Statistical Considerations in Multilevel Mediation Analysis

William Ruth

Collaborators: Rado Ramasy, Rowin Alfaro, Ariel Mundo, Bruno Remillard, Bouchra Nasri

CANSSI INCASS

Université de Montréal

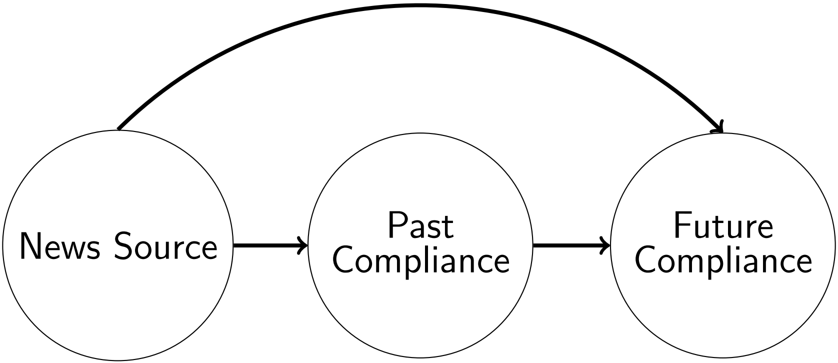
Outline

1) The Problem
2) Multilevel Causal Mediation Analysis
3) Uncertainty Quantification

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



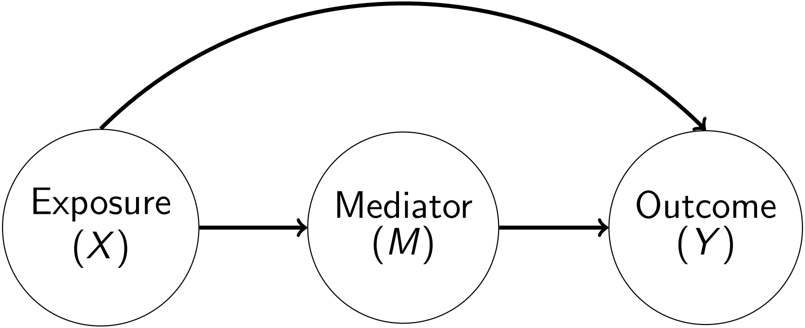
Example

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
  - δ-method

Uncertainty Quantification

- Quasi-Bayesian Monte Carlo
    - Monte Carlo δ-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 δ-Method
- Advantage: Flexible
- Disadvantage: Computational
- Existing implementation in `R`: *mediation*
  - Limited

Uncertainty Quantification

- δ-Method

1. Estimate (asymptotic) sampling distribution of regression parameters
2. Compute Jacobian of map from regression parameters to mediation effects
3. Multiply asymptotic covariance by Jacobian

Uncertainty Quantification

- δ-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 δ- and MC δ-methods
- Also build Wald interval using Monte Carlo (empirical) covariance matrix

Comparison

Effect	Scale	δ	MC δ	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 δ- and MC δ-methods
- Also build Wald interval using Monte Carlo (empirical) covariance matrix

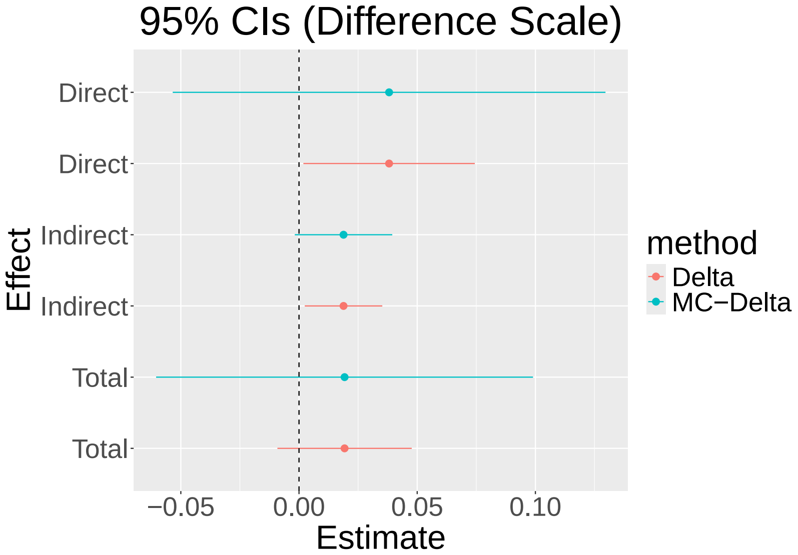
Comparison

Effect	Scale	δ	MC δ	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

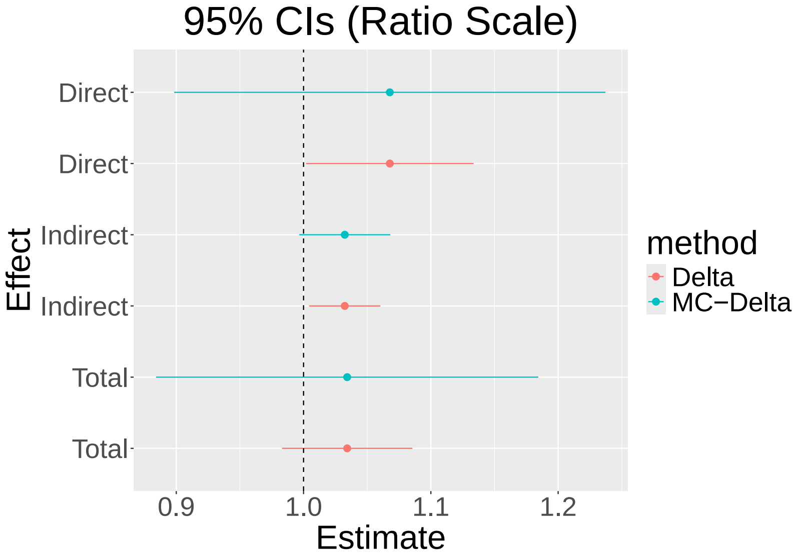
Trust Study

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

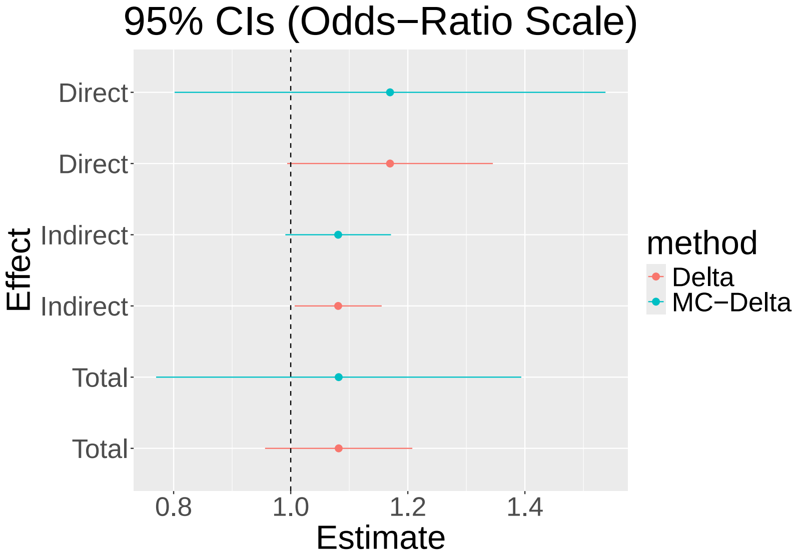
Trust Study


95% CIs (Difference Scale)
Direct
Direct
Indirect
Indirect
Total
Total
Effect
−0.05
0.00
0.05
0.10
Estimate
method
Delta
MC−Delta

Trust Study


95% CIs (Ratio Scale)
Direct
Direct
Indirect
Indirect
Total
Total
Effect
0.9
1.0
1.1
1.2
Estimate
method
Delta
MC−Delta

Trust Study



95% CIs (Odds−Ratio Scale)
Effect
Direct
Direct
Indirect
Indirect
Total
Total
0.8
1.0
1.2
1.4
Estimate
method
Delta
MC−Delta

Next Steps

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

Acknowledgements

Collaborators:

- Rado Ramasy
- Rowin Alfaro
- Ariel Mundo
- Bruno Remillard
- Bouchra Nasri

Funding:

- Canadian Statistical Sciences Institute

Thank You