Introduction to mediation analysis

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In many research contexts we might be interested in the extent to which the effect of some exposure $X$ on some outcome $Y$ is mediated by an intermediate variable $M$. 
• In many research contexts we might be interested in the extent to which the effect of some exposure $X$ on some outcome $Y$ is mediated by an intermediate variable $M$.

• In other words we are interested in the study of mediation.
Focus on **distal exposures for later life outcomes:**

- Health in childhood
- Psychosocial factors in childhood
- Psychosocial factors in adulthood
- Social Disadvantage in childhood
- Educational achievement
- Health outcome in adulthood
Focus on **distal** exposures for **later** life outcomes:

Interest: disentangle the underlying **processes**.
Other examples

- What proportion of the effect of prenatal care on infant mortality is mediated by medically-induced pre-term birth?
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- Is cognitive behavioral therapy acting via increased compliance in reducing suicide rates?
Other examples

- What proportion of the effect of prenatal care on infant mortality is mediated by medically-induced pre-term birth?
- Is cognitive behavioral therapy acting via increased compliance in reducing suicide rates?
- Is the effect of tamoxifen on CVD mediated/modified by other drugs taken to control its symptoms?
Two main strands in the literature for the study of mediation:

- Social sciences / psychometrics (Baron and Kenny, 1986)
- Causal inference literature (Robins and Greenland, 1992; Pearl, 2001)

The first more accessible, but also misused/misunderstood

The second more rigorous and general, but more complex
The study of mediation

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- The second more rigorous and general, but more complex

Aims:
- outline these two approaches
- compare them and show important differences
- show an application
Outline

1. SEM framework
2. Causal inference framework
3. Comparison
4. A life course epidemiology example
5. Summary
Exposure $X$, mediator $M$, outcome $Y$ and confounders $C$. 
Exposure $X$, mediator $M$, outcome $Y$ and confounders $C$. Mediation leads to separate the two pathways: indirect
Exposure $X$, mediator $M$, outcome $Y$ and confounders $C$. Mediation leads to separate the two pathways: indirect and direct.
1. SEM framework

2. Causal inference framework

3. Comparison

4. A life course epidemiology example

5. Summary
Consider the LSEM corresponding to this diagram:
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\[
\begin{align*}
M &= \alpha_0 + \alpha_x X + \alpha_c C + \epsilon_m \\
Y &= \beta_0 + \beta_x X + \beta_m M + \beta_c C + \epsilon_y
\end{align*}
\] (1)

\(\epsilon_m\) and \(\epsilon_y\) uncorrelated error terms, also uncorrelated with the explanatory variables in their equations.
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- **direct effect of** $X$ **on** $Y$: $\beta_x$
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- **the marginal effect of** $X$ is $(\beta_x + \alpha_x \beta_m) \Rightarrow$ **indirect effect is** $\alpha_x \beta_m$
If the model is correctly specified:

- direct effect of $X$ on $Y$: $\beta_x$
- the marginal effect of $X$ is $(\beta_x + \alpha_x \beta_m) \Rightarrow$ indirect effect is $\alpha_x \beta_m$

Estimation via ML/OLS; delta method/ bootstrapping to obtain SEs for the indirect effect.
Here \( L \) is an intermediate confounder (endogenous variable) because it is influenced by \( X \). If \( L \) is a continuous variable:
Here $L$ is an intermediate confounder (endogenous variable) because it is influenced by $X$. If $L$ is a continuous variable:

$$
\begin{align*}
L &= \gamma_0 + \gamma_x X + \gamma_c C + \epsilon_l \\
M &= \alpha_0 + \alpha_x X + \alpha_l L + \alpha_c C + \epsilon_m \\
Y &= \beta_0 + \beta_x X + \beta_m M + \beta_l L + \beta_c C + \epsilon_y
\end{align*}
$$

$\epsilon_l$, $\epsilon_m$, and $\epsilon_y$ uncorrelated error terms, also uncorrelated with the explanatory variables in their equation.
Following the same steps as before we find, if the model is correctly specified:

• Marginal effect of $X$ on $Y$ is
  
  $$\beta_x + \alpha_x \beta_m + \gamma_x \alpha_l \beta_m + \gamma_x \beta_l$$

• Effect mediated via $M$, the indirect effect is
  
  $$\alpha_x \beta_m + \gamma_x \alpha_l \beta_m$$

• Effect not mediated by $M$, the direct effect:
  
  $$\beta_x + \gamma_x \beta_l$$
Following the same steps as before we find, if the model is correctly specified:

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Following the same steps as before we find, if the model is correctly specified:

- **Marginal effect of** $X$ **on** $Y$ **is** $(\beta_x + \alpha_x \beta_m + \gamma_x \alpha_l \beta_m + \gamma_x \beta_l)$
- **Effect mediated via** $M$, the **indirect effect** is $(\alpha_x \beta_m + \gamma_x \alpha_l \beta_m)$
- **Effect not mediated by** $M$, the **direct effect**: $(\beta_x + \gamma_x \beta_l)$
• Extension to the case with intermediate confounder $L$ is straightforward
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• Models can only be linear for $Y$, $M$ and $L$, with no interactions nor other non-linearities (e.g. $M^2$)
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• Derivations of direct and indirect effects are always specific to a particular model
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Models can only be linear for $Y$, $M$ and $L$, with no interactions nor other non-linearities (e.g. $M^2$)

Derivations of direct and indirect effects are always specific to a particular model

For non-linear settings: approximate solutions (and for defining indirect effects only) (Hayes and Preacher, 2010)
1 SEM framework

2 Causal inference framework

3 Comparison

4 A life course epidemiology example

5 Summary
In this framework, definitions of direct and indirect effects do not depend on the specification of a particular statistical model.
The causal inference framework

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- Explicitly aiming for causal statements, this approach invokes the notion of "how the world would have been had something been different."
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• Explicitly aiming for causal statements, this approach invokes the notion of “how the world would have been had something been different.”

• Hence use of quantities that are not all observable: potential outcomes and the potential mediators.
**Potential outcomes**

- $Y(x)$: the potential values of $Y$ that would have occurred had $X$ been set, possibly counter to fact, to the value $x$.

- $M(x)$: the potential values of $M$ that would have occurred had $X$ been set, possibly counter to fact, to the value $x$.

- $Y(x, m)$: the potential values of $Y$ that would have occurred had $X$ been set, possibly counter to fact, to the value $x$ and $M$ to $m$. 
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- $Y(x, m)$: the potential values of $Y$ that would have occurred had $X$ been set, possibly counter to fact, to the value $x$ and $M$ to $m$.

- For simplicity consider the case where $X$ is binary

- It also helps to start with the definition of total causal effect
The average total causal effect of $X$, comparing exposure level $X = 1$ to $X = 0$, can be defined as the linear contrast $^1$:

$$TCE = E[Y(1)] - E[Y(0)]$$

This is a comparison of two hypothetical worlds: in the first, $X$ is set to 1, and in the second $X$ is set to 0.
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$$TCE = E[Y(1)] - E[Y(0)]$$

This is a comparison of two hypothetical worlds: in the first, $X$ is set to 1, and in the second $X$ is set to 0.

In general: $TCE \neq E[Y|X = 1] - E[Y|X = 0]$

hence $TCE$ cannot be naively estimated from the data.
To identify \( TCE \) we need to infer \( E[Y(1)] \) and \( E[Y(0)] \) from the data.

This is possible under certain assumptions. Those most invoked are:

(i) no interference: \( Y_i \) is not influenced by \( X_j, i \neq j \)
To identify $TCE$ we need to infer $E[Y(1)]$ and $E[Y(0)]$ from the data.

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(ii) consistency: $Y(x)$ can be inferred from observed $Y$ when $X = x$
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(iii) conditional exchangeability: $Y(x)$ can be inferred from $Y(x)$ of comparable others when $X \neq x$: 
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(iii) **conditional exchangeability**: $Y(x)$ can be inferred from $Y(x)$ of comparable others when $X \neq x$: *i.e.* no unmeasured confounding between $X$ and $Y$:

If these are satisfied, we can infer the *TCE* from the data

$$
\sum_c \{ E(Y|X = 1, C = c) - E(Y|X = 0, C = c) \} Pr(C = c)
$$
The average controlled direct effect of $X$ on $Y$, when $M$ is controlled at $m$, is:

$$CDE(m) = E[Y(1,m)] - E[Y(0,m)]$$
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- In the first, $X$ is set to 1, and in the second $X$ is set to 0.
- In both worlds, $M$ is set to $m$.
- By keeping $M$ fixed at $m$, we are getting at the direct effect of $X$, unmediated by $M$. 
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- In the first, $X$ is set to 1, and in the second $X$ is set to 0.
- In both worlds, $M$ is set to $m$.
- By keeping $M$ fixed at $m$, we are getting at the direct effect of $X$, unmediated by $M$.
- In general $CDE(m)$ varies with $m$
Identification possible under extensions of the earlier assumptions:

(i) no interference

(ii) consistency: extended to include

\[ Y = Y(x, m) \text{ if } X = x \text{ and } M = m \]
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(iii) sequential conditional exchangeability:

If these assumptions are satisfied we can infer the \( CDE(m) \) from the observed data

\[
\sum_c \{ E( Y|X = 1, M = m, C = c) - E( Y|X = 0, M = m, C = c) \} \cdot \frac{Pr(C = c)}{Pr(C = c)}
\]
The average Pure Natural Direct Effect of $X$ on $Y$ is:

$$PNDE = E[Y(1, M(0))] - E[Y(0, M(0))]$$
Pure Natural Direct Effect (PNDE): definition

The average Pure Natural Direct Effect of $X$ on $Y$ is:

$$PNDE = E[Y(1, M(0))] - E[Y(0, M(0))]$$

This is a comparison of two hypothetical worlds:

- In the first, $X$ is set to 1, and in the second $X$ is set to 0.
- In both worlds, $M$ is set to the natural value $M(0)$, i.e. the value it would take if $X$ were set to 0.
- Since $M$ is the same (within individual) in both worlds, we are still getting at the direct effect of $X$, unmediated by $M$. 
Identification possible, as before, under extensions of the earlier assumptions:

(i) no interference

(ii) consistency, extended to include:

\[ Y = Y(x, m) \] if \( X = x \) and \( M = m \),
\[ M = M(x) \] if \( X = x \), and
\[ Y = Y \{x, M(x^*)\} \] if \( X = x \) and \( M = M(x^*) \).
Identification possible, as before, under extensions of the earlier assumptions:

(i) no interference

(ii) consistency, extended to include:

\[ Y = Y(x, m) \text{ if } X = x \text{ and } M = m, \]
\[ M = M(x) \text{ if } X = x, \text{ and} \]
\[ Y = Y \{x, M(x^*)\} \text{ if } X = x \text{ and } M = M(x^*). \]

(iii) sequential conditional exchangeability extended to include no unmeasured \( X - M \) confounding
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(ii) **consistency**, extended to include:
\[ Y = Y(x, m) \text{ if } X = x \text{ and } M = m, M = M(x) \text{ if } X = x, \text{ and} \]
\[ Y = Y \{x, M(x^*)\} \text{ if } X = x \text{ and } M = M(x^*). \]

(iii) **sequential conditional exchangeability** extended to include no unmeasured \( X - M \) confounding

(iv) either **no intermediate confounders** or some restrictions on \( X - M \) interactions in their effect on \( Y \)
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Y = Y(x, m) \text{ if } X = x \text{ and } M = m, \quad M = M(x) \text{ if } X = x, \text{ and} \\
Y = Y\{x, M(x^*)\} \text{ if } X = x \text{ and } M = M(x^*).
\]

(iii) sequential conditional exchangeability extended to include no unmeasured $X - M$ confounding

(iv) either no intermediate confounders or some restrictions on $X - M$ interactions in their effect on $Y$

If these assumptions are satisfied: we can infer the \textit{NDE} from the observed data
The average Total Natural Indirect Effect of $X$ on $Y$ is:

$$TNIE = TCE - PNDE = E[Y(1, M(1))] - E[Y(1, M(0))]$$
The average **Total Natural Indirect Effect** of $X$ on $Y$ is:

$$TNIE = TCE - PNDE = E[Y(1, M(1))] - E[Y(1, M(0))]$$

This is a comparison of two hypothetical worlds: In both $X$ is set to 1, while $M$ is set to the natural value when $X$ is set to 1 or 0. The same assumptions as for $PNDE$ are required to identify the $TNIE$. 
Each of these estimands can be identified under certain assumption and via an identification equation, e.g.

\[
CDE(m) = \sum_c \left\{ E(Y|X = 1, M = m, C = c) - E(Y|X = 0, M = m, C = c) \right\} Pr(C = c)
\]

\[
PNDE = \sum_c \left\{ \sum_m \left\{ E(Y|X = 1, M = m, C = c) - E(Y|X = 0, M = m, C = c) \right\} \right. \\
\left. \sum_m Pr(M = m|X = 0, C = c) \right\} Pr(C = c)
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The identification equations

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CDE(m) = \sum_{c} \{E(Y|X = 1, M = m, C = c) - E(Y|X = 0, M = m, C = c)\} Pr(C = c)
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\[
PNDE = \sum_{c} \left\{ \sum_{m} \{E(Y|X = 1, M = m, C = c) - E(Y|X = 0, M = m, C = c)\} \right\} Pr(M = m|X = 0, C = c) Pr(C = c)
\]

- These equations can be extended to deal with continuous \(M\) and \(C\) and to include intermediate confounders \(L\).
The identification equations

- Each of these estimands can be identified under certain assumption and via an identification equation, e.g.

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PNDE = \sum_c \left\{ \sum_m \left\{ E(Y|X = 1, M = m, C = c) - E(Y|X = 0, M = m, C = c) \right\} \right\} Pr(M = m|X = 0, C = c) Pr(C = c)
\]

- These equations can be extended to deal with continuous \(M\) and \(C\) and to include intermediate confounders \(L\).

- Their essence is the specification of conditional expectations of \(Y\), conditional distributions for \(M\) (and \(L\)) (and marginal distributions for \(C\)).
Wide range of options, for most combinations of $M$ and $Y$:

- **G-computation**—very flexible and efficient but heavy on parametric modelling assumptions:
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- **G-computation**—very flexible and efficient but heavy on parametric modelling assumptions:
  - It is the direct implementation of the identification equations
  - requires correct specification of all relevant conditional expectations and distributions
  - implemented in `gformula` command in Stata
Wide range of options, for most combinations of $M$ and $Y$:

- **G-computation**—very flexible and efficient but heavy on parametric modelling assumptions:
  - It is the direct implementation of the identification equations
  - requires correct specification of all relevant conditional expectations and distributions
  - implemented in `gformula` command in Stata

- 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 understand
Outline

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Revisiting SEMs

Structural assumptions with no intermediate confounders
Disturbances are mutually uncorrelated
Disturbances are mutually uncorrelated

Disturbances are uncorrelated with the exogenous variables
Disturbances are mutually uncorrelated

Disturbances are uncorrelated with the exogenous variables

‘Same’ as no unaccounted common causes for $M - Y$, $X - Y$, $X - M$. 
SEM requires $\epsilon_l$ to be uncorrelated with $\epsilon_x$, $\epsilon_m$ and $\epsilon_y$. Modern causal inference does not require the equivalent assumption. This is not required for SEM mediation analysis either (De Stavola et al.)
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SEM requires $\epsilon_l$ to be uncorrelated with $\epsilon_x$, $\epsilon_m$ and $\epsilon_y$

Modern causal inference does not require the equivalent assumption

This is not required for SEM mediation analysis either (De Stavola et al.)

With linear models, structural assumptions for mediation analysis from the two schools are essentially equivalent
If a structural model is linear and does not include interactions or other non-linear terms:

- identifying equation for modern causal inference would lead to same estimands as adopting an SEM approach:
  - $\text{CDE}(m) = \text{PNDE} = \beta_x$
  - $\text{TNIE} = \alpha_x \beta_m$

Limitations of SEMs can be lifted by adopting the estimands defined within the 'modern' school but still using the machinery of SEM framework:

Estimation-by-combination
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  - $TNIE = \alpha_x \beta_m$

- Limitations of SEMs can be lifted by adopting the estimands defined within the ‘modern’ school but still using the machinery of SEM framework:

  Estimation-by-combination
Consider a more general linear SEM:

\[
\begin{align*}
L &= \gamma_0 + \gamma_x X + \gamma_c C + \epsilon_l \\
M &= \alpha_0 + \alpha_x X + \alpha_l L + \alpha_c C + \epsilon_m \\
Y &= \beta_0 + \beta_x X + \beta_l L + \beta_m M + \beta_{mm} M^2 + \beta_c C + \beta_{xm} X M + \epsilon_y
\end{align*}
\]

Applying the appropriate identification equations leads to:

\[
\begin{align*}
\text{CDE}(m) &= \beta_x + \beta_l \gamma_x + \beta_{xm} m \\
\text{PNDE} &= \beta_x + \beta_l \gamma_x + \beta_{xm} \left[ \alpha_0 + \alpha_l \left( \gamma_0 + \gamma_c \overline{C} \right) + \alpha_c \overline{C} \right] \\
\text{TNIE} &= \left( \beta_m + \beta_{xm} \right) \left( \alpha_x + \gamma_x \alpha_l \right) + \\
&\quad + \beta_{mm} \left[ \left( \alpha_x + \gamma_x \alpha_l \right)^2 + 2 \left( \alpha_x + \gamma_x \alpha_l \right) \left( \alpha_0 + \alpha_l \left( \gamma_0 + \gamma_c \overline{C} \right) + \alpha_c \overline{C} \right) \right]
\end{align*}
\]

where each of these parameters can be estimated by the model above, leading to the same results as from g-computation.
### Comparison of G-computation and estimation-by-combination

Datasets of size=1,000,000 generated according to specified model with $N(0, 1)$ errors and binary $C$ ($p = 0.5$).

Standard errors obtained via bootstrap for g-computation and the delta method for estimation-by-combination.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Method</th>
<th>PNDE estimate (s.e.)</th>
<th>Estimand</th>
<th>TNIE estimate (s.e.)</th>
<th>CDE(0) estimate (s.e.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Y, M, \text{with } C, MX$</td>
<td>true</td>
<td>0.730 -</td>
<td>0.240 -</td>
<td>0.400 -</td>
<td></td>
</tr>
<tr>
<td></td>
<td>g-estimation</td>
<td>0.731 (0.003)</td>
<td>0.238 (0.003)</td>
<td>0.405 (0.003)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>combination</td>
<td>0.731 (0.002)</td>
<td>0.239 (0.001)</td>
<td>0.405 (0.003)</td>
<td></td>
</tr>
<tr>
<td>$Y, M, \text{with } MX$ and $M^2$</td>
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<td>0.344 -</td>
<td>0.400 -</td>
<td></td>
</tr>
<tr>
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<td>g-estimation</td>
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<td>0.341 (0.004)</td>
<td>0.406 (0.003)</td>
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</tr>
<tr>
<td>$Y, M, L, \text{with } MX, M^2$</td>
<td>true</td>
<td>0.806 -</td>
<td>0.787 -</td>
<td>0.520 -</td>
<td></td>
</tr>
<tr>
<td></td>
<td>g-estimation</td>
<td>0.806 (0.007)</td>
<td>0.783 (0.008)</td>
<td>0.527 (0.004)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>combination</td>
<td>0.807 (0.002)</td>
<td>0.783 (0.003)</td>
<td>0.527 (0.004)</td>
<td></td>
</tr>
<tr>
<td>$Y, M, L, \text{with } C, U$</td>
<td>true</td>
<td>0.520 -</td>
<td>0.156 -</td>
<td>0.520 -</td>
<td></td>
</tr>
<tr>
<td></td>
<td>g-estimation</td>
<td>0.521 (0.003)</td>
<td>0.158 (0.003)</td>
<td>0.521 (0.004)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>combination</td>
<td>0.520 (0.002)</td>
<td>0.157 (0.001)</td>
<td>0.520 (0.002)</td>
<td></td>
</tr>
</tbody>
</table>
With continuous endogenous variables represented by a recursive linear system:

- **structural assumptions** for mediation made by the two approaches **closely related**, even in the presence of intermediate confounders

- **fully parametric estimation** via g-computation is achievable within an **SEM framework**, even in the presence of interactions and other non-linearities, and even if there is unmeasured $L - Y$ confounding.
1 SEM framework
2 Causal inference framework
3 Comparison
4 A life course epidemiology example
5 Summary
Eating disorders (ED) in adolescence

- ED comprise a variety of heterogeneous diseases
- Maternal factors possibly important
- Childhood BMI a possible mediator
- Data:
  - **Outcome**: ED scores derived from parental questionnaire on the child’s psychological distress when aged 13.5y: today focus on “**Binge eating**”
  - **Exposure**: pre-pregnancy maternal BMI (binary, > 25kg/m²)
  - **Mediator**: Childhood BMI (around age 7, age-standardized)
  - **Confounders**: pre-pregnancy maternal mental illness, maternal education, girl’s birth weight
Maternal BMI, childhood BMI and eating disorders

The causal question
How much of the effect of maternal BMI on her daughter's ED score is due to its effect on the child's BMI?
The causal question

How much of the effect of maternal BMI on her daughter’s ED score is due to its effect on the child’s BMI?
More specifically... 

We can ask either of these question:

**What effect does intervening on maternal BMI have on later ED if we could also intervene on each child BMI and set it to a particular level?**

- **Controlled Direct Effect**

**What effect does intervening on maternal BMI has on later ED in a world where the effect of maternal BMI has no effect on her child BMI?**

- **Natural Direct Effect**
Identification requires assumptions that allows us to use observed data to derive potential outcomes. According to the estimand, varying specifications of:

(i) no interference
(ii) consistency
(iii) no unmeasured confounding
(iv) for PNDE and TNIE: some parametric restrictions
**Maternal BMI, childhood BMI and eating disorders**

Results from g-computation and estimation-by-combination

<table>
<thead>
<tr>
<th>Model</th>
<th>Estimand</th>
<th>Method</th>
<th>G-computation</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Estimate</td>
<td>Estimate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(s.e.)</td>
<td>(s.e.)</td>
</tr>
<tr>
<td><strong>Model 1:</strong> no $X-M$ interaction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$TCE$</td>
<td></td>
<td>0.287</td>
<td>0.287</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.049)</td>
<td>(0.052)</td>
</tr>
<tr>
<td></td>
<td>$PNDE$</td>
<td></td>
<td>0.103</td>
<td>0.102</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.047)</td>
<td>(0.050)</td>
</tr>
<tr>
<td></td>
<td>$TNIE$</td>
<td></td>
<td>0.184</td>
<td>0.185</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.019)</td>
<td>(0.021)</td>
</tr>
<tr>
<td><strong>Model 2:</strong> $CDE(m)$ does not vary with $M(0)$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$TCE$</td>
<td></td>
<td>0.297</td>
<td>0.297</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.047)</td>
<td>(0.049)</td>
</tr>
<tr>
<td></td>
<td>$PNDE$</td>
<td></td>
<td>0.102</td>
<td>0.103</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.051)</td>
<td>(0.051)</td>
</tr>
<tr>
<td></td>
<td>$TNIE$</td>
<td></td>
<td>0.195</td>
<td>0.194</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.026)</td>
<td>(0.028)</td>
</tr>
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</table>
Maternal BMI, childhood BMI and eating disorders
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<table>
<thead>
<tr>
<th>Model</th>
<th>Estimand</th>
<th>G-computation Estimate (s.e.)</th>
<th>Combination Estimate (s.e.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>TCE</strong> 0.287 (0.049)</td>
<td><strong>TCE</strong> 0.287 (0.052)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>PNDE</strong> 0.103 (0.047)</td>
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<td></td>
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</table>

Which of these models is best?
## Maternal BMI, childhood BMI and eating disorders

### Structural model for Bingeing/Overeating

<table>
<thead>
<tr>
<th>Expl. var.</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No ( X - M ) interaction</td>
<td>No ( X - L ) nor ( L^2 )</td>
<td>No constraints</td>
</tr>
<tr>
<td></td>
<td>Estimate (s.e.)</td>
<td>Estimate (s.e.)</td>
<td>Estimate (s.e.)</td>
</tr>
<tr>
<td>( X )</td>
<td>0.072 (0.048)</td>
<td>0.084 (0.049)</td>
<td>0.068 (0.050)</td>
</tr>
<tr>
<td>( M )</td>
<td>0.315 (0.019)</td>
<td>0.313 (0.021)</td>
<td>0.312 (0.021)</td>
</tr>
<tr>
<td>( M^2 )</td>
<td>0.044 (0.012)</td>
<td>0.042 (0.012)</td>
<td>0.043 (0.012)</td>
</tr>
<tr>
<td>( L )</td>
<td>0.034 (0.022)</td>
<td>0.054 (0.020)</td>
<td>0.034 (0.022)</td>
</tr>
<tr>
<td>( L^2 )</td>
<td>0.032 (0.012)</td>
<td>-</td>
<td>0.032 (0.012)</td>
</tr>
<tr>
<td>( XL )</td>
<td>0.078 (0.045)</td>
<td>-</td>
<td>0.078 (0.045)</td>
</tr>
<tr>
<td>( XM )</td>
<td>-</td>
<td>0.017 (0.045)</td>
<td>0.014 (0.045)</td>
</tr>
<tr>
<td>( C_1 )</td>
<td>-0.011 (0.036)</td>
<td>-0.011 (0.036)</td>
<td>-0.011 (0.036)</td>
</tr>
<tr>
<td>( C_2 )</td>
<td>0.207 (0.054)</td>
<td>0.209 (0.054)</td>
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</tbody>
</table>
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  (b) While modern causal inference focuses on summary effects, SEMs help closer examination of specifications (novel semi-parametric approaches should not however be overlooked!).
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Thank you!


• Pearl J. Direct and indirect effects. *Proceedings of the Seventeenth Conference on Uncertainty and Artificial Intelligence* 2001; San Francisco: Morgan Kaufmann.