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Interpretation and Identification of Causal Mediation

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This article reviews the foundations of causal mediation analysis and offers a general and transparent account of the conditions necessary for the identification of natural direct and indirect effects, thus facilitating a more informed judgment of the plausibility of these conditions in specific applications. I show that the conditions usually cited in the literature are overly restrictive and can be relaxed substantially without compromising identification. In particular, I show that natural effects can be identified by methods that go beyond standard adjustment for confounders, applicable to observational studies in which treatment assignment remains confounded with the mediator or with the outcome. These identification conditions can be validated algorithmically from the diagrammatic description of one's model and are guaranteed to produce unbiased results whenever the description is correct. The identification conditions can be further relaxed in parametric models, possibly including interactions, and permit one to compare the relative importance of several pathways, mediated by interdependent variables.

Keywords: mediation formula, identification, confounding, graphical models

Mediation analysis aims to uncover causal pathways along which changes are transmitted from causes to effects. Interest in mediation analysis stems from both scientific and practical considerations. Scientifically, mediation tells us how nature works, and practically, it enables us to predict behavior under a rich variety of conditions and policy interventions. For example, in coping with the age-old problem of gender discrimination (Bickel, Hammel, & O'Connell, 1975; Goldberger, 1984), a policymaker may be interested in assessing the extent to which gender disparity in hiring can be reduced by making hiring decisions gender-blind, compared with eliminating gender inequality in education or job qualifications. The former concerns the *direct effect* of gender on hiring, while the latter concerns the *indirect effect* or the effect *mediated* via job qualification.

The example illustrates two essential ingredients of modern mediation analysis. First, the indirect effect is not merely a modeling artifact formed by suggestive combinations of parameters but an intrinsic property of reality that has tangible policy implications. In this example, reducing employers' prejudices and launching educational reforms are two contending policy options that involve costly investments and different implementation efforts. Knowing in advance which of the two, if successful, has a greater impact on reducing hiring disparity is essential for planning and depends critically on mediation analysis for resolution. Second, the policy decisions in this example concern the enabling and disabling of processes (hiring vs. education) rather than lowering or raising values of specific variables. These two considerations lead to the analysis of natural direct and indirect effects.

Mediation analysis has its roots in the literature of structural equation models (SEMs), going back to Wright's (1923, 1934) method of path analysis and continuing in the social sciences from the 1960s to 1980s through the works of Baron and Kenny (1986), Bollen (1989), Duncan (1975), and Fox (1980). The bulk of this work was carried out in the context of linear models, in which effect sizes are represented as sums and products of structural coefficients. The definition, identification, and estimation of these coefficients required a commitment to a particular parametric and distributional model and fell short of providing a general, causally defensible measure of mediation (Glynn, 2012; Hayes, 2009; Kraemer, Kiernan, Essex, & Kupfer, 2008; MacKinnon, 2008).

This has changed in the past 2 decades. Counterfactual thinking in statistics (Holland, 1988; Rubin, 1974) and epidemiology (Robins & Greenland, 1992), together with a formal semantics based on nonparametric structural equations (Balke & Pearl, 1995; Halpern, 1998; Pearl, 2001), has given causal mediation analysis a sound theoretical basis and extended its scope from linear to nonlinear models. The definitions of direct and indirect effects that emerge from this graphical-counterfactual symbiosis (summarized in the Natural Direct and Indirect Effects section, below) require no commitment to functional or distributional forms and are therefore applicable to models with arbitrary nonlinear interactions, arbitrary dependencies among the random variables, and both continuous and categorical variables.

This article concerns the conditions under which direct and indirect effects can be estimated from observational studies. In particular, I focus on the *natural* mediated effect, which is defined (roughly) as the expected change in the output when one lets the mediator change *as if* the input did (see the Natural Direct and

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Indirect Effects section, below, for formal definition). This counterfactual entity, which has engendered the transition from linear to nonlinear models, cannot, in general, be estimated from controlled experiments, even when it is feasible to randomize both the treatment and the mediating variables.[1] This limitation, noted by Robins and Greenland in 1992, resulted in 9 years of abandonment, during which natural effects were considered void of empirical content and were not investigated (S. Kaufman, Kaufman, & MacLenose, 2009).

Interest in natural effects rekindled when identification conditions were uncovered that circumvented this limitation, mediation formulas were derived, and the role of natural effects in policy making was made explicit (Pearl, 2001). While the identification conditions relied on untestable assumptions, those assumptions were conceptually meaningful and not substantially different from standard requirements of *no confounding* or *no common causes* that are made routinely in causal analysis.[2]

These developments, coupled with the capability of expressing and visualizing causal assumptions in graphical forms, have given rise to an explosion of mediation studies that have taken natural effects as the gold standard for analysis (e.g., Albert & Nelson, 2011; Coffman & Zhong, 2012; Hafeman & Schwartz, 2009; Huber, 2012; Imai, Keele, Tingley, & Yamamoto, 2011; Imai, Keele, & Yamamoto, 2010; Jo, Stuart, MacKinnon, & Vinokur, 2011; Joffe, Small, & Hsu, 2007; J. Kaufman, 2010; Mortensen, Diderichsen, Smith, & Andersen, 2009; Petersen, Sinisi, & van der Laan, 2006; Richiardi, Bellocco, & Zugna, 2013; Robins, 2003; Sobel, 2008; Ten Have, Elliott, Joffe, Zanutto, & Datto, 2004; Valeri & VanderWeele, 2013; VanderWeele & Vansteelandt, 2009; Vansteelandt, Bekaert, & Lange, 2012). These studies have also adopted the mediation formulas of natural effects as targets for estimation and as benchmarks for sensitivity analysis (Imai, Keele, & Yamamoto, 2010; Sjölander, 2009).

However, although the identification conditions invoked in current mediation analysis are based on the same formal principles (see Appendix B),[3] the articulation of these conditions in common scientific terms becomes highly varied and unreliable, making it hard for researchers to judge their plausibility in any given application. This stems from the difficulty of discerning conditional independencies among counterfactual variables, which must be undertaken by rank-and-file researchers whenever natural effects need be identified (Imai, Keele, & Yamamoto, 2010; Pearl, 2001; Petersen et al., 2006; Robins, 2003; VanderWeele & Vansteelandt, 2009). The verification of such independencies, often called *strong ignorability*, *conditional ignorability*, or *sequential ignorability*, presents a formidable judgmental task to most researchers if unaided by structural models (Joffe, Yang, & Feldman, 2010).

Recently, efforts have been made to interpret these conditions in more conceptually meaningful way, so as to enable researchers to judge whether the necessary assumptions are scientifically plausible (Coffman & Zhong, 2012; Imai, Jo, & Stuart, 2011; Imai, Keele, & Tingley, 2010; Muthén, 2011; Richiardi et al., 2013; Valeri & VanderWeele, 2013; VanderWeele, 2009). Invariably, these efforts strive to replace *ignorability* vocabulary with notions such as *no unmeasured confounders*, *no unmeasured confounding*, *as if randomized*, *effectively randomly assigned*, or *essentially random*, which are clearly more meaningful to empirical researchers.

Unfortunately, these interpretations are marred by two sources of ambiguity. First, the notion of a confounder varies significantly from author to author. Some define a confounder (say, of X and Y) as a variable that affects both X and Y. Some define a confounder as a variable that is associated with both X and Y. Others allow for a confounder to affect X and be associated with Y. Worse yet, the expression *no unmeasured confounders* is sometimes used to exclude the very existence of such confounders and sometimes to affirm our ability to neutralize them by controlling other variables, not necessarily confounders. Second, the interpretations have taken sequential ignorability as a starting point and consequently are overly stringent—sequential ignorability is a sufficient but not necessary condition for identifying natural effects. Weaker conditions can be articulated in a transparent and unambiguous language providing a greater identification power and a greater conceptual clarity.

A typical example of overly stringent conditions that can be found in the literature reads as follows:

> The sequential ignorability assumption must be satisfied in order to identify the average mediation effects. This key assumption implies that the treatment assignment is essentially random after adjusting for observed pretreatment covariates and that the assignment of mediator values is also essentially random once both observed treatment and the same set of observed pretreatment covariates are adjusted for. (Imai, Jo, & Stuart, 2011, pp. 863–864)[4]

I show that milder conditions are sufficient for identification. First, there is no need to require that covariates be pretreatment, as long as they are causally unaffected by the treatment. Second, the treatment assignment need not be random under any adjustment; identification can be achieved with treatment assignment remaining highly confounded under every set of observed covariates. Finally, one need not insist on using "the same set of observed pretreatment covariates"; two or three different sets can sometimes accomplish what the same set cannot.

On the other extreme, there is also a tendency among researchers to treat the necessary adjustments as totally independent of each other. A common misconception presumes that control of confounding between the treatment and the mediator can be accomplished independently of how one controls confounding between the mediator and the outcome. I show this not be the case;

[1] This is because there is no way to rerun history and measure each subject's response under conditions he or she has not actually experienced.

[2] Discussion about the philosophical and practical implications of this limitation can be found in Pearl (2009b, pp. 35, 391) and Robins and Richardson (2011). The rest of the article assumes that the investigator is in possession of scientific knowledge to judge the plausibility of *no confounding* type of assumptions that underlie all current research on mediation whether under the rubric of *sequential ignorability* (e.g., Imai, Keele, & Yamamoto, 2010) or *uncorrelated error terms.*

[3] Imai, Keele, and Yamamoto (2010) and Imai, Keele, Tingley, and Yamamoto (2011) discussed similarities and differences among several versions of the identifying assumptions, and Shpitser and VanderWeele (2011) delineated the context under which a restricted version of the conditions established in Pearl (2001) coincide with those established in Imai, Keele, and Yamamoto.

[4] A formal description of this and other identification strategies can be found in Imai, Keele, and Tingley (2010, Section 3.3) and Imai, Keele, Tingley, and Yamamota (2011); the latter supplements the description with graphs to facilitate communication.

adjusting for mediator-outcome confounders may constrain the choices of covariates admissible for the treatment-mediator adjustment.

The main purpose of this article is to offer a concise list of conditions that are sufficient for identifying the natural direct effect (the same holds for the indirect effect) and are milder than those articulated in the mainstream literature (Coffman & Zhong, 2012; Imai, Keele, & Tingley, 2010; Valeri & VanderWeele, 2013) yet still expressible in familiar and precise terms. With the help of these conditions, I extend mediation analysis to models in which standard control for confounders is infeasible, including models using auxiliary, treatment-dependent covariates and models with multiple mediators.

A second and perhaps equally important aim of this article is to present readers with a methodology that frees investigators from the need to understand, articulate, examine, and judge the plausibility of the assumptions needed for identification. Instead, the method can confirm or disconfirm these assumptions algorithmically from a deeper set of assumptions, as encoded in the structural or data-generating model itself. I show through examples that standard causal diagrams, no different from those invoked in conventional SEM studies, allow simple path-tracing routines to replace much of the human judgment deemed necessary in mediation analysis; the judgment invoked in the construction of the diagrams is sufficient.

The Structural Approach to Mediation

In this section, I introduce mediation analysis from the perspective of nonparametric SEMs.[5] This approach integrates the potential outcome framework of Splawa-Neyman (1923/1990) and Rubin (1974) with that of SEM, thus combining mathematical rigor with the merits of staying intimately informed by the data-generating process or its graphical representation.

Mediation Analysis in the Parametric Tradition

Figure 1 depicts the basic mediation structure that I later embed in wider contexts. It consists of three random variables: *T*, often called *treatment*; *Y*, the *outcome*; and *M*, the *mediator*, whose role in transmitting the effect of *T* on *Y* I wish to assess. As a running example, one could imagine an *encouragement design* (Holland, 1988) where *T* stands for a type of educational program that a student receives, *M* stands for the amount of homework a student does, and *Y* stands for a student's score on the exam. In the linear case (see Figure 1a), the causal relationships in this example would be modeled in three linear equations:

$$t = u_T, \qquad m = \alpha t + u_M, \qquad y = \beta t + \gamma m + u_Y, \tag{1}$$

where lowercase symbols (*t*, *m*, *y*) represent the values that the variables (*T*, *M*, *Y*) may take and U_T, U_M, and U_Y stand for omitted factors that explain variations in *T*, *M*, and *Y*. The coefficients α, β, and γ represent the structural parameters that need to be estimated from the data and that define the direct (β), indirect (αγ) and total ($\tau = \beta + \alpha\gamma$) effects of *T* on *Y*.

As structural parameters, α, β, and γ are causal quantities whose meaning is independent of the methods used in their estimation. γ, for example, stands for the increase in a student's score (*Y*) per unit increase in study time (*M*), keeping all other factors (*T* and U_Y) constant. This unit-based, ceteris paribus definition of structural parameters may lend itself to experimental verification when certain conditions hold. The assumption of linearity, for example, renders structural coefficients constant across individuals and permits one to estimate them by controlled experiments at the population level. One can imagine, for example, an investigator going to a district where *T* is not available, recruiting interested students (and their parents) and then randomly assigning $T = 1$ to some and $T = 0$ to others, and estimating α through the difference in the mean of *M* between the two experimental groups, which we write as $E[M \mid do(T = 1)] - E[M \mid do(T = 0)]$.[6] At the same experiment, the investigator can also measure students' scores, *Y*, and estimate the total effect

$$\tau = E[Y \mid do(T = 1)] - E[Y \mid do(T = 0)] = \beta + \alpha\gamma.$$

To estimate γ would require a more elaborate experiment in which both *T* and *M* are simultaneously randomized, thus deconfounding all three relationships in the model and permitting an unbiased estimate of γ:

$$\gamma = E[Y \mid do(T = 0), do(M + 1)] - E[Y \mid do(T = 0), do(M)].$$

The latter can also be estimated in an encouragement design where *M* is controlled not directly but through a randomized incentive for homework. However, most traditional work on mediation focused on nonexperimental estimation, treating the structural equations in Equation 1 as regression equations, assuming that each *U* term is uncorrelated with the predictors in the same equation.

The regression analysis of mediation, most notably the one advanced by Baron and Kenny (1986), can be stated as follows: To test the contribution of a given mediator *M* to the effect of *T* on *Y*, first regress *Y* on *T*, and estimate the regression coefficient R_{YT}, to be equated with the *total effect* τ. Second, include *M* in the regression, and estimate the partial regression coefficient $R_{YT \cdot M}$

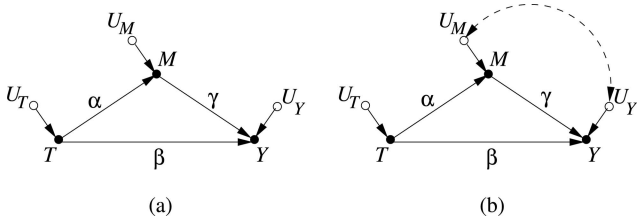

Figure 1. a: The basic (unconfounded) mediation model. b: A confounded version of a, showing correlation between U_M and U_Y. Solid bullets represent observed variables; hollow circles represent unobserved (or latent) variables. *M* = mediator; *T* = treatment; *U* = omitted factors; *Y* = outcome; α, β, γ = structural coefficients.

[5] Readers familiar with nonparametric SEM as introduced in Pearl (2009b, 2010b, 2012a), Petersen et al. (2006), and VanderWeele (2009) may go directly to the Interpretable Conditions for Identification section.

[6] It is of utmost importance to emphasize that the mean difference between treatment and control groups in the experiment is not equal to the difference $E[M \mid X = 1] - E[M \mid X = 0]$, which would obtain where *T* is available to students as an optional service. The two will differ substantially when *X* and *M* are confounded as, for example, when students who are highly motivated for self-study (*M*) are more likely to choose the treatment option. The *do*-operator was devised to make this distinction formal (Pearl, 1993).

when M is controlled for (or conditioned on or adjusted for). The difference between the two slopes, $R_{YT} - R_{YT \cdot M}$, would then measure the reduction in the total effect due to controlling for M and should quantify the effect mediated through M.

The rationale behind this estimation scheme follows from Figure 1a. If the total effect of T on Y through both pathways is $\tau = \beta + \alpha\gamma$, by adjusting for M, one severs the M-mediated path, and the effect is reduced to β. The difference between the two regression slopes gives the indirect, or mediated effect

$$\tau - \beta = \alpha\gamma. \quad (2)$$

Alternatively, one can venture to estimate α and γ independently of τ. This is done by first estimating the regression slope of M on T to get α, then estimating the regression slope of Y on M controlling for T, which gives us γ; multiplying the two slopes together gives us the mediated effect $\alpha\gamma$.

The validity of these two estimation methods depends of course on the assumption that the error terms, U_T, U_M, and U_Y, are uncorrelated. Otherwise, some of the structural parameters might not be estimable by simple regression, and both the difference-in-coefficients and product-of-coefficients methods will produce biased results. In randomized trials, where U_T can be identified with the randomized treatment assignment, we are assured that U_T is uncorrelated with both U_M and U_Y, so the regressional estimates of τ and α will be unbiased. However, randomization does not remove correlations between U_M and U_Y. If such correlation exists (as depicted in Figure 1b), adjusting for M will create spurious correlation between T and Y, which will prevent the proper estimate of γ or β. In other words, the regression coefficient $R_{YZ \cdot X}$ will no longer equal γ, and the difference $R_{YX} - R_{MX}R_{YM \cdot X}$ will no longer equal β. This follows from the fact that controlling or adjusting for M in the analysis (by including M in the regression equation) does not physically disable the paths going through M; it merely matches samples with equal M values and thus induces spurious correlations among other factors in the analysis (see Bullock, Green, & Ha, 2010; Cole & Hernán, 2002; Pearl, 1998; VanderWeele & Vansteelandt, 2009).[7] Such correlations cannot be detected by statistical means, so theoretical knowledge must be invoked to identify the sources of these correlations and control for common causes (so called "confounders") of M and Y whenever they are observable.[8]

This approach to mediation has two major drawbacks. One (mentioned above) is its reliance on the untested assumption of uncorrelated errors, and the second is its reliance on linearity and, in particular, on a property of linear systems called *effect constancy* (or *no interaction*): The effect of one variable on another is independent of the level at which we hold a third. This property does not extend to nonlinear systems; in such systems, the level at which we control M would in general modify the effect of T on Y. For example, if the output Y requires both T and M to be present, then holding M at zero would disable the effect of T on Y, while holding M at a high value would enable the latter.

As a consequence, additions and multiplications are not self-evident in nonlinear systems. It may not be appropriate, for example, to define the indirect effect in terms of the difference in the total effect, with and without control. Nor would it be appropriate to multiply the effect of T on M by that of M on Y (keeping X at some level)—multiplicative compositions demand their justifications. Indeed, all attempts to define mediation by generalizing the difference and product strategies to nonlinear system have resulted in distorted and irreconcilable results (Glynn, 2012; MacKinnon, Fairchild, & Fritz, 2007; MacKinnon, Lockwood, Brown, Wang, & Hoffman, 2007; Pearl, 2012b).

The next section removes these nonlinear barriers by defining *effect* as a counterfactual notion, independent of any statistical or parametric manifestation, thus availing mediation analysis to a broad spectrum of new applications, primarily those involving categorical data and highly nonlinear processes. The first limitation, the requirement of error independence (or *no unmeasured confounders*, as it is often called) is also relaxed, since the new definition opens new ways of overcoming correlations among the U terms.

Causes and Counterfactuals in Nonparametric Structural Models

In the most general case, the structural mediation model will have the form of Figure 2b:

$$t = f_T(u_T), \qquad m = f_M(t, u_M), \qquad y = f_Y(t, m, u_Y), \quad (3)$$

where T, M, Y are discrete or continuous random variables, f_T, f_M, and f_Y are arbitrary functions, and U_T, U_M, and U_Y represent, respectively, omitted factors that influence T, M, and Y but are not influenced by them. In our example, U_M represents all factors that explain variations in study time (M) among students at the same treatment (T). The triplet $U = (U_T, U_M, U_Y)$ is a random vector that accounts for all variations between individual students. It is sometimes called *unit*, for it offers a complete characterization of a subject's behavior as reflected in T, M, and Y. The distribution of U, denoted $P(U = u)$, uniquely determines the distribution $P(t, m, y)$ of the observed variables through the three functions in Equation 3.

In Figure 2a, the omitted factors are assumed to be arbitrarily distributed but mutually independent, written $U_T \perp\!\!\!\perp U_M \perp\!\!\!\perp U_Y$. In Figure 2b, the dashed arcs connecting U_T and U_M (as well as U_M and U_T) encode the understanding that the factors in question may be dependent. Figure 2c is a shorthand notation for Figure 2b. Here, the U factors are not shown explicitly, and their dependencies are encoded in the form of dashed arcs going directly to the affected variables.

Referring to the student-encouragement example, it is not hard to imagine sources of possible dependencies among the omitted factors. For example, if U_Y includes student's intelligence and the amount of time studied varies systematically with intelligence, U_M and U_Y will be dependent, as shown in the model of Figure 2b. Likewise, if U_T includes the propensity of students to enter the program (T) and this propensity depends on whether students have adequate conditions for

[7] This can be readily shown using classical path-tracing rules (Pearl, 2013); if U_M and U_Y are correlated, the regression coefficient $R_{YX \cdot Z}$ will not equal γ. Remarkably, the regressional estimates of the difference in coefficients and the product of coefficients will always be equal.

[8] Although Judd and Kenny (1981) recognized the importance of controlling for mediator-output confounders, the point was not mentioned in the influential article of Baron and Kenny (1986), and as a result, it has been ignored by most researchers in the social and psychological sciences (Judd & Kenny, 2010).

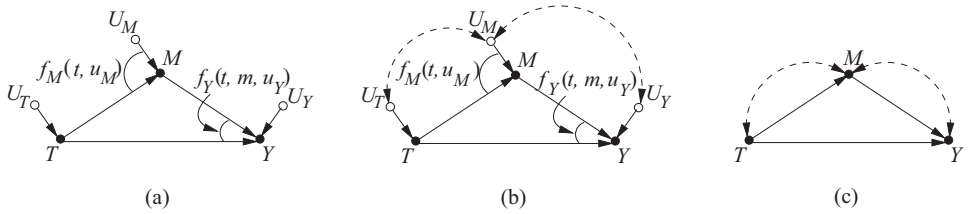

Figure 2. a: The basic nonparametric mediation model. b: A confounded mediation model in which dependence exists between U_M and (U_T, U_Y). c: A shorthand notation for b. M = mediator; T = treatment; U = omitted factors; Y = outcome; f = structural function; t = value of T; u = value of U; m = value of M.

home studies (U_M), then an arc between U_T and U_M is needed to encode their dependence (see Figure 2b). In general, as soon as one associates a diagram to a research context, interesting issues arise of possible associations among measured and unmeasured variables. Some can be decided by scientific considerations, and some may be debated by experts in the field. The purpose of the diagram is to provide an unambiguous description of the scientific context of a given application. While the application itself is usually shrouded in ambiguities and disagreements, the diagram represents a hypothetical consensus on what is plausible and important versus that which is deemed negligible or implausible.

In this article, I emphasize the use of diagrams as faithful conveyers of the scientific context in any given application, with the understanding that the actual causal story behind the context may vary from problem to problem and that questions regarding the statistical and counterfactual implications of the diagrams can be answered mechanically by simple path-tracing routines.[9] Notably, a model like that shown in Figure 2c allows for the existence of millions of unobserved subprocesses that make up the functions f_T, f_M, and f_Y; these do not alter questions concerning the mediating role of M.

Since every SEM can be translated into an equivalent counterfactual (or potential outcome) model (Pearl, 2009b, Definition 7.1.5), we can give the mediation model of Equation 3 a counterfactual interpretation as follows. Define the counterfactual variables M_t, Y_t, and $Y_{t,m}$ by

$$M_t = f_M(t,\ U), \qquad Y_t = f_Y(t,\ M_t,\ U), \qquad Y_{t,m} = f_Y(t,\ m,\ U), \tag{4}$$

where $U = (U_T, U_M, U_Y)$ is the random variable representing all omitted factors. In other words, the counterfactual variable M_t stands for the value that M would take when we set the subscripted variable T to a constant t and allow the other variables in the equation (i.e., U) to vary. Similarly, $Y_{t,m}$ stands for the value that Y would take when we set the subscripted variables T and M to constants, t and m, and allow U to vary. Accordingly, the independence assumption $U_T \perp\!\!\!\perp (U_M, U_Y)$ depicted in Figures 1b and 2a can be given a counterfactual form (called *treatment ignorability*):

$$T \perp\!\!\!\perp (M_t,\ Y_{t',m}) \quad \text{for all } t \text{ and } t',^{10} \tag{5}$$

while $(U_T, U_M) \perp\!\!\!\perp U_Y$ (depicted in Figure 2a) conveys the independence:

$$(T, M_t) \perp\!\!\!\perp Y_{t',m} \quad \text{for all } t \text{ and } t'. \tag{6}$$

This translation from independence of omitted factors into independence of counterfactuals reflects the fact that the statistical variations of $Y_{t,m}$ are caused solely by variations in U_Y, since t and m are constants, and similarly, variations of M_t are caused solely by those of U_M.

Since the functions f_T, f_M, and f_Y are unknown to investigators, mediation analysis commences by first defining total, direct, and indirect effects in terms of those functions and then asking whether they can be expressed in terms of the available data, which we assume are given in the form of random samples (t, m, y) drawn from the joint probability distribution $P(t, m, y)$. Whenever such a translation is feasible, we say that the respective effect is *identifiable*.

Natural Direct and Indirect Effects

Using the structural model of Equation 3, four types of effects can be defined for the transition from $T = 0$ to $T = 1$.[11]

Total effect (*TE*).

$$\begin{aligned} TE &= E\{f_Y[1, f_M(1, u_M), u_Y] - f_Y[0, f_M(0, u_M), u_Y]\} \\ &= E[Y_1 - Y_0] \\ &= E[Y|do(T = 1)] - E[Y|do(T = 0)]. \end{aligned} \tag{7}$$

TE measures the expected increase in the outcome Y as the treatment changes from $T = 0$ to $T = 1$, while the mediator is allowed to track the change in T as dictated by the function f_M.

Controlled direct effect (*CDE*).

$$\begin{aligned} CDE(m) &= E\{f_Y[1, M = m, u_Y] - f_Y[0, M = m, u_Y]\} \\ &= E[Y_{1,m} - Y_{0,m}] \\ &= E[Y|do(T = 1, M = m)] - E[Y|do(T = 0, M = m)]. \end{aligned} \tag{8}$$

[9] Readers who wish to read the statistical dependencies that a given context entails are advised to do so through the tool of *d*-separation (gently introduced in Appendix A), but this is not absolutely necessary, since *d*-separation and other graph-based techniques are mechanized on several available software programs (e.g., Kyono, 2010; Textor, Hardt, & Knüppel, 2011).

[10] Assumption $U_T \perp\!\!\!\perp U_M$ is in fact stronger than $T \perp\!\!\!\perp M_t$ and implies $T \perp\!\!\!\perp (M_{t_1}, M_{t_2}, \ldots, M_{t_n})$ where $\{t_1, t_2, \ldots, t_n\}$ are the values of T (Pearl, 2009b, p. 101). To keep the notation simple, I use a single generic subscript (e.g., t) to convey joint counterfactual independencies.

[11] Generalizations to arbitrary reference point, say, from $T = t$ to $T = t'$, are straightforward. These definitions apply at the population levels; the unit-level effects are given by the expressions under the expectation. All expectations are taken over the factors U_M and U_Y.

CDE measures the expected increase in the outcome Y as the treatment changes from $T = 0$ to $T = 1$, while the mediator is set to a prespecified level $M = m$ uniformly over the entire population.

Natural direct effect (*NDE*).

$$NDE = E\{f_Y[1, f_M(0, u_M), u_Y] - f_Y[0, f_M(0, u_M), u_Y]\} = E[Y_{1,M_0} - Y_{0,M_0}]. \quad (9)$$

NDE measures the expected increase in Y as the treatment changes from $T = 0$ to $T = 1$, while setting the mediator variable to whatever value it *would have attained* (for each individual) prior to the change, that is, under $T = 0$.

Natural indirect effect (*NIE*).

$$NIE = E\{f_Y[0, f_M(1, u_M), u_Y] - f_Y[0, f_M(0, u_M), u_Y]\} = E[Y_{0,M_1} - Y_{0,M_0}]. \quad (10)$$

NIE measures the expected increase in Y when the treatment is held constant, at $T = 0$, and M changes to whatever value it would have attained (for each individual) under $T = 1$.

Semantically, *NDE* measures the portion of the total effect that would be transmitted to Y absent M's ability to respond to T, while *NIE* measures the portion transmitted absent Y's ability to respond to changes in T, except those transmitted through M. The difference $TE - NDE$ quantifies the extent to which the response of Y is *owed* to mediation, while *NIE* quantifies the extent to which it is *explained* by mediation. These two components of mediation, the *necessary* and the *sufficient*, coincide into one in models void of interactions (e.g., linear) but differ substantially under moderation (see the Numerical Example section, below).

We remark that a controlled version of *NIE* does not exist because there is no way of disabling the direct effect of T on Y by setting a variable to a constant. Note also that the natural effects, *NDE* and *NIE*, are not accompanied by *do*-expressions because these effects are defined counterfactually and cannot be estimated from controlled experiments. The choice of the appropriate effect type in policy making is discussed in Pearl (2001, 2011), Robins and Richardson (2011), and VanderWeele (2009) and are illustrated in the Illustrations section, below. Whereas the controlled direct effect is of interest when policy options exert control over values of *variables* (e.g., raising the level of a substance in patients' blood to a prespecified concentration), the natural direct effect is of interest when policy options enhance or weaken *mechanisms* or *processes* (e.g., freezing a substance at its current level of concentration [for each patient], but preventing it from responding to a given stimulus).

This is an appropriate point to relate the definitions of natural effects to the standard definitions of direct and indirect effects used in parametric structural equation. When we apply the definitions above to the linear system of Equation 1, we readily obtain the expected results:

$$TE = \beta + \alpha\gamma, \quad NDE = CDE(m) = \beta, \quad NIE = \alpha\gamma. \quad (11)$$

A key conceptual difference between the causal and the traditional approaches is that, in the former, every effect is defined a priori, in a way that makes it applicable to any model, including confounded, unidentified, or nonlinear models. The statistical approach, on the other hand, requires that the model satisfies certain restrictions before the definition (of effects) obtains its legitimacy. This is somewhat paradoxical, for one must know what one seeks to estimate before imposing the appropriate restrictions on the model.

The equalities in Equation 10, for example, are derived from the basic definitions of Equations 6–9 and the linearity of Equation 1; they are sustained therefore in all linear systems, even when one does not make the assumption of *no omitted variables* (or *ignorability*). Likewise, the constancy of the controlled direct effect in linear system, $CDE(m) = \alpha$, is not an assumption but a consequence of how $CDE(m)$ is defined (see Equation 8).

In the classical approach, on the other hand, the assumption of no omitted variables must precede all definitions (Judd & Kenny, 1981, 2010) because the classical vocabulary was restricted to the statistical notion of *controlling for M* instead of the intended causal notion of *setting M to a constant*, and the two coincide only under the *no omitted variables* assumption.[12] (See Bollen & Pearl, 2013, for further discussion of this important observation, which is often overlooked in the potential-outcome literature; e.g., Rubin, 2010; Sobel, 2008.)

Finally, note that, in general, the total effect can be decomposed as

$$TE = NDE - NIE_r, \quad (12)$$

where NIE_r stands for the natural indirect effect under the reverse transition, from $T = 1$ to $T = 0$. This implies that *NIE* is identifiable whenever *NDE* and *TE* are identifiable. In linear systems, where reversal of transitions amounts to negating the signs of their effects, one has the standard additive formula, $TE = NDE + NIE$. Moreover, since each term in Equation 12 is based on an independent operational definition, this equality constitutes a formal justification for the additive formula taken for granted in linear systems.[13]

The Counterfactual Derivation of Natural Effects

To make this article self-contained, Appendix B provides a formal proof of the conditions for direct effect identification, as it appeared in Pearl (2001). It starts with the counterfactual definition of the natural direct effect and then goes through three steps. First, it seeks a set of covariates W that reduces nested counterfactuals to simple counterfactuals. Second, it reduces all counterfactuals to *do*-expressions, that is, expressions that are estimable from controlled randomized experiments. Finally, it poses conditions for identifying the *do*-expressions from observational studies. These three steps are echoed in the informal conditions articulated in the next section. (See also Shpitser & VanderWeele, 2011, and especially Shpitser, 2013, for refinements and elaborations.)

[12] It is interesting to note that Equation 10 remains valid under temporal reversal of the $T \rightarrow M$ relationship, that is, $\alpha = 0$ and $T = \delta M + U_T$. In such a model, Equations 7–10 give the correct result: $TE = NDE = CDE = \beta$, $NIE = 0$. The statistical definition, on the other hand, with its vocabulary confined to regression slopes, would not recognize *NIE* as zero because the regression slope of M on T is nonzero.

[13] Some authors (e.g., VanderWeele, 2009; Vansteelandt, 2012, Chapter 4.4), take $NIE = TE - NDE$ as the definition of the natural indirect effect, which ensures additivity a priori but presents a problem of interpretation; the resulting indirect effect, aside from being redundant, does not represent the same direction of change, from $T = 0$ to $T = 1$, as do the total and direct effects. This makes it hard to compare the effect attributed to mediating paths with that attributed to unmediated paths under the same conditions of change.

Interpretable Conditions for Identification

Preliminary Notation and Nomenclature

In this section, I provide precise identification conditions based solely on the notion of *unconfoundedness*. I say that the relationship between T and Y is *unconfounded* if the factors that influence T are independent of all factors that influence Y when T is held fixed. Given a set W of covariates, I say that *W renders a relationship unconfounded* if the relationship is unconfounded in every stratum $W = w$ of W. Finally, I use the expression *W deconfounds a relationship* as a shorthand substitute for *W renders a relationship unconfounded.* This definition also provides a model-based interpretation of *conditional strong ignorability*, written $T \perp\!\!\!\perp (Y_1, Y_0) | W$, and can be given a simple graphical representation called *backdoor* (see Appendix A), as is illustrated in the next section. Deconfounding occurs, for example, if W consists of all common causes of T and Y but may hold for other types of covariates as well (known as *sufficient* or *admissible*; see Appendix A), which neutralize the effect of common causes. Figuratively, such deconfounders can be recognized by intercepting, or blocking, all spurious (noncausal) paths between T and Y, namely, all paths that end with an arrow toward T (also called backdoor paths).[14]

In Figure 1a, for example, the relationship between M and Y is confounded by T, the common cause of M and Y. T is also a deconfounder of this relationship because T blocks the (one and only) backdoor path between M and Y. In Figure 1b, on the other hand, the relationship between M and Y is confounded by T as well as by latent common causes represented by the dashed arc between them. In fact, no measured set W exists that deconfounds this relationship because the latent backdoor path cannot be blocked by any measured variable. However, if U_M were to be observed, then the set $W = \{T, U_M\}$ (similarly $W = \{T, U_Y\}$) would deconfound the $M \rightarrow Y$ relationship by blocking all backdoor paths from M to Y. Note that U_M in this case is a deconfounder though it is not a common cause of M and Y.

I focus my discussion on the natural direct effect, *NDE*, though all conditions are applicable to the indirect effect as well, by virtue of the pseudoadditive decomposition of the total effect (see Equation 12). I assume that readers are familiar with the notion of identifiability as applied to causal or counterfactual relations (see, e.g., Appendix A). In particular, I say that the *W-specific* causal effect of T on Y is identifiable if the effect is consistently estimable from nonexperimental data for every stratum level w. In other words, the causal effect $P(y \mid do(t), w)$ can be expressed in terms of conditional probabilities of observed variables.[15] It is important to note that the problem of deciding whether such reduction exists has been fully solved using the *do*-calculus (Shpitser & Pearl, 2008; Tian & Shpitser, 2010). Consequently, effective algorithms are available that, given any causal diagram, can reduce any *do*-expression—in particular, *TE*, *CDE*(m), and $P(y \mid do(t_1, t_2, \ldots, t_k), (w_1, w_2, \ldots, w_k))$—to regression expressions, whenever such reduction exists. I therefore regard the identifiability of *do*-expressions as a solved problem and focus my attention on the question of whether *NDE* and *NIE* can be thus expressed and how.

Sufficient Conditions for Identifying Natural Effects

The following are two sets of assumptions or conditions, marked *A* and *B*, that are sufficient for identifying both direct and indirect natural effects. Each condition is communicated by a verbal description followed by its formal expression. Each set of conditions is followed by its graphical version, marked A_G and B_G, with all graphs representing nonparametric SEMs,[16] as in Figure 2. Assumption Set *B* is the stronger of the two and represents assumptions commonly invoked in the mediation literature (Coffman & Zhong, 2012; Imai, Jo, & Stuart, 2011; Imai, Keele, & Yamamoto, 2010; Shpitser & VanderWeele, 2011; VanderWeele & Vansteelandt, 2009; Vansteelandt et al., 2012; Vansteelandt & Lange, 2012). Assumption Set *A* is weaker and echoes more faithfully the derivation in Appendix B. For completeness, I also present a third assumption set, *C*, representing a compromise between *A* and *B*, which is based solely on the presence of deconfounding covariates, thus echoing more closely the way assumptions are articulated in the literature (e.g., Valeri & VanderWeele, 2013). Following a listing of the three assumption sets, Theorem 1 then presents the general formula for the natural direct effect (*NDE*) that results from Assumption Set *A*. The corresponding formula that results from Assumption Set *B* is given in Corollary 2. The corresponding formulas for the *NIE* follow from Equation 12 and are explicated in Equation 14b.

Assumption Set *A*. There exists a set W of measured covariates such that

A-1. No member of W is affected by treatment;

A-2. W deconfounds the mediator-outcome relationship (holding T constant):

$$[M_t \perp\!\!\!\perp Y_{t',m} \mid W] \quad \text{(alternatively, } [U_M \perp\!\!\!\perp U_Y | W]);$$

A-3. The W-specific effect of the treatment on the mediator is identifiable by some means:

$$[P(m \mid do(t), w) \quad \text{is identifiable}]; \text{ and}$$

A-4. The W-specific joint effect of {treatment + mediator} on the outcome is identifiable by some means:

$$[P(y \mid do(t, m), w) \quad \text{is identifiable}].$$

[14] By *path*, I mean any sequence of adjacent edges, regardless of directionality. By *blocking*, I mean disconnecting the path in the *d*-separation sense (see Appendix A).

[15] The expression $P(y \mid do(t), w)$ stands for the conditional probability $P_t(Y = y \mid T = t, W = w)$ obtained in a controlled experiment in which T is randomized and in which only units for which $W = w$ are recorded. *TE* and *CDE*(m) are *do*-expressions and can, therefore, be estimated from experimental data; not so the natural effects. *NDE* and *NIE* can be estimated from experimental data only when additional *no confounding* conditions hold (see Footnote 11) to be explicated below. The *do*-calculus (Pearl, 1995, 2009b, pp. 85–88) is a method of systematically reducing *do*-expressions to ordinary conditional probabilities but is not needed in this article.

[16] The distinction between graphs representing SEMs versus interventional models is discussed at length in Pearl (2009b, pp. 22–38) and is further elaborated in Robins and Richardson (2011). The latter models are also known as *causal Bayesian networks*; they represent experimental findings (i.e., *do*-expressions) but do not sanction counterfactual inferences.

Graphical version of Assumption Set *A*. There exists a set W of measured covariates such that

A_G-1. No member of W is a descendant of T;

A_G-2. W blocks all backdoor paths from M to Y not traversing T;[17]

A_G-3. The W-specific effect of T on M is identifiable (possibly using auxiliary variables); and

A_G-4. The W-specific joint effect of $\{T, M\}$ on Y is identifiable (possibly using auxiliary variables).

Illustration of A_G. Figure 3a provides an example where all A_G conditions are satisfied by $W = W_1$. First, W_1 satisfies A_G-1 and A_G-2 by virtue of being a nondescendant of T and blocking the path $M \leftarrow W_1 \rightarrow Y$, the only backdoor path from M to Y that does not traverse $T \rightarrow M$ or $T \rightarrow Y$ or that is not already blocked (by $\{\varnothing\}$). Next, A_G-3 is satisfied because the set (W_1, W_2) deconfounds the $T \rightarrow M$ relationship. This renders the W_1-specific causal effect of T on M identifiable by adjusting for W_2 and yields $P(m|do(t), w_1) = \sum_{w_2} P(m|t, w_2, w_1)P(w_2)$. The same applies to A_G-4, using adjustment for W_3 to identify the W_1-specific effect of $\{T, M\}$ on Y, yielding $P(y|do(t, m), w_1) = \sum_{w_3} P(y|t, m, w_3, w_1)P(w_3)$.

Assumption Set *B* (sequential ignorability, Imai, Keele, & Yamamoto, 2010). There exists a set W of measured covariates such that

B-1. W and T deconfound the mediator-outcome relationship, keeping T fixed:

$$[Y_{t',m} \perp\!\!\!\perp M_t \mid T, W]; \text{ and}$$

B-2. W deconfounds the treatment-{mediator, outcome} relationship:

$$[T \perp\!\!\!\perp (Y_{t',m}, M_t) \mid W].$$

Graphical version of Assumption Set *B*. There exists a set W of measured covariates such that

B_G-1. W and T block all T-avoiding backdoor paths from M to Y; and

B_G-2. W blocks all backdoor paths from T to M or to Y, and no member of W is a descendant of T.

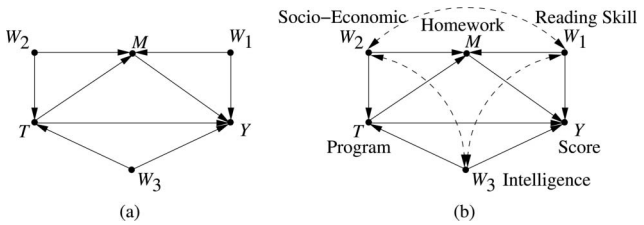

Figure 3. a: A mediation model with three independent confounders, permitting the decomposition of Equation 18. b: A model with dependent deconfounders, satisfying conditions *A* and *B*. M = mediator; T = treatment; W = covariates; Y = outcome.

Illustration of B_G. Figure 3a provides an example where all B_G conditions are satisfied using $W = \{W_1, W_2, W_3\}$. First, we examine all T-avoiding backdoor paths from M to Y (in particular, $M \leftarrow W_1 \rightarrow Y$) and note that $\{W, T\} = \{W_1, W_2, W_2, T\}$ block those paths, thus satisfying B_G-1. Next, complying with B_G-2, the set $\{W_1, W_2, W_2,\}$ blocks the paths $T \leftarrow W_2 \rightarrow M$ and $T \leftarrow W_3 \rightarrow Y$, the only ones with arrows into T. Finally, none of W_1, W_2, W_3 is a descendant of T, thus satisfying B_G-2.

Note that conditions A-3 and B-2 are automatically satisfied if T is randomized and A-4 is satisfied when both T and M are randomized, but the same is not true of A-2 and B-1; these may not hold even when we randomize both T and M (see Footnote 1).

If we limit the identification conditions to only those that invoke adjustment for covariates (giving up the options of using more elaborate identification methods, as in A-3 and A-4) Assumption Set A can be articulated more concisely thus:

Assumption Set *C* (piecemeal deconfounding). There exists three sets of measured covariates $W = \{W_1, W_2, W_3\}$ such that

C-1. No member of W_1 is affected by the treatment;

C-2. W_1 deconfounds the $M \rightarrow Y$ relationship (holding T constant);

C-3. $\{W_2, W_1\}$ deconfounds the $T \rightarrow M$ relationship; and

C-4. $\{W_3, W_1\}$ deconfounds the $\{T, M\} \rightarrow Y$ relationship.

Note that C-4 is sufficient for identifying the controlled direct effect (see Equation 8), C-3 and C-4 are sufficient for identifying the total effect (see Equation 7), and all four conditions are needed for the natural effects.

Theorem 1 (Pearl, 2001): When Conditions A-1 through A-2 hold, the natural direct effect is identified and is given by[18]

$$\begin{aligned} NDE = \sum_m \sum_w [&E(Y \mid do(T = 1, M = m)), W = w) \\ &- E(Y \mid do(T = 0, M = m), W = w)] \\ &P(M = m \mid do(T = 0), W = w)P(W = w). \end{aligned} \tag{13}$$

Corollary 1: If Conditions A-1 and A-2 are satisfied by a set W that also deconfounds the relationships in A-3 and A-4, then the *do*-expressions in Equation 13 are reducible to conditional expectations, and the natural direct and indirect effects become[19]

[17] This provision reflects the constancy of T in Assumption A-2 as depicted in Figure 2b. Both U_M and U_Y are defined relative to the condition where T is held constant, a condition that precludes T from passing information (or creating dependencies) between U_M and Y_Y.

[18] Summations should be replaced by integration when applied to continuous variables, as in Imai, Keele, and Yamamoto (2010). Note that Equation 13 is still valid if only A-1 and A-2 are satisfied by W; A-3 and A-4 are needed solely for identifying the *do*-expressions in the equation.

[19] Equations 14a–14b are identical to the ones derived by Imai, Keele, and Yamamoto (2010) using sequential ignorability (i.e., Assumptions B-1 and B-2) and subsequently rederived by a number of other authors (Lindquist, 2012; Wang & Sobel, 2013).

$$NDE = \sum_m \sum_w [E(Y \mid T = 1, M = m, W = w) - E(Y \mid T = 0, M = m, W = w)] P(M = m \mid T = 0, W = w) P(W = w). \quad (14a)$$

$$NIE = \sum_m \sum_w [P(M = m \mid T = 1, W = w) - P(M = m \mid T = 0, W = w)] E(Y \mid T = 0, M = m, W = w). \quad (14b)$$

Equations 14a and 14b are the averages (over w) of the mediation formula (i.e., Equations 17 and 27 in Pearl, 2001; see Footnote 20 below) and were called the *adjustment formula* in Shpitser and VanderWeele (2011).

Corollary 2: If conditions *B*-1 and *B*-2 are satisfied by a set W, then the natural direct and indirect effects are identified and are given by Equations 14a and 14b.

Corollary 2 follows from Theorem 1 by noting that, in structural models, any set W that satisfies *B*-1 and *B*-2 also deconfounds the relationships in *A*-3 and *A*-4 (Shpitser & VanderWeele, 2011).

Corollary 3: If Conditions *A*-1 and *A*-2 are satisfied with $W = \{\varnothing\}$ and two other sets of covariates exist, W_2 and W_3, such that W_2 deconfounds the $T \rightarrow M$ relationship and W_3 deconfounds the $\{TM\} \rightarrow Y$ relationship, then, regardless of possible dependencies between W_2 and W_3, the natural direct effect is identified and is given by

$$NDE = \sum_m \sum_{w_3} [E(Y \mid T = 1, M = m, W_3 = w_3) - E(Y \mid T = 0, M = m, W_3 = w_3)] P(W_3 = w_3) \sum_{w_2} P(M = m \mid T = 0, W = w_2) P(W = w_2). \quad (15)$$

Remarks. Assumption Set *A* differs from Assumption Set *B* on two main provisions. First, *A*-3 and *A*-4 permit the identification of these causal effects by all methods, while *B*-2 and *B*-3 insist that identification be accomplished by adjustment. Second, whereas *A*-3 and *A*-4 allow for the invocation of any set of covariates in order to identify the *W*-specific effect in question, *B* requires that the same set W of covariates deconfound both the mediator-outcome and treatment-{mediator, outcome} relationships.

It should be noted that, whereas this article concerns identification in observational studies, Conditions *A*-3 and *A*-4 open the door to experimental studies, when such are feasible. For example, one may venture to estimate the causal effect of T on M by randomizing T or by using instrumental variables or auxiliary intermediate variables. Only the latter are considered here. The restrictions on all such designs are the same, namely, that they lead to the identification of *W*-specific effects, where W is a set of attributes satisfying *A*-1 and *A*-2. Assumption *A*-2, on the other hand, cannot be satisfied by any experimental design since it involves cross-world independence, from t-worlds to t'-worlds. Identifiability requires that such independencies hold naturally in the population under study, not in a population crafted by design (see Footnote 1).

Appendix C explains why I must insist that W be unaffected by the treatment. This requirement is implicit in *B*-2 but not in *A*-2; it must therefore be stated explicitly in *A*-1 (and B_G-2) for, otherwise, *A*-3 and *A*-4 will not be sufficient for identifying *NDE*, as is shown below.

Illustrations

To illustrate and compare the conditions articulated in the previous section, I start with simple models that satisfy the strong conditions of *B* (and B_G), and then examine how the process of identification can benefit from the relaxed conditions given in *A* (and A_G).

How the Natural Effects Are Identified

Figure 4a illustrates the classical mediation model, with no confounding; all omitted factors (not shown in the diagram) affecting T, M, and Y are assumed to be independent, so both the mediator process, $T \rightarrow M$, and the outcome process, $\{T, M\} \rightarrow Y$, are unconfounded. In this model, the null set $W = \{\varnothing\}$ satisfies the conditions in *B* (as well as in *A*), and Equations 13 and 14a are reduced to

$$NDE = \sum_m [E(Y \mid T = 1, M = m) - E(Y \mid T = 0, M = m)] P(M = m \mid T = 0). \quad (16)$$

Likewise, the natural indirect effect (see Equation 14a) becomes[20]

$$NIE = \sum_m E(Y \mid T = 0, M = m) [P(M = m \mid T = 1) - P(M = m \mid T = 0)]. \quad (17)$$

The intuition behind Equation 16 is simple; the natural direct effect is the weighted average of the controlled direct effect $CDE(m)$, shown in the square brackets, using the no-treatment distribution $P(M = m \mid T = 0)$ as a weighting function. Equation 16 can be estimated by a two-step regression, as is shown below. The intuition behind Equation 17 is somewhat different and unveils a nonparametric version of the product-of-coefficients estimator (see the Mediation Analysis in the Parametric Tradition section, above). The term $E(Y \mid T = 0, M = m)$ plays the role of γ in Figure 1a, for it describes how Y responds to M for fixed treatment condition ($T = 0$). The term in the square brackets plays the role of α, for it captures the impact of the transition from $T = 0$ to $T = 1$ on the probability of M. One sees that what was a simple product operation in linear systems is replaced by a composition operator that involves summation over all values of M and thus allows for heterogeneous populations where both M and its effect on Y may vary from individual to individual.

Figure 4b illustrates a confounded mediation model in which a variable, W (or a set of variables), confounds all three relationships

[20] Equations 16 and 17 were called the mediation formula in Pearl (2009b, p. 132; see also Pearl, 2009a, 2012a). Since the *NDE* and *NIE* are connected to each other via Equation 12, all our discussions concerning the identification of *NDE* should apply to *NIE* as well (Pearl, 2009b, p. 132; see also Pearl, 2009a, 2012a).

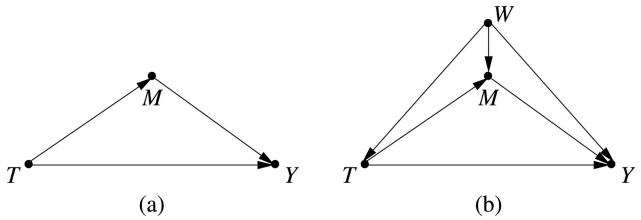

Figure 4. a: The basic unconfounded mediation model (same as Figure 1b, with omitted factors not shown). b: A confounded mediation model with covariate set W that deconfounds both the $T \rightarrow M$, $T \rightarrow Y$ and the $M \rightarrow Y$ relationships. M = mediator; T = treatment; W = covariates; Y = outcome.

in the model. Because W is not affected by T and is observed, adjusting for W renders all relationships unconfounded, and the conditions of B (as well as A) are satisfied. Accordingly, the natural direct effect estimand is given by Equation 14b, which invokes the mediation formula (see Equation 16) in each stratum of w of W, averaged over w.

Numerical Example

To anchor these mediation formulas in a concrete example, I return to the encouragement-design example of the introduction and assume that $T = 1$ stands for participation in an enhanced training program, $Y = 1$ for passing the exam, and $M = 1$ for a student spending more than 3 hours per week on homework. Assume further that the data described in Table 1 were obtained in a randomized trial with no mediator-to-outcome confounding (see Figure 4a). The data show that training tends to increase both the time spent on homework and the rate of success on the exam. Moreover, training and time spent on homework together are more likely to produce success than each factor alone.

Our research question asks for the extent to which students' homework contributes to their increased success rates. The policy implications of such questions lie in evaluating policy options that either curtail or enhance homework efforts, for example, by counting homework effort in the final grade or by providing students with adequate work environments at home. An extreme explanation of the data, with significant impact on educational policy, might argue that the program does not contribute substantively to students' success, save for encouraging students to spend more time on homework, an encouragement that could be obtained through less expensive means. Opposing this theory, there may be teachers who argue that the program's success is substantive, achieved mainly due to the unique features of the curriculum covered, while the increase in homework efforts, although catalytical, cannot alone account for the success observed.

Substituting these data into Equations 16–17 gives

$$NDE = (0.40 - 0.20)(1 - 0.40) + (0.80 - 0.30)0.40 = 0.32,$$

$$NIE = (0.75 - 0.40)(0.30 - 0.20) = 0.035,$$

$$TE = 0.80 \times 0.75 + 0.40 \times 0.25 - (0.30 \times 0.40 + 0.20 \times 0.10) = 0.46,$$

$$NIE/TE = 0.07, \quad NDE/TE = 0.696, \quad 1 - NDE/TE = 0.304.$$

In conclusion, the program as a whole has increased the success rate by 46% and that a significant portion, 30.4%, of this increase is due to the capacity of the program to stimulate improved homework effort. At the same time, only 7% of the increase can be explained by stimulated homework alone without the benefit of the program itself.

Let me now illustrate the use of Equation 14a in cases marred by confounding. Assume that W stands for gender, which, as shown in Figure 4b, confounds all three relations in the models. Equation 14a instructs us to conduct the analysis separately on males ($W = 1$) and females ($W = 0$) and average the results according to the gender mix in the population. For example, if the data in Table 1 represent the male population and a similar yet different table represents females, we take our estimate $NDE(W = 1) = 0.32$ and the corresponding $NDE(W = 0)$ from the female table and form the overall NDE by taking the weighted average of the two.

The purpose of this example is to demonstrate how the linear barriers that restricted classical mediation analysis can be broken by nonparametric formulas, Equations 16 and 17, that have emerged from the structural-counterfactual analysis. It shows how these mediation formulas are applicable to highly interacting variables, both continuous and categorical, without making any assumptions about the error distribution or about the functions that tie the variables together. Imai, Keele, and Yamamoto (2010) further analyzed the asymptotic variance of the estimands in Equations 16 and 17 and developed powerful software for sensitivity analysis.

In the next section, I deal with more intricate patterns of confounders, both measured and unmeasured, and show how Conditions A_G-1 to A_G-4 can guide us toward identification in the presence of those confounders.

The Benefits of Independent Adjustments

A benefit of the weaker conditions expressed in A is that A-3 and A-4 allow for covariates outside W to assist in the identification. This results in a greater flexibility in allocating covariates for the various adjustments invoked in Equation 14a. It also simplifies the process of justifying the assumptions that support these adjustments and leads, in turns, to a simpler overall estimand. Specifically, in choosing covariates to deconfound the $\{T, M\} \rightarrow Y$ relationship, one is free to ignore those chosen to deconfound the $T \rightarrow M$ relationship.

The model in Figure 3a demonstrates this flexibility. Although the set $W = \{W_1, W_2, W_3\}$ satisfies all the conditions in A and B, Assumption Set A permits us to handle each of the three covariates individually, so as to simplify the resulting estimand. Since W_1 alone renders the mediator-to-outcome relationship unconfounded

Table 1
Dependence of Success Rate on Treatment and Homework

Treatment T	Homework M	Success rate $E(Y \mid T = t, M = m)$
1	1	0.80
1	0	0.40
0	1	0.30
0	0	0.20

Homework $E(M \mid T = t)$
0.40
0.75

(for fixed T), we are at liberty to choose W_1 to satisfy Conditions A-1 and A-2. In the next step, we seek a set of covariates that, together with W_1, would deconfound the $T \rightarrow M$ relationship, and since W_2 alone meets this requirement, we can remove W_3 from the factor $P(M = m \mid T = 0, W = w) = P(M = m \mid T = 0, W_1 = w_1, W_2 = w_2, W_3 = w_3)$ of Equation 14a. Next, we seek a set of covariates that, together with W_1, would deconfound the $\{T, M\} \rightarrow Y$ relationship, and realizing that W_3 meets this requirement, we can remove W_2 from the factors $E(Y \mid T = 1, M = m, W = w)$ and $E(Y \mid T = 0, M = m, W = w)$ of Equation 14a. The resulting estimand for *NDE* becomes

$$\begin{aligned} NDE = \sum_m \sum_{w_2, w_3, w_1} & P(W_2 = w_2, W_3 = w_3, W_1 = w_1) \\ & \times P(M = m \mid T = 0, W_2 = w_2, W_1 = w_1) \\ & \times [E(Y \mid T = 1, M = m, W_1 = w, W_3 = w_3) \\ & - E(Y \mid T = 0, M = m, W_1 = w, W_3 = w_3)], \end{aligned} \tag{18}$$

with only one of W_3 and W_2 appearing in each of the last two factors.

Note that covariates need not be pretreatment to ensure identification; B and A require merely that W be causally unaffected by the treatment. Indeed, W_3 in Figure 3 may well be a posttreatment variable, the control of which is essential for identifying *NDE*.

Figure 3b associates a research context to the model of Figure 4a using our running example of student-encouragement design. Here, we assume that W_1 = reading skill is the sole confounder of the homework → score relation. Likewise, we assume that socioeconomic background confounds program (T) and homework (M) ostensibly because students from high socioeconomic backgrounds are more likely to have facilities that are conducive to doing homework and they (or their parents) are more likely to seek out the educational programs offered (T). Finally, we associate W_3 with students' natural intelligence, arguing that this is a significant factor in enticing students to enroll in the program (T) and simultaneously enables students to learn faster and score higher on exams.

As mentioned in the Structural Approach to Mediation section, above, as soon as one associates a diagram to a research context, issues arise of possible unforeseen associations among variables that may threaten identification and complicate estimation. In our example, mutual associations may naturally be suspected among language skills (W_1), socioeconomic background (W_2), and intelligence (W_3), with no clear origin or explanation. Such associations are depicted by the dashed arcs in Figure 3b, and the question arises, Do these present a problem to identification?[21] Such questions can be readily answered by Assumption Set A, using A_G-1 to A_G-4, though it is a bit hard to imagine how they can be handled by Assumption Set B.

Guided by A_G, note that all arguments previously used in deciding the identification of *NDE* in Figure 3a (see the Sufficient Conditions for Identifying Natural Effects section, Illustration of A_G subsection, above) are still valid for Figure 3b. Specifically,

(i) W_1 satisfies A_G-2 by virtue of blocking the two backdoor paths going from M to Y, $M \leftarrow W_1 \rightarrow Y$ and $M \leftarrow W_1 \leftrightarrow W_3 \rightarrow Y$;

(ii) $\{W_2, W_1\}$ blocks all backdoor paths from T to M (explicitly: $T \leftarrow W_2 \rightarrow M$, $T \leftarrow W_2 \leftrightarrow W_1 \rightarrow M$, $T \leftarrow W_3 \leftrightarrow W_1 \rightarrow M$, etc.); and

(iii) $\{W_3, W_1\}$ blocks all backdoor paths from $\{T, M\}$ to Y (explicitly: $T \leftarrow W_3 \rightarrow Y$, $T \leftarrow W_2 \leftrightarrow W_3 \rightarrow Y$, $T \leftarrow W_3 \leftrightarrow W_1 \rightarrow Y$, $T \leftarrow W_2 \leftrightarrow W_2 \leftrightarrow W_3 \rightarrow Y$, . . .).

We are thus led to the conclusion that the added associations between W_1, W_2, and W_3 do not interfere with the identification of *NDE*.

We are also led to appreciate the guidance provided by graphical procedures, without which decisions concerning identification could easily become unmanageable. Fortunately, these procedures are easily mechanizable by present-day software since they are driven entirely by the graph structure. Once a researcher hypothesizes the model structure, a simple algorithm can go through the graphical tests above and, if identifiability is established, deliver the proper mediation formula or estimate it from the data.

The next section discusses examples where the restrictiveness of Assumption Set B may hinder identification and where a careful examination of the A_G criteria would be needed to produce unbiased estimates of *NDE*.

Comparing Identification Power

In comparing the identification power of Assumption Sets A versus B, we note that A draws its increased power from two sources:

(a) Divide and conquer—covariates may be found capable of deconfounding the mediator and outcome processes separately but not simultaneously; and

(b) Identification by mediating instruments—intermediate covariates may be measured, enabling one to identify causal effects through multistep procedures, not through a one-step adjustment, as required by B.

Divide and conquer. To highlight the extra power of Assumption Set A, we examine the six models in Figure 5. The results of this examination are detailed in Table 2 and can be summarized as follows:

Both A and B deem the *NDE* identifiable in Models a and e and nonidentifiable in Model d. However, Assumption Set A correctly identifies *NDE* in Models b, c, and f, while B mistakes it to be nonidentifiable in these models.

The reasoning behind these determinations can best be followed in Figure 5b, which clearly demonstrates how the *divide and conquer* flexibility translates into increased identification power. Here, there are no backdoor paths from M to Y, so A_G-2 is satisfied by the null set $W = \{\varnothing\}$. Still, to deconfound the $T \rightarrow M$ relationship, A_G-3 requires an adjustment for W_2. Likewise, to deconfound the $\{T, M\} \rightarrow Y$ relationship, A_G-4 requires an adjustment for W_3. If we make the two adjustments separately, both relationships can be deconfounded, and by Corollary 3, *NDE* reduces to the estimand of Equation 15. However, if we were to adjust for W_2 and W_3

[21] This question was asked by one of the reviewers of this article. I assume it is a question faced by many researchers.

simultaneously, as required by Assumption Set *B*, the $T \rightarrow M$ relationship would become confounded along the path[22] $T \leftarrow o \rightarrow W_3 \leftrightarrow W_2 \leftarrow o \rightarrow M$. In other words, the full set of A_G (or B_G) cannot be satisfied by the same set of *W* elements. As a result, Assumption Set *B* would deem the *NDE* to be unidentifiable; there is no covariates set that simultaneously satisfies B_G-1 and B_G-2.

We note that treatment assignment in this model is not random under any one of the two needed adjustments; *T* remains confounded (or nonignorable) either with *M* or with *Y*. It is for this reason that the term *deconfounded* is less ambiguous than *random* or *as if randomized.*

Figure 5f further illustrates why Assumptions *A*-3 and *A*-4 insist on identifying *w*-specific effects and, consequently, the extra precautions that this requirement imposes on choosing *W*, even in cases where *NDE* is identified. If $W = W_1$ is chosen to deconfound the $M \rightarrow Y$ relationship, then *NDE* can be properly estimated (using W_2 to deconfound $T \rightarrow M$ and W_3 to deconfound $\{T, M\} \rightarrow Y$). However, if W_3 is chosen to deconfound the $M \rightarrow Y$ relationship, the $T \rightarrow M$ relationship is no longer deconfoundable, that is, no set of measured variables is available to block all the confounding paths from *T* to *M*. The conclusion is twofold. First, any software that tells us if *NDE* is identifiable may need to search the space of candidate sets *W* before a determination can be made; an independent control for confounding in each of the three relationships, $M \rightarrow Y$, $T \rightarrow M$, and $T \rightarrow Y$, is not sufficient for identifying natural effects. Second, if we venture to skip over this search and estimate the *NDE* by adjusting for all measured variables, the result is likely to become biased; Figures 5b, 5c, and 5f exemplify this danger.

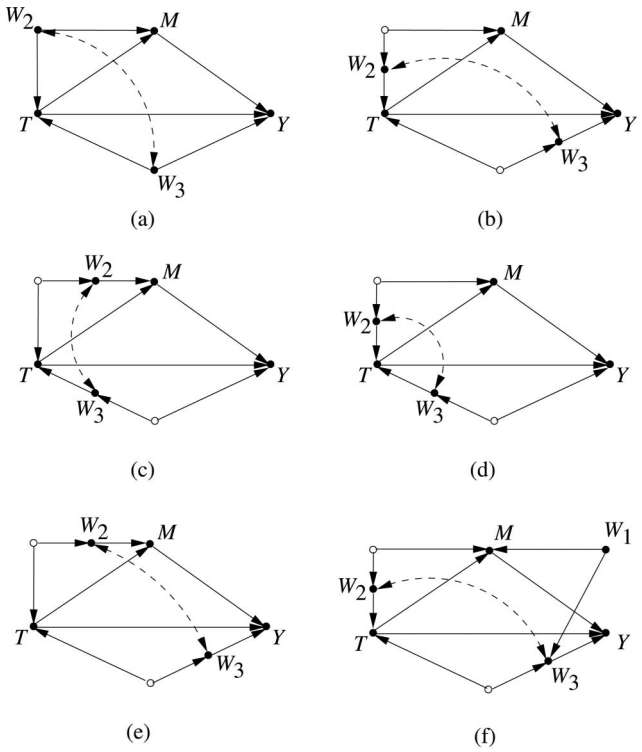

Figure 5. Showing six confounded models for comparing Assumption Sets *A* and *B*. The former is satisfied in all cases except d; the latter is satisfied in a and e only. Explanations are given in Table 2. *M* = mediator; *T* = treatment; *W* = covariates; *Y* = outcome.

Table 2
Sets of Covariates Needed for Deconfounding Each of the Two Relationships of Interest

Case	(i) Mediator process $T \rightarrow M$	(ii) Output process $\{T, M\} \rightarrow Y$
a	W_2 or $\{W_2, W_3\}$	W_3 or $\{W_2, W_3\}$
b	W_2 only	W_3 or $\{W_2, W_3\}$
c	W_2 or $\{W_2, W_3\}$	W_3 only
d	$\{W_2, W_3\}$	Not deconfoundable
e	W_2 or $\{W_2, W_3\}$	W_3 or $\{W_2, W_3\}$
f	Not deconfoundable if we choose $W = W_3$; deconfoundable by W_2 if we choose $W = W_1$	W_3 or $\{W_2, W_3\}$

Note. Assumption Set *B* is satisfied in Cases a and e only, where the set $\{W_2, W_3\}$ deconfounds both relationships. Assumption Set *A* is satisfied in all cases except for Case d.

Identification by mediating instruments. Figure 6 displays another model for which Assumption Set *A* permits the identification of the natural direct effect, while *B* does not. *NDE* achieves its identifiability through auxiliary mediating variables (*Z*) but not through adjustment for pretreatment covariates, as demanded by *B*.

In this model, the null set $W = \{\varnothing\}$ satisfies Condition *B*-1 but not Condition *B*-2; there is no set of covariates that would enable us to deconfound the treatment-mediator relationship. Referring to our encouragement-design example, such a model acknowledges the existence of unmeasured factors that affect both student choice to enroll in the program ($T = 1$) and student ability to devote time for homework ($M = 1$). The intermediate variable, *Z*, that stands between *T* and *M* may represent, for example, students' perception of the importance of homework to their progress, which can be monitored by auxiliary means (e.g., a questionnaire) at some intermediate stage of the study. It can be shown that the availability of such intermediate measurements can make up for the unobservability of all factors that confound *T* and *M* (Morgan & Winship, 2007, Chapter 3; Pearl, 2000a, Chapter 3).

Indeed, Condition *A*-3 requires only that we identify the effect of *T* on *M* by *some* means, not necessarily by rendering *T* random or unconfounded (or ignorable). The presence of the observed variable *Z* permits us to identify this causal effect using an estimator called *front-door* (Pearl, 1995; Pearl, 2009b, pp. 81–85). The resultant *NDE* estimand will be

$$NDE = \sum_m [E(Y \mid T = 1, M = m) - E(Y \mid T = 0, M = m)] \\ P(M = m \mid do(T = 0)), \quad (19)$$

where $P(M = m \mid do(T = 0))$ is given by

[22] This follows from the fact that both W_3 and W_2 are colliders (i.e., receiving two incoming arrows) along the path; each permits the flow of information when it is conditioned on and stops the flow when not conditioned on (see Appendix A).

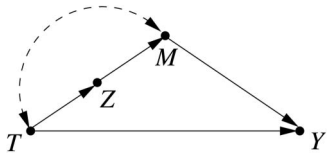

Figure 6. Measuring Z permits the identification of the effect of T on M through the front-door procedure (see Equation 20 in the text). Z satisfies the front-door condition since it intercepts all paths from T to M, and receives no other arrow except for $T \rightarrow Z$. M = mediator; T = treatment; Y = outcome; Z = covariate.

$$\sum_{z} P(Z = z \mid T = 0) \sum_{t'=0,1} P(M = m \mid Z = z, T = t')P(T = t'). \tag{20}$$

Numerical examples for the computation of Equation 20 were given in Pearl (2009b, pp. 83–84) and Morgan and Winship (2007). Application of the front-door estimator to problems in economics and social science was described in Chalak and White (2011) and in Knight and Winship (2013). The asymptotic efficiency of the front-door estimator (see Equation 20) was analyzed in Ramsahai (2012).

Figure 7 demonstrates the use of a mediating instrument, Z, situated on the causal pathway between T and Y. In this model, conditioning on W deconfounds both the $M \rightarrow Y$ and $T \rightarrow M$ relationships but confounds the $T \rightarrow Y$ relationship (see Appendix A). Fortunately, the ability to observe Z renders the W-specific joint effect of $\{T, M\}$ on Y identifiable (using the front-door estimand) and permits us to satisfy A-4. This example demonstrates the importance of requiring A-4 as a separate assumption and not insisting that it be satisfied by the same covariates W that satisfy A_2; had Z not been observed, Conditions A-1 to A-3 would have been satisfied, but not A-4, rendering *NDE* nonidentifiable.

Figure 8 tempts us to apply the front-door estimator to the $M \rightarrow Y$ relationship, which is confounded by unobserved common causes of M and Y (represented by the dashed arc). Unfortunately, although the causal effect of $\{T, M\}$ on Y and the controlled direct effect $CDE(m)$ are both identifiable (through the front-door estimator), Condition A-2 cannot be satisfied; no covariate can be measured that deconfounds the $M \rightarrow Y$ relationship. The front-door estimator provides a consistent estimate of the population causal effect, $P(Y = y \mid do(M = m))$, while unconfoundedness, as defined above in the Preliminary Notation and Nomenclature section,

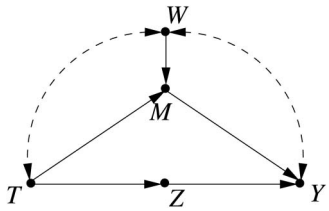

Figure 7. The natural direct effect is identified by adjusting for W and by using Z as auxiliary variable to identify $P(y \mid do(t, m), w)$ as required by A-4. M = mediator; T = treatment; W = covariate; Y = outcome; Z = covariate.

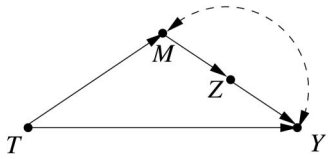

Figure 8. The natural direct effect is not identifiable even though all causal effects are identifiable. Assumption A-2 requires unconfoundedness of $M \rightarrow Y$ in every stratum of the (unobserved) confounder W, which is a stronger requirement than effect identification. M = mediator; T = treatment; Y = outcome; Z = covariate.

requires independence of U_M and U_Y, which measurement of Z cannot induce.

Figure 9 demonstrates the use of a covariate situated along the path from M to Y. In this model, the mediator → outcome relationship is unconfounded (since X is a collider), so we are at liberty to choose $W = \{\varnothing\}$ to satisfy condition A-2. The treatment → outcome relationship is confounded and requires an adjustment for X. The $\{T, M\} \rightarrow Y$ relationship, however, cannot be deconfounded by any covariate; conditioning on X would confound the $M \rightarrow Y$ relationship, while not conditioning on X would leave the $T \rightarrow Y$ relationship confounded along the path $T \leftarrow X \leftarrow L_1 \rightarrow Y$ (in violation of Condition A-4). Here, the presence of Z comes to our help, for it permits us to estimate $P(y \mid do(t, m), x)$ using the front-door estimator, as in Equations 19–20, thus rendering *NDE* identifiable.

Coping With Treatment-Dependent Confounders

Figure 8 is the first example we encountered in which the natural direct effect is nonidentifiable while the controlled direct effect is identifiable. Another such example is shown in Figure 10 (see Appendix B). Here, W can serve to deconfound both the $M \rightarrow Y$ and the $T \rightarrow M$ relationships, but alas, W is a descendant of T, so it violates Condition A-1 and renders *NDE* nonidentifiable. The controlled direct effect, on the other hand, is easily identifiable using the truncated product formula (see Appendix C). Figure 10 unveils a general pattern that prevents identification of natural effects in any nonparametric model (Avin, Shpitser, & Pearl, 2005; Robins, 2003): Whenever a variable exists, be it measured or unmeasured, that is a descendant of T and an ancestor of both M and Y (W in our examples), *NDE* is not identifiable.

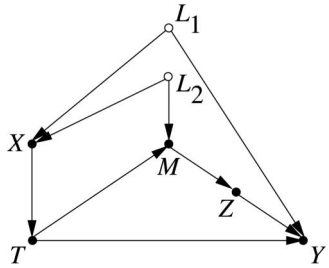

Figure 9. The confounding created by adjusting for X can be removed using measurement of Z to identify the effect of (T, M) on Y. L = latent variables; M = mediator; T = treatment; X = covariate; Y = outcome; Z = covariate.

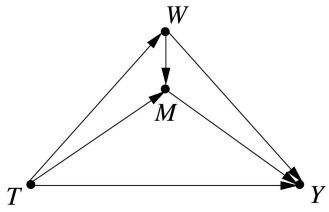

Figure 10. The natural direct effect is not identifiable because Condition *A*-1 cannot be satisfied—*W* is a descendant of *T*. *M* = mediator; *T* = treatment; *W* = covariate; *Y* = outcome.

This restriction however does not apply to linear structural models, where parameter identification is all that is needed for the identification of all effects, even when a confounder *W* of $M \rightarrow Y$ is affected by the treatment. The reason is that, with the values of all parameters given, the model equations becomes completely specified, from which we can derive all counterfactuals, including those invoked in the definition of natural effect (see Equations 9–10). The same applies to other parametric structural models, such as linear models with interaction terms. This increased identification power comes, of course, at the cost of increasing the danger of misspecification because our commitment to a specific functional form may be incorrect.

To illustrate, consider the parametric version of Figure 10:[23]

$$y = \beta_1 m + \beta_2 t + \beta_3 tm + \beta_4 w + u_t, \tag{21}$$

$$m = \gamma_1 t + \gamma_2 w + u_m, \tag{22}$$

$$w = \alpha t + u_y, \tag{23}$$

with $\beta_3 tm$ representing an interaction term. The basic definition of the natural effects (see Equations 9–10) gives (for the transition from $T = 0$ to $T = 1$, treating *M* as the mediator)

$$NDE(M) = \beta_2 + \alpha\beta_4. \tag{24}$$

$$NIE(M) = \beta_1(\gamma_1 + \alpha\gamma_2). \tag{25}$$

$$TE = \beta_2 + (\gamma_1 + \alpha\gamma_2)(\beta_3 + \beta_1) + \alpha\beta_4. \tag{26}$$

$$TE - NDE(M) = (\beta_1 + \beta_3)(\gamma_1 + \alpha\gamma_2). \tag{27}$$

We see that, due to treatment-mediator interaction, $\beta_3 tm$, the portion of the effect for which mediation is *necessary* ($TE - NDE$) can differ significantly from the portion for which mediation is *sufficient* (*NIE*; Pearl, 2012a). The fact that *W* is affected by the treatment does not hinder the identification of these effects (as long as the structural parameters are identifiable), though the choice of terms for each of those effects is not trivial and needs to be guided carefully by the formal, counterfactual definitions of *NDE* and *NIE* (Pearl, 2012b). Even in the simple model of Equations 21–23, with β_3 the only interaction term, it is not at all obvious that β_3 should affect the necessary and sufficient components of mediation in the manner shown in Equations 24–27. The task is much more intricate in the presence of multiple interacting mediators, each acting as both a mediator and a moderator.

For nonparametric models, Avin et al. (2005) derived a necessary and sufficient condition for identifying (natural) path-specific effects in any graph structure with no unmeasured confounders. For example, suppressing the $T \rightarrow W$ or $T \rightarrow M$ processes in Figure 10 would lead to identifiable effects, while suppressing the $W \rightarrow Y$ or $M \rightarrow Y$ processes would not. Shpitser (2013) generalized this result and gave a complete algorithm for path specific effects with multiple treatments, multiple outcomes, and hidden variables.

Figure 10 can in fact be regarded as having two interacting mediators, *M* and *W*, and the results of Avin et al. (2005) highlight a fundamental difference between the two. Whereas effects mediated through *W* are identifiable, those mediated through *M* are not. For example, the natural direct and indirect effects viewing *W* as the mediator can be obtained directly from Equations 16 and 17, exchanging *m* with *w*, since the relationships $T \rightarrow W$ and $(TW) \rightarrow Y$ are unconfounded. This gives

$$NDE(W) = \sum_w [E(Y \mid T = 1, W = w) - E(Y \mid T = 0, W = w)]P(W = w \mid T = 0),$$

$$NIE(W) = \sum_w E(Y \mid T = 0, W = w)[P(W = w \mid T = 1) - P(W = w \mid T = 0)],$$

in which *M* is not invoked, since it is regarded as part of the direct effect from *T* and *Y*.[24]

For comparison, the parametric version of Figure 10 given in Equations 21–23 yields the following effects when *W* is considered the mediator:

$$NDE(W) = \beta_2 + \gamma_1\beta_1. \tag{28}$$

$$NIE(W) = \alpha(\beta_4 + \gamma_2\beta_1). \tag{29}$$

$$TE = \beta_2 + (\gamma_1 + \alpha\gamma_2)(\beta_3 + \beta_1) + \alpha\beta_4. \tag{30}$$

$$TE - NDE(W) = \alpha(\gamma_2\beta_3 + \beta_4 + \gamma_2\beta_1 + \gamma_1\beta_3). \tag{31}$$

Comparing Equations 28–31 to Equations 24–27 allows an investigator to assess the relative contribution of each mediator, *W* and *M*, to the overall effect of *T* on *Y*.

Figure 11 depicts the parameterized model of Equations 21–23 and compares the subgraphs carrying the effects (*NIE*) mediated by *M* and *W*, respectively.

Conclusions

I have presented a concise, general, and interpretable set of conditions for identifying natural effects, and demonstrated by examples how they can be tested in a given model and how they lead to improved identification power. In particular, the new conditions open the door for identification methods that go beyond standard adjustment for covariates and leverage auxiliary variables and multistep procedures that operate in the presence of confounded treatment and mediator relationships.

[23] Such models have been analyzed extensively in the literature, some using a purely statistical approach (Jo, 2008; Kraemer et al., 2008; MacKinnon, 2008; Preacher, Rucker, & Hayes, 2007) and some applying the mediation formula of Equations 16 and 17 (Coffman & Zhong, 2012; Imai, Keele, & Yamamoto, 2010; Muthén, 2011; Pearl, 2010a, 2012a; Valeri & VanderWeele, 2013; VanderWeele & Vansteelandt, 2009). However, the problem of dealing with two interacting mediators (e.g., *M* and *W* in Figure 10) has not received much attention.

[24] Remarkably, if *W* were merely correlated with *M*, rather than causally affecting it, the effect mediated by either *M* or *W* would not be identified, since no measured covariate can satisfy Assumptions *A*-1 and *A*-2.

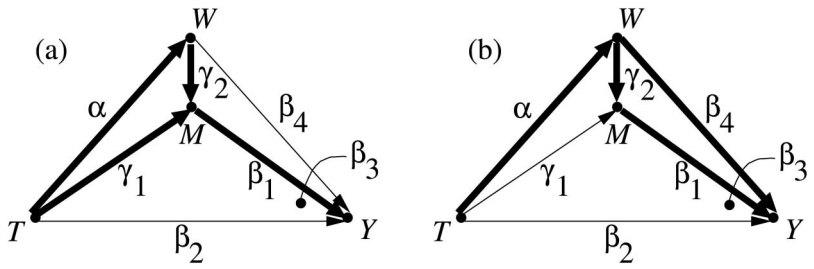

Figure 11. A parameterized version of Figure 10 in which the heavy arrows represent (a) paths carrying the natural indirect effect when M is considered as the mediator. b: Same with W considered as the mediator. M = mediator; T = treatment; W = covariate; Y = outcome; α, β, γ = structural coefficients.

Applying these conditions to linear models with interaction terms, I have shown how path-specific effects can be estimated in models with multiple pathways and interacting mediators.

An important feature of the conditions formulated in this article is their *mechanizability*. Simple graphical algorithms exist (and are cited in the reference list) that examine the structure of the model, test whether the identification conditions are satisfied in the model, and, depending on *how* they are satisfied, produce an unbiased estimate of the desired mediated effect. This feature relieves researchers from the task of interpreting and judging the validity of each identifying assumption in isolation; it is the plausibility of the postulated model structure (i.e., the diagram) that one needs to judge and defend. The structure itself dictates both the choices by which the identification conditions can be satisfied and the estimation procedures appropriate for each choice.

Naturally, to apply these identification procedures to real-life data, one needs to be certain of the causal scenario behind the data and that the scientific context of that scenario is faithfully depicted in the diagram. The question arises whether it is realistic to assume that investigators would possess such certainties in real-life applications. Here, one should recall that anchoring one's analysis in specific causal scenarios does not imply a commitment to the validity of those scenarios. It implies willingness to explore their ramifications, to evoke critiques of one's assumptions, and to understand which variants of each scenario are critical for identification and for choosing the correct estimator. The alternative, of course, is to sweep these uncertainties under the rug of no unmeasured confounders or sequential ignorability. This article replaces such sweeping assumptions with specific scientific contexts (encoded graphically) that investigators can scrutinize for plausibility, submit to statistical tests,[25] and appeal to mechanical procedures for identification analysis. This departure from ignorability-based approaches to mediation should provide researchers with a deeper understanding of the nature of mediation and the tools available for its analysis.

[25] The testable implications of causal diagrams are discussed in Appendix A (see Bollen & Pearl, 2013; Pearl, 2009b, pp. 140–144).

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(*Appendices follow*)

Appendix A

Covariate Selection: *d*-Separation and the Backdoor Criterion

Consider an observational study where we wish to find the effect of treatment (T) on outcome (Y), and assume that the factors deemed relevant to the problem are structured as in Figure A1; some are affecting the outcome, some are affecting the treatment, and some are affecting both treatment and response. Some of these factors may be unmeasurable, such as genetic trait or lifestyle, while others are measurable, such as gender, age, and salary level. Our problem is to select a subset of these factors for measurement and adjustment so that if we compare treated versus untreated subjects having the same values of the selected factors, we get the correct treatment effect in that subpopulation of subjects. Such a set of factors is called a *sufficient set*, *admissible set*, or a set *appropriate for adjustment* (see Greenland, Pearl, & Robins, 1999; Pearl, 2000b, 2009a). In this article, I call such a set a *deconfounder* of the $T \rightarrow Y$ relationship.

I now describe a criterion named *backdoor* (Pearl, 1993), which provides a graphical method of selecting such a set of factors for adjustment. It is based on the simple idea that, when we adjust for a set S of covariates, we should block, or disable, all spurious paths from T to Y and leave intact all causal paths between the two. To operationalize this idea, we need the notion of *d*-separation (the *d* stands for directional), which provides a formal characterization of what it means to block a path and also allows us to detect all the testable implications that a given model entails.

Definition 1 (*d*-separation): A set S of nodes is said to block a path p if either (a) p contains at least one arrow-emitting node that is in S or (b) p contains at least one collision node that is outside S and has no descendant in S. If S blocks all paths from set T to set Y, it is said to *d*-separate T and Y, and then, variables T and Y are independent given S, written $T \perp\!\!\!\perp Y | S$.[A1]

The intuition behind *d*-separation can best be recognized if we regard paths in the graph as conveyers of probabilistic information, with nodes acting as *information switches*. In causal chains $i \rightarrow m \rightarrow j$ and causal forks $i \leftarrow m \rightarrow j$, the two extreme variables are marginally dependent but become independent of each other (i.e., blocked) once we condition on (i.e., know the value of) the middle variable. Figuratively, conditioning on m appears to block the flow of information along the path, since learning about i has no effect on the probability of j, given m. Inverted forks $i \rightarrow m \leftarrow j$, representing two causes having a common effect, act the opposite way; if the two extreme variables are (marginally) independent, they become dependent (i.e., connected through unblocked path) once we condition on the middle variable (i.e., the common effect) or any of its descendants. This special handling of collision nodes (or *colliders*), reflects a general phenomenon known as *Berkson's paradox* (Berkson, 1946), whereby observations on a common consequence of two independent causes render those causes dependent. For example, the outcomes of two independent coins are rendered dependent by the testimony that at least one of them is a tail.

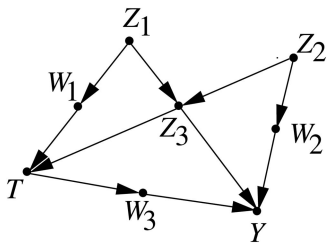

Figure A1. Graphical model illustrating the backdoor criterion. Error terms are not shown explicitly. T = treatment; W = covariates; Y = outcome; Z = covariates.

To illustrate, the path $Z_1 \rightarrow W_1 \rightarrow T$ in Figure A1 is blocked by $S = W_1$, and the path $Z_1 \rightarrow Z_3 \rightarrow T$ is blocked by $S = Z_3$, since each of these nodes emits an arrow along its corresponding path. Moreover, all other paths from Z_1 to T (e.g., $Z_1 \rightarrow Z_3 \rightarrow Y \leftarrow W_3 \leftarrow T$) are blocked by $S = \{\varnothing\}$, since Y is a collider. Consequently, the set $S = \{W_1, Z_3\}$ *d*-separates Z_1 from T, and we can conclude that the conditional independence $Z_1 \perp\!\!\!\perp T | \{W_1, Z_3\}$ will be satisfied in any probability function that this model can generate, regardless of how we parameterize the arrows.

Similarly, the path $Z_1 \rightarrow Z_3 \leftarrow Z_2$ is blocked by the null set $\{\varnothing\}$, but it is not blocked by $S = \{Y\}$ since Y is a descendant of the collision node Z_3. Consequently, the marginal independence $Z_1 \perp\!\!\!\perp Z_2$ will hold in the distribution, but $Z_1 \perp\!\!\!\perp Z_2 | Y$ will most likely not hold.

Each conditional independence implied by a *d*-separation condition in the diagram offers a statistical test that can be performed on the data to confirm or refute the validity of the model. These tests can easily be enumerated by attending to each missing edge in the graph and selecting a set of variables that *d*-separate the pair of variables corresponding to that missing edge.

For example, in Figure A1, three of the missing edges are Z_1–Z_2, Z_1–Y, and Z_2–T, with separating sets $\{\varnothing\}$,$\{T, Z_2, Z_3\}$, and $\{Z_1, Z_3\}$, respectively. Accordingly, the testable implications of M include $Z_1 \perp\!\!\!\perp Z_2$, $Z_1 \perp\!\!\!\perp Y | \{T, Z_2, Z_3\}$, and $Z_2 \perp\!\!\!\perp T | \{Z_1, Z_3\}$. In linear systems, these conditional independence constraints translate into zero partial correlations, or zero coefficients in the corresponding regression equations. For example, the three implications above translate into the following constraints: $r_{Z_1 Z_2} = 0$,$r_{YZ_1 \cdot TZ_2 Z_3} = 0$, and $r_{Z_2 T \cdot Z_1 Z_3} = 0$.

[A1] In other words, the conditional independence $T \perp\!\!\!\perp Y | S$ can be shown to hold in every distribution that the model can generate, regardless of the functional form of the equations in the model and regardless of the distribution of the omitted factors (Pearl & Verma, 1991). See Hayduk et al. (2003), Mulaik (2009), Elwert (2013), and Pearl (2009b, p. 335) for gentle introductions to *d*-separation.

(*Appendices continue*)

Such tests are easily conducted by routine regression techniques, and they provide valuable diagnostic information for model modification, in case any of them fails (see Pearl, 2009b, pp. 143–145). Software routines for automatic detection of all such tests, as well as other implications of graphical models, are reported in Kyono (2010).

Armed with the tool of *d*-separation or *path blocking*, we are ready to tackle the issue of identification using the backdoor criterion. This criterion provides a graphical method of selecting admissible sets of factors and demonstrates that causal quantities such as $P(y \mid do(t))$ can often be identified with no knowledge of the functional form of the equations or the distributions of the latent variables in M.

Definition 2 (admissible sets—the backdoor criterion): A set S is admissible (or sufficient) for estimating the causal effect of T on Y if two conditions hold:

1. No element of S is a descendant of T.
2. The elements of S block all backdoor paths from T to Y—namely, all paths that end with an arrow pointing to T.

Based on this criterion we see, for example, that, in Figure A1, the sets $\{Z_1, Z_2, Z_3\}$, $\{Z_1, Z_3\}$, $\{W_1, Z_3\}$, and $\{W_2, Z_3\}$ (among others) are each sufficient for adjustment because each blocks all backdoor paths between T and Y. The set $\{Z_3\}$, however, is not sufficient for adjustment because it does not block the path $T \leftarrow W_1 \leftarrow Z_1 \rightarrow Z_3 \leftarrow Z_2 \rightarrow W_2 \rightarrow Y$.

The intuition behind the backdoor criterion is as follows. The backdoor paths in the diagram carry spurious associations from T to Y, while the paths directed along the arrows from T to Y carry causative associations. Blocking the former paths (by conditioning on S) ensures that the measured association between T and Y is purely causal, namely, it correctly represents the target quantity: the causal effect of T on Y. The reason for excluding descendants of T (e.g., W_3 or any of its descendants) are discussed in Appendix C, while conditions for relaxing this restriction are given in Pearl (2009b, p. 338) and Shpitser, VanderWeele, and Robins (2010).

The implication of finding a sufficient set, S, is that stratifying on S is guaranteed to remove all confounding bias relative to the causal effect of T on Y. In other words, it renders the causal effect of T on Y identifiable, via

$$P(Y = y \mid do(T = t)) = \sum_s P(Y = y \mid T = t, S = s)P(S = s). \quad \text{(A1)}$$

Since all factors on the right-hand side of the equation are estimable (e.g., by regression) from preinterventional data, the causal effect can likewise be estimated from such data without bias. Moreover, the counterfactual implication of S can be written as $T \perp\!\!\!\perp Y_t \mid S$, also known as *conditional ignobility* (Rosenbaum & Rubin, 1983).

The backdoor criterion allows us to write Equation A1 by inspection, after selecting a sufficient set, S, from the diagram. The selection criterion can be applied systematically to diagrams of any size and shape, thus freeing analysts from judging whether "T is conditionally ignorable given S," a formidable mental task required in the potential-response framework. The criterion also enables the analyst to search for an optimal set of covariates—namely, a set, S, that minimizes measurement cost or sampling variability (Tian, Paz, & Pearl, 1998).

(*Appendices continue*)

Appendix B

Formal Derivation of Conditions for Natural Direct Effect Identification (After Pearl, 2001)

Notation

We retain the notation used in the rest of the article and let T be the control variable (whose effect we seek to assess) and Y be the response variable. We let M stand for the set of all intermediate variables between T and Y that, in the simplest case considered, would be a single variable M as in Figure 4 in the main text.

We use the counterfactual notation $Y_t(u)$ to denote the value that Y would attain in unit (or situation) $U = u$ under the control regime $do(T = t)$. See Equation 4 in the main text and Pearl (2000a, Chapter 7) for formal semantics of these counterfactual expressions. Many concepts associated with direct and indirect effect require comparison to a reference value of T, that is, a value relative to which we measure changes. We designate this reference value by t^*.

Natural Direct Effects: Formulation

Definition 3 (unit-level natural direct effect; qualitative): An event $T = t$ is said to have a natural direct effect on variable Y in situation $U = u$ if the following inequality holds:

$$Y_{t^*}(u) \neq Y_{t,M_{t^*}(u)}(u). \tag{B1}$$

In words, the value of Y under $T = t^*$ differs from its value under $T = t$ even when we keep M at the same value ($M_{t^*}(u)$) that M attains under $T = t^*$.

We can easily extend this definition from events to variables by defining T as having a *natural* direct effect on Y (in model M and situation $U = u$) if there exist two values, t^* and t, that satisfy Equation B1. Note that this definition does not require that we specify a value m for M; that value is determined naturally by the model, once we specify t, t^*, and u.

If one is interested in the magnitude of the natural direct effect, one can take the difference

$$Y_{t,M_{t^*}(u)}(u) - Y_{t^*}(u) \tag{B2}$$

and designate it by the symbol $NDE(t, t^*; Y, u)$ (acronym for natural direct effect). If we are further interested in assessing the average of this difference in a population of units, we have the following:

Definition 4 (average natural direct effect): The average natural direct effect of event $T = t$ on a response variable Y, denoted $NDE(t, t^*; Y)$, is defined as

$$NDE(t, t^*; Y) = E(Y_{t,M_{t^*}}) - E(Y_{t^*}). \tag{B3}$$

Natural Direct Effects: Identification

As noted in Robins and Greenland (1992), we cannot generally evaluate the average natural direct effect from empirical data. Formally, this means that Equation B3 is not reducible to expressions of the form

$$P(Y_t = y) \text{ or } P(Y_{t,m} = y);$$

the former governs the causal effect of T on Y (obtained by randomizing T), and the latter governs the causal effect of T and M on Y (obtained by randomizing both T and M).

We now present conditions under which such reduction is nevertheless feasible.

Theorem 2 (experimental identification): If there exists a set W of covariates, nondescendants of T or M, such that

$$Y_{t,m} \perp\!\!\!\perp M_{t^*} \mid W \quad \text{for all } m \tag{B4}$$

(read: $Y_{t,m}$ is conditionally independent of M_{t^*}, given W), then the average natural direct effect is experimentally identifiable, and it is given by

$$NDE(t, t^*; Y) = \sum_{w,m} [E(Y_{t,m} \mid w) - E(Y_{t^*m} \mid w)] P(M_{t^*} = m \mid w) P(w). \tag{B5}$$

Proof

The first term in Equation B3 can be written

$$E(Y_{t,M_{t^*}} = y) = \sum_w \sum_m E(Y_{t,m} = y \mid M_{t^*} = m, W = w) P(M_{t^*} = m \mid W = w) P(W = w). \tag{B6}$$

Using Equation B4, we obtain

$$E(Y_{t,M_{t^*}} = y) = \sum_w \sum_m E(Y_{t,m} = y \mid W = w) P(M_{t^*} = m \mid W = w) P(W = w). \tag{B7}$$

Each factor in Equation B7 is identifiable: $E(Y_{t,m} = y \mid W = w)$, by randomizing T and M for each value of W, and $P(M_{t^*} = m \mid W = w)$, by randomizing T for each value of W. This proves the assertion in the theorem. Substituting Equation B7 into Equation B3 and using the law of composition $E(Y_{t^*}) = E(Y_{t^*M_{t^*}})$ (Pearl 2000a, p. 229) gives Equation B5 and completes the proof of Theorem 2.

(*Appendices continue*)

The conditional independence relation in Equation B4 can easily be verified from the causal graph associated with the model. Using a graphical interpretation of counterfactuals (Pearl, 2000a, pp. 214–215), this relation reads

$$(Y \perp\!\!\!\perp M \mid W)_{G_{\underline{TM}}}. \tag{B8}$$

In words, W *d*-separates Y from M in the graph formed by deleting all (solid) arrows emanating from T and M.

Figure B1a illustrates a typical graph associated with estimating the direct effect of T on Y. The identifying subgraph is shown in Figure B1b and illustrates how W separates Y from M. The separation condition in Equation B8 is somewhat stronger than Equation B4, since the former implies the latter for every pair of values, t and t^*, of T (see Pearl 2000a, p. 214).

The identification of the natural direct effect from *nonexperimental* data requires stronger conditions. From Equation B5, we see that it is sufficient to identify the conditional probabilities of two counterfactuals: $P(Y_{t,m} = y \mid W = w)$ and $P(M_{t^*} = m \mid W = w)$, where W is any set of covariates that satisfies Equation B4 (or Equation B8). This yields the following criterion for identification:

> **Theorem 3 (nonexperimental identification):** The average natural direct effect $NDE(t, t^*;Y)$ is identifiable in nonexperimental studies if there exists a set W of covariates, nondescendants of T or M, such that for all values m and w we have
>
> (i) $Y_{tm} \perp\!\!\!\perp M_{t^*} \mid W$;
>
> (ii) $P(Y_{t,m} = y \mid W = w)$ and $P(Y_{t^*m} = y \mid W = w)$ are identifiable; and
>
> (iii) $P(M_{t^*} = m \mid W = w)$ is identifiable.
>
> Moreover, if Conditions (i)–(iii) are satisfied, the natural direct effect is given by Equation B5, in which all counterfactual expressions are replaced by their probabilistic estimands.
>
> In particular, for confounding-free models, we obtain the mediation formulas of Equations 16–17 in the main text.

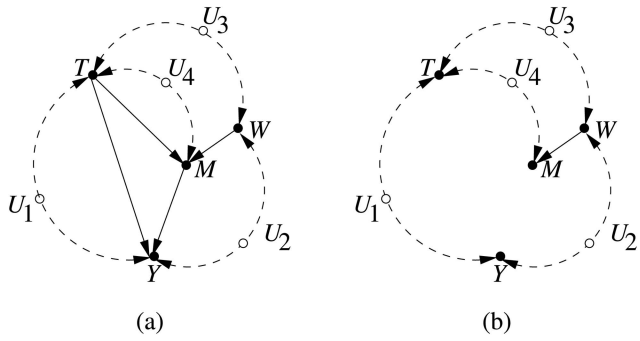

Figure B1. a: A causal model with latent variables (Us) where the natural direct effect can be identified in experimental studies. b: The subgraph $G_{T,M}$ illustrating the criterion of experimental identifiability (see Equation B8): W *d*-separates Y from M. M = mediator; T = treatment; W = covariate; Y = outcome.

(*Appendices continue*)

Appendix C

Why Treatment-Dependent Covariates Cannot Be Used to Deconfound the Mediator-Outcome Process

Assumption Sets A and B both insist that no member of W be affected by the treatment, which is a requirement distinct to the identification of natural effects. For example, to identify the controlled direct effect $CDE(m)$ in Figure 10 in the main text, we can condition on $W = w$, and, using the truncated product formula (Pearl, 2000a, p. 72), we can write

$$\begin{aligned} CDE(m) &= E[Y \mid do(T = 1, M = m)] - E[Y \mid do(T = 0, M = m)] \\ &= \sum_w E[Y \mid T = 1, M = m, W = w]P(T = 1, W = w) \\ &\quad - E[Y \mid T = 0, M = m, W = w]P(T = 0, W = w). \end{aligned}$$

The reason such conditioning does not work for the natural direct effect is that the latter is defined not in terms of a population experiment (i.e., control M to level $M = m$, and change T from $T = 0$ to $T = 1$) but in terms of a hypothetical manipulation at the unit level, namely, for each individual u, freeze M at whatever level it attained for that individual, then change T from $T = 0$ to $T = 1$ and observe the change in Y.

Appendix A shows that in order to convert this unit-based operation to a population-based operation (expressible as a $do(t)$ expression), we must first find a W that deconfounds M from Y (with T fixed) and then, conditioned on that same W, identify the counterfactual expression

$$P(M_t = m \mid W = w).$$

When W is affected by the treatment, this expression is not identifiable even when T is randomized. To see that, we recall that M_t stands for all factors affecting M when T is held fixed. These factors are none other but the omitted factors (or disturbance terms) that affect M, namely, U_M in Figure 1 in the main text. When we condition on W, those factors become correlated with T, which renders T confounded with M.

This can also be seen from the graph, using virtual colliders. The expression $P(M_t = m \mid W = w)$ stands for the causal effect of T on M within a stratum w of W. It is identifiable using the backdoor criterion, which demands that W not be affected by T because, as soon as W is a descendant of any intermediate variable from T to M (including M itself), a virtual collider is formed and a new backdoor path is opened by conditioning on W (Pearl, 2009b, p. 339).

Another way of seeing this is to resort to *do*-calculus. If W is not affected by the treatment, we have $W_t = W$, and we can write

$$\begin{aligned} P(M_t = m \mid W = w) &= P(M_t = m \mid W_t = w) \\ &= \frac{P(M_t = m, W_t = w)}{P(W_t = w)} \\ &= \frac{P(M = m, W = w \mid do(T = t))}{P(W = w \mid do(T = t))} \\ &= P(M = m \mid do(T = t), W = w). \end{aligned}$$

The last expression stands for the causal effect of T on M given that $W = w$ is the posttreatment value of W. It is identifiable by the *do*-calculus, whenever the model permits such identification (Shpitser & Pearl, 2008).

(*Appendices continue*)

It is worth mentioning at this point that treatment-dependent confounders hinder only nonparametric identification of natural effects as defined in Equation B3. The difficulty disappears when we have a parametric representations (as in Equations 21–23 in the main text) or when we compromise on the requirement of freezing M completely at the value it attained prior to the change in treatment. For example, if, in Figure 10 in the main text, we merely disable the process $T \rightarrow M$ and allow M to respond to W as we change T from $T = 0$ to $T = 1$, the resulting direct effect will be identified. These types of direct and indirect effects, which I would like to call *seminatural effects*,[C1] are defined (using parenthetical notation) as

$$SNDE = E[Y(T = 1), M(T = 0, W(T = 1)), W(T = 1)] - E[Y(T = 0)],$$
$$SNIE = E[Y(T = 0), M(T = 1, W(T = 0)), W(T = 0)] - E[Y(T = 0)].$$

Using the derivation leading to Equation B5, one can show that these seminatural effects are identifiable by

$$SNDE = \sum_{mw} E(Y \mid T = 1, M = m, W = w)P(M = m \mid T = 0, W = w) P(W = w \mid T = 1) - E(Y \mid T = 0),$$
$$SNIE = \sum_{mw} E(Y \mid T = 0, M = m, W = w)P(M = m \mid T = 1, W = w) P(W = w \mid T = 0) - E(Y \mid T = 0).$$

Accordingly, the parametric model of Equations 21–23 in the main text would yield the following seminatural effects:

$$SNDE = \beta_2 + \alpha(\beta_4 + \gamma_2\beta_1),$$
$$SNIE = \gamma_1\beta_1,$$
$$TE = \beta_2 + (\gamma_1 + \alpha\gamma_2)(\beta_3 + \beta_1) + \alpha\beta_4,$$
$$TE - SNDE = \gamma_1(\beta_1 + \beta_3) + \beta_3\alpha\gamma_2.$$

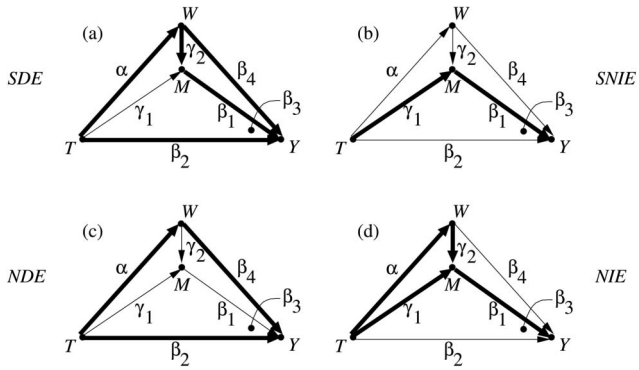

Figure C1. Subgraphs supporting the seminatural direct and indirect effects (*SNDE* in panel a, *SNIE* in Panel b) and those supporting the natural direct and indirect effects (*NDE* in Panel c, *NIE* in Panel d). M = mediator; T = treatment; W = covariate; Y = outcome; α, β, γ = structural coefficients.

Figure C1 depicts the path that supports the *SNDE* (seminatural direct effect) and *SNIE* (seminatural indirect effect) compared with those supporting the *NDE* (natural direct effect) and *NIE* (natural indirect effect) in Equations 24–27 in the main text. We see that the criterion of Avin et al. (2005) is satisfied in the latter, but not the former.

[C1] Huber (2012) called them *partial indirect effects.*

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COMMENT

Comment on Pearl: Practical Implications of Theoretical Results for Causal Mediation Analysis

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Mediation analysis has been extensively applied in psychological and other social science research. A number of methodologists have recently developed a formal theoretical framework for mediation analysis from a modern causal inference perspective. In Imai, Keele, and Tingley (2010), we have offered such an approach to causal mediation analysis that formalizes identification, estimation, and sensitivity analysis in a single framework. This approach has been used by a number of substantive researchers, and in subsequent work we have also further extended it to more complex settings and developed new research designs. In an insightful article, Pearl (2014) proposed an alternative approach that is based on a set of assumptions weaker than ours. In this comment, we demonstrate that the theoretical differences between our identification assumptions and his alternative conditions are likely to be of little practical relevance in the substantive research settings faced by most psychologists and other social scientists. We also show that our proposed estimation algorithms can be easily applied in the situations discussed in Pearl (2014). The methods discussed in this comment and many more are implemented via mediation, an open-source software (Tingley, Yamamoto, Hirose, Keele, & Imai, 2013).

Keywords: causal inference, causal mechanisms, direct and indirect effects, identification, sensitivity analysis

We begin by congratulating Judea Pearl (2014) on his insightful article and thanking Patrick Shrout for giving us an opportunity to provide a comment. In our 2010 *Psychological Methods* article, we proposed a general approach to causal mediation analysis that is based on the formal statistical framework of potential outcomes (Imai, Keele, & Tingley, 2010). Our approach is applicable to a wide range of statistical models, going beyond the traditional linear structural equation framework (see, e.g., Judd & Kenny, 1981; MacKinnon, 2008). We offered a set of identification assumptions, a general estimation strategy, and sensitivity analyses. All of our proposed methodology is implemented in the companion open-source software mediation (Tingley, Yamamoto, Hirose, Keele, & Imai, 2013). Some have extended our methodology to other settings (e.g., Albert & Want, 2014) and implemented it in other software (see, e.g., Muthén, 2011, for Mplus implementation). We are pleased to see that a number of psychologists and other substantive researchers from other disciplines have utilized our methodology in their research (e.g., Fang et al., 2013; Foster, 2013; Gadarian & Albertson, 2014; Linden & Karlson, 2013; Varese, Barkus, & Bentall, 2012; Walters, 2011, 2013, 2014; Yeager, Miu, Powers, & Dweck, 2013; Zeitzoff, 2013).

In his article, Pearl (2014) claimed that the assumption underlying our proposed methodology, which we called *sequential ignorability*, is "overly restrictive and can be relaxed substantially without compromising identification" (p. XXX). In this comment, we demonstrate that the theoretical differences between our identification assumptions and his alternative conditions are likely to be of little practical relevance in the substantive research settings faced by most psychologists and other social scientists. We also show that our proposed estimation algorithms can be easily applied in the situations discussed in Pearl (2014). Thus, although there are theoretical differences between Pearl's approach and ours, these differences have little practical implications for substantive researchers.

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Financial support from the National Science Foundation (SES-0918968) is acknowledged. The original article, in which we proposed a general approach to causal mediation analysis, appeared in this journal as Imai, Keele, and Tingley (2010). The easy-to-use software for implementing the proposed methodology (Tingley et al., 2013) is freely available at the Comprehensive R Archive Network (http://cran.r-project.org/web/packages/mediation).

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To begin, we show that when the treatment is randomized, our assumptions and Pearl's are equivalent. This result implies that in a randomized experiment, where causal mediation analysis is often used, the methodology we proposed in Imai, Keele, and Tingley (2010) is directly applicable without any modification. Similarly, we show that if the treatment and the mediator are "as-if randomized" given potentially different sets of pretreatment covariates in an observational study, our methodology, by adjusting for the full set of covariates, still provides valid estimates of causal mediation effects.[1] Therefore, in these common scenarios, we maintain the recommendation made in Imai, Keele, and Tingley (2010). Namely, substantive researchers should condition on the full set of covariates in order to guard against omitted variable bias.

Next, we consider observational studies where our sequential ignorability assumption fails to hold but Pearl's (2014) alternative assumption identifies the causal mechanism. In these cases, conditioning on the full set of pretreatment covariates leads to biased inference. We derive several practical implications of this theoretically interesting finding. First, if researchers possess precise knowledge of what covariates confound the treatment–mediator and the mediator–outcome relationships, they can still use our general estimation algorithms with different sets of covariates. Our software, mediation, can handle this case in a straightforward manner. Second and more important, we argue that in many observational studies, social science researchers do not possess such definite knowledge. To make the matter worse, it is often difficult to use the observed data to identify a single causal structure from the large number of possible structures.

Our recommendation, therefore, is to conduct a sensitivity analysis. As we explained in Imai, Keele, and Tingley (2010), a sensitivity analysis quantifies the degree to which the key identification assumption must be violated in order for a researcher's original conclusion to be reversed. Fortunately, as discussed in more detail later, this can be implemented straightforwardly by conditioning on different sets of covariates with our method of estimation. This sensitivity analysis is different from the one discussed in Imai, Keele, and Tingley (2010) because different sensitivity analyses are required to examine different violations of sequential ignorability. For example, Imai and Yamamoto (2013) developed yet another sensitivity analysis in the context of multiple mechanisms. For this reason, it is not possible to come up with a sensitivity analysis that covers all scenarios. What is underlying all of these sensitivity analyses, however, is the need to investigate the robustness of one's empirical findings to potential violations of untestable assumptions.

In what follows, we examine the aforementioned results regarding causal mediation analysis in experimental and observational studies. We then briefly discuss some of the remaining methodological challenges for causal mediation analysis and report initial progress we and others have made since our 2010 article. The final section summarizes what we think substantive researchers should take away from this exchange.

Causal Mediation Analysis in Randomized Experiments

We first consider causal mediation analysis in randomized experiments. Although Pearl (2014) confined the scope of his discussion to observational studies, causal mediation analysis is frequently employed with experimental data, particularly in psychology. Thus, it is important to examine whether Pearl's arguments have any practical implications for substantive researchers who conduct mediation analysis within the context of randomized experiments.

Consider the standard experimental design where we randomize the binary treatment variable, T. This means that the treatment assignment T is statistically independent of all observed pretreatment covariates W, unobserved covariates, and potential outcomes $Y(t)$. Now, consider Pearl's (2014) Assumption Set A, where a set of observed covariates W deconfounds the mediator (M)–outcome (Y) relationship, holding the treatment assignment T constant. In the Appendix, we formally show that that Assumption Set A is equivalent to Assumption Set B, or the sequential ignorability assumption used by Imai and colleagues (Imai, Keele, & Tingley, 2010,Imai, Keele, & Yamamoto, 2010). This implies that our proposed methodology provides a valid estimate under Pearl's alternative set of conditions when the treatment assignment is randomized.

Causal Mediation Analysis in Observational Studies

We next consider causal mediation analysis in observational studies, which is the focus of Pearl's (2014) article. Here, we examine two cases. First is the scenario where researchers assume that both the treatment and potential mediators are as-if randomized, given possibly different sets of observed pretreatment covariates. In this case, we show that our methodology, by adjusting for a full set of pretreatment covariates, gives valid estimates of causal mediation effects under Pearl's alternative set of conditions. We then investigate the situation where our sequential ignorability assumption fails to hold and yet researchers can deconfound treatment and mediator by a clever use of covariates.

When Treatment and Mediator Are As-If Randomized, Given Covariates

We begin by considering the situation where the treatment and the observed mediators are as-if randomized after adjustment for possibly different sets of pretreatment covariates. By as-if randomization, we mean the assumption that, once the researcher adjusts for pretreatment covariates that systematically affect the assignment process of the treatment or the naturally observed values of the mediator, the remaining observed variation in the treatment or the mediator is entirely due to chance. That is, the treatment and observed mediator are assigned as if randomized experiments were conducted by nature within a relevant strata defined by the pretreatment covariates (and the treatment in case of the mediator).

We argue that this is the assumption substantive researchers in social sciences often have in mind when they attempt to draw causal inference in observational studies with regression, propensity score matching, weighting, and so forth. Although this is

[1] As is standard in the causal inference literature, by "pretreatment" covariates, we mean that these covariates are not affected by the treatment. Pearl (2014) appears to be unaware of this common usage of the term when he describes one of the limitations of our assumption as follows: "There is no need to require that covariates be pretreatment, as long as they are causally unaffected by the treatment" (p. XXX).

mathematically a stronger assumption than standard ignorability assumptions such as Assumption A-2, B-1, and B-2 in Pearl (2014) (see the Appendix for a formal discussion), many substantive researchers employ this line of reasoning when justifying their ignorability assumptions. In particular, they often appeal to this logic with observational data from natural experiments with haphazard treatment assignments (see Dunning, 2012, for a list of such studies). In a study of election monitoring, for example, Hyde (2007) stated, "I present a natural experiment in which international observers were assigned to polling stations on election day using a method that I did not supervise but that comes very close to random assignment" (p. 46).

What are the practical implications of Pearl's (2014) theoretical findings when the treatment and observed mediator are as-if randomized? In the Appendix, we formally show that, in these settings, our proposed estimation method provides unbiased estimates of causal mediation effects under Pearl's alternative conditions even if one adjusts for a full set of covariates. We illustrate this result with Pearl's education example. In that example, there are two pretreatment covariates, reading skill (V) and the availability of a tutor (W), that confound the relationships between the treatment and the mediator and between the mediator and the outcome, respectively. Reading skill (V) may influence both the enrollment in the educational program (T) and the amount of homework (M). In addition, the availability of a tutor (W) may affect the amount of homework students do (M) as well as their test scores (Y). Now, assume that the enrollment in educational program (T) is as-if random (i.e., randomly assigned among the students who have the same level of reading skill, V). Let us also assume that the variation in the observed amount of homework (M) is due to chance alone once we adjust for the enrollment status (T) and the availability of a tutor (W).

What happens if we adjust for the full set of pretreatment covariates (i.e., $X = \{V, W\}$) when modeling the mediator and the outcome in this setting, as suggested by Imai, Keele, and Tingley (2010)? The result in the Appendix implies that this strategy also leads to the consistent estimates of average causal mediation effects. Although this approach is slightly more complex than the approach Pearl (2014) suggested (because it may involve additional covariates in each model), the inference based on our approach is still valid.

More important, for most substantive researchers, it is unlikely they will know with great certainty which covariates confound the treatment–mediator relationship but do not confound the mediator–outcome relationship (or vice versa). Rather, all observed pretreatment covariates are often candidate confounders for both treatment–mediator and mediator–outcome relationships. In Pearl's example, intelligence and socioeconomic status may also affect the amount of homework (M) and test scores (Y) as well as the program enrollment (T). Whenever there is such uncertainty, it is better to adjust for the full set of pretreatment covariates (X). The reason is simple. Doing so will protect one against the potential bias that results from failing to adjust for relevant confounders. In contrast, under the assumption that the both treatment and observed mediator are as-if randomized, adjusting for the full set of covariates (X) does not induce bias even when some covariates are irrelevant.

What if researchers actually know for sure what covariates to include in each model? In this rare but favorable situation, as Pearl (2014) showed, the mediator model only needs to adjust for V; similarly, it is sufficient to adjust for W when modeling the outcome. Fortunately, this can be easily accommodated within the general estimation algorithm proposed in Imai, Keele, and Tingley (2010) and implemented in our software, mediation. The only change that needs to be made to the algorithm is to estimate the mediator and outcome regression models with the different sets of covariates (V for the mediator and W for the outcome). The rest of the estimation procedure can proceed without modification.

When the Unobserved Confounders Are Deconfoundable

Next, we consider the cases where adjusting for the full set of covariates (X) in observational studies induces bias. Unlike the situations considered so far, these settings represent a key difference between the assumptions presented by Pearl (2014) and the assumption used in Imai, Keele, and Tingley (2010). In particular, our assumption fails to identify causal mediation effects if there exist unobserved pretreatment confounders and yet they can be deconfounded via a clever use of observed pretreatment confounders.

When might this occur? Pearl (2014) described examples like these in Figure 5 of his article. Consider model (c) of the figure, which is reproduced here in Figure 1. In Pearl's example, suppose that an unobserved variable (represented by an open circle at the upper left corner), which confounds the treatment (program take-up) and mediator (amount of homework), is parents' language skill and yet we only observe students' language skill, W_2. Here, the key assumption is that parent's language skill affects the amount of homework done by students only through student's language skill. Similarly, the model posits that there exists another unobserved variable (represented by an open circle at the bottom), say parents' intelligence, which confounds the treatment and the outcome (students' test scores). We observe student's intelligence, W_3. Another key assumption of this causal structure is that parents' intelligence influences program take-up only through students' intelligence. In addition, the model assumes that students' language skill affects neither the treatment nor the outcome directly and that students' intelligence affects neither the mediator nor the outcome directly. Under this situation, Pearl is correct in that adjusting for a full set of observed covariates (i.e., W_2 and W_3) leads to biased inference.

We argue that, in many substantive research settings, scholars are unlikely to possess such precise knowledge about the structure of confounding. In Pearl's (2014) example, with a small number of covariates, one can reason about causal structure. In most observational research, however, researchers measure a large number of covariates, and the exact structure between these covariates and unobservables is usually highly uncertain.

If our theoretical knowledge fails to guide us to the correct specification of the causal structure, could the observed data be used to inform our decision? The answer is a qualified yes. As Pearl (2009) showed in his related foundational work, the models such as those in his Figure 5 sometimes have implications about the conditional independences among observed variables, which we might then test statistically using the observed data. The problem, however, is that in practice such statistical tests are likely to suffer from false positives and negatives due to small sample size and multiple testing. Thus, it is likely that there will remain

substantial ambiguity about the "correct" specification of a causal model in substantive research.

In the presence of such ambiguity, what should empirical researchers do in practice? We again recommend a sensitivity analysis. Researchers should first identify a set of plausible models based on their prior knowledge. Such models may include a scenario like the one above, where there exist unobserved confounders and yet observed covariates can deconfound them. Under each of the selected models, researchers can estimate the average causal mediation effects while adjusting for different sets of observed covariates in the mediator and outcome models. As mentioned earlier, our algorithms and software can easily accommodate these different models. Researchers could then present a range of average causal mediation effect estimates that are possible under these alternative identification assumptions.[2]

Causal Mediation Analysis With Multiple Mediators

In the section entitled "Coping With Treatment-Dependent Confounders," Pearl (2014) studied a case of multiple mediators, whose directed acrylic graph (DAG) is reproduced here in Figure 2. As we also noted in Imai, Keele, and Tingley (2010) and our other related works, Pearl reminded us of an important fact that whenever there exists a treatment-dependent confounder (i.e., W in this DAG), the causal mediation effect with respect to M is not identifiable under our sequential ignorability assumption or Pearl's alternative set of assumptions.

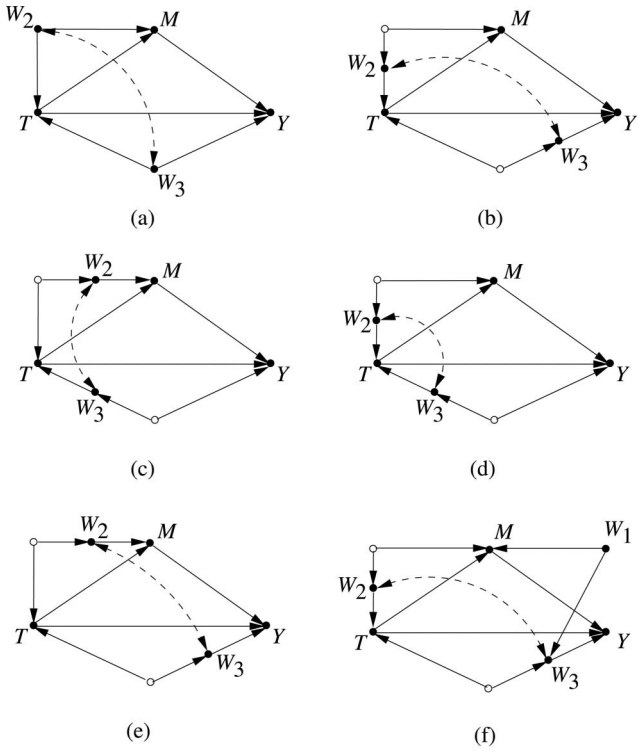

Figure 1. From "Interpretation and Identification of Causal Mediation," by J. Pearl, 2014, *Psychological Methods, 19,* p. XXX. Copyright 2014 by the American Psychological Association.

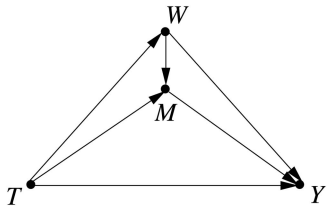

Figure 2. From "Interpretation and Identification of Causal Mediation," by J. Pearl, 2014, *Psychological Methods, 19,* p. XXX. Copyright 2014 by the American Psychological Association.

In Imai and Yamamoto (2013), we studied the same DAG using the following semiparametric varying-coefficient model,

$$Y_i = \beta_{1i}M_i + \beta_{2i}T_i + \beta_{3i}T_iM_i + \beta_{4i}W_i + U_{1i}. \quad (1)$$

$$M_i = \gamma_{1i}T_i + \gamma_{2i}W_i + U_{2i}. \quad (2)$$

$$W_i = \alpha_iT_i + U_{3i}. \quad (3)$$

This model is more general than the standard linear structural equation model studied in Pearl (2014). The difference is that we allow coefficients to vary, in an arbitrary fashion, across individual observations. In the standard linear structural equation model, these coefficients are assumed to be constant across observations (e.g., $\beta_{1i} = \beta_1$ for all i).

Under this general setting, Imai and Yamamoto (2013) showed that the average causal mediation effect, which corresponds to the combined paths of $T \rightarrow M \rightarrow Y$ and $T \rightarrow W \rightarrow M \rightarrow Y$, is not identifiable. This contrasts with the result given in Pearl (2014) under the standard structural linear equation model. Imai and Yamamoto (2013) showed that, in essence, when a treatment-dependent confounder exists, the interaction effect heterogeneity (i.e., the fact that the coefficient β_{3i} may vary across observations) makes the identification difficult. They then proposed a sensitivity analysis by characterizing the average causal mediation effect as a function of the degree of this interaction effect heterogeneity; namely, the variance of β_{3i}. As before, the key idea here is that when an untestable assumption is required for identification of causal effects, a sensitivity analysis is useful for quantifying the robustness of empirical findings to the potential violation of the assumption.

We believe that the investigation of multiple mediators is a relatively unexplored area of research, and yet in most substantive research there exist multiple mediators that are causally dependent of one another. Some researchers have already started to make progresses on this important problem (e.g., Albert & Nelson, 2011; Tchetgen Tchetgen & VanderWeele, 2014), and we look forward to further developments in the future.

Toward More Credible Causal Mediation Analysis

As evident from this discussion, causal mediation analysis is difficult because it requires untestable assumptions for identification. To

[2] Of importance, this form of sensitivity analysis is different from the one proposed in Imai, Keele, and Tingley (2010). That form of sensitivity analysis is still valid for a broad range of situations discussed by Pearl (2014), but it is not valid for the cases discussed in this section, where conditioning on the same set of confounders can produce bias.

cope with this problem, in Imai, Keele, and Tingley (2010) and here, we have suggested the use of sensitivity analyses. Such analyses allow us to investigate the robustness of our empirical findings to the potential violation of these untestable assumptions. Nevertheless, sensitivity analyses have their own limitations. Although such analyses can tell us a range of possible answers, they cannot be used to identify causal mediation effects themselves.

To make progress toward more credible causal mediation analysis, we need better research design strategies. In Imai, Tingley, and Yamamoto (2013), we have considered several experimental designs where the average causal mediation effects can be identified with assumptions that are potentially more plausible than those required under a standard experiment where the treatment assignment alone is randomized. Our new experimental designs are based on the possibility that the mediator can be either directly or indirectly manipulated in certain situations. We show that when such manipulation is possible, causal mediation effect estimates can be bounded in an informative manner without assuming the ignorability of the mediator, as in Assumption Sets A and B. These experimental designs can also serve as templates for observational studies, as we illustrate with political science examples in Imai, Keele, Tingley, and Yamamoto (2011). We believe that such a design-based approach is the most effective way to improve the credibility of causal mediation analysis. And when design based approaches are unavailable, sensitivity analysis remains essential to credible causal mediation analysis.

Concluding Remarks

Once again Pearl (2014) has demonstrated how DAGs can highlight important subtleties in the identification of causal effects. In this comment, we focused on the practical implications of his theoretical results. We also briefly described our initial attempts toward the remaining methodological challenges of causal mediation analysis; namely, multiple mediator and research design issues. We conclude by outlining what we think are the key points that substantive researchers should take away from this exchange.

- Randomization of treatment assignment protects against the complex nature of adjustments raised in Pearl (2014). We proved that when the treatment is randomized, Pearl's alternative assumption is equivalent to our sequential ignorability assumption.
- In observational studies, when both the treatment and the observed values of the mediator are as-if random, it is advisable to adjust for the full set of pretreatment covariates. Failure to include relevant confounders can result in bias. Including irrelevant covariates may complicate the modeling, but it does not introduce bias under this scenario.
- As Pearl (2014) has shown, even when unobserved confounders exist, it is sometimes possible to consistently estimate the average causal mediation effect by adjusting for observed covariates in a clever way. However, in practice, theoretical knowledge is unlikely to be precise enough to lead to such an analytic strategy. We therefore recommend a sensitivity analysis, estimating causal mediation effects under various plausible scenarios and examining the robustness of one's empirical findings to potential violations of key assumptions.
- For the analysis of multiple mediators, analysts should prefer the method of Imai and Yamamoto (2013) over the one outlined by Pearl (2014), because the former imposes weaker assumptions than the latter. We emphasize that new research designs are needed to improve the credibility of causal mediation analysis. Some initial attempts in this direction are described in Imai et al. (2011) and Imai et al. (2013).

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Appendix

Mathematical Proofs

First, we restate Assumption Sets A and B from Pearl (2014) using our current notation.

ASSUMPTION SET A *There exists a set W of observed covariates such that:*

A-1: *No member of W is affected by treatment T.*

$$\text{A-2: } M(t) \perp\!\!\!\perp Y(t', m) \mid W.$$

$$\text{A-3: } p(M(t) = m \mid W) \text{ is identifiable.}$$

$$\text{A-4: } p(Y(t, m) = y \mid W) \text{ is identifiable.}$$

ASSUMPTION SET B *There exists a set W of observed covariates such that:*

$$\text{B-1: } M \perp\!\!\!\perp Y(t', m) \mid T = t, W.$$

$$\text{B-2: } T \perp\!\!\!\perp \{Y(t', m), M(t)\} \mid W.$$

We now prove that Assumption Sets A and B are equivalent when T is randomized. That is, we consider the following additional assumption D to represent the randomization of T:

$$\text{D: } T \perp\!\!\!\perp \{Y(t', m), M(t), W\}.$$

Pearl (2014) showed that Assumption Set A is necessary for Assumption Set B. The proof of sufficiency is immediate by noting that A-2 and D imply B-1 and that D implies B-2.

Next, we prove that Assumption Set B is also satisfied when T and M are as-if randomized conditional on V and $\{T, W\}$, respectively, where $X = \{V, W\}$. That is, we consider the following Assumption Set D′:

ASSUMPTION SET D′ *There exist two possibly overlapping sets W, V of observed covariates such that:*

$$\text{D′-1: } M \perp\!\!\!\perp \{Y(t', m), V\} \mid T = t, W.$$

$$\text{D′-2: } T \perp\!\!\!\perp \{Y(t', m), M(t), W\} \mid V.$$

We now show that Assumption Set D′ implies Assumption Set B. The proof is again immediate by noting that D′-1 and D′-2 imply B′-1 and D′-2 implies B′-2.

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REPLY

Reply to Commentary by Imai, Keele, Tingley, and Yamamoto Concerning Causal Mediation Analysis

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This comment clarifies how structural causal models unify the graphical and potential outcome approaches to mediation, and why the resulting mediation formulas are identical in both frameworks. It further explains under what conditions ignorability-based assumptions are over-restrictive and why such assumptions require graphical interpretations before they can be judged for plausibility. Finally, the comment explains the key difference between traditional and modern methods of causal mediation, and demonstrates why the notion of mediation requires counterfactual rather than Bayes conditionals to be properly defined.

Keywords: mediation formula, seeing versus doing, sequential ignorability, graphical methods, structural causal models, counterfactuals

I am happy to join Imai, Keele, Tingley, and Yamamoto (2014) in celebrating the full convergence of our respective analyses toward a unified understanding of causal mediation. I am referring to the analysis presented in Pearl (2001; reproduced in Pearl, 2014a) on the one hand, and the analyses and implementations of Imai Keele, and Tingley (2010), Imai, Keele, Tingley, and Yamamoto (2010), and Imai, Keele, and Yamamoto (2010) on the other. In fact, when I first read Imai, Keele, and Yamamoto (2010), I had no doubt that despite some dissimilarities in the presentation of the assumptions, the two works would coincide on all fronts: definitions, basic assumptions, identification, and estimation algorithms. The reason for my confidence was that in 2001 I had approached the mediation problem from the symbiotic mathematical framework of structural causal models (SCM; Pearl, 2000, Chapter 7; Pearl, 2009a), which unifies the graphical, potential outcome and structural equation frameworks and permits researchers to combine the merits of each representation; structural equations and graphical models best represent what a researcher believes, while potential outcomes represent what a researcher seeks to estimate.

A logical analysis of SCM theory further revealed that structural equations and potential outcomes are logically equivalent; a theorem in one is a theorem in the other. They differ only in the language in which assumptions are cast; structural equations cast assumptions in the language in which scientific knowledge is stored, while potential outcomes cast those same assumptions in terms of quantities that one wishes to estimate (e.g., counterfactuals). This means that any researcher who accepts the potential outcome framework can use the power of graphs and structural equations for advantage and be assured the validity of the result. This also means that the power of graphs lies not merely in their clarity of visualizing assumptions, but also in computing complex implications of those assumptions. Typical implications are conditional independencies among variables and counterfactuals, what covariates need be controlled to remove confounding or selection bias, whether effects can be identified, and more. (Praising their transparency while ignoring their inferential power misses the main role that graphs play in modern causal analysis.)

Armed with these symbiotic tools, I derived identification conditions in the algebra of counterfactuals and presented them in two languages, potential outcomes and graphical. Not surprisingly, the mediation formulas derived in Imai, Keele, and Yamamoto (2010) coincide precisely with those derived in Pearl (2001), Equations 8, 17, 26, and 27. This is to be expected, since the two are but variants of the same mathematical umbrella, differing merely in the type of assumptions one is willing to posit and defend and the language one chooses to communicate the assumptions.

The assumptions posited in Imai, Keele, and Yamamoto (2010) added two restrictions to those articulated in Pearl (2001):

1. Commence the analysis with two ignorability assumptions (*B*-1 and *B*-2 in Pearl, 2014a). The latter is automatically satisfied in randomized studies.

2. Satisfy these two assumptions with the same set (W) of observed covariates.

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Clearly, all identification results produced under these restrictions will be valid in the symbiotic system of SCM (Pearl, 2001), in which these restrictions were not imposed.

In Pearl (2014a) I identified the set of circumstances in which these two added restrictions lead to missed opportunities, and the current commentary by Imai, Keele, et al. (2014) identified conditions under which the added restrictions will cause no practical loss of opportunities. The two studies complement each other and provide valuable information; they tell researchers when the inference systems of Imai and colleagues (Imai, Keele, & Tingley, 2010; Imai, Keele, et al., 2010; Imai, Keele, & Yamamoto, 2010) operate in perfect harmony with the methodology presented in Pearl (2001).

Specifically, Imai, Keele, et al. (2014) have shown that the restrictions imposed by sequential ignorability play a role in observational studies but not in studies where treatment is randomized. Additionally, the extra-restriction of conditioning on the same set of covariates may not be too severe in certain observational studies. I concur with most of these observations and commend Imai, Keele, et al. (2014) for bringing them to readers' attention.

I cannot accept, however, their conclusion that "including irrelevant covariates may complicate the modeling but does not compromise the identification of causal mediation effects under the as-if randomization assumption" (Imai, Keele, et al., 2014, pp. 482–487). Whether covariates are relevant or irrelevant depends on whether the "as-if randomization assumption" holds after their inclusion, which makes the sentence above circular, if not contradictory. The "as-if randomized" assumption can easily be violated by including what may appear to be irrelevant pretreatment covariates.[1] Moreover, the validity of the "as-if randomization assumption" may depend on many other assumptions encoded in the model; hence, no mortal can judge its plausibility without the aid of graphs.[2] Fortunately, the graphical procedure presented in Pearl (2014a) allow researchers to mechanize the choice of the relevant covariates, and I hope that Imai, Keele, et al., 2014 can implement this procedure in their flexible software. A prerequisite for accomplishing this function is to let users articulate assumptions in the language of scientific understanding—namely, graphs—and let estimation procedures and covariate selection be derived (mechanically) from those assumptions, rather than chosen a priori.

In the remainder of this article, I concentrate on an issue that is common to all players in causal mediation analysis. It concerns ways of improving the understanding of causal mediation among the uninitiated.

Impediments to such understanding come from several research communities.

1. Potential outcomes enthusiasts reject mediation when the mediator is nonmanipulable.

2. Traditional statisticians fear that without extensive reading of the philosophical writings of Aristotle, Kant, and Hume, they are not well equipped to tackle the subject of causation, especially when it involves claims based on untested assumptions.

3. Traditional mediation analysts do not understand the sudden intrusion of counterfactuals into their field, which thus far has been dominated by regression analysis.

4. Economists, who adore counterfactuals (although they find difficulties in defining them; Pearl, 2009b, p. 379) are not convinced that mediation analysis could help policy makers.

I will address the third group, namely, the traditional mediation analysts usually connected with the school of Baron and Kenny (1986), since the difficulties faced by this school are endemic among other groups as well and constitute the key impediment to a wider acceptance of causal mediation. As traditionalists examine modern definitions of direct and indirect effects, even those based on structural equations (e.g., Equations 7–10 in Pearl, 2014a), the thing that strikes them as odd is the absence of a conditioning operator in any of these definitions. Whereas in the linear structural equation modeling (SEM) tradition effects are associated with conditional expectations or regression slopes conditioned on holding some variables constant, here we plug the value of the variables we wish to keep constant (or control for) directly into the equation (or into the subscript of a counterfactual), but we never place that variable behind a conditioning bar. In other words, we write $E\{f_Y[1, M = m]\}$ or $E[Y_{1,m}]$ but not $E(Y \mid T = 1, M = m)$.

Readers versed in the distinction between "seeing" and "doing" (Lindley, 2002; Pearl, 1993; Pearl, 2009b, pp. 421–428; Spirtes, Glymour, & Scheines, 1993) or between "controlling for" and "setting" will recognize immediately that in mediation, the proper operator is "doing," not "seeing"; it is this difference that gives causal mediation analysis a claim to the title "causal." Most traditionalists, however, are not attuned to this distinction and when presented with the modern definitions of direct and indirect effect tend to voice skepticism: "Do we really need those counterfactuals?" or "Do we really need to treat a structural equation in this manner? Why not condition on $M = m$?"

The urge to condition on variables held constant is in fact so intense that I hold it accountable for a century of blunders and confusions; from "probabilistic causality" (Suppes, 1970; [Pearl, 2011b]) to "evidential decision theory" (Jeffrey, 1965; [Pearl, 2009b, pp. 108–109]) and Simpson's paradox (Simpson, 1951; [Pearl, 2009b, pp. 173–180; Pearl, 2014b]); from Fisher's error in handling mediation (Fisher, 1935; [Rubin, 2005]) to "principal stratification" mishandling of mediation (Rubin, 2004; [Pearl, 2011a]) from misinterpretations of structural equations (Freedman, 1987; Hendry, 1995; Holland, 1995; Sobel, 2008; Wermuth, 1992; [Bollen & Pearl, 2013; Pearl, 2009b, pp. 135–138]) to the

[1] For a lively discussion concerning the harm of including seemingly irrelevant covariates, see Pearl (2009c); Rubin (2009); Shrier (2009); Sjölander (2009). The collider X in Figure 9 of Pearl (2014a) is an example of a covariate that would compromise identification if included in the analysis (assuming a randomized treatment).

[2] Skeptics are invited to guess whether $M_t \perp T|Y$ holds in the model of Figure 1A, namely, whether the effect of T on M is ignorable conditional on Y. Graphs replace such formidable mental tasks with transparent scientific judgments on whether confounding factors exist between specific pairs of variables, satisfying the backdoor criterion (see Pearl, 2014a, Appendix A).

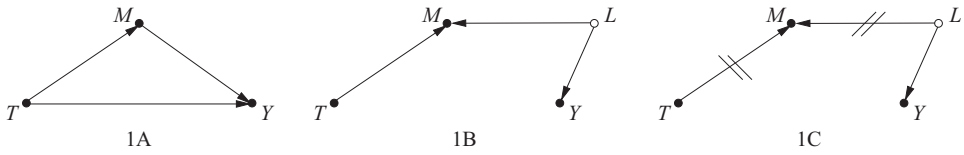

Figure 1. Demonstrating the difference between "controlling for *M*" and "fixing *M*." A: The classical mediation model. B: A model where the direct effect of *T* on *Y* is zero and yet "controlling for" *M* would yield a non-zero difference between units under $T = 0$ and those under $T = 1$. C: "Fixing" *M* amounts to overruling the influences of *T* and *L* on *M*, leading to correct estimate of the direct effect (= 0).

structural–regressional confusion in econometric textbooks today ([Chen & Pearl, 2013]).[3]

What caused this confusion, and how did it enter the world of mediation? The urge to condition stems from the absence of probabilistic notation for the notion of "holding *M* constant," which has forced generations of statisticians to use a surrogate in the form of "conditioning on *M*"—the only surrogate licensed to them by probability theory.

The history of mediation analysis offers a compelling narrative on why the conditioning habit took roots, and why it should be uprooted.

Examine the basic mediation model (Figure 1A) with *M* (partially) mediating between *T* and *Y*. Why are we tempted to "control" for *M* when we wish to estimate the direct effect of *T* on *Y*? The reason is that if we succeeded in preventing *M* from changing, then whatever changes we measure in *Y* would be attributable solely to variations in *T*, and we would then be justified in proclaiming the response observed as "direct effect of *T* on *Y*." Unfortunately, the language of probability theory does not possess the notation to express the idea of preventing *M* from changing or physically holding *M* constant. The only operator probability allows us to use is conditioning, which is what we do when we control for *M* in the conventional way. In other words, instead of physically holding *M* constant (say, at $M = m$) and comparing *Y* for units under $T = 1$ to those under $T = 0$, we allow *M* to vary but ignore all units except those in which *M* achieves the value $M = m$. Students of causality know that these two operations are profoundly different and give totally different results, except in the case of no omitted variables. Yet to most traditionalists, this would come as a total surprise and would elicit requests for explicit demonstration. Stunned by the cultural divide between the two camps, and having found no convincing demonstration in the literature,[4] I believe it is appropriate to provide one here; it is absolutely pivotal to the understanding of causal mediation.

Assume that there is a latent variable *L* causing both *M* and *Y* as shown in Figure 1B. To simplify the discussion, assume further that the structural equations are $Y = 0 \cdot T + 0 \cdot M + L$ and $M = T + L$. Obviously, the direct effect of *T* on *Y* in this case is zero, but this is not what we would get if we "control for *M*" and compare subjects under $T = 1$ to those under $T = 0$ at the same level of $M = 0$. In the former group we would find $Y = L = M - T = 0 - 1 = -1$, whereas in the latter group we would find $Y = L = M - T = 0 - 0 = 0$. In other words, in order to keep the same score of $M = 0$ for the two groups, *L* had to change from $L = -1$ to $L = 0$. Thus, we are unwittingly comparing apples and oranges (i.e., subjects for which $L = -1$ to those for which $L = 0$); not surprisingly, we obtain an erroneous estimate of (–1) for a direct effect that in reality is zero.

Now let us examine what we obtain from the counterfactual expression

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

for $M = 0$ (same for $M = 1$). Substituting the structural equation for the counterfactuals, we get

$$\begin{aligned} CDE(M = 0) &= E[Y(1, 0)] - E[Y(0, 0)] \\ &= E[0 \cdot 1 + 0 \cdot 0 + L] - E[0 \cdot 0 + 0 \cdot 0 + L], \\ &= E[L - L] = 0 \end{aligned}$$

as expected. The reason we obtained the correct result is that we simulated correctly what we set out to do: namely, to physically hold *M* constant rather than condition on *M*. In the former case *L* remains unchanged, because the physical operation of holding *M* constant and changing *T* does not affect *L*. In the latter, when we condition on a constant *M*, *L* must compensate for varying *T* to satisfy the equation $M = T + L$. In short, counterfactual conditioning reflects a physical intervention, whereas statistical conditioning reflects filtered observation. To avoid confusion between the two, I used the notation $E[Y \mid do(T = t)]$ as distinguished from ordinary conditional expectation, $E[Y \mid T = t]$ (Pearl, 2009b, Chapter 3).

The habit of translating "hold *M* constant" into "condition on *M*" became deeply entrenched in the statistical culture (see Lindley, 2002; Pearl, 1993; Spirtes et al., 1993), not by deliberate negligence but due to the coarseness of its language (probability theory), which fails to provide an appropriate operator for "holding *M* constant." Absent such an operator, statisticians (including Fisher, 1935) were pressed to use the only operator available to them—conditioning—and a century of confusion came into being.

Traditional mediation analysts of the Baron and Kenny school were not unaware of the dangers lurking from conditioning (Judd & Kenny, 1981, 2010). However, lacking an appropriate operator for "fixing *M*," they settled on a compromise; they defined the direct effect as

$$c' = E[Y|T = 1, M = 0)] - E[Y|T = 0, M = 0)]$$

and accompanied this definition with a warning that it is valid only under the assumption of "no omitted variables."

[3] In this paragraph, the unbracketed citations refer to articles where confusions are present, while citations in square brackets refer to articles where confusions are unveiled or resolved.

[4] The inappropriateness of conditioning on a mediator has been demonstrated in Pearl (1998) and Robins and Greenland (1992) and by many authors since. The demonstration provided below, however, is algebraic and may be more convincing to researchers new to graphical modeling.

Causal analysis circumvents this compromise upon realizing that the operator needed for "fixing M," while undefinable in probability theory, is well defined in SEM, both parametric and nonparametric, through the $do(M = m)$ operator. It calls for modifying the model by replacing the equation that determines M with a constant $M = m$ and keeping all other equations unaltered (Balke & Pearl, 1995; Pearl, 1993). This "surgical" operator permits researchers to state their intent using expressions such as $E(Y \mid do(M = m))$ or $Y(1,M)$, yielding $CDE(M) = E[Y(1,M)] - E[Y(0,M)]$. Modern treatment of direct and indirect effects owes its development to this notational provision and to the SEM semantics of interventions (Haavelmo, 1943/1995; Spirtes et al., 1993) and counterfactuals (Balke & Pearl, 1995).

I believe that, with this narrative in mind, traditional SEM analysts should not have any difficulties accepting the premises of causal mediation. First, these analysts already accept structural equations as the basis for modeling (most statisticians do not). Second, counterfactuals in our narrative enter naturally, as abbreviated structural equations (see Equation 4 in Pearl, 2014a). Third, traditional SEM analysts can easily appreciate the benefits of causal mediation analysis, since it endows them with two new capabilities: (a) extending mediation analysis to nonlinear functions and highly interactive variables, continuous as well as discrete; and (b) distinguishing between the necessary and sufficient notions of mediation.

I hope this exchange helps clarify the logic and scope of causal mediation analysis as well as the unifying power of the SCM methodology. I thank Imai, Keele, et al. (2014)for commenting on my article and contributing to this clarification.

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New Editors Appointed, 2016–2021

The Publications and Communications Board of the American Psychological Association announces the appointment of 9 new editors for 6-year terms beginning in 2016. As of January 1, 2015, manuscripts should be directed as follows:

- *History of Psychology* (http://www.apa.org/pubs/journals/hop/), **Nadine M. Weidman, PhD,** Harvard University
- *Journal of Family Psychology* (http://www.apa.org/pubs/journals/fam/), **Barbara H. Fiese, PhD,** University of Illinois at Urbana–Champaign
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