An introduction to causal mediation analysis

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“To mediate”

according to Merriam-Webster, has two meanings in the English language

1. to intervene to resolve conflict/dispute/disagreement
2. to convey or to transmit as an intermediate mechanism or intermediary agent

the second meaning is relevant

Mediation model

According to Wikipedia, a mediation model

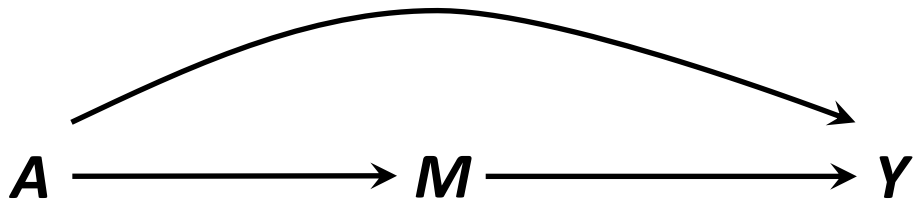
- seeks to explain the mechanism/process that underlies an observed relationship between an independent variable and a dependent variable via the inclusion of a third variable – a mediator or intermediate variable
- proposes that the independent variable influences the mediator variable, which in turn influences the dependent variable

Mediation model

- assumes variable M on the causal pathway from A to Y

Mediation model

- assumes variable M on the causal pathway from A to Y
- and considers effects through and not through M



Example: Treatment for Adolescents with Depression Study (TADS)

A: 4 treatment arms: pharmacological therapy (fluoxetine), cognitive behavior therapy (CBT), fluoxetine-CBT combination, and pill placebo

Y: depressive symptoms and secondary outcomes

$A \rightarrow Y$ findings:

- combination therapy most effective, followed by fluoxetine, in reducing depressive symptoms (TADS Team 2004)
- combination improved functioning, global health and quality of life; fluoxetine improved functioning (Vitiello et al. 2006)

Example: TADS

A: pharmacological therapy (fluoxetine), cognitive behavior therapy (CBT), fluoxetine-CBT combination, and pill placebo

Y: depressive symptoms

M: cognitive factors: positive outlook, solution-focused thinking, perfectionism, cognitive distortion and cognitive avoidance

$A \to Y \to M$ findings:

- reduction in perfectionism mediates effect of combination on depressive symptoms at 12 weeks (Jacob et al. 2009)
- increased positive outlook mediated effect of any active treatment on symptoms at 36 weeks (Jacob at al. 2014)

Why study mediation?

- Gain better understanding of how things happen: explain mechanisms of effect of an intervention or natural exposure
- Ask questions such as
  - if could block the direct path from A to Y, what would be the effect on Y?
  - if could block the effect of A on M, what would remain of effect of A on Y?
  - if could fix M at a specific level m, what would be the effect of A on Y?
- Improve/innovate on interventions by targeting certain mediators and/or tweaking how we influence mediators
- Justify the use of proximal/intermediate/surrogate outcomes in place of the ultimate outcome of interest

Mediation model is causal model: temporality

The arrows imply causal relationships.

This requires appropriate temporality among the variables A, M, Y.

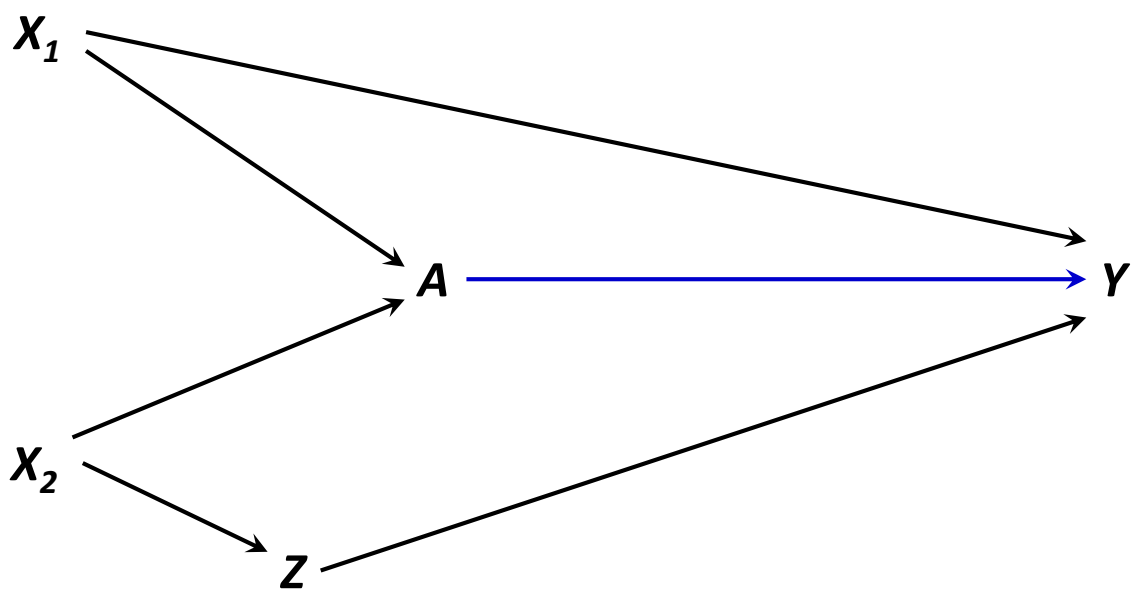
Mediation model is causal model: confounding

Also, the model is usually more complex, where these variables are embedded in a larger causal graph with other relevant variables.

Mediation model is causal model: confounding

Recall the simpler non-mediation case with just A and Y

To infer the causal effect of A on Y, have to control confounding



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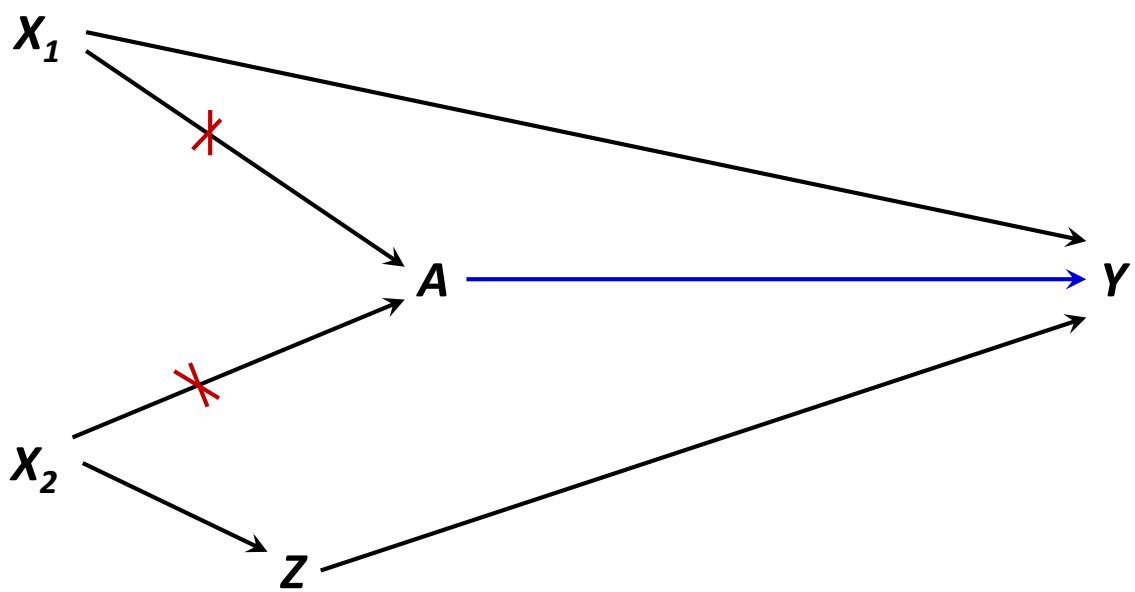
- by removing the X-A associations: randomizing A or otherwise balancing distribution of X between levels of A

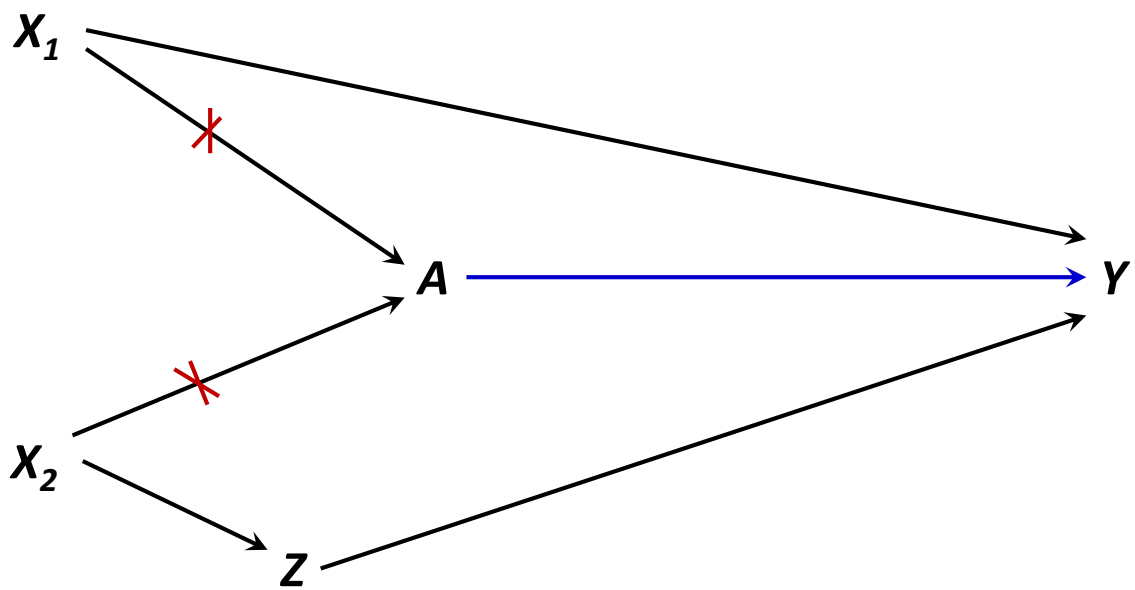


Mediation model is causal model: confounding

Recall the simpler non-mediation case with just A and Y

To infer the causal effect of A on Y, have to control confounding

- by removing the X-A associations: randomizing A or otherwise balancing distribution of X between levels of A
- and perhaps additionally adjusting for X in a model for Y

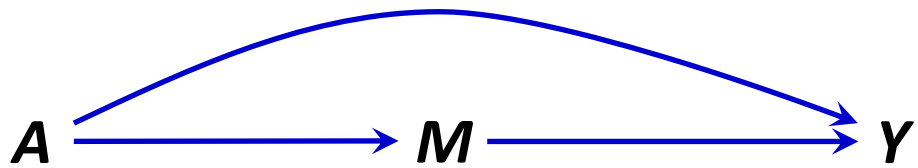


Mediation model is causal model: confounding

With mediation, confounding of $A \to M$, $A \to Y$ and $M \to Y$

Need to draw a causal graph that captures the confounding

- start with A, M, Y



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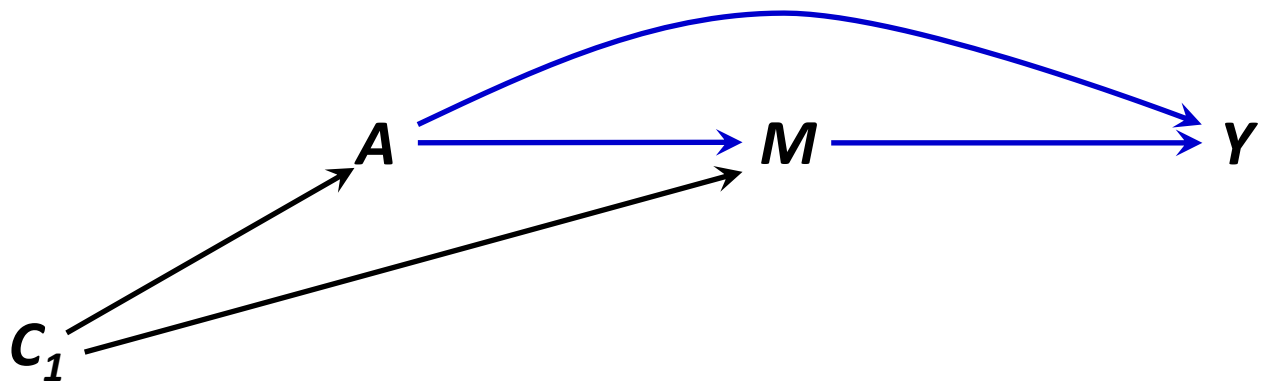
- C_1 are confounders of $A \rightarrow M$

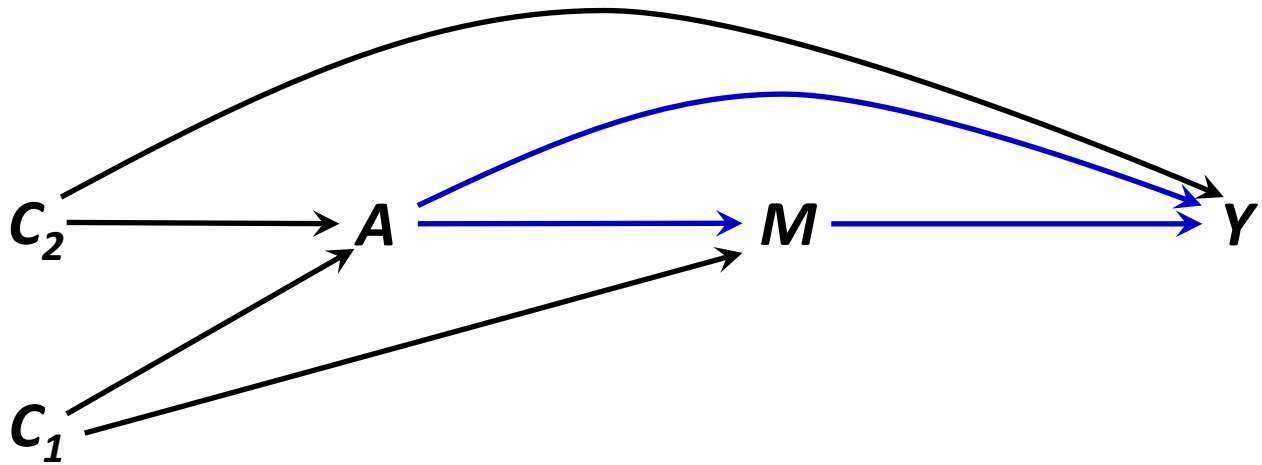


Mediation model is causal model: confounding

With mediation, confounding of $A \rightarrow M$, $A \rightarrow Y$ and $M \rightarrow Y$

Need to draw a causal graph that captures the confounding

- C_2 are confounders of $A \rightarrow Y$



Mediation model is causal model: confounding

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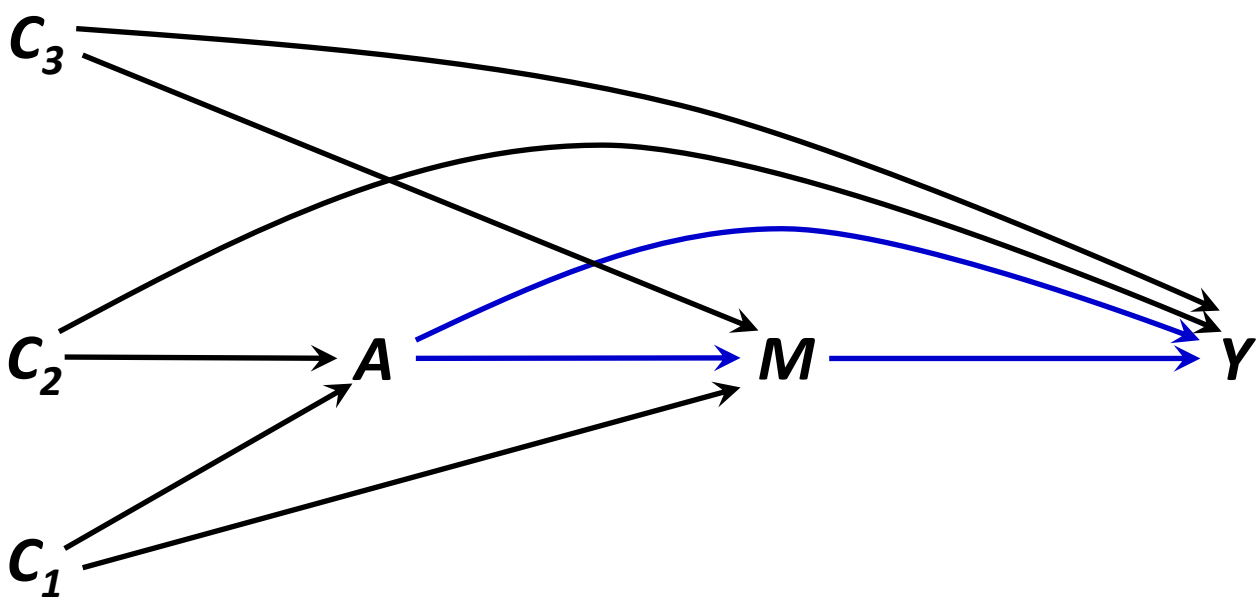
Need to draw a causal graph that captures the confounding

- C_3 are pre-treatment confounders of $M \rightarrow Y$

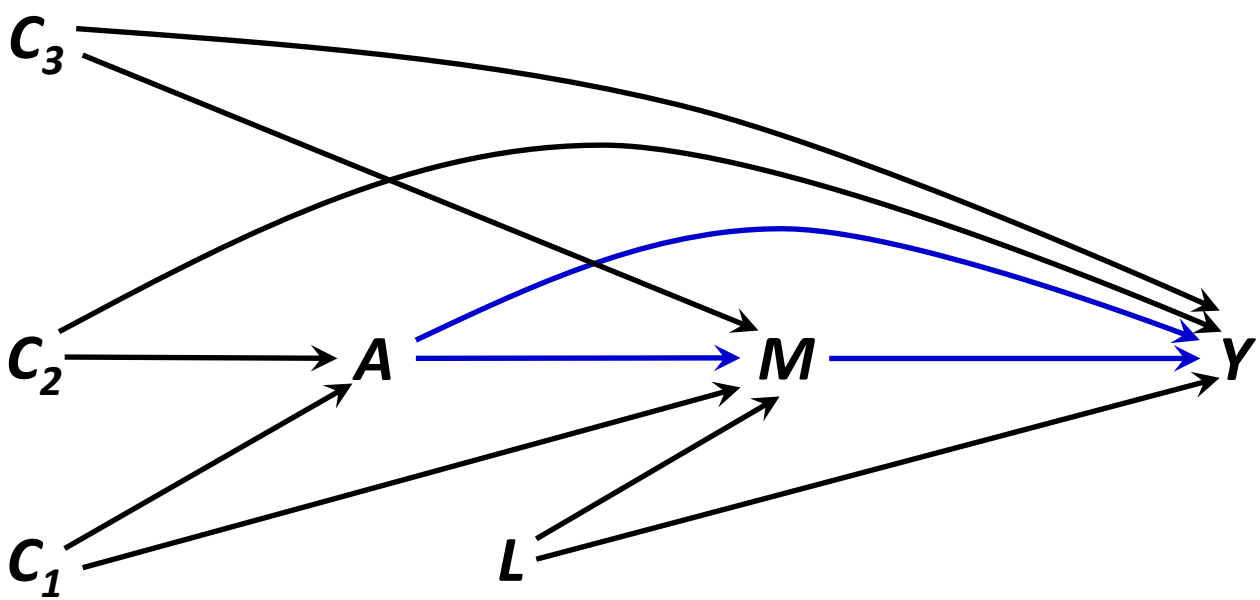


Mediation model is causal model: confounding

With mediation, confounding of $A \rightarrow M$, $A \rightarrow Y$ and $M \rightarrow Y$

Need to draw a causal graph that captures the confounding

- L are post-treatment confounders of $M \rightarrow Y$

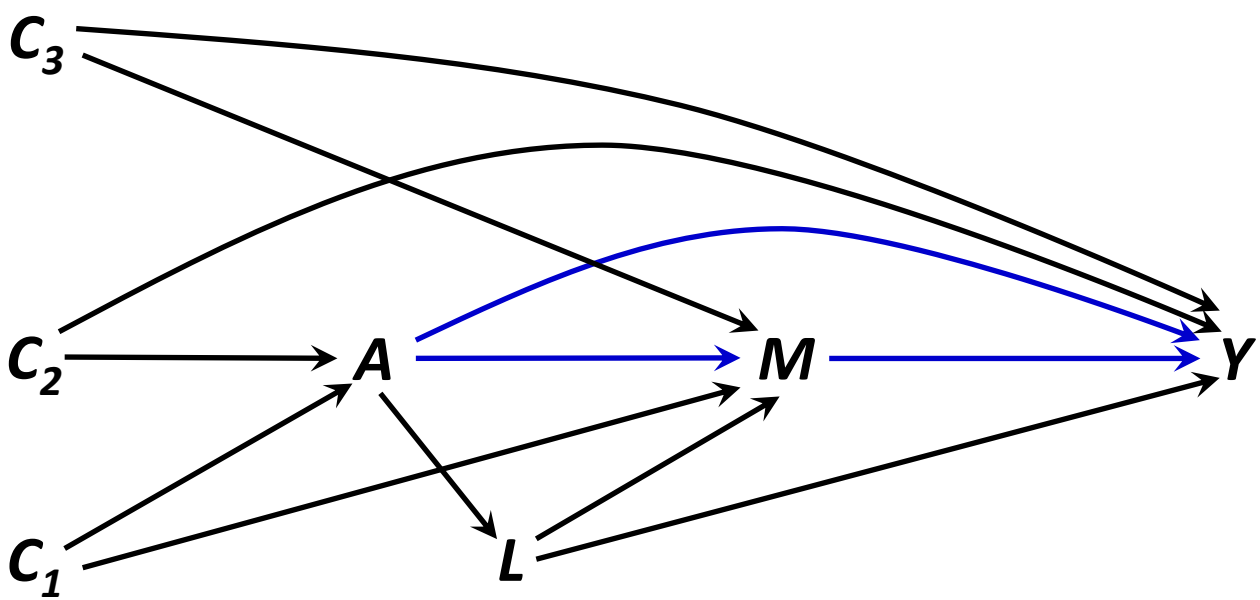


Mediation model is causal model: confounding

With mediation, confounding of $A \rightarrow M$, $A \rightarrow Y$ and $M \rightarrow Y$

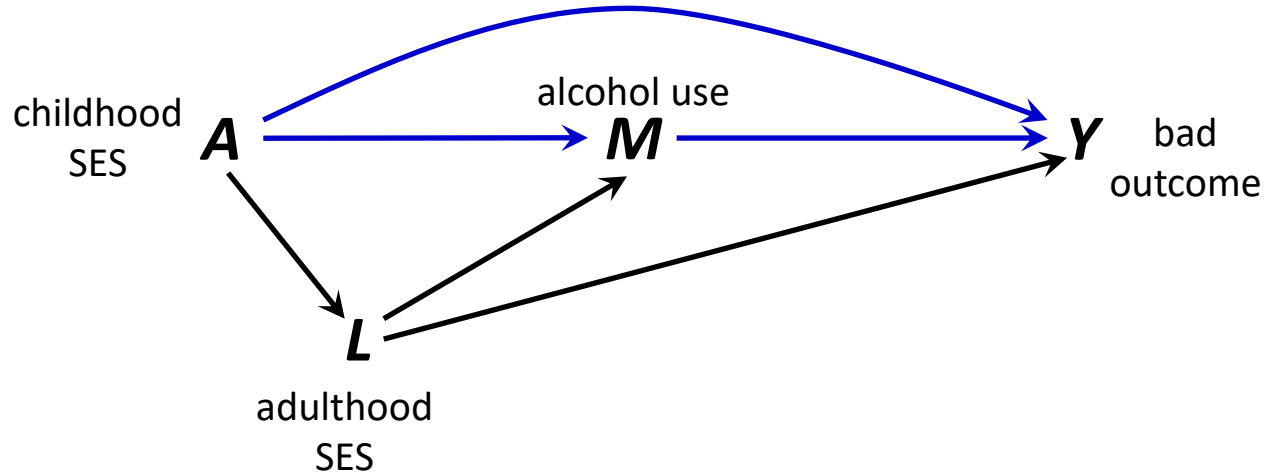
Need to draw a causal graph that captures the confounding

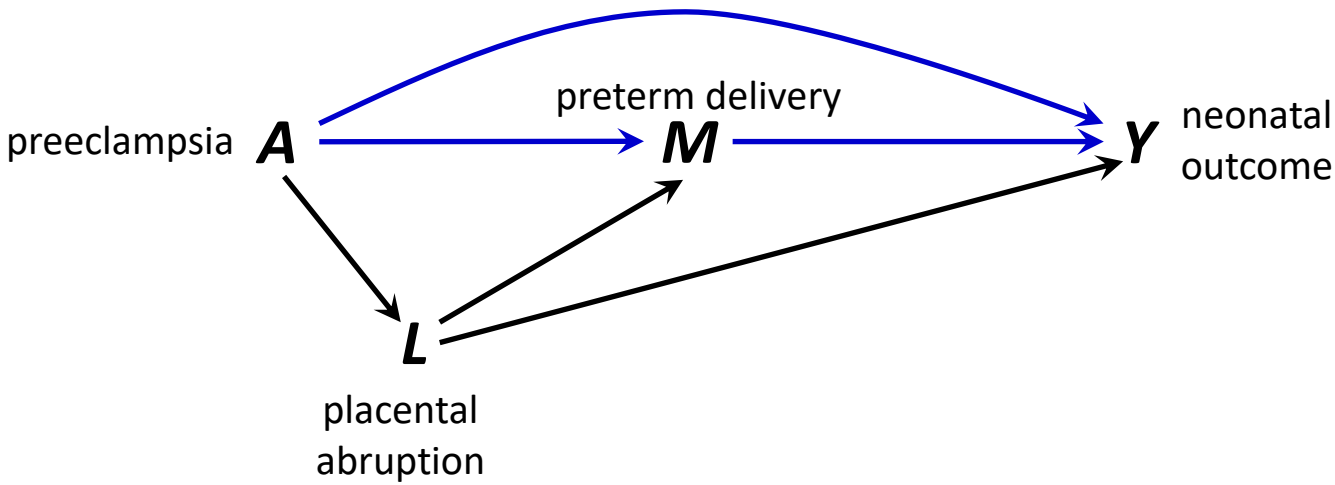
- L may very well be influenced by A



Mediation model is a causal model: confounding

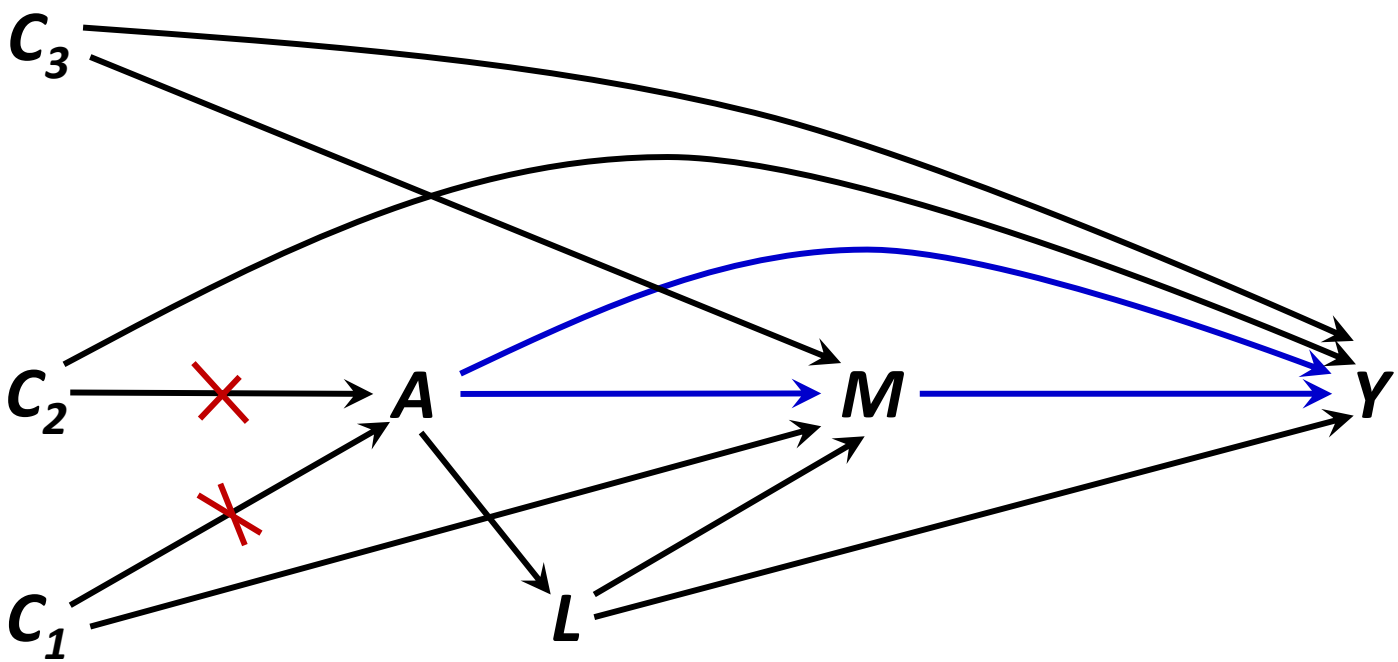
Examples of L – here leaving C out for clarity





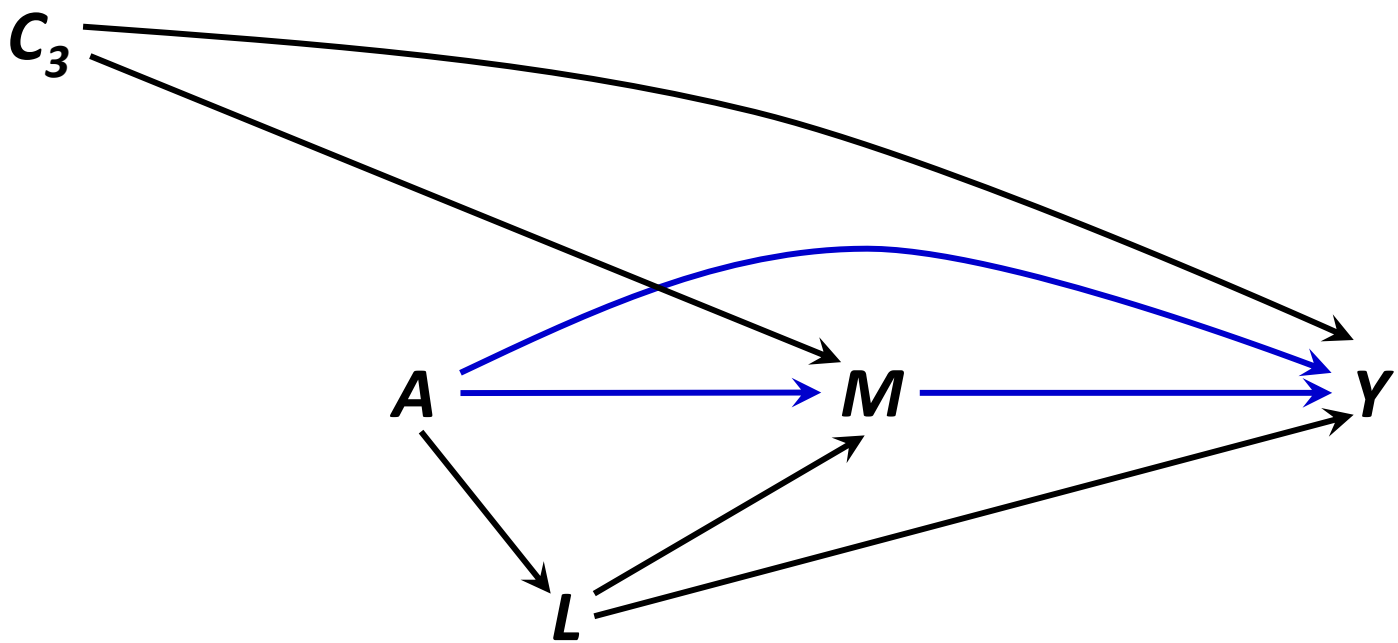
Mediation model is causal model: confounding

- Randomization of A simplifies but doesn't remove confounding



Mediation model is causal model: confounding

- With A randomized, there is still confounding of $M \rightarrow Y$



But let's back up... and go about it the proper way

- define the *estimand*
  - the effect of interest, which is a function of the distribution of potential outcomes
- clarify *identifiability* and identifying assumptions
  - translate the estimand into a function of the distribution of observed data
- consider *estimation* methods and additional assumptions

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- consider *estimation* methods and additional assumptions

We will revisit the non-mediation $A \rightarrow Y$ case before talking about mediation.

Example: $A \rightarrow Y$

For simplification, let A be binary (1=treatment, 0=control), and define effects on the difference scale.

With a RCT, a standard estimator of the treatment effect is $\overline{Y}_{A=1} - \overline{Y}_{A=0}$ (the difference b/w sample mean outcome in the treatment group and sample mean outcome in the control group).

What are we estimating with this estimator?

Example: $A \rightarrow Y$

ESTIMAND

The estimand here is the Average Treatment Effect (ATE), i.e., the average of the individual treatment effects

Treatment effect for individual i: $\text{effect}_i = Y_i(1) - Y_i(0)$

Average treatment effect: $\text{ATE} = \text{E}[Y(1) - Y(0)]$

Example: $A \rightarrow Y$

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Average treatment effect: $\text{ATE} = \text{E}[Y(1) - Y(0)]$

The ATE can also be re-expressed as $\text{E}[Y(1)] - \text{E}[Y(0)]$

Example: $A \to Y$

IDENTIFICATION for RCT

Due to randomization, have *ignorability*, i.e., $(Y(1), Y(0)) \perp\!\!\!\perp A$, so

$$\mathrm{E}[Y(1)] = \mathrm{E}[Y(1) \mid A = 1].$$

With some other assumptions (*consistency*, *no interference*),

$$\mathrm{E}[Y(1) \mid A = 1] = \mathrm{E}[Y \mid A = 1].$$

It follows that

$$\mathrm{E}[Y(1) - Y(0)] = \mathrm{E}[Y \mid A = 1] - \mathrm{E}[Y \mid A = 0].$$

The ATE is identified – RHS function of observed data distribution.

Example: $A \to Y$

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The ATE is identified – RHS function of observed data distribution.

(note: individual effects are not identifiable)

Example: $A \to Y$

ESTIMATION for RCT

The identification result means that a simple estimator is

$$\widehat{\text{ATE}} = \overline{Y}_{A=1} - \overline{Y}_{A=0}.$$

(not the only estimator)

Example: $A \to Y$

IDENTIFICATION for observational study

without randomization, don't have *ignorability*. instead, assume

conditional ignorability, i.e., $(Y(1), Y(0)) \perp\!\!\!\perp A \mid C$, where C is a set of pre-treatment variables (confounders), plus
positivity, i.e., $0 < \mathrm{P}(A = 1 \mid C = c) < 1$ for all c. then

$$\mathrm{E}[Y(1) - Y(0)] = \mathrm{E}\{\mathrm{E}[Y \mid A = 1, C] - \mathrm{E}[Y \mid A = 0, C]\}$$

Example: $A \to Y$

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ESTIMATION for observational study

different methods which rely on assuming a treatment assignment model, or an outcome regression model, or both

Mediation: different types of causal effects (estimands)

- Mediation analysis often concerned w/ partitioning the causal effect into mediated/indirect and unmediated/direct effects.
- Hence, the ATE is now referred to as the Total Effect (TE). More precisely, it is the Average Total Treatment Effect.

$$\text{TE} = \text{E}[Y(1) - Y(0)].$$

- There are different types of effects – which one is relevant depends on the research question
  - controlled direct effect (easiest to explain)
  - natural indirect and direct effects (intuitive and popular)
  - interventional indirect and direct effects (newer and nice)
- Will cover definitions and identification assumptions of all three types, and talk a bit about estimation of natural effects.

Mediation: controlled direct effect (CDE) – definition

- Answers question: if we could hypothetically fix the mediator to a specific level for everyone, what would be the average effect of intervention A on outcome Y?
  - e.g., bike helmet, car seat belt, hot water safe temperature

Mediation: controlled direct effect (CDE) – definition

- Answers question: if we could hypothetically fix the mediator to a specific level for everyone, what would be the average effect of intervention A on outcome Y?
- Recall definition of TE
  - $Y_i(a)$: potential outcome if assigned treatment a
  - each individual has two of these, $Y_i(1)$ and $Y_i(0)$
  - only one of which is observed $Y_i = Y_i(A_i)$ (*consistency*)

$$\text{TE}_i = Y_i(1) - Y_i(0)$$

$$\text{TE} = \text{E}[Y_i(1) - Y_i(0)]$$

Mediation: controlled direct effect (CDE) – definition

- Answers question: if we could hypothetically fix the mediator to a specific level for everyone, what would be the average effect of intervention A on outcome Y?

- Definition of the CDE extends this idea
  - $Y_i(a, m)$: potential outcome if assigned treatment a and mediator value m
  - each individual may have many of these (if many m values)
  - only one of which is observed $Y_i = Y_i(A_i, M_i)$ (*composition*)

$$\text{CDE}_i(m) = Y_i(1, m) - Y_i(0, m)$$

$$\text{CDE}(m) = \text{E}[Y(1, m) - Y(0, m)]$$

  - CDE depends on m

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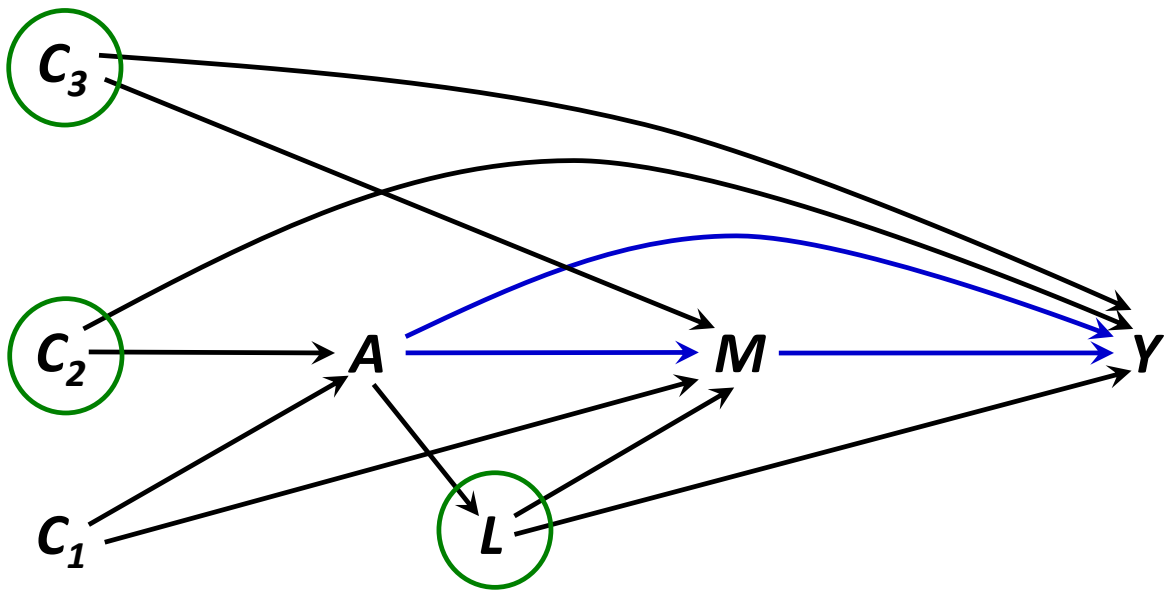
  - CDE depends on m

- CDE is not paired with an indirect effect

Mediation: CDE – identification assumptions

- two confounding-related assumptions:
  - no unmeasured $A \to Y$ confounders: $Y(a, m) \perp\!\!\!\perp A \mid C$
  - no unmeasured $M \to Y$ confounders: $Y(a, m) \perp\!\!\!\perp M \mid A, C, L$



- plus the usual causal inference assumptions: consistency (and composition), positivity of A and of $M = m$, no interference...

Mediation: natural indirect and direct effects – definition

- Partition TE: what is the effect that goes through M and what is the effect that does not go through M?
  - if could block the effect through M, i.e., keep the mediator at the level under control, what effect would we see?
  - if could block the direct path and let A affect Y only through M, what effect would we see?

Mediation: natural indirect and direct effects – definition

- Partition TE: what is the effect that goes through M and what is the effect that does not go through M?

- Requires nested potential outcomes: $Y(a, M(a'))$
  - each individual has four of these:
    - $Y_i(1, M_i(1)) = Y_i(1)$
    - $Y_i(0, M_i(0)) = Y_i(0)$
    - $Y_i(1, M_i(0))$
    - $Y_i(0, M_i(1))$
  - only one (of the first two) observed
  - the last two completely hypothetical so not observable

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  - only one (of the first two) observed
  - the last two completely hypothetical so not observable
- TE is contrast between first two potential outcomes
- Using one of last two potential outcomes, can partition TE

Mediation: natural indirect and direct effects – definition

- Two different TE = NDE + NIE decompositions
  - Contrasting $\mathrm{E}[Y(0, M(0))], \mathrm{E}[Y(1, M(0))], \mathrm{E}[Y(1, M(1))]$

$$\mathrm{NDE}(\cdot 0) = \mathrm{E}[Y(1, M(0))] - \mathrm{E}[Y(0, M(0))]$$
$$\mathrm{NIE}(1 \cdot) = \mathrm{E}[Y(1, M(1))] - \mathrm{E}[Y(1, M(0))]$$

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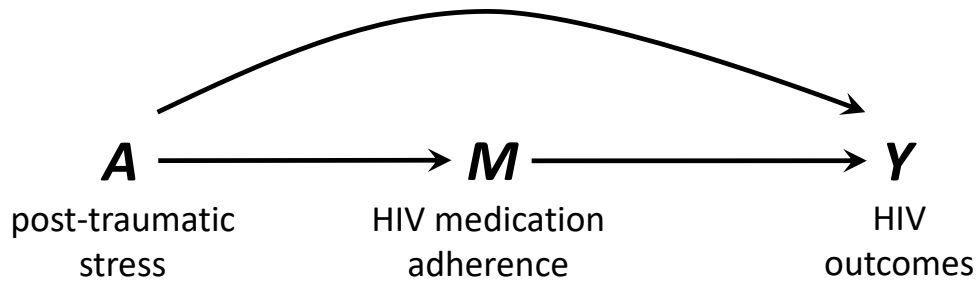

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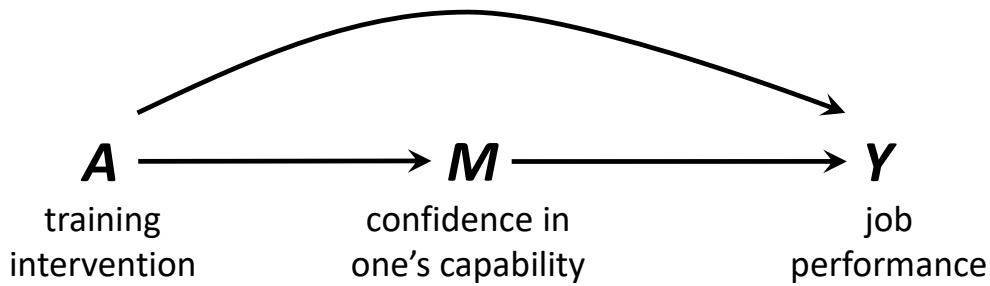
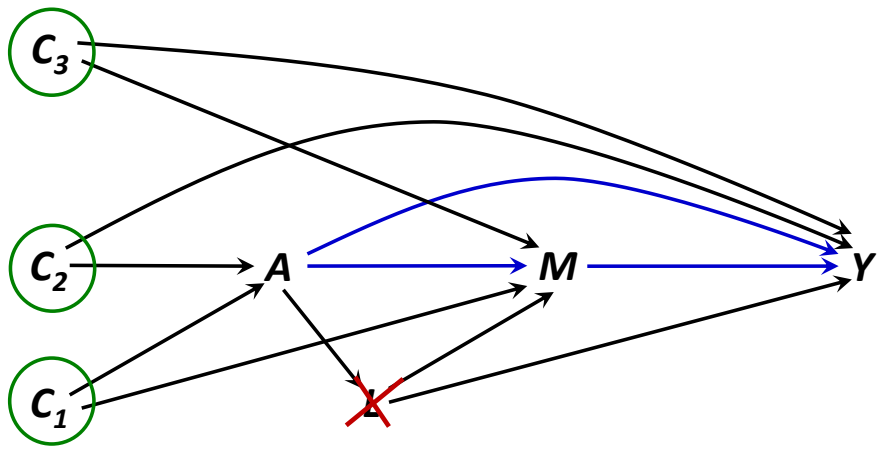


Mediation: NIE, NDE – identification assumptions

- four confounding-related assumptions:
  - no unmeasured $A \to Y$ confounders: $Y(a, m) \perp\!\!\!\perp A \mid C$
  - no unmeasured $A \to M$ confounders: $M(a) \perp\!\!\!\perp A \mid C$
  - no unmeasured $M \to Y$ confounders, and
  - no confounder of $M \to Y$ influenced by A
    $Y(a, m) \perp\!\!\!\perp M \mid A, C$



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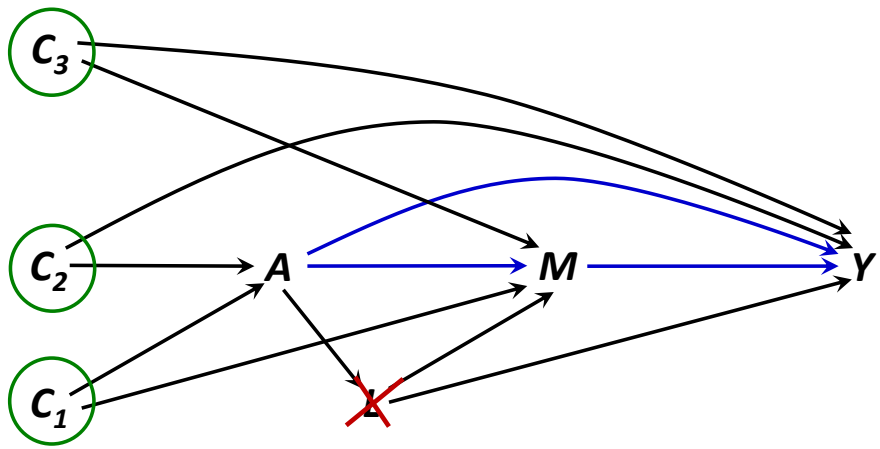

- also called *sequential conditional ignorability*
  - ignorability of A given C
  - ignorability of M given A, C

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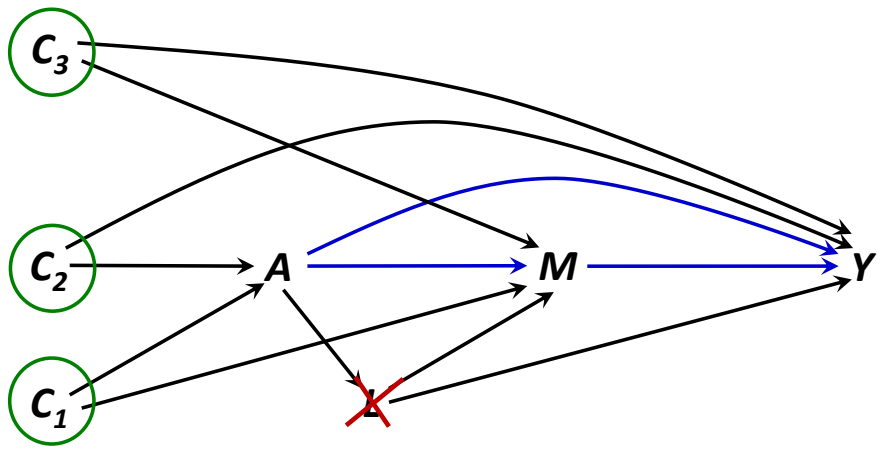
  - no confounder of $M \to Y$ influenced by A
    $Y(a, m) \perp\!\!\!\perp M \mid A, C$



- also called *sequential conditional ignorability*
  - ignorability of A given C
  - ignorability of M given A, C
- plus other usual causal inference assumptions
  - positivity of M now means $M(1)$ and $M(0)$ same range given C

Mediation: NIE, NDE – identification intuition

We don't estimate individual effects. This exercise is only to build intuition.

Mediation: NIE, NDE – identification intuition

Consider a specific person i with $A_i = 1$.

Observe $\begin{array}{l} Y_i(1, M_i(1)) = Y_i(1) = Y_i = y^* \\ M_i(1) = M_i = m^* \\ Y_i(1, m^*) = Y_i(1, M_i) = y^* \end{array}$. Want $\begin{array}{l} Y_i(0, M_i(0)) = Y_i(0) \\ Y_i(1, M_i(0)) \end{array}$.

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Learn about $Y_i(0)$ in one step:

- Under the no unmeasured $A \to Y$ confounding assumption, $Y_i(0)$ should be similar to the outcomes of persons j in the control condition who have the same C_2 values as person i. For persons j, $Y_j = Y_j(0)$. So we can take, for example, $\hat{Y}_i(0) = \bar{Y}_j = y^{**}$.

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and about $Y_i(1, M_i(0))$ in two steps:

- Under the no unmeasured $A \to M$ confounding assumption, $M_i(0)$ should be similar to the mediator values of persons k in the control condition who have the same C_1 values as person i. We can take $\hat{M}_i(0) = \bar{M}_k = m^{**}$.
- Under the no unmeasured $M \to Y$ confounding and no $M \to Y$ confounder affected by A assumptions, $Y_i(1, M_i(0)) \approx Y_i(1, m^{**})$ should be similar to the outcomes of persons l in the treatment condition who have the same C_3 values as person i but whose mediator value is $M_l = m^{**}$. We can then take $\hat{Y}_i(1, M_i(0)) = \bar{Y}_l = y^{***}$.

Mediation: NIE, NDE – identification formula

Potential outcomes:

$$\mathrm{E}[Y(a, M(a'))]$$
$$= \sum_c \sum_m \mathrm{E}[Y(a, m) \mid C = c]\mathrm{P}[M(a') = m \mid C = c]\mathrm{P}(C = c)$$
$$= \sum_c \sum_m \mathrm{E}[Y \mid A = a, M = m, C = c]\mathrm{P}(M = m \mid A = a', C = c)\mathrm{P}(C = c)$$

Natural direct and indirect effects:

$$\mathrm{NDE}(\cdot a) = \mathrm{E}[Y(1, M(a))] - \mathrm{E}[Y(0, M(a))]$$
$$= \sum_c \sum_m \left\{ \begin{matrix} \mathrm{E}[Y \mid A = 1, M = m, C = c] - \\ \mathrm{E}[Y \mid A = 0, M = m, C = c] \end{matrix} \right\} \mathrm{P}(M = m \mid A = a, C = c)\mathrm{P}(C = c)$$

$$\mathrm{NIE}(a' \cdot) = \mathrm{E}[Y(a', M(1))] - \mathrm{E}[Y(a', M(0))]$$
$$= \sum_c \sum_m \mathrm{E}[Y \mid A = a', M = m, X = x] \left[\begin{matrix} \mathrm{P}(M = m \mid A = 1, C = c) - \\ \mathrm{P}(M = m \mid A = 0, C = c) \end{matrix} \right] \mathrm{P}(C = c)$$

Mediation: NIE, NDE – estimation

Recall the non-mediation $A \to Y$ case, with confounders C

To estimate the ATE, options are

0. non-parametric estimation
   - if C balanced (RCT), difference in sample mean Y
   - if C just a few values, stratify by C, estimate and combine
1. rely on a model for treatment assignment
   - estimate $\mathrm{P}(A = 1 \mid C)$, weight/match to obtain balance on C, and take the difference between sample means of Y
2. rely on an outcome model (or models for potential outcomes)
   - simplest: regress Y on A, C
   - better: fit models two two arms separately to estimate $\mathrm{E}[Y \mid A = 1, C]$ and $\mathrm{E}[Y \mid A = 0, C]$ and average their difference over the distribution of C
3. rely on both models
   - combine 2. and 3.
   - double robustness: consistent if one model correctly specified

Mediation: NIE, NDE – estimation

For the mediation case with A, M, Y and C, there is a huge literature for different methods. Broadly, these methods rely on

1. a mediator model and an outcome model
   - regression with analytic results
   - regression-based simulation
2. a treatment assignment model and an model
   - weighting based on probability of treatment assignment and imputation of cross-world potential outcome
3. a treatment assignment model and a mediator model
   - weighting based on probability of treatment assignment and mediator assignment

   3b. a variation is weighting based on different models for treatment assigned, conditional on C and conditional on (C, M)
4. three models for treatment assignment, mediator and outcome
   - triply robust estimators

Mediation: NIE, NDE – estimation

We will now go over the first strategies (regression with analytic results and regression-based simulation) with the simplest case (continuous mediator and continuous outcome).

For more cases and strategies, see notes from my mini-course (`https://trang-q-nguyen.weebly.com/teaching.html`) from two years ago. There is a lot that is not included; this is a fast growing literature.

The course also addresses multiple mediators cases (simultaneous, sequential) to some extent.

Example: Continuous outcome and continuous mediator – strategy: linear regression with analytic results

- Assume linear potential mediators/outcomes models
- Allow treatment-mediator interaction

$$M_i(a) = \alpha_0 + \alpha_1 a + \alpha_2 C_i + \epsilon_{M_{i,a}}$$
$$Y_i(a, m) = \beta_0 + \beta_1 a + \beta_2 m + \beta_3 am + \beta_4 C_i + \epsilon_{Y_{i,a,m}}$$

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- Under identifying assmptns, estimate paras using regression models

$$\mathrm{E}[M|A=a, C=c] = \alpha_0 + \alpha_1 a + \alpha_2 c$$
$$\mathrm{E}[Y|A=a, M=m, C=c] = \beta_0 + \beta_1 a + \beta_2 m + \beta_3 am + \beta_4 c$$

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$$\mathrm{E}[Y|A=a, M=m, C=c] = \beta_0 + \beta_1 a + \beta_2 m + \beta_3 am + \beta_4 c$$

- If interested in CDEs, get estimates from second model

$$\mathrm{CDE}(m) = \mathrm{E}[Y_{1m}] - \mathrm{E}[Y_{0m}] = (\beta_1 + \beta_3 m)$$

Example: Continuous outcome and continuous mediator – strategy: linear regression with analytic results

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$$\mathrm{E}[Y|A=a, M=m, C=c] = \beta_0 + \beta_1 a + \beta_2 m + \beta_3 am + \beta_4 c$$

- The two models combined give conditional mean potential outcomes

$$\mathrm{E}[Y_{aM_{a'}}|C=c] = \beta_0 + \beta_1 a + (\beta_2 + \beta_3 a)(\alpha_0 + \alpha_1 a' + \alpha_2 c) + \alpha_4 c$$

Example: Continuous outcome and continuous mediator – strategy: linear regression with analytic results

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- Allow treatment-mediator interaction

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$$\mathrm{E}[Y_{aM_{a'}}|C=c] = \beta_0 + \beta_1 a + (\beta_2 + \beta_3 a)(\alpha_0 + \alpha_1 a' + \alpha_2 c) + \alpha_4 c$$

- which give the natural effects

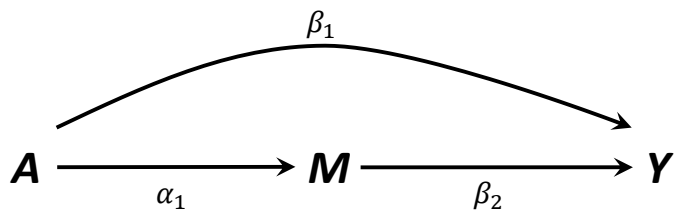
$$\mathrm{NDE}(\cdot a) = \mathrm{E}[Y_{1M_a}] - \mathrm{E}[Y_{0M_a}] = \beta_1 + \beta_3(\alpha_0 + \alpha_1 a + \alpha_2 \mathrm{E}C)$$
$$\mathrm{NIE}(a\cdot) = \mathrm{E}[Y_{aM_1}] - \mathrm{E}[Y_{aM_0}] = (\beta_2 + \beta_3 a)\alpha_1$$

Example: Continuous outcome and continuous mediator – strategy: linear regression with analytic results

- Given assumed models, the natural effects are

$$\text{NDE}(\cdot a) = \text{E}[Y_{1M_a}] - \text{E}[Y_{0M_a}] = \beta_1 + \beta_3(\alpha_0 + \alpha_1 a + \alpha_2 \text{E}C)$$
$$\text{NIE}(a\cdot) = \text{E}[Y_{aM_1}] - \text{E}[Y_{aM_0}] = (\beta_2 + \beta_3 a)\alpha_1$$

- Note that if no AM interaction
  - $\text{NDE}(\cdot 1) = \text{NDE}(\cdot 0) = \text{CDE} = \beta_1$
  - $\text{NIE}(1\cdot) = \text{NIE}(0\cdot) = \beta_2\alpha_1$



- These agree w/ Baron & Kenny's (1986) product-of-coefs formula
  - Causal mediation analysis generalizes B&K's mediation analysis
- However, AM interaction term recommended for model flexibility

Example: Continuous outcome and continuous mediator – strategy: linear regression with analytic results

- Implementation in SAS, SPSS (Valeri & VanderWeele 2013), Stata (Emsley et al. 2014)
  - default NDE(·0), NIE(1·)
  - CDE if specified
  - Delta/bootstrap SEs & CIs

- Can be used for a broad combination of models.

- SAS macro `mediation`:

```
%mediation(data=yrbs,
    yvar=depressSympts, avar=minority, mvar=bully,
    cvar=grade11 grade12 age gender hhses2 hhses3 hhses4,
    a0=0, a1=1, m=2.5, nc=8,
    yreg=linear, mreg=linear, interaction=true,
    boot=true)
run;
```

Example: Continuous outcome and continuous mediator – strategy: linear regression with analytic results

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    yvar=depressSympts / avar=minority / mvar=bully /
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    NC=8 / a0=0 / a1=1 / m=2.5 /
    yreg=LINEAR / mreg=LINEAR / interaction=TRUE /
    boot=TRUE
```

Example: Continuous outcome and continuous mediator – strategy: linear regression with analytic results

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  - default NDE(·0), NIE(1·)
  - CDE if specified
  - Delta/bootstrap SEs & CIs
- Can be used for a broad combination of models.
- Stata command `paramed`:

```
paramed dressSympts, avar=(minority) mvar(bully)
    cvar(grade11 grade12 age gender hhses2 hhses3 hhses4)
    a0=(0) a1(1) m(2.5) yreg(linear) mreg(linear)
    boot reps(1000) seed(12345) level(95)
```

Example: Continuous outcome and continuous mediator – strategy: linear regression with analytic results

NDEs and NIEs from Mplus: first compute means of X variables, then run:

```
MODEL:
bully ON minority (a1);
bully ON grade11  (a2);
bully ON grade12  (a3);
bully ON age      (a4);
bully ON gender   (a5);
bully ON hhses2   (a6);
bully ON hhses3   (a7);
bully ON hhses4   (a8);
[bully] (a0);

depressSympts ON minority       (b1);
depressSympts ON bully          (b2);
depressSympts ON minority_bully (b3);
depressSympts ON grade11 grade12 age gender hhses2 hhses3 hhses4;

MODEL CONSTRAINT:
NEW(nde0 nde1 nie0 nie1);
nde0 = b1 + b3*(a0   +a2*.33+a3*.29+a4*16.4+a5*.48+a6*.3+a7*.2+a8*.1);
nde1 = b1 + b3*(a0+a1+a2*.33+a3*.29+a4*16.4+a5*.48+a6*.3+a7*.2+a8*.1);
nie0 =  b2    *a1;
nie1 = (b2+b3)*a1;
```

Example: Continuous outcome and continuous mediator – strategy: linear regression with analytic results

NDEs and NIEs from Mplus: or center X variables at their means:

```
VARIABLE:
...
DEFINE:
CENTER grade11 grade12 age gender hhses2 hhses3 hhses4 (GRANDMEAN);

MODEL:
bully ON minority (a1);
bully ON grade11 grade12 age gender hhses2 hhses3 hhses4;
[bully] (a0);

depressSympts ON minority       (b1);
depressSympts ON bully          (b2);
depressSympts ON minority_bully (b3);
depressSympts ON grade11 grade12 age gender hhses2 hhses3 hhses4;

MODEL CONSTRAINT:
NEW(nde0 nde1 nie0 nie1);
nde0 = b1 + b3* a0;
nde1 = b1 + b3*(a0+a1);
nie0 =  b2    *a1;
nie1 = (b2+b3)*a1;
```

Example: Continuous outcome and continuous mediator – strategy: regression-based simulation (Imai et al. 2010)

Works for broad combinations of parametric/nonparametric models.

Example: Continuous outcome and continuous mediator – strategy: regression-based simulation (Imai et al. 2010)

Algorithm 1 – parametric bootstrap (bootstrap the parameters)

- fit models
- sample sets of parameters from their estimated distribution, assuming multivariate normal
- with each set of parameters:
  - sample potential mediators and potential outcomes
  - compute NIE and NDE
- summarize the sample of NIE and NDE

Algorithm 2 – non-parametric bootstrap (bootstrap the data)

- draw bootstrap samples from the data
- with each bootstrap dataset:
  - fit models
  - using estimated parameters, sample potential mediators and potential outcomes
  - compute NIE and NDE
- summarize the sample of NIE and NDE

Example: Continuous outcome and continuous mediator – strategy: regression-based simulation (Imai et al. 2010)

`mediation` package in `R` (Imai et al. 2010b, 2013; Tingley et al. 2014):

- natural effects only (no CDE); default output both NIE/NDE pairs
- also outputs proportion mediated
- allows different sets of X variables for the two models if wanted (I think)
- accommodates M-X interaction as well (`covariates=` option)

```
library(mediation)
mod.m <- lm(bully~minority+grade+age+gender+hhses, data=yrbs)
mod.y <- lm(depressSympts~minority*bully+grade+age+gender+hhses,
                                data=yrbs)
out <- mediate(mod.m, mod.y, sims=1000, boot=true,
               treat="minority", mediator="bully")
summary(out)
```

Mediation: "interventional" direct and indirect effects – definition

This is not a set of effects, but a class of effects

Involve hypothetical "interventions" that shift the values or distribution of the mediator

Recall that the natural effects contrast the averages of the individual nested potential outcomes of the form

$$Y_i(0, M_i(0)), Y_i(1, M_i(0)), Y_i(1, M_i(1))$$

The NIE/NDEs are thus based on the idea that for each individual, "moving" from a factual world to a counterfactual work requires "swapping" their mediator for their own other potential mediator.

This causes unidentifiability when there is a post-treatment confounder.

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Say person i's mediator is $M_i = M_i(1)$. Instead of swapping for $M_i(0)$, we swap for an $M_{\text{draw}} \sim p(M \mid A = 0, C = C_i)$.

Other than this detail, the direct and indirect effects are defined the same way as the natural effects.

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They are also called "randomization analog" because we can think about these random draws as the analogue of randomizing the mediator (conditional on covariates).

Mediation: "interventional" direct and indirect effects – comment

The natural effects are interpreted as"explaining the mechanisms of the causal effect. Yet from the point of view of "nature", it seems somewhat arbitrary whether we choose to decompose TE into natural effects in one way or in the other way.

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The "interventional" effects may better reflect what we were choosing when we had such a preference.

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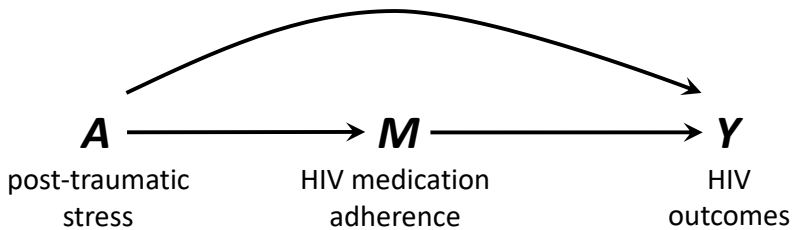
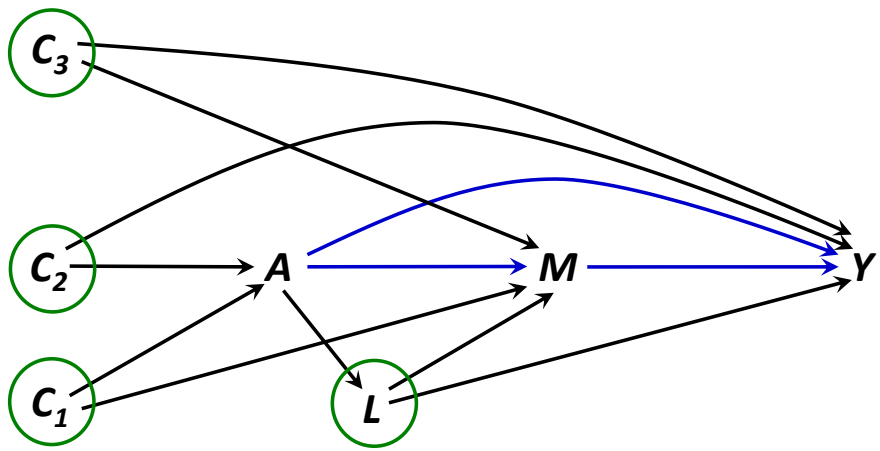


Imagine an intervention that helps people with PTSD adhere to HIV meds at same level as people without PTSD that are similar in covariates

Mediation: "interventional" direct and indirect effects – identification assumptions

- three confounding-related assumptions:
  - no unmeasured $A \to Y$ confounders: $Y(a, m) \perp\!\!\!\perp A \mid C$
  - no unmeasured $A \to M$ confounders: $M(a) \perp\!\!\!\perp A \mid C$
  - no unmeasured $M \to Y$ confounders: $Y(a, m) \perp\!\!\!\perp M \mid A, C, L$



- plus other usual causal inference assumptions

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