Chapter 386

Mixed Models Tests for Two Proportions in a 2-Level Hierarchical Design (Level-2 Randomization)

Introduction

This procedure calculates power and sample size for a two-level hierarchical mixed-effects logistic regression in which clusters (groups, classes, hospitals, etc.) of subjects are measured one time (cross-sectional) on a binary variable. The goal of the study is to compare the two group proportions.

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).

Technical Details

Our formulation comes from Ahn, Heo, and Zhang (2015), chapter 5, section 5.7.1, pages 177-179. The hierarchical mixed-effects logistic regression model that is adopted is

$$\log\left(\frac{p_{ij}}{1-p_{ij}}\right) = \beta_0 + \delta X_{ij} + u_i$$

where

Y_{ij} is the binary response of the jth subject in the ith cluster.

p_{ij} is $\text{E}(Y_{ij}|X_{ij})$. Assume $\left[p_{ij}|(X_{ij}=0)\right] = p_2$ and $\left[p_{ij}|(X_{ij}=1)\right] = p_1$

β_0 is the fixed intercept.

δ is the treatment effect of interest.

X_{ij}	is an indicator variable that is = 1 if cluster i is assigned to group 1 (treatment) and 0 if cluster i is assigned to group 2 (control).
u_i	is a random effect (subject-specific intercept) term for the ith cluster the is distributed as $N(0, \sigma_u^2)$.
σ_u^2	is variance of the level two (cluster) random effects.
ρ	is the intraclass correlation (ICC), where $\rho = Corr(Y_{ij}, Y_{ij'}) = (\sigma_u^2/(\sigma_u^2 + \pi^2/3))$.

The test of significance of the δ coefficient in the logistic regression analysis is the test statistic of interest.

The power can be calculated using

$$Power = \Phi \left\{ \frac{|p_1 - p_2|\sqrt{K_2 M/[1 + (M-1)\rho]} - \Phi(1 - \alpha/2)\sqrt{\left(1 + \frac{1}{\lambda}\right)\bar{p}(1 - \bar{p})}}{\sqrt{p_2(1 - p_2) + p_1(1 - p_1)/\lambda}} \right\}$$

where

K_m	is the number of clusters in group m, m = 1 or 2.
M	is the average number of subjects per cluster in both groups.
λ	is K_1/K_2.
$\bar{p}$	is $\left(\frac{p_1 + \lambda p_2}{1 + \lambda}\right)$.

This power function is used in a binary search algorithm to determine p_1, K_1, or M.

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 *Effect Size*, *Power*, *K1*, or *M*.

Under most situations, you will select either *Power* to calculate power or *K1* to calculate the number of clusters. Occasionally, you may want to fix the number of clusters and find the necessary cluster size.

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 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 Clusters and Subjects –
Number of Clusters

K1 (Number of Group 1 Clusters)

This is the number of clusters in group 1, which we have designated as the treatment group. The sample size for this group is equal to the number of clusters times the number of subjects per cluster.

Range

This value must be a positive number.

It can be a decimal (fractional) number such as '12.7'. The resulting value of N1 will be rounded to an 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.

K2 (Number of Group 2 Clusters)

This is the number of clusters in group 2, which we have designated as the control group. The sample size for this group is equal to the number of clusters times the number of subjects per cluster.

Range

This value must be a positive number.

It can be a decimal (fractional) number such as '12.7'. The resulting value of N2 will be rounded to an integer.

Using Multiples of K1

If you simply want a multiple of the value for group one, you would enter the multiple followed by "K1", with no blanks. If you want to use K1 directly, you do not have to enter the leading "1". For example, all of the following are valid entries:

10K1 2K1 0.5K1 K1.

List

You can use a list of values such as "10 20 30" or "K1 2K1 3K1".

Sample Size – Number of Clusters and Subjects – Number of Subjects Per Cluster

M (Number of Subjects Per Cluster)

This is the average number of items (subjects) per cluster in both groups.

Range

This value must be a positive number that is at least 1.

It can be a decimal (fractional) number such as '2.7'. The resulting values of N1 and N2 will be rounded to integers.

List

You can use a list of values such as "100 150 200". A separate analysis will be run for each element in the list.

Effect Size

P1 Input Type

Indicate what type of values to enter to specify the effect size: P1 - P2. Regardless of the entry type chosen, the test statistics used in the power and sample size calculations are the same. The value of P1 is calculated from the value entered. This option is simply given for convenience in specifying the effect size.

The choices are

- **Proportions**

    Enter P1 (Group 1 Proportion|H1) and P2 (Group 2 Proportion).

- **Differences**

    Enter D1 (Difference|H1 = P1-P2) and P2 (Group 2 Proportion).

- **Ratios**

    Enter R1 (Ratio|H1 = P1/P2) and P2 (Group 2 Proportion).

- **Odds Ratios**

    Enter OR1 (Odds Ratio|H1 = Odds1/Odds2) and P2 (Group 2 Proportion).

P1 (Group 1 Proportion |H1)

Enter a value for the proportion in group 1 (the experimental or treatment group) under the alternative hypothesis, H1. The power calculations assume that this is the actual value of the proportion.

You can enter a single value such as 0.1 or a series of values such as 0.1 0.2 0.3 or 0.1 to 0.9 by 0.1.

Note that values must be between zero and one and cannot be equal to P2.

D1 (Difference|H1 = P1 – P2)

This option specifies the difference between the two proportions under the alternative hypothesis, H1. This difference is used with P2 to calculate the value of P1 using the formula: P1=Diff+P2.

The power calculations assume that P1 is the actual value of the proportion in group 1 (experimental or treatment group).

You can enter a single value such as 0.05 or a series of values such as 0.03 0.05 0.10 or 0.01 to 0.05 by 0.01.

Differences must be between -1 and 1. They cannot take on the values -1, 0, or 1.

R1 (Ratio|H1 = P1/P2)

This option specifies the ratio between the two proportions P1 and P2. This ratio is used with P2 to calculate the value of P1 using the formula: P1=(Ratio) x (P2).

The power calculations assume that P1 is the actual value of the proportion in group 1 (experimental or treatment group).

You can enter a single value such as 0.5 or a series of values such as 0.5 0.6 0.7 0.8 or 1.25 to 2.0 by 0.25.

Ratios must be greater than zero. They cannot take on the value of one.

OR1 (Ratio|H1 = Odds1/Odds2)

This option specifies the ratio of P1 and P2, where P1 is the proportion in group 1 under the alternative hypothesis. This ratio is used with P2 to calculate the value of P1 using the formula: P1 = R1 x P2. The power calculations assume that P1 is the actual value of the proportion in group 1 (experimental or treatment group).

You may enter a range of values such as *0.5 0.6 0.7 0.8* or *1.25 to 2.0 by 0.25*. Ratios must be greater than zero. They cannot take on the value of one.

P2 (Group 2 Proportion)

Enter a value for the proportion in group 2 (the control, baseline, standard, or reference group).

Values must be between 0 and 1.

You can enter a single value such as 0.1 or a series of values such as 0.1 0.2 0.3 or 0.1 to 0.5 by 0.1.

Effect Size – Intracluster Correlation

ρ (Intracluster Correlation, ICC)

This is the value of the intracluster (or intraclass) correlation coefficient. It may be interpreted as the correlation between any two observations in the same cluster. It may also be thought of as the proportion of the variation in response that can be accounted for by the between-cluster variation.

Possible values are from 0 to just below 1. Typical values are between 0.0001 and 0.05.

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 only one measurement per subject and treatments will be applied to clusters (level-two units). The analysis will be a mixed-effect logistic regression. The following parameter settings are to be used for the power analysis: $P1 = 0.6$; $P2 = 0.5$; $\rho = 0.01$; $M = 20$ or 30; $\alpha = 0.05$; and $K1 = K2 = 10$ to 40 by 10.

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 Two Proportions in a 2-Level Hierarchical Design (Level-2 Randomization)** 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**
K1 (Number of Group 1 Clusters)........... **10 20 30 40**
K2 (Number of Group 2 Clusters)........... **K1**
M (Number of Subjects Per Cluster)....... **20 30**
P1 Input Type .... **Proportions**
P1 (Group 1 Proportion|H1).................... **0.6**
P2 (Group 2 Proportion) **0.5**
ρ (Intracluster Correlation, ICC).............. **0.01**

Annotated Output

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

Numeric Results

Power	Total Subjects N	Group 1 Clusters K1	Group 2 Clusters K2	Cluster Size M	Group 1 Prop P1	Group 2 Prop P2	Prop Diff P1-P2	Odds Ratio OR	ICC ρ	Alpha
0.45306	400	10	10	20	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.58262	600	10	10	30	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.74190	800	20	20	20	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.86672	1200	20	20	30	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.89211	1200	30	30	20	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.96434	1800	30	30	30	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.95855	1600	40	40	20	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.99151	2400	40	40	30	0.6000	0.5000	0.1000	1.500	0.0100	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.

Report Definitions

Power is the probability of rejecting a false null hypothesis.

N is the total number of subjects in the study.

K1 and K2 are the number of clusters in groups 1 and 2, respectively.

M is the average number of items (subjects) per cluster.

P1 is the proportion for group 1 (treatment group) assuming the alternative hypothesis.

P2 is the proportion for group 2 (control group). This is the proportion in the standard, reference, baseline, or control group.

Prop Diff = P1 - P2 is the difference in the group proportions assumed by the alternative hypothesis.

Odds Ratio = Odds1/Odds2 is the odds ratio assuming the alternative hypothesis.

ICC is the intracluster correlation.

Alpha is the probability of rejecting a true null hypothesis.

Summary Statements

Sample sizes of 25 in group one and 25 in group two, which were obtained by sampling 5 clusters
in group one and 5 clusters in group two with an average of 5 subjects per cluster, achieve 41%
power to detect a difference between the group means of at least 1. The standard deviation of
subjects is 1.00. The intracluster correlation coefficient is 0.010. 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
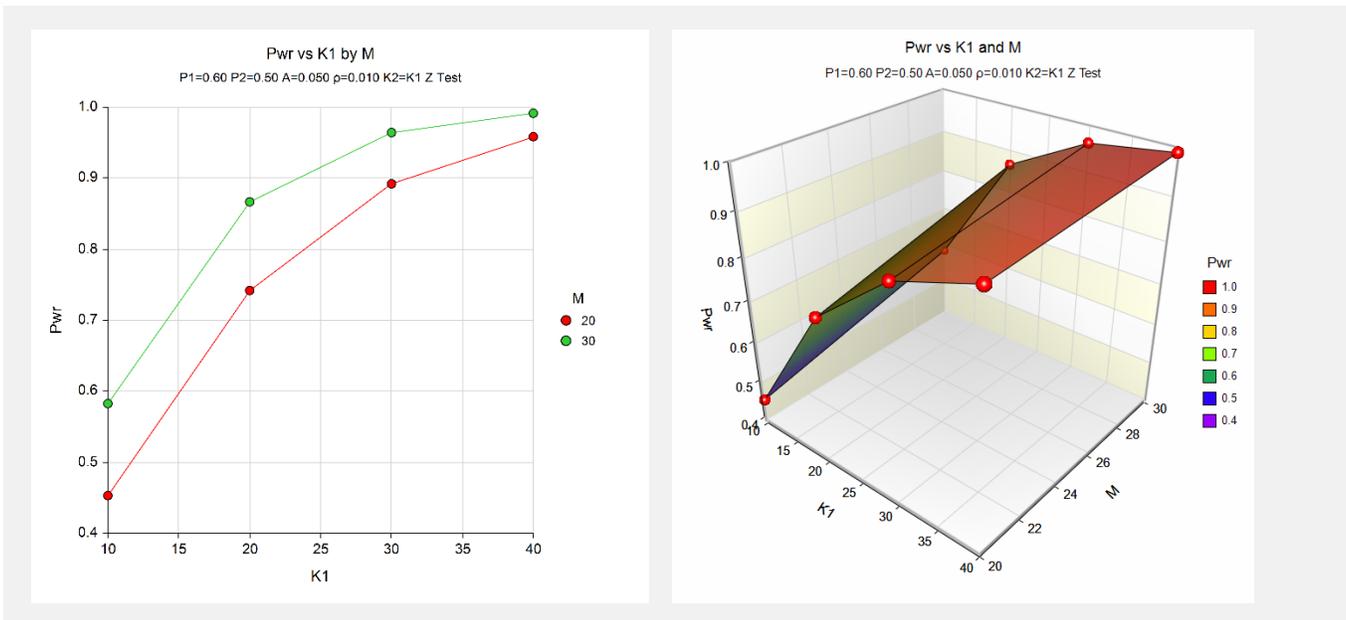
These plots show the power versus the cluster count for the two cluster size values.

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

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 Two Proportions in a 2-Level Hierarchical Design (Level-2 Randomization)** 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	**K1 (Number of Clusters)**
Power...	**0.90**
Alpha...	**0.05**
K2 (Number of Group 2 Clusters)...........	**K1**
M (Number of Subjects Per Cluster).......	**20 30**
P1 Input Type	**Proportions**
P1 (Group 1 Proportion|H1)....................	**0.6**
P2 (Group 2 Proportion)	**0.5**
ρ (Intracluster Correlation, ICC)..............	**0.01**

Output

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

Numeric Results

Power	Total Subjects N	Group 1 Clusters K1	Group 2 Clusters K2	Cluster Size M	Group 1 Prop P1	Group 2 Prop P2	Prop Diff P1-P2	Odds Ratio OR	ICC ρ	Alpha
0.90162	1240	31	31	20	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.90890	1380	23	23	30	0.6000	0.5000	0.1000	1.500	0.0100	0.050

This report shows the power for each of the scenarios.

Example 3 – Calculating Sample Size (Number of Subjects)

Continuing with the last example, suppose the researchers want to determine the number of subjects per cluster needed to achieve 90% power for all values of K1 and K2.

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 Two Proportions in a 2-Level Hierarchical Design (Level-2 Randomization)** 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	**M (Number of Subjects Per Cluster)**
Power..	**0.90**
Alpha..	**0.05**
K1 (Number of Group 1 Clusters)...........	**10 20 30 40**
K2 (Number of Group 2 Clusters)...........	**K1**
P1 Input Type	**Proportions**
P1 (Group 1 Proportion|H1)....................	**0.6**
P2 (Group 2 Proportion)	**0.5**
ρ (Intracluster Correlation, ICC).............	**0.01**

Output

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

Numeric Results

Power	Total Subjects N	Group 1 Clusters K1	Group 2 Clusters K2	Cluster Size M	Group 1 Prop P1	Group 2 Prop P2	Prop Diff P1-P2	Odds Ratio OR	ICC ρ	Alpha
0.90076	2140	10	10	107	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.90237	1400	20	20	35	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.90377	1260	30	30	21	0.6000	0.5000	0.1000	1.500	0.0100	0.050
0.90447	1200	40	40	15	0.6000	0.5000	0.1000	1.500	0.0100	0.050

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 179 provide a table in which several scenarios are reported. We will validate this procedure by duplicating the first two table entries.

The following parameter settings were used: Power = 0.80; *P1* = 0.6; *P2 = 0.4*; ρ = 0.1; *M* = 10 and 20; *ICC* = 0.1; and α = 0.05. The reported values of *K*1 and *K*2 are 19 and 15. The realized power values are 0.812 and 0.826

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 Two Proportions in a 2-Level Hierarchical Design (Level-2 Randomization)** procedure window. You may then make the appropriate entries as listed below, or open **Example 4** by going to the **File** menu and choosing **Open Example Template**.

Design Tab
Solve For .... **K1 (Number of Clusters)**
Power.. **0.80**
Alpha... **0.05**
K2 (Number of Group 2 Clusters)........... **K1**
M (Number of Subjects Per Cluster)....... **10 20**
P1 Input Type .... **Proportions**
P1 (Group 1 Proportion|H1).................... **0.6**
P2 (Group 2 Proportion) **0.4**
ρ (Intracluster Correlation, ICC)............. **0.1**

Output

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

Numeric Results

Power	Total Subjects N	Group 1 Clusters K1	Group 2 Clusters K2	Cluster Size M	Group 1 Prop P1	Group 2 Prop P2	Prop Diff P1-P2	Odds Ratio OR	ICC ρ	Alpha
0.81229	380	19	19	10	0.6000	0.4000	0.2000	2.250	0.1000	0.050
0.82529	600	15	15	20	0.6000	0.4000	0.2000	2.250	0.1000	0.050

PASS calculates the same values of K1: 19 and 15. Note that the realized power values are identical.

(We noticed two typos in Table 5.9, page 179. The last two entries for p1 are 0.5 and 0.6. We believe these should be 0.6 and 0.7.)