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Let Ω_M denote the range of M. In a randomized study or an observational study with measured confounders $\mathbf{X}_i$, for every $\mathbf{x}$,

$$M_i(0), M_i(1), \{Y_i(0, m), Y_i(1, m) : m \in \Omega_M\} \perp\!\!\!\perp Z_i \mid \mathbf{X}_i = \mathbf{x}.$$

Then

$$\begin{aligned} E(Y_i \mid Z_i = z, M_i = m, \mathbf{X}_i = \mathbf{x}) &= E(Y_i(z, m) \mid Z_i = z, M_i = m, \mathbf{X}_i = \mathbf{x}) \\ &= E(Y_i(z, m) \mid Z_i = z, M_i(z) = m, \mathbf{X}_i = \mathbf{x}) \\ &= E(Y_i(z, m) \mid M_i(z) = m, \mathbf{X}_i = \mathbf{x}). \end{aligned}$$

Thus

$$\begin{aligned} &E(Y_i \mid Z_i = 1, M_i = m, \mathbf{X}_i = \mathbf{x}) - E(Y_i \mid Z_i = 0, M_i = m, \mathbf{X}_i = \mathbf{x}) \\ &\quad = E(Y_i(1, m) \mid M_i(1) = m, \mathbf{X}_i = \mathbf{x}) - E(Y_i(0, m) \mid M_i(0) = m, \mathbf{X}_i = \mathbf{x}), \end{aligned}$$

which is not a causal comparison in general.

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To identify CDE($\mathbf{x}$), an additional condition is required.

$$Y_i(z, m) \perp\!\!\!\perp M_i(z) \mid \mathbf{X}_i = \mathbf{x} \tag{1}$$

or

$$Y_i(z, m) \perp\!\!\!\perp M_i \mid \mathbf{X}_i = \mathbf{x}, Z_i = z \tag{2}$$

The previous conditions
$M_i(0), M_i(1), \{Y_i(0, m), Y_i(1, m) : m \in \Omega_M\} \perp\!\!\!\perp Z_i \mid \mathbf{X}_i = \mathbf{x}$ and (1) or (2)
imply $E(Y_i \mid Z_i = z, M_i = m, \mathbf{X}_i = \mathbf{x}) = E(Y_i(z, m) \mid \mathbf{X}_i = \mathbf{x})$.

n.b. these conditons do not suffice to identify the average direct and indirect effects, as pointed out, for example in Robins (2003), except in the special case where additivity holds,

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To identify average direct/indirect effects when additivity does not hold, we must identify $E(Y_i(z, M_i(z^*)) \mid \mathbf{X}_i)$ for $z = z^*$ and $z \neq z^*$.

$$Y_i(z, M_i(z)) \perp\!\!\!\perp Z_i \mid \mathbf{X}_i = \mathbf{x}.$$

In the second case, using iterated expectations,

$$\begin{aligned} E(Y_i(z, M_i(z^*)) \mid \mathbf{X}_i = \mathbf{x}) &= EE(Y_i(z, M_i(z^*)) \mid M_i(z^*) = m, \mathbf{X}_i = \mathbf{x}) \\ &= EE(Y_i(z, m) \mid (M_i(z^*)) = m, \mathbf{X}_i = \mathbf{x}), \end{aligned}$$

where the expectation is iterated over the distribution of $M_i(z^*) \mid \mathbf{X}_i = \mathbf{x}$ and the second equality follows from the assumption that $M_i(z^*) = m$ implies $Y_i(z, M_i(z^*)) = Y_i(z, m)$.

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We make the additional assumption $E(Y_i(z,m) \mid (M_i(z^*) = m, \mathbf{X}_i = \mathbf{x}) = E(Y_i(z,m) \mid \mathbf{X}_i = \mathbf{x})$, which is implied by the condition (Vanderweele 2015)

$$Y_i(z,m) \perp\!\!\!\perp M_i(z^*) \mid \mathbf{X}_i = \mathbf{x},$$

then we can use the previously given conditions for the controlled effects to identify $E(Y_i(z,m) \mid \mathbf{X}_i = \mathbf{x})$, and we only need to average this over the distribution of $M_i(z^*) \mid \mathbf{X}_i = \mathbf{x}$;

Since

$$M_i(0), M_i(1), \{Y_i(0,m), Y_i(1,m) : m \in \Omega_M\} \perp\!\!\!\perp Z_i \mid \mathbf{X}_i = \mathbf{x},$$

this is the conditional distribution of M_i given $Z_i = z^*$ and $\mathbf{X}_i = \mathbf{x}$.

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The identification conditions can be weakened somewhat (e.g. Imai, Keele and Yamamoto 2010). However, in most studies, if the conditions above are not reasonable, neither are the weaker conditions.

It is important to point out that neither condition $Y_i(z, m) \perp\!\!\!\perp M_i(z) \mid \mathbf{X}_i = \mathbf{x}$ nor condition $Y_i(z, m) \perp\!\!\!\perp M_i \mid \mathbf{X}_i = \mathbf{x}, Z_i = z$ follow in either a randomized study or an observational study with confounders $\mathbf{X}$.

These conditions essentially state that values of the mediator under the treatment (control) condition act as if randomly assigned, within values of the pretreatment covariates $\mathbf{X}$. But this is not plausible in many contexts.

e.g. in the randomized encouragement study with time studied as mediator (Holland, 1988), condition $Y_i(z, m) \perp\!\!\!\perp M_i(z) \mid \mathbf{X}_i = \mathbf{x}$ states that the potential outcomes $Y_i(1, m)$ for encouraged subjects are independent of the amount of time actually studied given measured covariates.

But students who are not as bright and therefore have lower test scores might choose to study more than brighter students. It seems unlikely $Y_i(z, m) \perp\!\!\!\perp M_i(z) \mid \mathbf{X}_i = \mathbf{x}$ would hold without measuring additional covariates.

If the investigator measured additional covariates such as IQ, motivation, etc., such an assumption might be more credible. Especially if the time between the measurement of the covariates and the test score was relatively short.

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e.g. unemployed participants are assigned to a control group receiving no training or a treatment group in which job search skills (resume writing, presentation of self, information on where jobs are located) are taught. The mediator is a measure of job search activity. The outcome is employment status.

Given training status, might we expect job search activity to behave as if randomized? If so, there are no potentially confounding variables that affect both job search activity and employment status.

A potential confounder that comes to mind immediately is confidence. Confidence affects both the quality of job search and the likelihood of employment.

An investigator might try to measure confidence with a vector of covariates $\mathbf{X}$. But $\mathbf{X}$ includes only pre-treatment variables and pre-treatment confidence is likely to be changed by treatment.

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As the study is randomized, the investigator assumes

$$M_i(z), C_i(z), Y_i(z, m) \perp\!\!\!\perp Z_i,$$

and to take into account the post-treatment confounding by C_i, he/she assumes

$$Y_i(z, m) \perp\!\!\!\perp M_i(z) \mid C_i(z) = c.$$

Under these conditions, it is easy to see that

$$E(Y_i \mid Z_i = z, M_i = m, C_i = c) = E(Y_i(z, m) \mid C_i(z) = c)$$

Thus $E(Y_i \mid Z_i = 1, M_i = m, C_i = c) - E(Y_i \mid Z_i = 0, M_i = m, C_i = c) = E(Y_i(1, m) \mid C_i(1) = c) - E(Y_i(0, m) \mid C_i(0) = c)$ compares different groups of participants and is not a causal comparison.

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This illustrates that the conditions established to study mediation do not allow for post-treatment confounding. This suggests that mediation analyses relying on the assumptions above will often be of limited value in practice.

It is still important to make explicit the types of conditions upon which inferences about mediation depend and by developing sensitivity analyses which researchers can use to assess the impact of deviations from assumptions upon substantive conclusions.