

## Chapter 162

# Multi-Arm Superiority by a Margin Tests for the Difference Between Treatment and Control Proportions

---

## Introduction

This module computes power and sample size for multi-arm, superiority by a margin tests of the difference between treatment and control proportions. This procedure is based on the results in Machin, Campbell, Tan, and Tan (2018). In this design, there are  $k$  treatment groups and one control group. The groups are independent and are sampled using simple random sampling. A proportion is measured in each group. A total of  $k$  hypothesis tests are anticipated each comparing a treatment group with the common control group using a simple superiority by a margin test of the difference between two proportions.

The Bonferroni multiplicity adjustment of the type I error rate may be optionally made because several tests are being constructed from the same data. Making a multiplicity adjustment is usually recommended, but not always. In fact, Saville (1990) advocates not applying it and Machin, Campbell, Tan, and Tan (2018) include omitting it as a possibility.

Whether you want to test several doses of a single treatment or several types of treatments, good research practice requires that each treatment be compared with a control. For example, a popular three-arm design consists of three groups: control, treatment A, and treatment B. Two tests are run: treatment A versus control and treatment B versus the same control. This avoids having to obtain a second control group for treatment B. Besides the obvious efficiency in subjects, it may be easier to recruit subjects if their chances of receiving a new treatment are better than 50%.

---

## Example

Suppose that the current treatment for a disease works 70% of the time. Unfortunately, this treatment is expensive and occasionally exhibits serious side-effects. Two promising new treatments have been developed and are now ready to be tested. Hence, three groups are needed to complete this study. Two superiority by a margin hypotheses are to be tested in this study: whether each new treatment is better than the current treatment.

Clinicians are willing to adopt a new treatment only if it is more effective than the current treatment by clinically significant amount. They must determine, however, how much more effective the new treatment must be and still 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 a response of at least 77% is achieved, the new treatment will be adopted. The difference between these two percentages is called the *superiority margin*. The superiority margin in this example is 7%.

## Multi-Arm Superiority by a Margin Tests for the Difference Between Treatment and Control Proportions

The developers must design an experiment to test the hypothesis that the response rate of the new treatment is at least 0.77. The statistical hypotheses to be tested are

$$H_0: P_A \leq P_C + \delta_0 \quad \text{vs.} \quad H_1: P_A > P_C + \delta_0$$

$$H_0: P_B \leq P_C + \delta_0 \quad \text{vs.} \quad H_1: P_B > P_C + \delta_0$$

where  $\delta_0 = 0.07$ .

Notice that when the null hypothesis is rejected, the conclusion is that the response rate is at least 0.77. Note that even though the response rate of the current treatment is 0.70, the hypothesis test is about a response rate of 0.77. Also note that a rejection of the null hypothesis results in the conclusion of interest.

---

## Technical Details

Suppose you have  $k$  treatment groups with response probabilities  $P_i$  of size  $N_i$  and one control group with response probability  $P_C$  of size  $N_C$ . The total sample size is  $N = N_1 + N_2 + \dots + N_k + N_C$ .

The  $k$  one-sided superiority tests are

$$H_{0i}: P_i \leq P_C + \delta_0 \quad \text{vs.} \quad H_{1i}: P_i > P_C + \delta_0 \quad \text{for } i = 1, 2, \dots, k$$

Note that if higher proportions are better,  $\delta_0 > 0$  and if lower proportions are better,  $\delta_0 < 0$ .

If we define  $\delta_i = P_i - P_C$ , these are equivalent to

$$H_{0i}: \delta_i \leq \delta_0 \quad \text{vs.} \quad H_{1i}: \delta_i > \delta_0 \quad \text{for } i = 1, 2, \dots, k$$

For convenience, these hypotheses are collectively referred to as

$$H_0: \delta \leq \delta_0 \quad \text{vs.} \quad H_1: \delta > \delta_0$$

---

## Test Statistics

Several test statistics are available in this routine. These are

### 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

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

## Multi-Arm Superiority by a Margin Tests for the Difference Between Treatment and Control Proportions

where

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

$$\bar{p} = \frac{n_i \hat{p}_i + n_c \hat{p}_c}{n_i + n_c}$$

### Z Test (Unpooled)

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

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

where

$$\hat{\sigma}_2 = \sqrt{\frac{\hat{p}_i(1 - \hat{p}_i)}{n_i} + \frac{\hat{p}_c(1 - \hat{p}_c)}{n_c}}$$

### Z Test with Continuity Correction (Pooled)

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

$$z_t = \frac{\hat{p}_i - \hat{p}_c - \delta_0 + \frac{F}{2} \left( \frac{1}{n_i} + \frac{1}{n_c} \right)}{\hat{\sigma}_1}$$

where

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

$$\bar{p} = \frac{n_i \hat{p}_i + n_c \hat{p}_c}{n_i + n_c}$$

where  $F$  is -1 for lower-tailed hypotheses and 1 for upper-tailed hypotheses.

## Z Test with Continuity Correction (Unpooled)

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

$$z_t = \frac{\hat{p}_i - \hat{p}_C - \delta_0 - \frac{F}{2} \left( \frac{1}{n_i} + \frac{1}{n_C} \right)}{\hat{\sigma}_2}$$

where

$$\hat{\sigma}_2 = \sqrt{\frac{\hat{p}_i(1 - \hat{p}_i)}{n_i} + \frac{\hat{p}_C(1 - \hat{p}_C)}{n_C}}$$

where  $F$  is -1 for lower-tailed hypotheses and 1 for upper-tailed hypotheses.

## 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,  $\hat{p}_i$  and  $\hat{p}_C$ , are used in the numerator of the score statistic while MLE's  $\tilde{p}_i$  and  $\tilde{p}_C$ , constrained so that  $\tilde{p}_i - \tilde{p}_C = \delta_0$ , 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

$$z_{MND} = \frac{\hat{p}_i - \hat{p}_C - \delta_0}{\hat{\sigma}_{MND}}$$

where

$$\hat{\sigma}_{MND} = \sqrt{\left( \frac{\tilde{p}_i \tilde{q}_i}{n_i} + \frac{\tilde{p}_C \tilde{q}_C}{n_C} \right) \left( \frac{N}{N-1} \right)}$$

$$\tilde{p}_i = \tilde{p}_C + \delta_0$$

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

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

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

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

## Multi-Arm Superiority by a Margin Tests for the Difference Between Treatment and Control Proportions

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

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

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

$$L_3 = N$$

$$m_1 = \text{number of successes}$$

### 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,  $\hat{p}_i$  and  $\hat{p}_C$ , are used in the numerator of the score statistic while MLE's  $\tilde{p}_i$  and  $\tilde{p}_C$ , constrained so that  $\tilde{p}_i - \tilde{p}_C = \delta_0$ , 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

$$z_{FMD} = \frac{\hat{p}_i - \hat{p}_C - \delta_0}{\sqrt{\left(\frac{\tilde{p}_i \tilde{q}_i}{n_i} + \frac{\tilde{p}_C \tilde{q}_C}{n_C}\right)}}$$

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

### 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 corrects 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

$$\tilde{\gamma} = \frac{\tilde{V}^{3/2}(\delta)}{6} \left( \frac{\tilde{p}_i \tilde{q}_i (\tilde{q}_i - \tilde{p}_i)}{n_i^2} - \frac{\tilde{p}_C \tilde{q}_C (\tilde{q}_C - \tilde{p}_C)}{n_C^2} \right)$$

---

### Asymptotic Approximation to Power

A large sample approximation is used to compute power. The large sample approximation is made by replacing the values of  $\hat{p}_i$  and  $\hat{p}_C$  in the z statistic with the corresponding values of  $P_i$  and  $P_C$ , 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.

## Multiplicity Adjustment

Because  $k$  z-tests between treatment groups and the control group are run when analyzing the results of this study, many statisticians recommend that the Bonferroni adjustment be applied. This adjustment is easy to apply: the value of alpha that is used in the test is found by dividing the original alpha by the number of tests. For example, if the original alpha is set at 0.05 and the number of treatment (not including the control) groups is five, the individual tests will be conducted using an alpha of 0.01.

The main criticism of this procedure is that if there are many tests, the value of alpha becomes very small. To mitigate against this complaint, some statisticians recommend separating the treatment groups into those that are of primary interest and those that are of secondary interest. The Bonferroni adjustment is made by the using the number of primary treatments rather than the total number of treatments.

There are some who advocate ignoring the adjustment entirely in the case of randomized clinical trials. See for example Saville (1990) and the discussion in chapter 14 of Machin, Campbell, Tan, and Tan (2018).

---

## Size of the Control Group

Because the control group is used over and over, some advocate increasing the number of subjects in this group. The standard adjustment is to include  $\sqrt{k}$  subjects in the control group for each subject in one of the treatment groups. See Machin, Campbell, Tan, and Tan (2018, pages 231-232). Note that often, the treatment groups all have the same size.

## Example 1 – Finding the Sample Size

A parallel-group, clinical trial is being designed to compare three doses of a test compound against the standard therapy using three superiority by a margin tests. Suppose the standard therapy has a response rate of 60%. The investigators would like a sample size large enough to find statistical significance at an overall 0.05 level and an individual-test power of 0.80. The response rates of group 1 are 70%, 72%, or 74%. The response rate of group 2 is 75%. The response rate of group 3 is 80%. The superiority margin is 0.06 (10% of the standard therapy response rate).

Following common practice, the control-group sample-size multiplier will be set to  $\sqrt{k} = \sqrt{3} = 1.732$  since there are three treatment groups in this design.

### Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 1** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

#### Design Tab

Solve For .....	<b>Sample Size</b>
Higher Proportions Are .....	<b>Better (H1: <math>\delta &gt; \delta_0</math>)</b>
Test Type.....	<b>Z-Test (Unpooled)</b>
Power of Each Test .....	<b>0.8</b>
Overall Alpha .....	<b>0.05</b>
Bonferroni Adjustment .....	<b>Standard Bonferroni</b>
Group Allocation .....	<b>Enter Group Allocation Pattern, solve for group sample sizes</b>
$\delta_0$ (Superiority Difference).....	<b>0.06</b>
Control Proportion.....	<b>0.6</b>
Control Sample Size Allocation.....	<b>1.732</b>
Set A Number of Groups.....	<b>1</b>
Set A Proportion .....	<b>0.70 0.72 0.74</b>
Set A Sample Size Allocation .....	<b>1</b>
Set B Number of Groups.....	<b>1</b>
Set B Proportion .....	<b>0.75</b>
Set B Sample Size Allocation .....	<b>1</b>
Set C Number of Groups .....	<b>1</b>
Set C Proportion .....	<b>0.80</b>
Set C Sample Size Allocation .....	<b>1</b>
Set D Number of Groups .....	<b>0</b>
More.....	<b>Unchecked</b>

## Output

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

### Numeric Reports

#### Numeric Results

Solve For: [Sample Size](#)  
 Group Allocation: Enter Group Allocation Pattern, solve for group sample sizes  
 Test Type: Z-Test with Unpooled Variance  
 Higher Proportions Are: Better  
 Hypotheses:  $H_0: \delta \leq \delta_0$  vs.  $H_1: \delta > \delta_0$   
 Number of Groups: 4  
 Bonferroni Adjustment: Standard Bonferroni (Divisor = 3)

Comparison	Power		Sample Size		Proportion		Difference		Alpha	
	Target	Actual	Ni	Allocation	Pi H0 Pi.0	Pi H1 Pi.1	Superiority $\delta_0$	Actual $\delta_i$	Overall	Bonferroni- Adjusted
Control			3329	1.732	0.60	0.60				
vs A	0.8	0.80017	1922	1.000	0.66	0.70	0.06	0.10	0.05	0.016667
vs B	0.8	1.00000	1922	1.000	0.66	0.75	0.06	0.15	0.05	0.016667
vs C	0.8	1.00000	1922	1.000	0.66	0.80	0.06	0.20	0.05	0.016667
Total			9095							
Control			1444	1.732	0.60	0.60				
vs A	0.8	0.80029	834	1.000	0.66	0.72	0.06	0.12	0.05	0.016667
vs B	0.8	0.99231	834	1.000	0.66	0.75	0.06	0.15	0.05	0.016667
vs C	0.8	1.00000	834	1.000	0.66	0.80	0.06	0.20	0.05	0.016667
Total			3946							
Control			792	1.732	0.60	0.60				
vs A	0.8	0.80096	457	1.000	0.66	0.74	0.06	0.14	0.05	0.016667
vs B	0.8	0.89283	457	1.000	0.66	0.75	0.06	0.15	0.05	0.016667
vs C	0.8	0.99960	457	1.000	0.66	0.80	0.06	0.20	0.05	0.016667
Total			2163							

- Comparison: The group that is involved in the comparison between the treatment and control displayed on this report line. The comparison is made using the difference.
- Target Power: The power desired. Power is probability of rejecting a false null hypothesis for this comparison. This power is of the comparison shown on this line only.
- Actual Power: The power actually achieved.
- Ni: Sample Size. The number of subjects in the ith group. The total sample size, N, is shown as the last row of the column.
- Allocation: The group sample size allocation pattern. The value on each row represents the relative number of subjects assigned to the group.
- Pi.0: The response proportion in the ith group assumed by the null hypothesis, H0. Note that  $Pi.0 = P_c + \delta_0$ , where  $P_c$  is the control group proportion.
- Pi.1: The response proportion in the ith group at which the power is calculated.
- $\delta_0$ : The superiority difference in proportions is the boundary that separates a superior result and a non-superior result.
- $\delta_i$ : The difference between the ith group proportion (Pi.1) and the control group proportion ( $P_c$ ) at which the power is calculated. The formula is  $\delta_i = Pi.1 - P_c$ .
- Overall Alpha: The probability of rejecting at least one of the comparisons in this experiment when each null hypothesis is true.
- Bonferroni Alpha: The adjusted significance level at which each individual comparison is made.

#### Summary Statements

A parallel, 4-group design (with one control group and 3 treatment groups) will be used to test whether the proportion for each treatment group is superior to the control group proportion by a margin, with a superiority difference of 0.06 ( $H_0: \delta \leq 0.06$  vs.  $H_1: \delta > 0.06, \delta = P_i - P_c$ ). In this study, higher proportions are considered to be better. The superiority-by-a-margin hypotheses will be evaluated using 3 one-sided, two-sample, Bonferroni-adjusted Z-tests with unpooled variance, with an overall (experiment-wise) Type I error rate ( $\alpha$ ) of 0.05. The control group proportion is assumed to be 0.6. To detect the treatment proportions 0.7, 0.75, and 0.8 with at least 80% power for each test, the control group sample size needed will be 3329 and the number of needed subjects for the treatment groups will be 1922, 1922, and 1922 (totaling 9095 subjects overall).



## Multi-Arm Superiority by a Margin Tests for the Difference Between Treatment and Control Proportions

**Dropout-Inflated Sample Size**

Group	Dropout Rate	Sample Size Ni	Dropout- Inflated Enrollment Sample Size Ni'	Expected Number of Dropouts Di
1	20%	3329	4162	833
2	20%	1922	2403	481
3	20%	1922	2403	481
4	20%	1922	2403	481
Total		9095	11371	2276
1	20%	1444	1805	361
2	20%	834	1043	209
3	20%	834	1043	209
4	20%	834	1043	209
Total		3946	4934	988
1	20%	792	990	198
2	20%	457	572	115
3	20%	457	572	115
4	20%	457	572	115
Total		2163	2706	543

Group Lists the group numbers.

Dropout Rate The percentage of subjects (or items) that are expected to be lost at random during the course of the study and for whom no response data will be collected (i.e., will be treated as "missing"). Abbreviated as DR.

Ni The evaluable sample size for each group at which power is computed (as entered by the user). If Ni subjects are evaluated out of the Ni' subjects that are enrolled in the study, the design will achieve the stated power.

Ni' The number of subjects that should be enrolled in each group in order to obtain Ni evaluable subjects, based on the assumed dropout rate. Ni' is calculated by inflating Ni using the formula  $Ni' = Ni / (1 - DR)$ , with Ni' always rounded up. (See Julious, S.A. (2010) pages 52-53, or Chow, S.C., Shao, J., Wang, H., and Lohknygina, Y. (2018) pages 32-33.)

Di The expected number of dropouts in each group.  $Di = Ni' - Ni$ .

**Dropout Summary Statements**

Anticipating a 20% dropout rate, group sizes of 4162, 2403, 2403, and 2403 subjects should be enrolled to obtain final group sample sizes of 3329, 1922, 1922, and 1922 subjects.

## Multi-Arm Superiority by a Margin Tests for the Difference Between Treatment and Control Proportions

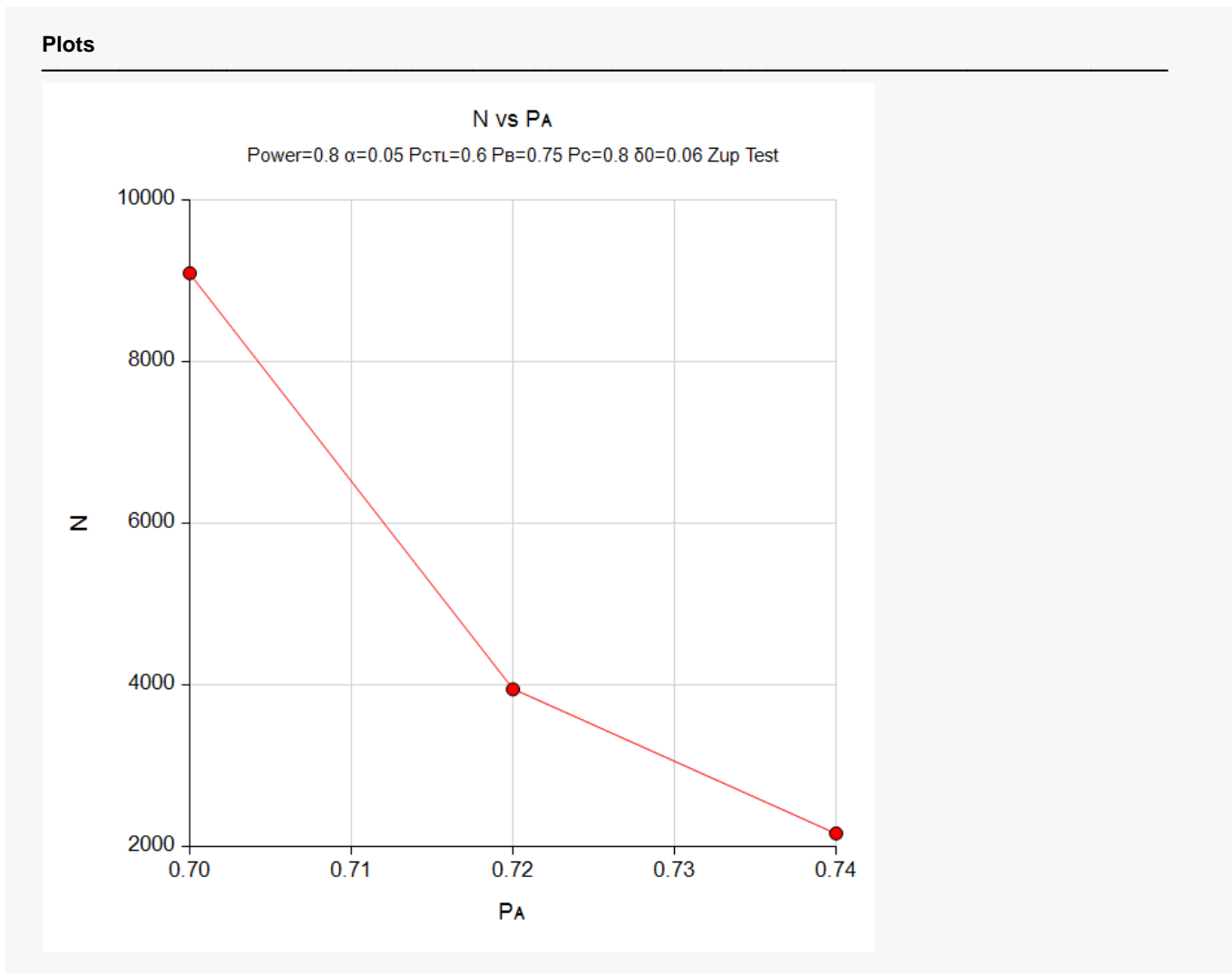
**References**

---

- Chow, S.C., Shao, J., Wang, H., and Lohknygina, Y. 2018. Sample Size Calculations in Clinical Research, 3rd Edition. Chapman & Hall/CRC. Boca Raton, FL. Pages 86-88.
- D'Agostino, R.B., Chase, W., and Belanger, A. 1988. 'The Appropriateness of Some Common Procedures for Testing the Equality of Two Independent Binomial Populations', *The American Statistician*, August 1988, Volume 42 Number 3, pages 198-202.
- 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, J.M. 2000. *Biostatistical Methods*. John Wiley & Sons. New York.
- Machin, D., Campbell, M.J., Tan, S.B, and Tan, S.H. 2018. *Sample Sizes for Clinical, Laboratory, and Epidemiology Studies*, 4th Edition. Wiley Blackwell.
- Miettinen, O.S. and Nurminen, M. 1985. 'Comparative analysis of two rates.' *Statistics in Medicine* 4: 213-226.
- 

This report shows the numeric results of this power study. Notice that the results are shown in blocks of three rows at a time. Each block represents a single design.

## Plots Section



This plot gives a visual presentation to the results in the Numeric Report. We can quickly see the impact on the sample size of decreasing the difference between the treatment and control proportions.

## Example 2 – Validation using a Previously Validated Procedure

We could not find a validation result in the statistical literature, so we will use a previously validated **PASS** procedure (**Superiority by a Margin Tests for the Difference Between Two Proportions**) to produce the results for the following example.

Suppose a parallel-group, clinical trial is being designed to compare three doses of a test compound against the standard therapy using three superiority by a margin tests. Suppose the standard therapy has a response rate of 60%. The investigators would like a sample size large enough to find statistical significance at an overall 0.05 level and an individual-test power of 0.80. The response rates of groups 1, 2, and 3 are 65%, 70%, and 75%, respectively. The superiority difference is 0.06 (10% of the standard therapy response rate). The analysis will use the unpooled Z-Test.

Following common practice, the control-group sample-size multiplier will be set to  $\sqrt{k} = \sqrt{3} = 1.732$  since there are three treatment groups in this design.

The **Superiority by a Margin Tests for the Difference Between Two Proportions** procedure is set up as follows.

Design Tab

Solve For ..... **Sample Size**  
 Power Calculation Method ..... **Normal Approximation**  
 Higher Proportions Are ..... **Better (H1: P1 - P2 > δ0)**  
 Test Type ..... **Z-Test (Unpooled)**  
 Power ..... **0.8**  
 Alpha ..... **0.016667** (which is Alpha / k)  
 Group Allocation ..... **Enter R = N2/N1, solve for N1 and N2**  
 R ..... **1.732** (which is Control SS Multiplier / Treatment SS Multiplier)  
 Input Type ..... **Mixture (δ0 and P1.1)**  
 δ0 (Superiority Difference) ..... **0.06**  
 P1.1 (Actual Proportion) ..... **0.7 0.75 0.8**  
 P2 (Group 2 Proportion) ..... **0.6**

This set of options generates the following report.

**Numeric Results**

Solve For: [Sample Size](#)  
 Test Statistic: Z-Test with Unpooled Variance  
 Hypotheses: H0: P1 - P2 ≤ δ0 vs. H1: P1 - P2 > δ0

Target Power	Actual Power*	N1	N2	N	Target R	Actual R	Ref. P2	P1 H0	P1 H1	Sup. Diff δ0	Diff δ1	Alpha
0.8	0.80017	1922	3329	5251	1.732	1.73205	0.6	0.66	0.70	0.06	0.10	0.01667
0.8	0.80003	355	615	970	1.732	1.73239	0.6	0.66	0.75	0.06	0.15	0.01667
0.8	0.80219	135	234	369	1.732	1.73333	0.6	0.66	0.80	0.06	0.20	0.01667

\* Power was computed using the normal approximation method.

Multi-Arm Superiority by a Margin Tests for the Difference Between Treatment and Control Proportions

In order to maintain a power of 80% for all three groups, it is apparent that the treatment groups will all need to have a sample size of 1922 and the control group should be 3329. We then calculate the powers of the three groups using these sample sizes. The results are displayed in the following table.

<b>Numeric Results</b>									
Solve For: <b>Power</b>									
Test Statistic: Z-Test with Unpooled Variance									
Hypotheses: H0: P1 - P2 ≤ δ0 vs. H1: P1 - P2 > δ0									
<b>Power*</b>	<b>N1</b>	<b>N2</b>	<b>N</b>	<b>Ref. P2</b>	<b>P1 H0 P1.0</b>	<b>P1 H1 P1.1</b>	<b>Sup. Diff δ0</b>	<b>Diff δ1</b>	<b>Alpha</b>
0.80017	1922	3329	5251	0.6	0.66	0.70	0.06	0.10	0.01667
1.00000	1922	3329	5251	0.6	0.66	0.75	0.06	0.15	0.01667
1.00000	1922	3329	5251	0.6	0.66	0.80	0.06	0.20	0.01667

\* Power was computed using the normal approximation method.

This table contains the validation values. We will now run these values through the current procedure and compare the results with these values.

## Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 2** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

<b>Design Tab</b>	
Solve For .....	<b>Sample Size</b>
Higher Proportions Are .....	<b>Better (H1: δ &gt; δ0)</b>
Test Type.....	<b>Z-Test (Unpooled)</b>
Power of Each Test .....	<b>0.8</b>
Overall Alpha .....	<b>0.05</b>
Bonferroni Adjustment .....	<b>Standard Bonferroni</b>
Group Allocation .....	<b>Enter Group Allocation Pattern, solve for group sample sizes</b>
δ0 (Superiority Difference).....	<b>0.06</b>
Control Proportion.....	<b>0.6</b>
Control Sample Size Allocation.....	<b>1.732</b>
Set A Number of Groups.....	<b>1</b>
Set A Proportion .....	<b>0.70</b>
Set A Sample Size Allocation .....	<b>1</b>
Set B Number of Groups.....	<b>1</b>
Set B Proportion .....	<b>0.75</b>
Set B Sample Size Allocation .....	<b>1</b>
Set C Number of Groups .....	<b>1</b>
Set C Proportion .....	<b>0.8</b>
Set C Sample Size Allocation .....	<b>1</b>

Multi-Arm Superiority by a Margin Tests for the Difference Between Treatment and Control Proportions

Set D Number of Groups ..... **0**  
 More..... **Unchecked**

## Output

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

### Numeric Results

Solve For: [Sample Size](#)  
 Group Allocation: Enter Group Allocation Pattern, solve for group sample sizes  
 Test Type: Z-Test with Unpooled Variance  
 Higher Proportions Are: Better  
 Hypotheses:  $H_0: \delta \leq \delta_0$  vs.  $H_1: \delta > \delta_0$   
 Number of Groups: 4  
 Bonferroni Adjustment: Standard Bonferroni (Divisor = 3)

Comparison	Power		Sample Size		Proportion		Difference		Alpha	
	Target	Actual	Ni	Allocation	PijH0 Pi.0	PijH1 Pi.1	Superiority $\delta_0$	Actual $\delta_i$	Overall	Bonferroni- Adjusted
	Control			3329	1.732	0.60	0.60			
vs A	0.8	0.80017	1922	1.000	0.66	0.70	0.06	0.10	0.05	0.016667
vs B	0.8	1.00000	1922	1.000	0.66	0.75	0.06	0.15	0.05	0.016667
vs C	0.8	1.00000	1922	1.000	0.66	0.80	0.06	0.20	0.05	0.016667
Total			9095							

As you can see, the sample sizes and powers match thus validating this procedure.