Chapter 837

Deming Regression

Introduction

This procedure provides sample size and power calculations for (unweighted) Deming regression when the goal of the study is to test whether the intercept is zero and the slope is one. An additional, simplifying assumption is made that the measurement standard deviation is constant throughout the range of the data. These results are based on the work of Linnet (1999).

Technical Details

Deming Regression

Deming regression is a technique for fitting a straight line to two-dimensional data where both variables, *X* and *Y*, are measured with error. This is different from simple linear regression where only the response variable, *Y*, is measured with error. Deming regression is often used for method comparison studies in clinical chemistry to look for systematic differences between two measurement methods. It is assumed that *X* represents the existing method and *Y* represents the new method.

Deming regression uses paired measurements, (x_i, y_i), measured with errors, ε_i and δ_i, where

$$x_i = X_i + \varepsilon_i$$

$$y_i = Y_i + \delta_i,$$

to estimate the intercept, A, and the slope, B, in the equation

$$\hat{Y}_i = A + B\hat{X}_i.$$

$\hat{X}_i$ and $\hat{Y}_i$ are estimates of the "true" (or expected) values of X_i and Y_i, respectively.

This procedure assumes that the measurement error ratio, $\lambda = V(\varepsilon_i)/V(\delta_i)$, is equal to one. Because of this, it gives the same result as orthogonal regression. It provides results using the unweighted method.

Hypotheses Concerning the Systematic Differences Between Methods

Using the Deming regression equation, the systematic difference, D_c, between the two methods at a particular level X_c is given by

$$D_c = Y_{est_c} - X_c = A + (B - 1)X_c$$

D_c is zero if A = 0 and B – 1 = 0. These two hypotheses can be tested using two t-tests:

$$t_A = (\hat{A} - 0)/SE(\hat{A})$$

$$t_B = (\hat{B} - 1)/SE(\hat{B})$$

One task that must be completed during the planning phase is to determine the size of D_c that is medically significant. This value can then be used to determine the corresponding values of *A* and *B* that should be used in the power calculations.

Experimental Design

This procedure assumes a very specific experimental design in which *N* objects are measured using both an existing method, *X*, and a new method, *Y*. To provide an estimate of the measurement error, each measurement is duplicated. Hence, each object is actually measured four times, twice using method *X* and twice using method *Y*.

Power of the Test that B = 1

This section will provide the formulas for calculating the power for the tests of *B* = 1 and *A* = 0. These results come from Linnet (1999, page 893).

The power of this test is computed as follows. First, compute t_B using

$$t_B = \frac{B - 1}{CV\,c_B}\sqrt{\frac{N}{2}} - \left|t_{\alpha/2,df}\right|$$

$$CV = \frac{\sigma_X}{x_m}$$

$$c_B = \sqrt{\frac{x_m^2}{U_V}}$$

$$U_V = \frac{(X_{max} - X_{min})^2}{12}$$

$$x_m = \frac{X_{max} + X_{min}}{2}$$

Note that U_V is used as an approximation of the sum of squares for *X*. It is the variance of a uniform random variable with boundaries X_{min} and X_{max} and σ_X^2 is the variance of the measurement error of *X*. This procedure makes the assumption that the variances of the measurement errors are approximately equal so that $\sigma_X^2 = \sigma_Y^2$. Note that σ_X^2 is estimated from the data using

$$\hat{\sigma}_X^2 = \frac{1}{2N}\sum_{i=1}^{N}(x_{1i} - x_{2i})^2$$

The power is computed as

$$\text{Power} = \mathrm{T}(-\infty < t_B)$$

where $T(x)$ is the CDF of a Student's t random variable with $df = N - 2$.

If the sample size is required, this power formula can be used in a binary search.

Power of the Test that the A = 0

The power of this test is computed as follows. First, compute t_A using

$$t_A = \frac{A}{c_A \sigma_X}\sqrt{\frac{N}{2}} - \left|t_{\alpha/2,df}\right|$$

where

$$c_A = \sqrt{1 + \frac{x_m^2}{U_V}}$$

The power is computed as

$$\text{Power} = \mathrm{T}(-\infty < t_A)$$

where $T(x)$ is the CDF of a Student's t random variable with $df = N - 2$.

If the sample size is required, this power formula can be used in a binary search.

Example 1 – Finding the Sample Size

Clinicians wish to conduct a method comparison study and analyze it with Deming Regression. They want to estimate the number of samples that must be measured when the significance level is 0.05, the power is 0.9, A is 0.2, B is 1.02 to 1.06, min X is 3, max X is 6, and CV is 0.02.

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**
Based On...**Both**
Power..**0.90**
Alpha...**0.05**
A (Intercept)..**0.2**
B (Slope)...**1.02 to 1.06 by 0.01**
Minimum X..**3**
Maximum X...**6**
Variation Input Type......................................**CV (Coefficient of Variation)**
CV (Coefficient of Variation) **0.02**

Output

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

Numeric Reports

Numeric Results

Solve For: Sample Size Based on the Minimum of the Intercept and Slope Powers
Regression Model: Y = A + BX
Intercept Hypotheses: H0: A = 0 vs. H1: A ≠ 0
Slope Hypotheses: H0: B = 1 vs. H1: B ≠ 1

Power		Sample Size	Regression Coefficients		X Method Statistics					
Intercept	Slope	N	Intercept	Slope	Min	Max	Mean	σ	CV	Alpha
1.00000	0.90030	286	0.2	1.02	3	6	4.5	0.09	0.02	0.05
0.99697	0.90201	129	0.2	1.03	3	6	4.5	0.09	0.02	0.05
0.94233	0.90018	73	0.2	1.04	3	6	4.5	0.09	0.02	0.05
0.90181	0.96059	62	0.2	1.05	3	6	4.5	0.09	0.02	0.05
0.90181	0.99325	62	0.2	1.06	3	6	4.5	0.09	0.02	0.05

Power (Intercept) The power of the t-test of the intercept regression coefficient.
Power (Slope) The power of the t-test of the slope regression coefficient.
Power The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N The number of samples that are measured by both methods. Two measurements are made using method X and another two measurements are made with method Y on each sample. This results in a total of four measurements per sample.
Intercept The value of the Y-intercept (A) regression coefficient in the Deming regression model: Y = A + BX. This is the value assumed by the alternative hypothesis. Under the null hypotheses, this value is zero.
Slope The value of the slope (B) regression coefficient in the Deming regression model: Y = A + BX. This is the value assumed by the alternative hypothesis. Under the null hypotheses, this value is one.
Min X The minimum measurement value possible for method X. Hence the range of X is [Min, Max]. Note that Min Y = Min X.
Max X The maximum measurement value possible for method X. Hence the range of X is [Min, Max]. Note that Max Y = Max X.
Mean X The population mean of the measurements made using method X. Note that Mean X = (Min X + Max X) / 2. This procedure makes the simplifying assumption that Mean Y = Mean X.
σ The population standard deviation of the difference in the duplicate measurements taken on each sample. This procedure makes the simplifying assumption that $\sigma_X = \sigma_Y = \sigma$.
CV The coefficient of variation of the measurements made by method X. CV = σ_X / (Mean X). This procedure makes the simplifying assumption that $CV_X = CV_Y = CV$.
Alpha The probability of rejecting a true null hypothesis.

Summary Statements

A method comparison study will be analyzed with Deming regression. A total of 286 samples will achieve 100% power for testing whether the intercept is zero and 90% power for testing whether the slope is one. Both tests are performed at the 0.05 level of significance. Duplicate measurements are made for each method on each sample for a total of four measurements per sample. Power is calculated assuming the intercept is 0.2 and the slope is 1.02. For both methods: the coefficient of variations are 0.02, the standard deviations are 0.09, the minimums are 3, the maximums are 6, and the means are 4.5.

Dropout-Inflated Sample Size

Dropout Rate	Sample Size N	Dropout-Inflated Enrollment Sample Size N'	Expected Number of Dropouts D
20%	286	358	72
20%	129	162	33
20%	73	92	19
20%	62	78	16
20%	62	78	16

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. 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. 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, 358 subjects should be enrolled to obtain a final sample size of 286 subjects.

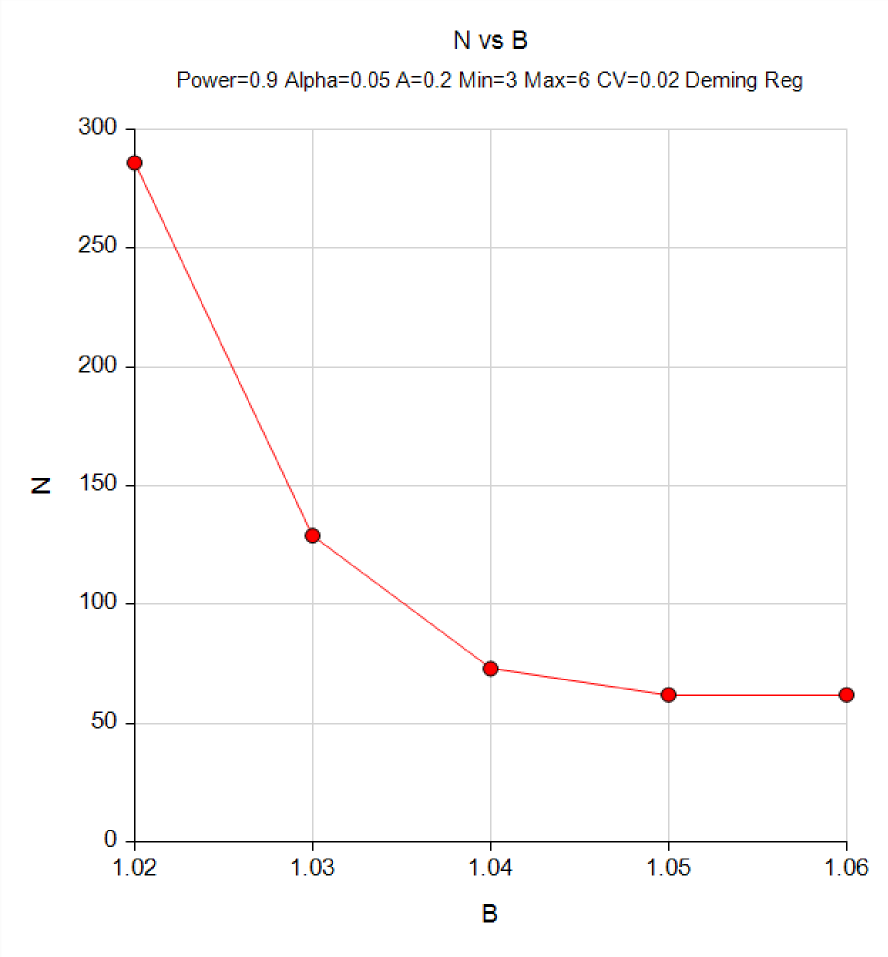
References

Linnet, Kristian. 1999. 'Necessary Sample Size for Method Comparison Studies Based on Regression Analysis.' Clinical Chemistry, Vol. 45:6, Pages 882-894.
Linnet, Kristian. 1990. 'Estimation of the Linear Relationship Between the Measurements of Two Methods with Proportional Errors.' Statistics in Medicine, Vol. 9, Pages 1463-1473.

These reports show the values of each of the parameters, one scenario per row.

Plots Section

Plots



This plot shows the relationship between the slope and sample size.

Example 2 – Validation using Linnet (1999)

Linnet (1999) pages 886-887 presents the following example which we will use to validate this procedure. In this example, the significance level is 0.05, the power is 0.9, A is 0.35, B is 1.058333, min X is 3, max X is 6, and CV is 0.02. The required sample size is 36.

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**
Based On.. **Both**
Power.. **0.90**
Alpha... **0.05**
A (Intercept) **0.35**
B (Slope)... **1.058333**
Minimum X... **3**
Maximum X.. **6**
Variation Input Type...................................... **CV (Coefficient of Variation)**
CV (Coefficient of Variation) **0.02**

Output

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

Numeric Results

Solve For: Sample Size Based on the Minimum of the Intercept and Slope Powers
Regression Model: Y = A + BX
Intercept Hypotheses: H0: A = 0 vs. H1: A ≠ 0
Slope Hypotheses: H0: B = 1 vs. H1: B ≠ 1

Power		Sample Size	Regression Coefficients		X Method Statistics					
Intercept	Slope	N	Intercept	Slope	Min	Max	Mean	σ	CV	Alpha
0.9884	0.90473	36	0.35	1.05833	3	6	4.5	0.09	0.02	0.05

PASS has also calculated the sample size as 36 which validate this procedure.

Note that the power of the intercept test is 0.9884 which is larger than the required 0.9 when N = 36.