Chapter 812

Lin's Concordance Correlation Coefficient

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 ρ, 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).

Technical Details

Following Lin et al. (2002), assume that *n* observations (Y_k, X_k) are selected from a bivariate population with means μ_Y and μ_X, variances σ_Y^2 and σ_X^2, and correlation ρ (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.

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:

where

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

where

$$\chi_a = \frac{2}{\upsilon^2 + \omega + \frac{1}{\omega}}$$

$$\omega = \frac{\sigma_Y}{\sigma_X}$$

$$\upsilon = \frac{|\mu_Y - \mu_X|}{\sqrt{\sigma_Y \sigma_X}}$$

The quantity ω is the *scale shift* and the quantity υ is the *location shift relative to scale*. The correlation ρ is a measure of precision and the quantity χ_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 ρ, υ, and ω.

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

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

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

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

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 ρ^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 by computed at λ_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

$\sigma_0 = \sigma(\rho_0, \upsilon_0, \omega_0, n)$ and $\sigma_1 = \sigma(\rho_1, \upsilon_1, \omega_1, n)$

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

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 ρ that can be tolerated is 0.97. Compute the power at ρ1 = 0.975, 0.980, and 0.985. The location shift, υ, is assumed to be 0.15 under H0 and 0.05 under H1. The scale shift, ω, 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

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 .... **Power**
Input... **General**
Alpha... **0.05**
n (Sample Size) .... **10 to 40 by 10**
ρ0 (Lower Boundary) **0.97**
ρ1 (ρ for Power).. **0.975 0.98 0.985**
υ0 (Upper Boundary) **0.15**
υ1 (υ for Power) **0.05**
ω0 (Upper Boundary)...................................... **1.15**
ω1 (ω for Power) **1.05**

Output

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

Numeric Reports

Numeric Results

Solve For: Power

Power	Sample Size n	Lin's CCC |H0 CCC0	Lin's CCC |H1 CCC1	ρ(Y,X) |H0 ρ0	ρ(Y,X) |H1 ρ1	|μY - μX| / √(σY σX) |H0 υ0	|μY - μX| / √(σY σX) |H1 υ1	σY / σX |H0 ω0	σY / σX |H1 ω1	Alpha
0.2784	10	0.95	0.973	0.97	0.975	0.15	0.05	1.15	1.05	0.05
0.4431	20	0.95	0.973	0.97	0.975	0.15	0.05	1.15	1.05	0.05
0.5740	30	0.95	0.973	0.97	0.975	0.15	0.05	1.15	1.05	0.05
0.6775	40	0.95	0.973	0.97	0.975	0.15	0.05	1.15	1.05	0.05
0.3844	10	0.95	0.978	0.97	0.980	0.15	0.05	1.15	1.05	0.05
0.6183	20	0.95	0.978	0.97	0.980	0.15	0.05	1.15	1.05	0.05
0.7711	30	0.95	0.978	0.97	0.980	0.15	0.05	1.15	1.05	0.05
0.8664	40	0.95	0.978	0.97	0.980	0.15	0.05	1.15	1.05	0.05

0.5308	10	0.95	0.983	0.97	0.985	0.15	0.05	1.15	1.05	0.05
0.8064	20	0.95	0.983	0.97	0.985	0.15	0.05	1.15	1.05	0.05
0.9263	30	0.95	0.983	0.97	0.985	0.15	0.05	1.15	1.05	0.05
0.9735	40	0.95	0.983	0.97	0.985	0.15	0.05	1.15	1.05	0.05

X The gold standard variable.
Y The new variable.
Power The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
n The sample size is the number of measurement pairs (new and gold-standard) in the study.
CCC0 The value of Lin's concordance correlation coefficient assuming H0. CCC0 serves as a lower bound on acceptable values of CCC.
CCC1 The value of Lin's concordance correlation coefficient assuming H1. It is the value at which the power is calculated.
ρ0 The correlation between the new measurement (Y) and the gold-standard measurement (X) assuming H0. It serves as a lower bound on acceptable values of ρ.
ρ1 The correlation between Y and X assuming H1. It is the value at which the power is calculated.
υ0 The location shift assuming H0, where $\upsilon = |\mu Y - \mu X| / \sqrt{(\sigma Y\ \sigma X)}$. υ0 serves as an upper bound on υ.
υ1 The location shift assuming H1. It is the value at which the power is calculated.
ω0 The scale shift assuming H0, where $\omega = \sigma Y / \sigma X$. ω0 serves as an upper bound on ω.
ω1 The scale shift assuming H1. It is the value at which the power is calculated.
Alpha The probability of rejecting a true null hypothesis.

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 0.95 under H0 and 0.973 under H1. The value of ρ, the correlation between Y and X, is 0.97 under H0 and 0.975 under H1. The value of υ, the relative bias, is 0.15 under H0 and 0.05 under H1. The value of ω, the ratio of the standard deviations, is 1.15 under H0 and 1.05 under H1.

Dropout-Inflated Sample Size

Dropout Rate	Sample Size n	Dropout-Inflated Enrollment Sample Size n'	Expected Number of Dropouts D
20%	10	13	3
20%	20	25	5
20%	30	38	8
20%	40	50	10

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 power is computed (as entered by the user). If n subjects are evaluated out of the n' subjects that are enrolled in the study, the design will achieve the stated power.
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. 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, 13 subjects should be enrolled to obtain a final sample size of 10 subjects.

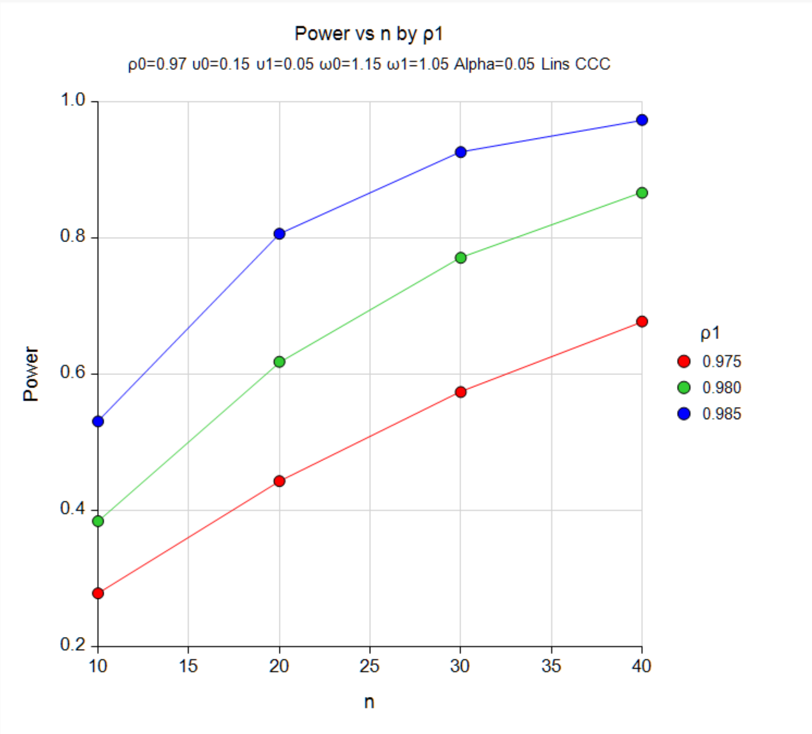
References

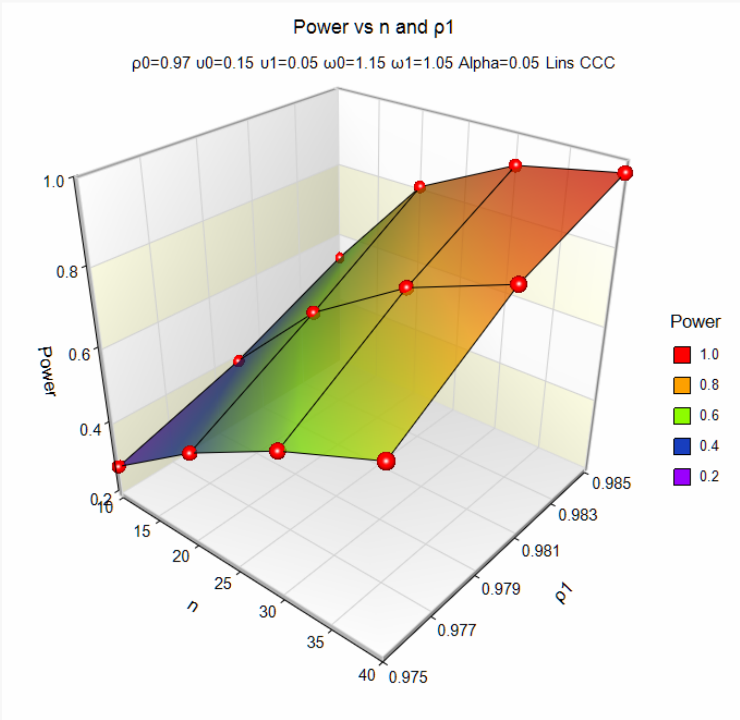
Lin, Lawrence I-Kuei. March, 1989. 'A Concordance Correlation Coefficient to Evaluate Reproducibility.' Biometrics 45, 255-268.
Lin, Lawrence I-Kuei. June, 1992. 'Assay Validation Using the Concordance Correlation Coefficient.' Biometrics 48, 599-604.
Lin, Lawrence I-Kuei. March, 2000. 'A Note on the 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), 257-270.
Lin, L., Hedayat, A.S., Wu, W. 2012. Statistical Tools for Measuring Agreement. Springer, New York.

This report shows the power for each of the scenarios.

Plots Section

Plots





These plots 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, $\upsilon 0$ = 0.15, $\upsilon 1$ = 0.05, $\omega 0$ = 1.15, $\omega 1$ = 1.05, alpha = 0.05, and n = 30, they obtain a power of 0.1936.

Setup

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 .... **Power**
Input... **General**
Alpha... **0.05**
n (Sample Size) **30**
ρ0 (Lower Boundary) **0.8**
ρ1 (ρ for Power).. **0.8332**
υ0 (Upper Boundary) **0.15**
υ1 (υ for Power) **0.05**
ω0 (Upper Boundary)..................................... **1.15**
ω1 (ω for Power) **1.05**

Output

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

Numeric Results

Solve For: Power

Power	Sample Size n	Lin's CCC |H0 CCC0	Lin's CCC |H1 CCC1	ρ(Y,X) |H0 ρ0	ρ(Y,X) |H1 ρ1	|μY - μX| / √(σY σX) |H0 υ0	|μY - μX| / √(σY σX) |H1 υ1	σY / σX |H0 ω0	σY / σX |H1 ω1	Alpha
0.1935	30	0.784	0.831	0.8	0.833	0.15	0.05	1.15	1.05	0.05

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