eAppendix. Empirical Formulae for Controlled Direct Effects and Natural Direct and Indirect Effects.

If conditions (1) and (2) hold then, it follows from Robins' g-formula[25,26] that the average controlled direct effect is given by:

$$\begin{aligned}\mathbb{E}[Y_{az} - Y_{a^*z}] \;=\;& \sum_x \sum_w \mathbb{E}[Y|A=a, Z=z, X=x, W=w]P(W=w|A=a, X=x)P(X=x)\\ &- \sum_x \sum_w \mathbb{E}[Y|A=a^*, Z=z, X=x, W=w]P(W=w|A=a^*, X=x)P(X=x).\end{aligned}$$

Note that if $W = \varnothing$ so that the set of variables X that suffices to control for confounding for the treatment-outcome relationship also suffices to control for confounding for the mediator-outcome relationship then the above expression reduces to

$$\mathbb{E}[Y_{az} - Y_{a^*z}] = \sum_x \{\mathbb{E}[Y|X=x, A=a, Z=z] - \mathbb{E}[Y|X=x, A=a^*, Z=z]\}P(X=x).^{10}$$

For natural direct effects it follows from the work of Pearl[8] that if conditions (1)-(4) hold then $\mathbb{E}[Y_{aZ_{a^*}} - Y_{a^*Z_{a^*}}]$

$$\begin{aligned}=\;& \sum_{x,w} \sum_z \{\mathbb{E}[Y|A=a, Z=z, X=x, W=w]P(W=w|A=a, X=x)P(Z=z|A=a^*, X=x)P(X=x)\\ &- \sum_{x,w} \sum_z \mathbb{E}[Y|A=a^*, Z=z, X=x, W=w]P(W=w|A=a^*, X=x)\}P(Z=z|A=a^*, X=x)P(X=x).\end{aligned}$$

If $W = \varnothing$ then the above expression reduces to

$$\mathbb{E}[Y_{aZ_{a^*}} - Y_{a^*Z_{a^*}}] = \sum_x \sum_z \{\mathbb{E}[Y|A=a, Z=z, X=x] - \mathbb{E}[Y|A=a^*, Z=z, X=x]\}P(Z=z|A=a^*, X=x)P(X=x).$$

If conditions (1)-(4) hold natural indirect effects can be computed by subtracting natural direct effect from total effects. Also if (1)-(4) hold then $\mathbb{E}[Y_{aZ_a} - Y_{aZ_{a^*}}]$

$$\begin{aligned}=\;& \sum_{x,w} \sum_z \mathbb{E}[Y|A=a, X=x, Z=z, W=w]P(W=w|A=a, X=x)P(Z=z|A=a, X=x)P(X=x)\\ &- \sum_{x,w} \sum_z \mathbb{E}[Y|A=a, X=x, Z=z, W=w]P(W=w|A=a, X=x)P(Z=z|A=a^*, X=x)P(X=x).\end{aligned}$$

If $W = \varnothing$ then the above expression reduces to

$$\begin{aligned}\mathbb{E}[Y_{aZ_a} - Y_{aZ_{a^*}}] \;=\;& \sum_x \sum_z \mathbb{E}[Y|A=a, Z=z, X=x]P(Z=z|A=a, X=x)P(X=x)\\ &- \sum_x \sum_z \mathbb{E}[Y|A=a, X=x, Z=z]P(Z=z|A=a^*, X=x)P(X=x).\end{aligned}$$