

Chapter 827

Joint Tests of Mediation in Linear Regression with Continuous Variables

Introduction

This procedure computes power and sample size for evaluating mediation analysis of a continuous dependent variable Y and continuous independent variables X and M . It is assumed that joint testing will be made of both links (regression models) of an indirect pathway assuming that the tests are asymptotically independent. The sample size calculations are based on the work of Vittinghoff and Neilands (2015).

Mediation Model

An in-depth discussion of mediation can be found in Hayes (2018). A popular method for testing for mediation is that of Baron and Kenny (1986). In this method, three regression models are fit where $M \sim N(\mu_M, \sigma_M^2)$ and $X \sim N(\mu_X, \sigma_X^2)$.

- (1) $M = \theta_0 + \theta_X X + e_M, e_M \sim N(0, \sigma_{e_M}^2)$
- (2) $Y = \beta_0 + \beta_X X + \beta_M M + e_Y, e_Y \sim N(0, \sigma_{e_Y}^2)$
- (3) $Y = \beta_0^* + \beta_X^* X + e_{Y^*}$

Vittinghoff, Sen, and McCulloch (2009) derived sample size formulas based on testing the significance of β_M in model 2. Vittinghoff and Neilands (2015) extended these results to give results for testing $\theta_X = 0$ in model 1 and $\beta_M = 0$ in model 2 simultaneously. They added adjustment factors for confounders in model 1 and model 2. They also added an adjustment for cluster randomized designs, if they are used.

Calculating the Power

Power calculations are based on standard normal distribution. They proceed as follows:

1. Determine the critical value $z_{1-\alpha}$ from the standard normal distribution where α is the probability of a type-I error.
2. Calculate: $z_{\beta_1} = \sqrt{\frac{N\sigma_X^2\theta_X^2(1-R_X^2)}{\delta\sigma_M^2(1-\rho_{XM}^2)}} - z_{1-\alpha}$.
2. Calculate: $z_{\beta_2} = \sqrt{\frac{N\sigma_M^2\beta_M^2(1-\rho_{XM}^2)(1-R_M^2)}{\delta\sigma_{e_Y}^2}} - z_{1-\alpha}$.
3. Calculate: Power = $\Phi(z_{\beta_1})\Phi(z_{\beta_2})$.

Notes

1. Use $\frac{\alpha}{2}$ instead of α for two-sided test.
2. $\rho_{XM} = \theta_X\sigma_X/\sigma_M$ must be between -1 and 1.
3. R_X^2 is squared multiple correlation of X on any confounding variables.
4. R_M^2 is squared multiple correlation of M on any confounding variables.
5. δ is the design effect which is defined as the ratio of the actual variance of Y with clustering to its variance under simple random sampling.

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.

Design Tab

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

Solve For

Solve For

This option specifies the parameter to be solved for from the other parameters. Under most situations, you will select either *Power* or *N (Sample Size)*.

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.

Test Direction

Alternative Hypothesis

Specify whether the hypothesis test is one-sided or two-sided. When a two-sided test is selected, the value of alpha is automatically divided by two. A two-sided test requires alpha to be less than 0.50.

Power and Alpha

Power

In this case of the joint testing of two hypotheses, Power is the product of the powers of those two individual hypotheses. This assumes that the two tests are approximately independent.

The two null hypotheses are

1. H01: $\theta_X = 0$ in model 1.
2. H02: $\beta_M = 0$ in model 2.

Range

Values must be between zero and one. Historically, the value of 0.80 (Beta = 0.20) was used for power. Now, 0.90 (Beta = 0.10) 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 (alpha) which is used for both tests. A type-I error occurs when you reject the joint null hypothesis when in fact it is true.

Values of alpha must be between zero and one. Historically, the value of 0.05 has been used for alpha. This means that about one test in twenty will falsely reject the null hypothesis. You should pick a value for alpha that represents the risk of a type-I error you are willing to take in your experimental situation.

You may enter a range of values such as *0.01 0.05 0.10* or *0.01 to 0.10 by 0.01*.

Sample Size

N (Sample Size)

This option specifies the value(s) for N , the sample size. Note that $3 < N$.

Effect Size

θ_X (Reg Coef of X in Model 1)

Enter one or more values for θ_X , which is the coefficient of X in model 1:

$$\text{Model 1: } M = \theta_0 + \theta_X(X) + e_M$$

where X is the primary predictor variable and M is the mediator variable.

Range

θ_X can be any value other than zero. It is in the same scale as σ_X .

β_M (Reg Coef of M in Model 2)

Enter one or more values for β_M , which is the coefficient of M in the regression model

$$Y = \beta_0 + \beta_X(X) + \beta_M(M) + e_Y$$

where X is the primary predictor variable and M is the mediator variable.

Range

β_M can be any value other than zero. It is in the same scale as σ_M .

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σ_X (Standard Deviation of X)

Enter one or more values for the standard deviation of X, the primary predictor variable.

Range

$$0 < \sigma_X.$$

σ_M (Standard Deviation of M)

Enter one or more values for the standard deviation of M, the mediator variable.

Range

$$0 < \sigma_M.$$

σ_e (Standard Deviation of e_Y)

Enter one or more values for the standard deviation of e_Y from the model

$$Y = \beta_0 + \beta_X(X) + \beta_M(M) + e_Y$$

Range

$$0 < \sigma_e.$$

DE (Design Effect)

DE is the design effect. It is used to adjust the sample size when a cluster randomized trial is being used. It is the ratio of actual variance of the outcome, Y, with clustering to its variance assuming simple random sampling.

Range

Any value greater than zero can be used. If you are NOT using a cluster randomized trial, then enter 1.0.

R^2_X (R^2 of Confounders in Model 1)

Enter one or more values of R^2_X . This value is used to form a correction factor when confounders are used in Model 1. This value is the value of R^2 that is achieved when X is regressed on the confounders.

Range

$$0 \leq R^2_X < 1.$$

If there are no confounders, enter '0'.

R^2_M (R^2 of Confounders in Model 2)

Enter one or more values of R^2_M . This value is used to form a correction factor when confounders are used in Model 2. This value is the value of R^2 that is achieved when M is regressed on the confounders.

Range

$$0 \leq R^2_M < 1.$$

If there are no confounders, enter '0'.

Example 1 – Finding Sample Size

Researchers are studying the relationship between a dependent variable (Y) and an independent variable (X). They want to understand the impact of a third variable (M) on the relationship between X and Y, so they decide to carry out a mediation analysis. They decide to determine the sample size based on the joint significance tests. Using prior analyses, they decide to use $\theta_x = 0.5, 0.7$; $\beta_M = 0.5, 0.6, 0.7$, $\sigma_x = \sigma_M = \sigma_e = DE = 1$; $R^2_x = 0.1$; and $R^2_M = 0.2$. They set the power at 0.9 and the two-sided significance level at 0.05.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Joint Tests of Mediation in Linear Regression with Continuous Variables** procedure. 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**.

| <u>Option</u> | <u>Value</u> |
|--|------------------------|
| Design Tab | |
| Solve For | N (Sample Size) |
| Alternative Hypothesis | Two-Sided |
| Power..... | 0.90 |
| Alpha..... | 0.05 |
| θ_x (Reg Coef of X in Model 1) | 0.5 0.7 |
| β_M (Reg Coef of M in Model 2) | 0.5 0.6 0.7 |
| σ_x (Standard Deviation of X) | 1 |
| σ_M (Standard Deviation of M) | 1 |
| σ_e (Standard Deviation of e_Y)..... | 1 |
| DE (Design Effect)..... | 1 |
| R^2_x (R^2 of Confounders in Model 1)..... | 0.1 |
| R^2_M (R^2 of Confounders in Model 2) | 0.2 |

Annotated Output

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

Numeric Results

| Numeric Results | | | | | | | | | | | | |
|----------------------------------|-------------------|-------------|---------------|---------------|-----------------|--------------|--------------|------------------|------------------|------------------|---------|-------|
| Two-sided alternative hypothesis | | | | | | | | | | | | |
| Joint Power | Individual Powers | Sample Size | Reg Coef of X | Reg Coef of M | Corr of X and M | Std Dev of X | Std Dev of M | Std Dev of e_Y | R^2 Conf Mdl 1 | R^2 Conf Mdl 2 | Des Eff | Alpha |
| | Pw1/Pw2 | N | θ_x | β_M | ρ_{XM} | σ_x | σ_M | σ_e | R^2_x | R^2_M | DE | |
| 0.9002 | 0.996/0.904 | 71 | 0.50 | 0.50 | 0.50 | 1.00 | 1.00 | 1.00 | 0.10 | 0.20 | 1.00 | 0.050 |
| 0.9030 | 0.979/0.923 | 53 | 0.50 | 0.60 | 0.50 | 1.00 | 1.00 | 1.00 | 0.10 | 0.20 | 1.00 | 0.050 |
| 0.9044 | 0.953/0.949 | 44 | 0.50 | 0.70 | 0.50 | 1.00 | 1.00 | 1.00 | 0.10 | 0.20 | 1.00 | 0.050 |
| 0.9027 | 1.000/0.903 | 104 | 0.70 | 0.50 | 0.70 | 1.00 | 1.00 | 1.00 | 0.10 | 0.20 | 1.00 | 0.050 |
| 0.9018 | 1.000/0.902 | 72 | 0.70 | 0.60 | 0.70 | 1.00 | 1.00 | 1.00 | 0.10 | 0.20 | 1.00 | 0.050 |
| 0.9024 | 1.000/0.902 | 53 | 0.70 | 0.70 | 0.70 | 1.00 | 1.00 | 1.00 | 0.10 | 0.20 | 1.00 | 0.050 |

| References | |
|--|--|
| Vittinghoff, E. and Neilands, T.B. 2015. 'Sample size for Joint Testing of Indirect Effects.' <i>Prevention Science</i> , Vol. 16(8), Pages 1128-1135. | |
| Vittinghoff, E., Sen, S., and McCulloch, C.E. 2009. 'Sample size calculations for evaluating mediation.' <i>Statistics in Medicine</i> , Vol. 28, Pages 541-557. | |

Joint Tests of Mediation in Linear Regression with Continuous Variables

Report Definitions

Hypotheses: $H_0: \beta_M = 0$ versus $H_1: \beta_M \neq 0$. (Two-Sided).

X is the primary predictor. It is an independent variable.

M is the mediator. It is the dependent variable in model 1 and an independent variable in model 2.

Model 1: $M = \theta_0 + \theta_x(X) + \epsilon_M$.

Model 2: is $Y = \beta_0 + \beta_x(X) + \beta_M(M) + \epsilon_Y$. The ϵ_Y 's are normally distributed.

Power is the probability of rejecting a false pair of null hypotheses that both θ_x and β_M are zero.

Pw1 is the probability of rejecting a false null hypotheses that θ_x is zero in model 1.

Pw2 is the probability of rejecting a false null hypotheses that β_x is zero in model 2.

N is the number of observations on which the multiple regressions are computed.

θ_x is the regression coefficient of X in model 2.

β_M is the regression coefficient of the mediator in model 2.

ρ_{XM} is the correlation between X and M.

σ_X is the standard deviation of X.

σ_M is the standard deviation of M.

σ_{ϵ_Y} is the standard deviation of the ϵ_Y in the model.

R^2_X is R^2 achieved when X is regressed on any confounder variables in model 1.

R^2_M is R^2 achieved when M is regressed on any confounder variables in model 2.

DE is the design effect (the ratio of actual variance of the outcome, Y, with clustering to its variance assuming simple random sampling).

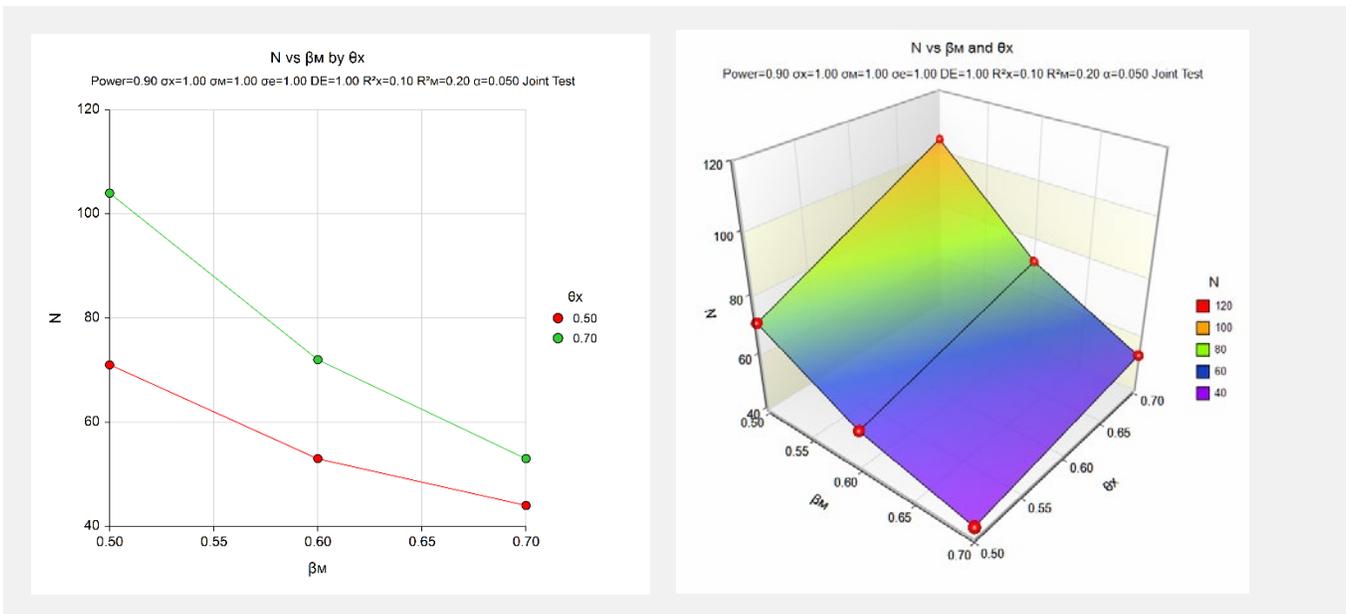
Alpha is the probability of rejecting a true null hypothesis. It should be small.

Summary Statements

A sample size of 71 achieves 90% joint power to detect $\theta_x = 0$ in model 1 and $\beta_M = 0$ in model 2 (assuming the independence of models 1 and 2) when the two-sided significance level (alpha) is 0.050. The individual power associated with model 1 is 100. The individual power associated with model 2 is 90. The regression coefficient, θ_x , in model 1 is 0.50. The regression coefficient, β_M , in model 2 is 0.50. The standard deviation of the primary predictor variable, X, is 1.00. The standard deviation of the mediator variable, M, is 1.00. The standard deviation of the residuals in model 2 is 1.00. The correlation between X (the primary predictor) and M (mediator) is 0.50. The R^2 achieved when X is regressed on any confounder variables in model 1 is 0.10. The R^2 achieved when M is regressed on any confounder variables in model 2 is 0.20. The design effect (the ratio of actual variance of the outcome, Y, with clustering to its variance assuming simple random sampling) is 1.00.

This report shows the necessary sample sizes. The definitions of each of the columns is given in the Report Definitions section.

Plots Section



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

Example 2 – Validation using Vittinghoff (2015)

Vittinghoff et al. (2015) present an example which $\theta_X = 0.25$; $\beta_M = 0.2$, $\sigma_X = \sigma_M = \sigma_e = DE = 1$; $R^2_X = 0.0$; and $R^2_M = 0.09$. They set the power at 0.8 and the two-sided significance level at 0.05. The computed N is 240.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Joint Tests of Mediation in Linear Regression with Continuous Variables** procedure. 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**.

| <u>Option</u> | <u>Value</u> |
|--|------------------------|
| Design Tab | |
| Solve For | N (Sample Size) |
| Alternative Hypothesis | Two-Sided |
| Power | 0.80 |
| Alpha | 0.05 |
| θ_X (Reg Coef of X in Model 1) | 0.25 |
| β_M (Reg Coef of M in Model 2) | 0.2 |
| σ_X (Standard Deviation of X) | 1 |
| σ_M (Standard Deviation of M) | 1 |
| σ_e (Standard Deviation of e_Y) | 1 |
| DE (Design Effect) | 1 |
| R^2_X (R^2 of Confounders in Model 1) | 0.0 |
| R^2_M (R^2 of Confounders in Model 2) | 0.09 |

Output

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

Numeric Results

| Numeric Results | | | | | | | | | | | | |
|----------------------------------|------------------------------|------------------|--------------------------------|-------------------------------|--------------------------------------|-------------------------------|-------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|---------------|-------|
| Two-sided alternative hypothesis | | | | | | | | | | | | |
| Joint Power | Individual Powers Pw1/Pw2 | Sample Size N | Reg Coef of X θ_X | Reg Coef of M β_M | Corr of X and M ρ_{XM} | Std Dev of X σ_X | Std Dev of M σ_M | Std Dev of e_Y σ_e | R^2 Conf Mdl 1 R^2_X | R^2 Conf Mdl 2 R^2_M | Des Eff DE | Alpha |
| 0.8014 | 0.980/0.818 | 241 | 0.25 | 0.20 | 0.25 | 1.00 | 1.00 | 1.00 | 0.00 | 0.09 | 1.00 | 0.050 |

PASS obtained 241 which is one higher than the 240 they calculated. It turns out that 240 has achieved a power that is slightly less than the 0.8 that was desired. Thus, 241 is the correct answer.