Chapter 370

Mixed Models Tests for Interaction in a 2×2 Factorial 2-Level Hierarchical Design (Level-2 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. All subjects in a particular cluster receive one of four possible treatments. Each treatment is a different combination of the two interventions.

Technical Details

Our formulation comes from Ahn, Heo, and Zhang (2015), chapter 5, section 5.5.1, pages 167-170. The hierarchical mixed model that is adopted is

$$Y_{ij} = \beta_0 + \delta_{X(2)}X_{ij} + \delta_{Z(2)}Z_{ij} + \delta_{XZ(2)}X_{ij}Z_{ij} + u_i + e_{ij}$$

where

Y_{ij} is the continuous response of the j^{th} subject in the i^{th} cluster.

β_0 is the fixed intercept.

$\delta_{X(2)}$ 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.

$\delta_{Z(2)}$ is the treatment effect of Z.

Z_{ij} is an indicator variable that is = 1 if cluster *i* is assigned to receive the Z intervention and 0 otherwise.

$\delta_{XZ(2)}$ 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 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(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.

$K_{0,0}$ is the number of level-2 units for which X = 0 and Z = 0.

$K_{0,1}$ is the number of level-2 units for which X = 0 and Z = 1.

$K_{1,0}$ is the number of level-2 units for which X = 1 and Z = 0.

$K_{1,1}$ is the number of level-2 units for which X = 1 and Z = 1.

M is the average number of level-1 units per level-2 unit.

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 $\delta_{XZ(2)}$ 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

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

where $f = 1 + (M - 1)\rho$.

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, K00, and M.

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

K00 (Group 00 Count (X=0, Z=0))

This is the number of level-2 units (e.g., classes) 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 for this group is equal to the number of level-2 units times the average number of level-1 (e.g., students) units per level-2 unit.

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

This value must be a positive integer.

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

K01 (Group 01 Count (X=0, Z=1))

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

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

Using Multiples of K00

If you simply want a multiple of the value for group 00, enter the multiple followed by "K00", with no blanks. If you want to use K00 directly, you do not have to enter a leading "1".

For example, all of the following are valid entries: 10K00 2K00 0.5K00 K00.

List

You can use a list of values such as "10 20 30" or "K00 2K00 3K00".

K10 (Group 01 Count (X=1, Z=0))

This is the number of level-2 units (e.g., classes) in group 10, which we have designated as the group in which X is one). The total sample size for this group is equal to the number of level-2 units times the average number of level-1 units per level-2 unit.

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

Using Multiples of K00

If you simply want a multiple of the value for group 00, enter the multiple followed by "K00", with no blanks. If you want to use K00 directly, you do not have to enter a leading "1".

For example, all of the following are valid entries: 10K00 2K00 0.5K00 K00.

List

You can use a list of values such as "10 20 30" or "K00 2K00 3K00".

K11 (Group 11 Count (X=1, Z=1))

This is the number of level-2 units (e.g., classes) in group 11, which we have designated as the group in which X is one and Z is one. The total sample size for this group is equal to the number of level-2 units times the average number of level-1 units per level-2 unit.

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

Using Multiples of K00

If you simply want a multiple of the value for group 00, enter the multiple followed by "K00", with no blanks. If you want to use K00 directly, you do not have to enter a leading "1".

For example, all of the following are valid entries: 10K00 2K00 0.5K00 K00.

List

You can use a list of values such as "10 20 30" or "K00 2K00 3K00".

M (Level-1 Unit Count Per Level-2 Unit)

This is the average number of level-1 units (e.g., subjects) per level-2 unit (e.g., class) in all four groups.

This value must be a positive number that is at least 1. It can be a decimal (fractional) number such as '2.7'.

List

You can use a list of values such as "10 15 20". A separate analysis will be run for each element in the list.

Effect Size

δ (Interaction = (μ11 - μ10) - (μ01 - μ00))

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 (μ11 - μ10) and (μ01 - μ00). 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 the four treatments will be applied to whole clusters (level-two units). 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: δ = 7; σ = 9.7; ρ = 0.06; M = 5 or 10; α = 0.05; and K00 = K01 = K10 = K11 = 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 2×2 Fact. 2-Level Hier. Design (Level-2 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**.

Option	Value
Design Tab	
Solve For	**Power**
Alpha	**0.05**
K00 (Group 00 Count (X=0, Z=0))	**5 10 15 20**
K01 (Group 01 Count (X=0, Z=1))	**K00**
K10 (Group 10 Count (X=1, Z=0))	**K00**
K11 (Group 11 Count (X=1, Z=1))	**K00**
M (Level-1 Unit Count Per Level-2 Unit)	**5 10**
δ (Interaction = (μ11 - μ10) - (μ01 - μ00))	**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 2×2 Factorial

Power	Total Level 1 Count N	Grp(0,0) Level 2 Count K00	Grp(0,1) Level 2 Count K01	Grp(1,0) Level 2 Count K10	Grp(1,1) Level 2 Count K11	Level 1 Count M	Inter Diff δ	Std Dev σ	ICC ρ	Alpha
0.3670	100	5	5	5	5	5	7.00	9.70	0.060	0.050
0.5382	200	5	5	5	5	10	7.00	9.70	0.060	0.050
0.6298	200	10	10	10	10	5	7.00	9.70	0.060	0.050
0.8283	400	10	10	10	10	10	7.00	9.70	0.060	0.050
0.8013	300	15	15	15	15	5	7.00	9.70	0.060	0.050
0.9453	600	15	15	15	15	10	7.00	9.70	0.060	0.050
0.8998	400	20	20	20	20	5	7.00	9.70	0.060	0.050
0.9843	800	20	20	20	20	10	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.

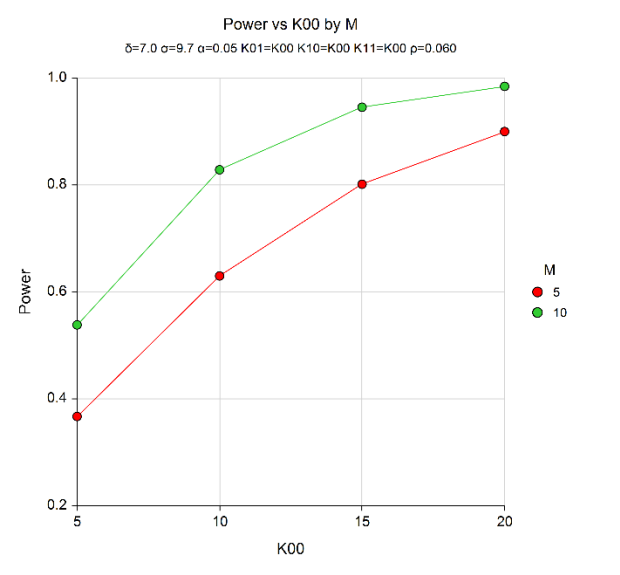
Mixed Models Tests for Interaction in a 2×2 Factorial 2-Level Hierarchical Design (Level-2 Randomization)

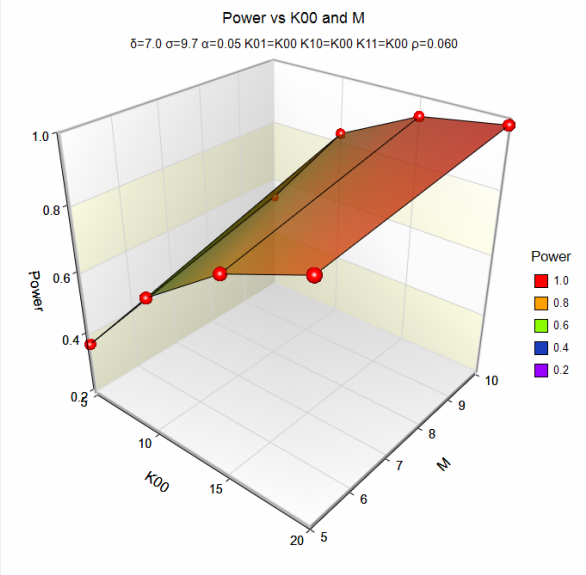
Report Definitions
Power is the probability of rejecting a false null hypothesis. It should be close to one.
N is the total number of level-1 units in the study.
K00 (Group 00 Count (F1=0, F2=0)) is the number of level-2 units in Group 00 (group in which F1 = 0 and F2 = 0).
K01 (Group 01 Count (F1=0, F2=1)) is the number of level-2 units in Group 01 (group in which F1 = 0 and F2 = 1).
K10 (Group 10 Count (F1=1, F2=0)) is the number of level-2 units in Group 10 (group in which F1 = 1 and F2 = 0).
K11 (Group 11 Count (F1=1, F2=1)) is the number of level-2 units in Group 11 (group in which F1 = 1 and F2 = 1).
M is the average number of level-1 units per level-2 unit.
δ is the interaction difference (μ11 - μ10) - (μ01 - μ00) 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 100 level-1 units, which were obtained by sampling 5 level-2 units in group 00, 5 level-2 units in group 01, 5 level-2 units in group 10, and 5 level-2 units in group 11 with an average of 5 level-1 units per level-2 unit, achieve 37% power to detect an interaction difference among the group means of at least 7.00. 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 (K00)

Continuing with the last example, suppose the researchers want to determine the value of K00 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 **Mixed Models Tests for Interaction in a 2×2 Fact. 2-Level Hier. Design (Level-2 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**.

Option	Value
Design Tab	
Solve For	**K00 (Group 00 Count of Level-2 Units)**
Power	**0.90**
Alpha	**0.05**
K01 (Group 01 Count (X=0, Z=1))	**K00**
K10 (Group 10 Count (X=1, Z=0))	**K00**
K11 (Group 11 Count (X=1, Z=1))	**K00**
M (Level-1 Unit Count Per Level-2 Unit)	**5 10**
δ (Interaction = (μ11 - μ10) - (μ01 - μ00))	**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 2×2 Factorial

Power	Total Level 1 Count N	Grp(0,0) Level 2 Count K00	Grp(0,1) Level 2 Count K01	Grp(1,0) Level 2 Count K10	Grp(1,1) Level 2 Count K11	Level 1 Count M	Inter Diff δ	Std Dev σ	ICC ρ	Alpha
0.9131	420	21	21	21	21	5	7.00	9.70	0.060	0.050
0.9123	520	13	13	13	13	10	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 170 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; $\delta = 0.4$; $\sigma = 1$; $\rho = 0.1$; $M = 10$; and $\alpha = 0.05$. The reported value of K00, K01, K10, K11 is 38 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 2×2 Fact. 2-Level Hier. Design (Level-2 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**.

Option	Value
Design Tab	
Solve For	**K00 (Group 00 Count of Level-2 Units)**
Power	**0.80**
Alpha	**0.05**
K01 (Group 01 Count (X=0, Z=1))	**K00**
K10 (Group 10 Count (X=1, Z=0))	**K00**
K11 (Group 11 Count (X=1, Z=1))	**K00**
M (Level-1 Unit Count Per Level-2 Unit)	**10**
δ (Interaction = (μ11 - μ10) - (μ01 - μ00))	**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 2×2 Factorial

Power	Total Level 1 Count N	Grp(0,0) Level 2 Count K00	Grp(0,1) Level 2 Count K01	Grp(1,0) Level 2 Count K10	Grp(1,1) Level 2 Count K11	Level 1 Count M	Inter Diff δ	Std Dev σ	ICC ρ	Alpha
0.8074	1520	38	38	38	38	10	0.40	1.00	0.100	0.050

PASS also calculates the value of K00 to be 38 and the power at 0.8074.