

# Statistical Considerations in Multilevel Mediation Analysis

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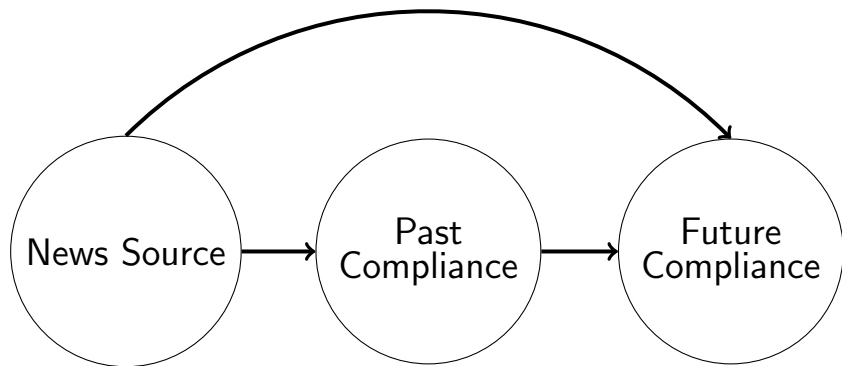
# Outline

- 1) The Problem
- 2) Mediation Analysis
- 3) Causal Inference
- 4) Mixed-Effects Models
- 234) Mixed-Effects Models in Causal Mediation Analysis

# Example

- Goal: Understand adherence to restrictive measures
  - E.g. Lockdowns
  - Both past and future
- Influence of news source
  - How trustworthy?
- Disentangle influence on future from influence on past

# Example

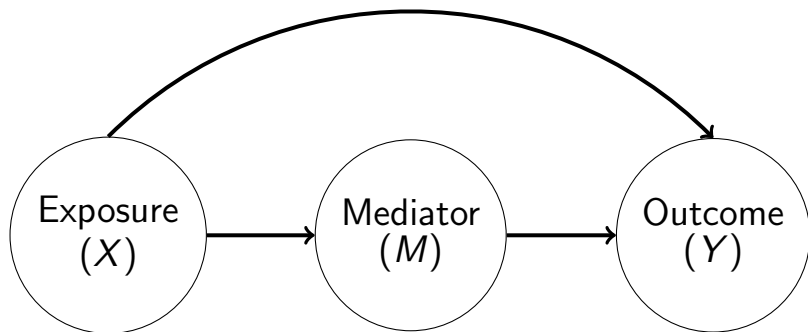


# Example

## Terminology

- Top path: Direct effect
- Center path: Indirect effect
- Combined: Total effect
- Exposure:  $X$
- Outcome:  $Y$
- Mediator:  $M$

# Mediation Analysis



# Mediation Analysis

- Separate **Total Effect** of  $X$  on  $Y$  into
  - **Direct Effect**
  - **Indirect Effect**
- Define mediation effects using counterfactuals
- Differences, ratios, odds-ratios

# Mediation Analysis

- We only observe one outcome per individual
- Explore population-level effects by averaging
- Identify expected counterfactuals with conditional expectations
  - Now it's a regression problem



# Mediation Analysis

- Fit two regression models
  - Mediator given exposure
  - Outcome given mediator and exposure
  - Both may include confounders
- Linear vs Logistic
- Fixed- vs Mixed-Effects
  - Single- vs Multi-Level

# Mediation Analysis

- Fit two regression models
  - Mediator given exposure
  - Outcome given mediator and exposure
  - Both may include confounders
- Linear vs **Logistic**
- Fixed- vs **Mixed-Effects**
  - Single- vs Multi-Level

# Mediation Analysis

- Model fitting involves intractable integrals over unobserved random effects
  - Evaluate using quadrature
- Estimated mediation effects depend on coefficients and RE covariances
- Uncertainty quantification:
  - Quasi-Bayesian Monte Carlo
  - $\delta$ -method

# Uncertainty Quantification

- Quasi-Bayesian Monte Carlo
  - Monte Carlo  $\delta$ -Method
- 1 Estimate sampling distribution of regression parameters
- 2 Simulate from estimated sampling distribution
- 3 Compute mediation effects for simulated parameters

# Uncertainty Quantification

- Quasi-Bayesian Monte Carlo
  - Monte Carlo  $\delta$ -Method
- Advantage: Flexible
- Disadvantage: Computational
- Existing implementation in R: *mediation*
  - Limited

# Uncertainty Quantification

- $\delta$ -Method
- 1 Estimate (asymptotic) sampling distribution of regression parameters
- 2 Compute Jacobian of map from reg pars to mediation effects
- 3 Multiply asymp. covariance by Jacobian

# Uncertainty Quantification

- $\delta$ -Method
- Advantage: Analytical
- Disadvantage: Asymptotic
- No existing R implementation
  - Until now!
  - Use glmmTMB, not lme4

# Comparison

- Simulate 200 datasets
  - **100** groups, **500** individuals per group
- Build confidence intervals using  $\delta$ - and MC  $\delta$ -methods
- Also build Wald interval using Monte Carlo (empirical) covariance matrix



# Comparison

Effect	Scale	$\delta$	MC $\delta$	Empirical
Total	Diff	0.940	0.940	0.940
	Ratio	0.935	0.930	0.955
	OR	0.955	0.960	0.950
Direct	Diff	0.960	0.960	0.960
	Ratio	0.935	0.930	0.945
	OR	0.970	0.970	0.950
Indirect	Diff	0.950	0.955	0.965
	Ratio	0.955	0.955	0.960
	OR	0.955	0.955	0.960

# Comparison

- Simulate 200 datasets
  - **10** groups, **1000** individuals per group
- Build confidence intervals using  $\delta$ - and MC  $\delta$ -methods
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# Comparison

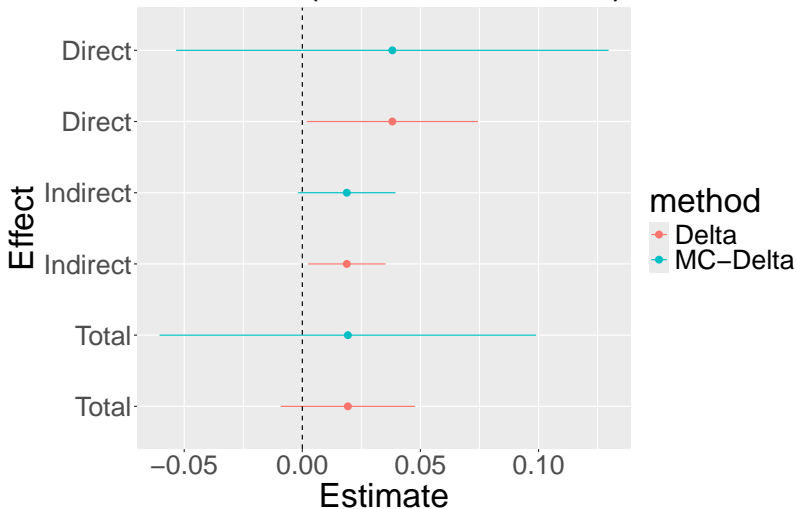
Effect	Scale	$\delta$	MC $\delta$	Empirical
Total	Diff	0.935	0.928	0.954
	Ratio	0.961	0.974	0.967
	OR	0.935	0.928	0.967
Direct	Diff	0.948	0.928	0.941
	Ratio	0.928	0.935	0.967
	OR	0.954	0.935	0.948
Indirect	Diff	0.974	0.967	0.961
	Ratio	0.980	0.974	0.961
	OR	0.948	0.928	0.948

# Trust Study

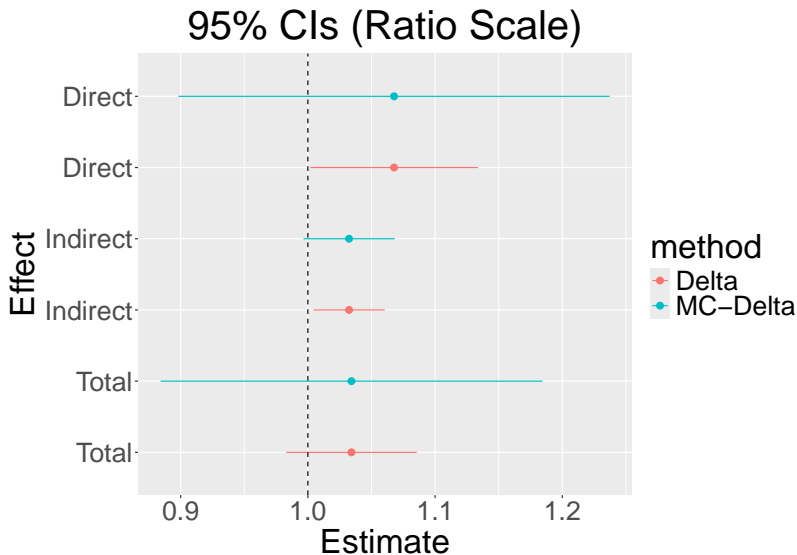
- Applying our method to the trust study dataset
  - Compare low-high trustworthiness
- CIs for all effect-scale pairs
  - 9 Intervals
- $\delta$  and MC  $\delta$

# Trust Study

## 95% CIs (Difference Scale)

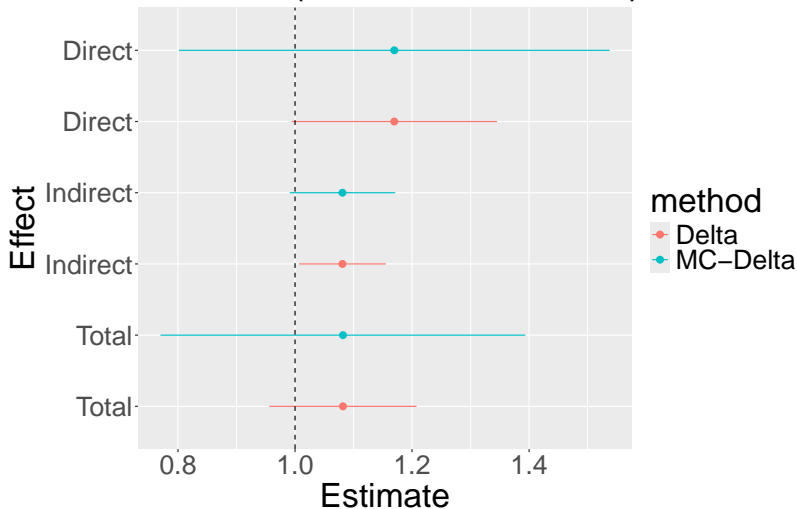


# Trust Study



# Trust Study

## 95% CIs (Odds-Ratio Scale)



# Next Steps

- Compare with Imai et al. (*mediation* package)
- Sensitivity to values of confounders
- Parametric bootstrap
- Group-specific effects



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- Rowin Alfaro
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- Bouchra Nasri

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# Thank You