Chapter 546

Tests for the Ratio of Two Poisson Rates (Zhu)

Introduction

This procedure may be used to calculate power and sample size for tests involving the ratio of two Poisson rates (count data). This procedure includes an option of accounting for over and under dispersion.

The calculation details upon which this procedure is based are found in Zhu (2017). 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 ($\varphi > 1$ implies over-dispersion; $\varphi < 1$ implies under-dispersion)

Average exposure time: μ_t

Event Rate Ratio | H0: $RR_0 = \lambda_2/\lambda_1$

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

Hypotheses

The three statistical hypotheses that can be used are

$$H_0: \frac{\lambda_2}{\lambda_1} \leq RR_0 \quad \text{vs.} \quad H_1: \frac{\lambda_2}{\lambda_1} > RR_0$$

$$H_0: \frac{\lambda_2}{\lambda_1} \geq RR_0 \quad \text{vs.} \quad H_1: \frac{\lambda_2}{\lambda_1} < RR_0$$

$$H_0: \frac{\lambda_2}{\lambda_1} = RR_0 \quad \text{vs.} \quad H_1: \frac{\lambda_2}{\lambda_1} \neq RR_0$$

Sample Size and Power Calculations

Sample Size Calculation

Zhu (2017) bases the sample size calculations on a non-inferiority test derived from a Poisson regression model. The sample size calculation is

$$N_1 \geq \frac{\left(z_\alpha\sqrt{V_0} + z_\beta\sqrt{V_1}\right)^2}{(\log(RR_0) - \log(\lambda_2/\lambda_1))^2}$$

$$N_2 = \theta N_1$$

where

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

and V_0 may be calculated in either of two ways.

V_0 Calculation Method 1 (using assumed true rates)

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

Using Method 1, V_0 and V_1 are equal.

V_0 Calculation Method 2 (fixed marginal total or restricted maximum likelihood estimation)

$$V_{02} = \frac{\varphi(1 + RR_0\theta)^2}{\mu_t RR_0\theta(\lambda_1 + \theta\lambda_2)}$$

Zhu (2017) did not give a recommendation regarding whether Method 1 or Method 2 should be used, except to say that "sample sizes calculated using Method 2 are slightly larger compared to those calculated by Method 1 for most simulated scenarios…".

Power Calculation

The corresponding power calculation to the sample size calculation above is

$$Power \geq 1 - \Phi\left(\frac{\sqrt{N_1}(\log(RR_0) - \log(\lambda_2/\lambda_1)) - z_\alpha\sqrt{V_0}}{\sqrt{V_1}}\right)$$

Example 1 – Calculating Sample Size

Researchers wish to determine whether the average Poisson rate of those receiving a new treatment is less than that of the current control. In this scenario, higher Poisson rates are worse than lower rates so a one-sided test will be used. The average exposure time for all subjects is 2.5 years. The event rate ratio of the null hypothesis is tested is 0.9. 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 1.4 to 1.8. Over-dispersion is set to 1.5.

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 as the true rates.

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	**Sample Size**
Alternative Hypothesis	**One-Sided (H1: λ2 / λ1 < RR0)**
Variance Calculation Method	**Using Assumed True Rates**
Power	**0.90**
Alpha	**0.025**
μ(t) (Average Exposure Time)	**2.5**
Group Allocation	**Equal (N1 = N2)**
RR0 (Non-Unity Ratio|H0)	**0.9**
λ1 (Event Rate of Group 1)	**2.2**
Enter λ2 or Ratio for Group 2	**λ2 (Event Rate of Group 2)**
λ2 (Event Rate of Group 2)	**1.4 1.6 1.8**
φ (Dispersion)	**1.5**

Output

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

Numeric Reports

Numeric Results

Solve For: Sample Size
Groups: 1 = Control, 2 = Treatment
Hypotheses: H0: λ2 / λ1 ≥ RR0 vs. H1: λ2 / λ1 < RR0
Variance Calculation Method: Using Assumed True Rates

	Sample Size			Average Exposure Time	Average Event Rate		Event Rate Ratio		Dispersion	
Power	N1	N2	N	μ(t)	λ1	λ2	Actual λ2 / λ1	Null RR0	φ	Alpha
0.90306	62	62	124	2.5	2.2	1.4	0.63636	0.9	1.5	0.025
0.90022	150	150	300	2.5	2.2	1.6	0.72727	0.9	1.5	0.025
0.90039	702	702	1404	2.5	2.2	1.8	0.81818	0.9	1.5	0.025

Power The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N1 and N2 The number of subjects in groups 1 and 2, respectively.
N The total sample size. N = N1 + N2.
μ(t) The average exposure (observation) time across subjects in both groups.
λ1 The event rate per time unit in Group 1 (control).
λ2 The event rate per time unit in Group 2 (treatment).
λ2 / λ1 The actual ratio of the average event rates under the alternative hypothesis.
RR0 The ratio of the average event rates under the null hypothesis.
φ The dispersion parameter (φ > 1 implies over-dispersion, φ < 1 implies under-dispersion).
Alpha The probability of rejecting a true null hypothesis.

Summary Statements

A parallel two-group design will be used to test whether the Poisson event rate ratio (λ2 / λ1 = λTrt / λCtrl) is less than 0.9 (H0: λ2 / λ1 ≥ 0.9 versus H1: λ2 / λ1 < 0.9). The comparison will be made using a one-sided Poisson regression coefficient test, with a Type I error rate (α) of 0.025. The average exposure time is assumed to be 2.5 and the dispersion parameter is assumed to be 1.5. The variance associated with the Poisson regression coefficient under consideration will be calculated using the assumed true rates. To detect an event rate ratio of 0.63636 (λ2 / λ1 = 1.4 / 2.2) with 90% power, the number of subjects needed will be 62 in Group 1 (control), and 62 in Group 2 (treatment).

Dropout-Inflated Sample Size

	Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
Dropout Rate	N1	N2	N	N1'	N2'	N'	D1	D2	D
20%	62	62	124	78	78	156	16	16	32
20%	150	150	300	188	188	376	38	38	76
20%	702	702	1404	878	878	1756	176	176	352

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.
N1, N2, and N: 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': The number of subjects that should be enrolled in the study in order to obtain 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., Wang, H., and Lokhnygina, Y. (2018) pages 32-33.)
D1, D2, and D: The expected number of dropouts. D1 = N1' - N1, D2 = N2' - N2, and D = D1 + D2.

Dropout Summary Statements

Anticipating a 20% dropout rate, 78 subjects should be enrolled in Group 1, and 78 in Group 2, to obtain final group sample sizes of 62 and 62, respectively.

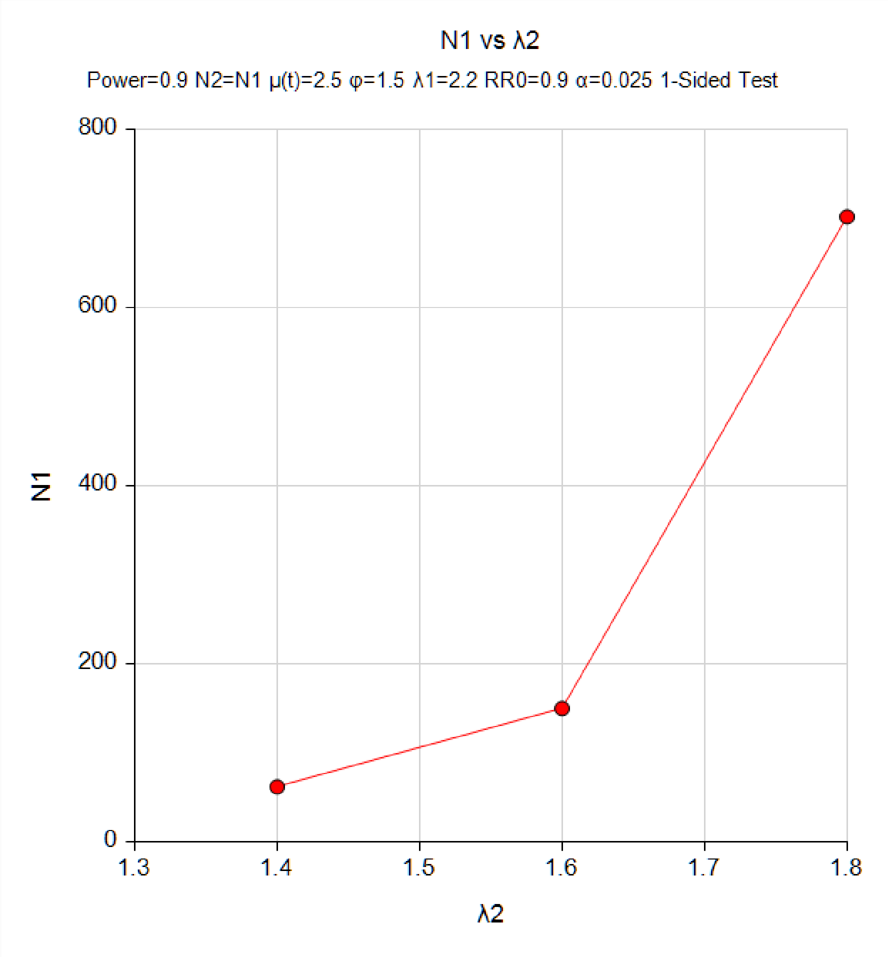
References

Zhu, H. 2017. 'Sample Size Calculation for Comparing Two Poisson or Negative Binomial Rates in Non-Inferiority or Equivalence Trials.' Statistics in Biopharmaceutical Research, 9(1), 107-115, doi:10.1080/19466315.2016.1225594.

This report shows the sample sizes for the indicated scenarios.

Plots Section

Plots



This plot represents the required sample sizes for various values of λ2.

Example 2 – Validation using Zhu (2017)

Zhu (2017) page 109 presents an example of solving for sample size where lower Poisson rates are better, the event rates are both 1.5, the over-dispersion is 1.35, the average duration is 0.85, the non-unity null rate is 1.1, the power is 0.9, and the significance rate is set to 0.025.

The calculated sample size was 2450.

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 .... **Sample Size**
Alternative Hypothesis .... **One-Sided (H1: λ2 / λ1 < RR0)**
Variance Calculation Method .... **Using Assumed True Rates**
Power... **0.90**
Alpha.. **0.025**
μ(t) (Average Exposure Time)....................... **0.85**
Group Allocation .... **Equal (N1 = N2)**
RR0 (Non-Unity Ratio|H0) **1.1**
λ1 (Event Rate of Group 1)........................... **1.5**
Enter λ2 or Ratio for Group 2........................ **λ2 (Event Rate of Group 2)**
λ2 (Event Rate of Group 2)........................... **1.5**
φ (Dispersion)... **1.35**

Output

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

Numeric Results

Solve For: Sample Size
Groups: 1 = Control, 2 = Treatment
Hypotheses: H0: λ2 / λ1 ≥ RR0 vs. H1: λ2 / λ1 < RR0
Variance Calculation Method: Using Assumed True Rates

	Sample Size			Average Exposure Time	Average Event Rate		Event Rate Ratio			
Power	N1	N2	N	μ(t)	λ1	λ2	Actual λ2 / λ1	Null RR0	Dispersion φ	Alpha
0.90006	2450	2450	4900	0.85	1.5	1.5	1	1.1	1.35	0.025

The sample size of 2450 calculated in **PASS** matches that of Zhu (2017) exactly.