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RE: A Practical Example Demonstrating the Utility of Single-world Intervention Graphs

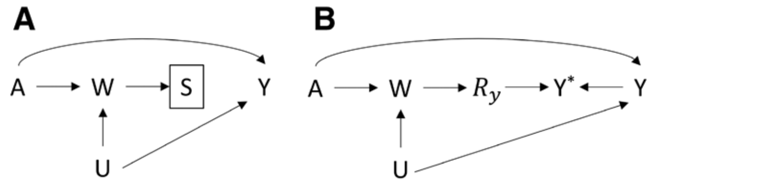

FIGURE. Causal diagrams for modeling attrition. A, Causal diagram of the vaccine trial used in the study by Breskin et al.[1]. B, The graphical representation of the vaccine trial when viewed as a missing data problem.

To the Editor:

In a recent communication, Breskin et al[1] aimed to demonstrate "how single-world intervention graphs can supplement traditional causal diagrams." The example used in their demonstration involved selection bias due to attrition, namely, subjects dropping out from a randomized trial before the outcome is observed. Here, we use the same example to demonstrate the opposite conclusion; the derivation presented by Breskin et al is in fact longer and more complicated than the standard, three-step derivation facilitated by traditional causal diagrams. We further show that more natural solutions to attrition problems are obtained when viewed as missing-data problems encoded in causal diagrams.

The trial example of Breskin et al is shown in the causal diagram of Figure A. The task is to estimate the average causal effect $E[Y|do(A=a)]$ in the general population, given complete data on A (vaccine assignment) and W (injection site pain), whereas data on Y (disease outcome) is available only for those subjects who did not drop out of the study ($S=0$). U stands for unmeasured health status, and participants with poor health ($U=1$) are assumed to be both more likely to experience pain and get the disease.

The standard strategy of causal diagrams is to convert the query expression, $E[Y|do\ (A=a)]$, into an equivalent expression that can be estimated from the available data.[2,3] The derivation goes as follows:

$$E[Y\,|do(A=a)]=E[Y\,|A=a] \quad (1)$$

$$=\sum_{W}E[Y\mid A=a,W=w]P(W=w\mid A=a) \quad (2)$$

$$=\sum_{w}E[Y|A=a,W=w,S=0]P(W=w|A=a) \quad (3)$$

The first equality is licensed by randomization (or null backdoor condition), the second by the law of total probability, and the latter by d-separation, that is, $Y \perp\!\!\!\perp S|\{A, W\}$. All components of the final expression can be estimated from the available data; the first factor from units who remained in the study ($S=0$), and the second from all units entering the trial. As noted in the study by Breskin et al, the same derivation holds if the arrows $A \rightarrow S$ and $W \rightarrow Y$ are added to the diagram.

The extreme simplicity and transparency of this derivation, vis-a-vis the elaborate derivation introduced by Breskin et al is an illustrative example of the utility of traditional causal diagrams in modeling attrition, censoring, selection bias, and missing data problems Single-world intervention graphs may be useful for researchers who are determined to verify ignorability conditions such as $Y(a) \perp\!\!\!\perp S(a)|W(a)$, but d-separation renders such efforts unnecessary. A wide variety of selection bias and cross-population problems can be solved by the same query-conversion strategy that we described above, operating on traditional causal diagrams.[2,3] General conditions for identifying causal effects under both confounding and selection bias are presented in the study by Correa et al.[4].

As a final remark, we note that the example presented by Breskin et al may be better formulated as a missing data problem. Such formulation would allow us to specify explicitly which variables are still measured for every subject who drops out of the study. For instance, in the current example, missingness only occurs in the outcome variable Y, a fact that is not represented in the diagram of Figure A. Missingness graphs,[5] on the other hand, allow us to formally encode this distinction, as shown in Figure B.

Here, the variable R_y replaces S and represents the "missingness mechanism" of the outcome variable Y, which is not observed directly. Instead, the variable Y^* stands for what we can observe of Y, such that $Y^* = Y$ when $R_y = 0$, and $Y^* =$ missing when $R_y = 1$. In this case, the derivation would proceed as before, but this formalism has some benefits: (1) it explicitly tells us that the two factors in Eq. 3 can be estimated from the same study and (2) more complicated missingness mechanisms can be easily accommodated. A comprehensive review of graphical methods for missing data can be found in the study by Mohan and Pearl.[6]

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The Authors Respond

To the Editor:

We read with keen interest Cinelli and Pearl's[1] response to our letter.[2] A key difference in our approaches can be appreciated by examining the first line of each of our derivations. In our derivation, the quantity we begin with is $E[Y(a)]$, but Cinelli and Pearl[1] begin with $E[Y \mid do(A=a)]$. Thus, a fundamental distinction, previously highlighted by Pearl,[3] is that our approach introduces new variables (in particular, the counterfactuals or potential outcomes $Y(a)$, $W(a)$, and $S(a)$), whereas Cinelli and Pearl[1] introduce a new operator (the *do* operator). Because these counterfactuals appear on the single world intervention graph in Figure B of our letter, the counterfactual independencies used in our derivation can be determined immediately using standard graphical criteria such as Pearl's d-separation. However, the causal diagram in Figure A of our letter only includes the observed factual random variables A, S, W, Y and the unobserved factual U, so it seems impossible to determine counterfactual independencies without additional context. In particular, if we equate $E[Y(a)]$ with $E[Y|do(A=a)]$ (Richardson and Robins,[4] page 7), then the first step in Cinelli and Pearl's[1] derivation becomes $E[Y(a)] = E[Y \mid A = a]$. However, because $Y(a)$ does not appear on the causal diagram, this step does not seem to be justified from the causal graph alone and requires knowledge that is not reflected by the causal diagram.

We appreciate the simplicity of Cinelli and Pearl's[1] derivation based on the causal diagram, but our intuition and insight are improved by working directly with counterfactuals. Before the introduction of single world intervention graphs, a shortcoming of the counterfactual approach was the conceptual difficulty of mapping knowledge of the factual variables to unobserved counterfactuals.[3] A key utility of single world intervention graphs is that they remove this difficulty. The first step in constructing a single world intervention graph is to construct a causal diagram based only on assumptions regarding the causal relationships between factuals.[4] This is then followed by applying an algorithm to map the causal relationships from the causal diagram to the single world intervention graph and thus the counterfactuals.[4] The construction of the single world intervention graph, therefore, explicitly links our assumptions regarding factuals to assumptions regarding counterfactuals.

We are pleased by the dialogue our letter has initiated. Causal inference holds a unique place at the intersection of many diverse fields, including epidemiology, statistics, philosophy, computer science, and economics, to name a few. Cross-disciplinary conversations like this provide valuable opportunities for us to learn alternate perspectives, minimize ambiguities, and enrich our understanding.

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A Call for Caution in Using Information Criteria to Select the Working Correlation Structure in Generalized Estimating Equations

To the Editor:

Generalized estimating equations (GEEs) are popular tools for estimating associations in clustered data settings. The semiparametric nature of this approach makes it highly appealing because unbiased effect estimators can be obtained without knowing the true distribution of the data being modeled. For example, it is unnecessary to specify a specific parametric distribution

All simulation code is available upon request from the corresponding author.
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