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.

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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.

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

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[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 acyclic 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.
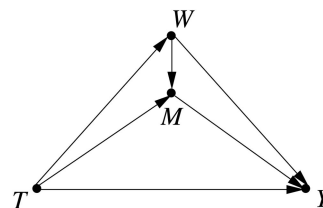

Figure 1. From "Interpretation and Identification of Causal Mediation," by J. Pearl, 2014, *Psychological Methods, 19,* p. XXX. Copyright 2014 by the American Psychological Association.

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
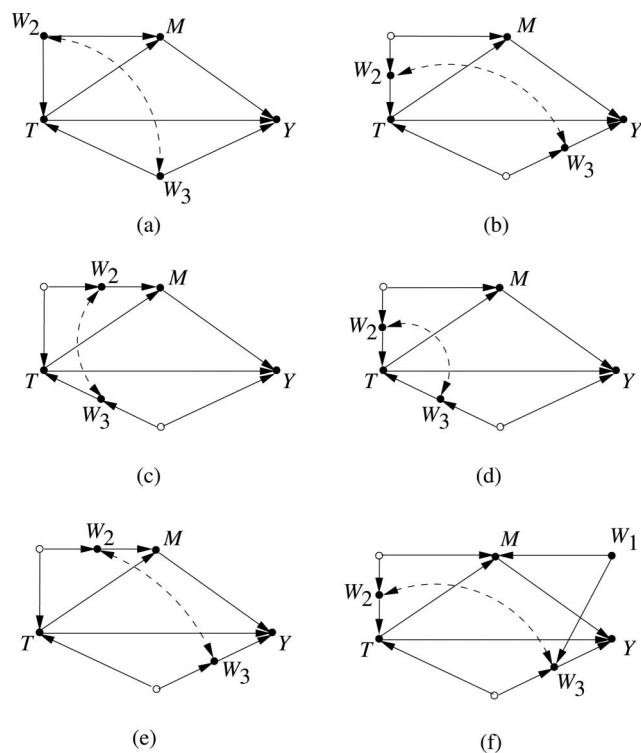
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[2] Of importance, this form of sensitivity analysis is different from the one proposed in Imai, Keele, and Tingley (2010). That form of sensitivity analysis is still valid for a broad range of situations discussed by Pearl (2014), but it is not valid 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.*

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

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

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

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

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

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:

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:*

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

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.