Organic direct and indirect effects with post-treatment common causes of mediator and outcome

JUDITH J. LOK*

Department of Biostatistics,

Harvard School of Public Health,

655 Huntington Avenue,

Boston, MA 02115,USA

jlok@hsph.harvard.edu

October 12, 2015

Abstract

Most of the literature on direct and indirect effects assumes that there are no post-treatment common causes of the mediator and the outcome. In contrast to natural direct and indirect effects, organic direct and indirect effects, which were introduced in Lok (2015), can be extended to provide an identification result for the case where there are post-treatment mediator-outcome confounders. This article provides a definition and an identification result for organic direct and indirect effects in the presence of post-treatment common causes of mediator and outcome.

Causal inference, Direct and indirect effect, Mediation, Organic direct and indirect effect, Post-treatment common causes of mediator and outcome.

1 Introduction

Most of the literature on direct and indirect effects assumes that there are no post-treatment common causes of the mediator and the outcome. In contrast to natural

direct and indirect effects, organic direct and indirect effects, which were introduced in Lok (2013), can be extended to provide an identification result for the case where there are post-treatment mediator-outcome confounders. This article provides a definition as well as an identification result for organic direct and indirect effects in the presence of post-treatment common causes of mediator and outcome. This provides another alternative to the three quantities described in VanderWeele et al. (2014). Just as organic direct and indirect effects in the absence of post-treatment mediator outcome confounding, organic direct and indirect effects in the presence of post-treatment mediator outcome confounding do not require that the mediator can be set to any specific value. It suffices that there are "organic" interventions on the mediator that change its distribution.

2   Setting and notation

Denote treatment by A, the mediator by M, the outcome by Y, pre-treatment common causes of the mediator and the outcome by C, and post-treatment common causes of the mediator and the outcome by L. I further adopt the notation from Lok (2013), including I for interventions on the mediator. Assume treatment A is randomized. For the current setting, the DAG is shown in Figure 1.

Figure 1: DAG summarizing the data in the presence of a post-treatment common cause of mediator and outcome L
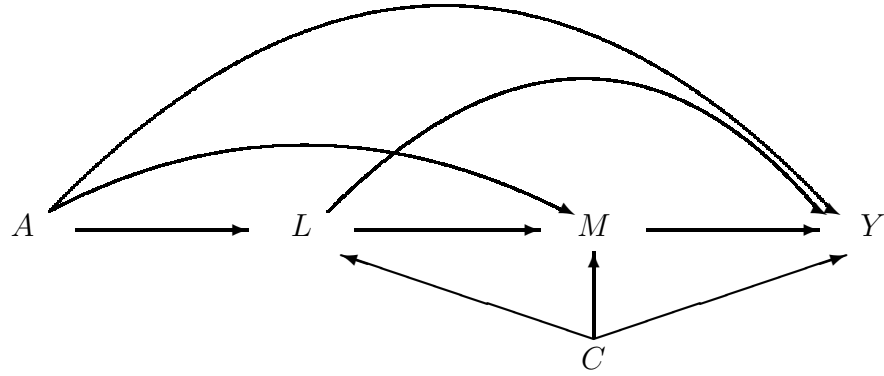
From the DAG notice that an intervention on the mediator may happen after L, because L is realized before the mediator. It is important to differentiate between interventions on M that happen before L and after L, because the distribution of L

under the intervention depends on when the intervention takes place. This article only considers organic interventions I on the mediator that happen after L.

3   Identifiability and estimation of organic direct and indirect effects with post-treat-ment common causes of mediator and outcome

If I happens after L, the value of L under the intervention and treatment equals the value of L_1. I define organic interventions in this setting as follows:

Definition 3.1 (Organic intervention in the presence of post-treatment common causes of mediator and outcome L). *An intervention I is an organic intervention if for all l, c,*

$$M_1^I|L_1 = l, C = c \sim M_0|L_0 = l, C = c \tag{1}$$

and

$$Y_1^I|M_1^I = m, L_1 = l, C = c \sim Y_1|M_1 = m, L_1 = l, C = c. \tag{2}$$

The idea behind mediation analysis is that under the intervention and treatment, M_1^I resembles M_0. Therefore, this article assumes that M_1^I depends on L and C in the same way as M_0, just as without L, this article assumes that M_1^I depends on C in the same way as M_0. Notice that without L, Definition 3.1 simplifies to Definition 4.1 from Lok (2013). Notice also that $M_1^I = M_0$ is no longer a special case of an organic intervention as defined in Definition 1.

Equation (2) means that given $C = c$ and $L_1 = l$, the prognosis under treatment of a unit "with $M_1^I = m$" is the same as the prognosis under treatment of a unit "with $M_1 = m$". In other words, given C and L_1, treated units with observed mediator equal to m are representative of treated units with $M_1^I = m$. Similar to Lok (2013), equation (2) can be relaxed to $E\left[Y_1^I|M_1^I = m, L_1 = l, C = c\right] = E\left[Y_1|M_1 = m, L_1 = l, C = c\right]$.

The consistency assumption is straightforward, but needs to include L:

Assumption 3.2 (Consistency). *If $A = 1$, then $L = L_1$, $M = M_1$ and $Y = Y_1$. If $A = 0$, then $L = L_0$, $M = M_0$ and $Y = Y_0$.*

The following identification result holds:

Theorem 3.3 (Organic direct and indirect effects: identification in the presence of post-treatment common causes of mediator and outcome.) *Under randomized treatment, consistency assumption 3.2 and definition of organic interventions 3.1, $E\left(Y_1^I\right)$, for an organic intervention I, is equal to*

$$\int_{(c,l,m)} E\left[Y|M=m, L=l, C=c, A=1\right] f_{M|L=l,C=c,A=0}(m) f_{L|C=c,A=1}(l) f_C(c) dm \, dl \, dc.$$

All objects on the right hand side of the equation in Theorem 3.3 depend on observables only and can be fitted using standard methods. Inference can be done along the lines of Section 6 of Lok (2013), see Section 4 below.

Proof of theorem 3.3

$$E\left(Y_1^I\right) = E\left(E\left[Y_1^I|M_1^I, L_1, C\right]\right)$$

$$= \int_{(c,l,m)} E\left[Y_1^I|M_1^I=m, L_1=l, C=c\right] f_{M_1^I|L_1=l,C=c}(m) dm \, f_{L_1|C=c}(l) dl \, f_C(c) dc$$

$$= \int_{(c,l,m)} E\left[Y_1|M_1=m, L_1=l, C=c\right] f_{M_0|L_0=l,C=c}(m) dm \, f_{L_1|C=c}(l) dl \, f_C(c) dc$$

$$= \int_{(c,l,m)} E\left[Y_1|M_1=m, L_1=l, C=c, A=1\right] f_{M_0|L_0=l,C=c,A=0}(m) dm f_{L_1|C=c,A=1}(l) dl f_C(c) dc$$

$$= \int_{(c,l,m)} E\left[Y|M=m, L=l, C=c, A=1\right] f_{M|L=l,C=c,A=0}(m) dm \, f_{L|C=c,A=1}(l) dl \, f_C(c) dc.$$

In this proof, the first two equalities follow from the definition of conditional expectation. The third equality follows from equations (2) and (1). The fourth equality follows from the fact that treatment was randomized; this implies that

$$A \per\!\!\!\perp (Y_1, M_1, L_1) \, | C \qquad \text{and} \qquad A \per\!\!\!\perp (M_0, L_0) \, | C.$$

The last equality follows from assumption 3.2. □

4   Organic direct and indirect effects with post-treatment common causes of mediator and outcome: inference

In the presence of post-treatment common causes L of the mediator and the outcome, inference can be done based on Section 3, Theorem 3.3. For example,

suppose that

$$M_1 \sim M_0 + \beta_1 + \beta_4 C + \beta_5 L | C, L \tag{3}$$

with $\beta_1 \in \mathbb{R}$, $\beta_4 \in \mathbb{R}^k$, and would be the case if, for example,

$$M = \beta_0 + \beta_1 A + \beta_2 C + \beta_3 L + \beta_4 AC + \beta_5 AL + \beta_6 CL + \epsilon,$$

where the random variable ϵ has the same distribution given (C, L) under treatment as without treatment, and with $\beta_0, \beta_1 \in \mathbb{R}$, $\beta_2, \beta_4 \in \mathbb{R}^k$, $\beta_3, \beta_5 \in \mathbb{R}^l$, and $\beta_6 \in \mathbb{R}^p$. Suppose in addition that the expected value of Y given M, L, and C under treatment follows some parametric model of the form

$$E[Y|M = m, L = l, C = c, A = 1] = f_\theta(m, l, c). \tag{4}$$

Then, Theorem 3.3 implies that

$$
\begin{aligned}
E&\left(Y^I_{1,M^I_1}\right) \\
&= \int_{(m,l,c)} E[Y|M = m, L = l, C = c, A = 1]\, f_{M|L=l,C=c,A=0}(m) f_{L|C=c,A=1}(l) f_C(c)\, dm\, dl\, dc \\
&= \int_{(c,l,m)} f_\theta(m, l, c) f_{M|L=l,C=c,A=1}(m + \beta_1 + \beta_4 c + \beta_5 l) f_{L|C=c,A=1}(l) f_C(c)\, dm\, dl\, dc \\
&= \int_{(c,l,\tilde{m})} f_\theta(\tilde{m} - \beta_1 - \beta_4 c - \beta_5 l, l, c) f_{M|L=l,C=c,A=1}(\tilde{m}) f_{L|C=c,A=1}(l) f_C(c)\, d\tilde{m}\, dl\, dc \\
&= E[f_\theta(M - \beta_1 - \beta_4 C - \beta_5 L, L, C)|A = 1], \tag{5}
\end{aligned}
$$

just as in Section 6 of Lok (2013). Expression (5) can be estimated by fitting models (3) and (4) above using standard methods, plugging the parameter estimates in (5), and replacing the expectation given $A = 1$ by its empirical average. Standard errors can be estimated using the bootstrap.

References

Lok, J. J. (2013). Defining and estimating causal direct and indirect effects: an intervention based approach. Technical report. Submitted to Biometrika.

VanderWeele, T. J., S. Vansteelandt, and J. M. Robins (2014). Effect decomposition in the presence of an exposure-induced mediator-outcome confounder. *Epidemiology 25*(2), 300–306.