Statistical Considerations in Multilevel Mediation Analysis

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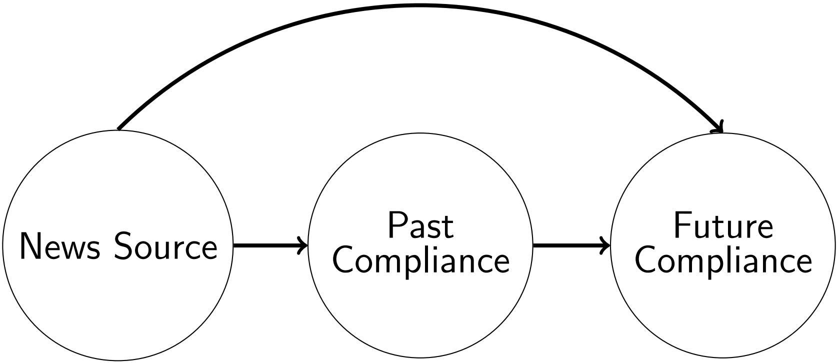
Outline

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



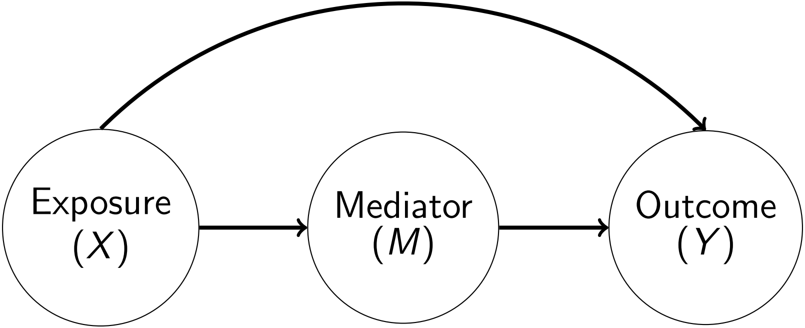
Example

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**

Traditionally, use regression

Mediation Analysis

Continuous outcome and mediator:

- $Y = \alpha_0 + \alpha_1 M + \alpha_2 X + \varepsilon_Y$
- $M = \beta_0 + \beta_1 X + \varepsilon_M$

Direct Effect: α_2

- "X in Y"

Indirect Effect: $\alpha_1 \cdot \beta_1$

- "M in Y" $\cdot$ "X in M"

Total Effect: $\alpha_2 + \alpha_1 \cdot \beta_1$

Mediation Analysis

Popular approach

- A bit outdated...

More popular: Causal mediation analysis

Causal Inference

Assume that X *causes* Y

Counterfactuals:

- What value would Y take if X were set to a particular level?
- Write Y_x for the value of Y when $X = x$
- If $X \neq x$ then Y_x is literally a "counterfactual"

Causal Inference

Example:

- Alice only reads scientific publications and will follow all lockdown mandates
- What if she instead only read Facebook?

- $Y_{Science}(Alice) = \text{follow}$
- $Y_{Facebook}(Alice) = \text{follow}$

Causal Inference

Example:

- Bob also only reads scientific publications and will follow all lockdown mandates, but is more susceptible to being influenced

- $Y_{Science}(Bob) = \text{follow}$
- $Y_{Facebook}(Bob) = \text{not follow}$

Causal Inference

- We only observe one outcome per individual
- Explore population-level effects by averaging
- Define mediation effects in terms of expected counterfactuals

Causal Inference

Total Effect: $\mathbb{E}(Y_{x'} - Y_x)$

- Effect on outcome when we change exposure from $X = x$ to $X = x'$

Other effects involve dependence on a mediator:

- Y_{xm}: Value of outcome when
  - Exposure (X) is set to x
  - Mediator (M) is set to m
- M_x: Value of mediator when
  - Exposure (X) is set to x
- "Nested Counterfactuals": Y_{xM_x} or $Y_{xM_{x'}}$

Causal Mediation Analysis

Controlled Direct Effect: $\mathbb{E}(Y_{x'm} - Y_{xm})$

- Effect of changing exposure with mediator held fixed

Natural Direct Effect: $\mathbb{E}(Y_{x'M_x} - Y_{xM_x})$

- Effect of changing exposure when we don't interfere with the mediator

Natural Indirect Effect: $\mathbb{E}(Y_{xM_{x'}} - Y_{xM_x})$

- Effect of changing which exposure value is seen by the mediator while holding fixed which exposure value is seen by the outcome

Causal Mediation Analysis

In our example

- Controlled Direct Effect: Effect of increasing news trustworthiness if the whole population followed guidelines in the past
- Natural Direct Effect: Effect of increasing news trustworthiness independent of any induced change in past compliance
- Natural Indirect Effect: Effect of changing past compliance if everyone only got news from Facebook

Causal Mediation Analysis

We can't measure all required counterfactuals

- E.g., Y_x or $Y_{x'}$, not both

Expected counterfactuals related to conditional expectations

- Under strong assumptions, $\mathbb{E} Y_x = \mathbb{E}(Y | X = x)$

Nested counterfactuals more complicated

- More on this later

Causal Mediation Analysis

How does causality change our analysis?

Still fit regression models, but include interaction terms between exposure and mediator

- $Y = \alpha_0 + \alpha_1 M + \alpha_2 X + \alpha_3 M \cdot X + \varepsilon_Y$
- $M = \beta_0 + \beta_1 X + \varepsilon_M$

Direct and indirect effects now depend on the levels of the exposure

Causal Mediation Analysis – Extensions

Discussion so far has involved continuous mediator and outcome

- What about binary or categorical?

Individuals might also be clustered

- E.g. Within countries

Causal Mediation Analysis – Extensions

Handling binary variables is pretty straightforward

- Instead of linear regression, use logistic regression
- Re-define mediation effects based on expected counterfactuals
    - I.e. Counterfactual probabilities
- New formulas for relating mediation effects to regression coefficients

Extend to more than 2 categories using binary indicators

Causal Mediation Analysis – Extensions

Clustered data more complicated

Standard approach is multi-level modelling

- I.e. Add random effects which vary across clusters

Combined with categorical variables:

- Generalized linear mixed models (GLMMs)

Mixed-Effects Models

The core idea is to augment our set of covariates

- Coefficients of these new covariates are random variables which vary across groups/clusters

In the linear setting:

- Old model: $Y = \alpha_0 + \alpha_1 X_1 + \ldots + \alpha_p X_p + \varepsilon$
- New model:
  $Y = \alpha_0 + \alpha_1 X_1 + \ldots + \alpha_p X_p + \mathbf{u_1 Z_1} + \ldots + \mathbf{u_q Z_q} + \varepsilon$

Mixed-Effects Models

The Z's are fixed, known covariates The u's are random variables

- I.e. Random effects

It's possible for the X's and Z's to overlap

- The coefficient on such a covariate has the form $\alpha_j + u_k$
- I.e. Mixed effect

Mixed-Effects Models

Extend to generalized linear models in the usual way

Choose response distribution and link function as for ordinary GLMs

Linear predictor now has a random effects component

Mixed-Effects Models

Why bother?

- E.g. Measured some but not all levels of a categorical variable
- Estimate covariance matrix of random effects
- Test for non-zero variance of each random effect

“Predict” level of random effects for each group

- Conditional mean or conditional mode of random effects given response

Mixed-Effects Models

In our example:

- Data collected from 11 different countries
- Explicitly model inter-country variability
- Predict country-specific random effects
- Use country-specific coefficients in formulas for mediation effects
- Test for significant mediation effects within each country

Multilevel Mediation Analysis

Uncertainty quantification for mixed-effects models can be challenging

Strategies include:

- Bootstrap
- Quasi-Bayesian Monte Carlo
- δ-method

Multilevel Mediation Analysis

Uncertainty quantification for mixed-effects models can be challenging

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- **Bootstrap**
- Quasi-Bayesian Monte Carlo
- δ-method

Multilevel Mediation Analysis

Uncertainty quantification for mixed-effects models can be challenging

Strategies include:

- Bootstrap
- Quasi-Bayesian Monte Carlo
- **δ-method**

Multilevel Mediation Analysis

Recall: Mediation effects defined using nested counterfactuals – $Y_{xM_{x'}}$

- Value of Y when X is set to x, and
- M is set to whatever value it would have if X were set to x'

Under strong assumptions, use the “Mediation Formula”

Multilevel Mediation Analysis

Mediation Formula:

$$\mathbb{E} Y_{x M_{x'}} = \mathbb{E}_{M|X=x'} \mathbb{E}(Y|X = x, M)$$

Multilevel Mediation Analysis

Mediation Formula:

$$
\begin{aligned}
\mathbb{E}Y_{xM_{x'}} &= \mathbb{E}_{M|X=x'}\mathbb{E}(Y|X=x,M) \\
&= \sum_{m=0}^{1} \mathbb{P}(Y=1|X=x,M=m)\mathbb{P}(M=m|X=x')
\end{aligned}
$$

Multilevel Mediation Analysis

Mediation Formula:

$$\mathbb{E}Y_{xM_{x'}} = \mathbb{E}_{M|X=x'}\mathbb{E}(Y|X=x,M) = \sum_{m=0}^{1}\mathbb{P}(Y=1|X=x,M=m)\mathbb{P}(M=m|X=x')$$

Logistic regression model makes this (relatively) simple:

$$\mathbb{P}(Y=1|X=x,M=m) = \mathrm{logit}^{-1}(\text{linear predictor})$$
$$\mathbb{P}(M=m|X=x') = \mathrm{logit}^{-1}(\text{different linear predictor})$$

Multilevel Mediation Analysis

Estimating $\mathbb{E}Y_{xM_{x'}}$ messy, but not *hard*

Uncertainty quantification based on asymptotic covariance of regression parameters

- Use δ-method
- Need derivatives of $\mathbb{E}Y_{xM_{x'}}$ wrt regression parameters
- Very messy, not particularly hard

Multilevel Mediation Analysis

Uncertainty quantification for mediation effects similar

- More δ-method

Very similar for GLMs and GLMMs

- Latter has more regression parameters
- Use `merDeriv` package to supplement `lme4`

Putting it All Together

- Define direct, indirect and total effects using counterfactuals
- Estimate these effects across countries using generalized linear mixed models
- Compute standard errors for estimated effects using the δ-method

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