Chapter 242

Tests for Two Proportions in a Stratified Cluster-Randomized Design (Cochran-Mantel-Haenszel Test)

Introduction

This procedure calculates power and sample size for tests for two proportions in a stratified cluster randomized design in which the outcome variable is binary. It uses the results of Xu, Zhu, and Ahn (2019) which extends previous results to include varying cluster size. Although response rates may vary among strata, hypotheses about the overall odds ratio are tested with the Cochran-Mantel-Haenszel test.

Technical Details

The following discussion summarizes the results in Xu, Zhu, and Ahn (2019).

Suppose you are interested in comparing the disease response rates of two groups (treatment and control). Further suppose that response rate is known to be related to other covariates (such as age, race, or gender). It is often desirable to remove the covariate's impact from the comparison of the two proportions. This is accomplished by stratifying on the covariates and forming hypotheses about a common odds ratio across all clusters and strata. It is assumed that the data will be analyzed using the Cochran-Mantel-Haenszel test.

In this design, assume that the randomization is balanced with an equal number of clusters assigned to each of the two groups. We denote the treatment group as group 1 and the control group as group 2. Denote the number of clusters in each of the two groups in stratum k by J_k. The number of strata is denoted as K.

Let the cluster sizes be denoted by n_{1jk} and n_{2jk} where j is the cluster in stratum k. It is assumed that these cluster sizes are independently and identically distributed with means μ_k and standard deviations $\tau_k, k = 1, \dots, K$. The total number of subjects in the study is $N = \sum_{k=1}^{K} \sum_{j=1}^{J_k} (n_{1jk} + n_{2jk})$.

Let Y_{1ijk} and Y_{2ijk} be the binary outcome variable with possible values 0 or 1. Let π_{1k} and π_{2k} be the corresponding response probabilities for these variables in the treatment and control groups of the kth stratum. Let $p_{1k} = \left(\sum_{j=1}^{J_k} \sum_{i=1}^{n_{1jk}} Y_{1ijk} \right) / \left(\sum_{j=1}^{J_k} n_{1jk} \right)$ and $p_{2k} = \left(\sum_{j=1}^{J_k} \sum_{i=1}^{n_{1jk}} Y_{2ijk} \right) / \left(\sum_{j=1}^{J_k} n_{2jk} \right)$ be the corresponding estimates of π_{1k} and π_{2k}.

Let ρ be the intracluster correlation coefficient (ICC) which is a measure of the similarity of subjects within the same cluster. Note that this correlation is assumed to be constant across all clusters.

Define the odds ratio between the treatment and control groups as

$$\psi_k = \frac{\dfrac{\pi_{1k}}{1-\pi_{1k}}}{\dfrac{\pi_{2k}}{1-\pi_{2k}}} = \frac{\pi_{1k}(1-\pi_{2k})}{\pi_{2k}(1-\pi_{1k})}$$

Further let ψ denote common odds ratio.

The task is to estimate the number of clusters needed for testing $H0: \psi = 1$ versus $H1: \psi \neq 1$ for a two-sided significance level α and a power of $1 - \beta$.

The Cochran-Mantel-Haenszel statistic for testing the above hypothesis is

$$C = \frac{\sum_{k=1}^{K} w_k (p_{1k} - p_{2k})}{\sqrt{\sum_{k=1}^{K} w_k^2 \left[\text{Var}(p_{1k}) + \text{Var}(p_{2k}) \right]}}$$

where

$$w_k = \frac{n_{1k} n_{2k}}{n_{1k} + n_{2k}}$$

$$n_{1k} = \sum_{j=1}^{J_k} n_{1jk}$$

$$n_{2k} = \sum_{j=1}^{J_k} n_{2jk}$$

The distribution of the statistic C is asymptotically standard normal.

Power Calculations

Three cases of statistical hypotheses are available. The power formula for each case is

1. $H0: \psi \geq 1$ versus $H1: \psi < 1$.

$$\text{Power} = 1 - \beta = 1 - \Phi\left(\frac{V\sqrt{N} - Tz_\alpha}{U} \right)$$

2. $H0: \psi \leq 1$ versus $H1: \psi > 1$.

$$\text{Power} = 1 - \beta = 1 - \Phi\left(\frac{-V\sqrt{N} + Tz_{1-\alpha}}{U} \right)$$

3. $H0: \psi = 1$ versus $H1: \psi \neq 1$.

$$\text{Power} = 1 - \beta = 2 - \Phi\left(\frac{V\sqrt{N} - Tz_{\alpha/2}}{U} \right) - \Phi\left(\frac{-V\sqrt{N} + Tz_{1-\alpha/2}}{U} \right)$$

where

$$T = \frac{1}{2}\sqrt{\sum_{k=1}^{K} f_k \left[\rho\mu_k + \rho\frac{\tau_k^2}{\mu_k} + (1-\rho)\right]\bar{\pi}_k(1-\bar{\pi}_k)}$$

$$U = \sqrt{\frac{1}{8}\sum_{k=1}^{K} f_k \left[\rho\mu_k + \rho\frac{\tau_k^2}{\mu_k} + (1-\rho)\right][\pi_{1k}(1-\pi_{1k}) + \pi_{2k}(1-\pi_{2k})]}$$

$$V = \frac{1}{4}\sum_{k=1}^{K} f_k(\pi_{1k} - \pi_{2K})$$

$$\bar{\pi}_k = \frac{(\pi_{1k} + \pi_{2K})}{2}$$

$$f_k = \frac{(n_{1k} + n_{2k})}{N}$$

$$\pi_{1k} = \frac{\psi\pi_{2k}}{1 - \pi_{2k} + \psi\pi_{2k}}$$

and $\Phi(x)$ is the standard normal cumulative distribution function.

These power formulas are used to conduct a binary search for sample size or odds ratio.

Example 1 – Finding Sample Size

A study is being planned to investigate the possible association between a certain drug and a certain disease. Since age is known to affect the disease rates, the population is stratified into four age groups with weights of 10%, 40%, 35%, and 15%. Furthermore, patients will be clustered by clinics. All patients in a clinic will receive either an intervention drug or a standard drug. The number of clinics receiving each treatment will be balanced.

Prior studies had shown the probability of this disease continuing after receiving the baseline treatment was 0.25, 0.20, 0.15, and 0.10, respectively, among the four age groups. The average number of patients per clinic has historically been 30, with a coefficient of variation of 0.4.

Two values of ICC will be used: 0.015 and 0.1. The significance level is set to 0.05 and the power is set to 0.8. The odds ratio is set to 1.5, 2, and 3.

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 ....**Sample Size**
Alternative Hypothesis ....**Two-Sided (H1: OR ≠ 1)**
Power...**0.8**
Alpha...**0.05**
OR (Actual Odds Ratio) **1.5 2 3**
ICC (Intracluster Correlation)................................**0.015 0.1**
Cluster Size Variation Input ....**Coefficient of Variation**

Set 1 Number of Strata **1**
Set 1 Percent of N in Each Stratum **10**
Set 1 Average of Cluster Sizes **30**
Set 1 Coefficient of Variation of Cluster Sizes **0.4**
Set 1 Pr(Success) in the Control Group (P2) **0.25**

Set 2 Number of Strata **1**
Set 2 Percent of N in Each Stratum **40**
Set 2 Average of Cluster Sizes **30**
Set 2 Coefficient of Variation of Cluster Sizes **0.4**
Set 2 Pr(Success) in the Control Group (P2) **0.2**

Set 3 Number of Strata **1**
Set 3 Percent of N in Each Stratum **35**
Set 3 Average of Cluster Sizes **30**
Set 3 Coefficient of Variation of Cluster Sizes **0.4**
Set 3 Pr(Success) in the Control Group (P2) **0.15**

Set 4 Number of Strata **1**
Set 4 Percent of N in Each Stratum **15**
Set 4 Average of Cluster Sizes **30**
Set 4 Coefficient of Variation of Cluster Sizes **0.4**
Set 4 Pr(Success) in the Control Group (P2) **0.1**

Output

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

Numeric Reports

Numeric Results of the Cochran-Mantel-Haenszel Test
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Solve For: Sample Size
Hypotheses: H0: OR = 1   vs.   H1: OR ≠ 1
Number of Strata: 4
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Power	Total Sample Size N	Anticipated Number of Clusters M	Actual Odds Ratio OR	Treatment Probability of Success P1	Control Probability of Success P2	Intracluster Correlation Coefficient ICC	Alpha
0.8	1815	60	1.5	0.2371	0.1725	0.015	0.05
0.8	5275	176	1.5	0.2371	0.1725	0.100	0.05
0.8	578	20	2.0	0.2919	0.1725	0.015	0.05
0.8	1681	56	2.0	0.2919	0.1725	0.100	0.05
0.8	212	7	3.0	0.3801	0.1725	0.015	0.05
0.8	617	20	3.0	0.3801	0.1725	0.100	0.05
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Power   The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N   The total sample size, i.e., the total number of subjects summed across all strata.
M   The anticipated number of clusters. Half of these clusters are assigned to the treatment group, while the other half
           are assigned to the control group.
OR   The overall odds ratio, [Odds1] / [Odds2] assumed by the alternative hypothesis. This is the OR at which the power
           is computed.
P1   The probability of a success in the treatment group. This is the weighted average of the individual P1's of all strata.
P2   The probability of a success in the control group. This is the weighted average of the individual P2's of all strata.
ICC   The intracluster correlation coefficient. This is the correlation between any two responses within a particular stratum.
Alpha   The probability of rejecting a true null hypothesis.

Summary Statements
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A stratified cluster-randomized design with 4 strata will be used to test whether the Group 1 (treatment) proportion
(P1) is different from the Group 2 (control) proportion (P2), by testing the odds ratio (OR = O1 / O2) against the null
value 1 (H0: OR = 1 versus H1: OR ≠ 1). The comparison will be made using a two-sided
Cochran-Mantel-Haenszel test, with a Type I error rate (α) of 0.05. To detect an odds ratio (O1 / O2) of 1.5 with
80% power, the total number of subjects needed will be 1815, from a total of 60 clusters (with half of the clusters in
Group 1 and half in Group 2, and balanced across the 4 strata).
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References
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Xu, X., Zhu, H., and Ahn, C. 2019. 'Sample size considerations for stratified cluster randomization design with
    binary outcomes and varying cluster size', Statistics in Medicine, Volume 38, Number 18, pages 3395-3404.
Donner, A. and Klar, N. 2000. Design and Analysis of Cluster Randomization Trials in Health Research. Arnold.
    London.
Nam, Jun-mo. 1992. 'Sample Size Determination for Case-Control Studies and the Comparison of Stratified and
    Unstratified Analyses,' Biometrics, Volume 48, pages 389-395.
Woolson, R.F., Bean, J.A., and Rojas, P.B. 1986. 'Sample Size for Case-Control Studies Using Cochran's Statistic,'
    Biometrics, Volume 42, pages 927-932.
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Strata-Detail Report

Strata-Detail Report
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Set	Number of Strata	Percent of N in Each Stratum	Average of Cluster Sizes	Standard Deviation of Cluster Sizes	Coefficient of Variation of Cluster Sizes	Pr(Success) in the Control Group P2
1	1	10	30	12	0.4	0.25
2	1	40	30	12	0.4	0.20
3	1	35	30	12	0.4	0.15
4	1	15	30	12	0.4	0.10
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Set	An identification number on the input screen.
Number of Strata	The number of strata defined by this set (input line).
Percent of N in Each Stratum	The percentage of the total sample size that is allocated to each stratum in this set.
Average of Cluster Sizes	The average cluster size (number of subjects) in each stratum of this set.
Standard Deviation of Cluster Sizes	The standard deviation of the cluster sizes in each stratum of this set.
Coefficient of Variation of Cluster Sizes	The coefficient of variation (CV) of the cluster sizes in each stratum of this set. CV = SD/Mean.
P2	Pr(Success) in the Control Group. The probability of a success in those clusters that are assigned to the control group in each stratum of this set.

This report shows the values of the individual, strata-level parameters that were used. These parameters are the same for all rows of the Numerical Results Report (shown above), so they are only displayed once.

Plots Section

Plots

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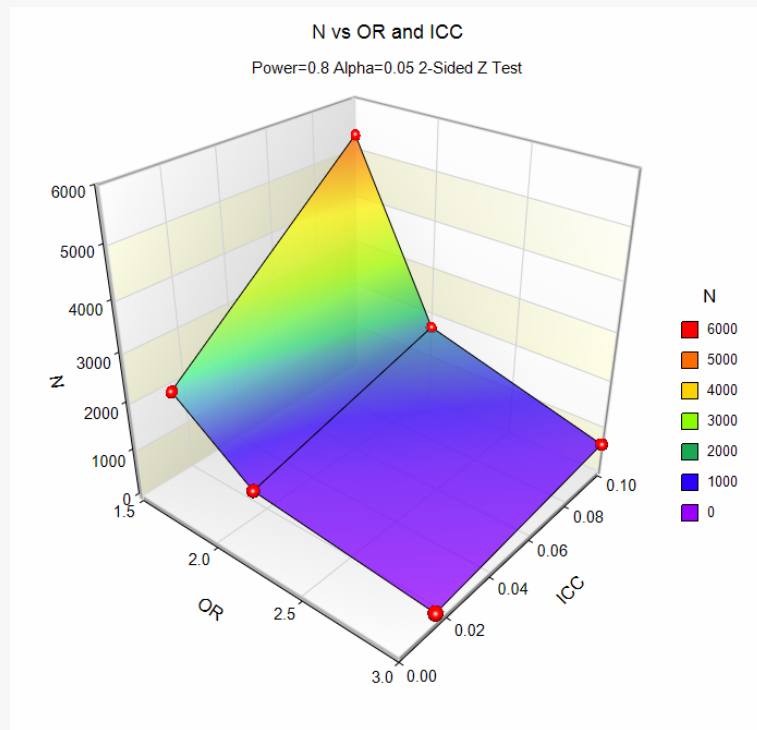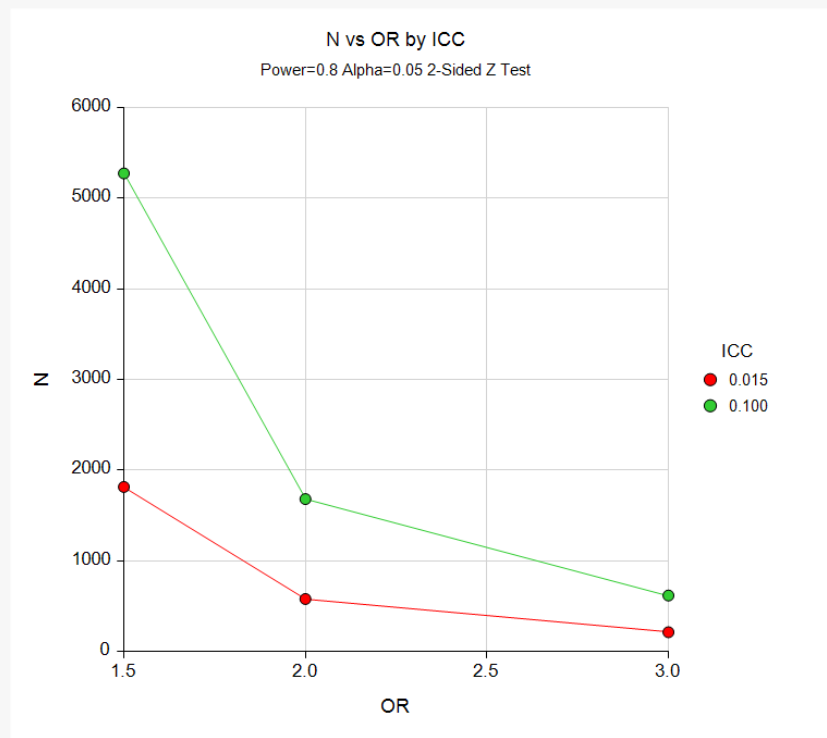
The values from the Numerical Results report are displayed in these plots.

Example 2 – Validation using Xu, Zhu, Ahn (2019)

Xu, Zhu, and Ahn (2019) provide an example of the power analysis of a stratified, cluster-randomized study. The data are to be analyzed by a two-sided Cochran-Mantel-Haenszel test. We will use their results to validate this procedure.

Their example had four strata with 4419, 4738, 4175, and 1093 subjects per stratum. (We will enter these numbers directly and let the program rescale them to percentages.)

The probability of success was 0.14 in each stratum. The average number of patients per cluster were 177, 119, 84, and 122. The corresponding standard deviations were 75, 53, 36, and 58.

The value of ICC was 0.015. The significance level is set to 0.05 and the power is set to 0.8. The odds ratio is set to 0.75923. They obtained a total sample size of 12387.

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
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Solve For .... **Sample Size**
Alternative Hypothesis .... **Two-Sided (H1: OR ≠ 1)**
Power.. **0.8**
Alpha.. **0.05**
OR (Actual Odds Ratio) **0.75923**
ICC (Intracluster Correlation) **0.015**
Cluster Size Variation Input .... **Standard Deviation**

Set 1 Number of Strata **1**
Set 1 Percent of N in Each Stratum **4419**
Set 1 Average of Cluster Sizes **177**
Set 1 Standard Deviation of Cluster Sizes.......... **75**
Set 1 Pr(Success) in the Control Group (P2) **0.14**

Set 2 Number of Strata **1**
Set 2 Percent of N in Each Stratum **4738**
Set 2 Average of Cluster Sizes **119**
Set 2 Standard Deviation of Cluster Sizes.......... **53**
Set 2 Pr(Success) in the Control Group (P2) **0.14**

Set 3 Number of Strata **1**
Set 3 Percent of N in Each Stratum **4175**
Set 3 Average of Cluster Sizes **84**
Set 3 Standard Deviation of Cluster Sizes.......... **36**
Set 3 Pr(Success) in the Control Group (P2) **0.14**

Set 4 Number of Strata **1**
Set 4 Percent of N in Each Stratum **1093**
Set 4 Average of Cluster Sizes **122**
Set 4 Standard Deviation of Cluster Sizes **58**
Set 4 Pr(Success) in the Control Group (P2) **0.14**

Output

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

Numeric Reports with Continuity Correction

Numeric Results of the Cochran-Mantel-Haenszel Test

Solve For: Sample Size
Hypotheses: H0: OR = 1   vs.   H1: OR ≠ 1
Number of Strata: 4

Power	Total Sample Size N	Anticipated Number of Clusters M	Actual Odds Ratio OR	Treatment Probability of Success P1	Control Probability of Success P2	Intracluster Correlation Coefficient ICC	Alpha
0.8	12387	106	0.7592	0.11	0.14	0.015	0.05

Strata-Detail Report

Set	Number of Strata	Percent of N in Each Stratum	Average of Cluster Sizes	Standard Deviation of Cluster Sizes	Coefficient of Variation of Cluster Sizes	Pr(Success) in the Control Group P2
1	1	30.63	177	75	0.4237	0.14
2	1	32.85	119	53	0.4454	0.14
3	1	28.94	84	36	0.4286	0.14
4	1	7.58	122	58	0.4754	0.14

PASS has also obtained a sample size of 12387, which validates this procedure.