

## Chapter 413

# One-Sample T-Tests for Superiority by a Margin

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## Introduction

This procedure computes power and sample size for superiority by a margin tests in one-sample designs in which the outcome is distributed as a normal random variable. This includes the analysis of the differences between paired values.

The details of sample size calculation for the one-sample design are presented in the One-Sample T-Tests chapter and they will not be duplicated here. This chapter only discusses those changes necessary for superiority by a margin tests. Sample size formulas for superiority by a margin tests of a single mean are presented in Chow et al. (2018) page 43.

The *one-sample t-test* is used to test whether a population mean is different from a specific value. When the data are differences between paired values, this test is known as the *paired t-test*.

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## Paired Designs

Paired data may occur because two measurements are made on the same subject or because measurements are made on two subjects that have been matched according to other variables. Hypothesis tests on paired data can be analyzed by considering the difference between the paired items as the response. The distribution of differences is usually symmetric. In fact, the distribution must be symmetric if the individual distributions of the two items are identical. Hence, the paired *t-test* is appropriate for paired data even when the distributions of the individual items are not normal.

In paired designs, the variable of interest is the difference between two individual measurements. Although the superiority hypothesis refers to the difference between two individual means, the actual values of those means are not needed. All that is needed is their difference.

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## The Statistical Hypotheses

Both non-inferiority and superiority tests are examples of directional (one-sided) tests and their power and sample size could be calculated using the One-Sample T-Tests procedure. However, at the urging of our users, we have developed this procedure which provides the input and output options that are convenient for superiority hypotheses. This section will review the specifics of superiority testing.

Remember that in the usual *t-test* setting, the null ( $H_0$ ) and alternative ( $H_1$ ) hypotheses for one-sided upper-tail tests are defined as

$$H_0: \mu \leq \mu_0 \quad \text{versus} \quad H_1: \mu > \mu_0$$

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Rejecting  $H_0$  implies that the mean is larger than the value  $\mu_0$ . This test is called an *upper-tail test* because  $H_0$  is rejected in samples in which the sample mean is larger than  $\mu_0$ .

The *lower-tail test* is

$$H_0: \mu \geq \mu_0 \quad \text{versus} \quad H_1: \mu < \mu_0$$

*Superiority by a margin* tests are special cases of the above directional tests. It will be convenient to adopt the following specialize notation for the discussion of these tests.

| <b>Parameter</b> | <b>PASS Input/Output</b> | <b>Interpretation</b>   |
|------------------|--------------------------|---|
| $\mu$            | $\mu$                    | <i>Population mean.</i> If the data are paired differences, this is the mean of those differences. This parameter will be estimated by the study.   |
| $\mu_1$          | $\mu 1$                  | <i>Actual population mean at which power is calculated.</i> This is the assumed population mean used in all calculations.   |
| $\mu_0$          | $\mu 0$                  | <i>Non-Inferiority Mean.</i> This is the smallest (or largest) value of the mean for which the new treatment will still be considered non-inferior to the reference.  |
| $\mu_R$          | $\mu R$                  | <i>Reference value.</i> Usually, this is the mean of a reference population. If the data are paired differences, this is the hypothesized value of the mean difference.   |
| $M_S$            | SM                       | <i>Margin of superiority.</i> This is a tolerance value that defines the magnitude of difference that is not of practical importance. This may be thought of as the smallest difference from the reference value that is considered to be of practical significance. This value is assumed to be a positive number. |

## Superiority by a Margin Tests

A *superiority by a margin test* tests that the mean is better than that of the baseline (reference) population by more than a small superiority margin. The actual direction of the hypothesis depends on the whether higher values of the response are good or bad.

### Case 1: High Values Good

In this case, higher values are better. The hypotheses are arranged so that rejecting the null hypothesis implies that the mean is greater than the reference value by at least the margin of superiority.

Equivalent sets of the null and alternative hypotheses are

$$\begin{array}{lll}
 H_0: \mu \leq \mu_0 & \text{versus} & H_1: \mu > \mu_0 \\
 H_0: \mu \leq \mu_R + M_S & \text{versus} & H_1: \mu > \mu_R + M_S \\
 H_0: \mu - \mu_R \leq M_S & \text{versus} & H_1: \mu - \mu_R > M_S
 \end{array}$$

## Case 2: High Values Bad

In this case, lower values are better. The hypotheses are arranged so that rejecting the null hypothesis implies that the mean is less than the reference value by at least the margin of superiority.

Equivalent sets of the null and alternative hypotheses are

$$\begin{aligned} H_0: \mu &\geq \mu_0 && \text{versus} && H_1: \mu < \mu_0 \\ H_0: \mu &\geq \mu_R - M_S && \text{versus} && H_1: \mu < \mu_R - M_S \\ H_0: \mu - \mu_R &\geq -M_S && \text{versus} && H_1: \mu - \mu_R < -M_S \end{aligned}$$

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## Example

A superiority test example will set the stage for the discussion of the terminology that follows. Suppose that a test is to be conducted to determine if a new cancer treatment substantially improves the mean bone density. The adjusted mean bone density (AMBD) in the population of interest is 0.002300 gm/cm with a standard deviation of 0.000300 gm/cm. Clinicians decide that if the treatment increases AMBD by more than 5% (0.000115 gm/cm), it provides a significant health benefit.

The hypothesis of interest is whether the AMBD in the treated group is greater than  $0.002300 + 0.000115 = 0.002415$ . The statistical test will be set up so that if the null hypothesis that the AMBD is greater than or equal to 0.002415 is rejected, the conclusion will be that the new treatment is superior, at least in terms of AMBD. The value 0.000115 gm/cm is called the *margin of superiority*.

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## One-Sample T-Test Statistic

The one-sample *t*-test assumes that the data are a simple random sample from a population of normally distributed values that all have the same mean and variance. This assumption implies that the data are continuous, and their distribution is symmetric. The calculation of the *t*-test proceeds as follows

$$t_{n-1} = \frac{\bar{X} - \mu_0}{s/\sqrt{n}}$$

where

$$\bar{X} = \frac{\sum_{i=1}^n X_i}{n},$$

$$s = \sqrt{\frac{\sum_{i=1}^n (X_i - \bar{X})^2}{n - 1}},$$

and  $\mu_0$  is the value of the mean hypothesized by the null hypothesis that incorporates both  $\mu_R$  and  $M_S$ .

The significance of the test statistic is determined by computing the p-value. If this p-value is less than a specified level (usually 0.05), the hypothesis is rejected. Otherwise, no conclusion can be reached.

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## Power Calculation for the One-Sample T-Test

When the standard deviation is unknown, the power is calculated as follows for a directional alternative (one-tailed test) in which  $\mu_1 > \mu_0$ .

1. Find  $t_\alpha$  such that  $1 - T_{df}(t_\alpha) = \alpha$ , where  $T_{df}(t_\alpha)$  is the area under a central- $t$  curve to the left of  $x$  and  $df = n - 1$ .
2. Calculate:  $X_1 = \mu_0 + t_\alpha \frac{\sigma}{\sqrt{n}}$ .
3. Calculate the noncentrality parameter:  $\lambda = \frac{\mu_1 - \mu_0}{\frac{\sigma}{\sqrt{n}}}$ .
4. Calculate:  $t_1 = \frac{X_1 - \mu_1}{\frac{\sigma}{\sqrt{n}}} + \lambda$ .
5. Power =  $1 - T'_{df,\lambda}(t_1)$ , where  $T'_{df,\lambda}(x)$  is the area to the left of  $x$  under a noncentral- $t$  curve with degrees of freedom  $df$  and noncentrality parameter  $\lambda$ .

## Example 1 – Power Analysis

Suppose that a test is to be conducted to determine if a new cancer treatment improves the mean bone density. The adjusted mean bone density (AMBD) in the population of interest ( $\mu_R$ ) is 0.002300 gm/cm with a standard deviation of 0.000300 gm/cm. Clinicians decide that if the treatment increases AMBD by more than 5% ( $M_S = 0.000115$  gm/cm such that  $\mu_0 = \mu_R + M_S = 0.002415$ ), it generates a significant health benefit. They also want to consider what would happen if the margin of superiority is set to 2.5% (0.0000575 gm/cm such that  $\mu_0 = \mu_R + M_S = 0.0023575$ ).

The analysis will be a superiority test using the  $t$ -test at the 0.025 significance level. Power is to be calculated assuming that the new treatment has 7.5% improvement on AMBD ( $\mu_1 = 0.0024725$ ). Several sample sizes between 20 and 300 will be analyzed. The researchers want to achieve a power of at least 90%. All numbers have been multiplied by 10000 to make the reports and plots easier to read.

### Setup

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

#### Design Tab

|                                     |   |
|-------------------------------------|---|
| Solve For .....                     | <b>Power</b>                                    |
| Higher Means Are .....              | <b>Better (H1: <math>\mu &gt; \mu_0</math>)</b> |
| Population Size .....               | <b>Infinite</b>                                 |
| Alpha .....                         | <b>0.025</b>                                    |
| N (Sample Size) .....               | <b>20 40 60 80 100 150 200 300</b>              |
| $\mu_0$ (Superiority Mean) .....    | <b>23.575 24.15</b>                             |
| $\mu_1$ (Actual Mean) .....         | <b>24.725</b>                                   |
| $\sigma$ (Standard Deviation) ..... | <b>3</b>  |

## One-Sample T-Tests for Superiority by a Margin

## Output

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

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**Numeric Results**


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Solve For: **Power**  
 Higher Means Are: **Better**  
 Hypotheses:  $H_0: \mu \leq \mu_0$  vs.  $H_1: \mu > \mu_0$

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| Power   | Sample Size<br>N | Mean                   |                   | Standard Deviation<br>$\sigma$ | Alpha |
|---------|------------------|------------------------|-------------------|--------------------------------|-------|
|         |                  | Superiority<br>$\mu_0$ | Actual<br>$\mu_1$ |                                |       |
| 0.36990 | 20               | 23.575                 | 24.725            | 3                              | 0.025 |
| 0.65705 | 40               | 23.575                 | 24.725            | 3                              | 0.025 |
| 0.83164 | 60               | 23.575                 | 24.725            | 3                              | 0.025 |
| 0.92317 | 80               | 23.575                 | 24.725            | 3                              | 0.025 |
| 0.96682 | 100              | 23.575                 | 24.725            | 3                              | 0.025 |
| 0.99658 | 150              | 23.575                 | 24.725            | 3                              | 0.025 |
| 0.99970 | 200              | 23.575                 | 24.725            | 3                              | 0.025 |
| 1.00000 | 300              | 23.575                 | 24.725            | 3                              | 0.025 |
| 0.12601 | 20               | 24.150                 | 24.725            | 3                              | 0.025 |
| 0.21844 | 40               | 24.150                 | 24.725            | 3                              | 0.025 |
| 0.30873 | 60               | 24.150                 | 24.725            | 3                              | 0.025 |
| 0.39493 | 80               | 24.150                 | 24.725            | 3                              | 0.025 |
| 0.47532 | 100              | 24.150                 | 24.725            | 3                              | 0.025 |
| 0.64517 | 150              | 24.150                 | 24.725            | 3                              | 0.025 |
| 0.76959 | 200              | 24.150                 | 24.725            | 3                              | 0.025 |
| 0.91135 | 300              | 24.150                 | 24.725            | 3                              | 0.025 |

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Power The probability of rejecting a false null hypothesis when the alternative hypothesis is true.  
 N The sample size, the number of subjects (or pairs) in the study.  
 $\mu_0$  The superiority mean. Since higher means are better,  $\mu_0 = \mu_R + SM$ , where  $\mu_R$  is the baseline, standard, or reference mean, and SM is the margin of superiority.  
 $\mu_1$  The actual value of the mean at which power and sample size are calculated.  
 $\sigma$  The standard deviation of the response (or standard deviation of differences for paired data). It measures the variability in the population.  
 Alpha The probability of rejecting a true null hypothesis.

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**Summary Statements**


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A single-group design will be used to test whether the mean is superior by a margin, with a margin of superiority added to a reference mean totaling 23.575 ( $H_0: \mu \leq 23.575$  versus  $H_1: \mu > 23.575$ ). The comparison will be made using a one-sided, one-sample t-test, with a Type I error rate ( $\alpha$ ) of 0.025. The underlying distribution standard deviation is assumed to be 3. To detect a mean of 24.725 with a sample size of 20, the power is 0.3699.

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## One-Sample T-Tests for Superiority by a Margin

**Dropout-Inflated Sample Size**

| Dropout Rate | Sample Size<br>N | Dropout-<br>Inflated<br>Enrollment<br>Sample Size<br>N' | Expected<br>Number of<br>Dropouts<br>D |
|--------------|------------------|---|--|
| 20%          | 20               | 25  | 5                                      |
| 20%          | 40               | 50  | 10                                     |
| 20%          | 60               | 75  | 15                                     |
| 20%          | 80               | 100   | 20                                     |
| 20%          | 100              | 125   | 25                                     |
| 20%          | 150              | 188   | 38                                     |
| 20%          | 200              | 250   | 50                                     |
| 20%          | 300              | 375   | 75                                     |

|              |  |
|--------------|--|
| 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.   |
| N            | The evaluable sample size at which power is computed (as entered by the user). If N subjects are evaluated out of the N' subjects that are enrolled in the study, the design will achieve the stated power.  |
| N'           | The total number of subjects that should be enrolled in the study in order to obtain N evaluable subjects, based on the assumed dropout rate. N' is calculated by inflating N using the formula $N' = N / (1 - DR)$ , with N' 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.) |
| D            | The expected number of dropouts. $D = N' - N$ .  |

**Dropout Summary Statements**

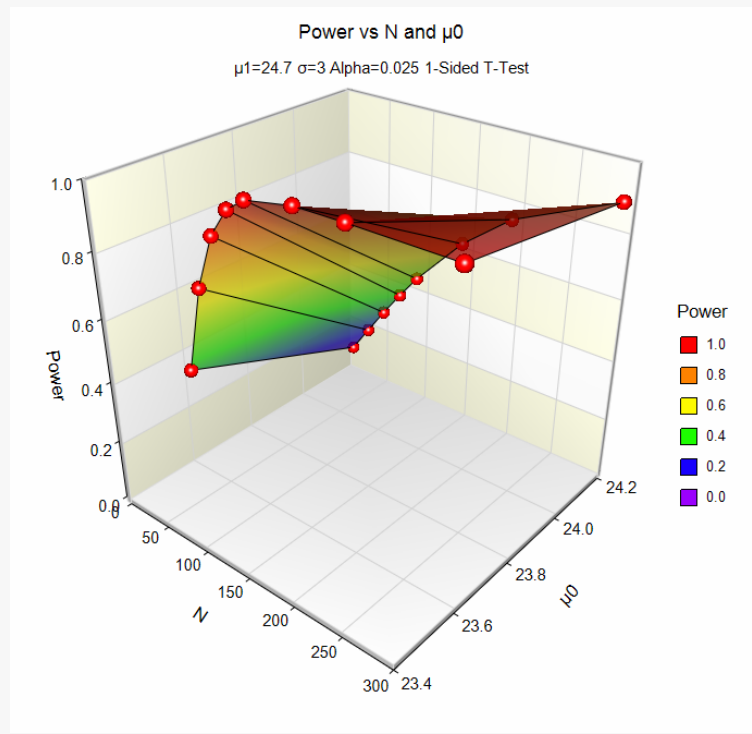
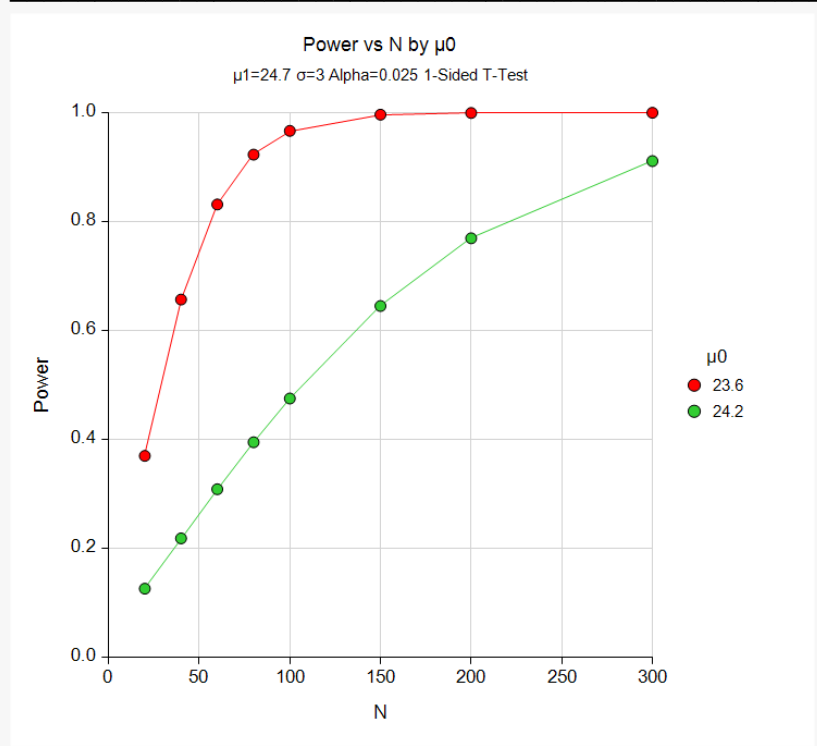
Anticipating a 20% dropout rate, 25 subjects should be enrolled to obtain a final sample size of 20 subjects.

**References**

- Chow, S.C., Shao, J., Wang, H., and Lohknygina, Y. 2018. Sample Size Calculations in Clinical Research, Third Edition. Taylor & Francis/CRC. Boca Raton, Florida.
- Julious, Steven A. 2004. 'Tutorial in Biostatistics. Sample sizes for clinical trials with Normal data.' Statistics in Medicine, 23:1921-1986.

One-Sample T-Tests for Superiority by a Margin

Plots



The above report shows that for  $\mu_0 = 24.15$  ( $SM = 1.15$ ), the sample size necessary to obtain 90% power is just under 300. However, if  $\mu_0 = 23.575$  ( $SM = 0.575$ ), the required sample size is about 75.



## Example 2 – Finding the Sample Size

Continuing with Example 1, the researchers want to know the exact sample size for each value of SM to achieve 90% power.

### 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.

| Design Tab                         |   |
|------------------------------------|---|
| Solve For .....                    | <b>Sample Size</b>                              |
| Higher Means Are .....             | <b>Better (H1: <math>\mu &gt; \mu_0</math>)</b> |
| Population Size .....              | <b>Infinite</b>                                 |
| Power.....                         | <b>0.90</b>                                     |
| Alpha.....                         | <b>0.025</b>                                    |
| $\mu_0$ (Superiority Mean) .....   | <b>23.575 24.15</b>                             |
| $\mu_1$ (Actual Mean) .....        | <b>24.725</b>                                   |
| $\sigma$ (Standard Deviation)..... | <b>3</b>  |

### Output

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

| Numeric Results   |  |                        |                   |                                |       |
|-------------------|--|------------------------|-------------------|--------------------------------|-------|
| Solve For:        | Sample Size                                |                        |                   |                                |       |
| Higher Means Are: | Better                                     |                        |                   |                                |       |
| Hypotheses:       | H0: $\mu \leq \mu_0$ vs. H1: $\mu > \mu_0$ |                        |                   |                                |       |
| Power             | Sample Size<br>N                           | Mean                   |                   | Standard Deviation<br>$\sigma$ | Alpha |
|                   |  | Superiority<br>$\mu_0$ | Actual<br>$\mu_1$ |                                |       |
| 0.90215           | 74   | 23.575                 | 24.725            | 3                              | 0.025 |
| 0.90005           | 288  | 24.150                 | 24.725            | 3                              | 0.025 |

This report shows the exact sample size requirement for each value of  $\mu_0$ .

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## Example 3 – Validation

This procedure uses the same mechanics as the One-Sample T-Tests for Non-Inferiority procedure. Refer to Example 3 of Chapter 415 for the validation.