Solve For: K1 (Number of Clusters)
Groups: 1 = Treatment, 2 = Control
Difference: δ = μ1 - μ2

	Number of Subjects			Number of Clusters			Number of				
Power	Group 1 N1	Group 2 N2	Total N	Group 1 K1	Group 2 K2	Total K	Subjects per Cluster M	Mean Difference δ	Standard Deviation σ	Intracluster Correlation ρ	Alpha
0.8074	190	190	380	19	19	38	10	0.4	1	0.1	0.05
0.8204	300	300	600	15	15	30	20	0.4	1	0.1	0.05

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