Chapter 368

Mixed Models Tests for Interaction in a 2×2 Factorial 3-Level Hierarchical Design (Level-2 Randomization)

Introduction

This procedure calculates power and sample size for a three-level hierarchical mixed model which is randomized at the **second** level. The cross-sectional study uses a 2-by-2 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 three-level hierarchical design, the level-1 units are nested in the level-2 units, which are nested in the level-3 units. For example, students might be nested in classes which are in turn nested within school.

This procedure is for cross-sectional (non-longitudinal) studies in which each subject is measured only one time.

In this case of level-2 randomization, each level-2 unit is randomly assigned to one of the four treatments combinations. All level-1 units within a specific level-2 unit receive the same interventions (treatment). For example, all students within a class receive the same treatment, but classes within a school might receive different treatments.

Technical Details

Our formulation comes from Ahn, Heo, and Zhang (2015), chapter 6, section 6.5.2, pages 213-216. The hierarchical mixed model that is adopted is

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

where

Y_{ijk} is the continuous response of the kth level-1 unit, within the jth level-2 unit, within the ith level-3 unit.

X_{ijk} is an indicator variable that is equal to "1" if the jth level-2 unit is assigned to receive intervention X and "0" otherwise. Thus, $X_{ijk} = Xj$ for all i and k.

Z_{ijk} is an indicator variable that is equal to "1" if the jth level-2 unit is assigned to receive intervention Z and "0" otherwise. Thus, $Z_{ijk} = Zj$ for all i and k.

β_0 is the fixed intercept.

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

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

$\delta_{XZ(2)}$ is the interaction effect of factors X and Z. In terms of the four group means, this effect is equal to $(\mu_{1,1} - \mu_{1,0}) - (\mu_{0,1} - \mu_{0,0})$. This is the term that is tested for this procedure.

u_i is the level-3 random intercept effect for the ith level-3 unit. It is distributed as $N(0, \sigma_3^2)$.

$u_{j(i)}$ is the level-2 random intercept effect for the $j(i)^{th}$ level-2 unit. It is distributed as $N(0, \sigma_2^2)$.

e_{ijk} is the level-1 random intercept effect that is distributed as $N(0, \sigma_e^2)$.

σ^2 is the variance of Y, where $\sigma^2 = \sigma_3^2 + \sigma_2^2 + \sigma_e^2$.

ρ_1 is the correlation among level-1 units which are in a particular level-2 unit.

ρ_2 is the correlation among level-2 units which are in a particular level-3 unit.

C is the number of level-3 units in the study.

$K_{0,0}$ 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 $f = 1 + (M - 1)\rho_1 - M\rho_2$.

Example 1 – Calculating Power

Suppose that a three-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 level-2 units. Five level-3 units are planned.

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: $\delta = 3$; $\sigma = 9.8$; $\rho_1 = 0.1$; $\rho_2 = 0.1$; $C = 5$; $M = 5$ or 10; $\alpha = 0.05$; 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**
C (Level 3 Units) **5**
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)) **3**
σ (Standard Deviation)...................................**9.8**
ρ1 (Correlation Among Level-1 Units)............**0.1**
ρ2 (Correlation Among Level-2 Units)............**0.05**

Output

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

Numeric Reports

Numeric Results

Solve For: Power

Power	Total Sample Size N	Number of Level-3 Units C	Number of Level-2 Units per Level-3 Unit					Number of Level-1 Units per Level-2 Unit M	Interaction δ	Standard Deviation σ	Correlation		
			Group 00 K00	Group 01 K01	Group 10 K10	Group 11 K11	Total K				Level 1 Units ρ1	Level 2 Units ρ2	Alpha
0.3579	500	5	5	5	5	5	20	5	3	9.8	0.1	0.05	0.05
0.5340	1000	5	5	5	5	5	20	10	3	9.8	0.1	0.05	0.05
0.6167	1000	5	10	10	10	10	40	5	3	9.8	0.1	0.05	0.05
0.8245	2000	5	10	10	10	10	40	10	3	9.8	0.1	0.05	0.05
0.7893	1500	5	15	15	15	15	60	5	3	9.8	0.1	0.05	0.05
0.9433	3000	5	15	15	15	15	60	10	3	9.8	0.1	0.05	0.05
0.8909	2000	5	20	20	20	20	80	5	3	9.8	0.1	0.05	0.05
0.9834	4000	5	20	20	20	20	80	10	3	9.8	0.1	0.05	0.05

Power   The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N   The total number of Level-1 units in the study.
C   The number of Level-3 units in the study.
K00   The number of Level-2 units per Level-3 unit in Group (0,0) (the group in which X = 0 and Z = 0).
K01   The number of Level-2 units per Level-3 unit in Group (0,1) (the group in which X = 0 and Z = 1).
K10   The number of Level-2 units per Level-3 unit in Group (1,0) (the group in which X = 1 and Z = 0).
K11   The number of Level-2 units per Level-3 unit in Group (1,1) (the group in which X = 1 and Z = 1).
K   The total number of Level-2 units.
M   The average number of Level-1 units per Level-2 unit.
δ   The interaction difference at which the power is calculated. $\delta = (\mu 11 - \mu 10) - (\mu 01 - \mu 00)$.
σ   The standard deviation of the subject responses.
ρ1   The intraclass correlation among Level-1 units within a single Level-2 unit.
ρ2   The intraclass correlation among Level-2 units within a single Level-3 unit.
Alpha   The probability of rejecting a true null hypothesis.

Summary Statements

A 2×2 factorial (X = 0,1 and Z = 0,1) 3-level hierarchical design will have level-1 units (e.g., students, subjects, or patients) in level-2 units (e.g., classes, clinics, or hospitals) in level-3 units (e.g., schools, regions, or networks) 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: $\delta = (\mu 11 - \mu 10) - (\mu 01 - \mu 00)$. The standard deviation of responses (σ) is assumed to be 9.8 (where σ² equals the sum of the error term variance, the level-2 random intercept variance, and the level-3 random intercept variance). The intraclass correlation coefficient of level-1 units is assumed to be 0.1, and the intraclass correlation coefficient of level-2 units is assumed to be 0.05. To detect a two-way interaction effect (δ) of at least 3, with 5 level-3 units, and within each level-3 unit, 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 500 level-1 units), the power is 0.3579.
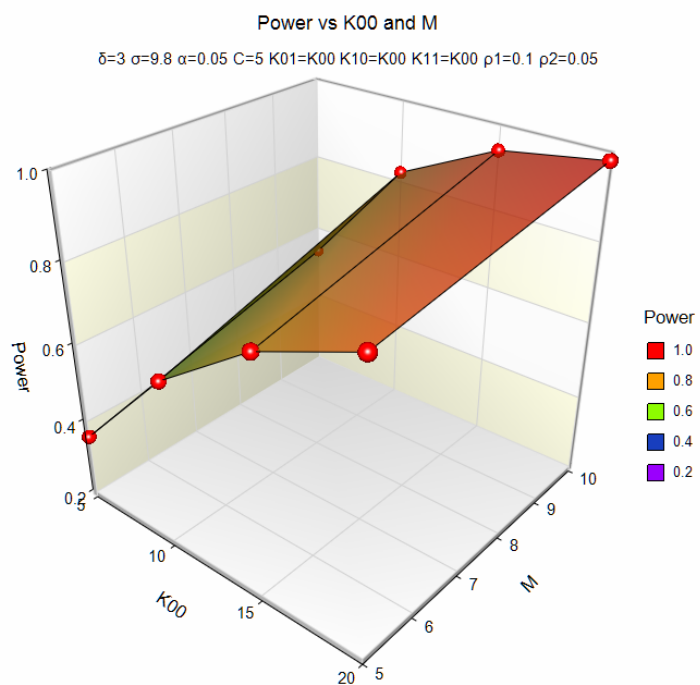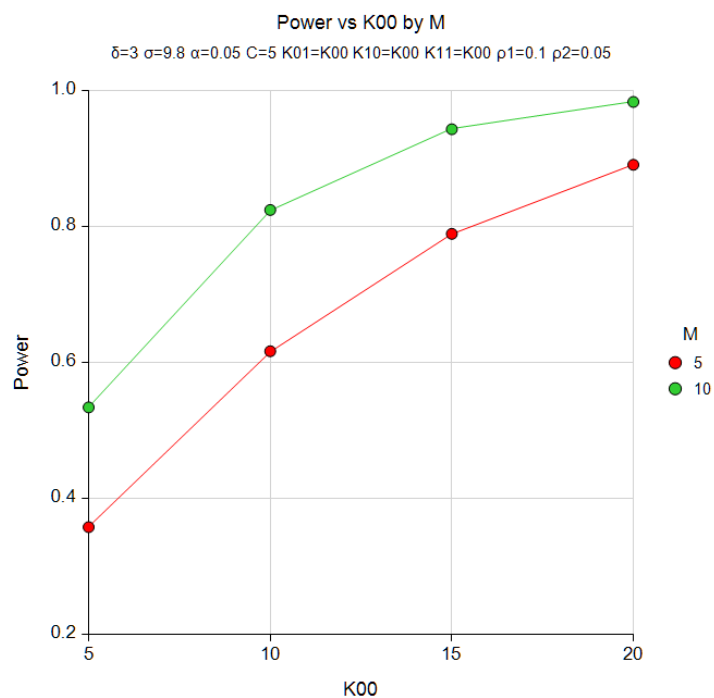
References

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
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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**
C (Level 3 Units) **5**
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))......**3**
σ (Standard Deviation)...................................**9.8**
ρ1 (Correlation Among Level-1 Units)............**0.1**
ρ2 (Correlation Among Level-2 Units)............**0.05**

Output

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

Numeric Results
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Solve For: K00 (Group 00 Count of Level-2 Units)
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| | | | Number of Level-2 Units per Level-3 Unit | | | | | Number of Level-1 Units per | | | Correlation | | |
| | Total Sample Size | Number of Level-3 Units | Group 00 | Group 01 | Group 10 | Group 11 | Total | Level-2 Unit | Interaction | Standard Deviation | Level 1 Units | Level 2 Units | |
Power	N	C	K00	K01	K10	K11	K	M	δ	σ	ρ1	ρ2	Alpha
0.9050	2100	5	21	21	21	21	84	5	3	9.8	0.1	0.05	0.05
0.9096	2600	5	13	13	13	13	52	10	3	9.8	0.1	0.05	0.05
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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 216 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 = 0.3; σ = 1; ρ_1 = 0.1; ρ_2 = 0.05; M = 5; C = 22; and α = 0.05. The value of K00, K01, K10, K11 is 4 and the resulting power is 0.835.

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 ....**Sample Size**
Alternative Hypothesis ....**Two-Sided (H1: σ²ʙᴛ/σ²ʙᴄ ≠ 1)**
Power...**0.80**
Alpha...**0.05**
Sequence Allocation ....**Equal (N1 = N2)**
M (Number of Replicates).............................**2**
R1 (Actual Variance Ratio) **0.5625**
σ²ʙᴄ (Control Variance)..................................**0.16**
σ²ᴡᴛ (Treatment Variance) **0.04**
σ²ᴡᴄ (Control Variance).................................**0.09**
ρ (Treatment, Control Correlation)................**0.75**

Output

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

Numeric Results

Solve For: Power

			Number of Level-2 Units per Level-3 Unit					Number of Level-1 Units per Level-2 Unit			Correlation		
Power	Total Sample Size N	Number of Level-3 Units C	Group 00 K00	Group 01 K01	Group 10 K10	Group 11 K11	Total K	M	Interaction δ	Standard Deviation σ	Level 1 Units ρ1	Level 2 Units ρ2	Alpha
0.835	1760	22	4	4	4	4	16	5	0.3	1	0.1	0.05	0.05

PASS also calculates the power at 0.8350.