

Chapter 458

Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates

Introduction

This procedure may be used to calculate power and sample size for non-inferiority tests involving the ratio of two Negative Binomial rates.

The calculation details upon which this procedure is based are found in Zhu (2016). Some of the details are summarized below.

Technical Details

Definition of Terms

The following table presents the various terms that are used.

Group	1 (Control)	2 (Treatment)
Sample size	N_1	N_2
Individual event rates	λ_1	λ_2

Dispersion parameter: φ (Negative Binomial dispersion)

Average exposure time: μ_t

Non-inferiority ratio: R_0 ($R_0 < 1$ when higher rates are better; $R_0 > 1$ when higher rates are worse)

Sample size ratio: $\theta = N_2/N_1$

Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates

Hypotheses

When higher rates are better, the non-inferiority test hypotheses are

$$H_0: \frac{\lambda_2}{\lambda_1} \leq R_0 \quad \text{vs.} \quad H_1: \frac{\lambda_2}{\lambda_1} > R_0$$

where $R_0 < 1$.

When higher rates are worse, the non-inferiority test hypotheses are

$$H_0: \frac{\lambda_2}{\lambda_1} \geq R_0 \quad \text{vs.} \quad H_1: \frac{\lambda_2}{\lambda_1} < R_0$$

where $R_0 > 1$.

Sample Size and Power Calculations

Sample Size Calculation

Zhu (2016) bases the sample size calculations on a non-inferiority test derived from a Negative Binomial regression model. The sample size calculation is

$$N_1 \geq \frac{(z_\alpha \sqrt{V_0} + z_\beta \sqrt{V_1})^2}{(\log R_0 - \log(\lambda_2/\lambda_1))^2}$$

$$N_2 = \theta N_1$$

where

$$V_1 = \frac{1}{\mu_t} \left(\frac{1}{\lambda_1} + \frac{1}{\theta \lambda_2} \right) + \frac{(1 + \theta)\varphi}{\theta}$$

and V_0 may be calculated in any of 3 ways.

V_0 Calculation Method 1 (using assumed true rates)

$$V_{01} = \frac{1}{\mu_t} \left(\frac{1}{\lambda_1} + \frac{1}{\theta \lambda_2} \right) + \frac{(1 + \theta)\varphi}{\theta}$$

Using Method 1, V_0 and V_1 are equal.

V_0 Calculation Method 2 (fixed marginal total)

$$V_{02} = \frac{(1 + R_0\theta)^2}{\mu_t R_0 \theta (\lambda_1 + \theta \lambda_2)} + \frac{(1 + \theta)\varphi}{\theta}$$

V_0 Calculation Method 3 (restricted maximum likelihood estimation)

$$V_{03} = \frac{2a}{\mu_t (-b - \sqrt{b^2 - 4ac})} \left(1 + \frac{1}{\theta R_0} \right) + \frac{(1 + \theta)\varphi}{\theta}$$

where

$$a = -\varphi \mu_t R_0 (1 + \theta),$$

$$b = \varphi \mu_t (\lambda_1 R_0 + \theta \lambda_2) - (1 + \theta R_0),$$

$$c = \lambda_1 + \theta \lambda_2$$

Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates

Zhu (2016) did not give a recommendation regarding whether Method 1, 2, or 3 should be used, except to say that “for many scenarios, Methods 1 and 2 gave the smallest and largest sample sizes, respectively, while the sample sizes given by Method 3 were between the other two methods and had the closest simulated power values to the targeted power.”

Power Calculation

The corresponding power calculation to the sample size calculation above is

$$Power \geq 1 - \Phi \left(\frac{\sqrt{N_1}(\log R_0 - \log(\lambda_2/\lambda_1)) - z_\alpha \sqrt{V_0}}{\sqrt{V_1}} \right)$$

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 Negative Binomial rates, sample sizes, alpha, and power.

Solve For

Solve For

This option specifies the parameter to be solved for from the other parameters.

Test

Higher Negative Binomial Rates Are

Specify whether higher Negative Binomial rates are better or worse. This selection determines the direction of the null and alternative hypotheses. When higher rates are better, the non-inferiority test hypotheses are

$H_0: \lambda_2 / \lambda_1 \leq R_0$ vs. $H_1: \lambda_2 / \lambda_1 > R_0$, and $R_0 < 1$.

When higher rates are worse (lower are better), the non-inferiority test hypotheses are

$H_0: \lambda_2 / \lambda_1 \geq R_0$ vs. $H_1: \lambda_2 / \lambda_1 < R_0$, and $R_0 > 1$.

Variance Calculation Method

Select among the three methods for calculating the V_0 variance component (see the documentation above for details).

- **Using Assumed True Rates**
For this choice, the variance component V_0 is based the values entered for λ_1 and λ_2 .
- **Fixed Marginal Total**
This method assumes a fixed number of events.
- **Restricted Maximum Likelihood Estimation**
This method uses the variance calculation based on restricted maximum likelihood estimation.

Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates

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 inferiority when in fact the treatment mean is non-inferior.

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. In this procedure, a type-I error occurs when rejecting the null hypothesis of inferiority when in fact the treatment group is not inferior to the reference group.

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*.

$\mu(t)$ (Average Exposure Time)

$\mu(t)$ (Average Exposure Time)

Enter a value (or range of values) for the average exposure (observation) time for each subject in each group. A value of one is commonly entered when exposure times are all equal. The range is $\mu(t) > 0$. You can enter a single value such as 1 or a series of values such as *0.8 0.9 1* or *0.8 to 1.2 by 0.1*.

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 $N2$, 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-Inferiority Tests for the Ratio of Two Negative Binomial Rates

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 ≥ 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 $N2$.
- **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 $N - N1$.

Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates

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 ≥ 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 ≥ 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 ≥ 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:

$$N2 = \lceil R \times N1 \rceil,$$

where the value $\lceil Y \rceil$ 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.

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.

Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates

Effect Size

R0 (Non-Inferiority Ratio)

Enter a value (or range of values) for the ratio of the two mean event rates assumed by the null hypothesis of non-inferiority. The range of possible values depends on the test direction. When higher rates are better, the non-inferiority test hypotheses are $H_0: \lambda_2 / \lambda_1 \leq R_0$ vs. $H_1: \lambda_2 / \lambda_1 > R_0$, and $R_0 < 1$. When higher rates are worse (lower are better), the non-inferiority test hypotheses are $H_0: \lambda_2 / \lambda_1 \geq R_0$ vs. $H_1: \lambda_2 / \lambda_1 < R_0$, and $R_0 > 1$.

λ_1 (Event Rate of Group 1)

Enter a value (or range of values) for the mean event rate per time unit in group 1 (control).

Example of Estimating λ_1

If 200 patients were exposed for 1 year (i.e. $t_1 = 1$ year) and 40 experienced the event of interest, then the mean event rate would be $\lambda_1 = 40/(200*1) = 0.2$ per patient-year. If 200 patients were exposed for 2 years (i.e. $t_1 = 2$ years) and 40 experienced the event of interest, then the mean event rate would be $\lambda_1 = 40/(200*2) = 0.1$ per patient-year.

λ_1 is used with λ_2 to calculate the event rate ratio as λ_2 / λ_1 . The range is $\lambda_1 > 0$. You can enter a single value such as 1 or a series of values such as 1 1.2 1.4 or 1 to 2 by 0.5.

Enter λ_2 or Ratio for Group 2

Indicate whether to enter the Group 2 event rate (λ_2) directly or the event rate ratio (λ_2 / λ_1) to specify λ_2 . The event rate ratio is calculated from λ_2 and λ_1 as λ_2 / λ_1 .

λ_2 (Event Rate of Group 2)

Enter a value (or range of values) for the mean event rate per time unit in group 2 (treatment).

Example of Estimating λ_2

If 200 patients were exposed for 1 year (i.e. $t_1 = 1$ year) and 40 experienced the event of interest, then the mean event rate would be $\lambda_2 = 40/(200*1) = 0.2$ per patient-year. If 200 patients were exposed for 2 years (i.e. $t_1 = 2$ years) and 40 experienced the event of interest, then the mean event rate would be $\lambda_2 = 40/(200*2) = 0.1$ per patient-year.

λ_1 is used with λ_2 to calculate the event rate ratio as λ_2 / λ_1 . The range is $\lambda_2 > 0$. You can enter a single value such as 1 or a series of values such as 1 1.2 1.4 or 1 to 2 by 0.5.

λ_2 / λ_1 (Ratio of Event Rates)

This is the (assumed, known, true) value of the ratio of the two event rates, λ_1 and λ_2 , at which the power is to be calculated. The event rate ratio is calculated from λ_1 and λ_2 as λ_2 / λ_1 . The range is $\lambda_2 / \lambda_1 > 0$ and $\lambda_2 / \lambda_1 \neq R_0$. When higher rates are better, $\lambda_2 / \lambda_1 > R_0$ and $R_0 < 1$. When higher rates are worse (lower are better), $\lambda_2 / \lambda_1 < R_0$, and $R_0 > 1$. You can enter a single value such as 1 or a series of values such as 0.9 0.95 1 1.05 1.1 or 0.9 to 1.1 by 0.05.

ϕ (Dispersion)

Enter a value or series of values for the anticipated Negative Binomial dispersion. You can enter a single value such as 0.4 or a series of values such as 0.2 0.3 0.4 0.5 or 0.2 to 0.5 by 0.1.

Example 1 – Calculating Sample Size

Researchers wish to determine whether the average Negative Binomial rate of those receiving a new treatment is non-inferior to a current control. In the scenario, higher rates are worse than lower rates. The average exposure time for all subjects is 2.5 years. The event rate ratio at which the new treatment will be considered non-inferior is 1.2. The event rate of the control group is 2.2 events per year. The researchers would like to examine the effect on sample size of a range of treatment group event rates from 1.8 to 2.4. Dispersion values ranging from 0.2 to 0.5 will be considered.

The desired power is 0.9 and the significance level will be 0.025. The variance calculation method used will be the method where the assumed rates are used.

Setup

This section presents the values of each of the parameters needed to run this example. First load the **Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates** procedure window from the menus. 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	Sample Size
Higher Negative Binomial Rates Are	Worse
Variance Calculation Method.....	Using Assumed True Rates
Power.....	0.90
Alpha.....	0.025
$\mu(t)$ (Average Exposure Time)	2.5
Group Allocation	Equal (N1 = N2)
R0 (Non-Inferiority Ratio).....	1.2
λ_1 (Event Rate of Group 1).....	2.2
Enter λ_2 or Ratio for Group 2	λ_2 (Event Rate of Group 2)
λ_2 (Event Rate of Group 2).....	1.8 to 2.4 by 0.1
ϕ (Dispersion)	0.2 to 0.5 by 0.05

Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates

Annotated Output

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

Numeric Results

Numeric Results for Non-Inferiority Tests of the Ratio of Two Negative Binomial Rates

Test Direction Assumption: Higher Negative Binomial Rates Are Worse

H0: $\lambda_2 / \lambda_1 \geq R_0$ vs. H1: $\lambda_2 / \lambda_1 < R_0$

Variance Calculation Method: Using Assumed True Rates

				Average Exposure Time	Grp 1 Cntrl Event Rate	Grp 2 Trt Event Rate	Event Rate Ratio	Non-Inf- eriority Ratio	Disper- sion	
Power	N1	N2	N	$\mu(t)$	λ_1	λ_2	λ_2 / λ_1	R0	ϕ	Alpha
0.90198	58	58	116	2.50	2.20	1.80	0.818	1.200	0.20	0.025
0.90018	77	77	154	2.50	2.20	1.90	0.864	1.200	0.20	0.025
0.90112	107	107	214	2.50	2.20	2.00	0.909	1.200	0.20	0.025
0.90008	155	155	310	2.50	2.20	2.10	0.955	1.200	0.20	0.025
0.90072	242	242	484	2.50	2.20	2.20	1.000	1.200	0.20	0.025
0.90016	418	418	836	2.50	2.20	2.30	1.045	1.200	0.20	0.025
0.90008	866	866	1732	2.50	2.20	2.40	1.091	1.200	0.20	0.025
0.90105	65	65	130	2.50	2.20	1.80	0.818	1.200	0.25	0.025
0.90110	87	87	174	2.50	2.20	1.90	0.864	1.200	0.25	0.025
0.90186	121	121	242	2.50	2.20	2.00	0.909	1.200	0.25	0.025
0.90158	176	176	352	2.50	2.20	2.10	0.955	1.200	0.25	0.025
0.90001	273	273	546	2.50	2.20	2.20	1.000	1.200	0.25	0.025
0.90058	474	474	948	2.50	2.20	2.30	1.045	1.200	0.25	0.025
0.90016	982	982	1964	2.50	2.20	2.40	1.091	1.200	0.25	0.025
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References

Zhu, H. 2016. 'Sample Size Calculation for Comparing Two Poisson or Negative Binomial Rates in Non-Inferiority or Equivalence Trials.' Statistics in Biopharmaceutical Research, Accepted Manuscript.

Report Definitions

Power is the probability of rejecting the null hypothesis when it is false.

N1 and N2 are the number of subjects in groups 1 and 2, respectively.

N is the total sample size. $N = N1 + N2$.

$\mu(t)$ is the average exposure (observation) time across subjects in both groups.

λ_1 is the event rate per time unit in Group 1 (control).

λ_2 is the event rate per time unit in Group 2 (treatment).

λ_2 / λ_1 is the (known, true, assumed) ratio of the two event rates.

R0 is the non-inferiority (boundary) ratio.

Dispersion (ϕ) is the Negative Binomial dispersion parameter.

Alpha is the probability of rejecting the null hypothesis when it is true.

Summary Statements

For a test of H0: $\lambda_2 / \lambda_1 \geq 1.200$ vs. H1: $\lambda_2 / \lambda_1 < 1.200$ (assuming higher Negative Binomial rates are worse), and using the variance calculation method with assumed true rates, samples of 58 and 58 subjects with average exposure time 2.50 achieve 90.198% power to detect an event rate ratio λ_2 / λ_1 of 0.818 when the event rate in group 1 (λ_1) is 2.20, the event rate in group 2 (λ_2) is 1.80, the dispersion is 0.20, and the significance level (alpha) is 0.025.

Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates

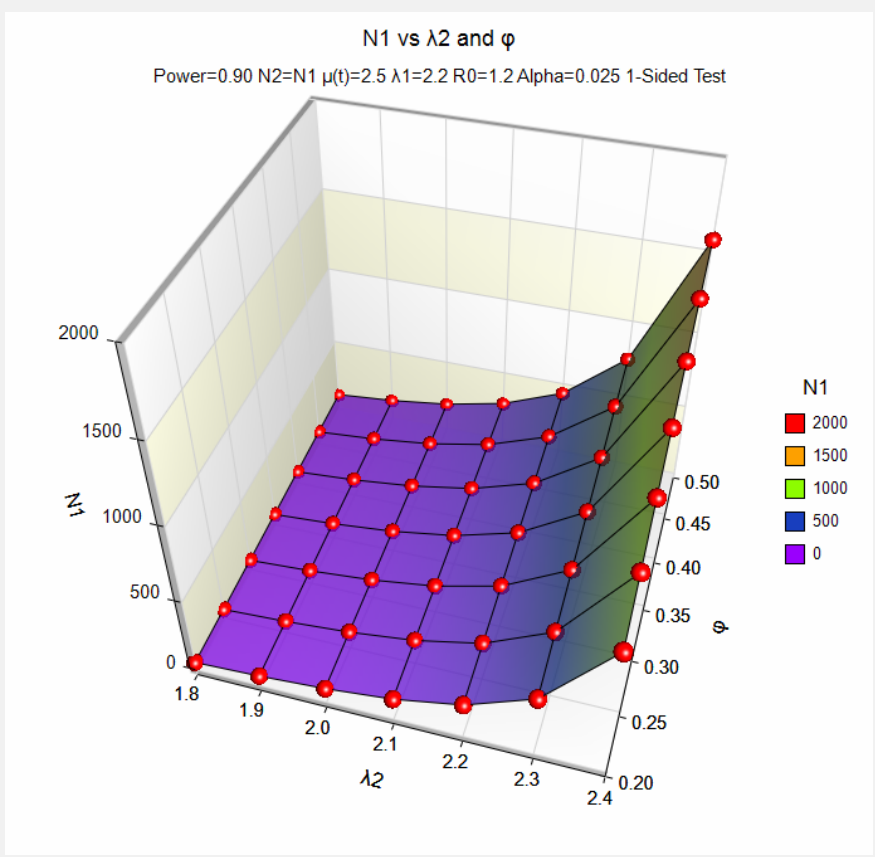
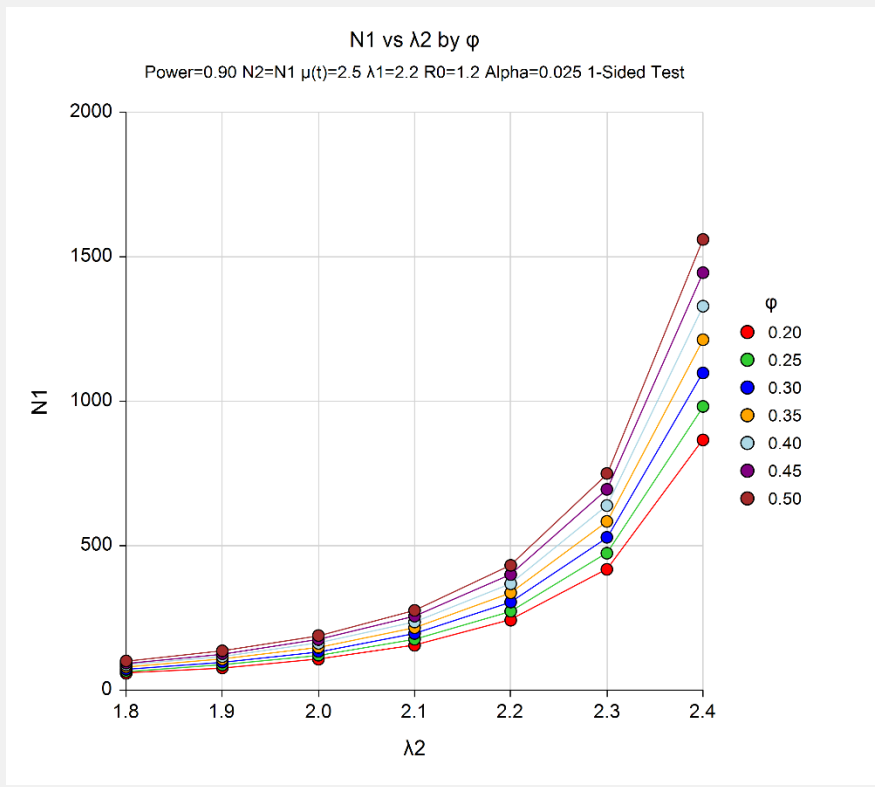
Dropout Rate	Dropout-Inflated Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
	Sample Size		N	Sample Size		N'	Dropouts		D
	N1	N2		N1'	N2'		D1	D2	
20%	58	58	116	73	73	146	15	15	30
20%	77	77	154	97	97	194	20	20	40
20%	107	107	214	134	134	268	27	27	54
20%	155	155	310	194	194	388	39	39	78
20%	242	242	484	303	303	606	61	61	122
20%	418	418	836	523	523	1046	105	105	210
20%	866	866	1732	1083	1083	2166	217	217	434
20%	65	65	130	82	82	164	17	17	34
20%	87	87	174	109	109	218	22	22	44
20%	121	121	242	152	152	304	31	31	62
20%	176	176	352	220	220	440	44	44	88
20%	273	273	546	342	342	684	69	69	138
20%	474	474	948	593	593	1186	119	119	238
20%	982	982	1964	1228	1228	2456	246	246	492
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Definitions
 Dropout Rate (DR) is 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").
 N1, N2, and N are the evaluable sample sizes at which power is computed. If N1 and N2 subjects are evaluated out of the N1' and N2' subjects that are enrolled in the study, the design will achieve the stated power.
 N1', N2', and N' are the number of subjects that should be enrolled in the study in order to end up with N1, N2, and N evaluable subjects, based on the assumed dropout rate. After solving for N1 and N2, N1' and N2' are calculated by inflating N1 and N2 using the formulas $N1' = N1 / (1 - DR)$ and $N2' = N2 / (1 - DR)$, with N1' and N2' always rounded up. (See Julious, S.A. (2010) pages 52-53, or Chow, S.C., Shao, J., and Wang, H. (2008) pages 39-40.)
 D1, D2, and D are the expected number of dropouts. $D1 = N1' - N1$, $D2 = N2' - N2$, and $D = D1 + D2$.

This report shows the sample sizes for the indicated scenarios.

Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates

Plots Section



These plots represent the required sample sizes for various values of λ_2 and the dispersion parameter.

Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates

Example 2 – Validation using Zhu (2016)

Zhu (2016) presents an example of solving for sample size where lower Negative Binomial rates are better, the event rates are both 1.5, the dispersion is 0.24, the average duration is 0.85, the non-inferiority ratio is 1.1, the power is 0.9, and the Type I error rate is 0.025.

The calculated sample sizes are 2370, 2373, and 2372 for the Assumed True Rate, Fixed Marginal Total, and REML variance calculation methods, respectively.

Setup

This section presents the values of each of the parameters needed to run this example. First load the **Non-Inferiority Tests for the Ratio of Two Negative Binomial Rates** procedure window from the menus. You may then make the appropriate entries as listed below, or open **Example 2 (a, b, or c)** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
Design Tab	
Solve For	Sample Size
Higher Negative Binomial Rates Are	Worse
Variance Calculation Method.....	Using Assumed True Rates (2nd run: Fixed Marginal Total 3rd run: Restricted Maximum Likelihood Estimation)
Power.....	0.90
Alpha.....	0.025
$\mu(t)$ (Average Exposure Time)	0.85
Group Allocation	Equal (N1 = N2)
R0 (Non-Inferiority Ratio).....	1.1
λ_1 (Event Rate of Group 1).....	1.5
Enter λ_2 or Ratio for Group 2	λ_2 (Event Rate of Group 2)
λ_2 (Event Rate of Group 2).....	1.5
ϕ (Dispersion)	0.24

Output

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

Numeric Results

Numeric Results for Non-Inferiority Tests of the Ratio of Two Negative Binomial Rates											
Test Direction Assumption: Higher Negative Binomial Rates Are Worse											
H0: $\lambda_2 / \lambda_1 \geq R_0$ vs. H1: $\lambda_2 / \lambda_1 < R_0$											
Variance Calculation Method: Using Assumed True Rates											
Power	N1	N2	N	Average Exposure Time $\mu(t)$	Grp 1 Cntrl Event Rate λ_1	Grp 2 Trt Event Rate λ_2	Event Rate Ratio λ_2 / λ_1	Non-Inferiority Ratio R0	Dispersion ϕ	Alpha	
0.90004	2370	2370	4740	0.85	1.50	1.50	1.000	1.100	0.24	0.025	
Variance Calculation Method: Fixed Marginal Total											
0.90011	2373	2373	4746	0.85	1.50	1.50	1.000	1.100	0.24	0.025	
Variance Calculation Method: Restricted Maximum Likelihood Estimation											
0.90004	2372	2372	4744	0.85	1.50	1.50	1.000	1.100	0.24	0.025	

The sample sizes calculated in **PASS** match those of Zhu (2016) exactly.