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 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.

$K_{0,0}$ 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

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

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

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

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**
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**

Output

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

Numeric Reports

Numeric Results

Solve For: Power

		Number of Level-2 Units									
Power	Total Sample Size N	Group 00 K00	Group 01 K01	Group 10 K10	Group 11 K11	Total K	Number of Level-1 Units per Level-2 Unit M	Interaction Difference δ	Standard Deviation σ	Intraclass Correlation ρ	Alpha
0.3670	100	5	5	5	5	20	5	7	9.7	0.06	0.05
0.5382	200	5	5	5	5	20	10	7	9.7	0.06	0.05
0.6298	200	10	10	10	10	40	5	7	9.7	0.06	0.05
0.8283	400	10	10	10	10	40	10	7	9.7	0.06	0.05
0.8013	300	15	15	15	15	60	5	7	9.7	0.06	0.05
0.9453	600	15	15	15	15	60	10	7	9.7	0.06	0.05
0.8998	400	20	20	20	20	80	5	7	9.7	0.06	0.05
0.9843	800	20	20	20	20	80	10	7	9.7	0.06	0.05

Level-2 Unit	A level-2 unit is a set of level-1 units. For example, the level-2 units might be clusters or classrooms and the level-1 units might be subjects or students within a level-2 unit.
Level-1 Unit	The first type of unit in a hierarchical model. For example, subjects (level-1) within clusters (level-2).
X	The first binary factor in the study. It has two levels: 0 and 1.
Z	The second binary factor in the study which also has two levels: 0 and 1.
Power	The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
Group	Each possible factor combination becomes a group. The means of the four groups are compared in the analysis.
N	The total number of level-1 units in the study. For example, the number of subjects.
K00	The number of level-2 units in group 00. This is the treatment group in which X = 0 and Z = 0.
K01	The number of level-2 units in group 01. This is the treatment group in which X = 0 and Z = 1.
K10	The number of level-2 units in group 10. This is the treatment group in which X = 1 and Z = 0.
K11	The number of level-2 units in group 11. This is the treatment group in which X = 1 and Z = 1.
K	The total number of level-2 units in the study.
M	The average number of level-1 units per level-2 unit. For example, the number of subjects per cluster.
δ	The interaction difference is the component of the model being tested. For this specific interaction, δ = (μ11 - μ10) - (μ01 - μ00).
σ	The standard deviation of the level-1 responses.
ρ	The intraclass correlation (ICC) among level-1 units within a single level-2 unit.
Alpha	The probability of rejecting a true null hypothesis.

Summary Statements

A 2×2 factorial (X = 0,1 and Z = 0,1) 2-level hierarchical design will have level-1 units (e.g., students, subjects, or patients) in level-2 units (e.g., classes, clinics, or hospitals) with random assignment of level-2 units to each of the 4 treatment arms (Groups 00, 01, 10, and 11) (level-2 randomization). This design will be used to test the two-way interaction term (X × Z) of the linear mixed-effects model, with a Type I error rate (α) of 0.05. This interaction is formed from the four group means using the following formula: δ = (μ11 - μ10) - (μ01 - μ00). The standard deviation of responses (σ) is assumed to be 9.7 (where σ^2 equals the sum of the error term variance and the level-2 random intercept variance). The intraclass correlation coefficient of level-1 units is assumed to be 0.06. To detect a two-way interaction effect (δ) of at least 7, with 5 level-2 units in Group 00 (X = 0, Z = 0), 5 level-2 units in Group 01 (X = 0, Z = 1), 5 level-2 units in Group 10 (X = 1, Z = 0), and 5 level-2 units in Group 11 (X = 1, Z = 1), with 5 level-1 units in each level-2 unit (for a grand total of 100 level-1 units), the power is 0.367.

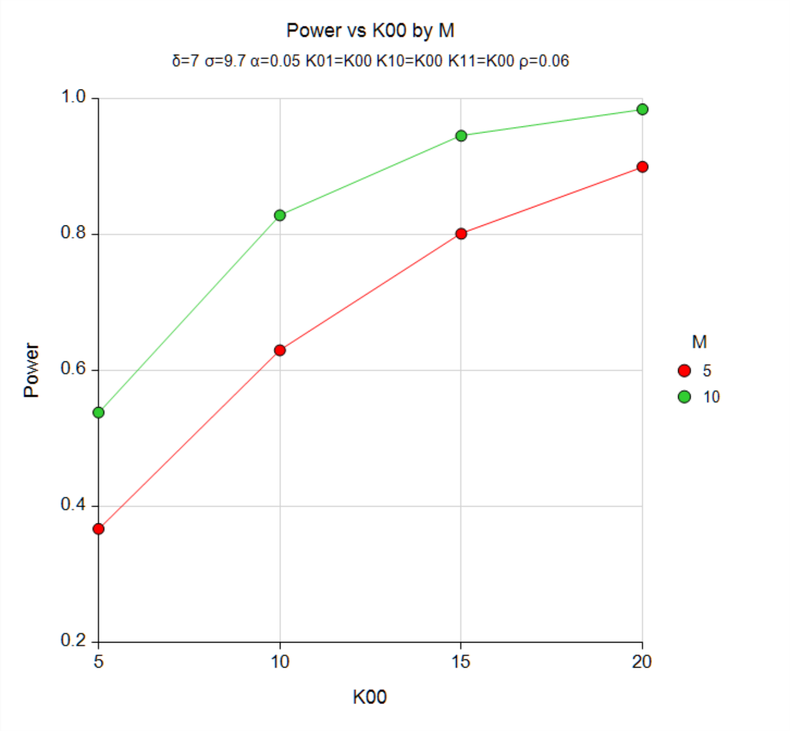
References

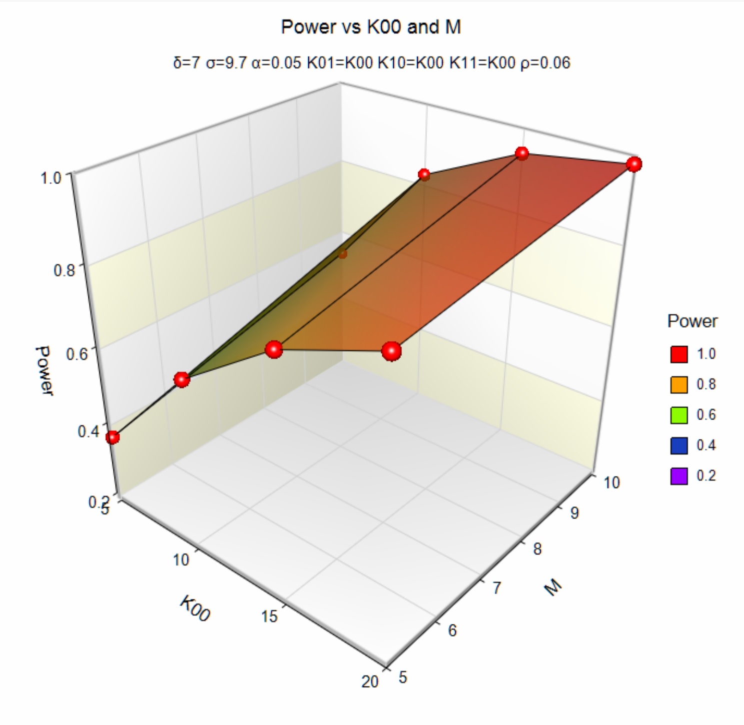
Ahn, C., Heo, M., and Zhang, S. 2015. Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research. CRC Press. New York.

This report shows the power for each of the scenarios.

Plots Section

Plots





These plots show the power 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

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 .... **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

Solve For: K00 (Group 00 Count of Level-2 Units)

Power	Total Sample Size N	Number of Level-2 Units: Group 00 K00	Group 01 K01	Group 10 K10	Group 11 K11	Total K	Number of Level-1 Units per Level-2 Unit M	Interaction Difference δ	Standard Deviation σ	Intraclass Correlation ρ	Alpha
0.9131	420	21	21	21	21	84	5	7	9.7	0.06	0.05
0.9123	520	13	13	13	13	52	10	7	9.7	0.06	0.05

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; δ = 0.4; σ = 1; ρ = 0.1; M = 10; and α = 0.05. The reported value of K00, K01, K10, K11 is 38 and the attained power at 0.807.

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 .... **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

Solve For: K00 (Group 00 Count of Level-2 Units)

Power	Total Sample Size N	Number of Level-2 Units Group 00 K00	Group 01 K01	Group 10 K10	Group 11 K11	Total K	Number of Level-1 Units per Level-2 Unit M	Interaction Difference δ	Standard Deviation σ	Intraclass Correlation ρ	Alpha
0.8074	1520	38	38	38	38	152	10	0.4	1	0.1	0.05

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