Chapter 744

Equivalence Tests for Simple Linear Regression

Introduction

This procedure computes power and sample size for equivalence tests of the slope in simple linear regression. Simple linear regression is a commonly used procedure in statistical analysis to model a linear relationship between a dependent variable Y and an independent variable X.

Difference between Simple Linear Regression and Correlation

The correlation coefficient is used when *X* and *Y* are from a bivariate normal distribution. That is, *X* is assumed to be a random variable whose distribution is normal. The values of X will not be known until the study is completed. In the simple linear regression context, no statement is made about the distribution of *X*. In fact, *X* does not have to be a random variable. In this procedure the distribution of Y is conditioned on X.

Fixed or Random X

Gatsonis and Sampson (1989) present power analysis results for two approaches: *unconditional* and *conditional*. This procedure provides a calculation for the *conditional* (fixed X) approach.

The *unconditional* approach assumes that X is normally distributed and is based on the correlation coefficient. The normality assumption might occasionally be met, but not frequently. Our impression is that usually the values of X will not be known at the planning stage, and they will not follow (even approximately) the normal distribution. Hence, the only option available is to proceed with the sample size calculation using the *conditional* approach and then estimate the standard deviation of the X's as best you can.

Technical Details

Suppose that the dependence of a variable *Y* on another variable *X* can be modeled using the simple linear equation

$$Y = A + BX$$

In this equation, *A* is the *Y*-intercept, *B* is the slope, *Y* is the dependent variable, and *X* is the independent variable.

The nature of the relationship between *Y* and *X* is studied using a sample of *N* observations. Each observation consists of a data pair: the *X* value and the *Y* value. The values of *A* and *B* are estimated from these observations using the method of least squares. Using these estimated values, each data pair may be modeled using the equation

$$Y_i = a + bX_i + e_i$$

Note that *a* and *b* are the least squares estimates of the population parameters *A* and *B*. The *e* values represent the discrepancies between the estimated values (*a* + *bX*) and the actual values *Y*. They are called the errors or residuals.

If it is assumed that these *e* values are normally distributed, tests of hypotheses about *A* and *B* can be constructed. Specifically, we can employ a pair of T-tests to test the equivalence of B compared to an interval defined by two equivalence limits, B_L and B_U.

The Statistical Hypotheses

PASS follows the two one-sided tests (TOST) approach for equivalence testing described by Schuirmann (1987) and power analysis using the bivariate, noncentral t distribution described by Phillips (1990). The bivariate, noncentral t is evaluated using the algorithm of Owen (1965).

Parameter	Interpretation	
B	*Population slope.*	This parameter will be estimated using the method of least squares.
B1	*Actual population slope at which power is calculated*.	
		This is the assumed population slope used in all calculations.
B_L, B_U	*Equivalence Limits*.	These are the boundaries of the slope between which the slope of the new group will still be considered equivalent to the reference slope.
B_R	*Reference value*.	This is the slope of the reference population.
EM	*Equivalence Margin.*	This is a tolerance value that defines the proportion of the slope that is not of practical importance. This may be thought of as the largest difference from the reference value that is still considered to be trivial.

Equivalence Tests

With $B_L < B_U$, the null hypothesis of non-equivalence is

$$H_0: B_R \leq B_L \ \text{ or } \ B_R \geq B_U.$$

The alternative hypothesis of equivalence is

$$H_1: B_L < B_R < B_U.$$

A pair of one-sample t-tests are used to analyze the data. The test assumes that the data are a simple random sample from a population of normally-distributed values that have the same variance. This assumption implies that the residuals are continuous and normal.

The calculation of the two, one-sided t-tests proceeds as follows

$$t_L = \frac{b - B_L}{s_b}$$

$$t_U = \frac{b - B_U}{s_b}$$

where s_b is the sample standard error of the regression coefficient. The test is usually calculated using a $100(1 - 2\alpha)\%$ confidence interval of the slope. If both limits of this confidence interval are between B_L and B_U, equivalence is concluded.

Power Calculation of the Equivalence Test of the Regression Coefficient, B

The power of this test is

$$\Pr\big(t_L \geq t_{1-\alpha, N-2} \ \text{ and } \ t_U \leq t_{\alpha, N-2} | \Delta_L, \Delta_U\big)$$

where t_L and t_U are distributed as the bivariate, noncentral t distribution with noncentrality parameters Δ_L and Δ_U given by

$$\Delta_L = \frac{B_R - B_L}{\sqrt{\sigma_e^2/(\sigma_X^2 N)}}$$

$$\Delta_U = \frac{B_R - B_U}{\sqrt{\sigma_e^2/(\sigma_X^2 N)}}.$$

The above probability is evaluated using the algorithm of Owen (1965) and Phillips (1990).

The sample size is found using a binary search with this power formula.

Calculation of σ_X

The above calculation requires the value of σ_X, the (population) standard deviation of the X values in the regression analysis. Except for the occasional experimental design that includes a specification of the X values (e.g., doses), the specific X values are unknown in the planning phase. Hence, a reasonable estimate must be found. **PASS** includes a special tool called the *Standard Deviation Estimator* that will aid in your search for accurate estimates of this parameter.

The following table provides examples of typical data configurations and their corresponding standard deviations.

σ_X	X Values	σ_X	X Values	σ_X	X Values	σ_X	X Values
0.500	1, 2	0.816	1, 2, 3	1.118	1, 2, 3, 4	1.414	1, 2, 3, 4, 5
1.000	1, 3	1.633	1, 3, 5	2.236	1, 3, 5, 7	2.828	1, 3, 5, 7, 9
1.500	1, 4	2.449	1, 4, 7	3.354	1, 4, 7, 10	4.243	1, 4, 7, 10, 13
2.000	1, 5	3.266	1, 5, 9	4.472	1, 5, 9, 13	5.657	1, 5, 9, 13, 17
4.000	1, 9	6.532	1, 9, 17	8.944	1, 9, 17, 25	11.314	1, 9, 17, 25, 33

Because of the direct impact on the power and sample size, it will be important to spend some time determining appropriate values for this parameter.

One final note: when a basic pattern is repeated, its population standard deviation remains the same. For example, the standard deviation of the values 1, 2, 1, 2, 1, 2 is 0.5. This is also the standard deviation of 1, 2 or 1, 2, 1, 2.

Example 1 – Calculating the Power

Suppose a power analysis is required for a simple linear regression study that will perform an equivalence test of the relationship between two variables, *Y* and *X*. Further suppose that in the past, the slope has been 1 and it will be advantageous to show that the slope of a new manufacturing process is similar. The equivalence limits are defined a 0.8 and 1.2.

The analysis will look at the power of several sample sizes between 300 and 1300. A significance level of 0.05 will be used. Based on previous studies, σe will be assumed to be 0.6. The value of σx will assume that X is binary with equally-likely values of 1 and 2. The power will be computed at B1 = 0.9, 0.95, and 1.

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**
Alpha..**0.05**
N (Sample Size)...**300 500 700 900 1100 1300**
Equivalence Limit Input Type........................**Upper and Lower Equivalence Limits**
Bu (Upper Equivalence Limit) **1.2**
BL (Lower Equivalence Limit)........................**0.8**
B1 (Slope|H1) **0.9 0.95 1**
σx Input Type..**List of X Values**
List of X Values..**1 2**
σe Input Type...**σe (Std Dev of Residuals)**
σe (Std Dev of Residuals)............................**0.6**

Output

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

Numeric Reports

Numeric Results

Solve For: Power
Hypotheses: $H0: B \leq B_L$ or $B \geq B_U$ vs. $H1: B_L < B < B_U$

| | | Slope | | | Standard Deviation | | | | |
| | | Equivalence Limits | | | | | | | |
Power	Sample Size N	Lower B_L	Upper B_U	H1 (Actual) B1	X σx	Y σY	Residuals σe	R-Squared R²	Alpha
0.4151	300	0.8	1.2	0.90	0.5	0.750	0.6	0.360	0.05
0.6716	300	0.8	1.2	0.95	0.5	0.765	0.6	0.385	0.05
0.7833	300	0.8	1.2	1.00	0.5	0.781	0.6	0.410	0.05
0.5855	500	0.8	1.2	0.90	0.5	0.750	0.6	0.360	0.05
0.8729	500	0.8	1.2	0.95	0.5	0.765	0.6	0.385	0.05
0.9622	500	0.8	1.2	1.00	0.5	0.781	0.6	0.410	0.05
0.7123	700	0.8	1.2	0.90	0.5	0.750	0.6	0.360	0.05
0.9516	700	0.8	1.2	0.95	0.5	0.765	0.6	0.385	0.05
0.9943	700	0.8	1.2	1.00	0.5	0.781	0.6	0.410	0.05
0.8037	900	0.8	1.2	0.90	0.5	0.750	0.6	0.360	0.05
0.9823	900	0.8	1.2	0.95	0.5	0.765	0.6	0.385	0.05
0.9992	900	0.8	1.2	1.00	0.5	0.781	0.6	0.410	0.05
0.8684	1100	0.8	1.2	0.90	0.5	0.750	0.6	0.360	0.05
0.9938	1100	0.8	1.2	0.95	0.5	0.765	0.6	0.385	0.05
0.9999	1100	0.8	1.2	1.00	0.5	0.781	0.6	0.410	0.05
0.9130	1300	0.8	1.2	0.90	0.5	0.750	0.6	0.360	0.05
0.9979	1300	0.8	1.2	0.95	0.5	0.765	0.6	0.385	0.05
1.0000	1300	0.8	1.2	1.00	0.5	0.781	0.6	0.410	0.05

Power   The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
N   The size of the sample drawn from the population.
B_L The lower equivalence limit of the slope.
B_U The upper equivalence limit of the slope.
B1   The slope at which the power is calculated.
σx   The standard deviation of the X values.
σY   The standard deviation of Y (ignoring X).
σe   The standard deviation of the residuals.
R²   The R-squared value when Y is regressed on X.
Alpha   The probability of rejecting a true null hypothesis.

Summary Statements

A simple linear regression (single group, Y versus X) design will be used to test the equivalence of a slope (B), with lower and upper equivalence limits of 0.8 and 1.2 (H0: B ≤ 0.8 or B ≥ 1.2 versus H1: 0.8 < B < 1.2). The comparison will be made using two one-sided simple linear regression slope t-tests, with an overall Type I error rate (α) of 0.05. The standard deviation of X is assumed to be 0.5 (calculated from the given list of X values), and the standard deviation of residuals is assumed to be 0.6 (corresponding to a standard deviation of Y of 0.75 and an R² of 0.36). To detect a slope of 0.9 with a sample size of 300, the power is 0.4151.

Dropout-Inflated Sample Size

Dropout Rate	Sample Size N	Dropout-Inflated Enrollment Sample Size N'	Expected Number of Dropouts D
20%	300	375	75
20%	500	625	125
20%	700	875	175
20%	900	1125	225
20%	1100	1375	275
20%	1300	1625	325

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, 375 subjects should be enrolled to obtain a final sample size of 300 subjects.

References

Blackwelder, W.C. 1998. 'Equivalence Trials.' In Encyclopedia of Biostatistics, John Wiley and Sons. New York.
    Volume 2, 1367-1372.
Phillips, Kem F. 1990. 'Power of the Two One-Sided Tests Procedure in Bioequivalence'. Journal of
    Pharmacokinetics and Biopharmaceutics, Volume 18, No. 2, Pages 137-144.
Owen, Donald B. 1965. 'A Special Case of a Bivariate Non-Central t-Distribution'. Biometrika, Volume 52, Pages
    437-446.
Mathews, Paul. 2010. Sample Size Calculations - Practical Methods for Engineers and Scientists. Mathews Malnar
    and Bailey. Fairport Harbor, OH.
Dupont, W.D. and Plummer, W.D. Jr. 1998. 'Power and Sample Size Calculations for Studies Involving Linear
    Regression'. Controlled Clinical Trials, Vol. 19, Pages 589-601.
Chow, S.C., Shao, J., Wang, H., and Lokhnygina, Y. 2018. Sample Size Calculations in Clinical Research, Third
    Edition. Taylor & Francis/CRC. Boca Raton, Florida.

This report shows the calculated power for each of the scenarios.

Plots Section
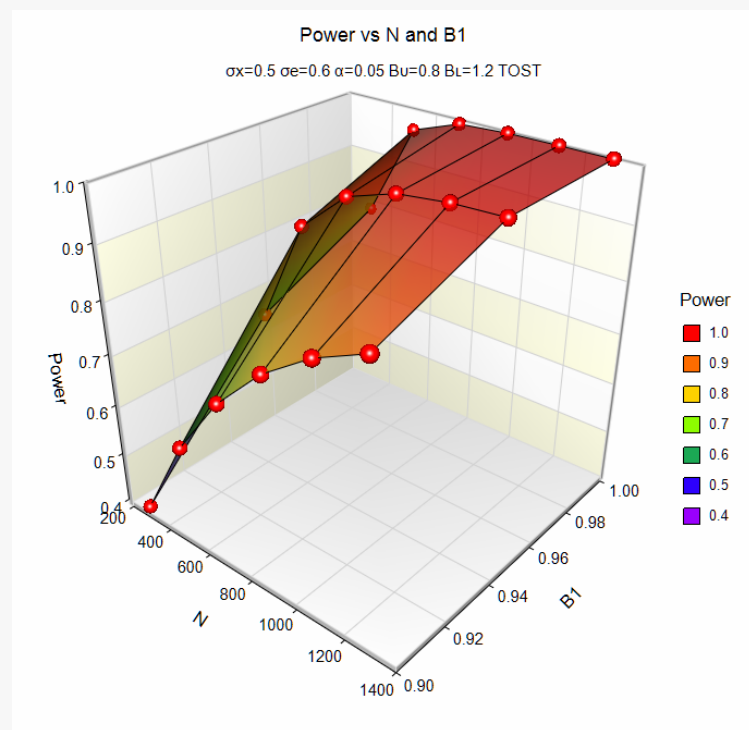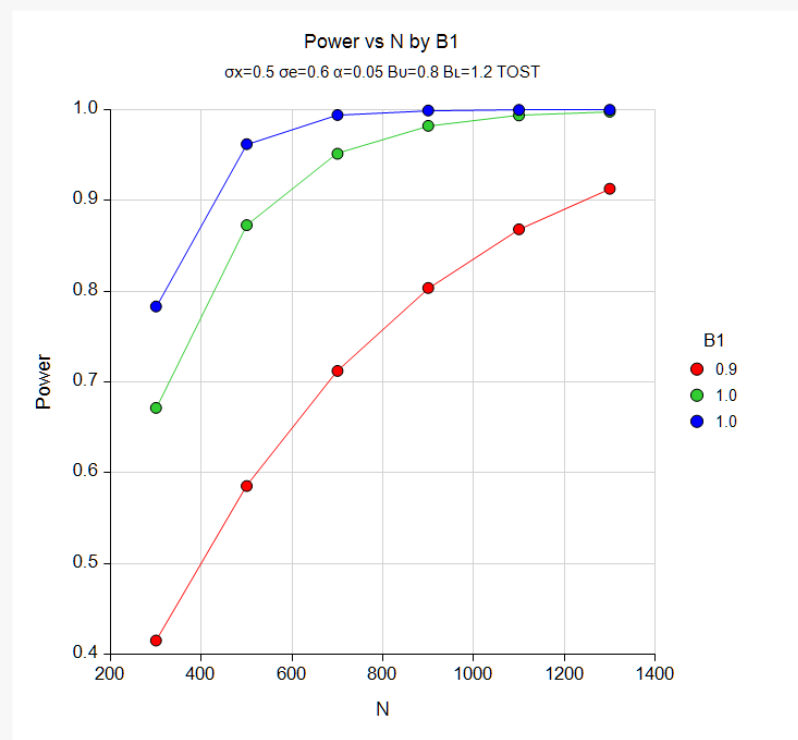
Plots
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These plots show the power versus the sample size for the three values of B1.

Example 2 – Validation using Another PASS Procedure

We could not find a validation example for this procedure in the literature. But since this procedure can be derived from the **One-Sample T-Tests for Equivalence** procedure, we will use an example from that previously validated procedure to validate this procedure.

In the other procedure, set the *Solve For* parameter to Sample Size. Also, set $Power = 0.9, EU = 1.2, EL = 0.8, \mu1 = 0.9\ 0.95\ 1, \alpha = 0.05$, and $\sigma = 0.6$.

The sample sizes are 310, 139, and 99.

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**
Power..**0.9**
Alpha...**0.05**
Equivalence Limit Input Type........................**Upper and Lower Equivalence Limits**
Bᴜ (Upper Equivalence Limit) **1.2**
Bʟ (Lower Equivalence Limit)........................**0.8**
B1 (Slope|H1) **0.9 0.95 1**
σx Input Type..**σx (Std Dev of X)**
σx (Std Dev of X) **1**
σe Input Type..**σe (Std Dev of Residuals)**
σe (Std Dev of Residuals)..............................**0.6**

Output

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

Numeric Results

Solve For: Sample Size
Hypotheses: H0: B ≤ Bʟ or B ≥ Bᴜ vs. H1: Bʟ < B < Bᴜ

		Slope				Standard Deviation			
	Sample Size N	Equivalence Limits							
		Lower Bʟ	Upper Bᴜ	H1 (Actual) B1	X σx	Y σY	Residuals σe	R-Squared R²	
Power									Alpha
0.9003	310	0.8	1.2	0.90	1	1.082	0.6	0.692	0.05
0.9005	139	0.8	1.2	0.95	1	1.124	0.6	0.715	0.05
0.9008	99	0.8	1.2	1.00	1	1.166	0.6	0.735	0.05

The sample sizes of 310, 139, and 99 match the results from the other procedure.