Chapter 272

Confidence Intervals for One-Sample Specificity

Introduction

This procedure calculates the (whole table) sample size necessary for a single-sample specificity confidence interval, based on a specified specificity, interval width, confidence level, and prevalence.

Caution: This procedure assumes that the specificity of the future sample will be the same as the specificity that is specified. If the sample specificity is different from the one specified when running this procedure, the interval width may be narrower or wider than specified.

Specificity (True Negative Rate)

The specificity (or true negative rate) is the proportion of the individuals with a known negative condition for which the predicted condition is negative.

		Predicted Condition		
		Positive	Negative	
True Condition	Positive	True Positive (A)	False Negative (C)	
	Negative	False Positive (B)	**True Negative (D)**	Specificity = D / (B + D)

Prevalence

The prevalence is the overall proportion of individuals with a positive condition.

		Predicted Condition		
		Positive	Negative	
True Condition	**Positive**	**True Positive (A)**	**False Negative (C)**	Prevalence = (A + C) / (A + B + C + D)
	Negative	False Positive (B)	True Negative (D)	

Technical Details

In general terms, the required sample size is determined by first calculating the sample size needed for the specificity proportion confidence interval, followed by a prevalence adjustment. The initial sample size calculation for the specificity confidence interval gives the number of individuals with a negative condition that are needed. The prevalence adjustment is used to add the number of individuals with a positive condition that are needed. The resulting sample size is the total number of individuals needed to obtain a table where the number of negative condition individuals will give the needed confidence interval width for the specificity.

Similarly, when calculating the confidence interval width for a given sample size, the given sample size is first used to produce the number of negative condition individuals, according to the given prevalence, and then the width based on the resulting negative condition count is then calculated.

If prevalence is to be ignored, a value of 0 may be used for prevalence, or the Confidence Intervals for One Proportion procedure may be used, as the scenario has been reduced to a simple confidence interval of a single proportion.

Confidence Interval Formulas

Many methods have been devised for computing confidence intervals for a single proportion. Five of these methods are available in this procedure. The five confidence interval methods are

1. Exact (Clopper-Pearson)
2. Score (Wilson)
3. Score with continuity correction
4. Simple Asymptotic
5. Simple Asymptotic with continuity correction

For a comparison of methods, see Newcombe (1998a).

For each of the following methods, let *p* be the population specificity, and let *r* represent the number of true negatives with *n* total negatives. Let $\hat{p} = r / n$.

Exact (Clopper-Pearson)

Using a mathematical relationship (see Fleiss et al (2003), p. 25) between the *F* distribution and the cumulative binomial distribution, the lower and upper confidence limits of a 100(1-α)% exact confidence interval for the true proportion *p* are given by

$$\left[\frac{r}{r + (n - r + 1)F_{1-\alpha/2;2(n-r+1),2r}}, \frac{(r + 1)F_{1-\alpha/2;2(r+1),2(n-r)}}{(n - r) + (r + 1)F_{1-\alpha/2;2(r+1),2(n-r)}}\right]$$

One-sided limits may be obtained by replacing $\alpha/2$ by α.

Score (Wilson)

The Wilson Score confidence interval, which is based on inverting the z-test for a single proportion, is calculated using

$$\frac{\left(2n\hat{p} + z_{1-\alpha/2}^2\right) \pm z_{1-\alpha/2}\sqrt{z_{1-\alpha/2}^2 + 4n\hat{p}(1-\hat{p})}}{2\left(n + z_{1-\alpha/2}^2\right)}$$

One-sided limits may be obtained by replacing $\alpha/2$ by α.

Score with Continuity Correction

The Score confidence interval with continuity correction is based on inverting the z-test for a single proportion with continuity correction. The $100(1-\alpha)\%$ limits are calculated by

$$Lower\ Limit = \frac{\left(2n\hat{p} + z_{1-\alpha/2}^2 - 1\right) - z_{1-\alpha/2}\sqrt{z_{1-\alpha/2}^2 - \{2 + (1/n)\} + 4\hat{p}\{n(1-\hat{p}) + 1\}}}{2\left(n + z_{1-\alpha/2}^2\right)}$$

$$Upper\ Limit = \frac{\left(2n\hat{p} + z_{1-\alpha/2}^2 + 1\right) + z_{1-\alpha/2}\sqrt{z_{1-\alpha/2}^2 + \{2 - (1/n)\} + 4\hat{p}\{n(1-\hat{p}) - 1\}}}{2\left(n + z_{1-\alpha/2}^2\right)}$$

One-sided limits may be obtained by replacing $\alpha/2$ by α.

Simple Asymptotic

The simple asymptotic formula is based on the normal approximation to the binomial distribution. The approximation is close only for very large sample sizes. The $100(1-\alpha)\%$ confidence limits are given by

$$\hat{p} \pm z_{1-\alpha/2}\sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$$

One-sided limits may be obtained by replacing $\alpha/2$ by α.

Simple Asymptotic with Continuity Correction

This formula is identical to the previous one, but with continuity correction. The $100(1-\alpha)\%$ confidence limits are

$$\left(\hat{p} - z_{1-\alpha/2}\sqrt{\frac{\hat{p}(1-\hat{p})}{n}} - \frac{1}{2n}, \hat{p} + z_{1-\alpha/2}\sqrt{\frac{\hat{p}(1-\hat{p})}{n}} + \frac{1}{2n}\right)$$

One-sided limits may be obtained by replacing $\alpha/2$ by α.

Interval Widths (One-Sided vs. Two-Sided)

For two-sided intervals, the distance from the sample specificity to each of the limits may be different. Thus, instead of specifying the distance to the limits we specify the width of the interval, *W*.

The basic equation for determining sample size for a two-sided interval when *W* has been specified is

$$W = U - L$$

For one-sided intervals, the distance from the sample specificity to limit, *D*, is specified.

The basic equation for determining sample size for a one-sided upper limit when *D* has been specified is

$$D = U - \hat{p}$$

The basic equation for determining sample size for a one-sided lower limit when *D* has been specified is

$$D = \hat{p} - L$$

Each of these equations can be solved for any of the unknown quantities in terms of the others.

Example 1 – Calculating Sample Size

Suppose a study is planned in which the researcher wishes to construct a two-sided 95% exact (Clopper-Pearson) confidence interval for the population specificity such that the width of the interval is no wider than 0.06. The anticipated specificity estimate is 0.7, but a range of values from 0.5 to 0.9 will be included to determine the effect of the specificity estimate on necessary sample size. Instead of examining only the interval width of 0.06, widths of 0.04, 0.08, and 0.10 will also be considered.

The goal is to determine the total sample size needed when also accounting for 30% prevalence.

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.......................... **Exact (Clopper-Pearson)**
Interval Type .... **Two-Sided**
Confidence Level **0.95**
Confidence Interval Width (Two-Sided) **0.04 0.06 0.08 0.10**
Specificity.. **0.5 to 0.9 by 0.05**
Prevalence.. **0.3**

Output

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

Numeric Reports

Numeric Results

Solve For: Sample Size
Confidence Interval Formula: Exact (Clopper-Pearson)
Confidence Interval Type: Two-Sided

Confidence Level	Sample Size N	Confidence Interval Width: Target	Confidence Interval Width: Actual	Specificity	Confidence Interval Limits: Lower	Confidence Interval Limits: Upper	Prevalence	Number of Negatives
0.95	3499	0.04	0.04	0.50	0.480	0.520	0.3	2449
0.95	3465	0.04	0.04	0.55	0.530	0.570	0.3	2425
0.95	3362	0.04	0.04	0.60	0.580	0.620	0.3	2353
0.95	3190	0.04	0.04	0.65	0.630	0.670	0.3	2233
0.95	2950	0.04	0.04	0.70	0.680	0.720	0.3	2065
0.95	2642	0.04	0.04	0.75	0.730	0.770	0.3	1849
0.95	2265	0.04	0.04	0.80	0.779	0.819	0.3	1585
0.95	1819	0.04	0.04	0.85	0.829	0.869	0.3	1273
0.95	1306	0.04	0.04	0.90	0.879	0.919	0.3	914
0.95	1569	0.06	0.06	0.50	0.470	0.530	0.3	1098
0.95	1555	0.06	0.06	0.55	0.520	0.580	0.3	1088
0.95	1509	0.06	0.06	0.60	0.570	0.630	0.3	1056
0.95	1432	0.06	0.06	0.65	0.620	0.680	0.3	1002
0.95	1326	0.06	0.06	0.70	0.669	0.729	0.3	928
0.95	1189	0.06	0.06	0.75	0.719	0.779	0.3	832
0.95	1022	0.06	0.06	0.80	0.769	0.829	0.3	715
.	.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.	.

Confidence Level	The proportion of confidence intervals (constructed with this same confidence level, sample size, etc.) that would contain the population specificity.
N	The size of the sample drawn from the population.
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.
Specificity	The assumed sample specificity, or true negative rate.
Confidence Interval Limits	The lower and upper limits of the confidence interval.
Prevalence	The assumed overall proportion of individuals with a positive condition.
Number of Negatives	The count upon which the confidence interval width calculation is based. Number of Negatives = Sample Size × (1 - Prevalence), with appropriate rounding.

Summary Statements

A single-group diagnostic test design will be used to obtain a two-sided 95% confidence interval for the specificity. The Exact (Clopper-Pearson) formula will be used to calculate the confidence interval. The sample specificity is assumed to be 0.5 and the prevalence is assumed to be 0.3. To produce a confidence interval with a width of no more than 0.04, 3499 subjects will be needed.

Dropout-Inflated Sample Size

Dropout Rate	Sample Size N	Dropout-Inflated Enrollment Sample Size N'	Expected Number of Dropouts D
20%	3499	4374	875
20%	3465	4332	867
20%	3362	4203	841
20%	3190	3988	798
20%	2950	3688	738
20%	2642	3303	661
20%	2265	2832	567
20%	1819	2274	455
20%	1306	1633	327
20%	1569	1962	393
20%	1555	1944	389
20%	1509	1887	378
20%	1432	1790	358
20%	1326	1658	332
20%	1189	1487	298
20%	1022	1278	256
.	.	.	.
.	.	.	.
.	.	.	.

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 the confidence interval is computed. If N subjects are evaluated out of the N' subjects that are enrolled in the study, the design will achieve the stated confidence interval.
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. After solving for N, 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 Lokhnygina, Y. (2018) pages 32-33.)
D The expected number of dropouts. D = N' - N.

Dropout Summary Statements

Anticipating a 20% dropout rate, 4374 subjects should be enrolled to obtain a final sample size of 3499 subjects.

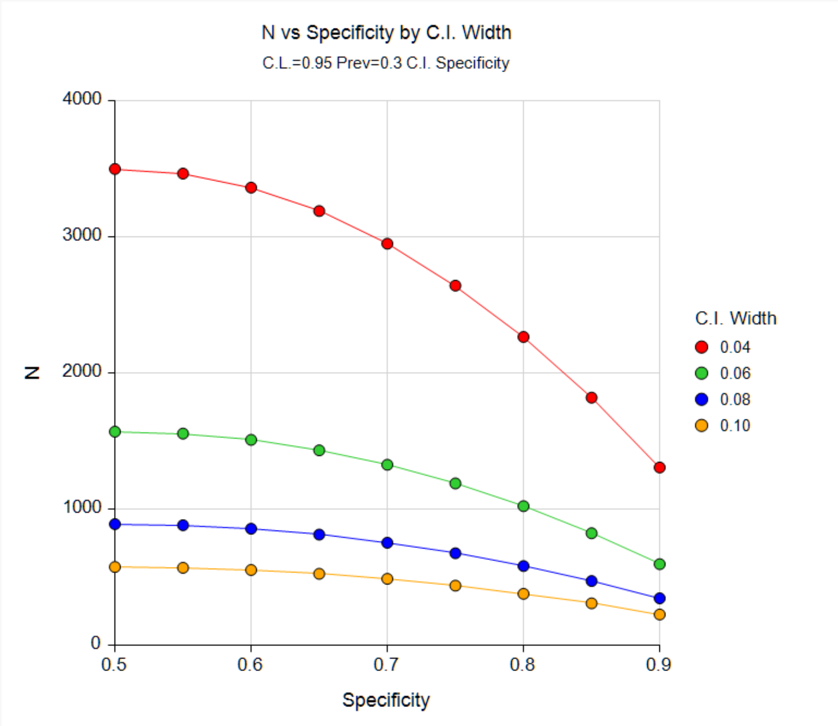
References

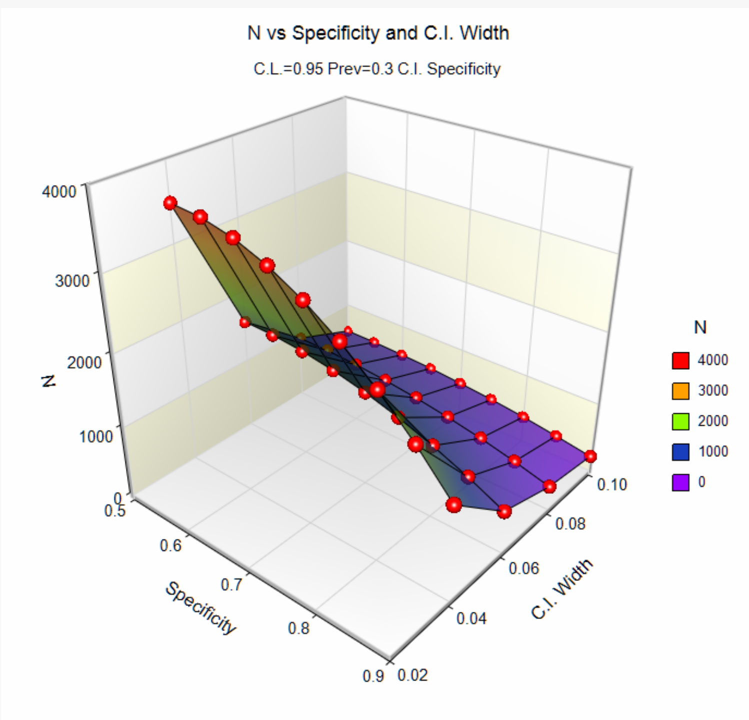
Hajian-Tilaki, K. 2014. 'Sample size estimation in diagnostic test studies of biomedical informatics.' Journal of Biomedical Informatics, 48, pp. 193-204.
Fleiss, J. L., Levin, B., Paik, M.C. 2003. Statistical Methods for Rates and Proportions. Third Edition. John Wiley & Sons. New York.
Newcombe, R. G. 1998. 'Two-Sided Confidence Intervals for the Single Proportion: Comparison of Seven Methods.' Statistics in Medicine, 17, pp. 857-872.

These reports show the calculated sample size for each of the scenarios.

Plots Section

Plots





These plots show the sample size versus the sample specificity for the four confidence interval widths.

Example 2 – Validation using Hajian-Tilaki (2014)

Hajian-Tilaki (2014), page 196, gives an example of a calculation for a simple asymptotic two-sided confidence interval for a single specificity when the confidence level is 95%, the specificity is 0.8, the prevalence is 0.1, and the margin of error is 3% (With a margin of error (precision) of 3%, the width is 0.06). The necessary sample size is calculated to be 759.

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**
Confidence Interval Formula.......................... **Simple Asymptotic**
Interval Type .... **Two-Sided**
Confidence Level **0.95**
Confidence Interval Width (Two-Sided) **0.06**
Specificity.. **0.8**
Prevalence.. **0.1**

Output

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

Numeric Results

Solve For: Sample Size
Confidence Interval Formula: Simple Asymptotic
Confidence Interval Type: Two-Sided

		Confidence Interval Width			Confidence Interval Limits			
Confidence Level	Sample Size N	Target	Actual	Specificity	Lower	Upper	Prevalence	Number of Negatives
0.95	759	0.06	0.06	0.8	0.77	0.83	0.1	683

PASS also calculates the necessary sample size to be 759. For some entries in the table, the sample size calculated in **PASS** is slightly different from the article. In the article the sample sizes are calculated directly, while **PASS** calculates the sample size needed before prevalence is taken into account, and then adjusts for the prevalence.