

## Chapter 812

# Lin's Concordance Correlation Coefficient

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### Introduction

Lin's concordance correlation coefficient (CCC) is the concordance between a new test or measurement (Y) and a gold standard test or measurement (X). This statistic quantifies the agreement between these two measures of the same variable (e.g. chemical concentration).

Like a correlation, CCC ranges from -1 to 1, with perfect agreement at 1. It cannot exceed the absolute value of  $\rho$ , Pearson's correlation coefficient between Y and X. It can be legitimately calculated on as few as ten observations. The coefficient and associated sample size formulas are presented in Lin (1989, 1992, 2000), Lin, Hedayat, Sinha, and Yang (2002), and Lin, Hedayat, and Wu (2012).

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### Technical Details

Following Lin et al. (2002), assume that  $n$  observations  $(Y_k, X_k)$  are selected from a bivariate population with means  $\mu_Y$  and  $\mu_X$ , variances  $\sigma_Y^2$  and  $\sigma_X^2$ , and correlation  $\rho$  (the Pearson correlation coefficient). Here,  $Y$  represents a measure from a candidate test or method and  $X$  represents the corresponding measure from the gold standard test or method.

The degree of concordance between the two measures can be characterized by the expected value of their squared difference

$$E[(Y - X)^2] = (\mu_Y - \mu_X)^2 + \sigma_Y^2 + \sigma_X^2 - 2\rho\sigma_Y\sigma_X.$$

This is the expected squared perpendicular deviation from a 45° line through the origin.

## Lin's Concordance Correlation Coefficient

If every pair from the bivariate population is in exact agreement, the above expectation would be 0. In order to create an index of concordance scaled to between -1 and 1, use the formula:

$$\begin{aligned}
 CCC &= 1 - \frac{E[(Y - X)^2]}{E[(Y - X)^2 | \rho = 0]} \\
 &= 1 - \frac{(\mu_Y - \mu_X)^2 + \sigma_Y^2 + \sigma_X^2 - 2\rho\sigma_Y\sigma_X}{(\mu_Y - \mu_X)^2 + \sigma_Y^2 + \sigma_X^2} \\
 &= \frac{2\rho\sigma_Y\sigma_X}{(\mu_Y - \mu_X)^2 + \sigma_Y^2 + \sigma_X^2} \\
 &= \rho \left( \frac{2}{\frac{(\mu_Y - \mu_X)^2}{\sigma_Y\sigma_X} + \frac{\sigma_Y}{\sigma_X} + \frac{\sigma_X}{\sigma_Y}} \right) \\
 &= \rho \left( \frac{2}{v^2 + \omega + \frac{1}{\omega}} \right) \\
 &= \rho \chi_a
 \end{aligned}$$

where

$$\begin{aligned}
 \chi_a &= \frac{2}{v^2 + \omega + \frac{1}{\omega}} \\
 \omega &= \frac{\sigma_Y}{\sigma_X} \\
 v &= \frac{|\mu_Y - \mu_X|}{\sqrt{\sigma_Y\sigma_X}}
 \end{aligned}$$

The quantity  $\omega$  is the *scale shift* and the quantity  $v$  is the *location shift relative to scale*. The correlation  $\rho$  is a measure of precision and the quantity  $\chi_a$  is a measure of accuracy.

As stated earlier,  $CCC$  obeys the inequalities

$$-1 \leq -|\rho| \leq CCC \leq |\rho| \leq 1.$$

From the above, it is evident that  $CCC$  is a function of  $\rho$ ,  $v$ , and  $\omega$ .

The value of  $CCC$  is estimated from a sample by  $\hat{CCC}$  where the usual sample counterparts are substituted into the above formula to obtain

$$\hat{CCC} = \frac{2S_{YX}}{(\bar{Y} - \bar{X})^2 + S_Y^2 + S_X^2}$$

## Lin's Concordance Correlation Coefficient

In order to achieve a better approximation with the normal distribution, Lin (1989) transforms  $C\hat{C}C$  using Fisher's Z transformation to obtain

$$\lambda(C\hat{C}C) = \tanh^{-1}(C\hat{C}C) = \frac{1}{2} \ln \left( \frac{1 + C\hat{C}C}{1 - C\hat{C}C} \right).$$

This quantity has an asymptotically normal distribution with mean

$$\lambda = \tanh^{-1}(CCC) = \frac{1}{2} \ln \left( \frac{1 + CCC}{1 - CCC} \right)$$

and variance

$$\sigma(\rho, v, \omega, n)^2 = \frac{1}{n-2} \left\{ \frac{(1-\rho^2)CCC^2}{(1-CCC^2)\rho^2} + \frac{2CCC^3(1-CCC)v^2}{\rho(1-CCC^2)^2} - \frac{CCC^4v^4}{2\rho^2(1-CCC^2)^2} \right\}$$

Lin (1992) indicates that rather just testing whether  $CCC$  is zero, it is more logical in this case to test whether  $CCC$  is greater than a threshold value,  $CCC0$ . This is analogous to a non-inferiority test of  $CCC$ . The null and alternative hypotheses are

$$H_0 : CCC \leq CCC0$$

$$H_1 : CCC > CCC0$$

The test is carried out by computing a lower confidence interval for  $CCC$  and checking whether the lower limit is greater than  $CCC0$ . If it is, the null hypothesis is rejected and the concordance of the new test procedure is established.

Here,  $CCC0$  represents the least acceptable value of  $CCC$ . An appropriate value for  $CCC0$  may be found using

$$CCC0 = \chi_a \sqrt{\rho_0^2 - d}$$

where  $d$  represents the  $100d\%$  loss in precision that can be tolerated and  $\rho^2$  represents the R-squared achieved when  $Y$  is regressed on  $X$ .

As shown in Lin et al. (2012 pages 14 and 71), the power of the above one-sided hypothesis test can be computed at  $\lambda_1$  (corresponding to  $CCC1$ ) using

$$1 - \beta = 1 - \Phi \left[ \frac{(\lambda_0 - \lambda_1) + \Phi^{-1}(1 - \alpha)\sigma_0}{\sigma_1} \right]$$

where

$$\sigma_0 = \sigma(\rho_0, v_0, \omega_0, n) \text{ and } \sigma_1 = \sigma(\rho_1, v_1, \omega_1, n)$$

This formula can be rearranged to obtain a formula for sample size.

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## 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.

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### Design Tab

The Design tab contains most of the parameters and options that you will be concerned with.

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#### Solve For

##### Solve For

This option specifies the parameter to be solved for from the other parameters. Select either *Power* for a power analysis or *Sample Size* for sample size determination.

Select *Sample Size* when you want to calculate the sample size needed to achieve a given power and alpha level. Select *Power* when you want to calculate the power of an experiment.

##### Input

There are two ways in which the parameters may be specified.

##### Input – Simple (CCC)

The simple input only requires the values of  $CCC_0$  and  $CCC_1$ . In this case,  $\rho = CCC$ ,  $v_0 = v_1 = 0$ , and  $\omega_0 = \omega_1 = 1$ .

##### Input – General ( $\rho$ , $u$ , $\omega$ )

The general input requires the values of  $\rho_0$ ,  $\rho_1$ ,  $v_0$ ,  $v_1$ ,  $\omega_0$ , and  $\omega_1$ .

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#### Power and Alpha

##### Power

This option specifies one or more values for power. Power is the probability of rejecting a false null hypothesis, and is equal to one minus beta. Beta is the probability of a type-II error, which occurs when a false null hypothesis is not rejected. In this procedure, a type-II error occurs when you fail to reject the null hypothesis of equal CCC's when in fact they are different.

Values must be between zero and one. Historically, the value of 0.80 was used for power. Now, 0.90 is also commonly used.

A single value may be entered here or a range of values such as *0.8 to 0.95 by 0.05* may be entered.

##### Alpha

This option specifies one or more values for the probability of a type-I error. A type-I error occurs when a true null hypothesis is rejected. In this procedure, a type-I error occurs when you reject the null hypothesis of equal CCC's when in fact they are equal.

Values must be between zero and one. Historically, the value of 0.05 has been used for two-sided tests and 0.025 for one-sided tests.

You may enter a single value such as 0.05 or a range of values such as *0.025 0.05 0.10* or *0.025 to 0.10 by 0.025*.

## Lin's Concordance Correlation Coefficient

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**Sample Size****n (Sample Size)**

Enter a value (or range of values) for the sample size (number of subjects). These values are ignored when you are solving for  $n$ .

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**Concordance Correlation Coefficient (CCC)****CCC0 (Lower Boundary)**

This is the value of CCC assumed by the null hypothesis,  $H_0$ . This is your statement of the lower bound on tolerable values of CCC. When the lower limit of a confidence interval computed for CCC is less than this value, concordance is not established. Otherwise, concordance is established.

In this case,  $\rho_0 = CCC_0$ ,  $v_0 = 0$ , and  $\omega_0 = 1$ .

The value(s) of CCC1 should be greater than this value.

**CCC1 (CCC for Power)**

This is the value of CCC assumed by the alternative hypothesis,  $H_1$ . This is the value at which the power of the test is computed.

In this case,  $\rho_1 = CCC_1$ ,  $v_1 = 0$ , and  $\omega_1 = 1$ .

The value(s) of CCC0 should be less than this value.

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**Precision or Correlation:  $\rho(Y, X)$**  **$\rho_0$  (Lower Boundary)**

This is the value of  $\rho$  (correlation between Y and X) assumed by the null hypothesis,  $H_0$ . It also serves as a lower boundary on permissible values of  $\rho$  computed from the data. If the lower confidence limit of a confidence interval for  $\rho$  computed from the sample is less than this amount, the concordance of Y is not established.

Since this value is a correlation, it must be between -1 and 1. However, for power and sample size computations, you should set keep this value greater than 0.

 **$\rho_1$  ( $\rho$  for Power)**

This is the value of  $\rho$  (correlation between Y and X) assumed by the alternative hypothesis,  $H_1$ . This is the value at which the power is computed.

This value must be greater than  $\rho_0$  and less than one.

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**Accuracy of Location:  $v = |\mu_Y - \mu_X| / \sqrt{(\sigma_Y \sigma_X)}$**  **$v_0$  (Upper Boundary)**

This is the value of  $v$  assumed by the null hypothesis,  $H_0$ . It also serves as an upper boundary on permissible values of  $v$ . It must be greater than  $v_1$ . When this value is set to 0, the means are assumed to be equal under the null hypothesis.

The formula for this value is 
$$v = \frac{|\mu_Y - \mu_X|}{\sqrt{\sigma_Y \sigma_X}}$$

## Lin's Concordance Correlation Coefficient

**u1 (u for Power)**

This is the value of  $\nu$  assumed by the alternative hypothesis, H1. It must be less than or equal to  $\nu_0$ . When this value is set to 0, the means are assumed to be equal under that alternative hypothesis.

The formula for this value is 
$$\nu = \frac{|\mu_Y - \mu_X|}{\sqrt{\sigma_Y \sigma_X}}$$
.

**Accuracy of Scale:  $\omega = \sigma_Y / \sigma_X$**  **$\omega_0$  (Upper Boundary)**

This is the value of  $\omega$  assumed by the null hypothesis, H0. It also serves as an upper boundary on permissible values of  $\omega$ . It must be greater than  $\omega_1$ . When this value is set to 1, the standard deviations of Y and X are assumed to be equal under the null hypothesis.

 **$\omega_1$  ( $\omega$  for Power)**

This is the value of  $\omega$  assumed by the alternative hypothesis, H1. It must be less than or equal to  $\omega_0$ . When this value is set to 1, the standard deviations are assumed to be equal under that alternative hypothesis.

**Example 1 – Power for Several Sample Sizes**

This example will calculate power for several sample sizes of a study designed to compare a gold standard measurement with a new measurement. The minimum value of  $\rho$  that can be tolerated is 0.97. Compute the power at  $\rho_1 = 0.975, 0.980, \text{ and } 0.985$ . The location shift,  $\nu$ , is assumed to be 0.15 under H0 and 0.05 under H1. The scale shift,  $\omega$ , is 1.15 under H0 and 1.05 under H1. Alpha is set to 0.05 and  $n$  is 10, 20, 30, or 40.

**Setup**

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Lin's Concordance Correlation Coefficient** procedure window by selecting it from the **Correlation** menu. You may then make the appropriate entries, 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>Power</b>
Input .....	<b>General</b>
Alpha .....	<b>0.05</b>
$n$ (Sample Size) .....	<b>10 to 40 by 10</b>
$\rho_0$ (Lower Boundary) .....	<b>0.97</b>
$\rho_1$ ( $\rho$ for Power) .....	<b>0.975 0.98 0.985</b>
$\nu_0$ (Upper Boundary) .....	<b>0.15</b>
$\nu_1$ ( $\nu$ for Power) .....	<b>0.05</b>
$\omega_0$ (Upper Boundary) .....	<b>1.15</b>
$\omega_1$ ( $\omega$ for Power) .....	<b>1.05</b>

Lin's Concordance Correlation Coefficient

Annotated Output

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

Numeric Results

Power	Sample Size (n)	Lin's	Lin's	$\rho(Y,X)$	$\rho(Y,X)$	$ \mu Y - \mu X $	$ \mu Y - \mu X $	$\sigma Y / \sigma X$	$\sigma Y / \sigma X$	Alpha
		CCC  H0 (CCC0)	CCC  H1 (CCC1)			$\sqrt{(\sigma Y \sigma X)}$  H0 (u0)	$\sqrt{(\sigma Y \sigma X)}$  H1 (u1)			
0.2784	10	0.950	0.973	0.970	0.975	0.150	0.050	1.150	1.050	0.05
0.4431	20	0.950	0.973	0.970	0.975	0.150	0.050	1.150	1.050	0.05
0.5740	30	0.950	0.973	0.970	0.975	0.150	0.050	1.150	1.050	0.05
0.6775	40	0.950	0.973	0.970	0.975	0.150	0.050	1.150	1.050	0.05
0.3844	10	0.950	0.978	0.970	0.980	0.150	0.050	1.150	1.050	0.05
0.6183	20	0.950	0.978	0.970	0.980	0.150	0.050	1.150	1.050	0.05
0.7711	30	0.950	0.978	0.970	0.980	0.150	0.050	1.150	1.050	0.05
0.8664	40	0.950	0.978	0.970	0.980	0.150	0.050	1.150	1.050	0.05
0.5308	10	0.950	0.983	0.970	0.985	0.150	0.050	1.150	1.050	0.05
0.8064	20	0.950	0.983	0.970	0.985	0.150	0.050	1.150	1.050	0.05
0.9263	30	0.950	0.983	0.970	0.985	0.150	0.050	1.150	1.050	0.05
0.9735	40	0.950	0.983	0.970	0.985	0.150	0.050	1.150	1.050	0.05

References

Lin, Lawrence I-Kuei. March, 1989. 'A Concordance Correlation Coefficient to Evaluate Reproducibility.' Biometrics 45, 255-268.  
 Lin, Lawrence I-Kuei. June, 1992. 'Assay Validation Using the Concordance Correlation Coefficient.' Biometrics 48, 599-604.  
 Lin, Lawrence I-Kuei. March, 2000. 'A Note on the Concordance Correlation Coefficient.' Biometrics 56, 324-325.  
 Lin, L., Hedayat, A.S., Sinha, B, and Yang, M. 2002. Statistical Methods in Assessing Agreement. JASA, 97(457), Pages 257-270.  
 Lin, L., Hedayat, A.S., Wu, W. 2012. Statistical Tools for Measuring Agreement. Springer, New York.

Report Definitions

X is the gold standard variable.  
 Y is the new variable.  
 Power is the probability of rejecting a false null hypothesis.  
 Sample Size (n) is the number of measurement pairs (new and gold-standard) in the study.  
 CCC0 is the value of Lin's concordance correlation coefficient assuming H0. CCC0 serves as a lower bound on acceptable values of CCC.  
 CCC1 is the value of Lin's concordance correlation coefficient assuming H1. It is the value at which the power is calculated.  
 $\rho 0$  is correlation between the new measurement (Y) and the gold-standard measurement (X) assuming H0. It serves as a lower bound on acceptable values of  $\rho$ .  
 $\rho 1$  is correlation between Y and X assuming H1. It is the value at which the power is calculated.  
 $u 0$  is the location shift assuming H0, where  $u = |\mu Y - \mu X| / \sqrt{(\sigma Y \sigma X)}$ .  $u 0$  serves as an upper bound on  $u$ .  
 $u 1$  is the location shift assuming H1. It is the value at which the power is calculated.  
 $\omega 0$  is the scale shift assuming H0, where  $\omega = \sigma Y / \sigma X$ .  $\omega 0$  serves as an upper bound on  $\omega$ .  
 $\omega 1$  is the scale shift assuming H1. It is the value at which the power is calculated.  
 Alpha is the probability of rejecting a true null hypothesis. It should be small.

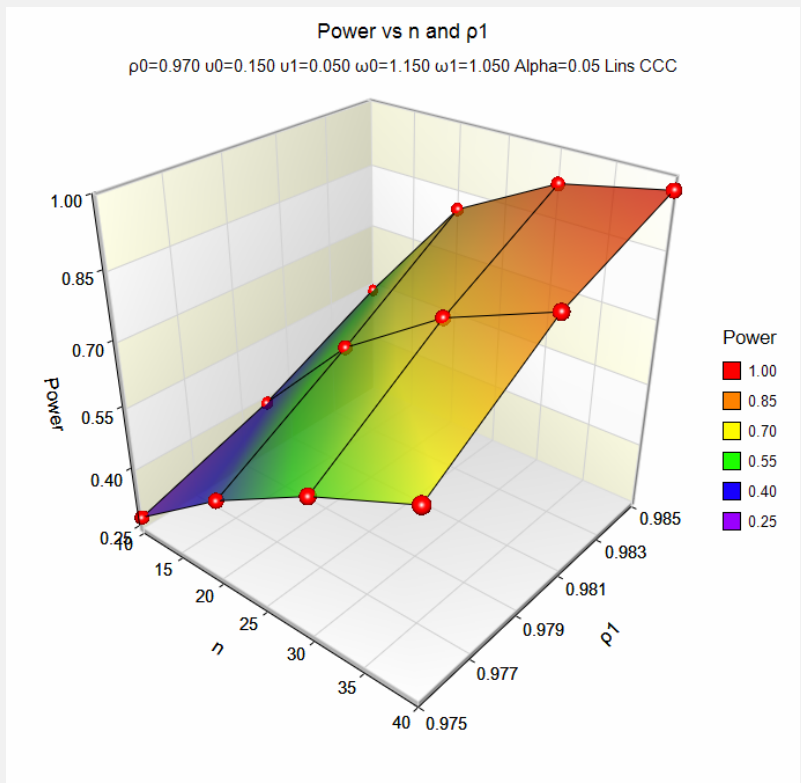
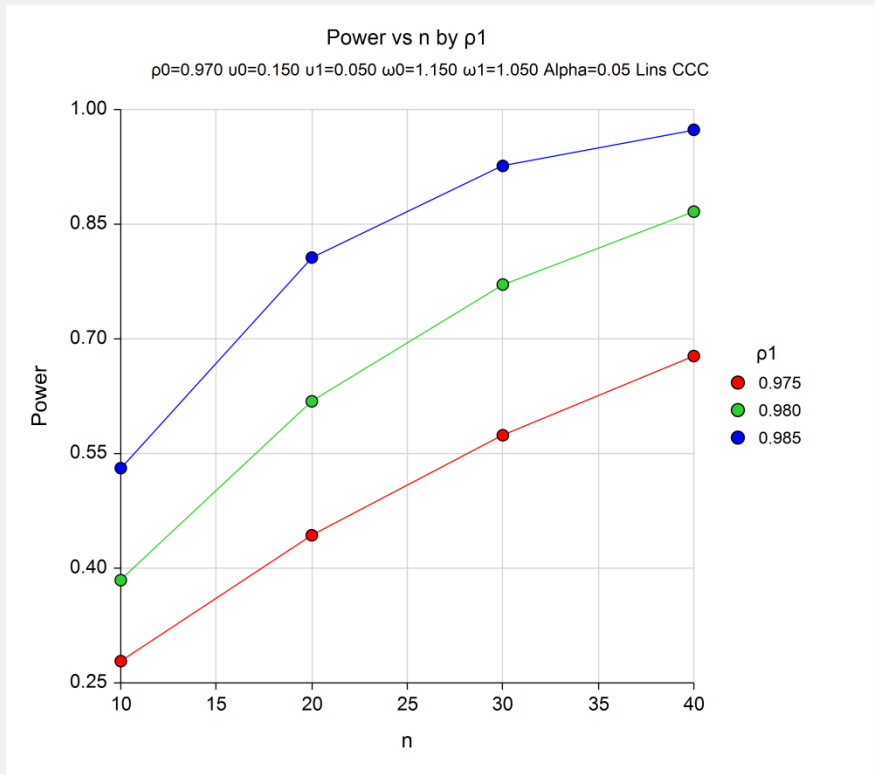
Summary Statements

In a study using Lin's concordance correlation coefficient to compare a new measurement method to the 'gold standard' method, a sample of 10 subjects results in 0.2784 power to determine whether the new method can be used instead of the gold standard. The statistical test uses a one-sided z test with a 0.05 significance level. The value of CCC is 0.950 under H0 and 0.973 under H1. The value of  $\rho$ , the correlation between Y and X, is 0.970 under H0 and 0.975 under H1. The value of  $u$ , the relative bias, is 0.150 under H0 and 0.050 under H1. The value of  $\omega$ , the ratio of the standard deviations, is 1.150 under H0 and 1.050 under H1.

This report shows the power for each of the scenarios.

Lin's Concordance Correlation Coefficient

Plots Section



This plot shows the relationship between power and sample size.



## Example 2 – Validation using Lin et al. (2002)

We will validate this procedure using the results of Lin et al. (2002). On page 264, in Table 1 of their article, they give the following example. With  $\rho_0 = 0.8$ ,  $\rho_1 = 0.8332$ ,  $\nu_0 = 0.15$ ,  $\nu_1 = 0.05$ ,  $\omega_0 = 1.15$ ,  $\omega_1 = 1.05$ ,  $\alpha = 0.05$ , and  $n = 30$ , they obtain a power of 0.1936.

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Lin's Concordance Correlation Coefficient** procedure window by selecting it from the **Correlation** menu. You may then make the appropriate entries, 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>Power</b>
Input .....	<b>General</b>
Alpha .....	<b>0.05</b>
n (Sample Size) .....	<b>30</b>
$\rho_0$ (Lower Boundary) .....	<b>0.8</b>
$\rho_1$ ( $\rho$ for Power) .....	<b>0.8332</b>
$\nu_0$ (Upper Boundary) .....	<b>0.15</b>
$\nu_1$ ( $\nu$ for Power) .....	<b>0.05</b>
$\omega_0$ (Upper Boundary) .....	<b>1.15</b>
$\omega_1$ ( $\omega$ for Power) .....	<b>1.05</b>

### Output

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

Numeric Results											
	Sample	Lin's	Lin's	$\rho(Y,X)$	$\rho(Y,X)$	$\frac{ \mu_Y - \mu_X }{\sqrt{(\sigma_Y \sigma_X)}}$	$\frac{ \mu_Y - \mu_X }{\sqrt{(\sigma_Y \sigma_X)}}$	$\frac{\sigma_Y}{\sigma_X}$	$\frac{\sigma_Y}{\sigma_X}$		
Power	Size	CCC	CCC	$\rho(Y,X)$	$\rho(Y,X)$	$\frac{ \mu_Y - \mu_X }{\sqrt{(\sigma_Y \sigma_X)}}$	$\frac{ \mu_Y - \mu_X }{\sqrt{(\sigma_Y \sigma_X)}}$	$\frac{\sigma_Y}{\sigma_X}$	$\frac{\sigma_Y}{\sigma_X}$		Alpha
0.1935	(n)	(CCC0)	(CCC1)	( $\rho_0$ )	( $\rho_1$ )	( $\nu_0$ )	( $\nu_1$ )	( $\omega_0$ )	( $\omega_1$ )		0.05
	30	0.784	0.831	0.800	0.833	0.150	0.050	1.150	1.050		

Note that PASS has calculated the power to be 0.1935, correct to within rounding.