

## Chapter 225

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

## Introduction

In a stratified design, the subjects are selected from two or more strata which are formed from important covariates such as gender, income level, or marital status. The number of subjects in each of the two groups in each stratum is set (fixed) by the design. A separate 2-by-2 table is formed for each stratum. Although response rates may vary among strata, hypotheses about the overall odds ratio can be tested using the Cochran-Mantel-Haenszel test. This module allows you to determine power and sample size for such a study.

## Technical Details

This procedure is based on the results of Woolson, Bean, and Rojas (1986) which were extended to include a continuity correction by Nam (1992). For more details, consult those articles or chapter 4 in Lachin (2000). We will now briefly summarize these results.

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 another covariate (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 covariate and forming hypotheses about a common odds ratio across all strata. Data from such a stratified design may be analyzed by the Cochran-Mantel-Haenszel test.

There are two versions of the Cochran-Mantel-Haenszel test: one that is continuity corrected and one that is not. The continuity-corrected test is more commonly used.

The computation of the test statistic is as follows. Suppose there are  $J$  strata. The result of each 2-by-2 table may be summarized as follows.

	<b>Groups</b>		
	<b>Group 1</b>	<b>Group 2</b>	
<b>Response</b>	<b>Treatment</b>	<b>Control</b>	<b>Total</b>
<b>Yes</b>	$x_{1j}$	$x_{2j}$	$x_j$
<b>No</b>	$n_{1j} - x_{1j}$	$n_{2j} - x_{2j}$	$N_j - x_j$
<b>Total</b>	$n_{1j}$	$n_{2j}$	$N_j$

where  $j = 1, 2, \dots, J$  and  $N = \sum_{j=1}^J N_j$ .

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

The parameters of interest are the success proportions  $p_{1j}$  and  $p_{2j}$ . These parameters are estimated by

$$\hat{p}_{1j} = \frac{x_{1j}}{n_{1j}} \text{ and } \hat{p}_{2j} = \frac{x_{2j}}{n_{2j}}$$

The odds of response in each of the two groups in each strata is given by

$$o_{1j} = \frac{p_{1j}}{1 - p_{1j}} \text{ and } o_{2j} = \frac{p_{2j}}{1 - p_{2j}}$$

The strata odds ratio  $\psi_j$  is calculated using the equation

$$\begin{aligned} \psi_j &= \frac{o_{1j}}{o_{2j}} \\ &= \frac{\left(\frac{p_{1j}}{1 - p_{1j}}\right)}{\left(\frac{p_{2j}}{1 - p_{2j}}\right)} \end{aligned}$$

In the sequel, it is assumed that the strata odds ratios are all equal. That is, it is assumed that  $\psi_1 = \psi_2 = \dots = \psi_j = \psi$ . Solving this relationship for  $p_{1j}$  in terms of  $\psi$  and  $p_{2j}$  gives

$$p_{1j} = \frac{\psi p_{2j}}{1 - p_{2j} + \psi p_{2j}}$$

If values for the odds ratio under the null hypothesis ( $\psi_0$ ), under the alternative hypothesis ( $\psi_1$ ), and  $p_{2j}$  are specified, values for  $p_{1j}$  under the null hypothesis ( $p_{1j0}$ ) and the alternative hypothesis ( $p_{1j1}$ ) can be calculated as follows

$$\begin{aligned} p_{1j0} &= \frac{\psi_0 p_{2j}}{1 - p_{2j} + \psi_0 p_{2j}}, \quad j = 1, 2, \dots, J \\ p_{1j1} &= \frac{\psi_1 p_{2j}}{1 - p_{2j} + \psi_1 p_{2j}}, \quad j = 1, 2, \dots, J \end{aligned}$$

Assuming a common odds ratio across all strata of  $\psi$  (that is, assuming  $\psi_1 = \psi_2 = \dots = \psi_j = \psi$ ), hypotheses of the form  $H_0: \psi \leq \psi_0$  versus  $H_1: \psi > \psi_0$  may be tested using Cochran's  $U$  statistic (Woolson et al. 1986, page 928)

$$U_G = \sum_{j=1}^J w_j \{(\hat{p}_{1j} - \hat{p}_{2j}) - (p_{1j0} - p_{2j})\}, \quad \text{where } w_j = \frac{n_{1j}n_{2j}}{N_j}$$

Note that when  $\psi_0 = 1$ ,  $U_G$  reduces to

$$U_0 = \sum_{j=1}^J w_j (\hat{p}_{1j} - \hat{p}_{2j}).$$

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

The value  $U_0$  is commonly used to form the Cochran-Mantel-Haenszel statistic.  $U_G$  is an extension of this statistic which allows  $\psi_0 \neq 1$ .

The calculation of the asymptotically normal test statistic,  $z_c$ , may or may not include a continuity correction factor depending on whether the parameter  $cc$  is set to 1/2 or 0. The formula for  $z_{CMH}$  is

$$z_{CMH} = \frac{U_G - cc}{\sqrt{v_0(U_G)}}$$

where

$$v_0(U_G) = \begin{cases} \sum_{j=1}^J w_j^2 \left\{ \frac{\hat{p}_{1j}(1 - \hat{p}_{1j})}{n_{1j}} + \frac{\hat{p}_{2j}(1 - \hat{p}_{2j})}{n_{2j}} \right\} & \text{if } \psi_0 \neq 1 \\ \sum_{j=1}^J w_j \hat{p}_j (1 - \hat{p}_j) & \text{if } \psi_0 = 1 \end{cases}$$

$$\hat{p}_j = \frac{x_j}{N_j}$$

The name *Cochran-Mantel-Haenszel test* actually refers to two tests: the Cochran test and the Mantel-Haenszel test. The difference is between these test is that Cochran's test uses  $v_0(U_G)$  to estimate the unconditional variance assuming that the group sample sizes are fixed, while the Mantel-Haenszel test replaces  $v_0(U_G)$  with an estimate of the conditional variance of  $U$  assuming that both row and column marginals are fixed. Asymptotically the two variances are equivalent, so the test is often called the Cochran-Mantel-Haenszel statistic.

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## Power Calculations

The asymptotic power of  $z_{CMH}$  for testing a one-sided hypothesis of the form  $H_0: \psi \leq \psi_0$  versus  $H_1: \psi > \psi_0$  is

$$Power = 1 - \Phi \left( \frac{z_{1-\alpha} \sqrt{V_0(U_G)} - E(U_G) + cc}{\sqrt{V_1(U_G)}} \right)$$

where

$$E(U_G) = \sum_{j=1}^J w_j \{ (p_{1j1} - p_{2j}) - (p_{1j0} - p_{2j}) \}$$

$$v_0(U_G) = \begin{cases} \sum_{j=1}^J w_j^2 \left\{ \frac{p_{1j0}(1 - p_{1j0})}{n_{1j}} + \frac{p_{2j}(1 - p_{2j})}{n_{2j}} \right\} & \text{if } \psi_0 \neq 1 \\ \sum_{j=1}^J w_j \bar{p}_j (1 - \bar{p}_j) & \text{if } \psi_0 = 1 \end{cases}$$

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

$$\bar{p}_j = p_{1j1} \left( \frac{n_{1j}}{N_j} \right) + p_{2j} \left( \frac{n_{2j}}{N_j} \right)$$

$$V_1(U_G) = \sum_{j=1}^J w_j^2 \left\{ \frac{p_{1j1}(1-p_{1j1})}{n_{1j}} + \frac{p_{2j}(1-p_{2j})}{n_{2j}} \right\}$$

Note that Woolson et al. (1986) and Nam (1992) give results for the usual case when  $\psi_0 = 1$ . The above results are our extension to the important case when  $\psi_0 \neq 1$ . We could not find published results for this case, so we have made this extension. When published results become available, we will adopt those results. If you have  $\psi_0 \neq 1$ , you must use  $U_G$ , rather than  $U_0$ , in the calculation of the test statistic.

Similar calculations may also be made for testing the other one-sided hypothesis  $H_0: \psi \geq \psi_0$  versus  $H_1: \psi < \psi_0$  and the two-sided hypothesis  $H_0: \psi = \psi_0$  versus  $H_1: \psi \neq \psi_0$ .

## Example 1 – Finding Power

Nam (1992) discusses a case-control study investigating the possible association between chlorinated water and colon cancer among males in Iowa. Since age is known to affect colon cancer rates, the population is stratified into four age groups with weights of 10%, 40%, 35%, and 15%. An equal number of cases and controls will be selected in each age-group. Prior studies had shown the probability of chlorinated water exposure among non-cancer subjects was 0.75, 0.70, 0.65, and 0.60, respectively, among the four age groups. The significance level is set to 0.05. The investigators want to consider various total sample sizes from 50 to 500. They also want to consider odds ratios of 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 .....	<b>Power</b>
Test Type .....	<b>Continuity-Corrected Z-Test</b>
Alternative Hypothesis .....	<b>One-Sided (H1: OR &gt; OR0)</b>
Alpha .....	<b>0.05</b>
M (Sample Size Multiplier) .....	<b>50 to 500 by 50</b>
OR0 (Odds Ratio   H0) .....	<b>1</b>
OR1 (Actual Odds Ratio) .....	<b>2 3</b>
Set 1 Number of Strata .....	<b>1</b>
Set 1 R1 = N1 / M .....	<b>0.05</b>
Set 1 R2 = N2 / M .....	<b>R1</b>
Set 1 Pr(Success) .....	<b>0.75</b>
Set 2 Number of Strata .....	<b>1</b>
Set 2 R1 = N1 / M .....	<b>0.20</b>
Set 2 R2 = N2 / M .....	<b>R1</b>
Set 2 Pr(Success) .....	<b>0.70</b>
Set 3 Number of Strata .....	<b>1</b>
Set 3 R1 = N1 / M .....	<b>0.175</b>
Set 3 R2 = N2 / M .....	<b>R1</b>
Set 3 Pr(Success) .....	<b>0.65</b>
Set 4 Number of Strata .....	<b>1</b>
Set 4 R1 = N1 / M .....	<b>0.075</b>
Set 4 R2 = N2 / M .....	<b>R1</b>
Set 4 Pr(Success) .....	<b>0.60</b>

## Output

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

### Numeric Results

#### Numeric Results of Cochran-Mantel-Haenszel Test of an Odds Ratio

Solve For: **Power**  
 Test Type: Continuity-Corrected Z-Test  
 Hypotheses:  $H_0: OR \leq OR_0$  vs.  $H_1: OR > OR_0$

Power	Sample Size				Odds Ratio		Alpha
	Total N	Group 1 N1	Group 2 N2	Multiplier M	Null OR0	Actual OR1	
0.17827	50	25	25	50	1	2	0.05
0.35051	100	50	50	100	1	2	0.05
0.49917	150	75	75	150	1	2	0.05
0.62148	200	100	100	200	1	2	0.05
0.71862	250	125	125	250	1	2	0.05
0.79373	300	150	150	300	1	2	0.05
0.85059	350	175	175	350	1	2	0.05
0.89289	400	200	200	400	1	2	0.05
0.92392	450	225	225	450	1	2	0.05
0.94639	500	250	250	500	1	2	0.05
0.33564	50	25	25	50	1	3	0.05
0.63373	100	50	50	100	1	3	0.05
0.81513	150	75	75	150	1	3	0.05
0.91213	200	100	100	200	1	3	0.05
0.96006	250	125	125	250	1	3	0.05
0.98247	300	150	150	300	1	3	0.05
0.99252	350	175	175	350	1	3	0.05
0.99688	400	200	200	400	1	3	0.05
0.99873	450	225	225	450	1	3	0.05
0.99949	500	250	250	500	1	3	0.05

- Group In a treatment vs. control design, the treatment group is 1 and the control group is 2.
- Power The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
- N The total sample size summed across all groups and strata.
- N1 and N2 The sample sizes from groups 1 and 2, respectively, summed across all strata.
- M The factor by which the values of R1 and R2 are multiplied to get the final sample sizes.
- OR0 The odds ratio  $[P1/(1-P1)] / [P2/(1-P2)]$  assuming the null hypothesis ( $H_0$ ).
- OR1 The value of the odds ratio at which the power is computed.
- Alpha The probability of rejecting a true null hypothesis.

#### Summary Statements

A two-group stratified design with 4 strata will be used to test whether the Group 1 (treatment) proportion ( $P_1$ ) is greater than the Group 2 (control) proportion ( $P_2$ ), by testing the odds ratio ( $OR = O_1 / O_2$ ) against the null value 1 ( $H_0: OR \leq 1$  versus  $H_1: OR > 1$ ). The comparison will be made using a one-sided Cochran-Mantel-Haenszel Continuity-Corrected Z-Test, with a Type I error rate ( $\alpha$ ) of 0.05. To detect an odds ratio ( $O_1 / O_2$ ) of 2 with sample sizes of 25 for Group 1 and 25 for Group 2 (divided across the 4 strata), the power is 0.17827.

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

**Dropout-Inflated Sample Size**

Dropout Rate	Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
	N1	N2	N	N1'	N2'	N'	D1	D2	D
20%	25	25	50	32	32	64	7	7	14
20%	50	50	100	63	63	126	13	13	26
20%	75	75	150	94	94	188	19	19	38
20%	100	100	200	125	125	250	25	25	50
20%	125	125	250	157	157	314	32	32	64
20%	150	150	300	188	188	376	38	38	76
20%	175	175	350	219	219	438	44	44	88
20%	200	200	400	250	250	500	50	50	100
20%	225	225	450	282	282	564	57	57	114
20%	250	250	500	313	313	626	63	63	126

Dropout Rate	The percentage of subjects (or items) that are expected to be lost at random during the course of the study and for whom no response data will be collected (i.e., will be treated as "missing"). Abbreviated as DR.
N1, N2, and N	The evaluable sample sizes at which power is computed (as entered by the user). If N1 and N2 subjects are evaluated out of the N1' and N2' subjects that are enrolled in the study, the design will achieve the stated power.
N1', N2', and N'	The number of subjects that should be enrolled in the study in order to obtain N1, N2, and N evaluable subjects, based on the assumed dropout rate. N1' and N2' are calculated by inflating N1 and N2 using the formulas $N1' = N1 / (1 - DR)$ and $N2' = N2 / (1 - DR)$ , with N1' and N2' always rounded up. (See Julious, S.A. (2010) pages 52-53, or Chow, S.C., Shao, J., Wang, H., and Lohknygina, Y. (2018) pages 32-33.)
D1, D2, and D	The expected number of dropouts. $D1 = N1' - N1$ , $D2 = N2' - N2$ , and $D = D1 + D2$ .

**Dropout Summary Statements**

Anticipating a 20% dropout rate, 32 subjects should be enrolled in Group 1, and 32 in Group 2, to obtain final group sample sizes of 25 and 25, respectively.

**References**

- Lachin, John M. 2000. Biostatistical Methods. John Wiley & Sons. New York.
- 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.

**Sample Sizes: N, N1, and N2**

The value of N is the sum of N1 and N2. The values of N1 and N2 are found by summing the individual strata-group sample sizes. These are found by multiplying R1 and R2 by M.

Note that this multiplication will usually result in fractional sample sizes across the strata. As a practical matter, we recommend rounding each fractional value up to the next integer when implementing a given design.

## Strata-Detail Report

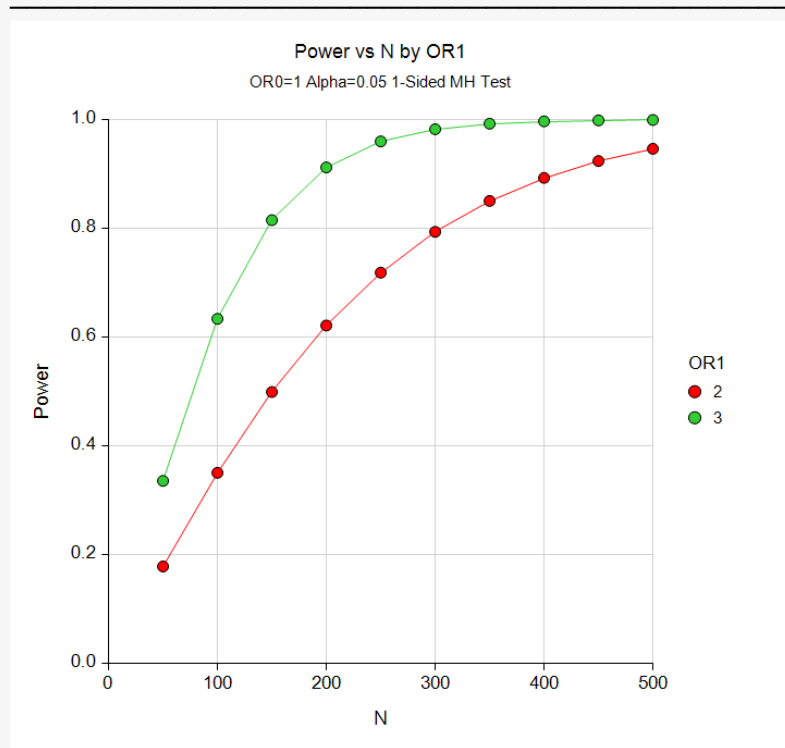
### Strata-Detail Report

Set	Number of Strata	Proportion of Total N in Each Stratum	Proportion of Stratum		Multiplier		Probability of Success Pr(Success)
			Group 1	Group 2	Group 1 R1	Group 2 R2	
1	1	0.10	0.5	0.5	0.050	0.050	0.75
2	1	0.40	0.5	0.5	0.200	0.200	0.70
3	1	0.35	0.5	0.5	0.175	0.175	0.65
4	1	0.15	0.5	0.5	0.075	0.075	0.60

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.

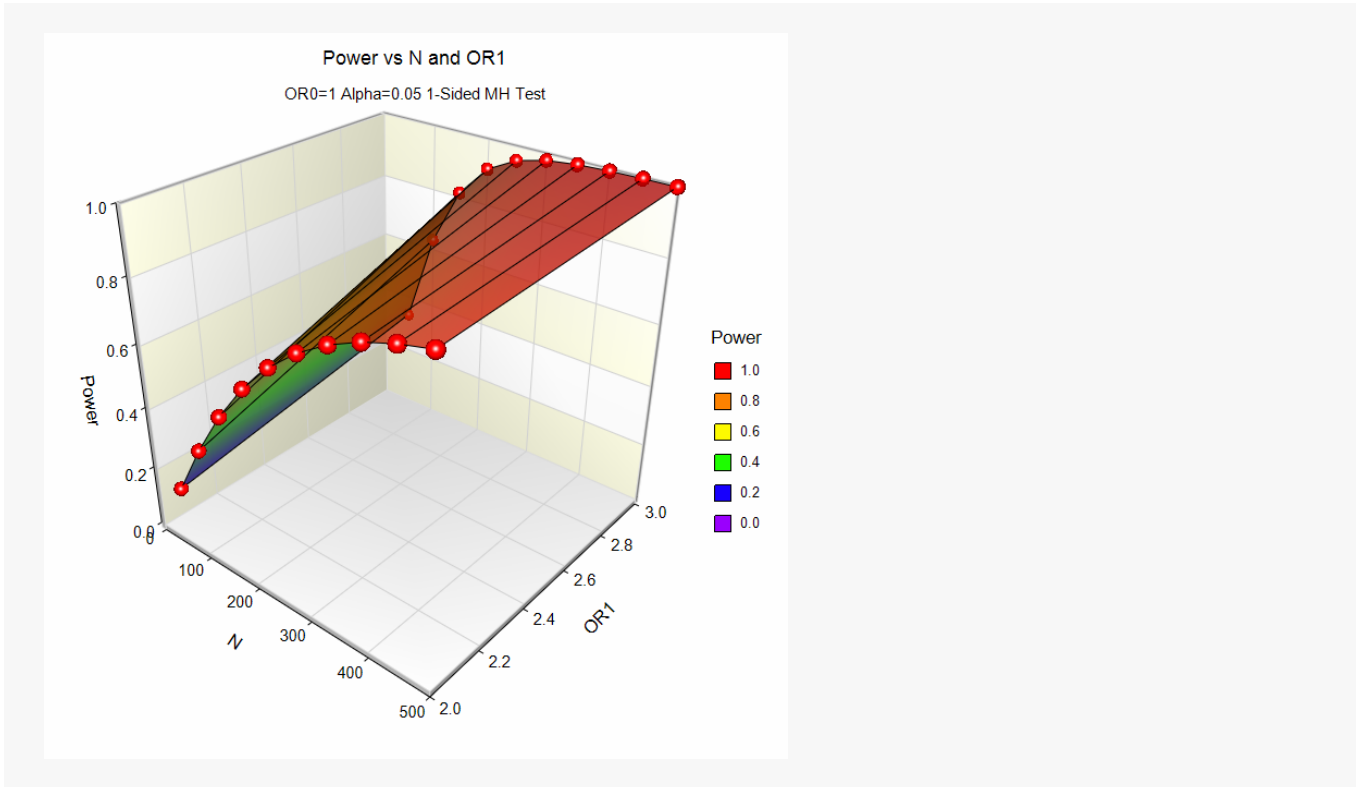
## Plots Section

### Plots





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



The values from the Numerical Results report are displayed in these plots. These charts provide a quick view of the power that is achieved for various sample sizes.

## Example 2 – Validation using Nam (1992)

To validate the procedure, we will compare **PASS's** results to those on page 392 of Nam (1992). Most of the settings in this example are the same as those of Example 1, except that the power is 90% and the odds ratio is 3. Nam (1992) found the necessary sample sizes to be 192 for the corrected test and 171 for the uncorrected test.

### 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 2a** 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 .....	<b>Sample Size</b>
Test Type.....	<b>Continuity-Corrected Z-Test</b>
Alternative Hypothesis .....	<b>One-Sided (H1: OR &gt; OR0)</b>
Power.....	<b>0.90</b>
Alpha.....	<b>0.05</b>
OR0 (Odds Ratio   H0).....	<b>1</b>
OR1 (Actual Odds Ratio) .....	<b>3</b>
Set 1 Number of Strata .....	<b>1</b>
Set 1 R1 = N1 / M .....	<b>0.05</b>
Set 1 R2 = N2 / M .....	<b>R1</b>
Set 1 Pr(Success).....	<b>0.75</b>
Set 2 Number of Strata .....	<b>1</b>
Set 2 R1 = N1 / M .....	<b>0.20</b>
Set 2 R2 = N2 / M .....	<b>R1</b>
Set 2 Pr(Success).....	<b>0.70</b>
Set 3 Number of Strata .....	<b>1</b>
Set 3 R1 = N1 / M .....	<b>0.175</b>
Set 3 R2 = N2 / M .....	<b>R1</b>
Set 3 Pr(Success).....	<b>0.65</b>
Set 4 Number of Strata .....	<b>1</b>
Set 4 R1 = N1 / M .....	<b>0.075</b>
Set 4 R2 = N2 / M .....	<b>R1</b>
Set 4 Pr(Success).....	<b>0.60</b>

## Output

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

### Numeric Results with Continuity Correction

#### Numeric Results of Cochran-Mantel-Haenszel Test of an Odds Ratio

Solve For: [Sample Size](#)  
 Test Type: Continuity-Corrected Z-Test  
 Hypotheses:  $H_0: OR \leq OR_0$  vs.  $H_1: OR > OR_0$

Power	Sample Size				Odds Ratio		Alpha
	Total N	Group 1 N1	Group 2 N2	Multiplier M	Null OR0	Actual OR1	
0.9	192	96	96	191.5	1	3	0.05

The value of 192 agrees exactly with that of Nam (1992) for the continuity-corrected test.

If you set Test Type to Z-Test (**Example 2b**) and rerun the analysis, you will get the following results.

Design Tab

Test Type.....**Z-Test**

### Numeric Results without Continuity Correction

#### Numeric Results of Cochran-Mantel-Haenszel Test of an Odds Ratio

Solve For: [Sample Size](#)  
 Test Type: Z-Test  
 Hypotheses:  $H_0: OR \leq OR_0$  vs.  $H_1: OR > OR_0$

Power	Sample Size				Odds Ratio		Alpha
	Total N	Group 1 N1	Group 2 N2	Multiplier M	Null OR0	Actual OR1	
0.9	171	85	85	170.7	1	3	0.05

The value of 171 agrees exactly with that of Nam (1992) for the uncorrected test.

## Example 3 – Finding Power of a Completed Experiment

Suppose you want to find the power for a completed experiment in which the individual strata sample sizes are known. In this example there are three strata with success probabilities 0.72, 0.66, and 0.69. The sample sizes for the treatment group in each stratum are 102, 113, and 97. The sample sizes for the control group in each stratum are 98, 110, and 114. The experiment was designed to detect an odds ratio of at least 1.5 with alpha equal to 0.05 for a one-sided test.

To calculate the power in this situation, we set M to 1 and enter the sample sizes directly into R1 and R2.

### 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 .....	<b>Power</b>
Test Type.....	<b>Continuity-Corrected Z-Test</b>
Alternative Hypothesis .....	<b>One-Sided (H1: OR &gt; OR0)</b>
Alpha.....	<b>0.05</b>
M (Sample Size Multiplier) .....	<b>1</b>
OR0 (Odds Ratio   H0).....	<b>1</b>
OR1 (Actual Odds Ratio) .....	<b>1.5</b>
Set 1 Number of Strata .....	<b>1</b>
Set 1 R1 = N1 / M .....	<b>102</b>
Set 1 R2 = N2 / M .....	<b>98</b>
Set 1 Pr(Success).....	<b>0.72</b>
Set 2 Number of Strata .....	<b>1</b>
Set 2 R1 = N1 / M .....	<b>113</b>
Set 2 R2 = N2 / M .....	<b>110</b>
Set 2 Pr(Success).....	<b>0.66</b>
Set 3 Number of Strata .....	<b>1</b>
Set 3 R1 = N1 / M .....	<b>97</b>
Set 3 R2 = N2 / M .....	<b>114</b>
Set 3 Pr(Success).....	<b>0.69</b>

## Output

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

### Numeric Results of Cochran-Mantel-Haenszel Test of an Odds Ratio

Solve For: [Power](#)  
 Test Type: Continuity-Corrected Z-Test  
 Hypotheses:  $H_0: OR \leq OR_0$  vs.  $H_1: OR > OR_0$

	Sample Size				Odds Ratio		Alpha
	Total N	Group 1 N1	Group 2 N2	Multiplier M	Null OR0	Actual OR1	
<b>Power</b>							
0.69797	634	312	322	1	1	1.5	0.05

The power to detect an odds ratio of 1.5 is only 0.69797 in this design.