Chapter 217

Confidence Intervals for the Ratio of Two Proportions

Introduction

This routine calculates the group sample sizes necessary to achieve a specified interval width of the ratio of two independent proportions.

Caution: These procedures assume that the proportions obtained from future samples will be the same as the proportions that are specified. If the sample proportions are different from those specified when running these procedures, the interval width may be narrower or wider than specified.

Technical Details

A background of the comparison of two proportions is given, followed by details of the confidence interval methods available in this procedure.

Comparing Two Proportions

Suppose you have two populations from which dichotomous (binary) responses will be recorded. The probability (or risk) of obtaining the event of interest in population 1 (the treatment group) is p_1 and in population 2 (the control group) is p_2. The corresponding failure proportions are given by $q_1 = 1 - p_1$ and $q_2 = 1 - p_2$.

The assumption is made that the responses from each group follow a binomial distribution. This means that the event probability p_i is the same for all subjects within a population and that the responses from one subject to the next are independent of one another.

Random samples of *m* and *n* individuals are obtained from these two populations. The data from these samples can be displayed in a 2-by-2 contingency table as follows

	Success	Failure	Total
Population 1	*a*	*c*	*m*
Population 2	*b*	*d*	*n*
Totals	*s*	*f*	*N*

The following alternative notation is sometimes used:

	Success	**Failure**	**Total**
Population 1	x_{11}	x_{12}	n_1
Population 2	x_{21}	x_{22}	n_2
Totals	m_1	m_2	N

The binomial proportions p_1 and p_2 are estimated from these data using the formulae

$$\hat{p}_1 = \frac{a}{m} = \frac{x_{11}}{n_1} \text{ and } \hat{p}_2 = \frac{b}{n} = \frac{x_{21}}{n_2}$$

When analyzing studies such as these, you usually want to compare the two binomial probabilities p_1 and p_2. The most direct methods of comparing these quantities are to calculate their difference or their ratio. If the binomial probability is expressed in terms of odds rather than probability, another measure is the odds ratio. Mathematically, these comparison parameters are

Parameter	**Computation**
Difference	$\delta = p_1 - p_2$
Risk Ratio	$\phi = p_1/p_2$
Odds Ratio	$\psi = \frac{p_1/q_1}{p_2/q_2} = \frac{p_1 q_2}{p_2 q_1}$

The choice of which of these measures is used might at first seem arbitrary, but it is important. Not only is their interpretation different, but, for small sample sizes, the coverage probabilities may be different. This procedure focuses on the ratio. Other procedures are available in **PASS** for computing confidence intervals for the difference and odds ratio.

Ratio

The (risk) ratio $\phi = p_1/p_2$ gives the relative change in the disease risk due to the application of the treatment. This parameter is also direct and easy to interpret. To compare this with the difference, consider a treatment that reduces the risk of disease for 0.1437 to 0.0793. Which single number is most enlightening, the fact that the absolute risk of disease has been decreased by 0.0644, or the fact that risk of disease in the treatment group is only 55.18% of that in the control group? In many cases, the percentage (risk ratio) communicates the impact of the treatment better than the absolute change.

Perhaps the biggest drawback to this parameter is that it cannot be calculated in one of the most common experimental designs: the case-control study.

Confidence Intervals for the Ratio (Relative Risk)

Many methods have been devised for computing confidence intervals for the ratio (relative risk) of two proportions $\phi = p_1/p_2$. Six of these methods are available in the Confidence Intervals for Two Proportions [Ratios] procedure. The six confidence interval methods are

1. Score (Farrington and Manning)

2. Score (Miettinen and Nurminen)

3. Score with Correction for Skewness (Gart and Nam)

4. Logarithm (Katz)

5. Logarithm + 1/2 (Walter)

6. Fleiss

Farrington and Manning's Score

Farrington and Manning (1990) proposed a test statistic for testing whether the ratio is equal to a specified value ϕ_0. The regular MLE's $\hat{p}_1$ and $\hat{p}_2$ are used in the numerator of the score statistic while MLE's $\tilde{p}_1$ and $\tilde{p}_2$ constrained so that $\tilde{p}_1/\tilde{p}_2 = \phi_0$ are used in the denominator. A correction factor of N/(N-1) is applied to increase the variance estimate. The significance level of the test statistic is based on the asymptotic normality of the score statistic.

Here is the formula for computing the test

$$z_{FMR} = \frac{\hat{p}_1/\hat{p}_2 - \phi_0}{\sqrt{\left(\frac{\tilde{p}_1\tilde{q}_1}{n_1} + \phi_0^2 \frac{\tilde{p}_2\tilde{q}_2}{n_2}\right)}}$$

where

$$\tilde{p}_1 = \tilde{p}_2\phi_0$$

$$\tilde{p}_2 = \frac{-B - \sqrt{B^2 - 4AC}}{2A}$$

$$A = N\phi_0$$

$$B = -[n_1\phi_0 + x_{11} + n_2 + x_{21}\phi_0]$$

$$C = m_1$$

as in the test of Miettinen and Nurminen (1985).

Farrington and Manning (1990) proposed inverting their score test to find the confidence interval. The lower limit is found by solving

$$z_{FMR} = \left| z_{\alpha/2} \right|$$

and the upper limit is the solution of

$$z_{FMR} = -\left| z_{\alpha/2} \right|$$

Miettinen and Nurminen's Score

Miettinen and Nurminen (1985) proposed a test statistic for testing whether the ratio is equal to a specified value ϕ_0. The regular MLE's $\hat{p}_1$ and $\hat{p}_2$ are used in the numerator of the score statistic while MLE's $\tilde{p}_1$ and $\tilde{p}_2$ constrained so that $\tilde{p}_1/\tilde{p}_2 = \phi_0$ are used in the denominator. A correction factor of N/(N-1) is applied to make the variance estimate less biased. The significance level of the test statistic is based on the asymptotic normality of the score statistic.

Here is the formula for computing the test

$$z_{MNR} = \frac{\hat{p}_1/\hat{p}_2 - \phi_0}{\sqrt{\left(\frac{\tilde{p}_1 \tilde{q}_1}{n_1} + \phi_0^2 \frac{\tilde{p}_2 \tilde{q}_2}{n_2} \right)\left(\frac{N}{N-1} \right)}}$$

where

$$\tilde{p}_1 = \tilde{p}_2 \phi_0$$

$$\tilde{p}_2 = \frac{-B - \sqrt{B^2 - 4AC}}{2A}$$

$$A = N\phi_0$$

$$B = -[n_1\phi_0 + x_{11} + n_2 + x_{21}\phi_0]$$

$$C = m_1$$

Miettinen and Nurminen (1985) proposed inverting their score test to find the confidence interval. The lower limit is found by solving

$$z_{MNR} = \left| z_{\alpha/2} \right|$$

and the upper limit is the solution of

$$z_{MNR} = -\left| z_{\alpha/2} \right|$$

Gart and Nam's Score

Gart and Nam (1988) page 329 proposed a modification to the Farrington and Manning (1988) ratio test that corrected for skewness. Let $z_{FM}(\phi)$ stand for the Farrington and Manning ratio test statistic described above. The skewness corrected test statistic z_{GN} is the appropriate solution to the quadratic equation

$$(-\tilde{\varphi})z_{GNR}^2 + (-1)z_{GNR} + (z_{FMR}(\phi) + \tilde{\varphi}) = 0$$

where

$$\tilde{\varphi} = \frac{1}{6\tilde{u}^{3/2}}\left(\frac{\tilde{q}_1(\tilde{q}_1 - \tilde{p}_1)}{n_1^2\tilde{p}_1^2} - \frac{\tilde{q}_2(\tilde{q}_2 - \tilde{p}_2)}{n_2^2\tilde{p}_2^2}\right)$$

$$\tilde{u} = \frac{\tilde{q}_1}{n_1\tilde{p}_1} + \frac{\tilde{q}_2}{n_2\tilde{p}_2}$$

Gart and Nam (1988) proposed inverting their score test to find the confidence interval. The lower limit is found by solving

$$z_{GNR} = |z_{\alpha/2}|$$

and the upper limit is the solution of

$$z_{GNR} = -|z_{\alpha/2}|$$

Logarithm (Katz)

This was one of the first methods proposed for computing confidence intervals for risk ratios.

For details, see Gart and Nam (1988), page 324.

$$L = \hat{\phi}\exp\left(-z\sqrt{\frac{\hat{q}_1}{n\hat{p}_1} + \frac{\hat{q}_2}{n\hat{p}_2}}\right)$$

$$U = \hat{\phi}\exp\left(z\sqrt{\frac{\hat{q}_1}{n\hat{p}_1} + \frac{\hat{q}_2}{n\hat{p}_2}}\right)$$

where

$$\hat{\phi} = \frac{\hat{p}_1}{\hat{p}_2}$$

Logarithm (Walters)

For details, see Gart and Nam (1988), page 324.

$$L = \hat{\phi} \exp(-z\sqrt{\hat{u}})$$

$$U = \hat{\phi} \exp(z\sqrt{\hat{u}})$$

where

$$\hat{\phi} = \exp\left(\ln\left(\frac{a + \frac{1}{2}}{m + \frac{1}{2}} \right) - \ln\left(\frac{b + \frac{1}{2}}{n + \frac{1}{2}} \right) \right)$$

$$\hat{u} = \frac{1}{a + \frac{1}{2}} - \frac{1}{m + \frac{1}{2}} + \frac{1}{b + \frac{1}{2}} - \frac{1}{n + \frac{1}{2}}$$

$$V = \left(\phi^2 \left(\frac{\tilde{q}_1}{m\tilde{p}_1} + \frac{\tilde{q}_2}{n\tilde{p}_2} \right) \right)^{-1}$$

$$\tilde{p}_1 = \phi\tilde{p}_2$$

$$\tilde{q}_1 = 1 - \tilde{p}_1$$

$$\tilde{q}_2 = 1 - \tilde{p}_2$$

$$\tilde{\mu}_3 = v^{3/2} \left(\frac{\tilde{q}_1(\tilde{q}_1 - \tilde{p}_1)}{(m\tilde{p}_1)^2} - \frac{\tilde{q}_2(\tilde{q}_2 - \tilde{p}_2)}{(n\tilde{p}_2)^2} \right)$$

$$v = \left(\frac{\tilde{q}_1}{m\tilde{p}_1} + \frac{\tilde{q}_2}{n\tilde{p}_2} \right)^{-1}$$

Iterated Method of Fleiss

Fleiss (1981) presents an improved confidence interval for the odds ratio and relative risk. This method forms the confidence interval using all the values of the odds ratio which would not be rejected by a chi-square hypothesis test. Fleiss gives the following details about how to construct this confidence interval. To compute the lower limit, do the following.

1. For a trial value of ψ, compute the quantities $X, Y, W, F, U,$ and V using the formulas

$$X = \psi(m + s) + (n - s)$$

$$Y = \sqrt{X^2 - 4ms\psi(\psi - 1)}$$

$$A = \frac{X - Y}{2(\psi - 1)}$$

$$B = s - A$$

$$C = m - A$$

$$D = f - m + A$$

$$W = \frac{1}{A} + \frac{1}{B} + \frac{1}{C} + \frac{1}{D}$$

$$F = \left(a - A - \frac{1}{2}\right)^2 W - z_{\alpha/2}^2$$

$$T = \frac{1}{2(\psi - 1)^2}\left(Y - n - \frac{\psi - 1}{Y}[X(m + s) - 2ms(2\psi - 1)]\right)$$

$$U = \frac{1}{B^2} + \frac{1}{C^2} - \frac{1}{A^2} - \frac{1}{D^2}$$

$$V = T\left[\left(a - A - \frac{1}{2}\right)^2 U - 2W\left(a - A - \frac{1}{2}\right)\right]$$

Finally, use the updating equation below to calculate a new value for the odds ratio using the updating equation

$$\psi^{(k+1)} = \psi^{(k)} - \frac{F}{V}$$

2. Continue iterating until the value of F is arbitrarily close to zero.

The upper limit is found by substituting $+\frac{1}{2}$ for $-\frac{1}{2}$ in the formulas for F and V.

Confidence limits for the *relative risk* can be calculated using the expected counts *A, B, C,* and *D* from the last iteration of the above procedure. The lower limit of the relative risk

$$\phi_{lower} = \frac{A_{lower}n}{B_{lower}m}$$

$$\phi_{upper} = \frac{A_{upper}n}{B_{upper}m}$$

Confidence Level

The confidence level, $1 - \alpha$, has the following interpretation. If thousands of random samples of size n_1 and n_2 are drawn from populations 1 and 2, respectively, and a confidence interval for the true difference/ratio/odds ratio of proportions is calculated for each pair of samples, the proportion of those intervals that will include the true difference/ratio/odds ratio of proportions is $1 - \alpha$.

Example 1 – Calculating Sample Size

Suppose a study is planned in which the researcher wishes to construct a two-sided 95% confidence interval for the ratio of proportions such that the width of the interval is no wider than 0.2. The confidence interval method to be used is the Logarithm (Katz) method. The confidence level is set at 0.95, but 0.99 is included for comparative purposes. The ratio estimate to be used is 1.2, and the estimate for proportion 2 is 0.6. Instead of examining only the interval width of 0.2, a series of widths from 0.1 to 0.3 will also be considered.

The goal is to determine the necessary sample size.

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**
Confidence Interval Formula..........................**Logarithm (Katz)**
Interval Type ....**Two-Sided**
Confidence Level (1 - Alpha) **0.95 0.99**
Group Allocation ....**Equal (N1 = N2)**
Confidence Interval Width (Two-Sided) ....**0.10 to 0.30 by 0.05**
Input Type..**Ratios**
P1/P2 (Ratio of Sample Proportions).............**1.2**
P2 (Proportion Group 2)................................**0.6**

Output

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

Numeric Reports

Numeric Results

Solve For: Sample Size
Confidence Interval Method: Logarithm (Katz)
Interval Type: Two-Sided

Confidence Level	Sample Size			Confidence Interval Width		Sample Proportions		Ratio	Confidence Interval Limits	
	N1	N2	N	Target	Actual	P1	P2	P1/P2	Lower	Upper
0.95	2337	2337	4674	0.10	0.10	0.72	0.6	1.2	1.15	1.25
0.95	1040	1040	2080	0.15	0.15	0.72	0.6	1.2	1.13	1.28
0.95	586	586	1172	0.20	0.20	0.72	0.6	1.2	1.10	1.30
0.95	376	376	752	0.25	0.25	0.72	0.6	1.2	1.08	1.33
0.95	261	261	522	0.30	0.30	0.72	0.6	1.2	1.06	1.36
0.99	4037	4037	8074	0.10	0.10	0.72	0.6	1.2	1.15	1.25
0.99	1796	1796	3592	0.15	0.15	0.72	0.6	1.2	1.13	1.28
0.99	1011	1011	2022	0.20	0.20	0.72	0.6	1.2	1.10	1.30
0.99	648	648	1296	0.25	0.25	0.72	0.6	1.2	1.08	1.33
0.99	451	451	902	0.30	0.30	0.72	0.6	1.2	1.06	1.36

Confidence Level   The proportion of confidence intervals (constructed with this same confidence level, sample size,
                                etc.) that would contain the true ratio of population proportions.
N1 and N2   The number of items sampled from each population.
N   The total sample size. N = N1 + N2.
Confidence Interval Width   The distance from the lower limit to the upper limit.
Target Width   The value of the width that is entered into the procedure.
Actual Width   The value of the width that is obtained from the procedure.
P1 and P2   The assumed sample proportions for sample size calculations.
P1/P2   The ratio of sample proportions at which sample size calculations are made.
Confidence Interval Limits   The lower and upper limits of the confidence interval for the true ratio of proportions (Population
                                Proportion 1 / Population Proportion 2).

Summary Statements

A parallel two-group design will be used to obtain a two-sided 95% confidence interval for the ratio of two
proportions (P1 / P2). The Group 1 sample proportion is assumed to be 0.72 and the Group 2 sample proportion is
assumed to be 0.6, giving a proportion ratio of 1.2. The Logarithm (Katz) method will be used to compute the
confidence interval limits. To produce a confidence interval width of 0.1, the number of subjects needed will be
2337 in Group 1 and 2337 in Group 2.

Dropout-Inflated Sample Size

Dropout Rate	Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
	N1	N2	N	N1'	N2'	N'	D1	D2	D
20%	2337	2337	4674	2922	2922	5844	585	585	1170
20%	1040	1040	2080	1300	1300	2600	260	260	520
20%	586	586	1172	733	733	1466	147	147	294
20%	376	376	752	470	470	940	94	94	188
20%	261	261	522	327	327	654	66	66	132
20%	4037	4037	8074	5047	5047	10094	1010	1010	2020
20%	1796	1796	3592	2245	2245	4490	449	449	898
20%	1011	1011	2022	1264	1264	2528	253	253	506
20%	648	648	1296	810	810	1620	162	162	324
20%	451	451	902	564	564	1128	113	113	226

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 the confidence interval 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 confidence interval.

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, 2922 subjects should be enrolled in Group 1, and 2922 in Group 2, to obtain final group sample sizes of 2337 and 2337, respectively.

References

Gart, John J. and Nam, Jun-mo. 1988. 'Approximate Interval Estimation of the Ratio of Binomial Parameters: A Review and Corrections for Skewness.' Biometrics, Volume 44, 323-338.

Koopman, P. A. R. 1984. 'Confidence Intervals for the Ratio of Two Binomial Proportions.' Biometrics, Volume 40, Issue 2, 513-517.

Katz, D., Baptista, J., Azen, S. P., and Pike, M. C. 1978. 'Obtaining Confidence Intervals for the Risk Ratio in Cohort Studies.' Biometrics, Volume 34, 469-474.

This report shows the calculated sample sizes for each of the scenarios.

Plots Section
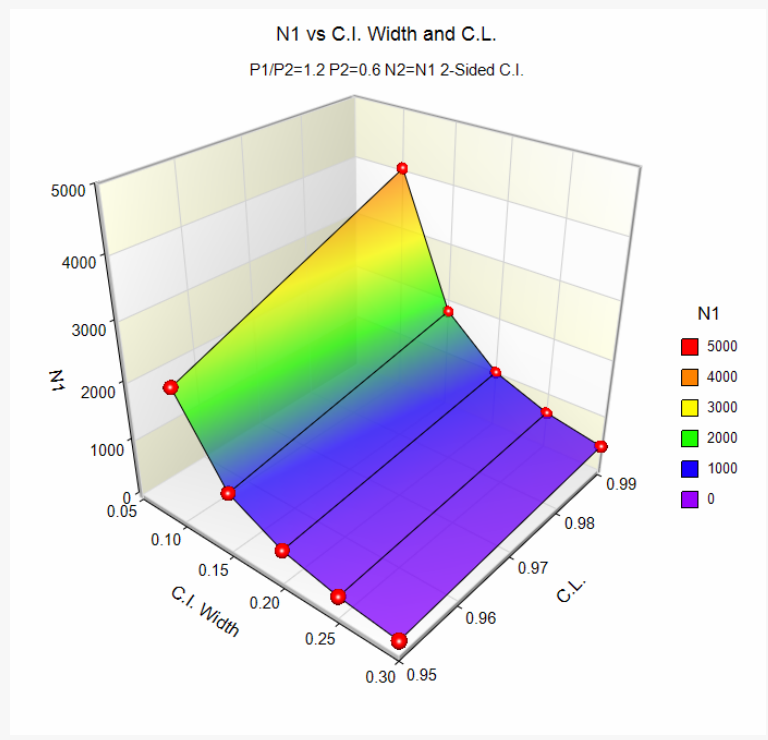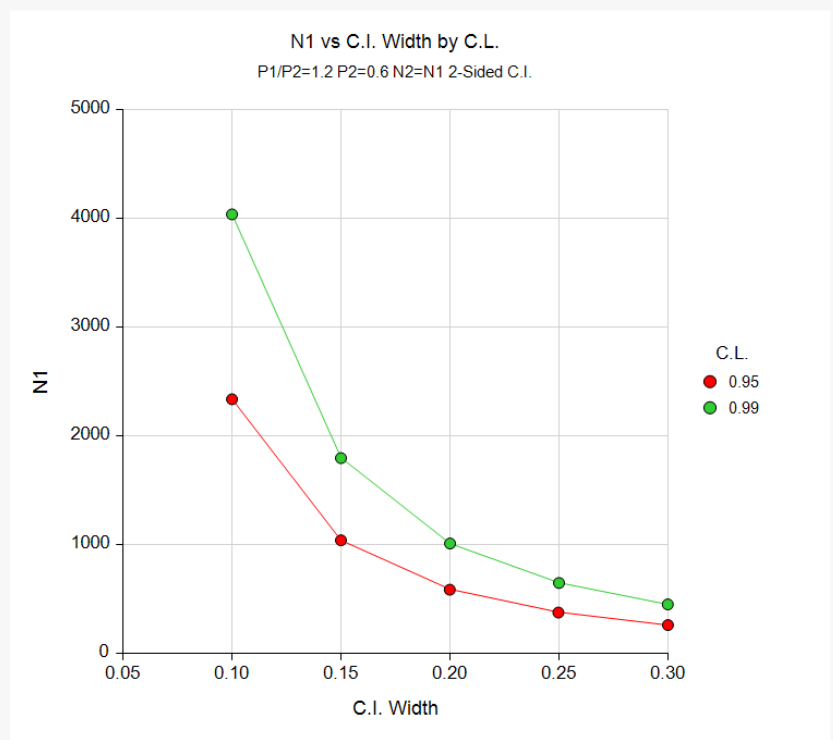
Plots
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These plots show the group sample size versus the confidence interval width for the two confidence levels.

Example 2 – Validation using Gart and Nam (1988)

Gart and Nam (1988) page 331 give an example (Example 2) of a calculation for a confidence interval for the ratio of proportions when the confidence level is 95%, the sample proportion ratio is 2 and the sample proportion 2 is 0.3, the sample size for group 2 is 20, and the interval width is 3.437 for the Logarithm + 1/2 (Walter) method, 3.751 for the Score (Farrington and Manning) method, and 4.133 for the Score w/Skewness (Gart and Nam) method. The necessary sample size for group 1 in each case is 10.

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(a-c)** 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**
Confidence Interval Formula.........................**Varies [Logarithm + 1/2 (Walter),**
                                                                                    Score (Farrington and Manning),
                                                                                    Score w/ Skewness (Gart and Nam)]
Interval Type..**Two-Sided**
Confidence Level **0.95**
Group Allocation ....**Enter N2, solve for N1**
N2 ....**20**
Confidence Interval Width (Two-Sided) ....**Varies [3.437, 3.751, 4.133]**
Input Type...**Ratios**
P1/P2 (Ratio of Sample Proportions).............**2**
P2 (Proportion Group 2)...............................**0.3**

Output

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

Logarithm + 1/2 (Walter)

Numeric Results

Solve For: Sample Size
Confidence Interval Method: Logarithm + 1/2 (Walter)
Interval Type: Two-Sided

Confidence Level	Sample Size			Confidence Interval Width		Sample Proportions		Ratio P1/P2	Confidence Interval Limits	
	N1	N2	N	Target	Actual	P1	P2		Lower	Upper
0.95	10	20	30	3.437	3.431	0.6	0.3	2	0.88	4.31

PASS also calculates the necessary sample size for Group 1 to be 10.

Score (Farrington and Manning)

Numeric Results

Solve For: Sample Size
Confidence Interval Method: Score (Farrington and Manning)
Interval Type: Two-Sided

Confidence Level	Sample Size			Confidence Interval Width		Sample Proportions		Ratio P1/P2	Confidence Interval Limits	
	N1	N2	N	Target	Actual	P1	P2		Lower	Upper
0.95	10	20	30	3.751	3.751	0.6	0.3	2	0.84	4.59

PASS also calculates the necessary sample size for Group 1 to be 10.

Score w/ Skewness (Gart and Nam)

Numeric Results

Solve For: Sample Size
Confidence Interval Method: Score with Correction for Skewness (Gart and Nam)
Interval Type: Two-Sided

Confidence Level	Sample Size			Confidence Interval Width		Sample Proportions		Ratio P1/P2	Confidence Interval Limits	
	N1	N2	N	Target	Actual	P1	P2		Lower	Upper
0.95	10	20	30	4.133	4.132	0.6	0.3	2	0.82	4.95

PASS also calculates the necessary sample size for Group 1 to be 10.

Example 3 – Validation using Katz et al (1978)

Katz et al (1978) pages 472-473 give an example of a calculation for a lower limit confidence interval for the ratio of proportions when the confidence level is 97.5%, the sample proportion ratio is 1.596078 and the sample proportion 2 is 0.153153, the sample size for group 2 is 111, and the distance from the ratio to the limit is 0.6223 for the Logarithm (Katz) method. The necessary sample size for group 1 is 225.

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 3** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab
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Solve For ....**Sample Size**
Confidence Interval Formula..........................**Logarithm (Katz)**
Interval Type...**Lower Limit**
Confidence Level (1 - Alpha) **0.975**
Group Allocation ....**Enter N2, solve for N1**
N2 ....**111**
Distance from Ratio to Limit (One-Sided) **0.6223**
Input Type..**Ratios**
P1/P2 (Ratio of Sample Proportions).............**1.596078**
P2 (Proportion Group 2)................................**0.153153**

Output

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

Numeric Results
_____

Solve For: Sample Size
Confidence Interval Method: Logarithm (Katz)
Interval Type: Lower Limit (One-Sided)
_____

| Confidence Level | Sample Size | | | Distance from Ratio to Limit | | Sample Proportions | | Ratio P1/P2 | Confidence Interval Limits | |
	N1	N2	N	Target	Actual	P1	P2		Lower	Upper
0.975	225	111	336	0.622	0.622	0.24	0.15	1.6	0.97	∞

PASS also calculates the necessary sample size for group 1 to be 225.