Paper PO-19

Sample Size Calculation to Evaluate Mediation Analysis

Rajendra Kadel, University of South Florida, Tampa, Florida

ABSTRACT

Mediation analysis is used to review the comparative change in the amount of strength of association of the primary predictor with the outcome after adjustment for the mediator. Mediation models are very widely used in social sciences and biomedical sciences. Before conducting mediation studies, researchers want to know the sample size (i.e. number of subjects) required for achieving the adequate power when testing for mediation. To the author's knowledge, there is no any SAS® procedure that produces sample size calculation for mediation analysis. The author presents a macro that implements the methodology for sample size calculation for mediation analysis written by Vittinghoff et al. (2009). It implements the methods to calculate sample sizes for the linear regression models. Very basic understanding of SAS is enough to use this macro. SAS Macro programming skill is not expected. When the macro is invoked, a series of windows will pop-up asking user to input required information. Output will be presented in SAS output window as well as in Microsoft word document. This macro is tested on Windows SAS 9.1 and above.

INTRODUCTION

Mediation analysis is used to review the comparative change in the amount of strength of association of the primary predictor with the outcome after adjustment for the mediator. Mediation models are very widely used in social sciences, especially in psychological studies. Before conducting mediation studies, researchers want to know the sample size (i.e. number of subjects) required for achieving the adequate power when testing for mediation. This problem of sample size calculation for testing the mediation effect of intermediate variable to the primary predictor is a common issue in epidemiologic and clinical research. To the author's knowledge, there is no any SAS procedure or that produces sample size calculation for mediation analysis. The SAS macro presented in this paper will be used to calculate sample for testing mediation effect based on Vittinghoff et al. (2009). They proposed the method based on variance inflation factor in regression that provide the exact sample size for linear model and approximations for logistic, Poisson, and Cox models. In this paper, I will present sample size calculation for linear models. The following four cases will be considered: (a) continuous primary predictor, continuous mediator (b) binary primary predictor, continuous mediator (c) continuous primary predictor, binary mediator, and (d) binary primary predictor, binary mediator. The authors argued that their method are also applicable to detecting the independent effect of a primary predictor in the presence of substantial confounding The method of sample size calculation is based on the Wald tests as these tests are more common in practice even though these methods are less reliable in case of small samples and if the alternative hypothesis are far from null.

SAMPLE SIZE CALCULATION FOR LINEAR MODEL

Let Y be the response, X_1 a primary predictor variable and X_2 is a mediator variable. The simple linear regression model takes the form

$$y_i = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \varepsilon_i,\ \varepsilon_i \sim N(0, \sigma_e^2) \qquad (1)$$

Where β_1 is the estimator of primary predictor (X_1) before the adjustment of mediator (X_2), β_2 is the regression coefficient for the mediator (X_2) and σ_e^2 is the variance of the random error term in the linear regression. If β_1^* is the estimator of the primary predictor (X_1) before the adjustment of mediator (X_2) in the full model (1), then proportion of treatment effect explained (PTE), which assess the mediation as the relative change in the strength of association of the primary predictor with the outcome after adjustment for the mediator, is of the form

$$\frac{\widehat{\beta_1^*} - \widehat{\beta_1}}{\widehat{\beta_1^*}} \qquad (2)$$

Vittinghoff et al. (2009) showed that for the linear regression (1), testing the mediation effect is equivalent to testing the null hypothesis H_0: $\beta_2 = 0$ versus the alternative hypothesis H_a: $\beta_2 \neq 0$. They also showed that, provided the full model is correctly specified, this is equivalent to testing PTE = 0 , provided the Pearson correlation of X_1 and X_2, $\rho \neq 0$. This will lead to the following equation to calculate sample size

$$n = \frac{(z_\alpha + z_\gamma)^2 \sigma_e^2}{{\beta_2}^2 \sigma_2^2 (1 - \rho^2)} \quad (3)$$

Where z_α and z_γ are the quintiles of the standard normal distribution corresponding to the specified one-sided type-I and type-II error rates, σ_e^2 is the residual variance of the outcome, σ_2^2 is the variance of the mediator (X_2) . Alternative to formula (3) are provided by Vittinghoff et al. (2009) if values of PTE, β_1^* and β_1 available. The following equations 4-6 are the alternative to equation (3)

$$n = \frac{(\mathrm{z}_\alpha + \mathrm{z}_\gamma)^2 \, \rho^2 \, \sigma_\mathrm{e}^2}{(\beta_1^* \sigma_1 PTE)^{\,2} (1 - \rho^2)} \quad (4)$$

$$n = \frac{(z_\alpha + z_\gamma)^2 \sigma_e^2}{(\beta_2 \sigma_2)^2 - (\beta_1^* \sigma_1 PTE)^2} \quad (5)$$

$$n = \frac{(z_\alpha + z_\gamma)^2 \sigma_e^2}{(\beta_2 \sigma_2)^2 - [(\beta_1^* - \beta_1)\sigma_1]^2} \quad (6)$$

If either of primary predictor X_1 and mediator X_2 is binary, its variance will be $\sigma_j^2 = f_j(1 - f_j)$, $j = 1,2$. Here, $f_j = Pr(X_j = 1)$ is the marginal prevalence. This indicates that formula (3) –(6) provided in Vittinghoff et al. (2009) can be used both for continuous and binary predictors.

PARAMETERS AND DEFAULT VALUES

The following are the list of the parameters and their default values that are used to calculate the sample size for mediation analysis in case of simple linear regression. The macro program will ask availability of certain parameter and uses one of the formulas (3) – (6) to calculate sample size. These formulas give user a choice depending upon which parameters can be most easily or readily available what information is available. However, it is not necessary for the user to indentify which formula to use in each of these cases. First three of the parameters listed below are required for each of four formulas and rest of them are based on what parameters are available. For example, if the variance of the predictors (X_1 and X_2) are available, then equation (5) will be used to calculate sample size. In that case, user will be asked to supply β_1^* , β_2 and PTE in addition to the following first three (a-c) required parameters.

(a) Type I Error (e.g. 0.05),
(b) Power desired (e.g. 0.8 for 80%),
(c) Residual Variance of Outcome ($e.g.\ \sigma_e^2 = 1.00$)
(d) Variance of Primary Predictor X_1 ($e.g\ \sigma_1^2 = 1$) , for continuous primary predictor or marginal prevalence ($e.g\ f_1 = 0.5$) if the predictor is binary
(e) Variance of Mediator X_2 ($e.g.\sigma_2^2 = 1$) , for continuous mediator or marginal prevalence ($e.g\ f_2 = 0.5$) of the mediator if it is binary
(f) Pearson Correlation Between X_1 and X_2 ($e.g.\ \rho = 0.30$)
(g) Estimate of X_1 before adjustment of X_2 ($e.g.\ \beta_1^* = 0.53$)
(h) Estimate of primary predictor X_1 after the adjustment of mediator X_2 , ($e.g.\ \beta_1 = 0.50$)
(i) Estimate of predictor X_2 in full model ,($e.g.\ \beta_2 = 0.10$) and
(j) Proportion of Treatment Effect ($e.g\ PTE = 5.66$).

SAMPLE SIZE CALCULATION MACRO

When we invoke the macro (attached in the Appendix), a series of windows will pop. The first window will be welcome window (Figure 1) as shown below. Users need to use [ENTER] key to move from one window to another window or one cell to next cell. The second (Figure 2) and third window (not shown here) will ask to choose if the primary predictor and mediators is continuous or binary. Fourth window (Figure 3) will be used to supply required parameters (Type I error, Power and Residual Variance). Rest of the windows will be based on the type of predictor (continuous or binary) choosen in second and third window. Once all the data are supplied, a window will pop up asking to open or save the Microsoft Word document that contains result (Figure 4 below).

Figure 1: Welcome Window

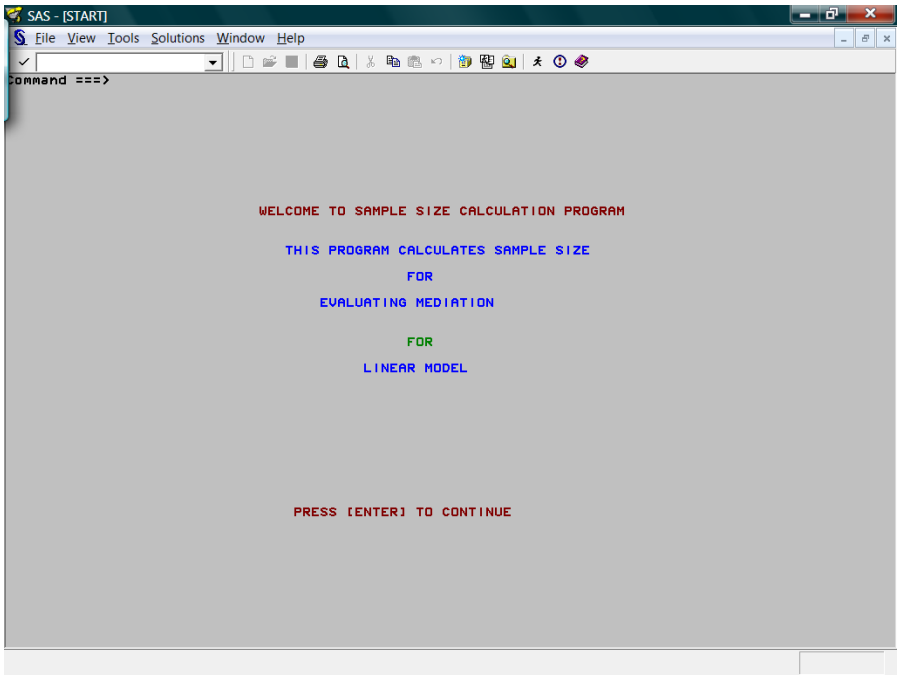

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Figure 2: Type of Primary Predictor X_1 Window

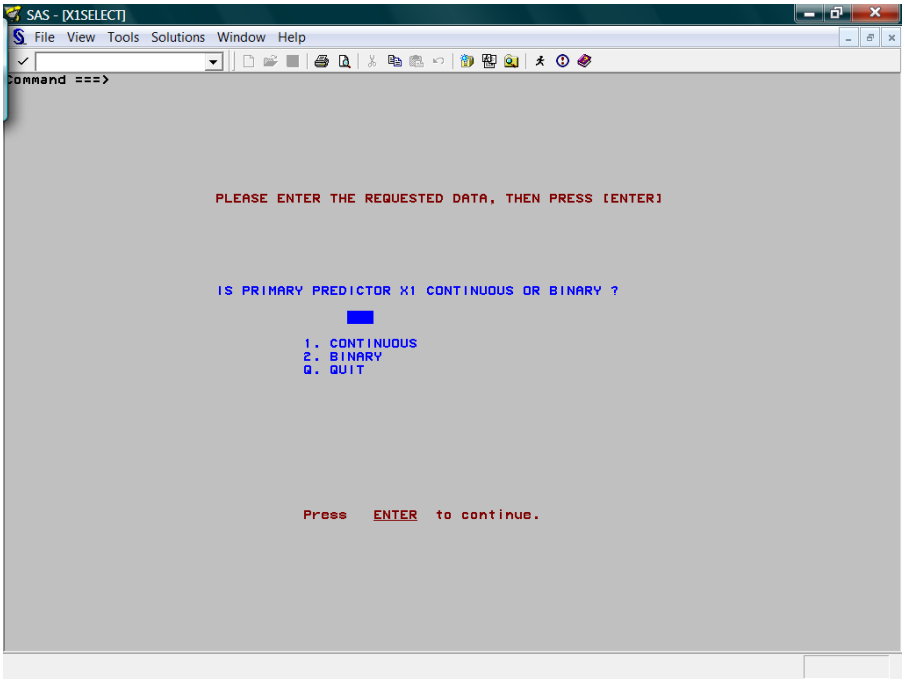
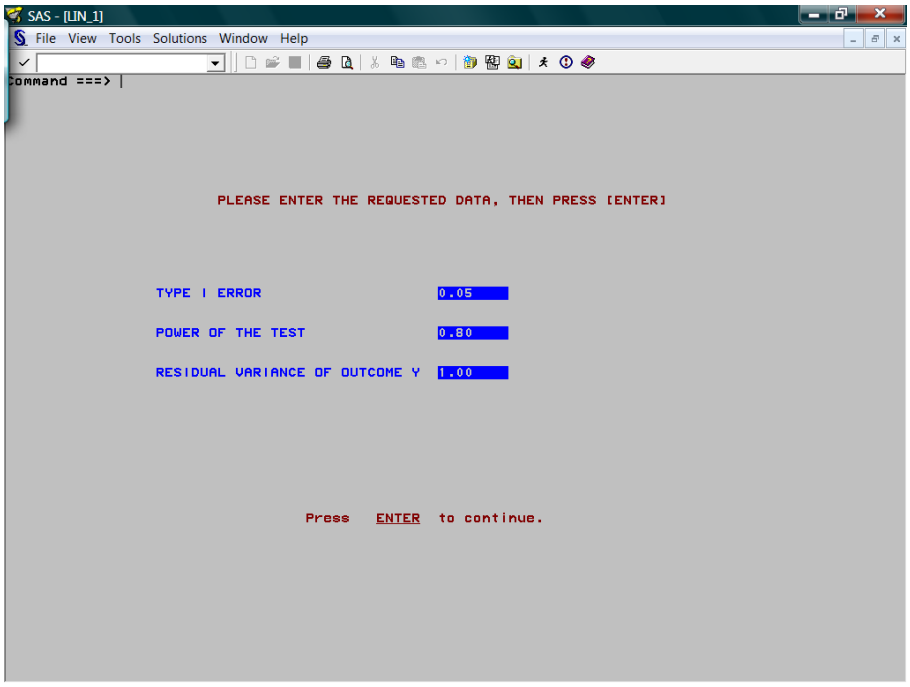


Figure 3: Required Parameters Window



As an example, consider the case where both (X_1) and mediator (X_2) are continuous with type I error rate 0.05, power 80% (i.e. 0.80), residual variance is 1, variance of primary predictor that is 1 but the variance of mediator X_2 is not available. In that such case, Pearson's Correlation between X_1 and X_2 ($\rho = 0.30$ for example), estimate of primary predictor X_1 before the adjustment of X_2 ($\beta_1^* = 0.53$ for example), Proportion of Treatment Effect (PTE = 5.66 for example) are supplied. Based on this information, the macro will automatically choose the formula (4) to calculate the sample size and the following table will be produced in the Microsoft Word document.

Figure 4: Microsoft Word Table

Sample Size Calculation for Linear Model

Variable Name	Description of Variable	Value
type1	TYPE I Error	0.05
power	Power	0.80
ResVar	Residual Variance of Outcome Y	1.00
VarX1	Variance of Primary Predictor X1	1.00
PreEstX1	Estimate of X1 before the adjustment of X2 (B1*)	0.53
Corr	Pearson's Correlation between X1 and X2	0.30
PTE	Proportion of Treatment Effect(PTE)	5.66
n	Sample Size (n)	863.00

CONCLUSION

SAS macro presented in this paper is a simple and user friendly macro that will calculate the sample size for evaluating mediation effect for linear regression. This macro can also be used to calculate sample size in the presence of a common set of confounding variable both in null and full model. Anyone who has basic knowledge of SAS programming and a basic understanding of mediation analysis can use this macro with ease.

REFERENCES

References: Vittinghoff E, Sen S, McCulloch CE . Sample size calculation for evaluating mediation. Statistics in Medicine 2009;28: 541-557.

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CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Rajendra Kadel,
University of South Florida
13201 Bruce B Downs, MDC56
Tampa, Florida 33612
(813) 794-0303
rkadel@health.usf.edu

APPENDIX

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/* SAMPLE SIZE CALCULATION MACRO */

%WINDOW START ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 color=GRAY
#9 @30 'WELCOME TO SAMPLE SIZE CALCULATION PROGRAM' C=RED
#12 @33 'THIS PROGRAM CALCULATES SAMPLE SIZE ' C=BLUE
#14 @47 'FOR'  C=BLUE  PERSIST=YES
#16 @37 'EVALUATING MEDIATION' C=BLUE
#19 @47 'FOR' C=BLUE
#21 @42 'LINEAR MODEL' C=BLUE
#32 @34 "PRESS [ENTER] TO CONTINUE" C=RED AUTOSKIP=YES;

%WINDOW X1SELECT ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#15 @25 'IS PRIMARY PREDICTOR X1 CONTINUOUS OR BINARY ?' C=blue
#17 @40 X1 1 A=REV_VIDEO C=blue  REQUIRED=YES
#17 @41 '  ' A=REV_VIDEO C=blue
#19 @35 '1. CONTINUOUS'  C=blue
#20 @35 '2. BINARY' C=blue
#21 @35 'Q. QUIT' C=blue
#32 @35 "Press" C=red @43 "ENTER"         A=underline C=red @50 "to continue." C=red ;


%WINDOW X2SELECT ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#15 @25 'IS  MEDIATOR VARIABLE X2 CONTINUOUS OR BINARY ?' C=blue
#17 @40 X2 1 A=REV_VIDEO C=blue  REQUIRED=YES
#17 @41 '  ' A=REV_VIDEO C=blue
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#19 @35 '1. CONTINUOUS'  C=blue
#20 @35 '2. BINARY' C=blue
#21 @35 'Q. QUIT' C=blue
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red ;

%WINDOW lin_1 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#15 @18 'TYPE I ERROR ' C= BLUE @50   type1 8 A=REV_VIDEO   C=blue REQUIRED=YES C=blue
#18 @18 'POWER OF THE TEST' C=BLUE @50  power 8  A=REV_VIDEO AUTOSKIP=YES C=blue
REQUIRED=YES
#21 @18 'RESIDUAL VARIANCE OF OUTCOME Y' C=BLUE  @50  ResVar 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red ;

%WINDOW lin_2 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#15 @25 'DO YOU HAVE VARIANCE  OF PRIMARY PREDICTOR X1 ?  ' C= BLUE
#17 @40 '(Y=YES, N=NO, Q=QUIT) ' C= BLUE
#19 @46 '  ' A=REV_VIDEO C=blue
#19 @45 VarX1YN 1 A=REV_VIDEO C=blue REQUIRED=YES
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_2_1 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#15 @17 'DO YOU HAVE MARGINAL PREVALANCE(f1) OF PRIMARY PREDICTOR X1 ?  ' C= BLUE
#17 @40 '(Y=YES, N=NO,  Q=QUIT) ' C= BLUE
#19 @46 '  ' A=REV_VIDEO C=blue
#19 @45 VarX1YN 1 A=REV_VIDEO C=blue REQUIRED=YES
#26 @18 "NOTE:" A=UNDERLINE
#26 @24 "MARGINAL PREVALANCE OF PRIMARY PREDICTOR X1  IS THE "
#27 @24 " PROPORTION OF 'YES' IN X1. "
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_3 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#14 @18 'VARIANCE OF MEDIATOR X2' C=BLUE @55 VarX2  8 A=REV_VIDEO  C=blue REQUIRED=YES C=blue
#17 @18 'CORRELATION COEF. BETWEEN X1 AND X2' C=BLUE @55 Corr 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#20 @18 'ESTIMATE OF X2 IN FULL MODEL (B2)' C=BLUE @55 EstX2 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_3_1 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#14 @18 'MARGINAL PREVALANCE OF MEDIATOR X2         (f2)' C=BLUE @60 f2  8 A=REV_VIDEO  C=blue
REQUIRED=YES C=blue
#17 @18 'CORRELATION COEF. BETWEEN X1 AND X2' C=BLUE @60 Corr 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#20 @18 'ESTIMATE OF X2 IN FULL MODEL (B2)' C=BLUE @60 EstX2 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_4 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#15 @25 'DO YOU HAVE VARIANCE  OF MEDIATOR X2 ?  ' C= BLUE
#17 @40 '(Y=YES, N=NO,  Q=QUIT) ' C= BLUE
#19 @46 '  ' A=REV_VIDEO C=blue
#19 @45 VarX2YN 1 A=REV_VIDEO C=blue REQUIRED=YES
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_4_1 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
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#15 @17 'DO YOU HAVE MARGINAL PREVALANCE(f2) OF MEDIATOR X2 ?  ' C= BLUE
#17 @40 '(Y=YES, N=NO,  Q=QUIT) ' C= BLUE
#19 @46 '  ' A=REV_VIDEO C=blue
#19 @45 VarX2YN 1 A=REV_VIDEO C=blue REQUIRED=YES
#26 @18 "NOTE:" A=UNDERLINE
#26 @24 "MARGINAL PREVALANCE OF MEDIATOR X2  IS THE "
#27 @24 " PROPORTION OF 'YES' IN X2. "
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_5 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#14 @18 'VARIANCE OF PRIMARY PREDICTOR X1' C= BLUE @68 VarX1  8 A=REV_VIDEO  C=blue
REQUIRED=YES C=blue
#17 @18 'CORRELATION COEFFICIENT. BETWEEN X1 AND X2' C=BLUE @68 Corr 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#20 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2 (B1*)' C=BLUE @68 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#23 @18 'PROPORTION OF TREATMENT EFFECT (PTE IN %)' C=BLUE @68 PTE 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#27 @18 "NOTE:" A=UNDERLINE
#27 @24 "PTE WILL BE BETWEEN 0 AND 100,eg 5.66 FOR 5.66%."
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_5_2 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#14 @18 'PREVALANCE OF PRIMARY PREDICTOR  X1 (f1)' C=BLUE @68 f1  8 A=REV_VIDEO  C=blue
REQUIRED=YES C=blue
#17 @18 'CORRELATION COEFFICIENT BETWEEN X1 AND X2' C=BLUE @68 Corr 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#20 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2 (B1*)' C=BLUE @68 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#23 @18 'PROPORTION OF TREATMENT EFFECT (PTE IN %)' C=BLUE @68 PTE 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#28 @18 "NOTE:" A=UNDERLINE
#28 @25 "PTE WILL BE BETWEEN 0 AND 100,eg 5.66 FOR 5.66%."
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_5_3 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#11 @18 'PREVALANCE OF PRIMARY PREDICTOR  X1 (f1)' C=BLUE @67 f1  8 A=REV_VIDEO  C=blue
REQUIRED=YES C=blue
#14 @18 'VARIANCE OF MEDIATOR X2' C=BLUE @67 VarX2 8  A=REV_VIDEO  C=blue REQUIRED=YES
#17 @18 'ESTIMATE OF PREDICTOR X2 IN FULL MODEL (B2)' C=BLUE @67  EstX2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#20 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2(B1*)' C=BLUE @67 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#23 @18 'PROPORTION OF TREATMENT EFFECT (PTE IN %)' C=BLUE @67 PTE 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#27 @18 "NOTE:" A=UNDERLINE
#27 @24 "PTE WILL BE BETWEEN 0 AND 100,eg 5.66 FOR 5.66%."
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_5_4 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#13 @18 'VARIANCE OF  PRIMARY PREDICTOR  X1' C=BLUE @67 VarX1  8 A=REV_VIDEO  C=blue
REQUIRED=YES C=blue
#15 @18 'PREVALANCE OF  MEDIATOR X2 (f2)' C=BLUE @67 f2 8  A=REV_VIDEO  C=blue REQUIRED=YES
#17 @18 'ESTIMATE OF PREDICTOR X2 IN FULL MODEL (B2)' C=BLUE @67 EstX2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#19 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2(B1*)' C=BLUE @67 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
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#21 @18 'PROPORTION OF TREATMENT EFFECT (PTE IN %)' C=BLUE @67 PTE 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#27 @18 "NOTE:" A=UNDERLINE
#27 @24 "PTE WILL BE BETWEEN 0 AND 100,eg 5.66 FOR 5.66%."
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_6 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#15 @25 'DO YOU HAVE PARAMETER ESTIMATE OF X1 AFTER ' C= BLUE
#17 @35 'ADJUSTMENT OF PREDICTOR X2 (B1) ?  ' C= BLUE
#19 @40 '(Y=YES, N=NO,  Q=QUIT) ' C= BLUE
#21 @46 '  ' A=REV_VIDEO C=blue
#21 @45 EstX1YN 1 A=REV_VIDEO C=blue REQUIRED=YES
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_6_1 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#13 @18 'VARIANCE OF  PRIMARY PREDICTOR  X1' C=BLUE @67 VarX1  8 A=REV_VIDEO  C=blue
REQUIRED=YES C=blue
#15 @18 'VARIANCE OF MEDIATOR X2' C=BLUE @67 VarX2 8  A=REV_VIDEO  C=blue REQUIRED=YES
#17 @18 'ESTIMATE OF PREDICTOR X2 IN FULL MODEL (B2)' C=BLUE @67 EstX2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#19 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2 (B1*)' C=BLUE @67 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#21 @18 'PROPORTION OF TREATMENT EFFECT (PTE IN %)' C=BLUE @67 PTE 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#27 @18 "NOTE:" A=UNDERLINE
#27 @24 "PTE WILL BE BETWEEN 0 AND 100,eg 5.66 FOR 5.66%."
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_6_2 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#13 @18 'MARGINAL PREVALANCE OF PRIMARY PREDICTOR X1 (f1)' C=BLUE @67 F1  8 A=REV_VIDEO
C=blue REQUIRED=YES C=blue
#15 @18 'VARIANCE OF MEDIATOR X2' C=BLUE @67 VarX2 8  A=REV_VIDEO  C=blue REQUIRED=YES
#17 @18 'ESTIMATE OF PREDICTOR X2 IN FULL MODEL (B2)' C=BLUE @67 EstX2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#19 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2 (B1*)' C=BLUE @67 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#21 @18 'PROPORTION OF TREATMENT EFFECT (PTE IN %)' C=BLUE @67 PTE 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#27 @18 "NOTE:" A=UNDERLINE
#27 @24 "PTE WILL BE BETWEEN 0 AND 100,eg 5.66 FOR 5.66%."
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_6_3 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#13 @18 'VARIANCE OF PRIMARY PREDICTOR X1 ' C=BLUE @67 VarX1  8 A=REV_VIDEO  C=blue
REQUIRED=YES C=blue
#15 @18 'MARGINAL PREVALANCE MEDIATOR X2 (f2)' C=BLUE  @67 f2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#17 @18 'ESTIMATE OF PREDICTOR X2 IN FULL MODEL (B2)' C=BLUE @67 EstX2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#19 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2 (B1*)' C=BLUE @67 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#21 @18 'PROPORTION OF TREATMENT EFFECT (PTE IN %)' C=BLUE @67 PTE 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#27 @18 "NOTE:" A=UNDERLINE
#27 @24 "PTE WILL BE BETWEEN 0 AND 100,eg 5.66 FOR 5.66%."
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_6_4 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
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#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#13 @18 'MARGINAL PREVALANCE OF PRIMARY PREDICTOR X1 (f1)' C=BLUE @67 f1  8 A=REV_VIDEO
C=blue REQUIRED=YES C=blue
#15 @18 'MARGINAL PREVALANCE OF MEDIATOR X2 (f2)' C=BLUE @67 f2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#17 @18 'ESTIMATE OF PREDICTOR X2 IN FULL MODEL (B2)' C=BLUE @67 EstX2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#19 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2 (B1*)' C=BLUE @67 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#21 @18 'PROPORTION OF TREATMENT EFFECT (PTE IN %)' C=BLUE @67 PTE 8 A=REV_VIDEO  C=blue
REQUIRED=YES
#27 @18 "NOTE:" A=UNDERLINE
#27 @24 "PTE WILL BE BETWEEN 0 AND 100,eg 5.66 FOR 5.66%."
#32 @35 "Press" C=red  @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_8_1 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#13 @18 'VARIANCE OF  PRIMARY PREDICTOR  X1' C=BLUE @67 VarX1  8 A=REV_VIDEO  C=blue
REQUIRED=YES C=blue
#15 @18 'VARIANCE OF MEDIATOR X2' C=BLUE @67 VarX2 8  A=REV_VIDEO  C=blue REQUIRED=YES
#17 @18 'ESTIMATE OF PREDICTOR X2 IN FULL MODEL (B2)' C=BLUE @67 EstX2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#19 @18 'ESTIMATE OF X1 AFTER THE ADJUSTMENT OF X2 (B1)' C=BLUE @67 EstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#21 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2 (B1*)' C=BLUE @67 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_8_2 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#13 @18 'MARGINAL PREVALANCE OF PRIMARY PREDICTOR X1 (F1)' C=BLUE @67 f1  8 A=REV_VIDEO
C=blue REQUIRED=YES C=blue
#15 @18 'VARIANCE OF MEDIATOR X2' C=BLUE @67 VarX2 8  A=REV_VIDEO  C=blue REQUIRED=YES
#17 @18 'ESTIMATE OF PREDICTOR X2 IN FULL MODEL (B2)' C=BLUE @67 EstX2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#19 @18 'ESTIMATE OF X1 AFTER THE ADJUSTMENT OF X2 (B1)' C=BLUE @67 EstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#21 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2 (B1*)' C=BLUE @67 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_8_3 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 Color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#13 @18 'VARIANCE OF PRIMARY PREDICTOR X1' C=BLUE @67 VarX1  8 A=REV_VIDEO  C=blue
REQUIRED=YES C=blue
#15 @18 'MARGINAL PREVALANCE MEDIATOR X2 (f2)' C=BLUE @67 f2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#17 @18 'ESTIMATE OF PREDICTOR X2 IN FULL MODEL (B2)' C=BLUE @67 EstX2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#19 @18 'ESTIMATE OF X1 AFTER THE ADJUSTMENT OF X2 (B1)' C=BLUE @67 EstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#21 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2 (B1*)' C=BLUE @67 PreEstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW lin_8_4 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 color=GRAY
#8  @25 "PRESS [ENTER], THEN INPUT REQUIRED DATA" C=red
#13 @18 'MARGINAL PREVALANCE PRIMARY PREDICTOR X1 (f1)' C=BLUE @67 f1  8 A=REV_VIDEO  C=blue
REQUIRED=YES C=blue
#15 @18 'MARGINAL PREVALANCE MEDIATOR X2 (f2)' C=BLUE @67 f2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
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#17 @18 'ESTIMATE OF PREDICTOR X2 IN FULL MODEL (B2)' C=BLUE @67 EstX2 8  A=REV_VIDEO  C=blue
REQUIRED=YES
#19 @18 'ESTIMATE OF X1 AFTER THE ADJUSTMENT OF X2 (B1)' C=BLUE @67 EstX1 8 A=REV_VIDEO
C=blue REQUIRED=YES
#21 @18 'ESTIMATE OF X1 BEFORE THE ADJUSTMENT OF X2 (B1*)' C=BLUE @67 PreEstX1 8 A=REV_VIDEO
AUTOSKIP=NO C=blue REQUIRED=YES
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;


%WINDOW ERRORWIN_2 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=80 color=GRAY
#8  @40 "INCORRECT INPUT!!!" C=red
#15 @18 "PLEASE ENTER 1 FOR 'CONTINUOUS' , 2 FOR 'BINARY' OR Q TO 'QUIT'. " C= BLUE
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%WINDOW ERRORWIN_3 ICOLUMN=5 IROW=5 ROWS=50 COLUMNS=83 color=GRAY
#8  @40 "INCORRECT INPUT!!!" C=red
#17 @20 "PLEASE ENTER  Y FOR 'YES' , N FOR 'NO' or Q FOR QUIT. " C= BLUE
#32 @35 "Press" C=red @43 "ENTER" A=underline C=red @50 "to continue." C=red;

%let X1=; %let X2=; %let p=0.5; %let type1=0.05; %let power=0.80;
%let ResVar=1.00; %let VarX1=1.00; %let VarX2=1.00;
%let VarX1YN=; %let VarX2YN=; %let EstX1YN=;%let f1=0.50; %let f2=0.50;
%let EstX1=; %let EstX2=; %let PTE=;%let PreEstX1=; %let Corr=;

/* inner macro */

%macro lin_samp;

data sampsize;type1=&type1;power=&power;zalpha=quantile('NORMAL',1-type1/2);
zbeta=quantile('NORMAL',power);ResVar=&ResVar;

%if &X1=1 and &X2=1 %then %do;VarX1=&VarX1;VarX2=&VarX2;
label VarX1="Variance of Primary Predictor X1";
%end;
%else %if &X1=2 and &X2=1 %then %do;VarX1=&f1*(1-&f1);VarX2=&VarX2;
label f1="Marginal Prevalance of Primary Predictor X1 (f1)";label VarX2="Variance of Mediator X2";
%end;

%else %if &X1=1 and &X2=2 %then %do;f2=&f2;VarX1=&VarX1;VarX2=f2*(1-f2);
label VarX1="Variance of Primary Predictor X1";
label f2="Marginal Prevalance of Mediator X2(f2)";%end;

%else %if &X1=2 and &X2=2 %then %do;
f1=&f1;f2=&f2;VarX1=f1*(1-f1);VarX2=f2*(1-f2);
label f1="Marginal Prevalance of Primary Predictor X1 (f1)";
label f2="Marginal Prevalance Mediator X2(f2)";
%end;

/* method1 */
%if %upcase(&VarX1YN)=N %then %do; method='method1';EstX2=&EstX2;Corr=&Corr;
bottom=((EstX2)**2*(VarX2)*(1-(Corr)**2));
label Corr="Pearson's Correlation between X1 and X2";
label EstX2="Estimate of Predictor X2 (B2)";drop varX1;%goto sampsize;
%end;

/* method2: */
%if %upcase(&VarX1YN)=Y and %upcase(&VarX2YN)=N %then %do;
method='method2';PreEstX1=&PreEstX1;Corr=&Corr;PTE=&PTE;
Bottom=(PreEstX1*PTE/100*1/Corr)**2*VarX1*(1-(Corr)**2);
label Corr="Pearson's Correlation between X1 and X2";
label PreEstX1="Estimate of X1 before the adjustment of X2 (B1*)";
label PTE="Proportion of Treatment Effect(PTE)";drop varX2 ;%goto sampsize;
```

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%end;

/*method 3 */
%if %upcase(&VarX1YN)=Y and %upcase(&VarX2YN)=Y  and %upcase(&EstX1YN)=N %then %do;
method='method3';EstX2=&EstX2;PreEstX1=&PreEstX1;PTE=&PTE;
Bottom=(EstX2)**2*(VarX2)-(PreEstX1*PTE/100)**2*VarX1;
label PreEstX1="Estimate of X1 before the adjustment of X2 (B1*)";
label EstX2="Estimate of Predictor X2 (B2)";
label PTE="Proportion of Treatment Effect(PTE)";%goto sampsize;
%end;

/* method 4*/
%if %upcase(&VarX1YN)=Y and %upcase(&VarX2YN)=Y  and %upcase(&EstX1YN)=Y %then %do;
method='method4';EstX1=&EstX1;EstX2=&EstX2;PreEstX1=&PreEstX1;
Bottom=(EstX2)**2*(VarX2)-(PreEstX1-EstX1)**2*VarX1;
label EstX1="Estimate of Predictor X2 (B1)";label EstX2="Estimate of Predictor X2 (B2)";
label PreEstX1="Estimate of X1 before the adjustment of X2 (B1*)";%goto sampsize;
%end;

%sampsize:
n=ceil(((zalpha+zbeta)**2*(ResVar))/Bottom); /* round to next integer */
label ResVar= "Residual Variance of Outcome Y";
label type1="TYPE I Error";label power="Power";label n="Sample Size (n)";

run;

proc transpose data=sampsize(drop=Bottom zalpha zbeta)out=sampsize2;run;

ods rtf  style=SASWeb  bodytitle; title 'Sample Size Calculation for Linear Model';
footnote1 j=l 'Source : Vittinghoff E, Sen S, McCulloch CE . Sample size calculation for evaluating mediation.';
footnote2 j=l 'Statistics in Medicine 2009;28: 541-557';
proc print data=sampsize2 label noobs;label _NAME_= "Variable Name";
label _LABEL_="Description of Variable";label COL1="Value";run;
ods rtf close;

%mend lin_samp;

/* outer macro */
%macro med_samplesize;
%display start ;

%first:
%let X1=; %let X2=; %let VarX1YN=; %let VarX2YN=; %let EstX1YN=;

%next1:
%display X1SELECT;
%if %upcase(&X1)=Q %then %do; %abort;%end;
%if %upcase(&X1)^=1 AND  %upcase(&X1)^=2 AND  %upcase(&X1)^=Q %then %do;
%display ERRORWIN_2;%let X1=;%goto next1;%end;

%next2:
%display X2SELECT;
%if %upcase(&X2)=Q %then %do; %abort;%end;
%if %upcase(&X2)^=1 AND  %upcase(&X2)^=2 AND  %upcase(&X2)^=Q %then %do;
%display ERRORWIN_2;%let X2=; %goto next2;%end;

%let ResVar=1.00; %let PreEstX1=0.53; %let EstX1=0.50; %let EstX2=0.10;
%let Corr=0.30; %let f1=0.50; %let f2=0.50; %let PTE=5.66;

%if &X1=2 %then %do; %let PTE=11.30; %end;
%if &X2=2 %then %do;%let EstX2=0.20;%end;
%display  lin_1;
```

```
%second:
%let VarX1YN=;
%if &X1=1 %then %do; %display  lin_2;%end;
%else %if &X1=2 %then %do; %display  lin_2_1; %end;

%if %upcase(&VarX1YN)=N %then %do;
%if &X2=1 %then %do; %display lin_3; %end;
%else %if &X2=2 %then %do; %display lin_3_1; %end;
%end;

%else %if %upcase(&VarX1YN)=Y %then %do;
%third:
%let VarX2YN=;
%if &X2=1 %then %do;%display  lin_4; %end;
%else %if &X2=2 %then %do;%display  lin_4_1;%end;
%if %upcase(&VarX2YN)=N %then %do;
%if &X1=1 %then %do; %display lin_5;%end;
%else %if &X1=2 %then %do; %display lin_5_2;%end;
%end;

%else %if %upcase(&VarX2YN)=Y %then %do;
%fourth:
%let EstX1YN=; %display lin_6;
%if %upcase(&EstX1YN)=N %then %do;
%if &X1=1 and &X2=1 %then %do; %display lin_6_1;%end;
%else %if &X1=2 and &X2=1 %then %do; %display lin_6_2;%end;
%else %if &X1=1 and &X2=2 %then %do; %display lin_6_3;%end;
%else %if &X1=2 and &X2=2 %then %do; %display lin_6_4;%end;
%end;

%else %if %upcase(&EstX1YN)=Y %then %do;
%if &X1=1 and &X2=1 %then %do;  %display lin_8_1;%end;
%else %if &X1=2 and &X2=1 %then %do;%display lin_8_2;%end;
%else %if &X1=1 and &X2=2 %then %do; %display lin_8_3;%end;
%else %if &X1=2 and &X2=2 %then %do; %display lin_8_4;%end;
%end;

%else %if  %upcase(&EstX1YN)=Q %then %do;%abort;%end;
%else %if %upcase(&EstX1YN)^=Y AND %upcase(&EstX1YN)^=N AND %upcase(&EstX1YN)^=Q %then %do;
%display ERRORWIN_3;%goto fourth;%end;
%end;

%else %if  %upcase(&VarX2YN)=Q %then %do; %abort;%end;
%else %if %upcase(&VarX2YN)^=Y AND %upcase(&VarX2YN)^=N AND %upcase(&VarX2YN)^=Q %then %do;
%display ERRORWIN_3; %goto third;%end;
%end;

%else %if  %upcase(&VarX1YN)=Q %then %do;%abort; %end;
%else %if %upcase(&VarX1YN)^=Y AND %upcase(&VarX1YN)^=N AND %upcase(&VarX1YN)^=Q %then %do;
%display ERRORWIN_3; %goto second;%end;

%lin_samp
%mend med_samplesize;
%med_samplesize
```