

Chapter 369

Mixed Models Tests for Interaction in a 2x2 Factorial 2-Level Hierarchical Design (Level-1 Randomization)

Introduction

This procedure calculates power and sample size for a two-level hierarchical mixed model in which clusters of subjects are measured one time (cross-sectional) on a continuous variable. The study uses a two-by-two factorial design with two binary factors, each with two possible values (0 and 1). This results in four treatment arms. The goal of the study is to test the significance of the two-way interaction between the two factors.

In this two-level hierarchical design, the subjects are the level-one units and the clusters are the level-two units. Each subject is individually randomized to receive one of the four possible treatments. Hence, all four treatments occur within each level-2 unit.

Technical Details

Our formulation comes from Ahn, Heo, and Zhang (2015), chapter 5, section 5.5.2, pages 170-172. The hierarchical mixed model that is adopted is

$$Y_{ij} = \beta_0 + \delta_{X(1)}X_{ij} + \delta_{Z(1)}Z_{ij} + \delta_{XZ(1)}X_{ij}Z_{ij} + u_i + e_{ij}$$

where

- Y_{ij} is the continuous response of the j^{th} subject in the i^{th} cluster.
- β_0 is the fixed intercept.
- $\delta_{X(1)}$ is the treatment effect of X.
- X_{ij} is an indicator variable that is = 1 if cluster i is assigned to receive the X intervention and 0 otherwise.
- $\delta_{Z(1)}$ is the treatment effect of Z.

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- Z_{ij} is an indicator variable that is = 1 if cluster i is assigned to receive the Z intervention and 0 otherwise.
- $\delta_{XZ(1)}$ is the interaction effect of X and Z. In terms of the four group means, this effect is equal to $(\mu_{1,1} - \mu_{1,0}) - (\mu_{0,1} - \mu_{0,0})$.
- u_i is a random effect 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(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). This is the correlation between any two level-1 units within a specific level-2 unit.
- K is the number of level-2 units in the study.
- $M_{0,0}$ is the number of level-1 units per level-2 unit for which X = 0 and Z = 0.
- $M_{0,1}$ is the number of level-1 units per level-2 unit for which X = 0 and Z = 1.
- $M_{1,0}$ is the number of level-1 units per level-2 unit for which X = 1 and Z = 0.
- $M_{1,1}$ is the number of level-1 units per level-2 unit for which X = 1 and Z = 1.

The test of significance of the product $X_{ij}Z_{ij}$ term in the mixed model analysis is the test statistic of interest. It tests whether the difference between the two levels of one factor at the high level of the other factor is equal to the corresponding difference at the low level of the second factor.

Assume that $\delta_{XZ(1)}$ is to be tested using a Wald test. The statistical hypotheses are $H_0: \delta_{XZ(2)} = 0$ vs. $H_a: \delta_{XZ(2)} \neq 0$.

The power is calculated using

$$Power = \Phi \left\{ \frac{\delta_{XZ(2)}}{\sigma} \sqrt{\frac{K}{f \left(\frac{1}{M_{0,0}} + \frac{1}{M_{1,1}} + \frac{1}{M_{1,0}} + \frac{1}{M_{0,1}} \right)}} - \Phi(1 - \alpha/2) \right\}$$

where $f = 1 - \rho$.

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 (Interaction), Power, K, and M00.

Under most situations, you will select either Power to calculate power or K00 to calculate the number of level-2 units. Occasionally, you may want to fix the number of level-2 units and find the necessary average number of level-1 units.

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 K00 and 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 Level-1 and Level-2 Units

K (Level-2 Unit Count)

This is the number of level-2 units (e.g., classes) in the study. This value must be a positive integer that is at least 1.

List

You can use a list of values such as "8 12 16". A separate analysis will be run for each element in the list.

M00 (Group 00 Count (X=0, Z=0))

This is the number of level-1 units (e.g., subjects) per level 2 unit in group 00, which we have designated as the group in which both of the binary factors X and Z are zero (i.e., control group). The total sample size (number of level-1 units) of this group is equal to $K \times M00$.

Each of the factors X and Z have two levels: 0 (no intervention) and 1 (intervention). Thus, in this group in which $X = 0$ and $Z = 0$, neither of the interventions occur. Hence, this is called the control group.

This value must be a positive 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.

M01 (Group 01 Count (X=0, Z=1))

This is the number of level-1 units (e.g., classes) per level 2 unit in group 01, which we have designated as the group in which X is zero and Z is one (i.e., only factor two is active). The total sample size (number of level-1 units) for this group is $K \times M01$.

Each of the factors X and Z have two levels: 0 (no intervention) and 1 (intervention). Thus, in this group in which $X = 0$ and $Z = 1$, an intervention occurs for the second factor but not the first.

Using Multiples of M00

If you simply want a multiple of the value for group 00, enter the multiple followed by "M00", with no blanks. If you want to use M00 directly, you do not have to enter a leading "1". For example, all of the following are valid entries: M00 10M00 2M00 0.5M00.

List

You can use a list of values such as "10 20 30" or "M00 2M00 3M00".

M10 (Group 01 Count (X=1, Z=0))

This is the number of level-1 units (e.g., classes) per level 2 unit in group 10, which we have designated as the group in which X is one and Z is zero (i.e., only factor one is active). The total sample size (number of level-1 units) for this group is $K \times M10$.

Each of the factors X and Z have two levels: 0 (no intervention) and 1 (intervention). Thus, in this group in which $X = 1$ and $Z = 0$, an intervention occurs for the first factor but not the second.

Using Multiples of M00

If you simply want a multiple of the value for group 00, enter the multiple followed by "M00", with no blanks. If you want to use M00 directly, you do not have to enter a leading "1". For example, all of the following are valid entries: M00 10M00 2M00 0.5M00.

Mixed Models Tests for Interaction in a 2x2 Factorial 2-Level Hierarchical Design (Level-1 Randomization)**List**

You can use a list of values such as "10 20 30" or "M00 2M00 3M00".

M11 (Group 11 Count (X=1, Z=1))

This is the number of level-1 units (e.g., classes) per level 2 unit in group 11, which we have designated as the group in which X is one and Z is one (i.e., both factors are active). The total sample size (number of level-1 units) for this group is $K \times M11$.

Each of the factors X and Z have two levels: 0 (no intervention) and 1 (intervention). Thus, in this group in which $X = 1$ and $Z = 1$, an intervention occurs for both factors.

Using Multiples of M00

If you simply want a multiple of the value for group 00, enter the multiple followed by "M00", with no blanks. If you want to use M00 directly, you do not have to enter a leading "1". For example, all of the following are valid entries: M00 10M00 2M00 0.5M00.

List

You can use a list of values such as "10 20 30" or "M00 2M00 3M00".

Effect Size **δ (Interaction = $(\mu_{11} - \mu_{10}) - (\mu_{01} - \mu_{00})$)**

Enter a value for the interaction among the four group means at which the study is to be powered. That is, the power is the probability of detecting a difference of at least this amount. This value is not necessarily the true interaction difference. Rather, it is the interaction difference that you want to be able to detect.

Interaction

The interaction is the difference of the differences. That is, it is constructed as the difference between the two differences $(\mu_{11} - \mu_{10})$ and $(\mu_{01} - \mu_{00})$. It is the failure of the two factors to act independently of each other.

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

Syntax

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 all 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 (Intraclass Correlation, ICC)

This is the value of the intraclass (or intracluster) correlation coefficient. It may be interpreted as the correlation between any two level-1 observations from the same level-2 unit.

Possible values are from 0 to just below 1. Typical values are between 0.0001 and 0.5. 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 two interventions. Each intervention will be whether one of two drugs is administered. There will be only one measurement per subject and each subject (level-1 unit) will be randomized to a group individually. The analysis will be a mixed model of continuous data using the model given earlier in this chapter. The following parameter settings are to be used for the power analysis: $\delta = 7$; $\sigma = 9.7$; $\rho = 0.06$; $K = 4$ or 6 ; $\alpha = 0.05$; and $M00 = M01 = M10 = M11 = 5$ to 20 by 5 . Find the power of each combination of parameter settings.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Mixed Models Tests for Interaction in a 2x2 Fact. 2-Level Hier. Design (Level-1 Rand.)** 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**.

<u>Option</u>	<u>Value</u>
Design Tab	
Solve For	Power
Alpha.....	0.05
K (Level-2 Unit Count)	4 6
M00 (Group 00 Count (X=0, Z=0))	5 10 15 20
M01 (Group 01 Count (X=0, Z=1))	M00
M10 (Group 10 Count (X=1, Z=0))	M00
M11 (Group 11 Count (X=1, Z=1))	M00
δ (Interaction = $(\mu_{11} - \mu_{10}) - (\mu_{01} - \mu_{00})$)	7
σ (Standard Deviation)	9.7
ρ (Intraclass Correlation, ICC)	0.06

Annotated Output

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

Numeric Results

Numeric Results for an Interaction in a 2x2 Factorial

	Total Level 1 Count	Level 2 Count	Grp(0,0) Level 1 Count	Grp(0,1) Level 1 Count	Grp(1,0) Level 1 Count	Grp(1,1) Level 1 Count	Inter Diff δ	Std Dev σ	ICC ρ	Alpha
Power	N	K	M00	M01	M10	M11				
0.3838	80	4	5	5	5	5	7.00	9.70	0.060	0.050
0.6531	160	4	10	10	10	10	7.00	9.70	0.060	0.050
0.8219	240	4	15	15	15	15	7.00	9.70	0.060	0.050
0.9145	320	4	20	20	20	20	7.00	9.70	0.060	0.050
0.5313	120	6	5	5	5	5	7.00	9.70	0.060	0.050
0.8219	240	6	10	10	10	10	7.00	9.70	0.060	0.050
0.9419	360	6	15	15	15	15	7.00	9.70	0.060	0.050
0.9829	480	6	20	20	20	20	7.00	9.70	0.060	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.

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Report Definitions

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

N is the total number of level-1 units in the study.

K is the number of level-2 units in the study.

M00 (Group 00 Count (F1=0, F2=0)) is the number of level-1 units per level-2 unit in Group 00 (F1 = 0 and F2 = 0).

M01 (Group 01 Count (F1=0, F2=1)) is the number of level-1 units per level-2 unit in Group 01 (F1 = 0 and F2 = 1).

M10 (Group 10 Count (F1=1, F2=0)) is the number of level-1 units per level-2 unit in Group 10 (F1 = 1 and F2 = 0).

M11 (Group 11 Count (F1=1, F2=1)) is the number of level-1 units per level-2 unit in Group 11 (F1 = 1 and F2 = 1).

δ is the interaction difference $(\mu_{11} - \mu_{10}) - (\mu_{01} - \mu_{00})$ at which the power is calculated.

σ is the standard deviation of the subject responses.

ρ (ICC) is the intraclass correlation among level-1 units within a single level-2 unit.

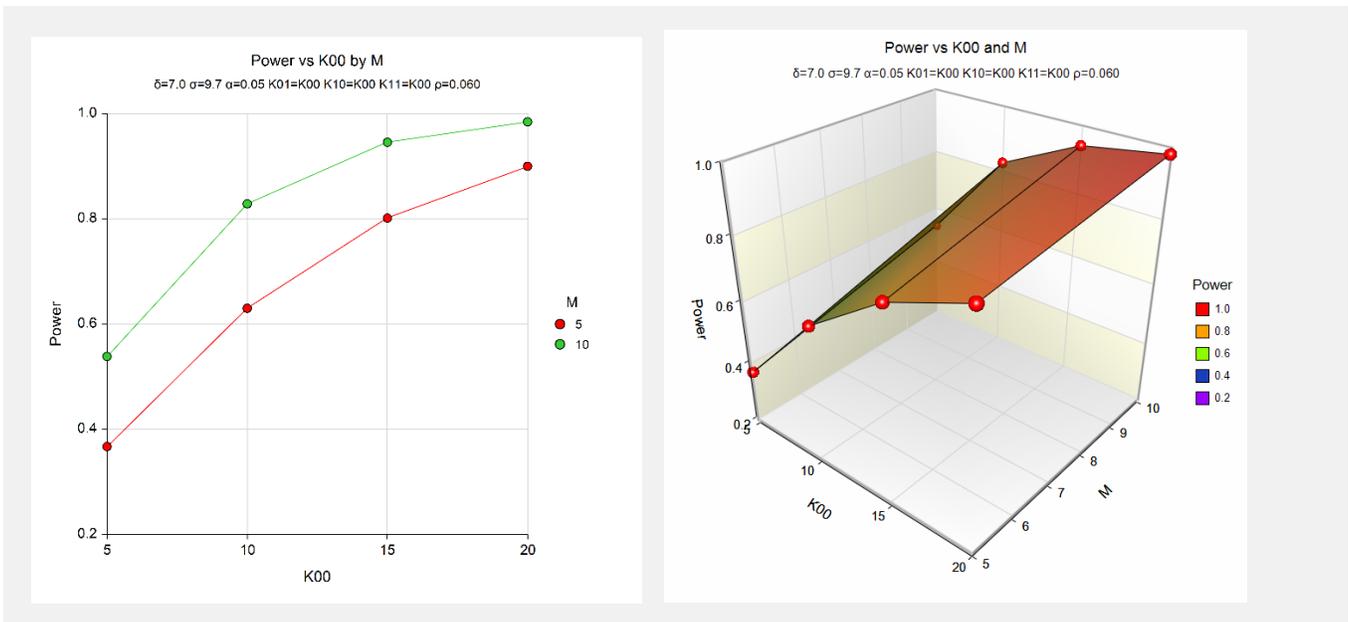
Alpha is the probability of rejecting a true null hypothesis, that is, rejecting when the means are actually equal.

Summary Statements

A total sample size of 80 level-1 units were obtained by sampling 4 level-2 units and then, from each level-2 unit, sampling 5 level-1 units in group 00, 5 level-1 units in group 01, 5 level-1 units in group 10, and 5 level-1 units in group 11. This sample achieves 38% power to detect an interaction difference among the group means of at least 7.00. This interaction difference was formed from the four group means using the following formula: $\delta = (\mu_{11} - \mu_{10}) - (\mu_{01} - \mu_{00})$. The standard deviation of subjects is 9.70. The intraclass correlation coefficient is 0.060. 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 for the various parameter settings.

Example 2 – Calculating Sample Size (M00)

Continuing with the last example, suppose the researchers want to determine the value of M00 needed to achieve 90% power for both values of K.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Mixed Models Tests for Interaction in a 2x2 Fact. 2-Level Hier. Design (Level-1 Rand.)** 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**.

<u>Option</u>	<u>Value</u>
Design Tab	
Solve For	M00 (Group 00 Count of Level-1 Units)
Power.....	0.90
Alpha.....	0.05
K (Level-2 Unit Count)	4 6
M01 (Group 01 Count (X=0, Z=1))	M00
M10 (Group 10 Count (X=1, Z=0))	M00
M11 (Group 11 Count (X=1, Z=1))	M00
δ (Interaction = $(\mu_{11} - \mu_{10}) - (\mu_{01} - \mu_{00})$)	7
σ (Standard Deviation)	9.7
ρ (Intraclass Correlation, ICC).....	0.06

Output

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

Numeric Results

Numeric Results for an Interaction in a 2x2 Factorial										
	Total Level 1 Count	Level 2 Count	Grp(0,0) Level 1 Count	Grp(0,1) Level 1 Count	Grp(1,0) Level 1 Count	Grp(1,1) Level 1 Count	Inter Diff	Std Dev	ICC	Alpha
Power	N	K	M00	M01	M10	M11	δ	σ	ρ	
0.9005	304	4	19	19	19	19	7.00	9.70	0.060	0.050
0.9077	312	6	13	13	13	13	7.00	9.70	0.060	0.050

This report shows the power for each of the scenarios.

Example 3 – Validation using Ahn, Heo, and Zhang (2015)

Ahn, Heo, and Zhang (2015) page 173 provide a table in which several scenarios are reported. We will validate this procedure by duplicating the top entry. The following parameter settings are used for the power analysis: Power = 0.80; $\delta = 0.4$; $\sigma = 1$; $\rho = 0.1$; M00, M01, M10, M11 are 10; and $\alpha = 0.05$. The value of K is found to be 18 and the attained power at 0.807.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Mixed Models Tests for Interaction in a 2x2 Fact. 2-Level Hier. Design (Level-1 Rand.)** 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**.

<u>Option</u>	<u>Value</u>
Design Tab	
Solve For	K (Level-2 Unit Count)
Power.....	0.80
Alpha.....	0.05
M00 (Group 00 Count (X=0, Z=0))	10
M01 (Group 01 Count (X=0, Z=1))	M00
M10 (Group 10 Count (X=1, Z=0))	M00
M11 (Group 11 Count (X=1, Z=1))	M00
δ (Interaction = $(\mu_{11} - \mu_{10}) - (\mu_{01} - \mu_{00})$)	0.4
σ (Standard Deviation)	1
ρ (Intraclass Correlation, ICC).....	0.1

Output

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

Numeric Results

Numeric Results for an Interaction in a 2x2 Factorial										
	Total		Grp(0,0)	Grp(0,1)	Grp(1,0)	Grp(1,1)				
	Level 1	Level 2	Level 1	Level 1	Level 1	Level 1	Inter	Std	ICC	
	Count	Count	Count	Count	Count	Count	Diff	Dev	ρ	Alpha
Power	N	K	M00	M01	M10	M11	δ	σ	ρ	Alpha
0.8074	720	18	10	10	10	10	0.40	1.00	0.100	0.050

PASS also calculates the value of K to be 18 and the power at 0.8074.