

## Chapter 273

# Confidence Intervals for One-Sample Sensitivity and Specificity

## Introduction

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

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

## Sensitivity (True Positive Rate)

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

		Predicted Condition		
		Positive	Negative	
True Condition	Positive	True Positive (A)	False Negative (C)	Sensitivity = $A / (A + C)$
	Negative	False Positive (B)	True Negative (D)	

## 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)	Specificity = $D / (B + D)$
	Negative	False Positive (B)	True Negative (D)	

## Confidence Intervals for One-Sample Sensitivity and Specificity

### 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 as the larger of two (whole table) sample sizes needed for each of the sensitivity and specificity confidence intervals, including appropriate prevalence adjustments.

### Sensitivity Confidence Interval Sample Size Calculation

The initial sample size calculation for the sensitivity confidence interval gives the number of individuals with a positive condition that are needed. The prevalence adjustment is used to add the number of individuals with a negative condition that are needed. The resulting sample size is the total number of individuals needed to obtain a table where the number of positive condition individuals will give the needed confidence interval width for the sensitivity.

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

### Specificity Confidence Interval Sample Size Calculation

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.

## 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 sensitivity, and let  $r$  represent the number of true positives with  $n$  total positives. 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  $100(1-\alpha)\%$  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  $\alpha$ .

### Score (Wilson)

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

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

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

### 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

$$\begin{aligned} \text{Lower Limit} &= \frac{(2n\hat{p} + z_{1-\alpha/2}^2 - 1) - z_{1-\alpha/2} \sqrt{z_{1-\alpha/2}^2 - \{2 + (1/n)\} + 4\hat{p}\{n(1 - \hat{p}) + 1\}}}{2(n + z_{1-\alpha/2}^2)} \\ \text{Upper Limit} &= \frac{(2n\hat{p} + z_{1-\alpha/2}^2 + 1) + z_{1-\alpha/2} \sqrt{z_{1-\alpha/2}^2 + \{2 - (1/n)\} + 4\hat{p}\{n(1 - \hat{p}) - 1\}}}{2(n + z_{1-\alpha/2}^2)} \end{aligned}$$

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

## Confidence Intervals for One-Sample Sensitivity and Specificity

### 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  $\alpha$ .

### 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  $\alpha$ .

---

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

For two-sided intervals, the distance from the sample sensitivity 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 sensitivity 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.

---

## 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 most of the parameters and options that you will be concerned with.

---

#### Solve For

##### Solve For

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

## Confidence Intervals for One-Sample Sensitivity and Specificity

---

### Confidence Interval Method

#### Confidence Interval Formula

Specify the formula to be used in calculation of confidence intervals.

- **Exact (Clopper-Pearson)**

The exact formula uses the binomial probabilities directly.

- **Score (Wilson)**

This formula is based on inverting a critical ratio test.

- **Score (Continuity Correction)**

This formula is based on inverting a critical ratio test with continuity correction.

- **Simple Asymptotic**

The simple asymptotic formula is based on the normal approximation to the binomial.

- **Simple Asymptotic (Continuity Correction)**

This formula is based on the normal approximation to the binomial with continuity correction.

---

### One-Sided or Two-Sided Interval

#### Interval Type

Specify whether the intervals to be used will be two-sided confidence intervals, intervals that have only an upper limit, or intervals that have only a lower limit.

---

### Confidence

#### Confidence Level

Enter the confidence level (or confidence coefficient). This is the proportion of confidence intervals (constructed with this same confidence level, sample size, etc.) that contain the population sensitivity or specificity.

Often, the values 0.95 or 0.99 are used. You can enter single values or a range of values such as *0.90, 0.95* or *0.90 to 0.99 by 0.01*.

---

### Sample Size

#### N (Sample Size)

Enter one or more values for the sample size. This is the number of individuals selected at random from the population to be in the study.

You can enter a single value or a range of values.

---

### Precision

#### Confidence Interval Width (Two-Sided)

This is the distance from the lower confidence limit to the upper confidence limit.

You can enter a single value or a list of values. The value(s) must be between 0 and 1.

## Confidence Intervals for One-Sample Sensitivity and Specificity

### Distance from Sensitivity to Limit (One-Sided)

This is the distance from the sample sensitivity or sample specificity to the lower or upper limit of the confidence interval, depending on whether the Interval Type is set to Lower One-Sided or Upper One-Sided.

You can enter a single value or a list of values. The value(s) must be between 0 and 1.

---

### Sensitivity

#### Sensitivity

Enter an estimate of the sensitivity (or true positive rate). The sample size and width calculations assume that the value entered here is the sensitivity estimate that is obtained from the sample. If the sample sensitivity is different from the one specified here, the width may be narrower or wider than specified.

You can enter a range of values such as *0.1 0.2 0.3* or *0.1 to 0.5 by 0.1*.

---

### Specificity

#### Specificity

Enter an estimate of the specificity (or true negative rate). The sample size and width calculations assume that the value entered here is the specificity estimate that is obtained from the sample. If the sample specificity is different from the one specified here, the width may be narrower or wider than specified.

You can enter a range of values such as *0.1 0.2 0.3* or *0.1 to 0.5 by 0.1*.

---

### Prevalence

#### Prevalence

Enter the value of the assumed prevalence. The Prevalence is the assumed overall proportion of individuals with a positive condition. The sample size calculations for the sensitivity and specificity confidence intervals are concerned with the number of positive condition and negative condition individuals, respectively. The prevalence is used to produce the total sample size needed to generate the proper number of positive condition and negative condition individuals.

You can enter a range of values such as *0.1 0.2 0.3* or *0.1 to 0.5 by 0.1*.

## Confidence Intervals for One-Sample Sensitivity and Specificity

## Example 1 – Calculating Sample Size

Suppose a study is planned in which the researcher wishes to construct two-sided 95% exact (Clopper-Pearson) confidence intervals for the population sensitivity and specificity such that the widths of the intervals are no wider than 0.06. The anticipated sensitivity estimate is 0.7, but a range of values from 0.5 to 0.9 will be included to determine the effect of the sensitivity estimate on necessary sample size. The anticipated specificity is 0.6. 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 20% to 60% prevalence.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Confidence Intervals for One-Sample Sensitivity and Specificity** procedure. You may 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>
<b>Design Tab</b>	
Solve For .....	<b>Sample Size</b>
Confidence Interval Formula .....	<b>Exact (Clopper-Pearson)</b>
Interval Type .....	<b>Two-Sided</b>
Confidence Level .....	<b>0.95</b>
Confidence Interval Width (Two-Sided) ..	<b>0.04 0.06 0.08 0.10</b>
Sensitivity .....	<b>0.5 to 0.9 by 0.05</b>
Specificity .....	<b>0.6</b>
Prevalence .....	<b>0.2 to 0.6 by 0.1</b>

### Annotated Output

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

### Numeric Results

**Numeric Results for Two-Sided Confidence Intervals for One-Sample Sensitivity and Specificity**  
Confidence Interval Formula: Exact (Clopper-Pearson)

Confidence Level	Prev	Target Width	Sensitivity	Sample Size for Sens. C.I.	Specificity	Sample Size for Spec. C.I.	Required Sample Size (N)	Sens. C.I. Width with N	Spec. C.I. Width with N
0.950	0.200	0.040	0.500	12245	0.600	2942	12245	0.040	0.020
0.950	0.300	0.040	0.500	8164	0.600	3362	8164	0.040	0.026
0.950	0.400	0.040	0.500	6123	0.600	3922	6123	0.040	0.033
0.950	0.500	0.040	0.500	4898	0.600	4706	4898	0.040	0.040
0.950	0.600	0.040	0.500	4082	0.600	5883	5883	0.033	0.041
0.950	0.200	0.040	0.550	12125	0.600	2942	12125	0.040	0.020
0.950	0.300	0.040	0.550	8084	0.600	3362	8084	0.040	0.026
0.950	0.400	0.040	0.550	6063	0.600	3922	6063	0.040	0.033
0.950	0.500	0.040	0.550	4850	0.600	4706	4850	0.040	0.040
0.950	0.600	0.040	0.550	4042	0.600	5883	5883	0.033	0.041
0.950	0.200	0.040	0.600	11765	0.600	2942	11765	0.040	0.020
0.950	0.300	0.040	0.600	7844	0.600	3362	7844	0.040	0.026
.	.	.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.	.	.

[report continues]

## Confidence Intervals for One-Sample Sensitivity and Specificity

### 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.

### Report Definitions

Confidence level is the proportion of confidence intervals (constructed with this same confidence level, sample size, etc.) that would contain the population sensitivity or specificity.

Prevalence is the assumed overall proportion of individuals with a positive condition.

Target Width is the desired distance from the lower limit to the upper limit.

Sensitivity is the assumed sample sensitivity, or true positive rate.

Sample Size for Sensitivity Confidence Interval is the whole table sample size needed to obtain the desired sensitivity confidence interval width.

Specificity is the assumed sample specificity, or true negative rate.

Sample Size for Specificity Confidence Interval is the whole table sample size needed to obtain the desired specificity confidence interval width.

Required Sample Size (N) is the whole table sample size that is needed to give the desired confidence interval width for both the sensitivity and specificity. It is the larger of the two sample sizes.

Sensitivity Confidence Interval Width with N is the distance from the sensitivity confidence interval lower limit to the upper limit when the sample size is N.

Specificity Confidence Interval Width with N is the distance between the specificity confidence interval lower limit to the upper limit when the sample size is N.

### Summary Statements

Assuming a prevalence of 0.200 and a sample sensitivity of 0.500, the sample size needed for a two-sided 95% sensitivity confidence interval with a width of at most 0.040, is 12245. Assuming a prevalence of 0.200 and a sample specificity of 0.600, the sample size needed for a two-sided 95% specificity confidence interval with a width of at most 0.040, is 2942. The whole table sample size required so that both confidence intervals have widths less than 0.040, is 12245, the larger of the two sample sizes.

### Dropout-Inflated Sample Size

Dropout Rate	Sample Size N	Dropout- Inflated Enrollment Sample Size N'	Expected Number of Dropouts D
20%	12245	15307	3062
20%	8164	10205	2041
20%	6123	7654	1531
20%	4898	6123	1225
20%	5883	7354	1471
20%	12125	15157	3032
20%	8084	10105	2021
20%	6063	7579	1516
20%	4850	6063	1213
20%	5883	7354	1471
20%	11765	14707	2942
.	.	.	.
.	.	.	.
.	.	.	.

### 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").

N is 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' is the total number of subjects that should be enrolled in the study in order to end up with 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., and Wang, H. (2008) pages 39-40.)

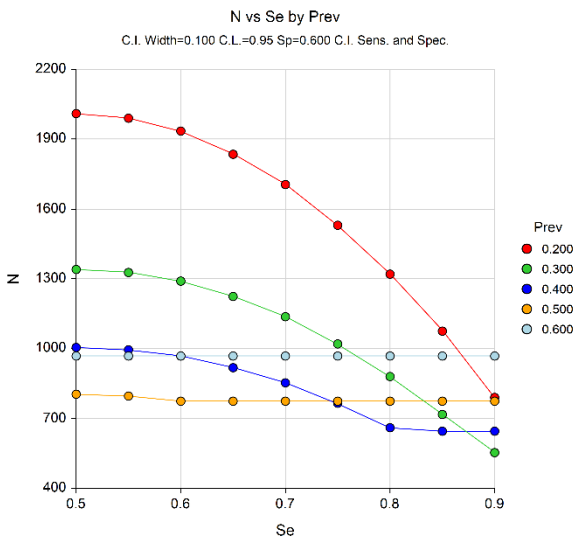
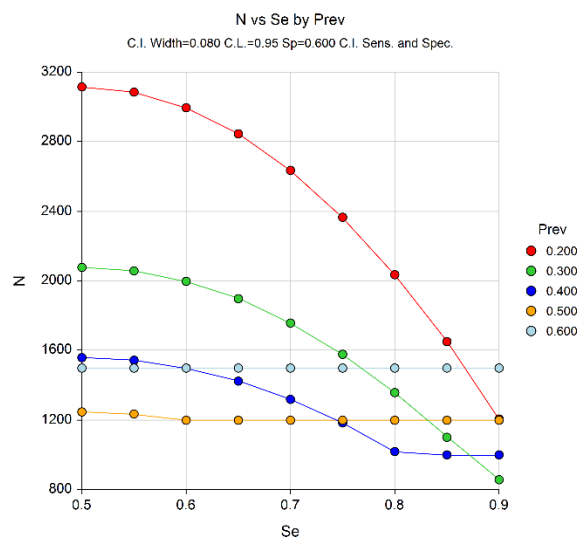
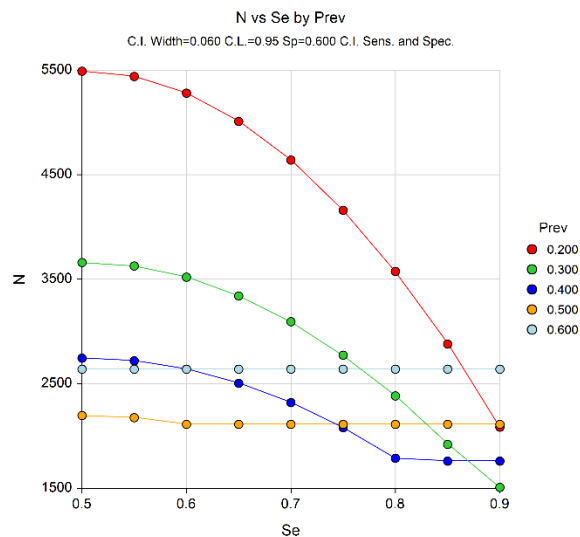
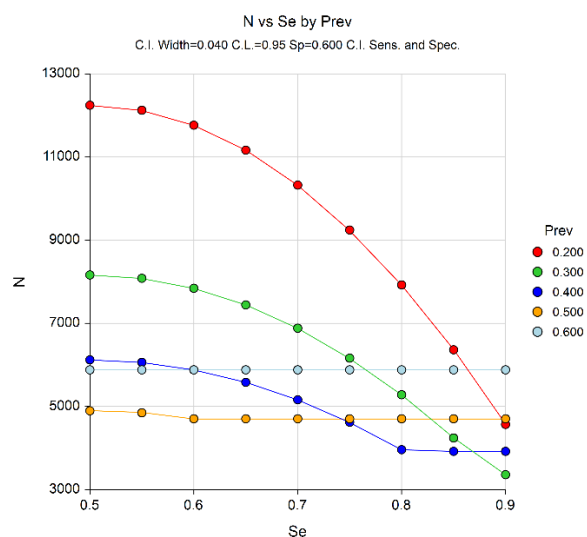
D is the expected number of dropouts.  $D = N' - N$ .

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

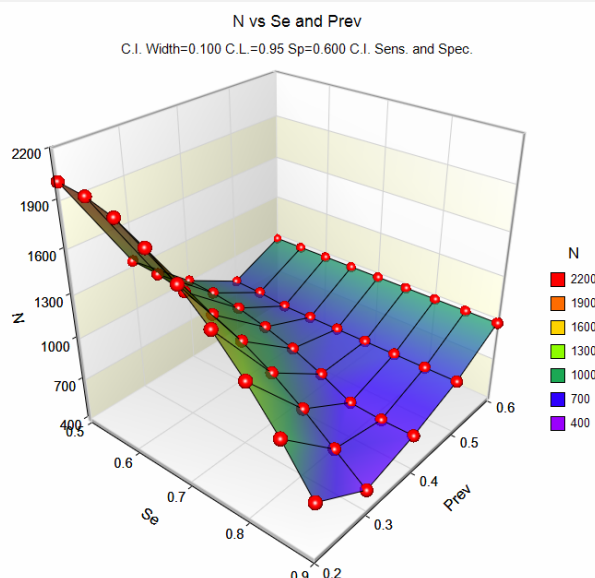
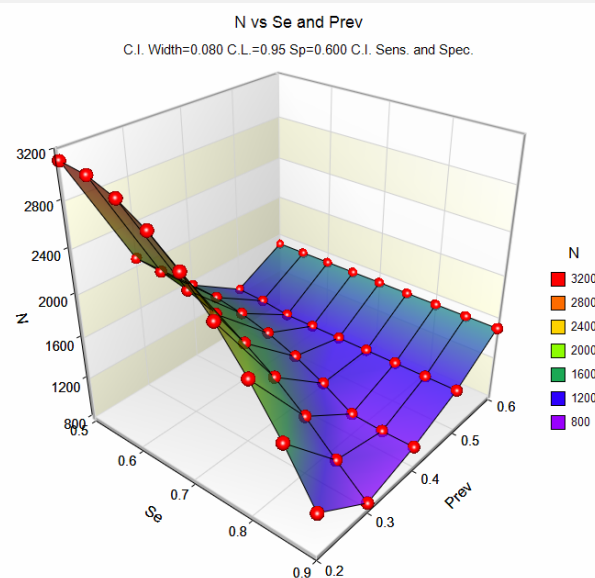
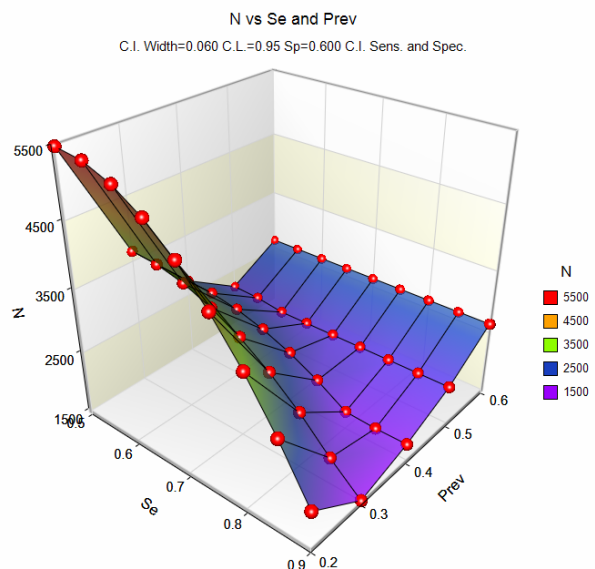
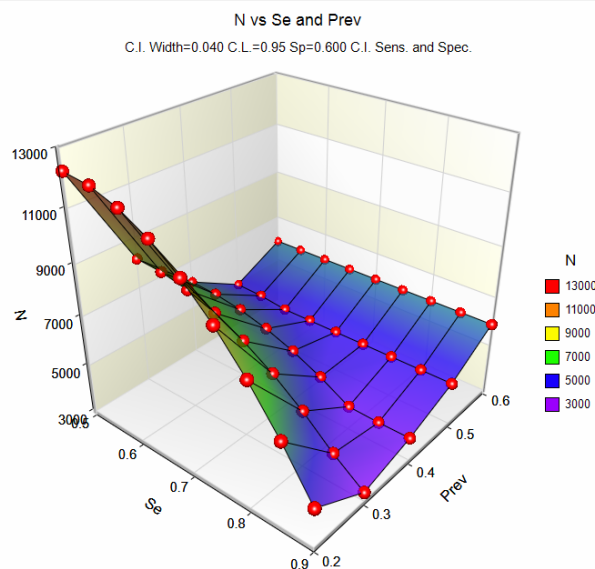


## Confidence Intervals for One-Sample Sensitivity and Specificity

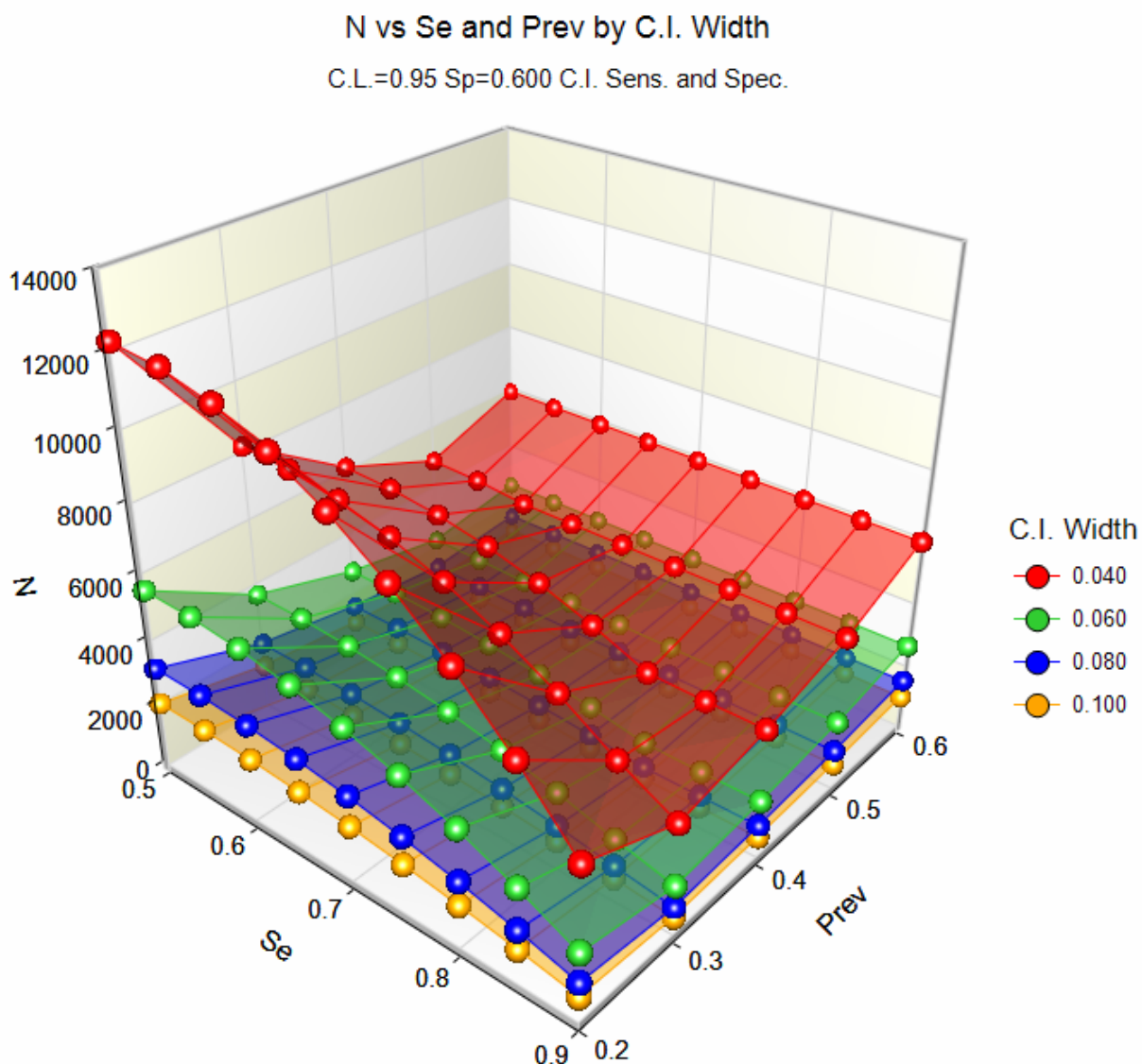
## Plots Section



## Confidence Intervals for One-Sample Sensitivity and Specificity



## Confidence Intervals for One-Sample Sensitivity and Specificity



These plots show the sample size versus the sample sensitivity and prevalence for the four confidence interval widths. It can be seen in the plots where the sample size depends on the sensitivity, and where it depends on the specificity.

## Example 2 – Validation for Sensitivity Confidence Interval using Hajian-Tilaki (2014)

Hajian-Tilaki (2014), page 195, gives an example of a calculation for a simple asymptotic two-sided confidence interval for a single sensitivity when the confidence level is 95%, the sensitivity is 0.8, the prevalence is 0.1, and the margin of error is 7% (With a margin of error (precision) of 7%, the width is 0.14). The necessary sample size is calculated to be 1254.

### Setup

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

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Sample Size</b>
Confidence Interval Formula .....	<b>Simple Asymptotic</b>
Interval Type .....	<b>Two-Sided</b>
Confidence Level .....	<b>0.95</b>
Confidence Interval Width (Two-Sided) ..	<b>0.14</b>
Sensitivity .....	<b>0.8</b>
Specificity .....	<b>0.8</b>
Prevalence .....	<b>0.1</b>

### Output

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

### Numeric Results

**Numeric Results for Two-Sided Confidence Intervals for One-Sample Sensitivity**  
Confidence Interval Formula: Simple Asymptotic

Confidence Level	Prev	Target Width	Sensitivity	Sample Size for Sens. C.I.	Specificity	Sample Size for Spec. C.I.	Required Sample Size (N)	Sens. C.I. Width with N	Spec. C.I. Width with N
0.950	0.100	0.140	0.800	<b>1260</b>	0.800	140	1260	0.140	0.047

PASS calculates the necessary sample size to be 1260. 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. With a sample size of 1254, the number of positives would be 125.4, which should be rounded up to 126. Adjusting 126 for prevalence gives 1260.

## Example 3 – Validation for Specificity Confidence Interval 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

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Confidence Intervals for One-Sample Sensitivity and Specificity** procedure. You may make the appropriate entries as listed below or open **Example 3** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
<b>Design Tab</b>	
Solve For .....	<b>Sample Size</b>
Confidence Interval Formula .....	<b>Simple Asymptotic</b>
Interval Type .....	<b>Two-Sided</b>
Confidence Level .....	<b>0.95</b>
Confidence Interval Width (Two-Sided) ..	<b>0.06</b>
Sensitivity .....	<b>0.8</b>
Specificity .....	<b>0.8</b>
Prevalence .....	<b>0.1</b>

### Output

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

### Numeric Results

Numeric Results for Two-Sided Confidence Intervals for One-Sample Sensitivity Confidence Interval Formula: Simple Asymptotic									
Confidence Level	Prev	Target Width	Sensitivity	Sample Size for Sens. C.I.	Specificity	Sample Size for Spec. C.I.	Required Sample Size (N)	Sens. C.I. Width with N	Spec. C.I. Width with N
0.950	0.100	0.060	0.800	6830	0.800	<b>759</b>	6830	0.060	0.020

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.