

## Chapter 205

# Non-Zero Null Tests for the Difference Between Two Proportions

## Introduction

This module computes power and sample size for hypothesis tests of the difference between two independent proportions where the null-hypothesized value is non-zero. The *non-offset* case is available in another procedure. This procedure compares the power achieved by each of several test statistics.

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

## Technical Details

Suppose you have two populations from which dichotomous (binary) responses will be recorded. The probability (or risk) of obtaining the event of interest in population 1 (the treatment group) is  $p_1$  and in population 2 (the control group) is  $p_2$ . The corresponding failure proportions are given by  $q_1 = 1 - p_1$  and  $q_2 = 1 - p_2$ .

An assumption is made that the responses from each group follow a binomial distribution. This means that the event probability,  $p_i$ , is the same for all subjects within the group and that the response from one subject is independent of that of any other subject.

Random samples of  $m$  and  $n$  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	$a$	$c$	$m$
Control	$b$	$d$	$n$
Total	$s$	$f$	$N$

The following alternative notation is sometimes used.

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

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

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

## Comparing Two Proportions

When analyzing studies such as this, you usually want to compare the two binomial probabilities,  $p_1$  and  $p_2$ . The most direct method of comparing these quantities is to calculate their difference or their ratio. If the binomial probability is expressed in terms of odds rather than probability, another measure is the odds ratio. Mathematically, these comparison parameters are

<u>Parameter</u>	<u>Computation</u>
Difference	$\delta = p_1 - p_2$
Risk Ratio	$\phi = p_1 / p_2$
Odds Ratio	$\psi = \frac{p_1 / (1 - p_1)}{p_2 / (1 - p_2)} = \frac{p_1 q_2}{p_2 q_1}$

The choice of which of these measures is used might seem arbitrary, but it is not. Not only will the interpretation be different, but, for small sample sizes, the powers of tests based on different parameters will be different. The non-null case is commonly used in equivalence and non-inferiority testing.

### Difference

The (risk) difference,  $\delta = p_1 - p_2$ , is perhaps the most direct method of comparison between the two event probabilities. This parameter is easy to interpret and communicate. It gives the absolute impact of the treatment. However, there are subtle difficulties that can arise with its interpretation.

One interpretation difficulty occurs when the event of interest is rare. If a difference of 0.001 were reported for an event with a baseline probability of 0.40, we would probably dismiss this as being of little importance. That is, there usually little interest in a treatment that decreases the probability from 0.400 to 0.399. However, if the baseline probability of a disease was 0.002 and 0.001 was the decrease in the disease probability, this would represent a reduction of 50%. Thus we see that interpretation depends on the baseline probability of the event.

A similar situation occurs when the amount of possible difference is considered. Consider two events, one with a baseline event rate of 0.40 and the other with a rate of 0.02. What is the maximum decrease that can occur? Obviously, the first event rate can be decreased by an absolute amount of 0.40, while the second can only be decreased by a maximum of 0.02.

So, although creating the simple difference is a useful method of comparison, care must be taken that it is appropriate for the situation.

## Hypothesis Tests

Although several statistical tests are available for testing the inequality of two proportions, only a few can be generalized to the non-null case. No single test is the champion in every situation, so one should compare the powers of the various tests to determine which to use.

### Difference

The (risk) difference,  $\delta = p_1 - p_2$ , is perhaps the most direct method for comparing two proportions. Three sets of statistical hypotheses can be formulated:

1.  $H_0: p_1 - p_2 = \delta_0$  versus  $H_1: p_1 - p_2 \neq \delta_0$ ; this is often called the *two-tailed test*.
2.  $H_0: p_1 - p_2 \leq \delta_0$  versus  $H_1: p_1 - p_2 > \delta_0$ ; this is often called the *upper-tailed test*.
3.  $H_0: p_1 - p_2 \geq \delta_0$  versus  $H_1: p_1 - p_2 < \delta_0$ ; this is often called the *lower-tailed 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 such a test.

1. Find the critical value (or values in the case of a two-sided test) 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. For example, for an upper-tailed test with a target alpha of 0.05, the critical value is 1.645.
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  $p_{1.1}$  ( $p_1$  under the alternative) 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  $p_{1.0}$  ( $p_1$  under the null) 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 is used. The large sample approximation is made by replacing the values of  $\hat{p}_1$  and  $\hat{p}_2$  in the  $z$  values with the corresponding values of  $p_1$  and  $p_2$  under the alternative hypothesis and then computing the results based on the normal distribution. Note that in large samples, the Farrington and Manning statistic is substituted for the Gart and Nam statistic. Also, for large samples, the results for the odds ratio have not (to our knowledge) been published. In this case, we substitute the calculations based on the ratio.

## Non-Zero Null Tests for the Difference Between Two Proportions

### Test Statistics

Several test statistics have been proposed for testing whether the difference, ratio, or odds ratio are different from a specified value. The main difference among the several test statistics is in the formula used to compute the standard error used in the denominator. These tests are based on the following  $z$ -test

$$z_t = \frac{\hat{p}_1 - \hat{p}_2 - \delta_0 - c}{\hat{\sigma}}$$

The constant,  $c$ , represents a continuity correction that is applied in some cases. When the continuity correction is not used,  $c$  is zero. In power calculations, the values of  $\hat{p}_1$  and  $\hat{p}_2$  are not known. The corresponding values of  $p_1$  and  $p_2$  under the alternative hypothesis are 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 you should use. The answer is simple: you should use the test statistic that you will use to analyze your data. 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 during power or sample calculations.

#### Z Test (Pooled)

This test was first proposed by Karl Pearson in 1900. Although this test is usually expressed directly as a chi-square statistic, it is expressed here as a  $z$  statistic so that it can be more easily used for one-sided hypothesis testing. The proportions are pooled (averaged) in computing the standard error. The formula for the test statistic is

$$z_t = \frac{\hat{p}_1 - \hat{p}_2 - \delta_0}{\hat{\sigma}_1}$$

where

$$\hat{\sigma}_1 = \sqrt{\bar{p}(1-\bar{p})\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}$$

$$\bar{p} = \frac{n_1\hat{p}_1 + n_2\hat{p}_2}{n_1 + n_2}$$

#### Z Test (Unpooled)

This test statistic does not pool the two proportions in computing the standard error.

$$z_t = \frac{\hat{p}_1 - \hat{p}_2 - \delta_0}{\hat{\sigma}_2}$$

where

$$\hat{\sigma}_2 = \sqrt{\frac{\hat{p}_1(1-\hat{p}_1)}{n_1} + \frac{\hat{p}_2(1-\hat{p}_2)}{n_2}}$$

## Non-Zero Null Tests for the Difference Between Two Proportions

### Z Test with Continuity Correction (Pooled)

This test is the same as Z Test (Pooled), except that a continuity correction is used. Recall that in the null case, the continuity correction makes the results closer to those of Fisher's Exact test.

$$z_t = \frac{\hat{p}_1 - \hat{p}_2 - \delta_0 + \frac{F}{2} \left( \frac{1}{n_1} + \frac{1}{n_2} \right)}{\hat{\sigma}_1}$$

$$\hat{\sigma}_1 = \sqrt{\bar{p}(1-\bar{p}) \left( \frac{1}{n_1} + \frac{1}{n_2} \right)}$$

$$\bar{p} = \frac{n_1 \hat{p}_1 + n_2 \hat{p}_2}{n_1 + n_2}$$

where  $F$  is -1 for lower-tailed, 1 for upper-tailed, and both -1 and 1 for two-sided hypotheses.

### Z Test with Continuity Correction (Unpooled)

This test is the same as the Z Test (Unpooled), except that a continuity correction is used. Recall that in the null case, the continuity correction makes the results closer to those of Fisher's Exact test.

$$z_t = \frac{\hat{p}_1 - \hat{p}_2 - \delta_0 - \frac{F}{2} \left( \frac{1}{n_1} + \frac{1}{n_2} \right)}{\hat{\sigma}_2}$$

$$\hat{\sigma}_2 = \sqrt{\frac{\hat{p}_1(1-\hat{p}_1)}{n_1} + \frac{\hat{p}_2(1-\hat{p}_2)}{n_2}}$$

where  $F$  is -1 for lower-tailed, 1 for upper-tailed, and both -1 and 1 for two-sided hypotheses.

### T-Test

Based on a detailed, comparative study of the behavior of several tests, D'Agostino (1988) and Upton (1982) proposed using the usual two-sample  $t$ -test for testing whether the two proportions are equal. One substitutes a '1' for a success and a '0' for a failure in the usual, two-sample  $t$ -test formula.

### Miettinen and Nurminen's Likelihood Score Test

Miettinen and Nurminen (1985) proposed a test statistic for testing whether the difference is equal to a specified, non-zero, value,  $\delta_0$ . The regular MLE's,  $\hat{p}_1$  and  $\hat{p}_2$ , are used in the numerator of the score statistic while MLE's  $\tilde{p}_1$  and  $\tilde{p}_2$ , constrained so that  $\tilde{p}_1 - \tilde{p}_2 = \delta_0$ , are used in the denominator. 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 this test statistic is

$$z_{MND} = \frac{\hat{p}_1 - \hat{p}_2 - \delta_0}{\hat{\sigma}_{MND}}$$

## Non-Zero Null Tests for the Difference Between Two Proportions

where

$$\hat{\sigma}_{MND} = \sqrt{\left(\frac{\tilde{p}_1 \tilde{q}_1}{n_1} + \frac{\tilde{p}_2 \tilde{q}_2}{n_2}\right) \left(\frac{N}{N-1}\right)}$$

$$\tilde{p}_1 = \tilde{p}_2 + \delta_0$$

$$\tilde{p}_2 = 2B \cos(A) - \frac{L_2}{3L_3}$$

$$A = \frac{1}{3} \left[ \pi + \cos^{-1} \left( \frac{C}{B^3} \right) \right]$$

$$B = \text{sign}(C) \sqrt{\frac{L_2^2}{9L_3} - \frac{L_1}{3L_3}}$$

$$C = \frac{L_2^3}{27L_3^3} - \frac{L_1 L_2}{6L_3^2} + \frac{L_0}{2L_3}$$

$$L_0 = x_{21} \delta_0 (1 - \delta_0)$$

$$L_1 = [n_2 \delta_0 - N - 2x_{21}] \delta_0 + m_1$$

$$L_2 = (N + n_2) \delta_0 - N - m_1$$

$$L_3 = N$$

### Farrington and Manning's Likelihood Score Test

Farrington and Manning (1990) proposed a test statistic for testing whether the difference is equal to a specified value,  $\delta_0$ . The regular MLE's,  $\hat{p}_1$  and  $\hat{p}_2$ , are used in the numerator of the score statistic while MLE's  $\tilde{p}_1$  and  $\tilde{p}_2$ , constrained so that  $\tilde{p}_1 - \tilde{p}_2 = \delta_0$ , are used in the denominator. 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

$$z_{FMD} = \frac{\hat{p}_1 - \hat{p}_2 - \delta_0}{\sqrt{\left(\frac{\tilde{p}_1 \tilde{q}_1}{n_1} + \frac{\tilde{p}_2 \tilde{q}_2}{n_2}\right)}}$$

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

## Non-Zero Null Tests for the Difference Between Two Proportions

### Gart and Nam's Likelihood Score Test

Gart and Nam (1990), page 638, proposed a modification to the Farrington and Manning (1988) difference test that corrected for skewness. Let  $z_{FMD}(\delta)$  stand for the Farrington and Manning difference test statistic described above. The skewness corrected test statistic,  $z_{GND}$ , is the appropriate solution to the quadratic equation

$$(-\tilde{\gamma})z_{GND}^2 + (-1)z_{GND} + (z_{FMD}(\delta) + \tilde{\gamma}) = 0$$

where

$$\tilde{\gamma} = \frac{\tilde{V}^{3/2}(\delta)}{6} \left( \frac{\tilde{p}_1 \tilde{q}_1 (\tilde{q}_1 - \tilde{p}_1)}{n_1^2} - \frac{\tilde{p}_2 \tilde{q}_2 (\tilde{q}_2 - \tilde{p}_2)}{n_2^2} \right)$$

## 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, differences, 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  $N_1$  and  $N_2 \leq$  Maximum  $N_1$  or  $N_2$  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.

## Non-Zero Null Tests for the Difference Between Two Proportions

---

### 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.

---

### Test

#### Alternative Hypothesis

Specify the direction of the alternative hypothesis, H1.

- **One-Sided (H1:  $P1 - P2 < D0$ )**  
Refers to a lower-tailed, one-sided test in which the alternative hypothesis is  $H1: P1 < P2 + D0$  or equivalently  $H1: P1 - P2 < D0$ .
- **One-Sided (H1:  $P1 - P2 > D0$ )**  
Refers to an upper-tailed, one-sided test in which the alternative hypothesis is  $H1: P1 > P2 + D0$  or equivalently  $H1: P1 - P2 > D0$ .
- **Two-Sided (H1:  $P1 - P2 \neq D0$ )**  
Refers to a two-sided test in which the alternative hypothesis is  $H1: P1 \neq P2 + D0$  or equivalently  $H1: P1 - P2 \neq D0$ .

For one-sided tests, the direction you select must match the values entered for D0 and D1. For example, if you select  $H1: P1 - P2 < D0$ , then the value(s) for D1 must be less than the value(s) for D0.

#### Test Type

Specify which test statistic is used in searching and reporting.

Note that *C.C.* is an abbreviation for *Continuity Correction*. This refers to the adding or subtracting  $1/(2n)$  to (or from) the numerator of the z-value to bring the normal approximation closer to the binomial distribution.



## Non-Zero Null Tests for the Difference Between Two Proportions

---

### 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. In this procedure, a type-II error occurs when you fail to reject the null hypothesis of equal proportions when in fact they are different.

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.

#### 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. For this procedure, a type-I error occurs when you reject the null hypothesis of equal proportions when in fact they are equal.

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.

## Non-Zero Null Tests for the Difference Between Two Proportions

### 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  $\geq 2$ . 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  $\geq 2$ . 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 Not 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  $N2$ .

## Non-Zero Null Tests for the Difference Between Two Proportions

- **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  $\geq 2$ . 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  $\geq 2$ . 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  $\geq 2$ . 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  $\geq Y$ .

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.

## Non-Zero Null Tests for the Difference Between Two Proportions

### 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

#### Input Type

Indicate what type of values to enter to specify the differences under the null and alternative hypotheses.

Regardless of the entry type chosen, the calculations are the same. This option is simply given for convenience in specifying the differences.

---

#### Effect Size – Differences (P1 – P2)

*These options are displayed only if Input Type = "Differences"*

##### D0 (Difference|H0 = P1.0 – P2)

This option specifies the difference between the two proportions given in the null hypothesis, H0. This difference is used with P2 to calculate the value of P1.0 using the formula:  $P1.0 = P2 + D0$ . Note that P1.0 here means the value of P1 under H0.

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

The power calculations use P1.0 as the value of the proportion in group 1 (the experimental or treatment group) under the null hypothesis. In this non-null case, the value of P1.0 is not equal to P2 as it is in the null case.

You may enter a range of values such as *0.03 0.05 0.10* or *0.01 to 0.05 by 0.01*.

##### D1 (Difference|H0 = P1.1 – P2)

This option specifies the difference between the P1.1 and P2. This difference is used with P2 to calculate the value of P1.1 using the formula:  $P1.1 = D1 + P2$ . Note that P1.1 here means the value of P1 under H1. Differences must be between -1 and 1. They cannot take on the values -1 or 1.

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

This option is only used if you are specifying *Differences*.

You may enter a range of values such as *0.03 0.05 0.10* or *0.01 to 0.05 by 0.01*.

## Non-Zero Null Tests for the Difference Between Two Proportions

---

### Effect Size – Group 1 (Treatment)

*These options are displayed only if Input Type = “Proportions”*

#### **P1.0 (Group 1 Proportion|H0)**

This option specifies the value of the group 1 proportion given the null hypothesis. The power calculations assume that P1.0 is the value of the P1 under the null hypothesis. In this non-null case, the value of P1.0 is not equal to P2 as it is in the null case.

You may enter a range of values such as *0.03 0.05 0.10* or *0.01 to 0.05 by 0.01*.

Proportions must be between zero and one. They cannot take on the values zero or one.

#### **P1.1 (Group 1 Proportion|H1)**

This is the value of P1 under the alternative hypothesis. It is written P1.1. The power calculations assume that this is the actual value of this proportion.

You may enter a range 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.

---

### Effect Size – Group 2 (Reference)

#### **P2 (Group 2 Proportion)**

Specify the value of P2, the control, baseline, or standard group's proportion. The null hypothesis is that the two proportions differ by a specified amount. Since P2 is a proportion, these values must be between zero and one.

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

## Non-Zero Null Tests for the Difference Between Two Proportions

### Example 1 – Finding Power

A study is being designed to study the effectiveness of a new treatment. Historically, the standard treatment has enjoyed a 60% cure rate. The new treatment reduces the seriousness of certain side effects that occur with the standard treatment. Thus, the new treatment will be adopted even if it is slightly less effective than the standard treatment. The researchers will recommend adoption of the new treatment if it has a cure rate of at least 55%.

The researchers plan to use the Farrington and Manning likelihood score test statistic to analyze the data. They want to study the power of the one-sided Farrington and Manning test at group sample sizes ranging from 50 to 2000 for detecting a difference significantly greater than -0.05 when the actual cure rate of the new treatment ranges from 57% to 70%. 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 **Non-Zero Null Tests for the Difference Between Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Test (Non-Zero Null)**, and then clicking on **Non-Zero Null Tests for the Difference Between 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
<b>Design Tab</b>	
Solve For .....	<b>Power</b>
Power Calculation Method.....	<b>Normal Approximation</b>
Alternative Hypothesis .....	<b>One-Sided (H1: P1 - P2 &gt; D0)</b>
Test Type .....	<b>Likelihood Score (Farr. &amp; Mann.)</b>
Alpha .....	<b>0.05</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Sample Size Per Group .....	<b>50 100 250 500 1000 1500 2000</b>
Input Type .....	<b>Differences</b>
D0 (Difference H0 = P1.0 - P2).....	<b>-0.05</b>
D1 (Difference H1 = P1.1 - P2).....	<b>-0.03 0.00 0.05 0.10</b>
P2 (Group 2 Proportion) .....	<b>0.6</b>

## Non-Zero Null Tests for the Difference Between Two Proportions

## 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:  $H_0: P_1 - P_2 \leq D_0$  vs.  $H_1: P_1 - P_2 > D_0$

Power*	N1	N2	N	Ref. P2	P1 H0 P1.0	P1 H1 P1.1	Diff H0 D0	Diff H1 D1	Alpha
0.07486	50	50	100	0.6000	0.5500	0.5700	-0.0500	-0.0300	0.0500
0.08748	100	100	200	0.6000	0.5500	0.5700	-0.0500	-0.0300	0.0500
0.11711	250	250	500	0.6000	0.5500	0.5700	-0.0500	-0.0300	0.0500
0.15829	500	500	1000	0.6000	0.5500	0.5700	-0.0500	-0.0300	0.0500
0.23101	1000	1000	2000	0.6000	0.5500	0.5700	-0.0500	-0.0300	0.0500
0.29755	1500	1500	3000	0.6000	0.5500	0.5700	-0.0500	-0.0300	0.0500
0.35965	2000	2000	4000	0.6000	0.5500	0.5700	-0.0500	-0.0300	0.0500

(Report continues)

\* 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,  $N_1 + N_2$ .
- 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 Group 1 proportion under the null hypothesis. P1.1 is the proportion for Group 1 under the alternative hypothesis at which power and sample size calculations are made.
- D0 is the difference ( $P_1 - P_2$ ) under the null hypothesis. D1 is the difference under the alternative hypothesis used for power and sample size calculations.
- Alpha is the probability of rejecting a true null hypothesis.

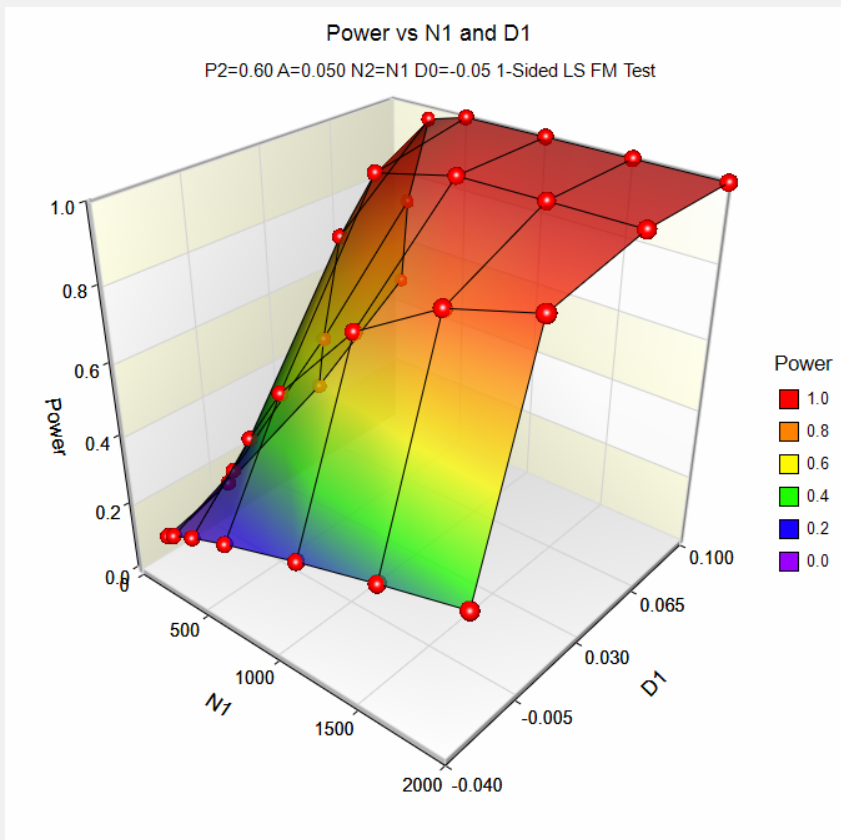
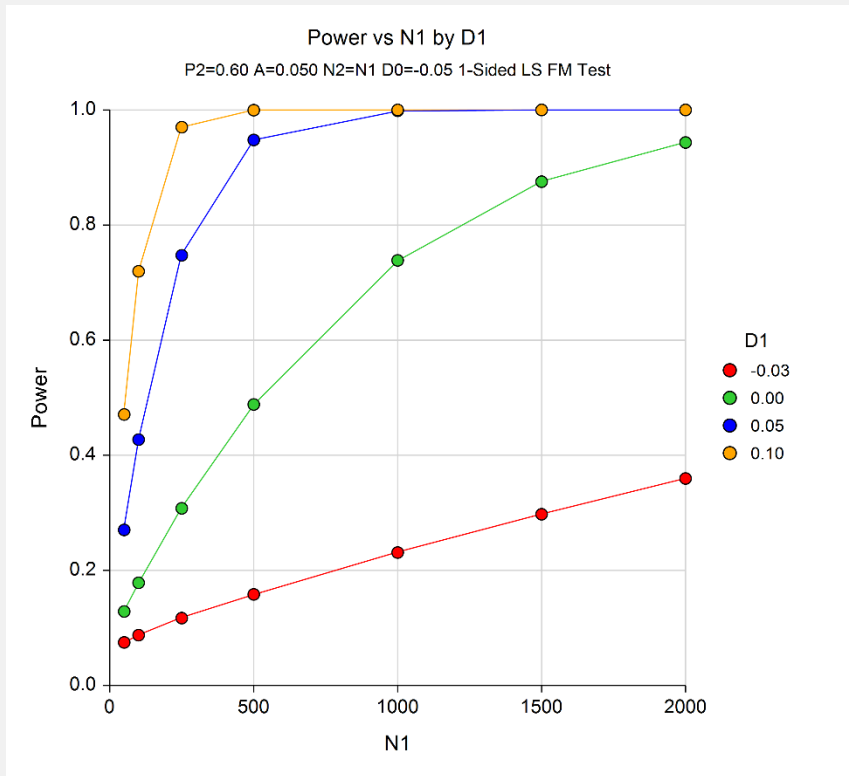
## Summary Statements

Group sample sizes of 50 in Group 1 and 50 in Group 2 achieve 7.486% power to detect a difference of -0.0300 when the null-hypothesized difference is -0.0500. The Group 2 proportion is 0.6000. The Group 1 proportion is assumed to be 0.5500 under the null hypothesis and 0.5700 under the alternative hypothesis. The test statistic used is the one-sided Score test (Farrington & Manning). The significance level of the test is 0.0500.

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

Non-Zero Null Tests for the Difference Between Two Proportions

Plots Section



The values from the table are displayed in the above charts. These charts give us a quick look at the sample size that will be required for various values of D1.



## Non-Zero Null Tests for the Difference Between Two Proportions

## Example 2 – Finding the Sample Size

Continuing with the scenario given in Example 1, the researchers want to determine the sample size needed to achieve 80% power for each value of D1.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Non-Zero Null Tests for the Difference Between Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Test (Non-Zero Null)**, and then clicking on **Non-Zero Null Tests for the Difference Between 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**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Sample Size</b>
Power Calculation Method.....	<b>Normal Approximation</b>
Alternative Hypothesis.....	<b>One-Sided (H1: P1 - P2 &gt; D0)</b>
Test Type.....	<b>Likelihood Score (Farr. &amp; Mann.)</b>
Power.....	<b>0.80</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Input Type.....	<b>Differences</b>
D0 (Difference H0 = P1.0 - P2).....	<b>-0.05</b>
D1 (Difference H1 = P1.1 - P2).....	<b>-0.03 0.00 0.05 0.10</b>
P2 (Group 2 Proportion) .....	<b>0.6</b>

### 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: P1 - P2 ≤ D0 vs. H1: P1 - P2 > D0

Target Power	Actual Power*	N1	N2	N	Ref. P2	P1 H0 P1.0	P1 H1 P1.1	Diff H0 D0	Diff H1 D1	Alpha
0.80	0.80003	7491	7491	14982	0.6000	0.5500	0.5700	-0.0500	-0.0300	0.0500
0.80	0.80019	1186	1186	2372	0.6000	0.5500	0.6000	-0.0500	0.0000	0.0500
0.80	0.80084	290	290	580	0.6000	0.5500	0.6500	-0.0500	0.0500	0.0500
0.80	0.80113	125	125	250	0.6000	0.5500	0.7000	-0.0500	0.1000	0.0500

\* Power was computed using the normal approximation method.

The required sample size will depend a great deal on the value of D1. The researchers should spend time determining the most accurate value for D1.

## Example 3 – Comparing the Power of Several Test Statistics

Continuing with Example 2, the researchers want to determine which of the eight 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 50 and 200 when  $D_1$  is 0.1.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Non-Zero Null Tests for the Difference Between Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Test (Non-Zero Null)**, and then clicking on **Non-Zero Null Tests for the Difference Between 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**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Power</b>
Power Calculation Method.....	<b>Binomial Enumeration</b>
Maximum N1 or N2 for Binomial Enumeration .....	<b>5000</b>
Zero Count Adjustment Method.....	<b>Add to zero cells only</b>
Zero Count Adjustment Value .....	<b>0.0001</b>
Alternative Hypothesis .....	<b>One-Sided (H1: P1 - P2 &gt; D0)</b>
Test Type.....	<b>Likelihood Score (Farr. &amp; Mann.)</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Sample Size Per Group .....	<b>50 100 150 200</b>
Input Type.....	<b>Differences</b>
D0 (Difference H0 = P1.0 - P2).....	<b>-0.05</b>
D1 (Difference H1 = P1.1 - P2).....	<b>0.05</b>
P2 (Group 2 Proportion) .....	<b>0.6</b>
<b>Reports Tab</b>	
Show Comparative Reports.....	<b>Checked</b>
<b>Comparative Plots Tab</b>	
Show Comparative Plots .....	<b>Checked</b>

Non-Zero Null Tests for the Difference Between Two Proportions

Output

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

Numeric Results and Plots

Power Comparison of Eight Different Tests

Hypotheses:  $H_0: P_1 - P_2 \leq D_0$  vs.  $H_1: P_1 - P_2 > D_0$

N1/N2	P2	P1.1	Target Alpha	Z(P) Test Power	Z(UnP) Test Power	Z(P) CC Test Power	Z(UnP) CC Test Power	T Test Power	F.M. Score Power	M.N. Score Power	G.N. Score Power
50/50	0.6000	0.6500	0.0500	0.2720	0.2720	0.2064	0.2096	0.2694	0.2720	0.2694	0.2720
100/100	0.6000	0.6500	0.0500	0.4207	0.4248	0.3663	0.3663	0.4178	0.4207	0.4207	0.4207
150/150	0.6000	0.6500	0.0500	0.5540	0.5540	0.5054	0.5054	0.5504	0.5540	0.5519	0.5519
200/200	0.6000	0.6500	0.0500	0.6654	0.6683	0.6286	0.6286	0.6624	0.6683	0.6654	0.6654

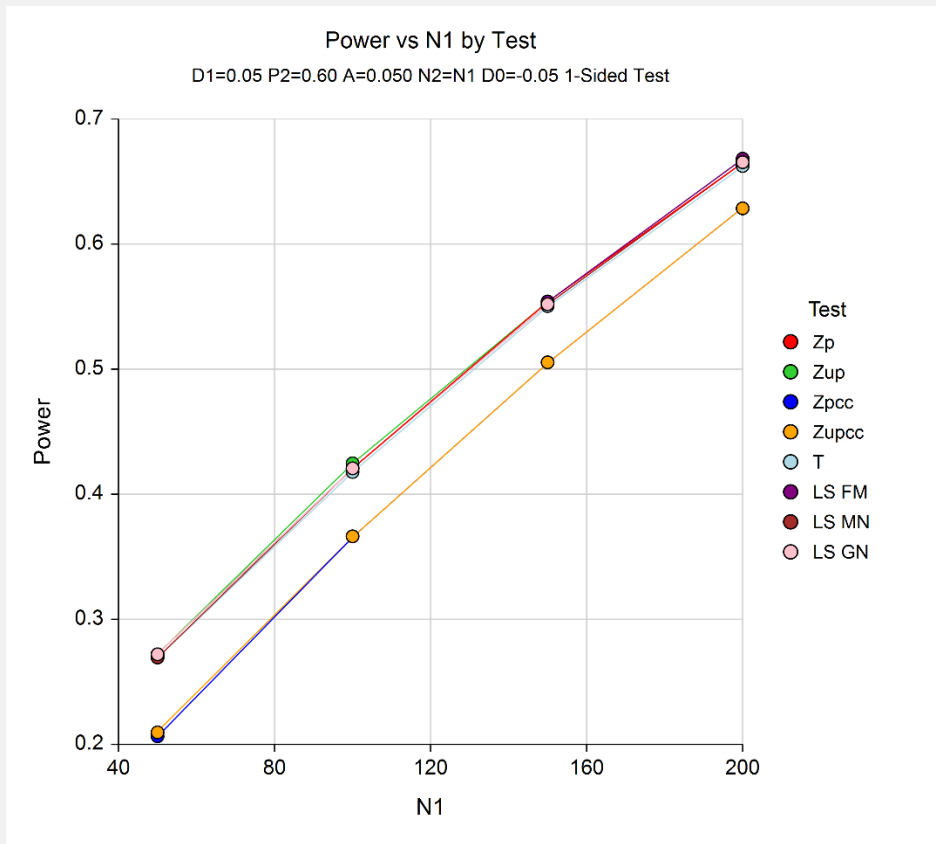
Note: Power was computed using binomial enumeration of all possible outcomes.

Actual Alpha Comparison of Eight Different Tests

Hypotheses:  $H_0: P_1 - P_2 \leq D_0$  vs.  $H_1: P_1 - P_2 > D_0$

N1/N2	P2	P1.1	Target Alpha	Z(P) Test Alpha	Z(UnP) Test Alpha	Z(P) CC Test Alpha	Z(UnP) CC Test Alpha	T Test Alpha	F.M. Score Alpha	M.N. Score Alpha	G.N. Score Alpha
50/50	0.6000	0.6500	0.0500	0.0527	0.0527	0.0342	0.0343	0.0526	0.0527	0.0526	0.0527
100/100	0.6000	0.6500	0.0500	0.0499	0.0500	0.0369	0.0369	0.0499	0.0499	0.0499	0.0499
150/150	0.6000	0.6500	0.0500	0.0509	0.0509	0.0398	0.0398	0.0509	0.0509	0.0509	0.0509
200/200	0.6000	0.6500	0.0500	0.0479	0.0482	0.0387	0.0387	0.0477	0.0482	0.0479	0.0479

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



It is interesting to note that the powers of the continuity-corrected test statistics are consistently lower than the other tests. This occurs because the actual alpha achieved by these tests is lower than for the other tests.

## Non-Zero Null Tests for the Difference Between Two Proportions

## 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 **Non-Zero Null Tests for the Difference Between Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Test (Non-Zero Null)**, and then clicking on **Non-Zero Null Tests for the Difference Between 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**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	Power
Power Calculation Method.....	Normal Approximation
Alternative Hypothesis.....	One-Sided (H1: P1 - P2 > D0)
Test Type.....	Likelihood Score (Farr. & Mann.)
Alpha.....	0.05
Group Allocation .....	Equal (N1 = N2)
Sample Size Per Group.....	50 100 150 200
Input Type.....	Differences
D0 (Difference H0 = P1.0 - P2).....	-0.05
D1 (Difference H1 = P1.1 - P2).....	0.05
P2 (Group 2 Proportion) .....	0.6
<b>Reports Tab</b>	
Show Power Detail Report .....	Checked

### Output

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

#### Numeric Results and Plots

<b>Power Detail Report</b>							
Test Statistic: Farrington & Manning Likelihood Score Test							
Hypotheses: H0: P1 - P2 ≤ D0 vs. H1: P1 - P2 > D0							
N1/N2	P2	D0	D1	Normal Approximation		Binomial Enumeration	
				Power	Alpha	Power	Alpha
50/50	0.6000	-0.0500	0.0500	0.27032	0.0500	0.27200	0.0527
100/100	0.6000	-0.0500	0.0500	0.42722	0.0500	0.42069	0.0499
150/150	0.6000	-0.0500	0.0500	0.55774	0.0500	0.55405	0.0509
200/200	0.6000	-0.0500	0.0500	0.66361	0.0500	0.66826	0.0482

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

## Example 5 – Finding the Power after Completing an Experiment

Researchers are studying the effectiveness of a new treatment for cancer. Historically, the standard treatment has enjoyed a 52% cure rate. The new experimental treatment is believed to be better, but it costs much more to administer. After weighing cost versus effectiveness, the researchers decided that they will adopt the new treatment if the cure rate is at least 59%. They conduct a study in which 200 patients are given the new treatment, and 200 are given the standard regimen. They find that 66% are cured by the new treatment, while 52% are cured by the standard treatment. The Farrington and Manning likelihood score test, however, indicates that the results are not statistically significant for  $\alpha = 0.05$ . They now desire to compute the power for a range of alternative values.

Note that a range of alternatives is used in computing the power instead of the actual difference from the study. The power should be computed at values representing practically significant differences from the null value.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Non-Zero Null Tests for the Difference Between Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Test (Non-Zero Null)**, and then clicking on **Non-Zero Null Tests for the Difference Between Two Proportions**. You may then make the appropriate entries as listed below, or open **Example 5** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Power</b>
Power Calculation Method.....	<b>Binomial Enumeration</b>
Maximum N1 or N2 for Binomial Enumeration .....	<b>5000</b>
Zero Count Adjustment Method.....	<b>Add to zero cells only</b>
Zero Count Adjustment Value .....	<b>0.0001</b>
Alternative Hypothesis .....	<b>One-Sided (H1: P1 - P2 &gt; D0)</b>
Test Type .....	<b>Likelihood Score (Farr. &amp; Mann.)</b>
Alpha .....	<b>0.05</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Sample Size Per Group .....	<b>200</b>
Input Type .....	<b>Differences</b>
D0 (Difference H0 = P1.0 - P2).....	<b>0.07</b>
D1 (Difference H1 = P1.1 - P2).....	<b>0.08 to 0.20 by 0.02</b>
P2 (Group 2 Proportion) .....	<b>0.52</b>

## Non-Zero Null Tests for the Difference Between Two Proportions

## Output

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

## Numeric Results and Plots

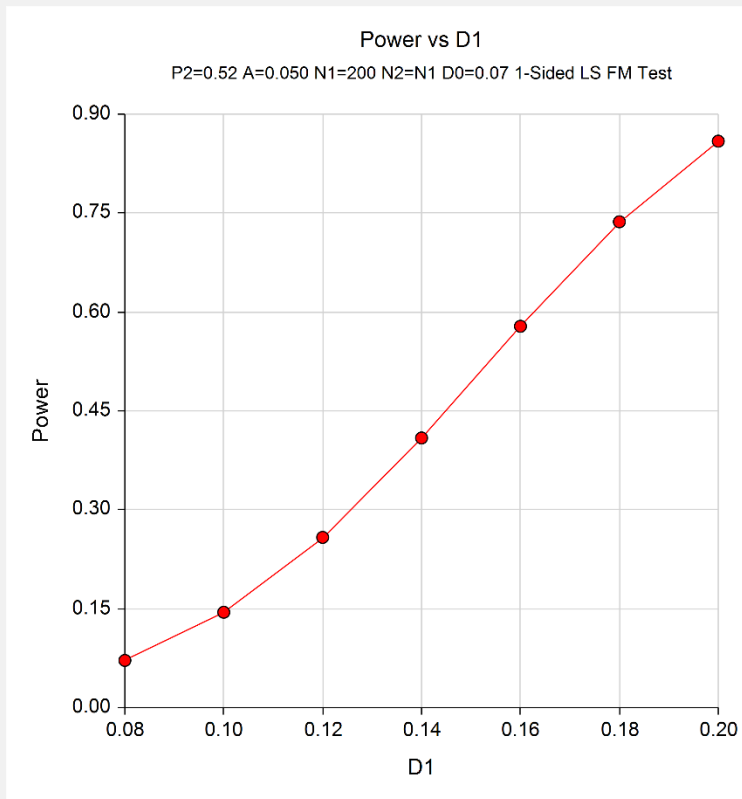
## Numeric Results

Test Statistic: Farrington & Manning Likelihood Score Test

Hypotheses:  $H_0: P_1 - P_2 \leq D_0$  vs.  $H_1: P_1 - P_2 > D_0$

Power*	N1	N2	N	Ref. P2	P1 H0 P1.0	P1 H1 P1.1	Diff H0 D0	Diff H1 D1	Target Alpha	Actual Alpha*
0.07152	200	200	400	0.5200	0.5900	0.6000	0.0700	0.0800	0.0500	0.0479
0.14459	200	200	400	0.5200	0.5900	0.6200	0.0700	0.1000	0.0500	0.0479
0.25814	200	200	400	0.5200	0.5900	0.6400	0.0700	0.1200	0.0500	0.0479
0.40895	200	200	400	0.5200	0.5900	0.6600	0.0700	0.1400	0.0500	0.0479
0.57829	200	200	400	0.5200	0.5900	0.6800	0.0700	0.1600	0.0500	0.0479
0.73684	200	200	400	0.5200	0.5900	0.7000	0.0700	0.1800	0.0500	0.0479
0.85910	200	200	400	0.5200	0.5900	0.7200	0.0700	0.2000	0.0500	0.0479

\* Power and actual alpha were computed using binomial enumeration of all possible outcomes.



The power depends a great deal on the value of D1 for this sample size. It is evident that the power is quite low for the majority of alternative values studied.

## Non-Zero Null Tests for the Difference Between Two Proportions

## Example 6 – Validation of Sample Size Calculation for the Farrington and Manning Test using Machin et al. (1997)

Machin et al. (1997), page 106, present a sample size study in which  $P_2 = 0.5$ ,  $D_0 = -0.2$ ,  $D_1 = 0$ , one-sided  $\alpha = 0.1$ , and  $\beta = 0.2$ . Using the Farrington and Manning test statistic, they found the sample size to be 55 in each group.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Non-Zero Null Tests for the Difference Between Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Test (Non-Zero Null)**, and then clicking on **Non-Zero Null Tests for the Difference Between Two Proportions**. You may then make the appropriate entries as listed below, or open **Example 6** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Sample Size</b>
Power Calculation Method.....	<b>Normal Approximation</b>
Alternative Hypothesis .....	<b>One-Sided (H1: P1 - P2 &gt; D0)</b>
Test Type .....	<b>Likelihood Score (Farr. &amp; Mann.)</b>
Power.....	<b>0.80</b>
Alpha.....	<b>0.10</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Input Type.....	<b>Differences</b>
D0 (Difference H0 = P1.0 - P2).....	<b>-0.2</b>
D1 (Difference H1 = P1.1 - P2).....	<b>0</b>
P2 (Group 2 Proportion) .....	<b>0.5</b>

### Output

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

### Numeric Results

<b>Numeric Results</b>											
Test Statistic: Farrington & Manning Likelihood Score Test											
Hypotheses: H0: P1 - P2 ≤ D0 vs. H1: P1 - P2 > D0											
Target Power	Actual Power*	N1	N2	N	Ref. P2	P1 H0 P1.0	P1 H1 P1.1	Diff H0 D0	Diff H1 D1	Alpha	
0.80	0.80009	55	55	110	0.5000	0.3000	0.5000	-0.2000	0.0000	0.1000	
* Power was computed using the normal approximation method.											

PASS found the required sample size to be 55, which corresponds exactly to the results of Machin et al. (1997).

## Non-Zero Null Tests for the Difference Between Two Proportions

## Example 7 – Validation of Sample Size Calculation using Farrington and Manning (1990)

Farrington and Manning (1990), page 1451, present a sample size study in which  $P_2 = 0.05$ ,  $D_0 = 0.2$ ,  $D_1 = 0.35$ , one-sided  $\alpha = 0.05$ , and  $\beta = 0.20$ . Using the Farrington and Manning test statistic, they found the sample size to be 80 in each group. They mention that the true power is 0.813.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Non-Zero Null Tests for the Difference Between Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Test (Non-Zero Null)**, and then clicking on **Non-Zero Null Tests for the Difference Between Two Proportions**. You may then make the appropriate entries as listed below, or open **Example 7(a or b)** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Sample Size</b>
Power Calculation Method.....	<b>Normal Approximation</b>
Alternative Hypothesis .....	<b>One-Sided (H1: P1 - P2 &gt; D0)</b>
Test Type .....	<b>Likelihood Score (Farr. &amp; Mann.)</b>
Power.....	<b>0.80</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Input Type.....	<b>Differences</b>
D0 (Difference H0 = P1.0 – P2).....	<b>0.2</b>
D1 (Difference H1 = P1.1 – P2).....	<b>0.35</b>
P2 (Group 2 Proportion) .....	<b>0.05</b>

### Output

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

### Numeric Results

<b>Numeric Results</b>											
Test Statistic: Farrington & Manning Likelihood Score Test											
Hypotheses: H0: P1 - P2 ≤ D0 vs. H1: P1 - P2 > D0											
Target Power	Actual Power*	N1	N2	N	Ref. P2	P1 H0 P1.0	P1 H1 P1.1	Diff H0 D0	Diff H1 D1	Alpha	
0.80	0.80068	80	80	160	0.0500	0.2500	0.4000	0.2000	0.3500	0.0500	
* Power was computed using the normal approximation method.											

PASS also calculated the required sample size to be 80.



### Non-Zero Null Tests for the Difference Between Two Proportions

Next, to calculate the true power based on binomial enumeration for this sample size, we make the following changes to the template.

Option	Value
<b>Design Tab</b>	
Solve For .....	<b>Power</b>
Power Calculation Method.....	<b>Binomial Enumeration</b>
Maximum N1 or N2 for Binomial Enumeration .....	<b>5000</b>
Zero Count Adjustment Method.....	<b>Add to zero cells only</b>
Zero Count Adjustment Value .....	<b>0.0001</b>
Sample Size Per Group.....	<b>80</b>

### Numeric Results

<b>Numeric Results</b>										
Test Statistic: Farrington & Manning Likelihood Score Test										
Hypotheses: H0: P1 - P2 ≤ D0 vs. H1: P1 - P2 > D0										
Power*	N1	N2	N	Ref. P2	P1 H0 P1.0	P1 H1 P1.1	Diff H0 D0	Diff H1 D1	Target Alpha	Actual Alpha*
<b>0.81320</b>	80	80	160	0.0500	0.2500	0.4000	0.2000	0.3500	0.0500	0.0553

PASS also calculated the true power to be 0.813.

## Example 8 – Validation of Sample Size Calculation for the Unpooled Z-Test using Chow, Shao, and Wang (2008)

Chow, Shao, and Wang (2008) page 92 gives the results of a sample size calculation for an unpooled Z-test for non-inferiority. This procedure can be used for the same test. When  $P_{1.0} = 0.55$  (from  $\delta = -0.1$ ),  $P_{1.1} = 0.85$ ,  $P_2 = 0.65$ , power = 0.8, and alpha = 0.05, Chow, Shao, and Wang (2008) reports a required sample size of 25.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Non-Zero Null Tests for the Difference Between Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Test (Non-Zero Null)**, and then clicking on **Non-Zero Null Tests for the Difference Between Two Proportions**. You may then make the appropriate entries as listed below, or open **Example 8** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Sample Size</b>
Power Calculation Method.....	<b>Normal Approximation</b>
Alternative Hypothesis .....	<b>One-Sided (H1: D1 &gt; D0)</b>
Test Type .....	<b>Z-Test (Unpooled)</b>
Power.....	<b>0.80</b>
Alpha.....	<b>0.05</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Input Type.....	<b>Proportions</b>
P1.0 (Group 1 Proportion H0).....	<b>0.55</b>
P1.1 (Group 1 Proportion H1).....	<b>0.85</b>
P2 (Group 2 Proportion) .....	<b>0.65</b>

### Output

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

### Numeric Results

Numeric Results										
Test Statistic: Z-Test with Unpooled Variance										
Hypotheses: H0: P1 - P2 ≤ D0 vs. H1: P1 - P2 > D0										
Target Power	Actual Power*	N1	N2	N	Ref. P2	P1 H0 P1.0	P1 H1 P1.1	Diff H0 D0	Diff H1 D1	Alpha
0.80	0.80858	25	25	50	0.6500	0.5500	0.8500	-0.1000	0.2000	0.0500
* Power was computed using the normal approximation method.										

PASS also found the required sample size to be 25.

## Example 9 – Validation of Sample Size Calculation for the Unpooled Z-Test using Julius and Campbell (2012)

Julius and Campbell (2012) presents Table XIII gives the results of sample size calculations for an unpooled Z-test for non-inferiority for P2 between 0.7 and 0.9,  $|D0|$  between 0.05 and 0.20 and D1 between -0.05 and 0.05. Sample sizes are calculated for 90% power and  $\alpha = 0.025$ . This example will replicate all values of D1 for P1 = 0.70 and  $|D0| = 0.20$  in the table.

The sample sizes reported in the table for D1 between -0.05 and 0.05 are 205, 179, 157, 139, 124, 111, 100, 90, 81, 74, and 67.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Non-Inferiority Tests for the Difference Between Two Proportions** procedure window by expanding **Proportions**, then **Two Independent Proportions**, then clicking on **Non-Inferiority**, and then clicking on **Non-Inferiority Tests for the Difference Between Two Proportions**. You may then make the appropriate entries as listed below, or open **Example 8** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Sample Size</b>
Power Calculation Method.....	<b>Normal Approximation</b>
Alternative Hypothesis .....	<b>One-Sided (H1: P1 - P2 &gt; D0)</b>
Test Type.....	<b>Z-Test (Unpooled)</b>
Power.....	<b>0.90</b>
Alpha.....	<b>0.025</b>
Group Allocation .....	<b>Equal (N1 = N2)</b>
Input Type.....	<b>Differences</b>
D0 (Difference H0 = P1.0 - P2).....	<b>-0.2</b>
D1 (Difference H1 = P1.1 - P2).....	<b>-0.05 to 0.05 by 0.01</b>
P2 (Group 2 Proportion) .....	<b>0.70</b>

## Non-Zero Null Tests for the Difference Between Two Proportions

## Output

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

## Numeric Results

## Numeric Results

Test Statistic: Z-Test with Unpooled Variance

Hypotheses:  $H_0: P_1 - P_2 \leq D_0$  vs.  $H_1: P_1 - P_2 > D_0$

Target Power	Actual Power*	N1	N2	N	Ref. P2	P1 H0 P1.0	P1 H1 P1.1	Diff H0 D0	Diff H1 D1	Alpha
0.90	0.90096	205	205	410	0.7000	0.5000	0.6500	-0.2000	-0.0500	0.025
0.90	0.90111	179	179	358	0.7000	0.5000	0.6600	-0.2000	-0.0400	0.025
0.90	0.90047	157	157	314	0.7000	0.5000	0.6700	-0.2000	-0.0300	0.025
0.90	0.90067	139	139	278	0.7000	0.5000	0.6800	-0.2000	-0.0200	0.025
0.90	0.90142	124	124	248	0.7000	0.5000	0.6900	-0.2000	-0.0100	0.025
0.90	0.90172	111	111	222	0.7000	0.5000	0.7000	-0.2000	0.0000	0.025
0.90	0.90257	100	100	200	0.7000	0.5000	0.7100	-0.2000	0.0100	0.025
0.90	0.90203	90	90	180	0.7000	0.5000	0.7200	-0.2000	0.0200	0.025
0.90	0.90049	81	81	162	0.7000	0.5000	0.7300	-0.2000	0.0300	0.025
0.90	0.90228	74	74	148	0.7000	0.5000	0.7400	-0.2000	0.0400	0.025
0.90	0.90073	67	67	134	0.7000	0.5000	0.7500	-0.2000	0.0500	0.025

\* Power was computed using the normal approximation method.

The sample sizes from **PASS** match Table XIII of Julius and Campbell (2012) exactly.

We should point out that the values reported in Table XIII for  $P_1 - P_2 = -0.04$  where  $|D_0| = 0.05$  (45845, 41537, 36178, etc.) are incorrect for all  $P_1$  given. If you calculate the table values using formula (30) of Julius and Campbell (2012) or using **PASS**, you'll find that each sample size in the table is 200 more than the correct value. All other values in Table XIII are correct.