

## Chapter 101

# Conditional Power of One Proportion Tests

## Introduction

In sequential designs, one or more intermediate analyses of the emerging data are conducted to evaluate whether the experiment should be continued. This may be done to conserve resources or to allow a data monitoring board to evaluate safety and efficacy when subjects are entered in a staggered fashion over a long period of time. *Conditional power* (a frequentist concept) is the probability that the final result will be significant, given the data obtained up to the time of the interim look. *Predictive power* (a Bayesian concept) is the result of averaging the conditional power over the posterior distribution of effect size. Both of these methods fall under the heading of *stochastic curtailment* techniques. Further reading about the theory of these methods can be found in Jennison and Turnbull (2000), Chow and Chang (2007), Chang (2008), Proschan et. al (2006), and Dmitrienko et. al (2005).

This program module computes conditional and predicted power for the case when a one-proportion  $z$  test is used to test whether a population proportion is greater than, less than, or not equal to a specific value.

## Technical Details

All details and assumptions usually made when using a one proportion  $z$  test continue to be in force here.

## Conditional Power

The power of an experiment indicates whether a study is likely to result in useful results, given the sample size. Low power means that the study is *futile*: little chance of statistical significance even though the alternative hypothesis is true. A study that is futile should not be started. However, futility may be determined only after the study has started. When this happens, the study is *curtailed*.

The futility of a study that is underway can be determined by calculating its *conditional power*: the probability of statistical significance at the completion of the study given the data obtained so far.

It is important to note that conditional power at the beginning of the study before any data are collected is equal to the unconditional power. So, conditional power will be high even if early results are negative. Hence, conditional power will seldom result in study curtailment very early in the study.

From Jennison and Turnbull (2000) pages 205 to 208, the general upper one-sided conditional power at stage  $k$  for rejecting a null hypothesis about a parameter  $\theta$  at the end of the study, given the observed test statistic,  $Z_k$ , is computed as

$$P_{uk}(\theta) = \Phi\left(\frac{Z_k\sqrt{I_k} - z_{1-\alpha}\sqrt{I_K} + \theta(I_K - I_k)}{\sqrt{I_K - I_k}}\right),$$

### Conditional Power of One Proportion Tests

the general lower one-sided conditional power at stage  $k$  is computed as

$$P_{lk}(\theta) = \Phi\left(\frac{-Z_k\sqrt{I_k} - z_{1-\alpha}\sqrt{I_K} - \theta(I_K - I_k)}{\sqrt{I_K - I_k}}\right),$$

and the general two-sided conditional power at stage  $k$  is computed as

$$P_k(\theta) = \Phi\left(\frac{Z_k\sqrt{I_k} - z_{1-\alpha/2}\sqrt{I_K} + \theta(I_K - I_k)}{\sqrt{I_K - I_k}}\right) + \Phi\left(\frac{-Z_k\sqrt{I_k} - z_{1-\alpha/2}\sqrt{I_K} - \theta(I_K - I_k)}{\sqrt{I_K - I_k}}\right),$$

where

$\theta$  = the parameter being tested by the hypothesis

$k$  = an interim stage at which the conditional power is computed ( $k = 1, \dots, K - 1$ )

$K$  = the stage at which the study is terminated and the final test computed

$Z_k$  = the test statistic calculated from the observed data that has been collected up to stage  $k$

$I_k$  = the information level at stage  $k$

$I_K$  = the information level at the end of the study

$z_{1-\alpha}$  = the standard normal value for the test with a type I error rate of  $\alpha$ .

For the test of a single proportion with null hypothesis  $H_0: P_1 = P_0$ , where  $P_1$  is the alternative proportion at which the power is calculated and  $P_0$  is the hypothesized proportion under the null hypothesis, these components are computed in Change (2008) page 70 as

$\theta = P_1 - P_0$  (the expected difference under the alternative hypothesis)

$Z_k = (p_{1k} - P_0)\sqrt{\hat{I}_k}$  (the  $z$  statistic computed from the observed data)

$I_k = n_k / \sigma^2$  (the interim information level)

$I_K = N / \sigma^2$  (the final information level)

where

$p_{1k}$  is the sample proportion, estimating  $P_1$  at stage  $k$

$\hat{I}_k$  is the estimated information from the sample at stage  $k$

$n_k$  is the sample size at stage  $k$

$N$  is the total sample size

$\sigma^2 = \bar{p}(1 - \bar{p})$  with  $\bar{p} = (P_1 + P_0)/2$

Computing conditional power requires you to set  $P_0$  and  $P_1$ . Their values can come from the values used during the planning of the study, from similar studies, or from estimates made from the data that has emerged.

## Conditional Power of One Proportion Tests

### Futility Index

The *futility index* is  $1 - P_k(\theta) | H_a$ . The study may be stopped if this index is above 0.8 or 0.9 (that is, if conditional power falls below 0.2 or 0.1).

### Predictive Power

*Predictive power* (a Bayesian concept) is the result of averaging the conditional power over the posterior distribution of effect size. From Jennison and Turnbull (2000) pages 210 to 213, the general upper one-sided predictive power at stage  $k$  is given by

$$P_{uk} = \Phi \left( \frac{Z_k \sqrt{I_K} - z_{1-\alpha} \sqrt{I_k}}{\sqrt{I_K - I_k}} \right).$$

the general lower one-sided predictive power at stage  $k$  is given by

$$P_{lk} = \Phi \left( \frac{-Z_k \sqrt{I_K} - z_{1-\alpha} \sqrt{I_k}}{\sqrt{I_K - I_k}} \right),$$

the general two-sided predictive power at stage  $k$  is given by

$$P_k = \Phi \left( \frac{|Z_k| \sqrt{I_K} - z_{1-\alpha/2} \sqrt{I_k}}{\sqrt{I_K - I_k}} \right) + \Phi \left( \frac{-|Z_k| \sqrt{I_K} - z_{1-\alpha/2} \sqrt{I_k}}{\sqrt{I_K - I_k}} \right),$$

with all terms defined as in the equations for conditional power.

## 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 most of the parameters and options that you will be concerned with.

### Test

#### Alternative Hypothesis

Specify the alternative hypothesis of the test. Since the null hypothesis is the opposite, specifying the alternative is all that is needed.

When you choose a one-sided test option, you must be sure that the value(s) of P0 and P1 match your choice. For example, if you select  $H_a: P1 < P0$ , the value of P1-P0 should be less than zero.

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### Alpha

#### Alpha

This option specifies one or more values for the probability of a type-I error at the end of the study. 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 two-sided tests and 0.025 for one-sided tests.

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

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### Sample Size

#### N (Target Sample Size)

This option specifies one or more values of the target sample size, the total number of subjects planned for the study. This value must be an integer greater than one. Note that you may enter a list of values using the syntax *50,100,150,200,250* or *50 to 250 by 50*.

#### nk (Sample Size at Look k)

Enter the sample size obtained through look k. If this value is greater than N, the value of N is increased to this amount.

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### Effect Size – Proportions

#### P0 (Null Proportion)

Enter a value for P0, the proportion assumed by the null hypothesis. Note that the difference between this and P1 is the value that is actually tested. Usually, the values for P0 and P1 are the values upon which the total sample size of the study was based.

You may enter a range of values such as *0 0.5 1* or *0 to 3 by 0.5*.

#### P1 (Alternative Proportion)

Enter a value for P1, the proportion assumed by the alternative hypothesis. Note that the difference between this and P0 is the value that is actually tested. Usually, the values for P0 and P1 are the values upon which the total sample size of the study was based.

You may enter a range of values such as *0 0.5 1* or *0 to 3 by 0.5*.

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### Effect Size – Current Test Statistic

#### Zk (Current Test Statistic)

Enter the value of the  $z$  statistic calculated from the data obtained through stage  $k$ . This value may be positive or negative. Typically, the  $z$  statistic ranges between -5 and 5.

## Conditional Power of One Proportion Tests

## Example 1 – Computing Conditional Power

Suppose a study has been planned to detect a change in response rate from 55% to 65% at an alpha of 0.05 using a one-sided z-test. The sample size is 50. An interim analysis will be run after half the data have been collected. The data monitoring board would like to have the conditional power calculated for z-values of 1.0, 1.5, 2.0, 2.5, and 3.0.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Conditional Power of One Proportion Tests** procedure window by expanding **Proportions**, then **One Proportion**, then clicking on **Conditional Power**, and then clicking on **Conditional Power of One Proportion Tests**. You may make the appropriate entries as listed below or open **Example 1** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Alternative Hypothesis .....	<b>Ha: P1 &gt; P0 (One-Sided)</b>
Alpha.....	<b>0.025</b>
N (Target Sample Size) .....	<b>50</b>
nk (Sample Size to Look k).....	<b>25</b>
P0 (Null Proportion) .....	<b>0.55</b>
P1 (Alternative Proportion) .....	<b>0.65</b>
Zk (Current Test Statistic).....	<b>1 1.5 2 2.5 3</b>

### Annotated Output

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

### Numeric Results

#### Numeric Results for the Conditional Power of the One Proportion Test

Null Hypothesis: P1 = P0    Alternative Hypothesis: P1 > P0

Cond. Power	Pred. Power	Total Sample Size N	Current Sample Size nk	Null Prop P0	Alt. Prop P1	Diff P1-P0	Test Statistic Zk	Alpha	Futility
0.22627	0.29262	50	25	0.5500	0.6500	0.1000	1.000	0.02500	0.77373
0.40083	0.56409	50	25	0.5500	0.6500	0.1000	1.500	0.02500	0.59917
0.59825	0.80743	50	25	0.5500	0.6500	0.1000	2.000	0.02500	0.40175
0.77302	0.94244	50	25	0.5500	0.6500	0.1000	2.500	0.02500	0.22698
0.89413	0.98878	50	25	0.5500	0.6500	0.1000	3.000	0.02500	0.10587

#### References

Jennison, C., and Turnbull, B.W. 2000. Group Sequential Methods with Applications to Clinical Trials. Chapman & Hall/CRC. New York.  
 Proschan, M., Lan, K.K.G., Wittes, J.T. 2006. Statistical Monitoring of Clinical Trials. Springer. NY, NY.  
 Chang, Mark. 2008. Classical and Adaptive Clinical Trial Designs. John Wiley & Sons. Hoboken, New Jersey.

#### Report Definitions

Conditional Power is the probability of rejecting a false null hypothesis at the end of the study given the data that have emerged so far.

Predicted Power is the average conditional power, averaged over the effect size.

N is the anticipated total sample size to be drawn.

nk is the sample size obtained through stage k.

P0 is the proportion assuming the null hypothesis.

P1 is the proportion assuming the alternative hypothesis.

Diff is the mean difference (P1 - P0) that is to be detected by the completed study.

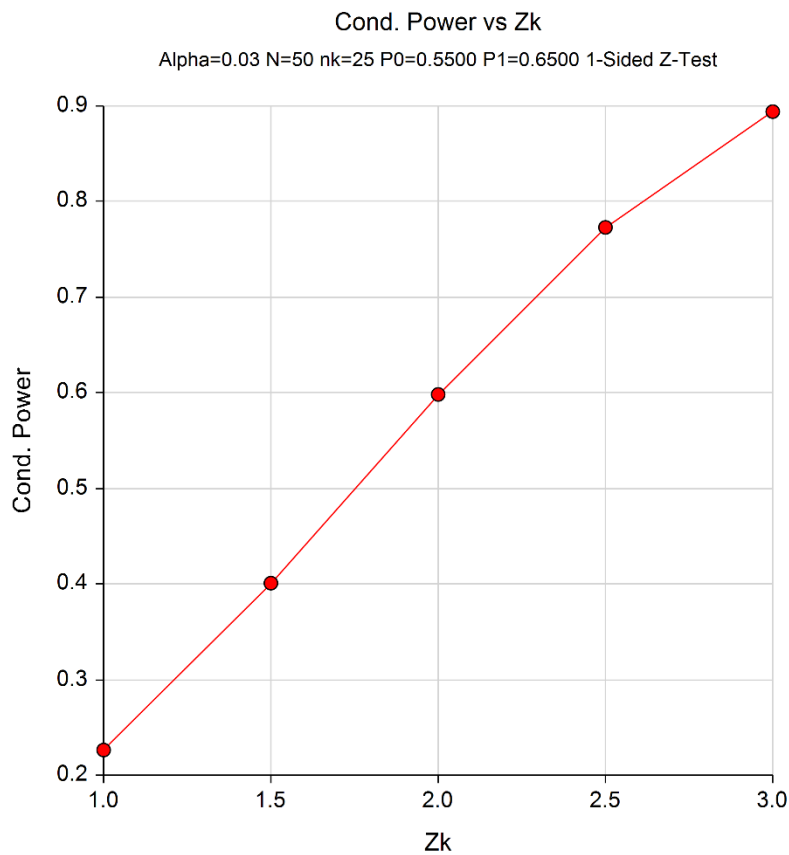
## Conditional Power of One Proportion Tests

$Z_k$  is the value of the test statistic from the observed data at stage  $k$ .  
Alpha is the probability of rejecting a true null hypothesis.  
Futility is one minus the conditional power. A value greater than 0.9 or 0.8 indicates the study should be stopped because there is little chance of achieving statistical significance.

**Summary Statements**

The first 25 of the planned 50 subjects achieve 23% conditional power to detect the difference of 0.1000 between the null proportion 0.5500 and the alternative proportion 0.6500 at a significance level of 0.02500 using a one-sided one-sample z-test. The z-value of the data that have emerged so far is 1.000. The futility index is 0.77373.

This report shows the values of each of the parameters, one scenario per row. The definitions of each column are given in the Report Definitions section.

**Plots Section**

This plot shows the relationship between conditional power and  $Z_k$ .

## Example 2 – Validation

We could not find an example of a conditional power calculation for a one-sample test in the literature. Since the calculations are relatively simple, we will validate the calculation of the third scenario of Example 1 by hand.

In this case

$$\begin{aligned}
 I_k &= n_k / \sigma^2 & I_K &= N / \sigma^2 \\
 &= \frac{25}{0.6(1-0.6)} & &= \frac{50}{0.6(1-0.6)} \\
 &= 104.1666667 & &= 208.3333333
 \end{aligned}$$

$$\begin{aligned}
 P_{uk}(\theta) &= \Phi\left(\frac{Z_k\sqrt{I_k} - z_{1-\alpha}\sqrt{I_K} + \theta(I_K - I_k)}{\sqrt{I_K - I_k}}\right) \\
 &= \Phi\left(\frac{2.0\sqrt{104.1666667} - (1.959964)\sqrt{208.3333333} + (0.65 - 0.55)(208.3333333 - 104.1666667)}{\sqrt{208.3333333 - 104.1666667}}\right) \\
 &= \Phi\left(\frac{2.5394376}{10.2062073}\right) \\
 &= \Phi(0.2488131) \\
 &= 0.5982473
 \end{aligned}$$

This value matches the third line of the report in Example 1.