Mediation Special Topics

- Causal Mediation Analysis
- Meta-analysis and data synthesis.
- Categorical Variables
- Multilevel Mediation Models
- Bayesian mediation analysis.

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Causal Inference in Mediation (Chapter 13)

- Assumptions of true causal relations and self-contained/comprehensive model for regression analysis for mediation.
- Blalock's (1979) presidential address states that about 50 variables are involved in sociological phenomenon and Weinstein's comprehensive versus limited health psychology models. How many variables are relevant in your research area?
- Problem with mediation analysis because M is not randomly assigned but is self-selected.
- Causal inference for mediation is an active research area (Frangakis & Rubin, 2002; Pearl, 2001; Pearl, 2009).

Counterfactual/ Potential Outcome Models

- Most modern causal inference approaches are based on a counterfactual or potential outcome model.
- In these models, all the possible counterfactual and actual conditions of an experiment are considered and the statistical model is based on all these possible or potential conditions.
- The Marginal Structural Model is the regression model for these counterfactual and actual conditions. It differs from the usual regression model because it is based on potential outcomes.
- Natural and Controlled Effects.

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Randomized Two Group Design

- Ideally we need the same individual in both the treatment and control conditions at the same time. Units (individual level) usually have observed data for one of two conditions but not the other—the fundamental problem of causal inference (Holland, 1986).
- Randomization of a large number of persons solves the fundamental problem of causal inference. The average in each group can be compared and is an estimator of a causal effect. It is called an average causal effect (ACE).

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Why *b* and *c'* Do Not Reflect a Causal Relation

- Because M is not under experimental control, *b* and *c'* do not necessarily represent causal effects. M is both a dependent and independent variable.
- Need: The relation between M and Y for participants in the treatment group if they were in the control group; the relation between M and Y for control participants if they instead were in the treatment group. Coefficients *b* and *c'* are not Average Causal Effects, because the counterfactuals for these relations are complicated because M is not randomly assigned.

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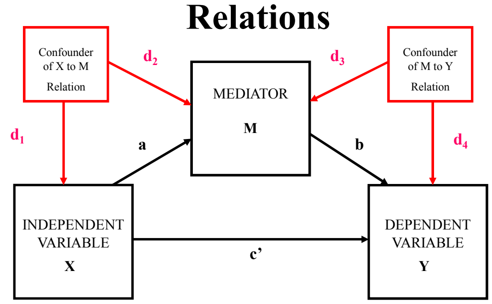
Confounders of Mediation Relations



True model needs d_1,d_2, d_3, d_4, otherwise coefficients are confounded.

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Sensitivity Analysis for Confounding

- How will results change with confounding of the M to Y relation, e.g. when X is randomized?
- VanderWeele (2010), confounder effect on Y and difference in proportions of the confounder between groups at level of M.
- Imai et al. (2010), confounder effect as the correlation between error terms.
- Adaptation of Left Out Variables Error (LOVE; Mauro, 1990) based on the correlation of a confounder with Y and the correlation of a confounder with M.
- See Cox et al., 2014, *Evaluation Review*.

Statistical Methods for Confounding

- Statistical approaches to improve causal inference from a mediation study. A way to deal with omitted variable bias.

1) Instrumental Variable Methods
2) Principal Stratification
3) Inverse Probability Weighting
4) G-estimation

- Active area of research (MacKinnon & Pirlott, 2015, *Personality and Social Psychology Review*)…

Inverse Probability Weighting

- Method to adjust results for confounders.
- Assumes no unmeasured confounding.
- Weights observations as a way to deal with confounding, missing data etc.
- Here weights are used to adjust for confounding of the M to Y relation when R is randomized.
- Marginal treatment effect under ignorability.

See Robins, Hernan, & Brumbeck (2000) and also Coffman (2011).Weighting has a long history starting in sampling (Horvitz & Thompson, 1952).

IPW is a General Procedure

- Can be used to adjust for confounders, lack of randomization, missing data, longitudinal data.
- Can be used for models with many variables but need a model to predict each variable, e.g., if X is not randomized, fit a propensity model for X and also M and conduct weighted analysis for M and Y.
- No unmeasured confounders assumption is likely better than no adjustment at all?
- Possible that adjustment would increase or decrease estimates based on weights.
- Weights can be unstable so there is research on different weighting methods (Cole & Hernan, 2008).

Design Approaches to Improving Causal Inference

- Statistical mediation analysis answers the following question, "How does a researcher use measures of the hypothetical intervening process to increase the amount of information from a research study?"
- Another question is, "What is the best next study or studies to conduct after a statistical mediation analysis to test mediation theory."

1. Designs to address **Consistency** of the mediation relation.
2. Designs to address **Specificity** of the mediation relation.

MacKinnon, 2008; MacKinnon & Pirlott, 2012 related to Hill's (1971) considerations. Also SMART designs (Almiral et al., 2014)

(1) Consistency Mediation Designs

- Consistency designs replicate mediation relations in new settings, groups, species (animals, humans), and times.
- Consistency designs also replicate mediation relations with alternative manipulations (X), alternative measures of the same mediator (M), and other related dependent measures (Y).
- Overall, consistency designs provide evidence that the mediation relation is consistently observed across many domains and variables.

(2) Specificity Mediation Designs

- Evidence for specificity of a mediation relation is obtained by comparing between groups (or variables) to demonstrate that the mediation relation is present in the predicted groups (or variables) but not present in other groups (or variables).
- Specificity designs demonstrate that mediation relations can be changed by different manipulations (X), mediation relations are observed for some mediators (M) but not others, and mediation is observed for some dependent measures (Y) but not others in a way that demonstrates a pattern of results consistent mediation theory.

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Blockage Specificity Designs

- The goal of blockage designs is to test a mediation relation with a manipulation that blocks the mediator from operating.
- For example, let's say that an exercise program appears to reduce depression by increasing endorphin levels -- the hypothesized mediator. A blockage manipulation would administer a drug to prevent endorphin production so that persons receiving the exercise program would no longer experience reduced depression if the endorphin level is the mediator.

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Enhancement Specificity Designs

- The goal of enhancement designs is to test interventions that enhance the effects of a hypothesized mediator.
- For example, let's say that a treatment program improves abstinence by increasing social support. An enhancement design would include a group where social support is increased even more to demonstrate a larger effect on abstinence. Social support may be increased by more sessions with counselors, increasing exposure non addicted friends and family etc. in addition to the typical program.

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Causal Mediation Summary

- Causal inference in mediation is challenging because M is not randomized.
- Can look at how effects would change for different confounder values.
- Can include measures of confounding variables in the statistical analysis.
- Experimental approaches to improving causal inference.
- Active research area with more to come.

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Mediation for Integrated Data Analysis and Meta-Analysis

- Methods to combine information across research studies.
- Estimates for X to M and M to Y relations.
- Relation of M to Y is more problematic because M is not randomized so relation between M and Y is correlational as it is for the single mediator model.
- Mediator constructs may differ across studies. Even if it is the same construct, measurement may differ. Weakness or a strength? Strengths: use as estimates of different aspects of a random process, measurement facets, Bayesian update estimates with each new study.

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Mediation with a Categorical Dependent Variable (Chapter 11)

A dependent variable is often binary such as whether a person litters or not, used a condom or not, dead or alive, diseased or not, or divorced or not. Counts of events.

In this case, Poisson, logistic or probit regression is the method of choice because of violation of assumptions if ordinary least squares regression is used.

Estimates of the mediated effect using logistic and probit regression can be distorted using conventional procedures.

Here binary or continuous X, continuous M, and binary Y is described in detail (Chapter 11).

MacKinnon 2008; MacKinnon et al., *Clinical Trials (2007)* and MacKinnon et al., under revision.

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Why *ab* and *c-c′* are not equal in Logistic and Probit Regression…

- The two estimators, *ab* and *c-c′* are not identical in logistic or probit regression because, unlike ordinary least squares regression where the residual variance varies across equations, in logistic regression the residual variance is fixed to equal $\pi^2/3$ (MacKinnon & Dwyer, 1993). So the logistic regression coefficients are a function of the relations among variables and the fixed value of the residual variance.
- There are solutions if you want *ab* and *c-c′* to be close.
- Or just focus on *ab* and its standard error to make confidence intervals or use Rmediation or the bootstrap.

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Options for Categorical M and Y #1

- Can just use product of coefficient methods with Rmediation or bootstrap.
- Or you could use Mplus which standardizes across equations. Mplus also allows for path analysis models with combinations of categorical and continuous variables.
- Sample size requirements are larger for binary dependent variable than for continuous dependent variable.
- With logistic or probit regression, *c-c'* does not always equal *ab*. Can standardize values to make *c* and *c'* in the same metric so the *c-c'* method is comparable to *ab*.

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Options for Categorical M and Y #2

Traditional and potential outcome approach to mediation coincide for linear models and log-linear models.

For non-linear models with interactions, methods based on the counterfactual model may yield different results.

If you are using nonlinear models with interactions you can use the SAS and SPSS macros described in Valeri & VanderWeele (2012) to investigate how results may differ. Or you could use Imai et al.'s R program. Mplus with the Model Constraint command will work and counterfactual quantities is estimated in Mplus Version 7.2.

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Multilevel Mediation (Chapter 9)

Mediation
Multilevel data as a nuisance and an opportunity
Mediation in Multilevel Models
Groups, schools, classes, clinics, cities, states….and also individuals.
Ecological and Atomistic Fallacies

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Multilevel mediation effects for two-level models

Level of X, M, and Y can be used to describe different types of multilevel models. Assume X, M, and Y are all measured at the individual level.

$1 \rightarrow 1 \rightarrow 1$; X, M, and Y measured at the individual level.

$2 \rightarrow 1 \rightarrow 1$; X at level 2, M and Y at the individual level.

$2 \rightarrow 2 \rightarrow 1$; X and M at level 2, Y at the individual level.

$2 \rightarrow 2 \rightarrow 2$; X, M, and Y level 2.

(Krull & MacKinnon, 1999)

Models with more than two levels, e.g., three levels.

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Multilevel mediation effects for three-level models

$3 \rightarrow 2 \rightarrow 1$; X (Schools), M (Classroom Observations), and Y (Individuals).

$3 \rightarrow 2 \rightarrow 1$; X (Schools), M (Person Norms), Y (Repeated Measures).

$1 \rightarrow 1 \rightarrow 1$; X, M, and Y measured at the individual level but the data have a three level structure, e.g., Individuals X, M, and Y within schools

See Preacher, K. J. (2011). Multilevel SEM strategies for evaluating mediation in three-level data. *Multivariate Behavioral Research*, *46*, 691-731, and Pituch, K. A., Murphy, D. L., & Tate, R. L. (2010). Three-level models for indirect effects in school- and class-randomized experiments in education. *Journal of Experimental Education, 78, 60*-95.

Four-level, Five-level,…

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Mediated Effects at Different Levels

Mediated effects at group and individual level are possible (MacKinnon, 2008).

Controversy about individual level mediated effects when X is at a higher level. For example in the 2 -1- 1 model, X is delivered at Level 2 and the M to Y relation is at Level 1. Does it make sense to consider this mediated effect at the individual level? It does not when only considering the data measured. But the population mediated effect is the intervention changing individuals even when X is at Level 2.

See Pituch, K.A., & Stapleton, L. M. (2012). Distinguishing between cross- and cluster-level mediation processes in the cluster randomized trial. *Sociological Methods and Research, 41*, 630-670.

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1-1-1 Model

Investigates mediation for each individual and also investigates mediation for the averages across people (MacKinnon & Valente, 2014).

Combines idiographic and nomothetic approaches in one analysis.

Important new mediation model.

Related to N of 1 research designs but also includes aggregation across persons.

Person-centered medicine, adaptive designs….

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1-1-1 Model Key Idea

There is a mediated effect for each individual and there is a variance of this mediated effect across individuals.

There is also an average mediated effect that combines information from each individual to compute the average mediated effect. This average mediated effect has more power and is usually the mediated effect of interest.

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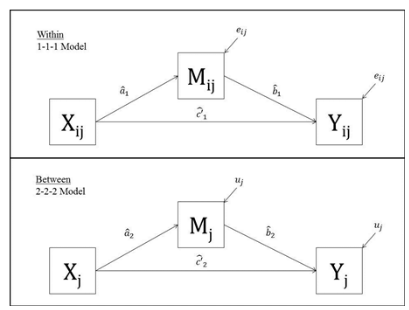
1-1-1 Figure



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Multilevel Structural Equation Modeling (MSEM)

1. Allows for measurement models for constructs to accommodate measurement error.
2. General model that allows for simultaneous estimation of model coefficients, e.g., mediation models, more complex models.
3. Some fit indices, estimation strategies available in SEM can be applied to multilevel data.

Software now available and growing Mplus (Muthen & Muthen, 2001), GLLAMM (Rabe-Hesketh et al., 2004)

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More information on MSEM

Mplus www.statmodel.com

GLLAMM www.gllamm.org

EQS http://www.mvsoft.com/products.htm

Lisrel http://www.ssicentral.com/lisrel/

HLM http://www.ssicentral.com/hlm/

UCLA mplus information http://www.ats.ucla.edu/mplus

Mlwin http://www.bristol.ac.uk/cmm/software/mlwin/

Joop Hox's homepage: http://www/joophox.net

Kris Preacher's Mplus program examples: http://www.quantpsy.org/pubs/syntax_appendix_081311.pdf

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Multilevel Summary

Two views of multilevel data: (1) a nuisance in the statistical analysis and (2) an opportunity to investigate effects at different levels.

New Mplus version allows for estimation of many different models including random *a* and *b* effects using MSEM.

Can have very complicated models with many levels and potential mediation across and between levels.

Need applications to real data. Need methods work for information on statistical testing….

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Bayesian Mediation Analysis: Fixed versus Random parameters

In frequentist statistics, parameters are fixed and unknown; we find point estimates and/or confidence intervals for parameters. The data are random.
p-value=P(data|H_0)

In Bayesian statistics, parameters are random and the data are fixed. We find point estimates (usually the mean or median of the posterior distribution) or probability intervals for the parameters.
Posterior probability=P(H_0|data)

Inverse probability was the original term for what Fisher called Bayesian (derisively). So you have probability (Frequentist) and inverse probability (Bayesian).
*Thanks to **Milica Miočević** for the next few slides.

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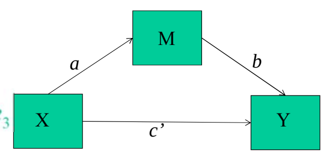
Bayesian Mediation

- All parameters get prior distributions

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

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



- Normal prior distributions are specified for regression coefficients *int2, a, int3, b,* and *c'*
- The variances of M and Y are inverse-gamma prior distributions

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Why Bayesian Mediation might be a better option than standard methods

1. Prior Information: It is a natural way to build knowledge about a phenomenon; the results of each study before the current one can be represented in prior information.
2. Prior Information: If the results of one study are completely divergent from the previous findings, it allows for the calibration of these anomalous findings when prior knowledge is incorporated into the analysis.
3. Credible Intervals: The estimates using Bayesian mediation have a probabilistic interpretation: instead of talking in terms of confidence, results are interpreted in terms of probability.
4. Small Samples: It is useful for small sample sizes

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Mplus code for Bayesian Mediation with diffuse prior distributions

```
title: Bayesian Mediation analysis with a diffuse prior;
data: file=f13secondstudynonames.csv;
variable:
names= id x m y;
usev= x-y;
analysis:
estimator=bayes;
process=2;
model:
m on x (a);
y on m (b)
X (cpr);
model constraint:
new (indirect);
indirect=a*b;
output: tech1 tech8 standardized;
plot:
type=plot2;
```

The only change in the code compared to maximum likelihood estimation

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Mplus output for Bayesian Mediation with diffuse prior distributions

```
MODEL RESULTS

                              Posterior  One-Tailed        95% C.I.
                   Estimate       S.D.     P-Value   Lower 2.5%  Upper 2.5%

 M          ON
    X                 5.969      0.577      0.000       4.993       7.068

 Y          ON
    M                 1.034      0.357      0.000       0.385       1.694
    X                -0.517      2.351      0.430      -5.901       4.000

 Intercepts
    M                 2.326      0.401      0.000       1.539       3.137
    Y                 5.975      1.139      0.000       3.949       8.044

 Residual Variances
    M                 2.156      0.500      0.000       1.567       3.405
    Y                 8.555      2.508      0.000       5.619      15.213

 New/Additional Parameters
    INDIRECT          6.129      2.307      0.000       2.334      10.478
```

Point estimate for the mediated effect

95% credibility limits

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Bayesian Mediation References

Enders, C. K., Fairchild, A. J., & MacKinnon, D. P. (2013). A Bayesian Approach for Estimating Mediation Effects With Missing Data. *Multivariate Behavioral Research*, *48*(3), 340-369.

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Gill, J. (2002). *Bayesian methods: A social and behavioral sciences approach*. CRC press.

Miočević, M. (2014). *Obtaining accurate estimates of the mediated effect with and without prior information. Masters Document.*

Miočević, M., & MacKinnon, D. P. *SAS® for Bayesian mediation analysis*. In Proceedings of the 39th annual meeting of SAS Users Group International. Cary, NC: SAS Institute, Inc.

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Muthén, B. & Asparouhov, T. (2012).Bayesian SEM: A more flexible representation of substantive theory. *Psychological Methods*, *17*, 313-335.

Yuan, Y., & MacKinnon, D. P. (2009). Bayesian mediation analysis. *Psychological methods*, *14*(4), 301.

Other Special Topics

Person-oriented Mediated Effects.

Mediation analysis with massive amounts of data.

Measurement of Mediating Variables.

Combining substantive review meta-analysis of mediating variables in each research area.