Mediation: Natural Direct and Indirect Effects

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April 28, 2025

Learning goals for today

At the end of class, you will be able to:

- 1. Define natural direct and indirect effects
- 2. Decompose total effects into these components
- 3. Understand how intermediate confounding complicates natural direct effects
- 4. Estimate natural direct and indirect effects

Recall from before: Controlled direct effects



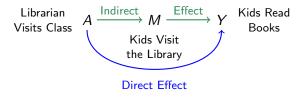
Recall from before: Controlled direct effects



Direct effect: Close the library

$$\mathsf{E}\left(Y^{10}-Y^{00}\right)$$

Recall from before: Controlled direct effects



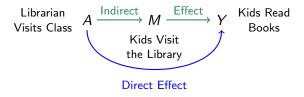
Direct effect: Close the library

$$E(Y^{10} - Y^{00})$$

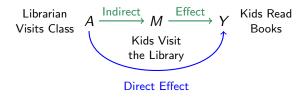
Direct effect: Make everyone visit the library

$$E(Y^{11}-Y^{01})$$





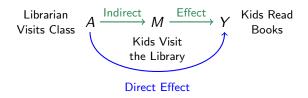
Let M^a be the potential mediator value under treatment A = a



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Direct effect (0): Effect of the librarian visiting in a world where kids visit the library as if the librarian didn't visit the class

$$\mathsf{E}\left(Y^{1M^0}-Y^{0M^0}\right)$$



Let M^a be the potential mediator value under treatment A = a

Direct effect (0): Effect of the librarian visiting in a world where kids visit the library as if the librarian didn't visit the class

$$\mathsf{E}\left(Y^{1M^0}-Y^{0M^0}\right)$$

Direct effect (1): Effect of the librarian visiting in a world where kids visit the library as if the librarian visited the class

$$\mathsf{E}\left(Y^{1M^1}-Y^{0M^1}\right)$$

$$\mathsf{E}\!\left(Y^1-Y^0\right)$$
 Total effect

$$\mathsf{E}\Big(Y^1-Y^0\Big)$$
 Total effect $\mathsf{E}\Big(Y^{1M^1}-Y^{0M^0}\Big)$ since $Y^a=Y^{aM^a}$

$$E\left(Y^{1}-Y^{0}\right)$$

$$=E\left(Y^{1M^{1}}-Y^{0M^{0}}\right)$$

$$=E\left(Y^{1M^{1}}\underbrace{-Y^{1M^{0}}+Y^{1M^{0}}}_{\text{Add }0}-Y^{0M^{0}}\right)$$
Total effect

$$E\left(Y^{1}-Y^{0}\right) \qquad \text{Total effect}$$

$$=E\left(Y^{1M^{1}}-Y^{0M^{0}}\right) \qquad \text{since } Y^{a}=Y^{aM^{a}}$$

$$=E\left(Y^{1M^{1}}\underbrace{-Y^{1M^{0}}+Y^{1M^{0}}-Y^{0M^{0}}}\right)$$

$$=\underbrace{E\left(Y^{1M^{1}}-Y^{1M^{0}}\right)}_{\text{Add 0}} +\underbrace{E\left(Y^{1M^{0}}-Y^{0M^{0}}\right)}_{\text{Direct Effect}}$$
(effect through M)

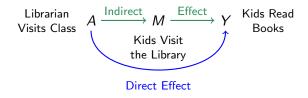


Librarian Visits Class
$$A \xrightarrow{\text{Indirect}} M \xrightarrow{\text{Effect}} Y \xrightarrow{\text{Kids Read}} \text{Books}$$

Kids Visit the Library Direct Effect

$$\tau(1) = \mathsf{E}(Y^{1M^1} - Y^{1M^0})$$

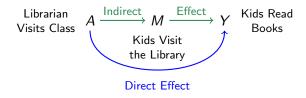
$$\tau(0) = \mathsf{E}(Y^{0M^1} - Y^{0M^0})$$



Indirect effect (1): Effect of visiting the library as much as you would if the librarian did vs did not visit, in a world where the librarian visits

$$\tau(1) = \mathsf{E}(Y^{1M^1} - Y^{1M^0})$$

$$\tau(0) = \mathsf{E}(Y^{0M^1} - Y^{0M^0})$$



Indirect effect (1): Effect of visiting the library as much as you would if the librarian did vs did not visit, in a world where the librarian visits

$$\tau(1) = \mathsf{E}(Y^{1M^1} - Y^{1M^0})$$

Indirect effect (0): Effect of visiting the library as much as you would if the librarian did vs did not visit, in a world where the librarian does not visit

$$\tau(0) = \mathsf{E}(Y^{0M^1} - Y^{0M^0})$$

Controlled direct effect

$$\frac{1}{n} \sum_{i=1}^{n} \left(Y_i^{11} - Y_i^{01} \right)$$

$$\frac{1}{n} \sum_{i=1}^{n} \left(Y_{i}^{1M_{i}^{1}} - Y_{i}^{0M_{i}^{1}} \right)$$

Controlled direct effect

$$\frac{1}{n}\sum_{i=1}^{n}\left(Y_{i}^{11}-Y_{i}^{01}\right)$$

 Y_i^{11} can be observed in an experiment

— Assign
$$A = 1$$
 and $M = 1$

Natural direct effect

$$\frac{1}{n} \sum_{i=1}^{n} \left(Y_{i}^{1M_{i}^{1}} - Y_{i}^{0M_{i}^{1}} \right)$$

Controlled direct effect

$$\frac{1}{n}\sum_{i=1}^n\left(Y_i^{11}-Y_i^{01}\right)$$

 Y_i^{11} can be observed in an experiment

— Assign A = 1 and M = 1

 Y_i^{01} can be observed in an experiment

— Assign A = 0 and M = 1

Natural direct effect

$$\frac{1}{n} \sum_{i=1}^{n} \left(Y_{i}^{1M_{i}^{1}} - Y_{i}^{0M_{i}^{1}} \right)$$

Controlled direct effect

$$\frac{1}{n}\sum_{i=1}^n\left(Y_i^{11}-Y_i^{01}\right)$$

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 Y_i^{01} can be observed in an experiment

— Assign
$$A = 0$$
 and $M = 1$

Natural direct effect

$$\frac{1}{n} \sum_{i=1}^{n} \left(Y_{i}^{1M_{i}^{1}} - Y_{i}^{0M_{i}^{1}} \right)$$

 $Y_i^{1M_i^1}$ can be observed in an experiment — Assign A = 1

Controlled direct effect

$$\frac{1}{n}\sum_{i=1}^n\left(Y_i^{11}-Y_i^{01}\right)$$

 Y_i^{11} can be observed in an experiment

— Assign
$$A = 1$$
 and $M = 1$

 Y_i^{01} can be observed in an experiment

— Assign
$$A = 0$$
 and $M = 1$

Natural direct effect

$$\frac{1}{n}\sum_{i=1}^n \left(Y_i^{1M_i^1} - Y_i^{0M_i^1}\right)$$

$$Y_i^{1M_i^1}$$
 can be observed in an experiment — Assign $A = 1$

$$Y_i^{0M_i^1}$$
 cannot be observed in an experiment — Because M_i^1 is unknown!

¹Imai, K., Tingley, D., & Yamamoto, T. (2013). Experimental designs for identifying causal mechanisms. Journal of the Royal Statistical Society: Series A (Statistics in Society), 176(1), 5-51.

Crossover design¹

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Crossover design¹

▶ In period 1, assign A = a. See outcome $M = M^a$

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Crossover design¹

- ▶ In period 1, assign A = a. See outcome $M = M^a$
- ▶ In period 2, assign A = a'. Assign $M = M^a$. See $Y^{a'M^a}$

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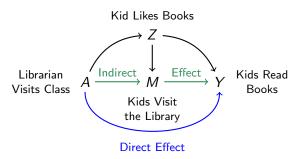
Crossover design¹

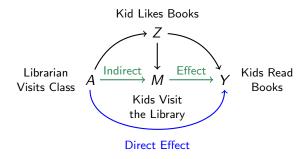
- ▶ In period 1, assign A = a. See outcome $M = M^a$
- ▶ In period 2, assign A = a'. Assign $M = M^a$. See $Y^{a'M^a}$

Works an assumption of no carry-over: current treatment is all that affects current outcome

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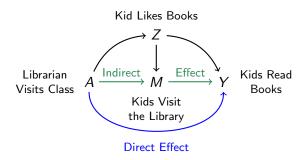




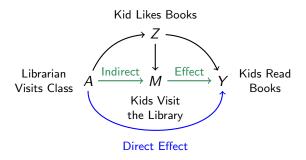


If Z is measured,

- ► The controlled direct effect E(Y^{1a} Y^{0a}) is nonparametrically identified
- ▶ but the natural direct effect $E(Y^{1M^a} Y^{0M^a})$ is not

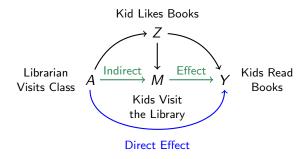


Why?



Why? For CDE:

$$E(Y^{10}) = E_{Z|A=1} (E(Y | A = 1, M = 0, Z))$$

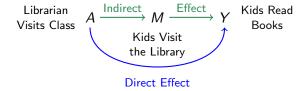


Why? For NDE:

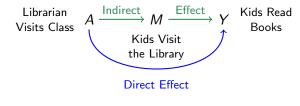
$$\mathsf{E}(Y^{1M^0}) = \mathsf{E}_{Z|A=1} \left(\mathsf{E} \left(Y \mid A=1, M=M^0, Z \right) \right)$$

but we never have $M=M^0$ with A=1, so that doesn't work

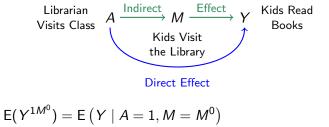
For NDE, this setting is nonparametrically identified

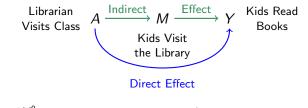


For NDE, this setting is nonparametrically identified



 $\mathsf{E}(Y^{1M^\circ})$





$$E(Y^{1M^0}) = E(Y \mid A = 1, M = M^0)$$

= $P(M^0 = 1)E(Y \mid A = 1, M = 1)$

Librarian Visits Class
$$A \xrightarrow{\text{Indirect}} M \xrightarrow{\text{Effect}} Y \xrightarrow{\text{Kids Read}} Books$$

Rids Visit the Library

Direct Effect

$$E(Y^{1M^0}) = E(Y \mid A = 1, M = M^0)$$

$$= P(M^0 = 1)E(Y \mid A = 1, M = 1)$$

$$+ P(M^0 = 0)E(Y \mid A = 1, M = 0)$$

$$= P(M = 1 \mid A = 0)E(Y \mid A = 1, M = 1)$$

Librarian Visits Class
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Rids Visit the Library

Direct Effect

$$E(Y^{1M^0}) = E(Y \mid A = 1, M = M^0)$$

$$= P(M^{0} = 1)E(Y \mid A = 1, M = 1)$$

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$$= P(M = 1 \mid A = 0)E(Y \mid A = 1, M = 1)$$

$$+ P(M = 0 \mid A = 0)E(Y \mid A = 1, M = 0)$$

For NDE, this setting is nonparametrically identified

Librarian Visits Class
$$A \xrightarrow{\text{Indirect}} M \xrightarrow{\text{Effect}} Y \xrightarrow{\text{Kids Read}} \text{Books}$$

Kids Visit the Library

Direct Effect

$$E(Y^{1M^0}) = E(Y \mid A = 1, M = M^0)$$

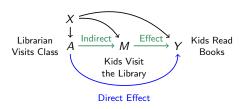
$$= P(M^0 = 1)E(Y \mid A = 1, M = 1)$$

$$+ P(M^0 = 0)E(Y \mid A = 1, M = 0)$$

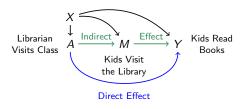
$$= P(M = 1 \mid A = 0)E(Y \mid A = 1, M = 1)$$

$$+ P(M = 0 \mid A = 0)E(Y \mid A = 1, M = 0)$$

Identified because no potential outcomes remain!



²Method implemented in the R package mediation and described on p. 773: Imai, K., Keele, L., Tingley, D., & Yamamoto, T. (2011). Unpacking the black box of causality: Learning about causal mechanisms from experimental and observational studies. American Political Science Review, 105(4), 765-789.



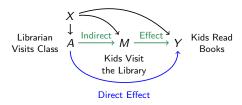
1. Model $E(M \mid X, A)$

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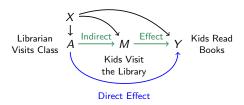
- 1. Model $E(M \mid X, A)$
 - ► Predict M^a for all a

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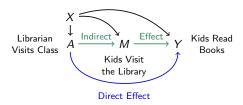
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- 2. Model $E(Y \mid X, A, M)$

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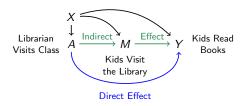
- 1. Model $E(M \mid X, A)$
 - ightharpoonup Predict M^a for all a
- 2. Model $E(Y \mid X, A, M)$
 - ▶ Predict Y^{a',M^a} for any pair a', a

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Bootstrap for confidence intervals

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Summary: Mediation decomposes causal effects

Controlled direct effects Example: $E(Y^{10} - Y^{00})$

- ▶ Idea: Intervene to hold the mediator at a fixed value
- ► ✓ Identified in a sequentially randomized experiment
- ▶ ✓ Identifiable with observed intermediate confounding
- ▶ X Direct and indirect effects are not additively decomposable

Natural direct and indirect effects Example: $E(Y^{1M^0} - Y^{0M^0})$

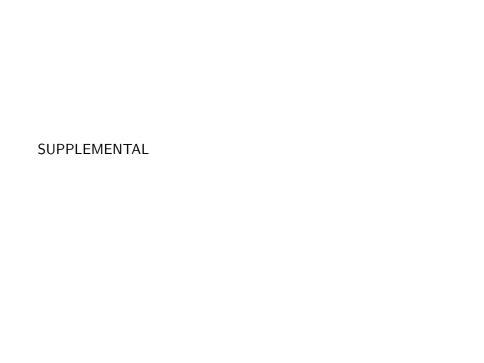
- ► Idea: Intervene to hold the mediator at the value in the absence of treatment
- ightharpoonup Not identified 3 in an experiment— Y^{1M^0} is unobservable
 - ► Crossover experiments can help with an extra assumption
- X Not identifiable with any intermediate confounding
- ▶ ✓ Direct and indirect effects are additively decomposable

³Each use of "identified" refers to nonparametric identification. Parametric identification is sometimes possible when nonparametric identification is not.

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- 3. Understand how intermediate confounding complicates natural direct effects
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Natural direct and indirect effects in SWIGs

Direct effect under mediator $M = M^1$

$$A \mid 1 \xrightarrow{M} M \mid M^1 \xrightarrow{} Y \qquad - \qquad A \mid 0 \xrightarrow{M} M \mid M^1 \xrightarrow{} Y$$

Direct effect under mediator $M = M^0$

$$A \mid 1 \longrightarrow M \mid M^0 \longrightarrow Y \qquad \qquad A \mid 0 \longrightarrow M \mid M^0 \longrightarrow Y$$

Indirect effect under treatment A = 1

$$A \mid 1 \xrightarrow{M} \mid M^1 \xrightarrow{Y} \qquad A \mid 1 \xrightarrow{M} \mid M^0 \xrightarrow{Y} Y$$

Indirect effect under treatment A = 0

$$A \mid 0 \xrightarrow{M} \mid M^1 \xrightarrow{Y} Y \qquad - \qquad A \mid 0 \xrightarrow{M} \mid M^0 \xrightarrow{Y} Y$$