PATHWAYS

Mediation and life course epidemiology: challenges and examples

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Methods for Longitudinal Data Analysis in the Social Sciences
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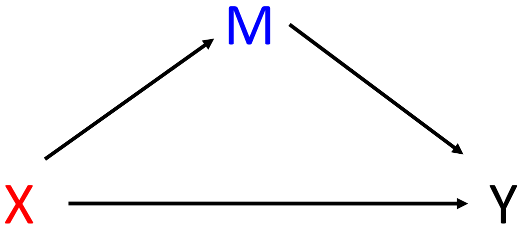
Mediation

- In many research contexts we might be interested in the extent to which the effect of some exposure X on some outcome Y acts via an intermediate variable M.



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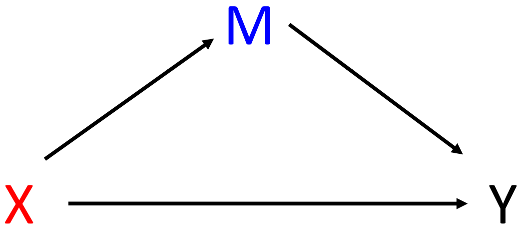
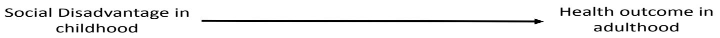


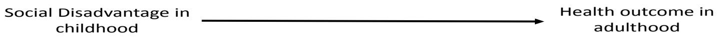
- In other words we are interested in the study of mediation.

Mediation in life course epidemiology



Focus on distal exposures for later life outcomes,

Mediation in life course epidemiology



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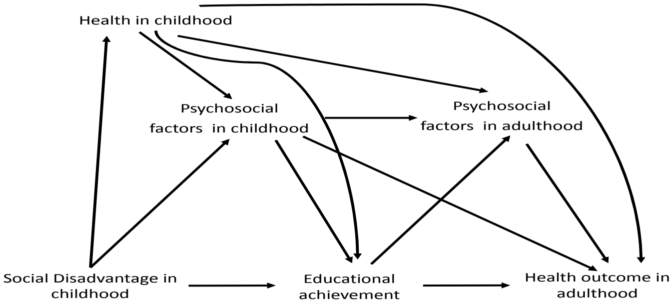

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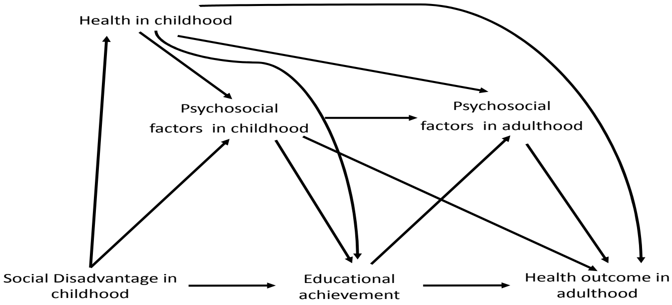

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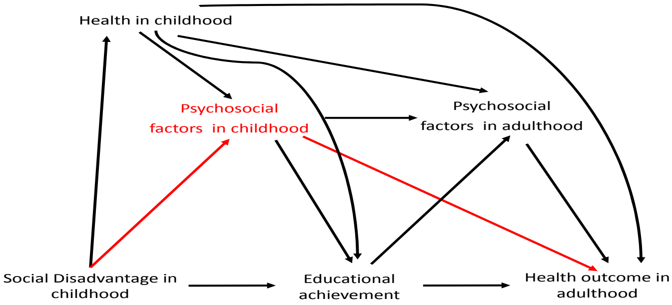

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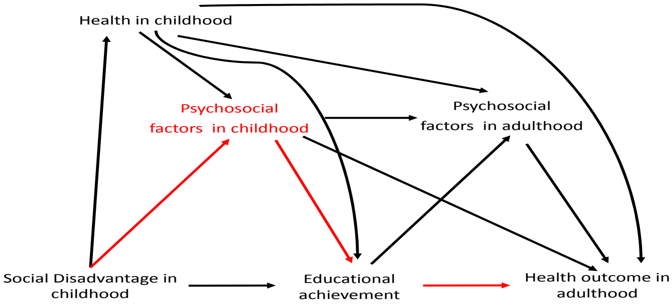

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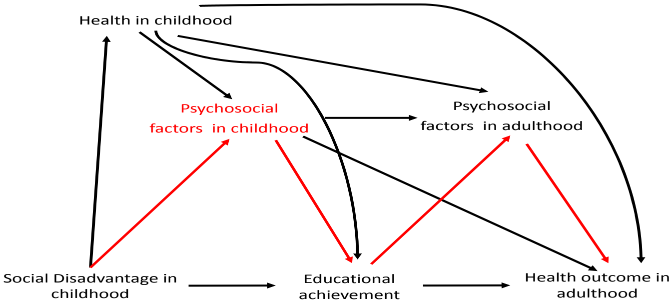

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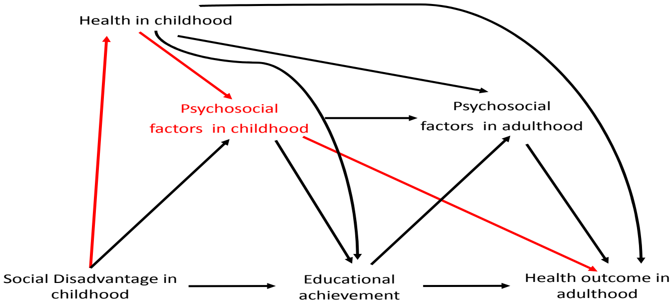

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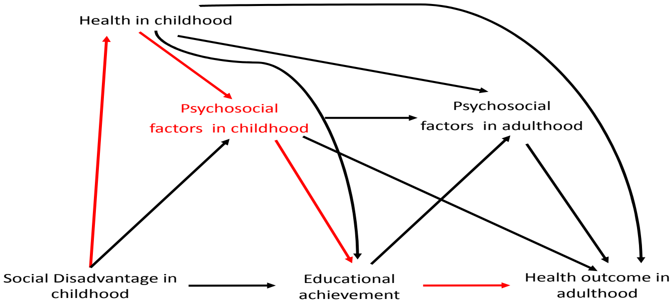

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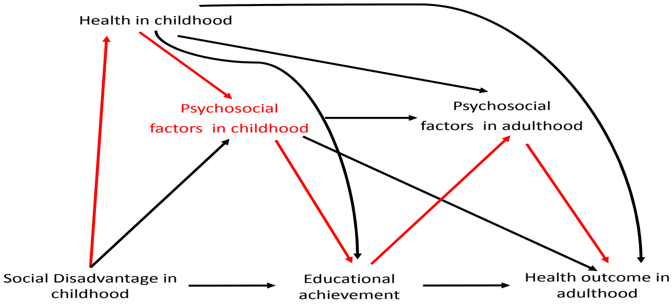

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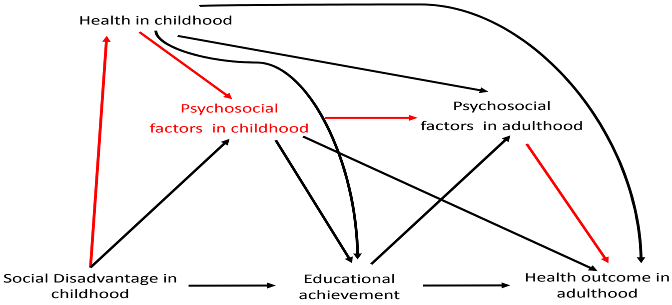

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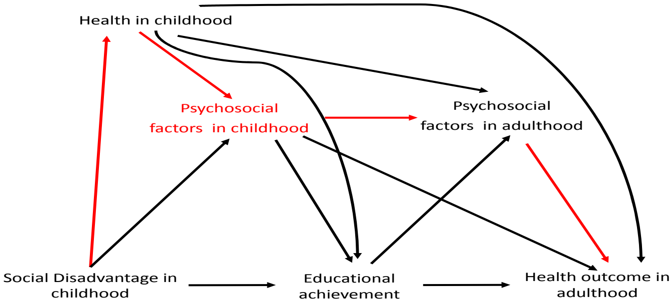

But how?

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The study of mediation

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

- Two main strands in the literature for the study of mediation:
  - Social sciences / psychometrics (MacKinnon, 1986)
  - Causal inference literature (Robins and Greenland, 1992; Pearl, 2001)
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Aims:

- Describe these approaches
- Discuss an example
- Outline some extensions

Outline

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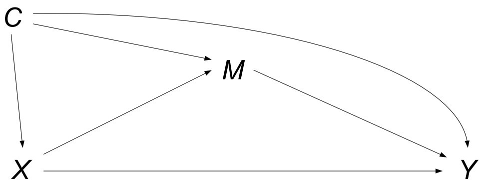
A simplified setting



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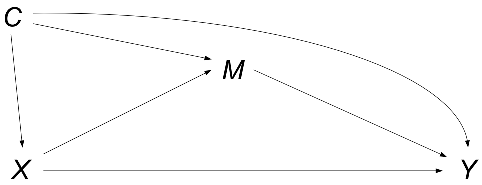

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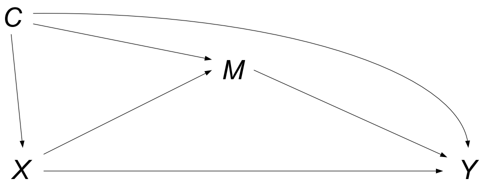
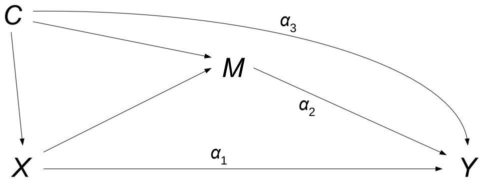


- Adding a vector of confounders C to our original diagram,
- and letting M and Y be continuous ...
- ...we now consider a linear structural equations model.

A linear Structural Equation Model

Wright, 1921



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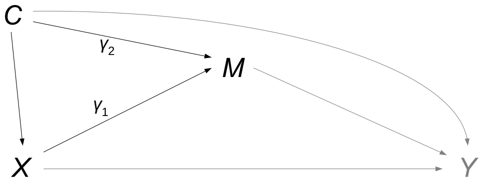

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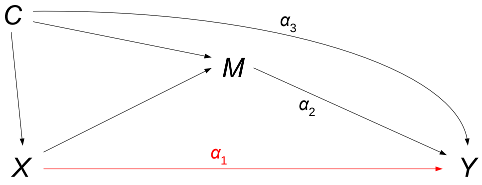

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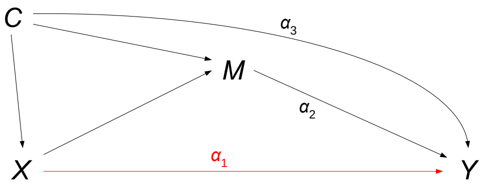

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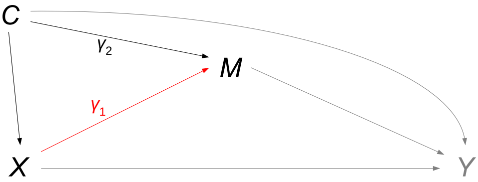

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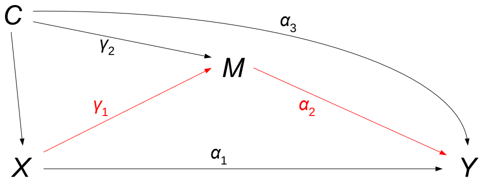

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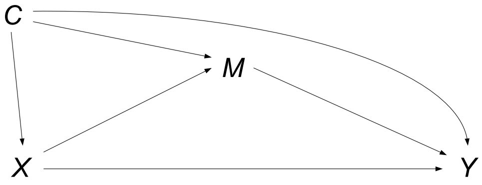

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Estimation (generally) via MLE.

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(Imai *et al.* , 2010; Vansteelandt, 2011)

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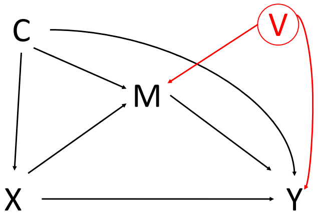

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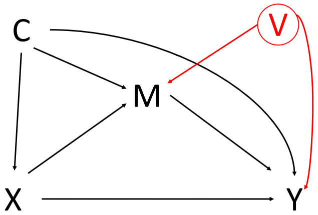

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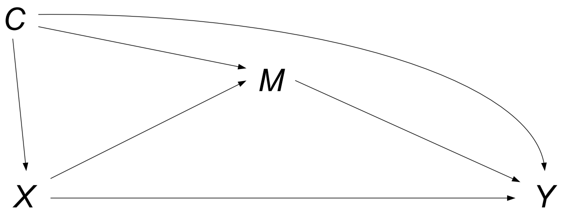
3. Intermediate confounding (De Stavola *et al.* , 2014).

Problem 3: intermediate confounding



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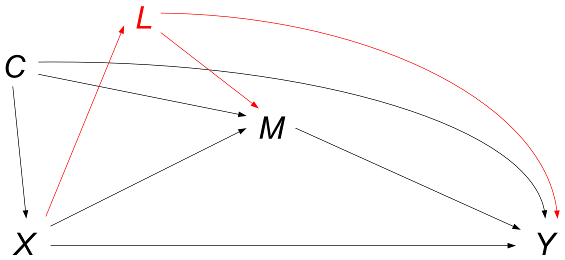

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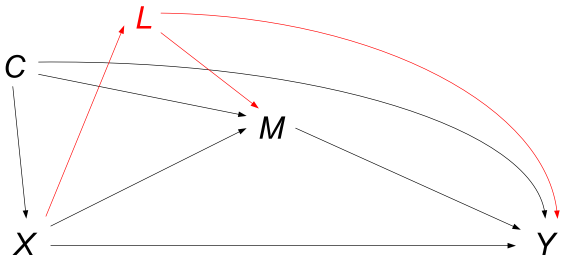

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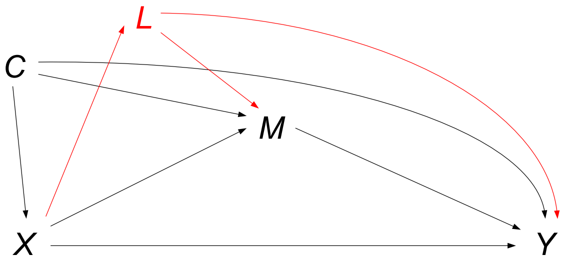

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- In a way we should and also should not condition on L when estimating α_1 and α_2.

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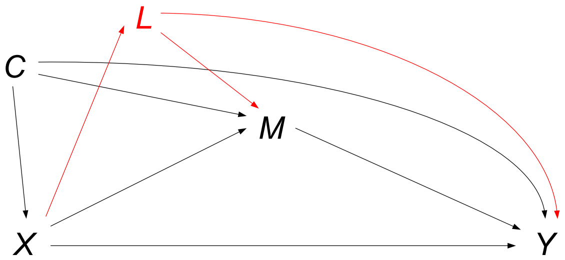

- Intermediate confounders L are common causes of M and Y

Recent contributions from the causal inference literature bring:

- clarity to these issues
- greater flexibility to the modelling

estimating α_1 and α_2.

Outline

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Potential outcomes and mediators

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For simplicity, consider the case where X is binary

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Note that this can also be written as

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Controlled direct effect

Pearl, 2001

- The controlled direct effect of X on Y when M is controlled at m, expressed as a mean difference is

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- For this reason, it is useful to have a different definition of a direct effect.

Natural direct effect

Pearl, 2001; Robins and Greenland, 1992

- The natural direct effect of X on Y expressed as a mean difference is

$$\text{NDE} = E\left[Y\left\{1, M(0)\right\}\right] - E\left[Y\left\{0, M(0)\right\}\right].$$

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- Since M is the same (*within* subject) in both worlds, we are still getting at the direct effect of X.
- If no individual-level interaction between X and M, $\text{CDE}\left(m\right) = \text{NDE} \ \ \forall m$.

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- X is allowed to influence Y only through its influence on M. Thus it is an indirect effect through M.

Comments

- Effect decomposition:
  The sum of the natural direct and indirect effects is the total causal effect:

$$\begin{aligned} \text{NDE} + \text{NIE} &= E\left[Y\left\{1, M(0)\right\}\right] - E\left[Y\left\{0, M(0)\right\}\right] \\ &+ E\left[Y\left\{1, M(1)\right\}\right] - E\left[Y\left\{1, M(0)\right\}\right] = \text{TCE} \end{aligned}$$

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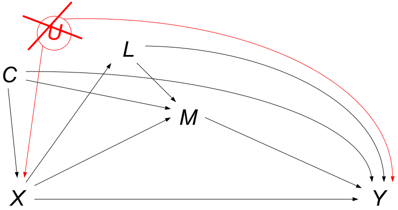
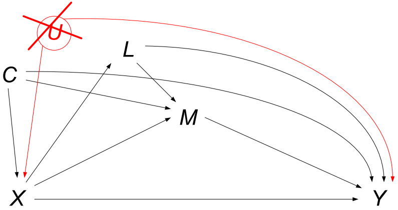
- Identification:
  As well as technical assumptions of no interference and consistency, there are no unmeasured confounding assumptions, and more…

Assumptions for identification: TCE



- No unmeasured confounding of the X–Y relationship.

Assumptions for identification: CDE



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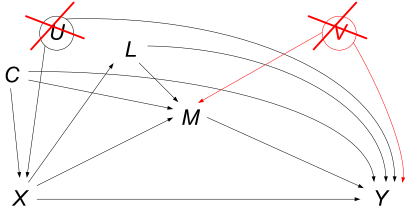

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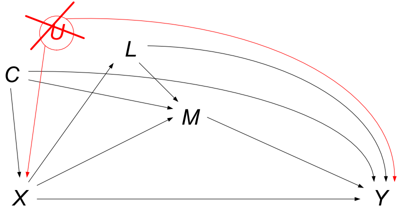

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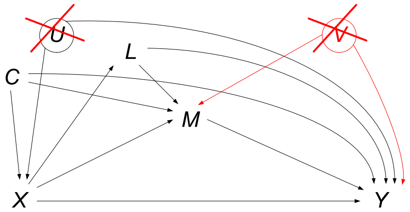

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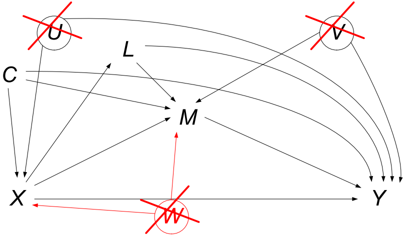

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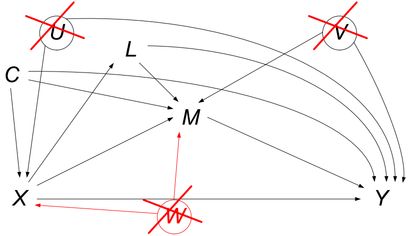

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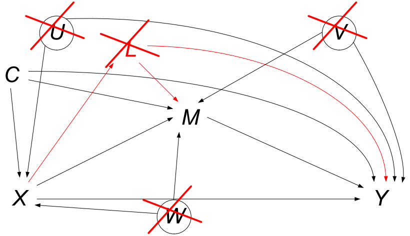

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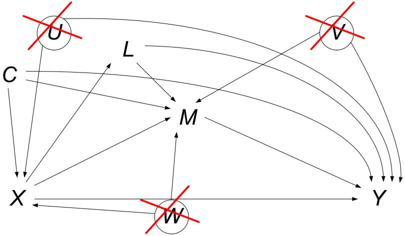

- No unmeasured confounding of the X–Y, M–Y, or X–M relationships.
- AND, in addition, either:
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  - Some restriction on the extent to which X and M interact in their effect on Y (Petersen et al, 2006).

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- Semi-parametric methods make fewer parametric assumptions:
  - Inverse probability of treatment weighting (IPTW):
    - not practical when M is continuous
  - Various flavours of G-estimation
    - generally more complex to implement and understand

Outline

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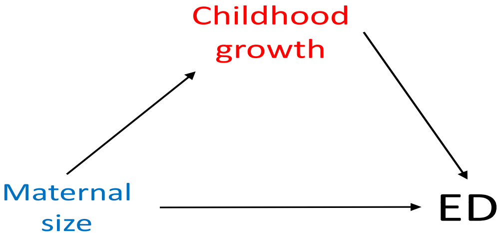

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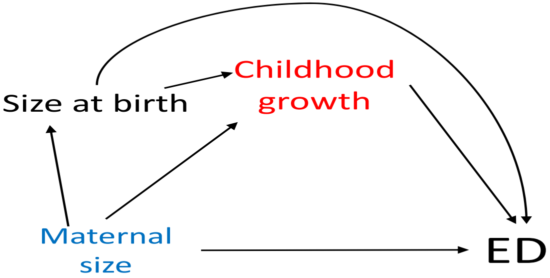

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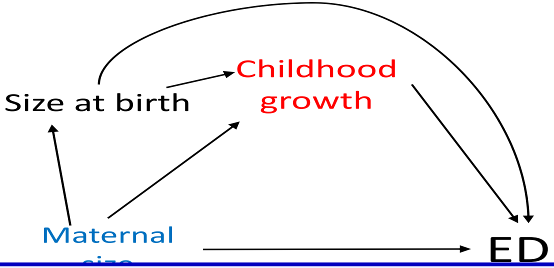

"Is the effect of maternal size on her daughter's ED scores mediated via childhood growth?"

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Estimation: Fully-parametric g-computation via Monte Carlo simulation (with imputation and bootstrapped SEs).

Results

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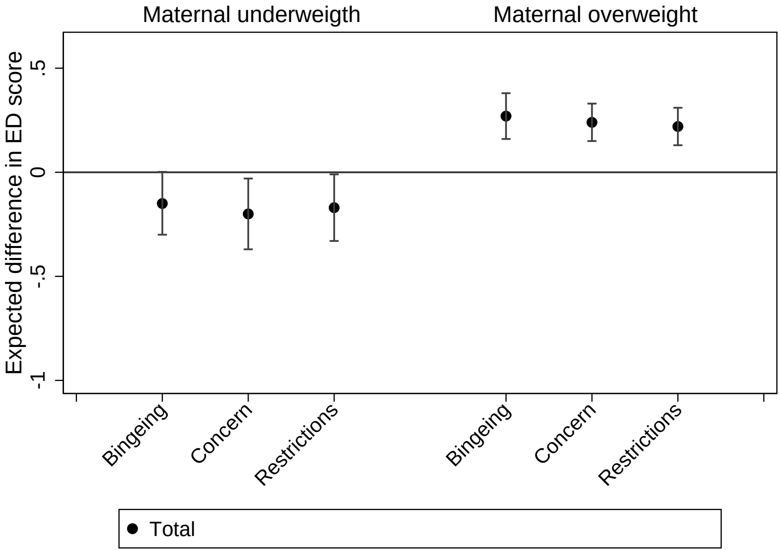

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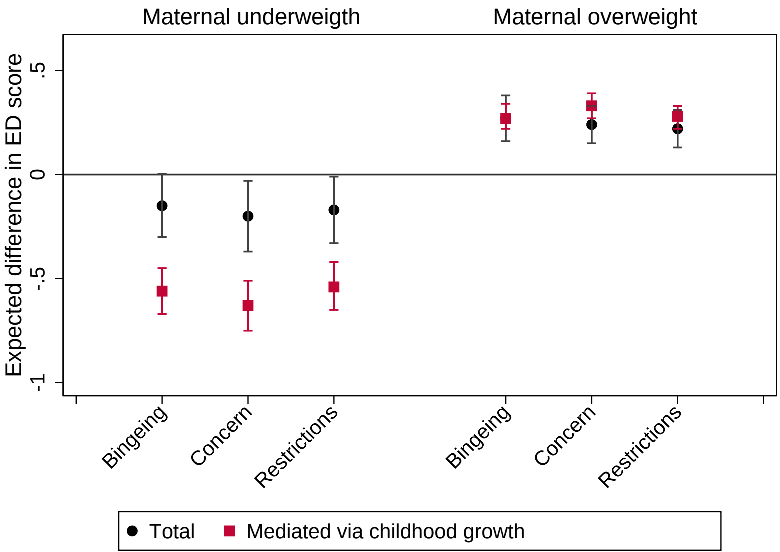

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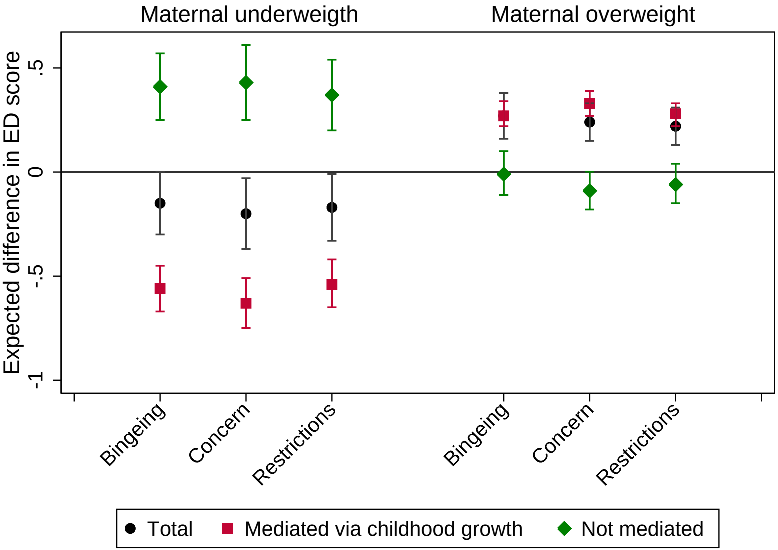

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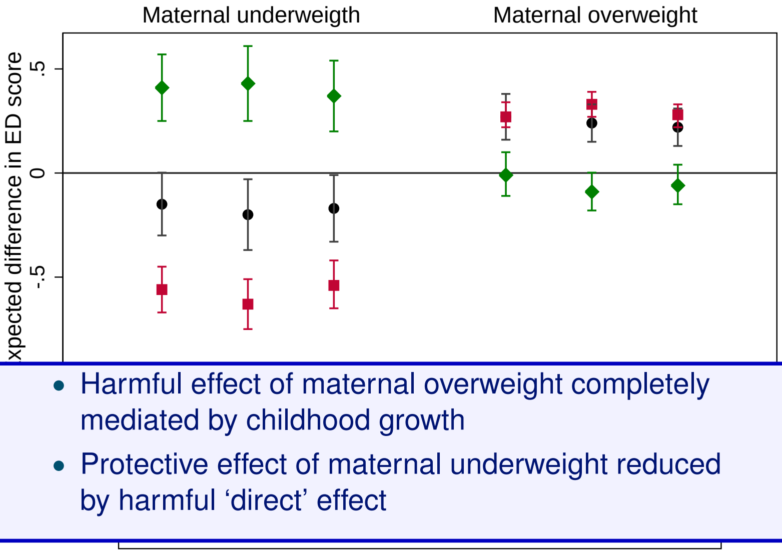

- Harmful effect of maternal overweight completely mediated by childhood growth
- Protective effect of maternal underweight reduced by harmful ‘direct’ effect

Outline

Multiple mediators

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    - Decomposition into mediated effects via individual mediators: there are several alternative options
    - Estimation: necessary to fix a parameter (κ) that is not estimable and carry out sensitivity analyses

Does birth weight also play a mediating role?

Results: Maternal overweight

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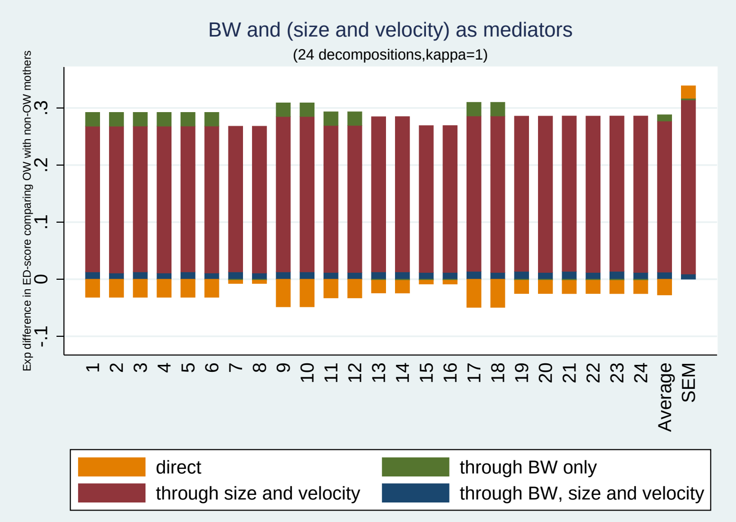

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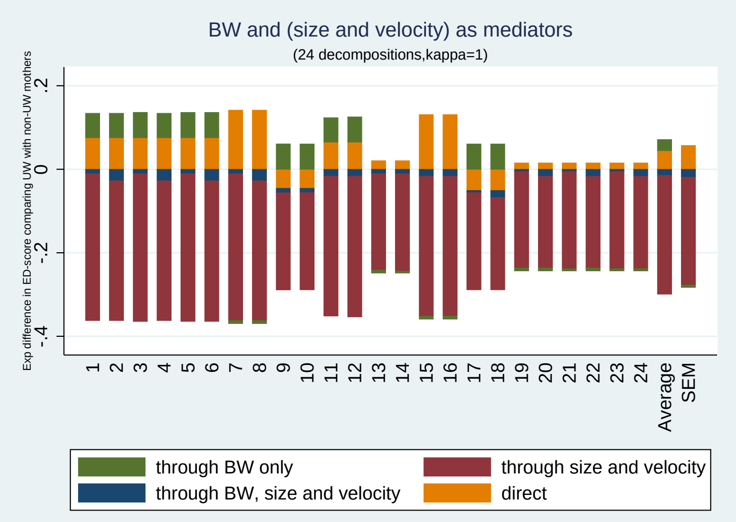

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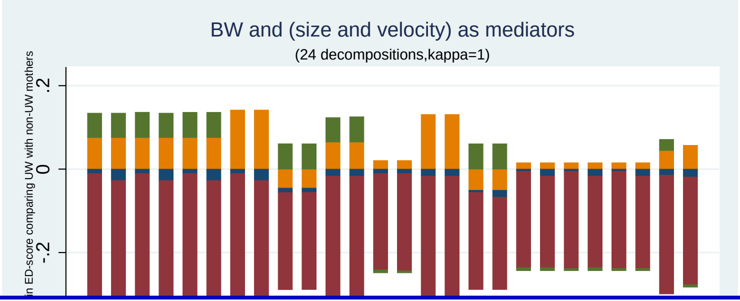

- Consistent harmful/protective effects primarily via childhood growth.
- Harmful direct effect for maternal underweight; also via BW only.
- (Hardly any variation with κ).

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Thank you!

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References

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