Chapter 197

Superiority by a Margin Tests for the Odds Ratio of Two Proportions

Introduction

This module provides power analysis and sample size calculation for superiority by a margin tests of the odds ratio in two-sample designs in which the outcome is binary. Users may choose between two popular test statistics commonly used for running the hypothesis test.

The power calculations assume that independent, random samples are drawn from two populations.

Example

A superiority by a margin test example will set the stage for the discussion of the terminology that follows. Suppose that the current treatment for a disease works 70% of the time. A promising new treatment has been developed to the point where it can be tested. The researchers wish to show that the new treatment is better than the current treatment by at least some amount. In other words, does a clinically significant higher number of treated subjects respond to the new treatment?

Clinicians want to demonstrate the new treatment is superior to the current treatment. They must determine, however, how much more effective the new treatment must be to be adopted. Should it be adopted if 71% respond? 72%? 75%? 80%? There is a percentage above 70% at which the difference between the two treatments is no longer considered ignorable. After thoughtful discussion with several clinicians, it was decided that if the odds ratio of new treatment to reference is at least 1.1, the new treatment would be adopted. This ratio is called the *margin of superiority*. The margin of superiority in this example is 1.1.

The developers must design an experiment to test the hypothesis that the odds ratio of the new treatment to the reference is at least 1.1. The statistical hypothesis to be tested is

$$H_0: O_1/O_2 \le 1.1 \quad \text{versus} \quad H_1: O_1/O_2 > 1.1$$

Notice that when the null hypothesis is rejected, the conclusion is that the odds ratio is at least 1.1. Note that even though the response rate of the current treatment is 0.70, the hypothesis test is about an odds ratio of 1.1. Also notice that a rejection of the null hypothesis results in the conclusion of interest.

Technical Details

The details of sample size calculation for the two-sample design for binary outcomes are presented in the chapter "Tests for Two Proportions," and they will not be duplicated here. Instead, this chapter only discusses those changes necessary for superiority by a margin tests.

This procedure has the capability for calculating power based on large sample (normal approximation) results and based on the enumeration of all possible values in the binomial distribution.

Suppose you have two populations from which dichotomous (binary) responses will be recorded. Assume without loss of generality that the higher proportions are better. The probability (or risk) of cure in population 1 (the treatment group) is p_1 and in population 2 (the reference group) is p_2. Random samples of n_1 and n_2 individuals are obtained from these two populations. The data from these samples can be displayed in a 2-by-2 contingency table as follows

Group	Success	Failure	Total
Treatment	x_{11}	x_{12}	n_1
Control	x_{21}	x_{22}	n_2
Totals	m_1	m_2	N

The binomial proportions, p_1 and p_2, are estimated from these data using the formulae

$$\hat{p}_1 = \frac{a}{m} = \frac{x_{11}}{n_1} \text{ and } \hat{p}_2 = \frac{b}{n} = \frac{x_{21}}{n_2}$$

Define $O_i = p_i/(1 - p_i)$. Let $p_{1.0}$ represent the group 1 proportion tested by the null hypothesis, H_0. The power of a test is computed at a specific value of the proportion which we will call $p_{1.1}$. Let ψ_0 represent the smallest odds ratio (margin of superiority) between the two proportions that still results in the conclusion that the new treatment is superior to the current treatment. For a superiority by a margin test, $\psi_0 > 1$ The set of statistical hypotheses that are tested is

$$H_0: O_1/O_2 \le \psi_0 \quad \text{versus} \quad H_1: O_1/O_2 > \psi_0$$

which can be rearranged to give

$$H_0: O_1 \le O_2\psi_0 \quad \text{versus} \quad H_1: O_1 > O_2\psi_0$$

There are three common methods of specifying the margin of superiority. The most direct is to simply give values for p_2 and $p_{1.0}$. However, it is often more meaningful to give p_2 and then specify $p_{1.0}$ implicitly by specifying the difference, ratio, or odds ratio. Mathematically, the definitions of these parameterizations are

<u>Parameter</u>	<u>Computation</u>	<u>Hypotheses</u>
Difference	$\delta_0 = p_{1.0} - p_2$	$H_0: p_1 - p_2 \le \delta_0 \quad \text{versus} \quad H_1: p_1 - p_2 > \delta_0$
Ratio	$\phi_0 = p_{1.0}/p_2$	$H_0: p_1/p_2 \le \phi_0 \quad \text{versus} \quad H_1: p_1/p_2 > \phi_0$
Odds Ratio	$\psi_0 = O_{1.0}/O_2$	$H_0: O_1/O_2 \le \psi_0 \quad \text{versus} \quad H_1: O_1/O_2 > \psi_0$

Odds Ratio

The odds ratio, $\psi = O_1/O_2 = (p_1/(1-p_1))/(p_2/(1-p_2))$, gives the relative change in the odds of the response. Testing superiority by a margin uses the formulation

$$H_0: O_1/O_2 \le \psi_0 \quad \text{versus} \quad H_1: O_1/O_2 > \psi_0$$

or equivalently

$$H_0: \psi \le \psi_0 \quad \text{versus} \quad H_1: \psi > \psi_0.$$

For superiority by a margin tests with higher proportions better, $\psi_0 > 1$. For superiority by a margin tests with higher proportions worse, $\psi_0 < 1$.

A Note on Setting the Significance Level, Alpha

Setting the significance level has always been somewhat arbitrary. For planning purposes, the standard has become to set alpha to 0.05 for two-sided tests. Almost universally, when someone states that a result is statistically significant, they mean statistically significant at the 0.05 level.

Although 0.05 may be the standard for two-sided tests, it is not always the standard for one-sided tests, such as superiority by a margin tests. Statisticians often recommend that the alpha level for one-sided tests be set at 0.025 since this is the amount put in each tail of a two-sided test.

Power Calculation

The power for a test statistic that is based on the normal approximation can be computed exactly using two binomial distributions. The following steps are taken to compute the power of these tests.

1. Find the critical value using the standard normal distribution. The critical value, $z_{critical}$, is that value of z that leaves exactly the target value of alpha in the appropriate tail of the normal distribution.

2. Compute the value of the test statistic, z_t, for every combination of x_{11} and x_{21}. Note that x_{11} ranges from 0 to n_1, and x_{21} ranges from 0 to n_2. A small value (around 0.0001) can be added to the zero-cell counts to avoid numerical problems that occur when the cell value is zero.

3. If $z_t > z_{critical}$, the combination is in the rejection region. Call all combinations of x_{11} and x_{21} that lead to a rejection the set A.

4. Compute the power for given values of $p_{1.1}$ and p_2 as

$$1 - \beta = \sum_A \binom{n_1}{x_{11}} p_{1.1}^{x_{11}} q_{1.1}^{n_1 - x_{11}} \binom{n_2}{x_{21}} p_2^{x_{21}} q_2^{n_2 - x_{21}}.$$

5. Compute the actual value of alpha achieved by the design by substituting $p_{1.0}$ for $p_{1.1}$ to obtain

$$\alpha^* = \sum_A \binom{n_1}{x_{11}} p_{1.0}^{x_{11}} q_{1.0}^{n_1 - x_{11}} \binom{n_2}{x_{21}} p_2^{x_{21}} q_2^{n_2 - x_{21}}.$$

Asymptotic Approximations

When the values of n_1 and n_2 are large (say over 200), these formulas often take a long time to evaluate. In this case, a large sample approximation can be used. The large sample approximation is made by replacing the values of $\hat{p}_1$ and $\hat{p}_2$ in the z statistic with the corresponding values of $p_{1.1}$ and p_2, and then computing the results based on the normal distribution.

Test Statistics

Two test statistics have been proposed for testing whether the odds ratio is different from a specified value. The main difference between the test statistics is in the formula used to compute the standard error used in the denominator. These tests are both

In power calculations, the values of $\hat{p}_1$ and $\hat{p}_2$ are not known. The corresponding values of $p_{1.1}$ and p_2 may be reasonable substitutes.

Following is a list of the test statistics available in **PASS**. The availability of several test statistics begs the question of which test statistic one should use. The answer is simple: <u>one should use the test statistic that will be used to analyze the data.</u> You may choose a method because it is a standard in your industry, because it seems to have better statistical properties, or because your statistical package calculates it. Whatever your reasons for selecting a certain test statistic, you should use the same test statistic when doing the analysis after the data have been collected.

Miettinen and Nurminen's Likelihood Score Test

Miettinen and Nurminen (1985) proposed a test statistic for testing whether the odds ratio is equal to a specified value, ψ_0. Because the approach they used with the difference and ratio does not easily extend to the odds ratio, they used a score statistic approach for the odds ratio. The regular MLE's are $\hat{p}_1$ and $\hat{p}_2$. The constrained MLE's are $\tilde{p}_1$ and $\tilde{p}_2$. These estimates are constrained so that $\tilde{\psi} = \psi_0$. A correction factor of N/(N-1) is applied to make the variance estimate less biased. The significance level of the test statistic is based on the asymptotic normality of the score statistic.

The formula for computing the test statistic is

$$z_{MNO} = \frac{\dfrac{(\hat{p}_1 - \tilde{p}_1)}{\tilde{p}_1 \tilde{q}_1} - \dfrac{(\hat{p}_2 - \tilde{p}_2)}{\tilde{p}_2 \tilde{q}_2}}{\sqrt{\left(\dfrac{1}{n_1 \tilde{p}_1 \tilde{q}_1} + \dfrac{1}{n_2 \tilde{p}_2 \tilde{q}_2}\right)\left(\dfrac{N}{N-1}\right)}}$$

where

$$\tilde{p}_1 = \frac{\tilde{p}_2 \psi_0}{1 + \tilde{p}_2 (\psi_0 - 1)}$$

$$\tilde{p}_2 = \frac{-B + \sqrt{B^2 - 4AC}}{2A}$$

$$A = n_2 (\psi_0 - 1)$$

$$B = n_1 \psi_0 + n_2 - m_1 (\psi_0 - 1)$$

$$C = -m_1$$

Farrington and Manning's Likelihood Score Test

Farrington and Manning (1990) indicate that the Miettinen and Nurminen statistic may be modified by removing the factor $N/(N-1)$.

The formula for computing this test statistic is

$$z_{FMO} = \frac{\dfrac{\left(\hat{p}_1 - \tilde{p}_1\right)}{\tilde{p}_1 \tilde{q}_1} - \dfrac{\left(\hat{p}_2 - \tilde{p}_2\right)}{\tilde{p}_2 \tilde{q}_2}}{\sqrt{\left(\dfrac{1}{n_1 \tilde{p}_1 \tilde{q}_1} + \dfrac{1}{n_2 \tilde{p}_2 \tilde{q}_2}\right)}}$$

where the estimates $\tilde{p}_1$ and $\tilde{p}_2$ are computed as in the corresponding test of Miettinen and Nurminen (1985) given above.

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 the parameters associated with this test such as the proportions, odds ratios, sample sizes, alpha, and power.

Solve For

Solve For

This option specifies the parameter to be solved for using the other parameters. The parameters that may be selected are *Power*, *Sample Size*, and *Effect Size*.

Select *Power* when you want to calculate the power of an experiment.

Select *Sample Size* when you want to calculate the sample size needed to achieve a given power and alpha level.

Power Calculation

Power Calculation Method

Select the method to be used to calculate power. When the sample sizes are reasonably large (i.e. greater than 50) and the proportions are between 0.2 and 0.8 the two methods will give similar results. For smaller sample sizes and more extreme proportions (less than 0.2 or greater than 0.8), the normal approximation is not as accurate so the binomial calculations may be more appropriate.

The choices are

- **Binomial Enumeration**

  Power for each test is computed using binomial enumeration of all possible outcomes when N1 and N2 ≤ Maximum N1 or N2 for Binomial Enumeration (otherwise, the normal approximation is used). Binomial enumeration of all outcomes is possible because of the discrete nature of the data.

- **Normal Approximation**

  Approximate power for each test is computed using the normal approximation to the binomial distribution.

Actual alpha values are only computed when "Binomial Enumeration" is selected.

Power Calculation – Binomial Enumeration Options

Only shown when Power Calculation Method = "Binomial Enumeration"

Maximum N1 or N2 for Binomial Enumeration

When both N1 and N2 are less than or equal to this amount, power calculations using the binomial distribution are made. The value of the "Actual Alpha" is only calculated when binomial power calculations are made.

When either N1 or N2 is larger than this amount, the normal approximation to the binomial is used for power calculations.

Zero Count Adjustment Method

Zero cell counts cause many calculation problems when enumerating binomial probabilities. To compensate for this, a small value (called the "Zero Count Adjustment Value") may be added either to all cells or to all cells with zero counts. This option specifies which type of adjustment you want to use.

Adding a small value is controversial, but may be necessary. Some statisticians recommend adding 0.5 while others recommend 0.25. We have found that adding values as small as 0.0001 seems to work well.

Zero Count Adjustment Value

Zero cell counts cause many calculation problems when enumerating binomial probabilities. To compensate for this, a small value may be added either to all cells or to all zero cells. This is the amount that is added. We have found that 0.0001 works well.

Be warned that the value of the odds ratio will be affected by the amount specified here!

Test

Higher Proportions Are

Use this option to specify the direction of the test. Note that OR = O1/O2.

If Higher Proportions are "Better", the alternative hypothesis is H1: OR > OR0.

If Higher Proportions are "Worse", the alternative hypothesis is H1: OR < OR0.

Test Type

Specify which test statistic is used in searching and reporting.

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 here or a range of values such as *0.8 to 0.95 by 0.05* may be entered.

Superiority by a Margin Tests for the Odds Ratio of Two Proportions

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. Historically, the value of 0.05 has been used for alpha. 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 (When Solving for Sample Size)

Group Allocation

Select the option that describes the constraints on *N1* or *N2* or both.

The options are

- **Equal (N1 = N2)**

  This selection is used when you wish to have equal sample sizes in each group. Since you are solving for both sample sizes at once, no additional sample size parameters need to be entered.

- **Enter N1, solve for N2**

  Select this option when you wish to fix *N1* at some value (or values), and then solve only for *N2*. Please note that for some values of *N1*, there may not be a value of *N2* that is large enough to obtain the desired power.

- **Enter N2, solve for N1**

  Select this option when you wish to fix *N2* at some value (or values), and then solve only for *N1*. Please note that for some values of *N2*, there may not be a value of *N1* that is large enough to obtain the desired power.

- **Enter R = N2/N1, solve for N1 and N2**

  For this choice, you set a value for the ratio of *N2* to *N1*, and then PASS determines the needed *N1* and *N2*, with this ratio, to obtain the desired power. An equivalent representation of the ratio, *R*, is

  $$N2 = R * N1.$$

- **Enter percentage in Group 1, solve for N1 and N2**

  For this choice, you set a value for the percentage of the total sample size that is in Group 1, and then PASS determines the needed *N1* and *N2* with this percentage to obtain the desired power.

N1 (Sample Size, Group 1)

This option is displayed if Group Allocation = "Enter N1, solve for N2"

N1 is the number of items or individuals sampled from the Group 1 population.

N1 must be ≥ 2. You can enter a single value or a series of values.

N2 (Sample Size, Group 2)

This option is displayed if Group Allocation = "Enter N2, solve for N1"

N2 is the number of items or individuals sampled from the Group 2 population.

N2 must be ≥ 2. You can enter a single value or a series of values.

R (Group Sample Size Ratio)

This option is displayed only if Group Allocation = "Enter R = N2/N1, solve for N1 and N2."

R is the ratio of *N2* to *N1*. That is,

$$R = N2 / N1.$$

Use this value to fix the ratio of *N2* to *N1* while solving for *N1* and *N2*. Only sample size combinations with this ratio are considered.

N2 is related to *N1* by the formula:

$$N2 = [R \times N1],$$

where the value *[Y]* is the next integer $\geq Y$.

For example, setting *R* = 2.0 results in a Group 2 sample size that is double the sample size in Group 1 (e.g., *N1* = 10 and *N2* = 20, or *N1* = 50 and *N2* = 100).

R must be greater than 0. If *R* < 1, then *N2* will be less than *N1*; if *R* > 1, then *N2* will be greater than *N1*. You can enter a single or a series of values.

Percent in Group 1

This option is displayed only if Group Allocation = "Enter percentage in Group 1, solve for N1 and N2."

Use this value to fix the percentage of the total sample size allocated to Group 1 while solving for *N1* and *N2*. Only sample size combinations with this Group 1 percentage are considered. Small variations from the specified percentage may occur due to the discrete nature of sample sizes.

The Percent in Group 1 must be greater than 0 and less than 100. You can enter a single or a series of values.

Sample Size (When <u>Not</u> Solving for Sample Size)

Group Allocation

Select the option that describes how individuals in the study will be allocated to Group 1 and to Group 2.

The options are

- **Equal (N1 = N2)**

  This selection is used when you wish to have equal sample sizes in each group. A single per group sample size will be entered.

- **Enter N1 and N2 individually**

  This choice permits you to enter different values for *N1* and *N2*.

- **Enter N1 and R, where N2 = R * N1**

  Choose this option to specify a value (or values) for *N1*, and obtain *N2* as a ratio (multiple) of *N1*.

- **Enter total sample size and percentage in Group 1**

  Choose this option to specify a value (or values) for the total sample size (*N*), obtain *N1* as a percentage of *N*, and then *N2* as *N - N1*.

Sample Size Per Group

This option is displayed only if Group Allocation = "Equal (N1 = N2)."

The Sample Size Per Group is the number of items or individuals sampled from each of the Group 1 and Group 2 populations. Since the sample sizes are the same in each group, this value is the value for *N1*, and also the value for *N2*.

The Sample Size Per Group must be ≥ 2. You can enter a single value or a series of values.

N1 (Sample Size, Group 1)

*This option is displayed if Group Allocation = "Enter N1 and N2 individually" or "Enter N1 and R, where N2 = R * N1."*

N1 is the number of items or individuals sampled from the Group 1 population.

N1 must be ≥ 2. You can enter a single value or a series of values.

N2 (Sample Size, Group 2)

This option is displayed only if Group Allocation = "Enter N1 and N2 individually."

N2 is the number of items or individuals sampled from the Group 2 population.

N2 must be ≥ 2. You can enter a single value or a series of values.

R (Group Sample Size Ratio)

*This option is displayed only if Group Allocation = "Enter N1 and R, where N2 = R * N1."*

R is the ratio of *N2* to *N1*. That is,

$$R = N2/N1$$

Use this value to obtain *N2* as a multiple (or proportion) of *N1*.

N2 is calculated from *N1* using the formula:

$$N2=[R \times N1],$$

where the value *[Y]* is the next integer ≥ *Y*.

For example, setting *R* = 2.0 results in a Group 2 sample size that is double the sample size in Group 1.

R must be greater than 0. If *R* < 1, then *N2* will be less than N1; if *R* > 1, then *N2* will be greater than *N1*. You can enter a single value or a series of values.

Total Sample Size (N)

This option is displayed only if Group Allocation = "Enter total sample size and percentage in Group 1."

This is the total sample size, or the sum of the two group sample sizes. This value, along with the percentage of the total sample size in Group 1, implicitly defines *N1* and *N2*.

The total sample size must be greater than one, but practically, must be greater than 3, since each group sample size needs to be at least 2.

You can enter a single value or a series of values.

Percent in Group 1

This option is displayed only if Group Allocation = "Enter total sample size and percentage in Group 1."

This value fixes the percentage of the total sample size allocated to Group 1. Small variations from the specified percentage may occur due to the discrete nature of sample sizes.

The Percent in Group 1 must be greater than 0 and less than 100. You can enter a single value or a series of values.

Effect Size – Odds Ratios

OR0 (Superiority Odds Ratio)

This option specifies the trivial odds ratio between P1 and P2. The power calculations assume that P1.0 is the value of the P1 under the null hypothesis. OR0 is used with P2 to calculate the value of P1.0.

When *Higher Proportions Are* is set to *Better*, the trivial odds ratio implicitly gives the amount by which P1 must be greater than P2 to have the treatment group declared superior to the reference group. OR0 should be greater than one for superiority by a margin tests. The reverse is the case when *Higher Proportions Are* is set to *Worse*.

Odds ratios must be positive. OR0 cannot take on the value of 1.

You may enter a range of values such as *0.95 0.97 0.99* or *0.91 to 0.99 by 0.02*.

OR1 (Actual Odds Ratio)

This option specifies the odds ratio of P1 and P2, where P1.1 is the actual proportion in the treatment group. The power calculations assume that P1.1 is the actual value of the proportion in group 1. This value is used with P2 to calculate the value of P1.1.

Odds ratios must be positive. You may enter a range of values such as *0.95 1 1.05* or *0.9 to 1 by 0.02*.

Effect Size – Group 2 (Reference)

P2 (Reference Group Proportion)

Specify the value of p_2, the reference, baseline, or control group's proportion. The null hypothesis is that the two proportions differ by no more than a specified amount. Since P2 is a proportion, these values must be between 0 and 1.

You may enter a range of values such as *0.1 0.2 0.3* or *0.1 to 0.9 by 0.1*.

Example 1 – Finding Power

A study is being designed to establish the superiority of a new treatment compared to the current treatment. Historically, the current treatment has enjoyed a 62.5% cure rate. The new treatment is hoped to perform better than the current treatment. Thus, the new treatment will be adopted if it is more effective than the current treatment by a clinically significant amount. The researchers will recommend adoption of the odds ratio of the new treatment to the old treatment is at least 1.5.

The researchers plan to use the Farrington and Manning likelihood score test statistic to analyze the data that will be (or has been) obtained. They want to study the power of the Farrington and Manning test at group sample sizes ranging from 50 to 500 when the actual odds ratio is 2.0. The significance level will be 0.05.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Superiority by a Margin Tests for the Odds Ratio of Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Superiority by a Margin**, and then clicking on **Superiority by a Margin Tests for the Odds Ratio of Two Proportions**. 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**
Power Calculation Method ....**Normal Approximation**
Higher Proportions Are...........................**Better (H1: OR > OR0)**
Test Type...**Likelihood Score (Farr. & Mann.)**
Alpha **0.05**
Group Allocation ....**Equal (N1 = N2)**
Sample Size Per Group..........................**50 to 500 by 50**
OR0 (Superiority Odds Ratio) **1.5**
OR1 (Actual Odds Ratio).......................**2.0**
P2 (Group 2 Proportion) **0.625**

Annotated Output

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

Numeric Results

```
Numeric Results ─────────────────────────────────────────────────────────────
Test Statistic: Farrington & Manning Likelihood Score Test
Hypotheses:  H0: OR ≤ OR0   vs.   H1: OR > OR0
```

Power*	N1	N2	N	Ref. P2	P1|H0 P1.0	P1|H1 P1.1	Sup. OR OR0	OR OR1	Alpha
0.16278	50	50	100	0.6250	0.7143	0.7692	1.500	2.000	0.050
0.23613	100	100	200	0.6250	0.7143	0.7692	1.500	2.000	0.050
0.30292	150	150	300	0.6250	0.7143	0.7692	1.500	2.000	0.050
0.36502	200	200	400	0.6250	0.7143	0.7692	1.500	2.000	0.050
0.42291	250	250	500	0.6250	0.7143	0.7692	1.500	2.000	0.050
0.47676	300	300	600	0.6250	0.7143	0.7692	1.500	2.000	0.050
0.52669	350	350	700	0.6250	0.7143	0.7692	1.500	2.000	0.050
0.57279	400	400	800	0.6250	0.7143	0.7692	1.500	2.000	0.050
0.61522	450	450	900	0.6250	0.7143	0.7692	1.500	2.000	0.050
0.65413	500	500	1000	0.6250	0.7143	0.7692	1.500	2.000	0.050

* Power was computed using the normal approximation method.

References
Chow, S.C., Shao, J., and Wang, H. 2008. Sample Size Calculations in Clinical Research, Second Edition.
　Chapman & Hall/CRC. Boca Raton, Florida.
Farrington, C. P. and Manning, G. 1990. 'Test Statistics and Sample Size Formulae for Comparative Binomial
　Trials with Null Hypothesis of Non-Zero Risk Difference or Non-Unity Relative Risk.' Statistics in
　Medicine, Vol. 9, pages 1447-1454.
Fleiss, J. L., Levin, B., Paik, M.C. 2003. Statistical Methods for Rates and Proportions. Third Edition. John
　Wiley & Sons. New York.
Gart, John J. and Nam, Jun-mo. 1988. 'Approximate Interval Estimation of the Ratio in Binomial Parameters: A
　Review and Corrections for Skewness.' Biometrics, Volume 44, Issue 2, 323-338.
Gart, John J. and Nam, Jun-mo. 1990. 'Approximate Interval Estimation of the Difference in Binomial
　Parameters: Correction for Skewness and Extension to Multiple Tables.' Biometrics, Volume 46, Issue 3,
　637-643.
Julious, S. A. and Campbell, M. J. 2012. 'Tutorial in biostatistics: sample sizes for parallel group clinical
　trials with binary data.' Statistics in Medicine, 31:2904-2936.
Lachin, John M. 2000. Biostatistical Methods. John Wiley & Sons. New York.
Machin, D., Campbell, M., Fayers, P., and Pinol, A. 1997. Sample Size Tables for Clinical Studies, 2nd
　Edition. Blackwell Science. Malden, Mass.
Miettinen, O.S. and Nurminen, M. 1985. 'Comparative analysis of two rates.' Statistics in Medicine 4: 213-226.

Report Definitions
Power is the probability of rejecting a false null hypothesis.
N1 and N2 are the number of items sampled from each population.
N is the total sample size, N1 + N2.
P2 is the proportion for Group 2, which is the standard, reference, or control group.
P1 is the proportion for Group 1, which is the treatment or experimental group. P1.0 is the smallest Group 1
　proportion that still yields a superiority conclusion. P1.1 is the proportion for Group 1 under the
　alternative hypothesis at which power and sample size calculations are made.
OR0 is the superiority odds ratio, [P1/(1-P1)] / [P2/(1-P2)], assuming H0. OR1 is the odds ratio under the
　alternative hypothesis used for power and sample size calculations.
Alpha is the probability of rejecting a true null hypothesis.

Summary Statements ───
Sample sizes of 50 in Group 1 and 50 in Group 2 achieve 16.278% power to detect an odds ratio
of 2.000 when the superiority odds ratio is 1.500. The reference group proportion is 0.6250.
The treatment group proportion is assumed to be 0.7143 under the null hypothesis. The power was
computed for the case when the actual treatment group proportion is 0.7692. The test statistic
used is the one-sided Score test (Farrington & Manning). The significance level of the test is
0.050.

This report shows the values of each of the parameters, one scenario per row.

Plots Section

Power vs N1

OR1=2.00 P2=0.63 A=0.050 N2=N1 OR0=1.50 1-Sided LS FM Test
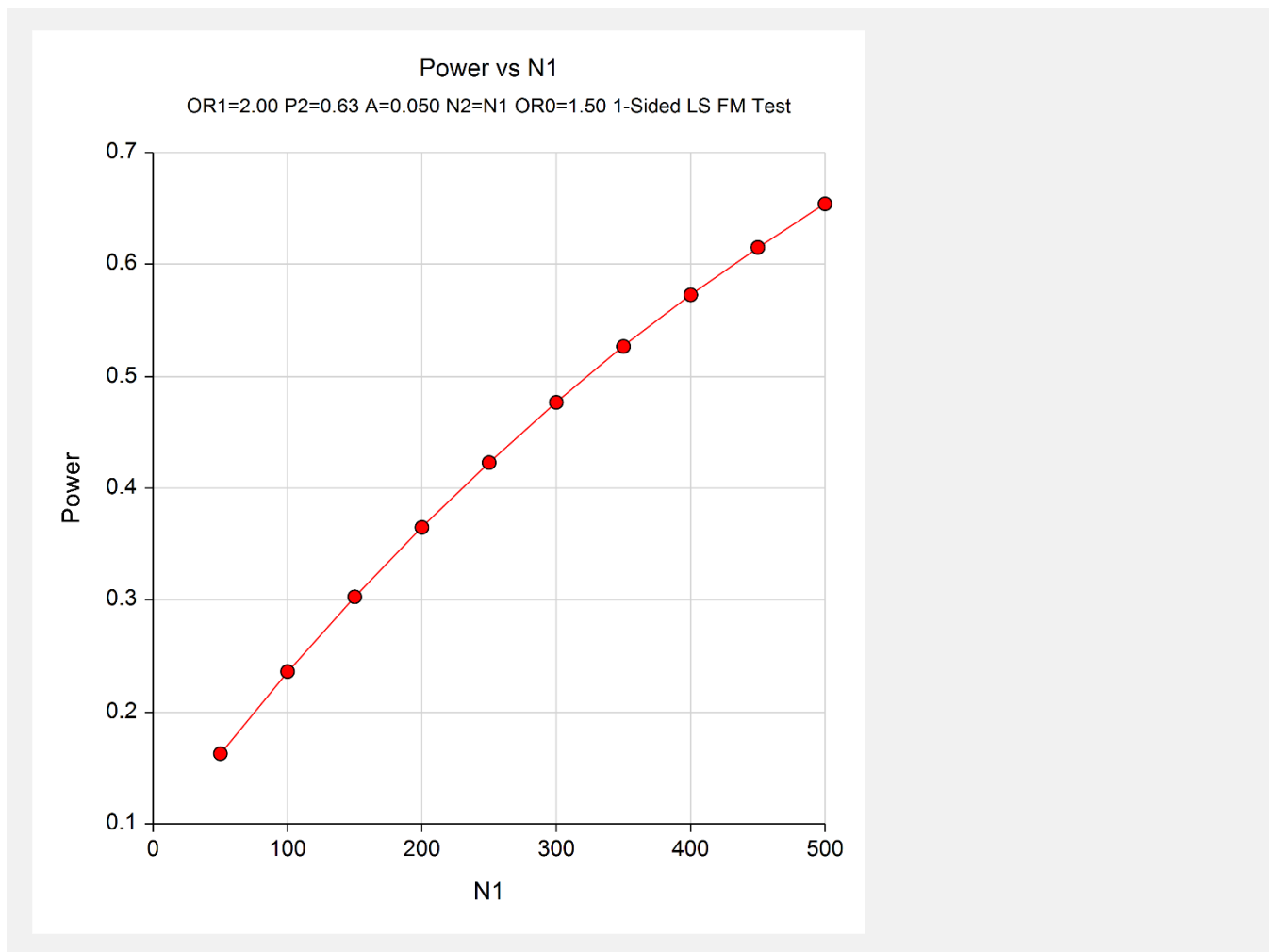
The values from the table are displayed in the above chart. These charts give us a quick look at the sample size that will be required for various sample sizes.

Example 2 – Finding the Sample Size

Continuing with the scenario given in Example 1, the researchers want to determine the sample size necessary to achieve a power of 0.80.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Superiority by a Margin Tests for the Odds Ratio of Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Superiority by a Margin**, and then clicking on **Superiority by a Margin Tests for the Odds Ratio of Two Proportions**. 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	**Sample Size**
Power Calculation Method	**Normal Approximation**
Higher Proportions Are..........................	**Better (H1: OR > OR0)**
Test Type...	**Likelihood Score (Farr. & Mann.)**
Power	**0.80**
Alpha	**0.05**
Group Allocation	**Equal (N1 = N2)**
OR0 (Superiority Odds Ratio)	**1.5**
OR1 (Actual Odds Ratio)	**2.0**
P2 (Group 2 Proportion)	**0.625**

Output

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

Numeric Results

Numeric Results ──
Test Statistic: Farrington & Manning Likelihood Score Test
Hypotheses: H0: OR ≤ OR0 vs. H1: OR > OR0

Target Power	Actual Power*	N1	N2	N	Ref. P2	P1|H0 P1.0	P1|H1 P1.1	Sup. OR OR0	OR OR1	Alpha
0.80	0.80002	745	745	1490	0.6250	0.7143	0.7692	1.500	2.000	0.050

* Power was computed using the normal approximation method.

The required sample size is 1035 per group.

Example 3 – Comparing the Power of the Two Test Statistics

Continuing with Example 2, the researchers want to determine which of the two possible test statistics to adopt by using the comparative reports and charts that **PASS** produces. They decide to compare the powers from binomial enumeration and actual alphas for various sample sizes between 1000 and 1200.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Superiority by a Margin Tests for the Odds Ratio of Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Superiority by a Margin**, and then clicking on **Superiority by a Margin Tests for the Odds Ratio of Two Proportions**. 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 ....**Power**
Power Calculation Method ....**Binomial Enumeration**
Maximum N1 or N2 for Binomial Enumeration **5000**
Zero Count Adjustment Method..........................**Add to zero cells only**
Zero Count Adjustment Value **0.0001**
Higher Proportions Are......................................**Better (H1: OR > OR0)**
Test Type...**Likelihood Score (Farr. & Mann.)**
Alpha **0.05**
Group Allocation ....**Equal (N1 = N2)**
Sample Size Per Group.....................................**600 700 800**
OR0 (Superiority Odds Ratio) **1.5**
OR1 (Actual Odds Ratio) **2.0**
P2 (Group 2 Proportion) **0.625**

Reports Tab
Show Comparative Reports ....**Checked**

Comparative Plots Tab
Show Comparative Plots....................................**Checked**

Output

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

Numeric Results and Plots

Power Comparison of Two Different Tests ———————————————————————————————
Hypotheses: H0: OR ≤ OR0   vs.   H1: OR > OR0

|			Target	F.M. Score	M.N. Score
N1/N2	**P2**	**P1.1**	**Alpha**	**Power**	**Power**
600/600	0.6250	0.7692	0.0500	0.7297	0.7297
700/700	0.6250	0.7692	0.0500	0.7862	0.7862
800/800	0.6250	0.7692	0.0500	0.8322	0.8313

Note: Power was computed using binomial enumeration of all possible outcomes.

Actual Alpha Comparison of Two Different Tests ———————————————————————————
Hypotheses: H0: OR ≤ OR0   vs.   H1: OR > OR0

			Target	F.M. Score	M.N. Score
N1/N2	**P2**	**P1.1**	**Alpha**	**Alpha**	**Alpha**
600/600	0.6250	0.7692	0.0500	0.0503	0.0503
700/700	0.6250	0.7692	0.0500	0.0502	0.0502
800/800	0.6250	0.7692	0.0500	0.0502	0.0501

Note: Actual alpha was computed using binomial enumeration of all possible outcomes.
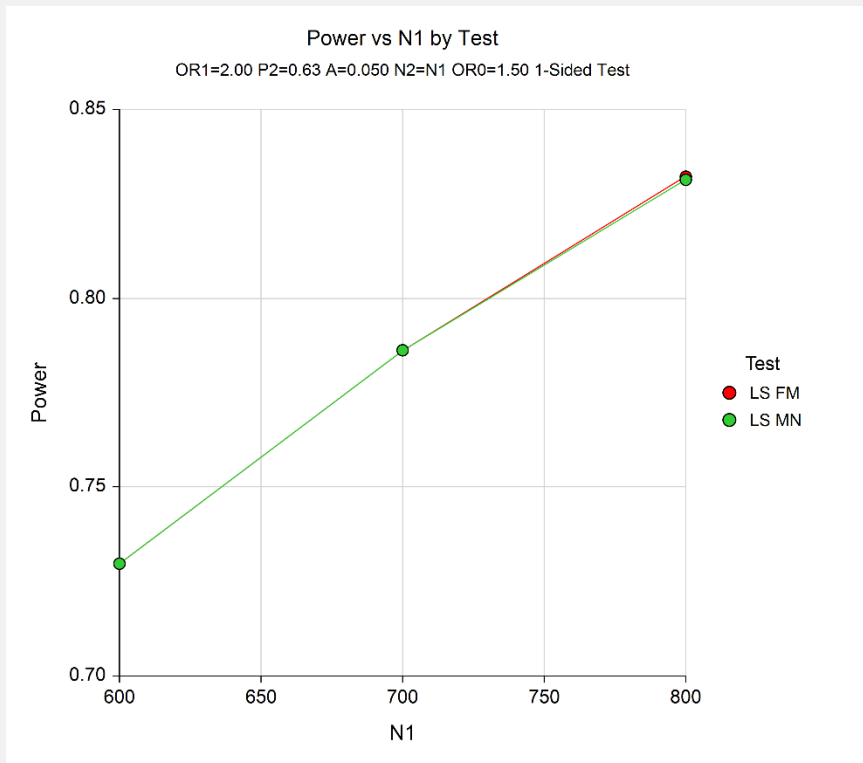
The power is almost exactly the same for both tests, which is not surprising given the large sample size.

Example 4 – Comparing Power Calculation Methods

Continuing with Example 3, let's see how the results compare if we were to use approximate power calculations instead of power calculations based on binomial enumeration.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Superiority by a Margin Tests for the Odds Ratio of Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Superiority by a Margin**, and then clicking on **Superiority by a Margin Tests for the Odds Ratio of Two Proportions**. 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**.

Option	Value
Design Tab	
Solve For	**Power**
Power Calculation Method	**Normal Approximation**
Higher Proportions Are..........................	**Better (H1: OR > OR0)**
Test Type..	**Likelihood Score (Farr. & Mann.)**
Alpha	**0.05**
Group Allocation	**Equal (N1 = N2)**
Sample Size Per Group.........................	**600 700 800**
OR0 (Superiority Odds Ratio)	**1.5**
OR1 (Actual Odds Ratio).......................	**2.0**
P2 (Group 2 Proportion)	**0.625**
Reports Tab	
Show Power Detail Report.....................	**Checked**

Output

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

Numeric Results and Plots

Power Detail Report ——
Test Statistic: Farrington & Manning Likelihood Score Test
Hypotheses: H0: OR ≤ OR0 vs. H1: OR > OR0

				Normal Approximation		Binomial Enumeration	
N1/N2	P2	OR0	OR1	Power	Alpha	Power	Alpha
600/600	0.6250	1.500	2.000	0.72209	0.050	0.72971	0.050
700/700	0.6250	1.500	2.000	0.77821	0.050	0.78622	0.050
800/800	0.6250	1.500	2.000	0.82407	0.050	0.83218	0.050

Notice that the approximate power values are close to the binomial enumeration values for all sample sizes.

Example 5 – Validation

We could not find a validation example for a superiority by a margin test for the odds ratio of two proportions. The calculations are basically the same as those for a superiority by a margin test of the ratio of two proportions, which has been validated using Blackwelder (1993). We refer you to Example 5 of Chapter 196, "Superiority by a Margin Tests for the Ratio of Two Proportions," for a validation example.