Chapter 102

Confidence Intervals for the Difference Between Two Correlated Proportions

Introduction

This routine calculates the sample sizes needed to achieve a specified confidence interval width for the difference between two correlated proportions. Correlated proportions occur when two binary variables are obtained on each subject.

Several formulas have been proposed to calculate confidence intervals for the difference between two correlated proportions. This procedure provides results for five methods.

Technical Details

This section provides the technical details of how the sample sizes are determined.

Comparing Two Proportions

Suppose two dichotomous responses (*Yt* and *Ys*) are obtained on each of *n* subjects. A common example is when *Ys* represents a pretest binary response and *Yt* represents a posttest response.

Suppose the probability of obtaining the event of interest in variable *Yt* is Pt. That is, $P(Yt = 1) = Pt$. Similarly, the probability of obtaining the event of interest in variable *Ys* is Ps. That is, $P(Ys = 1) = Ps$. The corresponding failure probabilities are given by $Qt = P(Yt = 0)$ and $Qs = P(Ys = 0)$. The purpose of the study is to compare *Pt* and *Ps* by evaluating their difference.

The following table gives both the marginal (total) probabilities and the joint (or cell) probabilities.

	Ys = 1	**Ys = 0**	**Totals**
Yt = 1	P_{11}	P_{10}	P_t
Yt = 0	P_{01}	P_{00}	Q_t
Totals	P_s	Q_s	1

Note that $P_t = P_{11} + P_{10}$ and $P_s = P_{11} + P_{01}$, so the quantity P_{11} is common to both terms. This shows that P_t and P_s are correlated.

An assumption is made that the responses for each variable follow binomial distributions. Since both variables are measured on the same individual, the variables are assumed to be correlated.

A random sample of *n* individuals (or pairs) are obtained, and the two variables are measured on each individual. The data from these samples can be displayed in a 2-by-2 contingency table as follows

	Ys = 1	Ys = 0	Totals
Yt = 1	f_{11}	f_{10}	$f_{1\bullet}$
Yt = 0	f_{01}	f_{00}	$f_{0\bullet}$
Totals	$f_{\bullet 1}$	$f_{\bullet 0}$	n

The binomial proportions P_t and P_s are estimated using the formulae

$$\hat{P}_t = p_t = \frac{f_{1\bullet}}{n} \text{ and } \hat{P}_s = p_s = \frac{f_{\bullet 1}}{n}$$

The (risk) difference $\delta = P_t - P_s$ is perhaps the most direct method of comparison between these two event probabilities. This parameter is easy to interpret and communicate. It gives the absolute impact of the treatment. However, there are subtle difficulties that can arise with its interpretation.

One interpretation difficulty occurs when the event of interest is rare. If a difference of 0.001 were reported for an event with a baseline probability of 0.40, it would probability be dismissed as being of little importance. That is, there is usually little interest in a treatment that decreases the probability from 0.400 to 0.399. However, if the baseline probably of a disease was 0.002 and 0.001 was the decrease in the disease probability, this would represent a reduction of 50%. Thus we see that interpretation of the size of the difference depends on the baseline probability of the event. So, although using the simple difference is a useful method of comparison, care must be taken that it fits the situation.

Confidence Intervals for the Difference (Pt – Ps)

Many formulas have been proposed for computing confidence intervals for the difference between two paired proportions. Five of these methods are available in this procedure.

It is difficult to recommend one procedure as the best. However, all comparisons in the literature that we have reviewed have found the *Wald* and the *Wald with continuity correction* to be lacking in several aspects. Therefore, we recommend avoiding these methods. They are provided because they often appear in elementary statistics texts. But, in real work, they should be avoided.

These confidence interval methods are as follows.

Wald

Fleiss *et al.* (2003, p. 378) and Newcombe (1998c) mention a confidence interval for the difference in proportions given by

$$(p_1 - p_2) \pm z_{1-\alpha/2} se_{p_1 - p_2}$$

where

$$se_{p_1 - p_2} = \frac{\sqrt{n(f_{10} + f_{01}) - (f_{10} - f_{01})^2}}{n\sqrt{n}}$$

Wald with Continuity Correction

Fleiss *et al.* (2003, p. 378) and Newcombe (1998c) mention a confidence interval for the difference in proportions given by

$$(p_1 - p_2) \pm \left(z_{1-\alpha/2} se_{p_1-p_2} + 1/n\right)$$

where

$$se_{p_1-p_2} = \frac{\sqrt{n(f_{10} + f_{01}) - (f_{10} - f_{01})^2}}{n\sqrt{n}}$$

Agresti and Min's Wald+2

Agresti and Min (2005) provide an improvement to the Wald Method which is made by adding two observations to the 2x2 table before calculating the interval. This modification improves the overall coverage probability and allows results to be calculated even though one or more marginal frequency totals are zero.

The modification is simply to add $\frac{1}{2}$ to each of the cell frequencies before making any calculations and then to calculate the confidence interval using the Wald method. They call this the "Wald + 2" method.

Bonett and Price's Adjusted Wald

Bonett and Price (2012) provide an improvement to the Wald method which is similar to the method of Agresti and Min method. The adjustment is made by adding two observations to the 2x2 table before calculating the interval. This modification improves the overall coverage probability and allows results to be calculated even though one or more marginal frequency totals are zero.

The modification is simply to add one to each of the non-diagonal cell frequencies before making any calculations and then calculate the confidence interval using the Wald method. Bonett and Price call this the "Adjusted Wald" method. They show that it performs well in most situations.

Newcombe's Score

Newcombe (1998c, p. 2639, method 10), Altman *et al.* (2000, p. 52), and Machin *et al.* (2018, p. 141-142) provide a formula for computing a confidence interval of the proportion difference. Through extensive analysis, Newcombe shows that this method is a very good choice.

Newcombe describes this method as using score intervals for the marginal proportions, but adding a continuity correction for the estimated correlation coefficient.

The lower limit is given by

$$D_L = (p_t - p_s) - W_L$$

where

$$W_L = \sqrt{(p_t - L_t)^2 - 2\rho(p_t - L_t)(U_s - p_s) + (U_s - p_s)^2}$$

and the upper limit is given by

$$D_U = (p_t - p_s) + W_U$$

where

$$W_U = \sqrt{(p_s - L_s)^2 - 2\rho(p_s - L_s)(U_t - p_t) + (U_t - p_t)^2}$$

$$p_t = \frac{f_{11} + f_{10}}{n}$$

$$p_s = \frac{f_{11} + f_{01}}{n}$$

$$L_t = \frac{A_t - B_t}{C_t}$$

$$U_t = \frac{A_t + B_t}{C_t}$$

$$A_t = 2np_t + z_{1-\alpha/2}^2$$

$$B_t = z_{1-\alpha/2}\sqrt{z_{1-\alpha/2}^2 + 4np_t(1 - p_t)}$$

$$C_t = 2\left(n + z_{1-\alpha/2}^2\right)$$

$$L_s = \frac{A_s - B_s}{C_s}$$

$$U_s = \frac{A_s + B_s}{C_s}$$

$$A_s = 2np_s + z_{1-\alpha/2}^2$$

$$B_s = z_{1-\alpha/2}\sqrt{z_{1-\alpha/2}^2 + 4np_s(1 - p_s)}$$

$$C_s = 2\left(n + z_{1-\alpha/2}^2\right)$$

The within subject correlation coefficient with continuity correction, ρ_{cc}, is calculated as follows.

If $f_{11} + f_{10},\ f_{01} + f_{00},\ f_{11} + f_{01},$ or $f_{10} + f_{00}$ then set $\rho_{cc} = 0$.

Otherwise, calculate

$$A = (f_{11} + f_{10})(f_{01} + f_{00})(f_{11} + f_{01})(f_{10} + f_{00})$$

$$B = (f_{11}f_{00}) - (f_{10}f_{01})$$

$$C = \begin{cases} B - \dfrac{n}{2} & \text{if } B > \dfrac{n}{2} \\ 0 & \text{if } 0 \le B \le \dfrac{n}{2} \\ B & B < 0 \end{cases}$$

and then calculate

$$\rho_{cc} = C/\sqrt{A}$$

The width of this interval is $D_U - D_L$.

Correlation of Yt and Ys (Pearson's Phi Coefficient)

The (uncorrected) correlation of the two binary variables, *Yt* and *Ys*, measured on each subject is sometimes called Pearson's phi coefficient, φ. It is be calculated as follows:

$$\rho = \varphi = \frac{P_{11}P_{00} - P_{10}P_{01}}{\sqrt{P_t P_s Q_t Q_s}}$$

This correlation may be used with the marginal probabilities to obtain the joint (cell) probabilities using the following relationships:

$$P_{11} = P_t P_s + \rho\sqrt{P_t P_s Q_t Q_s}$$

$$P_{10} = P_t Q_s - \rho\sqrt{P_t P_s Q_t Q_s}$$

$$P_{01} = Q_t P_s - \rho\sqrt{P_t P_s Q_t Q_s}$$

$$P_{00} = Q_t Q_s + \rho\sqrt{P_t P_s Q_t Q_s}$$

The lower and upper limits of this correlation is given by

$$\rho_L = \max\left\{-\sqrt{\frac{P_s P_t}{(1-P_s)(1-P_t)}}, -\sqrt{\frac{(1-P_s)(1-P_t)}{P_s P_t}}\right\}$$

$$\rho_U = \min\left\{\sqrt{\frac{P_s(1-P_t)}{P_t(1-P_s)}}, \sqrt{\frac{P_t(1-P_s)}{P_s(1-P_t)}}\right\}$$

Continuity Corrected Correlation

Newcombe's score method uses a continuity corrected correlation (phi) in the calculation of interval width. This correction, shown above, can be summarized as follows.

$$\rho_{cc} = \rho - \frac{1}{2n\sqrt{P_t P_s Q_t Q_s}}$$

To keep all input values consistent, always enter the uncorrected estimate of ρ. The program will make necessary adjustments when needed with Newcombe's method.

Alternative Ways of Setting the Parameter Values

The main parameter of interest is $\delta = P_t - P_s$. Most of the formulas for the confidence intervals of δ involve the joint probabilities. When the study is being planned it is usually very difficult to find estimates of the joint probabilities $(P_{11}, P_{10}, P_{01}, P_{00})$ from previous studies or from experts. However, estimates of the marginal probabilities (P_t, Q_t, P_s, Q_s) and the within-subject correlation (ρ) are usually much easier to obtain. Using the relationships given above, the values of the joint probabilities may be calculated from the marginal probabilities.

In order to make comparisons with other results easier, PASS allows for both input types: marginal probabilities or joint probabilities.

Example 1 – Calculating Sample Size

Suppose a study is planned in which the researcher wishes to compare the binary (yes/no) response to a certain treatment. The responses of each subject are measured before (Ys) and after (Yt) the treatment is administered.

The researchers want to estimate the sample size needed to construct a 95% confidence interval for the difference in response proportions such that the width of the interval is no wider than 0.1. Newcombe's score method will be used to construct the interval.

Previous studies provide a planning value for P_s of 0.41 and the (uncorrected) within-subject correlation will be between 0.51 and 0.62.

Planning values for P_t will be 0.5, 0.6, and 0.7.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. 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**.

Option	Value
Design Tab	
Solve For	**Sample Size**
Confidence Interval Formula	**Newcombe's Score**
Confidence Level (1 - Alpha)	**0.95**
WD (Width of Confidence Interval)	**0.1**
Probability Input Type	**Enter Marginal Probabilities**
Pt (Prob (Yt = 1))	**0.5 0.6 0.7**
Ps (Prob (Ys = 1))	**0.41**
ρ (Correlation of Yt and Ys)	**0.51 0.62**

Annotated Output

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

Numeric Results

Numeric Results
Confidence Interval Formula: Newcombe's Score

C.I. Width WD	Number of Pairs N	Prob Yt=1 Pt	Prob Ys=1 Ps	Corr Yt,Ys ρ	Pt-Ps Diff	Lower C.I. Segment Width WL	Upper C.I. Segment Width WU	Conf Level CL
0.09998	371	0.5	0.41	0.51	0.09	0.05044	0.04954	0.95
0.09999	289	0.5	0.41	0.62	0.09	0.05050	0.04949	0.95
0.09991	364	0.6	0.41	0.51	0.19	0.05094	0.04897	0.95
0.09984	284	0.6	0.41	0.62	0.19	0.05104	0.04881	0.95
0.09990	343	0.7	0.41	0.51	0.29	0.05149	0.04842	0.95
0.09990	268	0.7	0.41	0.62	0.29	0.05165	0.04825	0.95

References
Newcombe, R.G. 1998. 'Improved Confidence Intervals for the Difference Between Binomial Proportions Based on Paired Data.' Statistics in Medicine. Volume 17. Pages 2635-2650.
Altman, D.G, Machin, D., Bryant, T.N., Gardner, M.J. 2000. Statistics with Confidence, 2nd Edition. BMJ Publishing.
Agresti, A. and Min, Y. 2005. 'Simple improved confidence intervals for comparing matched proportions.' Statistics in Medicine. Volume 24. Pages 729-740. DOI: 10.1002/sim.1781.
Bonett, D.G. and Price, R.M. 2012. 'Adjusted Wald Confidence Interval for a Difference of Binomial Proportions

Based on Paired Data.' Journal of Educational and Behavioral Statistics. Volume 17, Number 4, Pages 479-488. DOI:10.3102/1076998611411915.
Machin, D., Campbell, M., Tan, S.B., and Tan, S.H. 2018. Sample Size Tables for Clinical, Laboratory and Epidemiology Studies, 4th Edition. John Wiley & Sons. Hoboken, NJ.

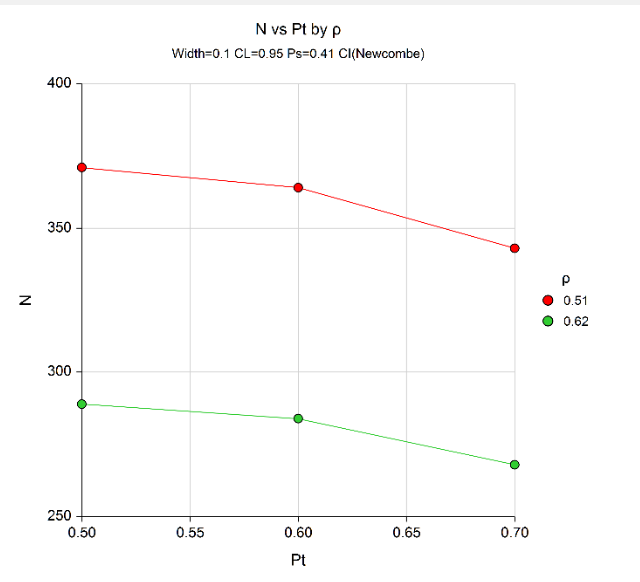
Report Definitions
W_D is the width of the confidence interval for the difference between the two proportions.
N is the number of pairs in the study.
Pt is the probability that the response variable Yt = 1.
Ps is the probability that the response variable Ys = 1.
ρ is the within-subject correlation between Yt and Ys. It is also called the phi (ϕ) coefficient.
Diff (Pt - Ps) is the difference between the two proportions, Pt and Ps. It is the parameter of interest.
W_L is the distance from the difference to the lower C.I. limit. Note that $W_D = W_L + W_U$.
W_U is the distance from the difference to the upper C.I. limit. Note that $W_D = W_L + W_U$.
CL is the confidence level of the confidence interval.

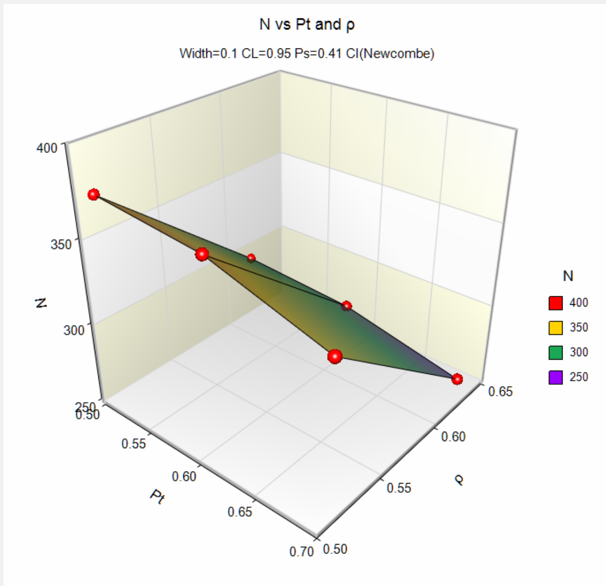
Summary Statements
A confidence interval is desired for the difference between two correlated binomial proportions based on paired data. A sample of 371 pairs (two variables measured on each subject) generates a confidence interval with a maximum width of 0.09998 at a confidence level of 0.95 for a difference in proportions of 0.09. The Newcombe's Score method is used to compute the confidence interval. The response proportion of the treatment variable is 0.5 and of the standard variable is 0.41. The within-subject correlation is assumed to be 0.51.

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

Chart Section

Chart Section





These plots show the group sample sizes for each of the scenarios. It appears that the value of the within-subject correlation has the largest impact on sample size in this study.

Example 2 – Validation of Newcombe's Score Method using Newcombe (1998c)

Newcombe (1998c, page 2641) presents a table from which we will use the second row as our validation example. In this row, $P_{11} = 0.4, P_{10} = 0.24, P_{01} = 0.04, P_{00} = 0.32,$ and $N = 50$. The resulting 95% confidence interval for the difference is 0.0562 to 0.3292 which gives a width of 0.273.

Setup

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

Option	Value
Design Tab	
Solve For	**C.I. Width**
Confidence Interval Formula	**Newcombe's Score**
Confidence Level (1 - Alpha)	**0.95**
N (Number of Pairs)	**50**
Probability Input Type	**Enter Joint (Cell) Probabilities**
P10 (Prob (Yt = 1, Ys = 0))	**0.24**
P01 (Prob (Yt = 0, Ys = 1))	**0.04**
P11 (Prob (Yt = Ys = 1))	**0.4**

Output

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

Numeric Results

Numeric Results
Confidence Interval Formula: Newcombe's Score

C.I. Width WD	Number of Pairs N	Prob Yt=1 and Ys=0 P10	Prob Yt=0 and Ys=1 P01	Prob Yt=1 and Ys=1 P11	Pt-Ps Diff	Lower C.I. Segment Width WL	Upper C.I. Segment Width WU	Conf Level CL
0.27305	50	0.24	0.04	0.4	0.2	0.14384	0.12921	0.95

This report gives the width as 0.27305 which validates this procedure.

Example 3 – Validation of the Wald Method using Newcombe (1998c)

Newcombe (1998c, page 2640) presents a table from which we will use the first row as our validation example. In this row, $P_{11} = 0.36, P_{10} = 0.24, P_{01} = 0.04, P_{00} = 0.36,$ and $N = 50$. The resulting 95% confidence interval for the difference is 0.0642 to 0.3358 which gives a width of 0.2716.

Setup

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

Option	Value
Design Tab	
Solve For	**C.I. Width**
Confidence Interval Formula	**Wald**
Confidence Level (1 - Alpha)	**0.95**
N (Number of Pairs)	**50**
Probability Input Type	**Enter Joint (Cell) Probabilities**
P10 (Prob (Yt = 1, Ys = 0))	**0.24**
P01 (Prob (Yt = 0, Ys = 1))	**0.04**

Output

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

Numeric Results

Numeric Results
Confidence Interval Formula: Wald

C.I. Width W_D	Number of Pairs N	Prob Yt=1 and Ys=0 P10	Prob Yt=0 and Ys=1 P01	Pt-Ps Diff	Std Error of Diff SE	Conf Level CL
0.27158	50	0.24	0.04	0.2	0.06928	0.95

This report shows gives the width as 0.27158 which validates this procedure since it rounds to 0.2716.

Example 4 – Validation of the Wald C.C. Method using Newcombe (1998c)

Newcombe (1998c, page 2640) presents a table from which we will use the second row as our validation example. In this row, $P_{11} = 0.36, P_{10} = 0.24, P_{01} = 0.04, P_{00} = 0.36,$ and $N = 50$. The resulting 95% confidence interval for the difference is 0.0442 to 0.3558 which gives a width of 0.3116.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. You may then make the appropriate entries as listed below, or open **Example 4** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**C.I. Width**
Confidence Interval Formula	**Wald with Continuity Correction**
Confidence Level (1 - Alpha)	**0.95**
N (Number of Pairs)	**50**
Probability Input Type	**Enter Joint (Cell) Probabilities**
P10 (Prob (Yt = 1, Ys = 0))	**0.24**
P01 (Prob (Yt = 0, Ys = 1))	**0.04**

Output

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

Numeric Results

Numeric Results
Confidence Interval Formula: Wald with Continuity Correction

C.I. Width W_D	Number of Pairs N	Prob Yt=1 and Ys=0 P10	Prob Yt=0 and Ys=1 P01	Pt-Ps Diff	Std Error of Diff SE	Conf Level CL
0.31158	50	0.24	0.04	0.2	0.06928	0.95

This report shows gives the width as 0.31158 which validates this procedure since it rounds to 0.3116.

Example 5 – Validation of the Agresti and Min Method using Agresti and Min (2005)

Agresti and Min (2005, page 736) present a Table V from which we will use the second row as our validation example. In this row, $P_{10} = \frac{8}{86} = 0.093023, P_{01} = \frac{16}{86} = 0.186047,$ and $N = 86$. The resulting 95% confidence interval for the difference is -0.019 to 0.201 which gives a rounded width of 0.22.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. You may then make the appropriate entries as listed below, or open **Example 5** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**C.I. Width**
Confidence Interval Formula	**Agresti and Min's Wald+2**
Confidence Level (1 - Alpha)	**0.95**
N (Number of Pairs)	**86**
Probability Input Type	**Enter Joint (Cell) Probabilities**
P10 (Prob (Yt = 1, Ys = 0))	**0.093023**
P01 (Prob (Yt = 0, Ys = 1))	**0.186047**

Output

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

Numeric Results

Numeric Results
Confidence Interval Formula: Agresti and Min's Wald + 2

C.I. Width Wᴅ	Number of Pairs N	Prob Yt=1 and Ys=0 P10	Prob Yt=0 and Ys=1 P01	Pt-Ps Diff	Std Error of Diff SE	Conf Level CL
0.21946	86	0.09302	0.18605	-0.09302	0.05599	0.95

This report gives the width as 0.21946 which validates this procedure since it is within rounding of 0.22.

Example 6 – Validation of the Bonett and Price Method using Bonett and Price (2012)

Bonett and Price (2012, page 484) present an example which we will use as our validation example. In this example, $P_{10} = \frac{50}{200} = 0.25, P_{01} = \frac{22}{200} = 0.11,$ and $N = 200$. The resulting 95% confidence interval for the difference is 0.057 to 0.220 which gives a width of 0.163.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. You may then make the appropriate entries as listed below, or open **Example 6** by going to the **File** menu and choosing **Open Example Template**.

Option	Value
Design Tab	
Solve For	**C.I. Width**
Confidence Interval Formula	**Bonett and Price's Adjusted Wald**
Confidence Level (1 - Alpha)	**0.95**
N (Number of Pairs)	**200**
Probability Input Type	**Enter Joint (Cell) Probabilities**
P10 (Prob (Yt = 1, Ys = 0))	**0.25**
P01 (Prob (Yt = 0, Ys = 1))	**0.11**

Output

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

Numeric Results

Numeric Results
Confidence Interval Formula: Bonett and Price's Adjusted Wald

C.I. Width W_D	Number of Pairs N	Prob Yt=1 and Ys=0 P10	Prob Yt=0 and Ys=1 P01	Pt-Ps Diff	Std Error of Diff SE	Conf Level CL
0.1625	200	0.25	0.11	0.14	0.04145	0.95

This report gives the width as 0.1625 which validates this procedure since it is within rounding of 0.163.