Modern Mediation Analysis Methods in the Social Sciences

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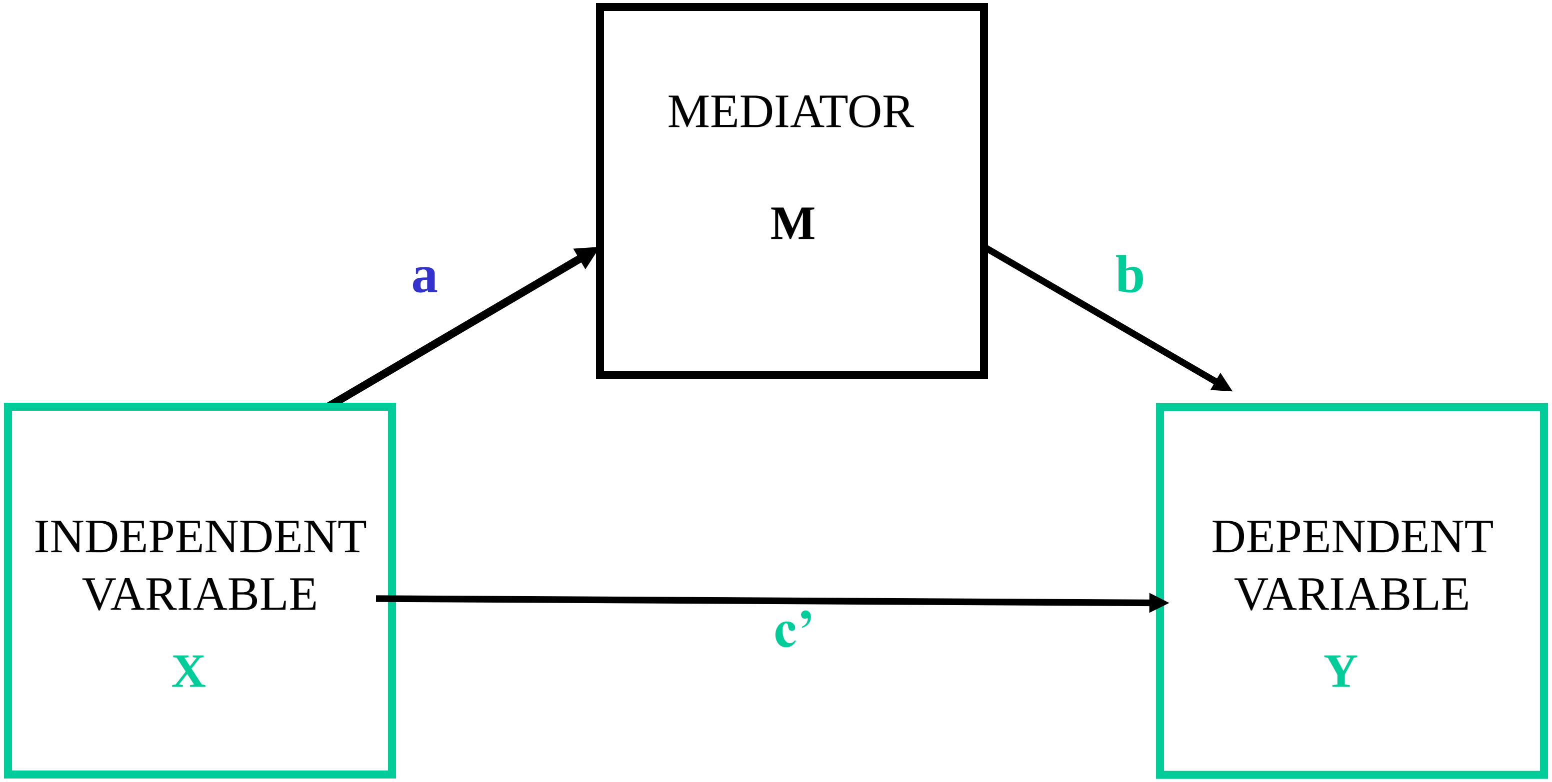
Introduction and Applications
Single Mediator Model
More Complicated Mediation Models
Longitudinal Mediation Models
Summary and Future Directions

*Thanks to National Institute on Drug Abuse and Centre for Statistical Methodology.

Mediation Statements

- If norms become less tolerant about smoking then smoking will decrease.
- If you increase positive parental communication then there will be reduced symptoms among children of divorce.
- If children are successful at school they will be less anti-social.
- If unemployed persons can maintain their self-esteem they will be more likely to be reemployed.

Single Mediator Model



Mediating Variable

A variable that is intermediate in the causal process relating an independent to a dependent variable.

- Attitudes (X) cause intentions (M) which then cause behavior (Y) (Ajzen & Fishbein, 1980)
- Prevention program (X) changes norms (M) which promotes healthy behavior (Y) (Judd & Kenny, 1981)
- Neglect/Abuse in childhood (X) impairs threat appraisal (M) which affects aggressive behavior (Y) (Dodge, Bates, & Petit, 1990)
- Parenting programs (X) reduce parents' negative discipline (M) which reduces symptoms among children with attention deficit (Y) (Hinshaw, 2002).

Mediation is important because …

- Central questions in many fields are about mediating processes
- Important for basic research on mechanisms of effects
- Critical for applied research, especially prevention and treatment
- Many interesting statistical and mathematical issues

Third-Variable Effects

- Most statistics focuses on two-variable effects, e.g., correlation, odds ratio between X and Y.
- More possible relations with three variables; names for third-variable effects: mediator, confounder, covariate, moderator.
- Complex even though only one more variable is added to a two-variable model. Usually only one variable is randomized.
- 4, 5, and more variables have even more complexity.

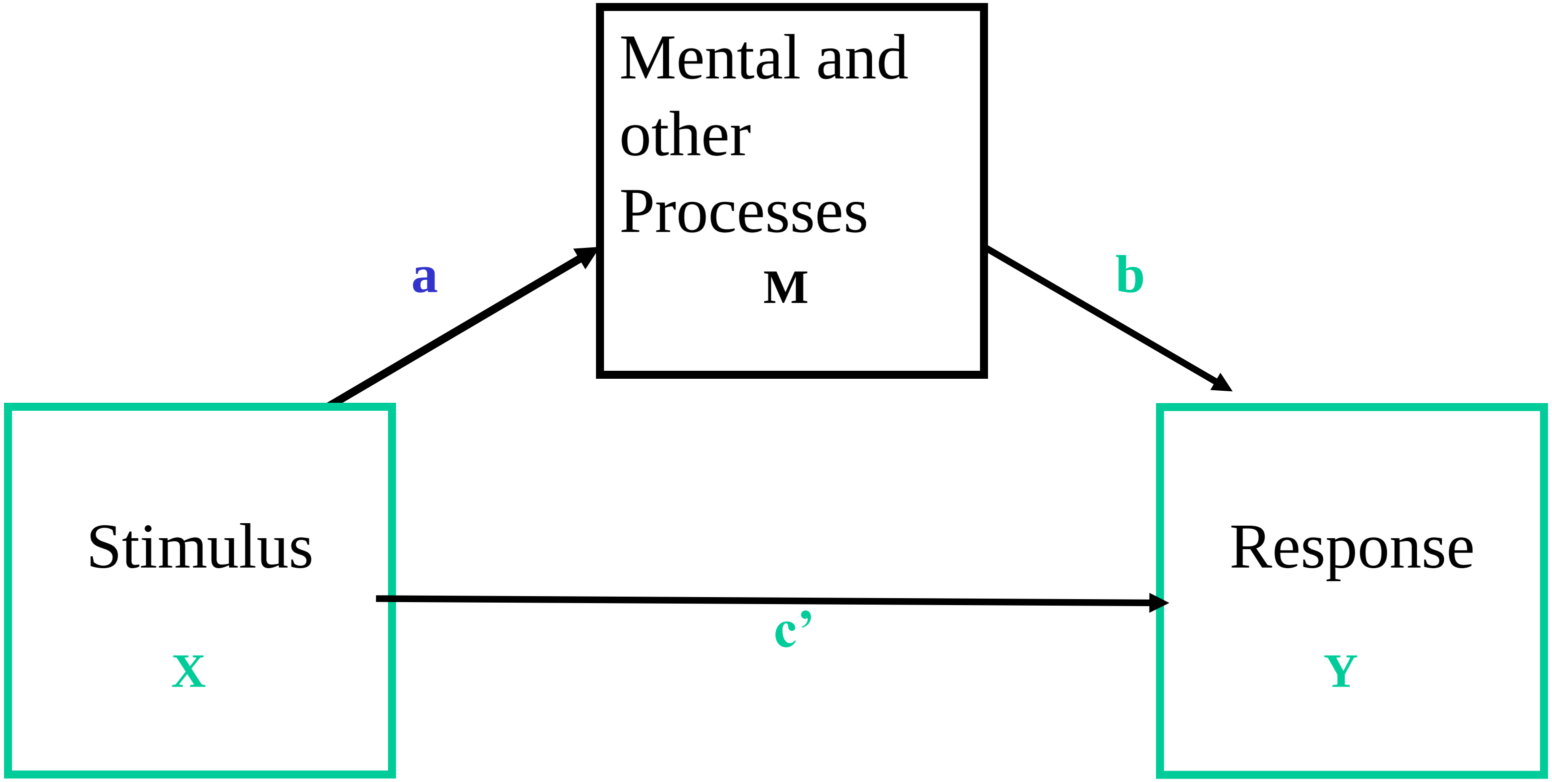
Mediator Definitions

- A mediator is a variable in a chain whereby an independent variable causes the mediator which in turn causes the outcome variable (Sobel, 1990)
- The generative mechanism through which the focal independent variable is able to influence the dependent variable (Baron & Kenny, 1986)
- A variable that occurs in a causal pathway from an independent variable to a dependent variable. It causes variation in the dependent variable and itself is caused to vary by the independent variable (Last, 1988)

S→O→R Theory I

- Stimulus→ Organism → Response (SOR) theory whereby the effect of a Stimulus on a Response depends on mechanisms in the organism (Woodworth, 1928). These mediating mechanisms translate the Stimulus to the Response. SOR theory is ubiquitous in psychology.
- Stimulus: Multiply 24 and 16
- Organism: You
- Response: Your Answer

Stimulus-Organism-Response (S-O-R) Mediation Model



Applications

Two overlapping applications of mediation analysis:

(1) Mediation for Elaboration

(2) Mediation by Design

Mediation for Elaboration

- Observed relation and try to elaborate it.
- Elaboration method described by Lazarsfeld and colleagues (1955; Hyman, 1955) where a third variable is included in an analysis to see if/how the observed relation changes.
- Replication (Covariate)
- Explanation (Confounder)
- Intervening (Mediator)
- Specification (Moderator)

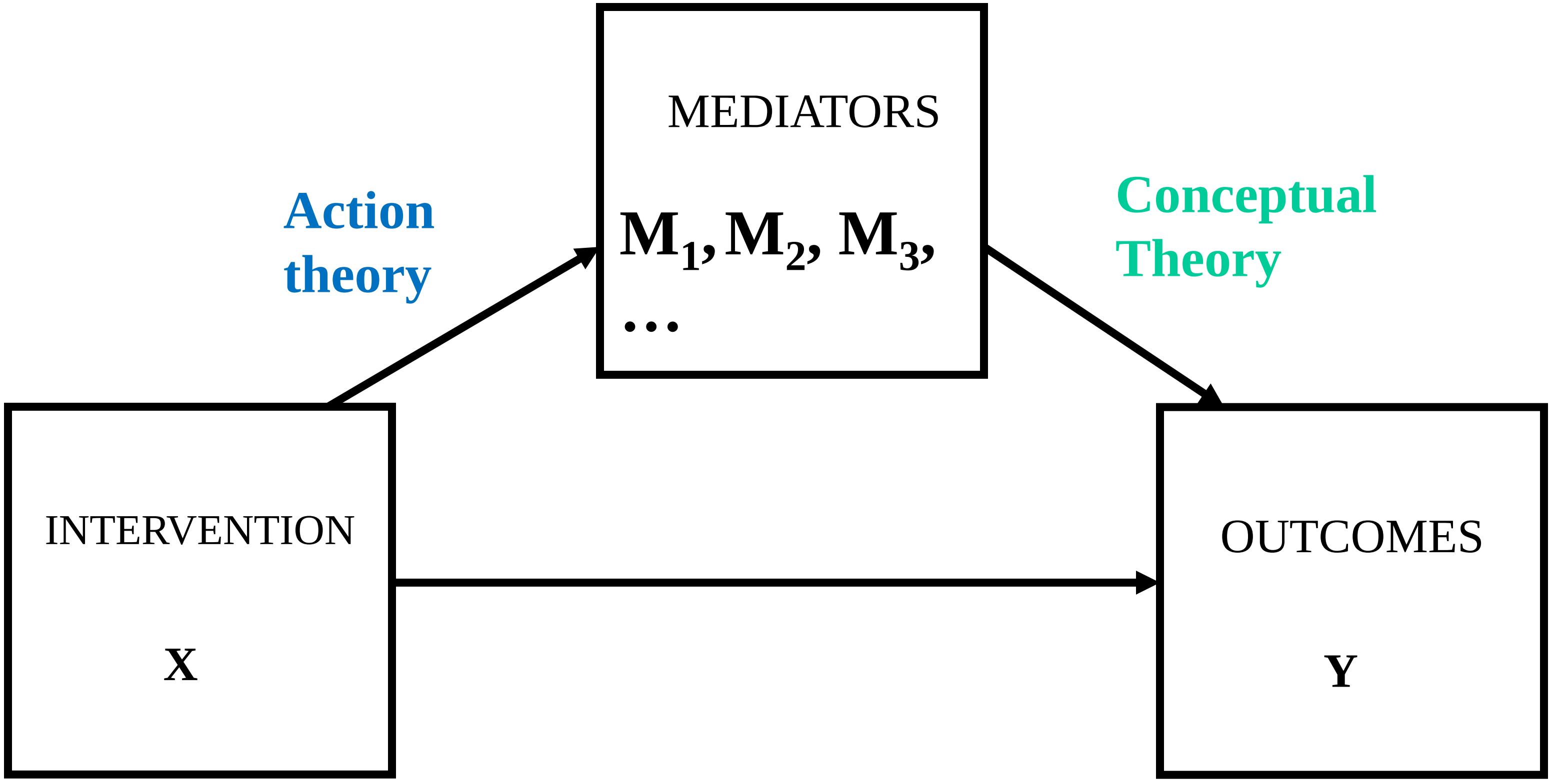
Mediation by Design

- Select mediating variables that are causally related to an outcome variable.
- Intervention is designed to change these mediators.
- If mediators are causally related to the outcome, then an intervention that changes the mediator will change the outcome.
- Common in applied research like prevention and treatment.

Mediation in Intervention Research Theory

- Conceptual Theory (Remission Theory, Etiological Theory) focuses on how the mediators are related to the dependent variables. Action theory corresponds to how the program will affect mediators. (Chen, 1990, Lipsey, 1993; MacKinnon, 2008).
- Mediation is important for intervention science. Practical implications include reduced cost and more effective interventions if the mediators of interventions are identified.

Intervention Mediation Model



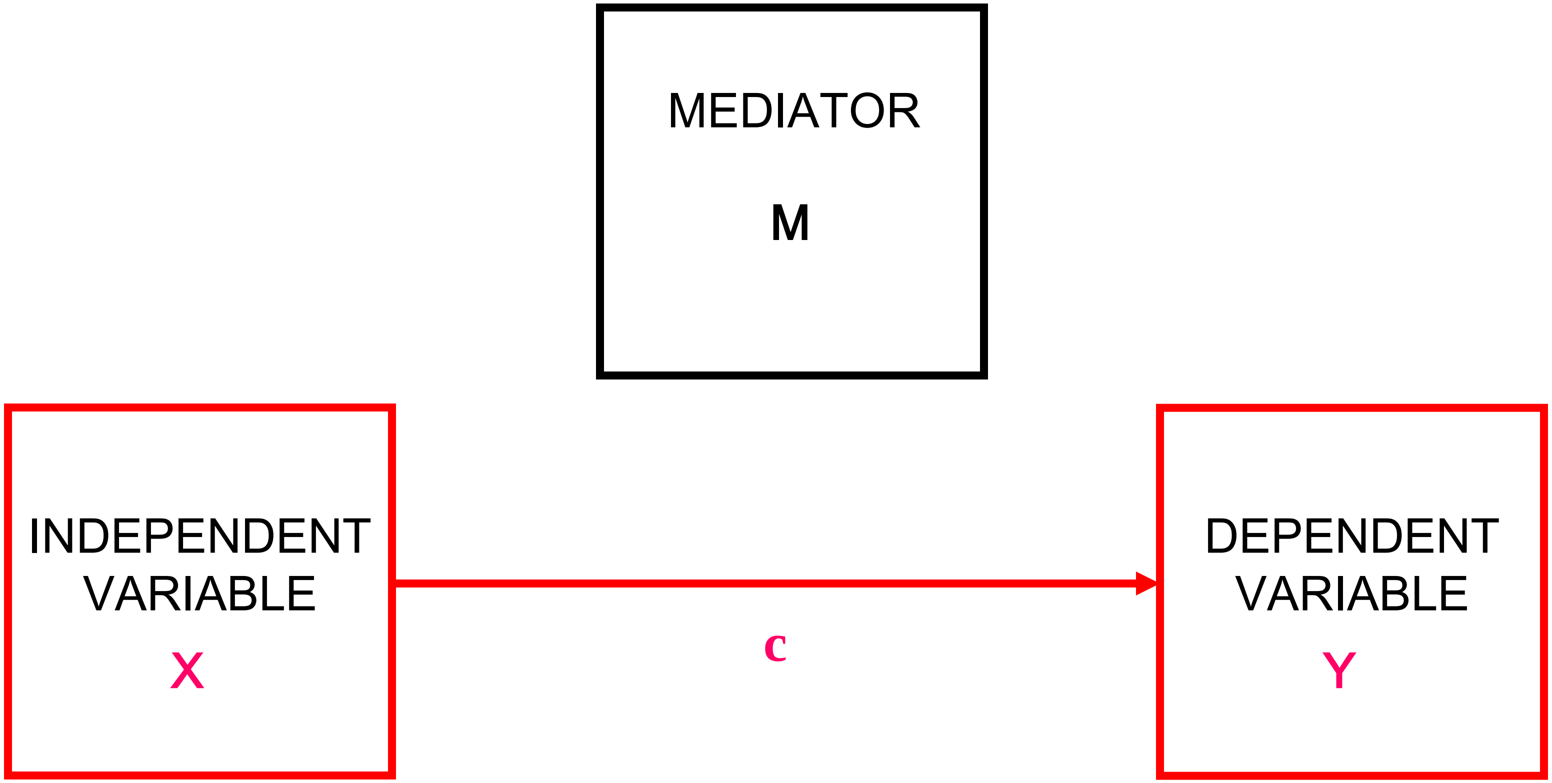
If the mediators selected are causally related to Y, then changing the mediators will change Y.

Mediation Regression Equations

- Tests of mediation for a single mediator use information from some or all of three equations.
- The coefficients in the equations may be obtained using methods such as ordinary least squares regression, covariance structure analysis, or logistic regression. The following equations are in terms of linear regression and expectations.

(Hyman, 1955; Judd & Kenny, 1981; Baron & Kenny, 1986; MacKinnon & Dwyer, 1993)

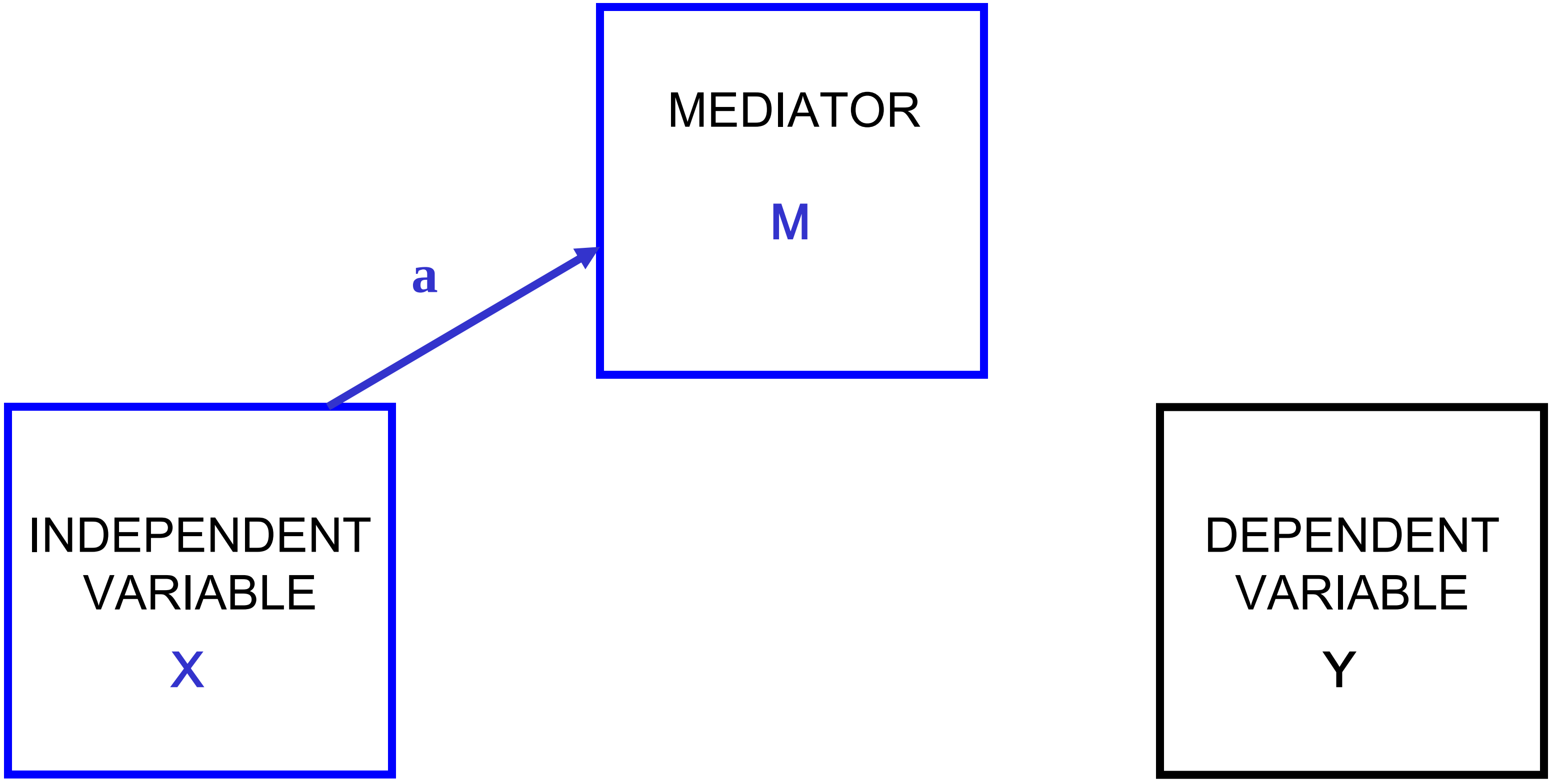
Equation 1 Social Science



1. The independent variable is related to the dependent variable:

$$Y = i_1 + \hat{c}X + e_1$$

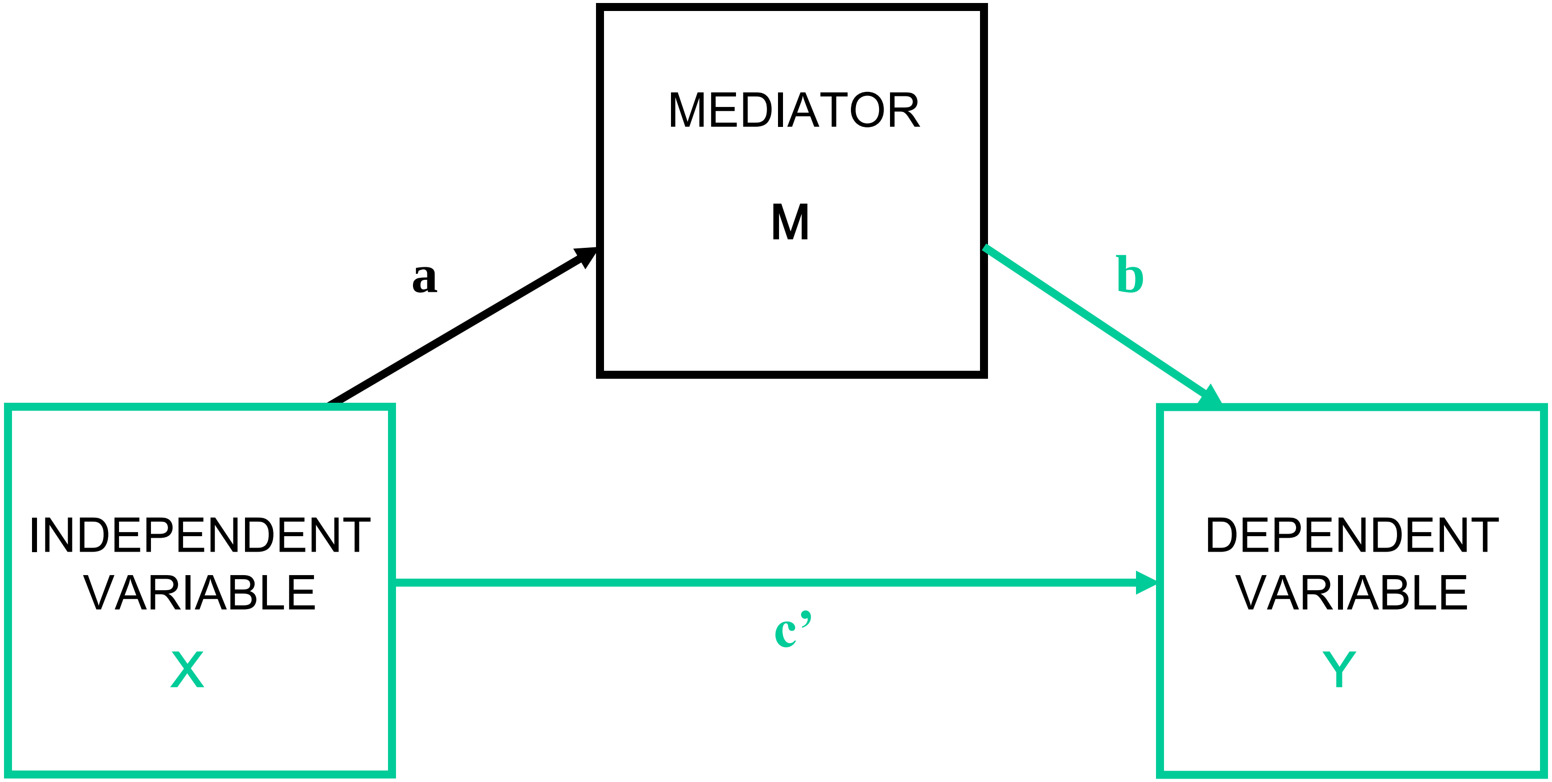
Equation 2 Social Science



2. The independent variable is related to the potential mediator:

$$M = i_2 + \hat{a}X + e_2$$

Equation 3 Social Science



3. The mediator is related to the dependent variable controlling for exposure to the independent variable:

$$Y = i_3 + \hat{c}' X + \hat{b} M + e_3$$

Effect Measures

Indirect Effect = ab = c - c'

ab = c - c' for ordinary least squares regression not nonlinear models like logistic regression.

Direct effect= c' Total effect= ab+ c'=c

Corresponding VanderWeele (2010) notation

Indirect Effect = $\boldsymbol{\beta}_1\boldsymbol{\theta}_2 = \phi_1 - \boldsymbol{\theta}_1$

Direct effect= $\boldsymbol{\theta}_1$ Total effect= $\boldsymbol{\beta}_1\boldsymbol{\theta}_2 + \boldsymbol{\theta}_1 = \phi_1$

Significance Testing and Confidence Limit Estimation

Product of coefficients estimation, *ab*, of the mediated effect and standard error is the most general approach with best statistical properties for the linear model given assumptions. Best tests are the Joint Significance, Distribution of the Product, and Bootstrap for confidence limit estimation and significance testing again under model assumptions.

For nonlinear models and/or violation of model assumptions, the usual estimators are not necessarily accurate. New developments based on potential outcome approaches provide more accurate estimators (Robins & Greenland, 1992; Pearl, 2001).

Social Science Equations with Covariate C.

$E[Y|X{=}x, C{=}c] = i_1 + c\,X + c_2\,C$ (1)

$E[M|X{=}x, C{=}c] = i_3 + a\,X + a_2\,C$ (2)

$E[Y|X{=}x, M{=}m, C{=}c] = i_2 + c'\,X + b\,M + c_3\,C$ (3)

With XM interaction

$E[Y|X{=}x, M{=}m, C{=}c] = i_4 + c'\,X + b\,M + h\,XM + c_4\,C$ (4)

Identification Assumptions

1. No unmeasured X to Y confounders given covariates.

2. No unmeasured M to Y confounders given covariates.

3. No unmeasured X to M confounders given covariates.

4. There is no effect of X that confounds the M to Y relation.

VanderWeele & VanSteelandt (2009)

Inferential Assumptions

- Reliable and valid measures.
- Data are a random sample from the population of interest.
- Coefficients, *a*, *b*, *c'* reflect the correct functional form.
- Mediation chain is correct. Temporal ordering is correct: X before M before Y.
- No moderator effects. The relation from X to M and from M to Y are homogeneous across subgroups or other participant characteristics.

Modern Causal Inference in Mediation

- Introduction of counterfactual/potential outcome model illustrates problems with the causal interpretation of results from mediation analysis.
- Counterfactual is central to modern causal inference. The counterfactual refers to conditions in which a participant could serve, not just the condition that they did serve in.
- Problem with mediation analysis because M is not randomly assigned but is self-selected.

Holland (1988)

Randomized Two Group Design

- Want Y(1) – Y(0) but this not possible for each person—the fundamental problem of causal inference.
- Randomization of a large number of persons solves the fundamental problem of causal inference. The average in each group is an estimator of a causal effect (ACE).
- Randomization does not solve the problem for mediation because some potential outcomes are impossible when M is considered.

Problem with Mediation Analysis

- We will **never get the value for M in the control group for an individual in the treatment group**. We will **never get the value for M in the treatment group, for an individual in the control group**.

- One solution is the natural indirect effect which **uses the value of M in the control group as the counterfactual to compare the value of M in the treatment group** and vice versa (Robins & Greenland, 1992; Pearl, 2001) with the assumptions described above (sequential ignorability).

Omitted Variables/Confounders

- (Judd & Kenny, 1981 p. 607): "… a mediational analysis may also yield biased estimates because of omitted variables that cause both the outcome and one or more of the mediating variables. If variables that affect the outcome and ….mediating variables are not controlled in the analysis, biased estimates of the mediation process will result, even .. a randomized experimental research design ..."

- (similar quote on James & Brett, 1984 p. 317-318, see also James, 1980)

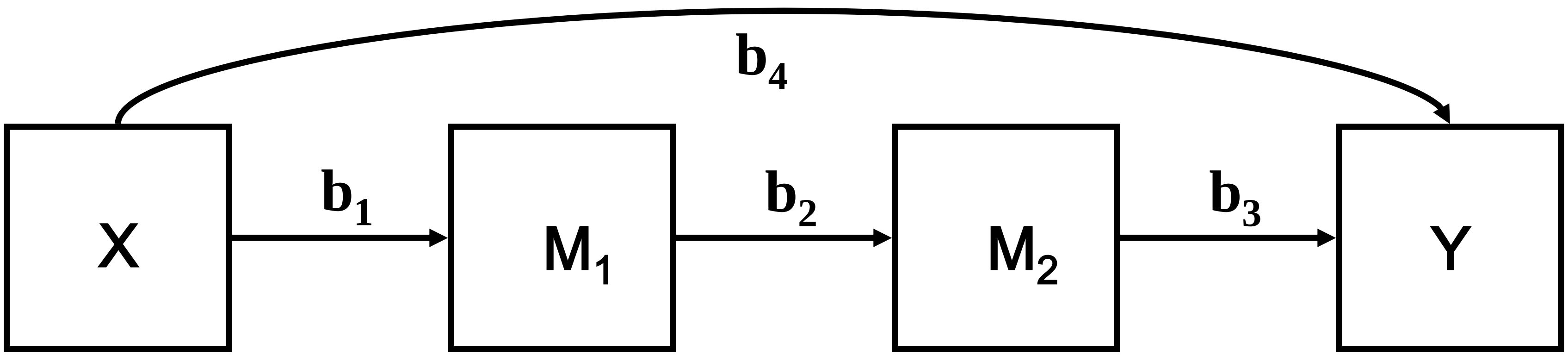
Confounding in the Social Sciences

Some areas such as psychology can easily run many randomized experiments to conduct a more fine grained investigation of mediation by removing effects of confounders by design.

The most common approach is to include all variables in a comprehensive model like Structural Equation Modeling (SEM). Make up for lack of clarity by having a more comprehensive model.

Discussion of alternative explanations of relations.

Three-Path Sequential Mediation Model

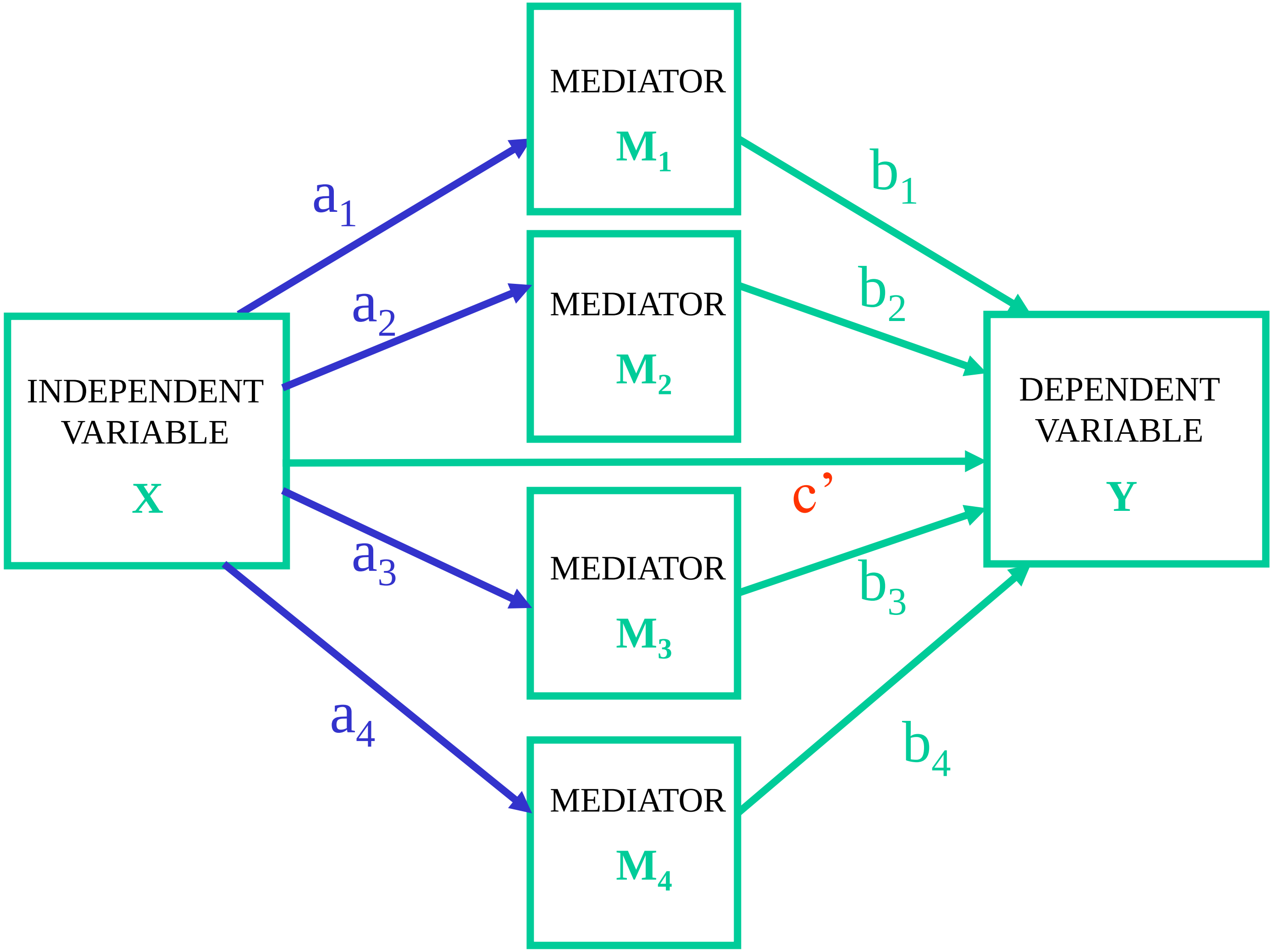


Mediated effect = $b_1 b_2 b_3$

$Var(b_1 b_2 b_3) = b_1^2 b_2^2 s_{b3}^2 + b_1^2 b_3^2 s_{b2}^2 + b_2^2 b_3^2 s_{b1}^2 + 2\, b_1 b_2 b_3^2 s_{b2b1}^2 +$
$2\, b_1 b_2^2 b_3 s_{b1b3}^2 + 2\, b_1^2 b_2 b_3 s_{b2b3}^2$

Standard Error$(b_1 b_2 b_3)$= $\sqrt{var(b_1 b_2 b_3)}$

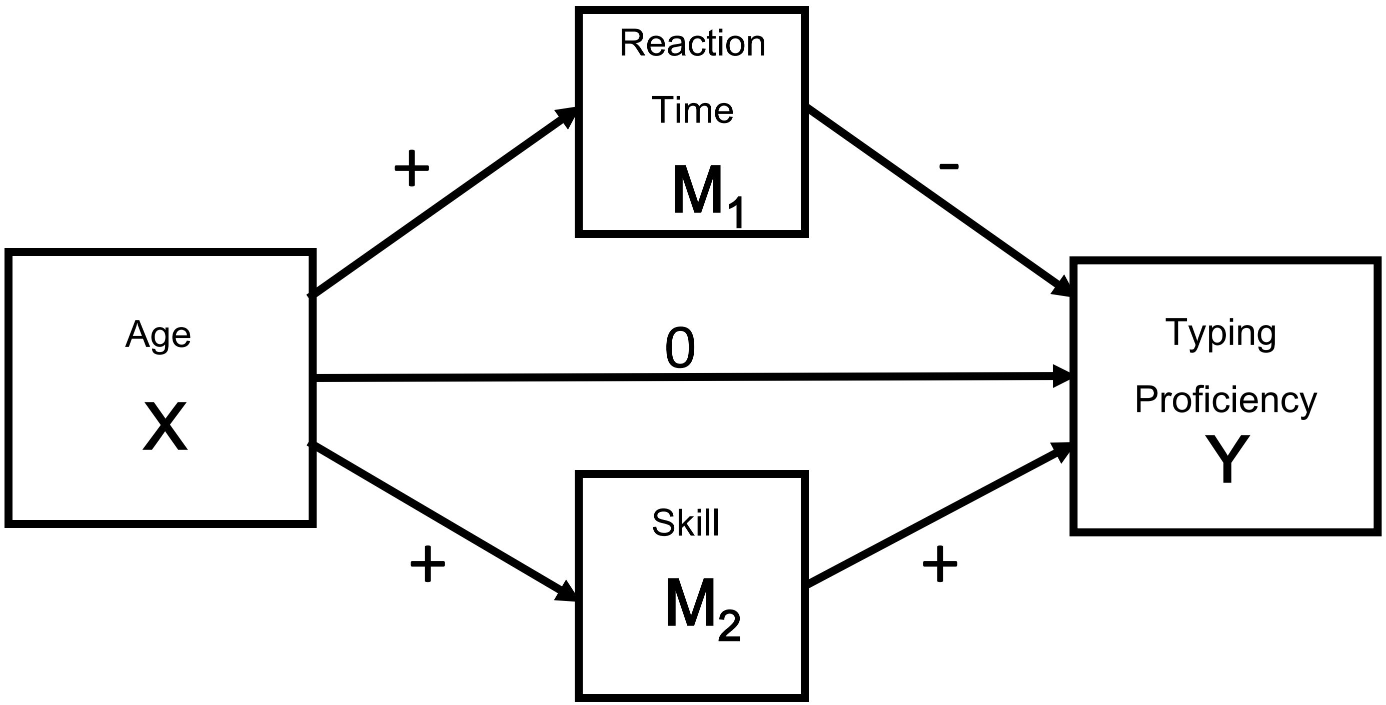
Parallel Four Mediator Model



Inconsistent Mediation Models

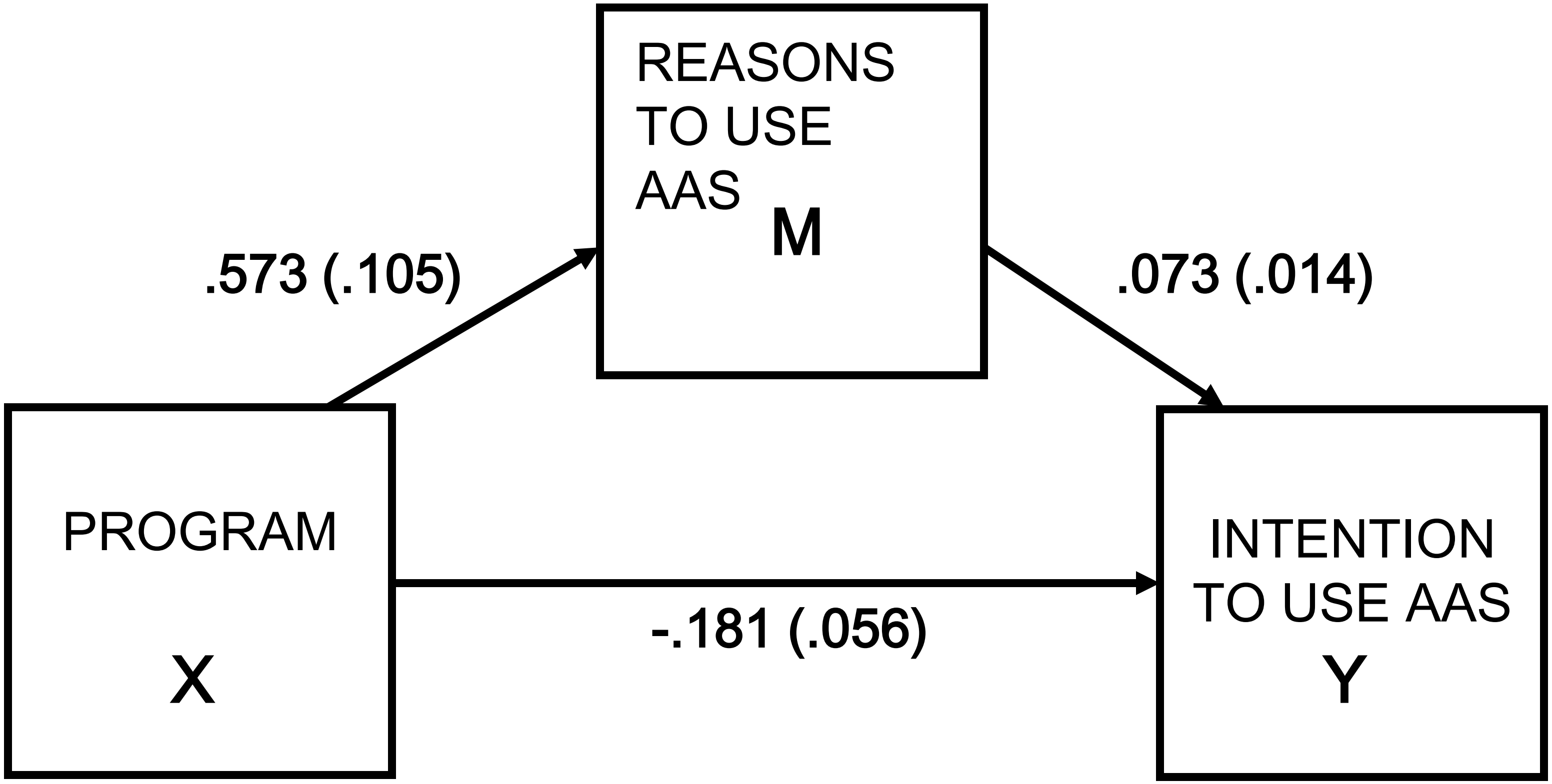
- An inconsistent mediation model has at least one mediated effect with a different sign than the direct effect or other mediated effects (MacKinnon et al., 2000)
- There is mediation because the mediator transmits the effect of the independent variable to the dependent variable. Inconsistent mediation can occur whether or not $\hat{c}$ is statistically significant.
- Intervention studies may have a mediator that is counterproductive. The best way to find these variables is to use mediation analysis.

Mediators of the null effect of age on typing (Salthouse, 1984)



Compensation - compensate for loss of capacity with other methods. Compensation implies opposing mediational processes for the effect of aging (Baltes, 1997).

Inconsistent Mediation in Steroid Prevention Study



Mediated effect = .042
Standard error = .011

More on Temporal Order

- Assume temporal ordering is correct: X before M before Y.
- Assume that relations among X, M, and Y are at equilibrium so the observed relations are not solely due to when they are measured, i.e., if measured 1 hour later a different model would apply.
- Assume correct timing and spacing of measures to detect effects.
- But manipulations target specific times with many patterns of change over time.

Mediation is a Longitudinal Model

- A mediator is a variable in a chain whereby an independent variable causes the mediating variable which in turn causes the outcome variable—these are longitudinal relations. X, M, and Y in single mediator model imply longitudinal relations even if measured at the same time.
- For a single mediator model, temporal order for X is clear when it represents random assignment, but the temporal order of M and Y must be based on prior research or theory.

Cross-sectional models

Cross-section is a snapshot of relations.

Models assume that a system has reached an equilibrium. But systems may be dynamic and change over time in complicated ways.

Meaning of cross-sectional relations (relation of rank order of level) is different from longitudinal relations (relation of rank order of change).

May take time for effects to occur. Size of effect depends on time lag-effect 1 day apart is likely different from an effect 1 year apart. Functional form over time may differ.

(Cole & Maxwell, 2003; Gollob & Reichardt, 1991; MacKinnon, 2008; Maxwell & Cole 2007; Maxwell et al., 2012 and Commentaries in *Multivariate Behavioral Research*)

Benefits of Longitudinal Data

- Time-ordering of X to M to Y is investigated. Can shed light on whether changes in M precede changes in Y.
- Both cross-sectional and longitudinal relations can be examined.
- Removes some alternative explanations of effects, e.g., effects of unchanging individual variables can be removed.

What if repeated measures of X, M, and Y are available?

- Measures of X, M, and Y at two time points allow for several options; difference score, ANCOVA, residualized change score, relative change…
- Measures of X, M, and Y at three or more time points allow for many alternative longitudinal models.
- For many examples, X is measured once and represents random assignment of participants to one of two groups. Other variables often do not represent random assignment.

Stability, Stationarity, and Equilibrium

- Stability-the extent to which the mean of a measure is the same across time.
- Stationarity-the extent to which relations among variables are the same across time.
- Equilibrium-the extent to which a system has stabilized so that the relations examined are the same over time.

Cole & Maxwell, 2003; Dwyer, 1983; Kenny, 1979; MacKinnon, 2008; Wohlwill, 1973

Timing of Relations

- When does X affect M or M affect Y?
- What is the functional form? Triggering, cascading, and other timing processes (Tang & DeRubeis, 1999; Howe et al., 2002).
- How are decisions made about timing? Not often considered in research projects except with respect to when a manipulation is made and the easiest time for data collection.
- Timing is crucial for deciding when to collect longitudinal measures (Collins & Graham, 2003).

Models for Three or More Waves

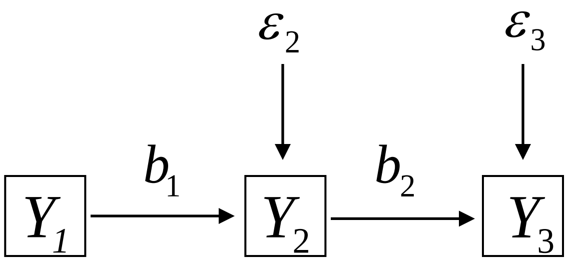
Autoregressive Models

Latent Growth Curve Models (LGM)

Latent Change Score Models (LCS)

Others: Autoregressive and Latent Growth Curve Models (ALT), Differential Equation Models, Area Under the Curve, Multilevel Structural Equation Models, Survival Analysis, fractional polynomial (Royston & Altman, 1994), spline (Borghi et al., 2006), functional data analysis (Ramsay, 2005)

Autoregressive (Jöreskog, 1974)

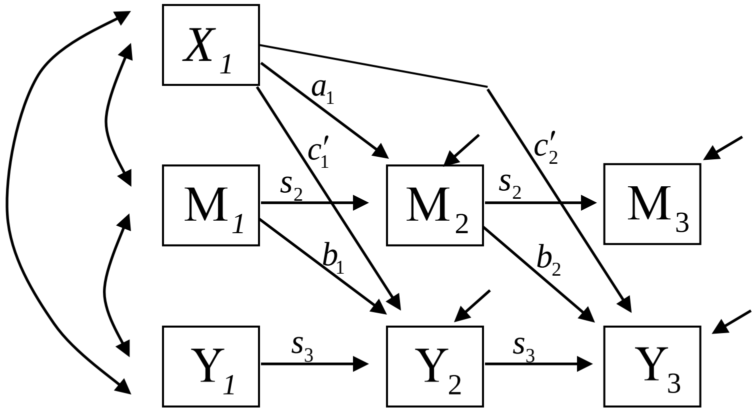


$$Y_2 = b_1 Y_1 + \varepsilon_2$$

$$Y_3 = b_2 Y_2 + \varepsilon_3$$

$$\sigma^2_{Y_1}, \sigma^2_{\varepsilon_2}, \sigma^2_{\varepsilon_3}, b_1, b_2$$

Autoregressive Model with Time-Ordered Mediation, Cole & Maxwell, (2003); MacKinnon (1994, 2008)

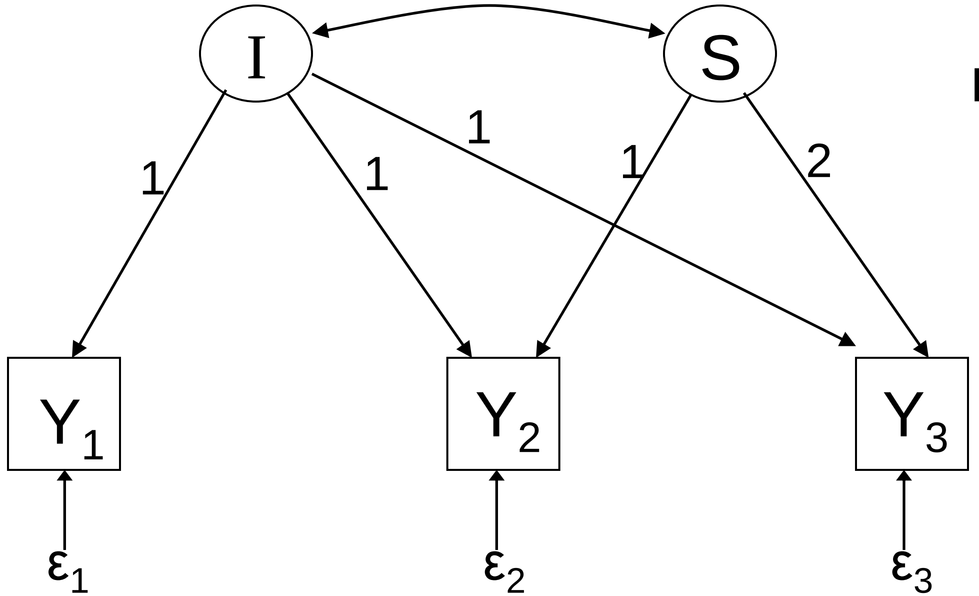


Note: Residuals at the same time are correlated

Autoregressive Models

- Many indirect effects. Standard error of the sum of (or any function) the indirect effects can be derived with the multivariate delta method or resampling methods.
- Model does not allow for random effects for individual change and does not typically include modeling of means. Change in growth of means is an important aspect of longitudinal data.

Latent Growth Model (LGM)



Meredith & Tisak (1990)

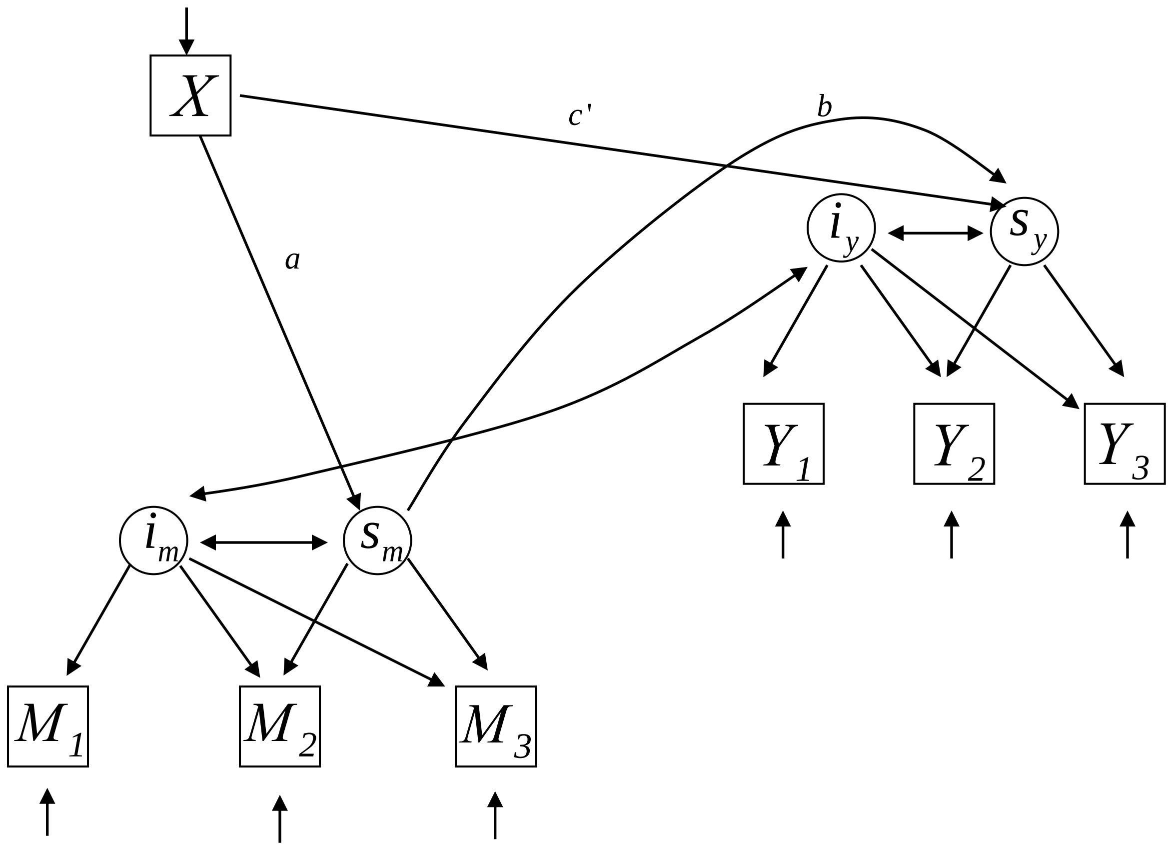
$$Y_1 = I + 0S + \varepsilon_1$$

$$Y_2 = I + 1S + \varepsilon_2$$

$$Y_3 = I + 2S + \varepsilon_3$$

$$\sigma^2_{\varepsilon_1}, \sigma^2_{\varepsilon_2}, \sigma^2_{\varepsilon_3}, \sigma^2_I, \sigma^2_S, \rho_{IS}, Means$$

Latent Growth Curve Model (Cheong et al., 2003)



Latent Growth Models (LGM)

- LGM models change over time by estimating an intercept and slope for change in variables. These models can be used to investigate mediation by estimating change over time for the mediator and change over time for the outcome (Cheong et al. 2003).
- Another LGM estimates change in the mediator at earlier time points to change in the outcome at later time points providing more evidence for temporal precedence of the mediator.
- Latent Change Score (LCS) models are also available (McArdle, 2001).

Modern Causal Inference for Longitudinal Data 1

Time varying effects lead to complexities when interpreting causal effects.

Changes at earlier waves could cause subsequent variables that complicate model interpretation.

For example, the relation of M to Y at each wave can lead to complications. Should earlier measures of M or Y be included in the prediction of later waves of data? Problem of collider bias.

Modern Causal Inference for Longitudinal Data 2

Specify longitudinal models in a potential outcome and causal framework.

G-computation ~ standardization where predictions are made for factual and counterfactual data.

G-estimation to obtain a parameter value that removes effect of interest.

Marginal Structural Model with inverse probability weighting to weight observations by amount of confounding.

(Robins 1986, 1989, 1999 and colleagues)

Marginal Structural Model IPW Example

Obtain predictors of M that will render M unaffected by confounders. Note that this assumes that all confounders are in the statistical model-the no unmeasured confounders assumption.

The method uses inverse probability weighting to reweight participants according to exposure to treatment and values of confounders. (Coffman, 2011; Robins, Hernan, & Brumbeck, 2000).

Longitudinal models for a steroid prevention project (ATLAS)

- Adolescents Teaching and Learning to Avoid Steroids (ATLAS) project randomized high school football teams in Oregon and Washington to receive the steroid prevention program or an information only group. Just individual data here.

- Measured the same persons at baseline and after half were randomized to receive a prevention program.

Linn Goldberg (OHSU) principal investigator. For more on the program see Goldberg et al. (1996) and for mediation see MacKinnon et al., (2001). LGM Cheong et al., (2003).

ATLAS IPW Analysis

- Confounders may explain the relation of M to Y in these data. It would be useful to apply a method that adjusts for possible confounding.
- A large number of measures were used in the propensity model, e.g., grades, body image, depression, perceptions of steroid use, attitudes…
- Program changes a social norm mediator which then affects nutrition behavior outcome.

ATLAS IPW Results

Parameter	Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept	-0.0035	0.0395	-0.0810	0.0739	-0.09	0.9290
X	0.4237	0.0681	0.2903	0.5572	6.22	<.0001
M	**0.1287**	**0.0323**	**0.0655**	**0.1920**	**3.99**	**<.0001**

***b* = 0.1715 se = 0.0315 with traditional analysis.**

Weights ranged from .2 to about 7

IPW Confidence Limits UCL=.113 LCL=.034

Usual Confidence Limiits UCL=.135 LCL=.059

Longitudinal Models Summary

- Many alternative longitudinal models.
- Generating the potential outcomes for longitudinal models is challenging.
- There are several potential outcome methods to look at effects at specific endpoints but these have been rarely applied in social science.
- Combination of person and variable approaches for mediation is an active area of research.

Summary

- Widespread application of mediation in the social sciences. Regression and Structural Equation Modeling are the most common methods.
- Growth in modern causal methods.
- Multiple mediator model is most likely for social science outcomes.
- Longitudinal mediation models shed light on temporal precedence.
- Methods work needed to understand these models: causal inference, model equivalence, validity of assumptions.
- Need examples of applying the models to real data.

Thank You

References available by sending me an e-mail at David.MacKinnon@asu.edu

Most topics are covered in MacKinnon (2008). Introduction to Statistical Mediation Analysis, Erlbaum; Mahwah, NJ. e.g., Causal Inference circa 2008 Chapter 13, Longitudinal Mediation models in Chapter 8, and background for mediation in Chapters 1 and 2. New edition will contain more information on causal mediation methods.

See website for Research In Prevention Laboratory

http://www.public.asu.edu/~davidpm/

Hypothesized Effects of Oxford Mediation Analysis Presentation