Chapter 320

Equivalence Tests for the Mean Ratio in a Three-Arm Trial (Normal Data) (Simulation)

Introduction

This procedure computes power and sample size of an equivalence test procedure that compares three means from independent groups using various mean ratios. Schuirmann's (1987) two one-sided tests (TOST) approach is used to test equivalence. The t-test is commonly used in this situation, but Welch's unequal variance test is also available.

Measurements are made on individuals that have been randomly assigned to one of three groups: treatment group, reference group, or placebo group. This *three-arm* design may be analyzed by an initial test of treatment superiority over the placebo followed by a two-arm equivalence test of the ratio of the treatment and reference means or of the ratio of the treatment – placebo means and the reference – placebo means. The details are found in Chang *et al.* (2014).

Because of the complicated analysis procedure (two tests), the power and sample size results are based on simulation. Chang et al. (2014) gives analytic results for the case of equal sample sizes, but a more flexible algorithm was needed for the case of unequal sample sizes and variances.

Technical Details

Computer simulation allows us to estimate the power and significance level that is actually achieved by a test procedure in situations that are not mathematically tractable.

The steps to a simulation study are as follows.

1. Specify how the tests are carried out. This includes indicating how the test statistics are calculated and how the significance levels are specified.

2. Generate random samples from the distributions specified by the <u>alternative</u> hypothesis. Calculate the test statistics from the simulated data and determine if the null hypothesis is accepted or rejected. Tabulate the number of rejections and use this to calculate the test's power.

3. Repeat step 2 several thousand times, tabulating the number of times the simulated data leads to a rejection of the null hypothesis. The power is the proportion of simulated samples in step 2 that lead to rejection.

Equivalence Assessment Methods

This section describes the analysis methods that can be used to assess equivalence that are available in this procedure. We begin with the design setting.

Suppose a pool of subjects is randomly assigned to one three groups: treatment, reference, or placebo. The subject responses from each group are assumed to be normally distributed with $X_T \sim N(\mu_T, \sigma_T^2)$, $X_R \sim N(\mu_R, \sigma_R^2)$, and $X_P \sim N(\mu_P, \sigma_P^2)$. Samples of size $n_T, n_R,$ and n_P are thus obtained from the three arms.

Chang *et al.* (2014) present three methods for conducting an analysis of various ratios of the means. Each results in different sample size requirements. Each of these methods is based on the following summary statistics:

$$\bar{X}_i = \frac{\sum_{k=1}^{n_i} X_{ik}}{n_i}$$

$$s_i^2 = \frac{\sum_{k=1}^{n_i} (X_{ik} - \bar{X}_i)^2}{n_i - 1}$$

where *i =T, R, P*.

(B) Treatment Efficacy Test followed by Treatment vs Reference Equivalence Test

This method first tests whether the treatment is better than the placebo. This is a one-sided test, so the significance level is set at 0.025. If this hypothesis is rejected, then a second equivalence test is run. This second test is based on the ratio of the treatment and the reference means. It uses a significance level of 0.05 for both TOST tests.

Hypotheses

The treatment efficacy hypotheses are:

$$H_0: \mu_T - \mu_P \leq 0 \text{ versus } H_1: \mu_T - \mu_P > 0.$$

The lower and upper equivalence hypotheses are

$$H_{0L}: \frac{\mu_T}{\mu_R} \leq E_L \text{ versus } H_{1L}: \frac{\mu_T}{\mu_R} > E_L \text{ and } H_{0U}: \frac{\mu_T}{\mu_R} \geq E_U \text{ versus } H_{1U}: \frac{\mu_T}{\mu_R} < E_U.$$

Unequal Variance Test Statistics

The treatment efficacy test uses the one-sided test statistics t_S. This is given by

$$t_S = \frac{\bar{X}_T - \bar{X}_P}{\sqrt{\frac{s_T^2}{n_T} + \frac{s_P^2}{n_P}}}$$

The degrees of freedom are

$$\nu_S = \frac{\left(\frac{s_T^2}{n_T} + \frac{s_P^2}{n_P}\right)^2}{\frac{s_T^4/n_T^2}{n_T - 1} + \frac{s_P^4/n_P^2}{n_P - 1}}$$

The equivalence tests use the pair of TOST test statistics t_L and t_U. These are given by

$$t_L = \frac{\bar{X}_T - E_L \bar{X}_R}{\sqrt{\frac{s_T^2}{n_T} + E_L^2 \frac{s_R^2}{n_R}}}$$

$$t_U = \frac{\bar{X}_T - E_U \bar{X}_R}{\sqrt{\frac{s_T^2}{n_T} + E_U^2 \frac{s_R^2}{n_R}}}$$

The degrees of freedom of these t-tests are

$$\nu_L = \frac{\left(\frac{s_T^2}{n_T} + E_L^2 \frac{s_R^2}{n_R}\right)^2}{\frac{s_T^4/n_T^2}{n_T - 1} + E_L^4 \left(\frac{s_R^4/n_R^2}{n_R - 1}\right)}$$

$$\nu_U = \frac{\left(\frac{s_T^2}{n_T} + E_U^2 \frac{s_R^2}{n_R}\right)^2}{\frac{s_T^4/n_T^2}{n_T - 1} + E_U^4 \left(\frac{s_R^4/n_R^2}{n_R - 1}\right)}$$

Equal Variance Test Statistics

The treatment efficacy test uses the one-sided test statistics t_S. This test statistic is given by

$$t_S = \frac{\bar{X}_T - \bar{X}_R}{\sqrt{s_{pool}^2 \left(\frac{1}{n_T} + \frac{1}{n_P}\right)}}$$

where

$$s_{pool}^2 = \frac{s_T^2(n_T - 1) + s_P^2(n_P - 1)}{n_T + n_P - 2}$$

The degrees of freedom of this test are $\nu_S = n_T + n_P - 2$.

The equivalence tests use the pair of TOST test statistics t_L and t_U. These are given by

$$t_L = \frac{\bar{X}_T - E_L \bar{X}_R}{\sqrt{s_{pool}^2 \left(\frac{1}{n_T} + E_L^2 \frac{1}{n_R}\right)}}$$

$$t_U = \frac{\bar{X}_T - E_U \bar{X}_R}{\sqrt{s_{pool}^2 \left(\frac{1}{n_T} + E_U^2 \frac{1}{n_R}\right)}}$$

$$s_{pool}^2 = \frac{s_T^2(n_T - 1) + s_R^2(n_R - 1)}{n_T + n_R - 2}$$

The degrees of freedom for both tests given by $\nu_L = \nu_U = n_T + n_R - 2$.

(C) Treatment Efficacy Test followed by Treatment vs Reference Equivalence Test of Mean Differences

This method first tests whether the treatment is better than the placebo. This is a one-sided test, so the significance level is set at 0.025.

If this hypothesis is rejected, then a second equivalence test is run. This second test is based on the ratio of the treatment mean minus the placebo mean and the reference mean minus the placebo mean. This equivalence test uses a significance level of 0.05 for both TOST tests.

Hypotheses

The treatment efficacy hypotheses are:

$$H_0: \mu_T - \mu_P \leq 0 \text{ versus } H_1: \mu_T - \mu_P > 0.$$

The lower and upper equivalence hypotheses are

$$H_{0L}: \frac{\mu_T - \mu_P}{\mu_R - \mu_P} \leq E_L \text{ versus } H_{1L}: \frac{\mu_T - \mu_P}{\mu_R - \mu_P} > E_L \text{ and } H_{0U}: \frac{\mu_T - \mu_P}{\mu_R - \mu_P} \geq E_U \text{ versus } H_{1U}: \frac{\mu_T - \mu_P}{\mu_R - \mu_P} < E_U.$$

Unequal Variance Test Statistics

The treatment efficacy test uses the one-sided test statistics t_S. This is given by

$$t_S = \frac{\bar{X}_T - \bar{X}_P}{\sqrt{\frac{s_T^2}{n_T} + \frac{s_P^2}{n_P}}}$$

The degrees of freedom are

$$\nu_S = \frac{\left(\frac{s_T^2}{n_T} + \frac{s_P^2}{n_P}\right)^2}{\frac{s_T^4/n_T^2}{n_T - 1} + \frac{s_P^4/n_P^2}{n_P - 1}}$$

The equivalence tests use the pair of TOST test statistics t_L and t_U. These are given by

$$t_L = \frac{\bar{X}_T - E_L \bar{X}_R - (1 - E_L)\bar{X}_P}{\sqrt{\frac{s_T^2}{n_T} + E_L^2 \frac{s_R^2}{n_R} + (1 - E_L)^2 \frac{s_P^2}{n_P}}}$$

$$t_U = \frac{\bar{X}_T - E_U \bar{X}_R - (1 - E_U)\bar{X}_P}{\sqrt{\frac{s_T^2}{n_T} + E_U^2 \frac{s_R^2}{n_R} + (1 - E_U)^2 \frac{s_P^2}{n_P}}}$$

The degrees of freedom of these t-tests are

$$\nu_L = \frac{\left(\frac{s_T^2}{n_T} + E_L^2 \frac{s_R^2}{n_R} + (1 - E_L)^2 \frac{s_P^2}{n_P}\right)^2}{\frac{s_T^4/n_T^2}{n_T - 1} + E_L^4 \left(\frac{s_R^4/n_R^2}{n_R - 1}\right) + (1 - E_L)^4 \left(\frac{s_P^4/n_P^2}{n_P - 1}\right)}$$

$$\nu_U = \frac{\left(\frac{s_T^2}{n_T} + E_U^2 \frac{s_R^2}{n_R} + (1 - E_U)^2 \frac{s_P^2}{n_P}\right)^2}{\frac{s_T^4/n_T^2}{n_T - 1} + E_U^4 \left(\frac{s_R^4/n_R^2}{n_R - 1}\right) + (1 - E_U)^4 \left(\frac{s_P^4/n_P^2}{n_P - 1}\right)}$$

Equal Variance Test Statistics

The treatment efficacy test uses the one-sided test statistics t_S. This test statistic is given by

$$t_S = \frac{\bar{X}_T - \bar{X}_R}{\sqrt{s_{pool}^2 \left(\frac{1}{n_T} + \frac{1}{n_P}\right)}}$$

where

$$s_{pool}^2 = \frac{s_T^2(n_T - 1) + s_P^2(n_P - 1)}{n_T + n_P - 2}$$

The degrees of freedom of this test are $\nu_S = n_T + n_P - 2$.

The equivalence tests use the pair of TOST test statistics t_L and t_U. These are given by

$$t_L = \frac{\bar{X}_T - E_L \bar{X}_R - (1 - E_L)\bar{X}_P}{\sqrt{s_{pool}^2 \left(\frac{1}{n_T} + \frac{E_L^2}{n_R} + \frac{(1 - E_L)^2}{n_P}\right)}}$$

$$t_U = \frac{\bar{X}_T - E_U \bar{X}_R - (1 - E_U)\bar{X}_P}{\sqrt{s_{pool}^2 \left(\frac{1}{n_T} + \frac{E_U^2}{n_R} + \frac{(1 - E_U)^2}{n_P}\right)}}$$

$$s_{pool}^2 = \frac{s_T^2(n_T - 1) + s_R^2(n_R - 1) + s_P^2(n_P - 1)}{n_T + n_R + n_P - 3}$$

The degrees of freedom for both tests given by $\nu_L = \nu_U = n_T + n_R + n_P - 3$.

(D) Treatment vs Reference Equivalence Test of Mean Differences

This method skips the treatment versus placebo test that was used in methods (B) and (C). This is replaced by the lower TOST test which is now conducted at a significance level of 0.025.

The equivalence test is run. This test is based on the ratio of the treatment mean minus the placebo mean and the reference mean minus the placebo mean. This equivalence test uses a significance level of 0.025 for t_L and 0.05 for t_U.

Hypotheses

The lower and upper equivalence hypotheses are

$$H_{0L}: \frac{\mu_T - \mu_P}{\mu_R - \mu_P} \leq E_L \text{ versus } H_{1L}: \frac{\mu_T - \mu_P}{\mu_R - \mu_P} > E_L \text{ and } H_{0U}: \frac{\mu_T - \mu_P}{\mu_R - \mu_P} \geq E_U \text{ versus } H_{1U}: \frac{\mu_T - \mu_P}{\mu_R - \mu_P} < E_U.$$

Unequal Variance Test Statistics

The equivalence tests use the pair of TOST test statistics t_L and t_U. These are given by

$$t_L = \frac{\bar{X}_T - E_L \bar{X}_R - (1 - E_L)\bar{X}_P}{\sqrt{\frac{s_T^2}{n_T} + E_L^2 \frac{s_R^2}{n_R} + (1 - E_L)^2 \frac{s_P^2}{n_P}}}$$

$$t_U = \frac{\bar{X}_T - E_U \bar{X}_R - (1 - E_U)\bar{X}_P}{\sqrt{\frac{s_T^2}{n_T} + E_U^2 \frac{s_R^2}{n_R} + (1 - E_U)^2 \frac{s_P^2}{n_P}}}$$

The degrees of freedom of these t-tests are

$$
\nu_L = \frac{\left(\frac{s_T^2}{n_T} + E_L^2 \frac{s_R^2}{n_R} + (1 - E_L)^2 \frac{s_P^2}{n_P}\right)^2}{\frac{s_T^4/n_T^2}{n_T - 1} + E_L^4 \left(\frac{s_R^4/n_R^2}{n_R - 1}\right) + (1 - E_L)^4 \left(\frac{s_P^4/n_P^2}{n_P - 1}\right)}
$$

$$
\nu_U = \frac{\left(\frac{s_T^2}{n_T} + E_U^2 \frac{s_R^2}{n_R} + (1 - E_U)^2 \frac{s_P^2}{n_P}\right)^2}{\frac{s_T^4/n_T^2}{n_T - 1} + E_U^4 \left(\frac{s_R^4/n_R^2}{n_R - 1}\right) + (1 - E_U)^4 \left(\frac{s_P^4/n_P^2}{n_P - 1}\right)}
$$

Equal Variance Test Statistics

The equivalence tests use the pair of TOST test statistics t_L and t_U. These are given by

$$
t_L = \frac{\bar{X}_T - E_L \bar{X}_R - (1 - E_L)\bar{X}_P}{\sqrt{s_{pool}^2 \left(\frac{1}{n_T} + \frac{E_L^2}{n_R} + \frac{(1 - E_L)^2}{n_P}\right)}}
$$

$$
t_U = \frac{\bar{X}_T - E_U \bar{X}_R - (1 - E_U)\bar{X}_P}{\sqrt{s_{pool}^2 \left(\frac{1}{n_T} + \frac{E_U^2}{n_R} + \frac{(1 - E_U)^2}{n_P}\right)}}
$$

$$
s_{pool}^2 = \frac{s_T^2(n_T - 1) + s_R^2(n_R - 1) + s_P^2(n_P - 1)}{n_T + n_R + n_P - 3}
$$

The degrees of freedom for both tests given by $\nu_L = \nu_U = n_T + n_R + n_P - 3$.

Solution by Simulation

Because of the complexity of the experimental procedure, power and sample size are solved for using simulation. The accuracy of the simulation depends heavily upon the number of simulations, M. Of course, as M is increased, the solution time also increases.

We have found the following strategy to be reasonable. Set M to 1000 (or even 500) while you are experimenting with various settings. Once you have a set of options that you like, set M to 5000 (or higher).

Note that Chang *et al.* (2014) present closed form approximations. Unfortunately, their results are only given for equal group sample sizes. This is often not the case for three-arm designs such as this.

Example 1 – Power at Various Sample Sizes

Researchers are planning a three-arm trial to determine if the response to a new drug is equivalent to the response to a reference drug. The average response level to the reference drug is approximately 63 with a standard deviation of 5 in all groups. The response at the placebo is 43. They want to investigate the power when the treatment response is also 63.

The researchers decide to use the (C) method for the analysis of the results. This method considers the ratio of the treatment - placebo difference to the reference – placebo difference. They set the equivalence boundaries at 0.8 and 1.25. The significance levels are 0.025 for the first test and 0.05 for the equivalence test.

An initial run of the procedure with only 500 simulations yielded a sample size of 25 per group, so they want to investigate the group sizes of 20, 25, and 30 when the number of simulations is 5000.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. 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**.

<u>Option</u>	<u>Value</u>
Design Tab	
Solve For	**Power**
Testing Procedure	**Chang (C): Equivalence of Mean Difference Ratio after Treatment Efficacy**
Test Type..	**T-Test Assuming Equal Variances**
Simulations	**5000**
Random Seed...	**5567949** (for reproducibility)
$\alpha 1$ (One-Sided Alpha)....................................	**0.025**
$\alpha 2$ (Equivalence Alpha)	**0.05**
Group Allocation Input Type	**Equal to ni (Sample Size Per Group)**
ni (Sample Size Per Group)............................	**20 25 30**
μ_T (Treatment Group Mean)	**63**
μ_R (Reference Group Mean)..........................	**63**
μ_P (Placebo Group Mean)	**43**
σ Input Type..	**Equal ($\sigma_T = \sigma_R = \sigma_P = \sigma$)**
σ (Group Standard Deviation)	**5**
E_L (Lower Equiv Limit)....................................	**0.8**
E_U (Upper Equiv Limit)...................................	**1.25**
Options Tab	
Random Normal Method	**Box - Muller**
Maximum N Before Search Termination	**5000**

Annotated Output

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

Numeric Results and Plots

Numeric Results ───

Testing Procedure:	Chang Test (C): Equivalence of Mean Difference Ratio after Treatment Efficacy
Test Type:	T-Test Assuming Equal Variances
Treatment Efficacy Hypotheses:	H0s: $\mu_T - \mu_P \leq 0$ vs. H1s: $\mu_T - \mu_P > 0$, Alpha = α_1
Lower Equivalence Hypotheses:	H0L: $(\mu_T - \mu_P) / (\mu_R - \mu_P) \leq E_L$ vs. H1L: $(\mu_T - \mu_P) / (\mu_R - \mu_P) > E_L$, Alpha = α_2
Upper Equivalence Hypotheses:	H0U: $(\mu_T - \mu_P) / (\mu_R - \mu_P) \geq E_U$ vs. H1U: $(\mu_T - \mu_P) / (\mu_R - \mu_P) < E_U$, Alpha = α_2

| | | | | | | —— Ratio of Mean Diffs —— | | | | —— Alphas —— | |
| | —— Sample Sizes —— | | | | —— Means —— | Lower Equiv Limit | Upper Equiv Limit | Actual | Std Dev | 1-Sided | Equiv |
Power	n_T	n_R	n_P	N	$\mu_T \mid \mu_R \mid \mu_P$	E_L	E_U	E_A	σ	α_1	α_2
0.728	20	20	20	60	63 | 63 | 43	0.8	1.25	1	5	0.025	0.05
0.848	25	25	25	75	63 | 63 | 43	0.8	1.25	1	5	0.025	0.05
0.915	30	30	30	90	63 | 63 | 43	0.8	1.25	1	5	0.025	0.05

Notes
Simulations: 5000. Run Time: 16.21 seconds. Random Normal Method: Box - Muller.
User-Entered Random Seed: 5567949

References
Chang, Y.W., Tsong, Y., Dong, X., Zhao, Z. 2014. 'Sample size determination for a three-arm equivalence trial of normally distributed responses.' Journal of Biopharmaceutical Statistics. Volume 24, Pages 1190-1202.
Blackwelder, W.C. 1998. 'Equivalence Trials.' In Encyclopedia of Biostatistics, John Wiley and Sons. New York. Volume 2, 1367-1372.
Devroye, Luc. 1986. Non-Uniform Random Variate Generation. Springer-Verlag. New York.

Report Definitions
Power is the probability of rejecting a false null hypothesis.
n_T is the sample size of the treatment group.
n_R is the sample size of the reference (control) group.
n_P is the sample size of the placebo group.
N is the total sample size of the trial.
$\mu_T \mid \mu_R \mid \mu_P$ are the means of the treatment, reference, and control groups, respectively. The power is calculated assuming these values.
E_L is the lower equivalence boundary of the ratio of mean differences, $(\mu_T - \mu_P) / (\mu_R - \mu_P)$.
E_U is the upper equivalence boundary of the ratio of mean differences, $(\mu_T - \mu_P) / (\mu_R - \mu_P)$.
E_A is the ratio of the mean differences assumed by the alternative hypothesis. That is, $E_A = (\mu_T - \mu_P) / (\mu_R - \mu_P)$.
σ is the common standard deviation of all the groups.
α_1 is the probability of rejecting a one-sided test.
α_2 is the probability of rejecting the equivalence test.

Summary Statements ───
Sample sizes of 20, 20, and 20 in the treatment, reference, and placebo groups achieve 73% power to detect equivalence when the margin of equivalence of the ratio is from 0.8 to 1.25 and the actual mean difference ratio is 1. The testing procedure is Chang's method (C): "the equivalence test of the mean difference ratio after a treatment efficacy test." The means of the treatment, reference, and placebo groups are 63, 63, and 43, respectively. All three group standard deviations are equal to 5. The significance level of the one-sided, treatment efficacy t-test is 0.025. The significance level of the two, one-sided equivalence t-tests is 0.05. These results are based on 5000 Monte Carlo samples.

This report shows the estimated power for each group sample size.

Chart Section

Chart Section ───

Power vs ni

E_L=0.8 E_U=1.25 α1=0.025 α2=0.05 $μ_T$=T-Test (C) $μ_R$=63 $μ_P$=43 σ=5 T-Test (C)
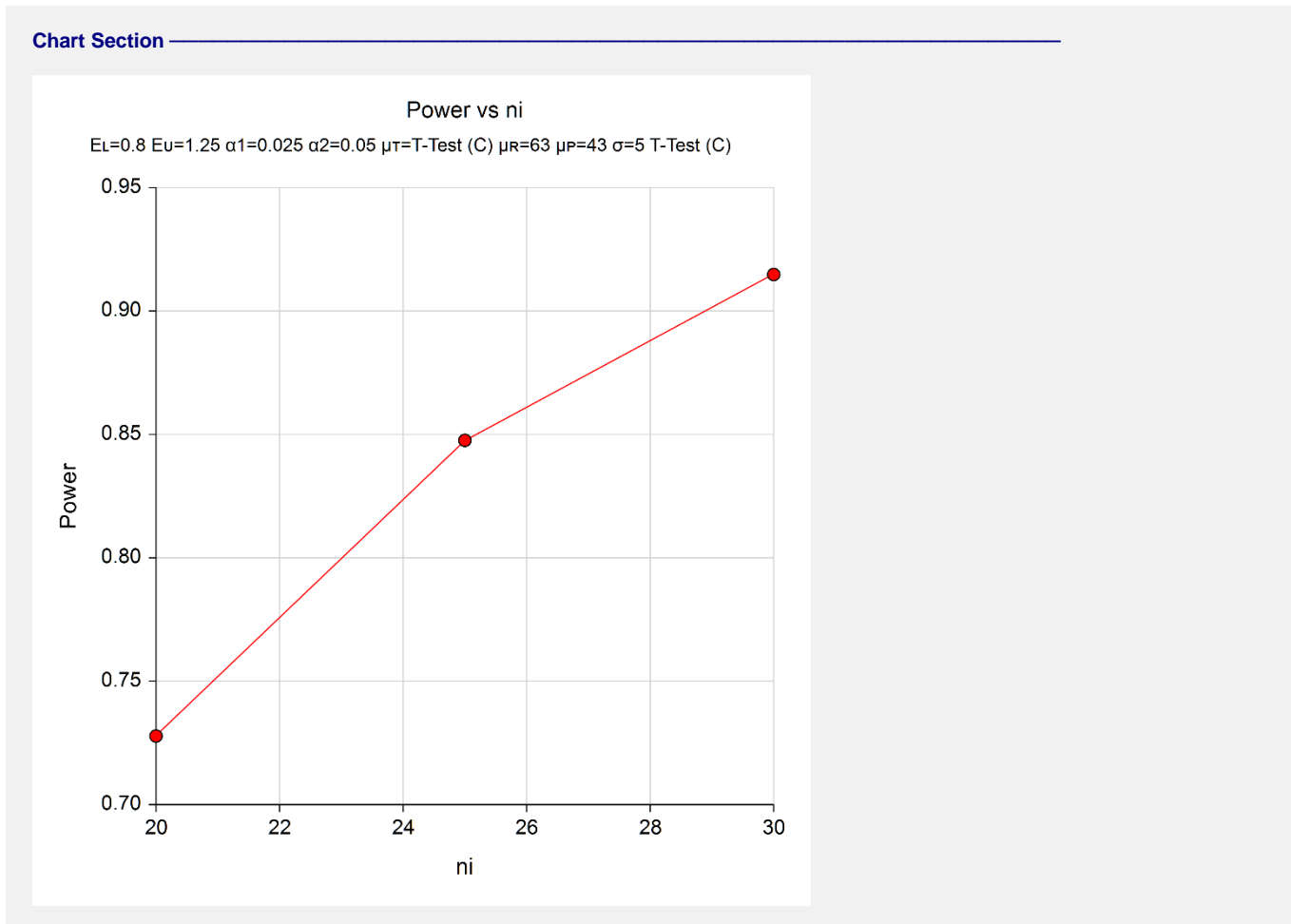
This plot presents the power for the various sample sizes.

Example 2 – Validation using Chang et al. (2014)

Chang *et al.* (2014) presents several tables of results for power and sample size procedures. We will use the second row of Table 4, page 1200, as the validation result for this procedure.

In this table, the average response level to the reference drug is approximately 10 with a standard deviation of 3 in all groups. The response at the placebo is 0. They want to investigate the power when the treatment response is also 10.

The (C) method is used for the analysis of the results. The equivalence boundaries are 0.8 and 1.25. The significance levels are 0.025 for the first test and 0.05 for the equivalence test. The power is to be 80%. The number of simulations is 5000.

The resulting group sample size is 33.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. You may then make the appropriate entries as listed below, or open **Example 2** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**Sample Size**
Testing Procedure	**Chang (C): Equivalence of Mean Difference Ratio after Treatment Efficacy**
Test Type..	**T-Test Assuming Equal Variances**
Simulations	**5000**
Random Seed..	**4638088** (for reproducibility)
Power..	**0.8**
$\alpha 1$ (One-Sided Alpha)....................................	**0.025**
$\alpha 2$ (Equivalence Alpha)	**0.05**
Group Allocation Input Type	**Equal Allocation ($A_T = A_R = A_P$)**
μ_T (Treatment Group Mean)	**10**
μ_R (Reference Group Mean)..........................	**10**
μ_P (Placebo Group Mean)	**0**
σ Input Type..	**Equal ($\sigma_T = \sigma_R = \sigma_P = \sigma$)**
σ (Group Standard Deviation)	**3**
E_L (Lower Equiv Limit)....................................	**0.8**
E_U (Upper Equiv Limit)....................................	**1.25**
Options Tab	
Random Normal Method	**Box - Muller**
Maximum N Before Search Termination	**5000**

Output

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

Numeric Results and Plots

Numeric Results ——

Testing Procedure:	Chang Test (C): Equivalence of Mean Difference Ratio after Treatment Efficacy
Test Type:	T-Test Assuming Equal Variances
Treatment Efficacy Hypotheses:	H0s: $\mu_T - \mu_P \le 0$ vs. H1s: $\mu_T - \mu_P > 0$, Alpha = α_1
Lower Equivalence Hypotheses:	H0L: $(\mu_T - \mu_P) / (\mu_R - \mu_P) \le E_L$ vs. H1L: $(\mu_T - \mu_P) / (\mu_R - \mu_P) > E_L$, Alpha = α_2
Upper Equivalence Hypotheses:	H0U: $(\mu_T - \mu_P) / (\mu_R - \mu_P) \ge E_U$ vs. H1U: $(\mu_T - \mu_P) / (\mu_R - \mu_P) < E_U$, Alpha = α_2

						—— Ratio of Mean Diffs ——				—— Alphas ——	
						Lower Equiv	Upper Equiv		Std		
	—— Sample Sizes ——			—— Means ——		Limit	Limit	Actual	Dev	1-Sided	Equiv
Power	n_T	n_R	n_P	N	$\mu_T \mid \mu_R \mid \mu_P$	E_L	E_U	E_A	σ	α_1	α_2
0.804	33	33	33	99	10 | 10 | 0	0.8	1.25	1	3	0.025	0.05

Notes
Simulations: 5000. Run Time: 81.69 seconds. Random Normal Method: Box - Muller.
User-Entered Random Seed: 4638088

PASS also finds the sample size to be 33 per group.