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Letter to Editor

When is an association truly causal? Revisiting causal inference in the era of artificial intelligence

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Dear Editor,

The rapid expansion of artificial intelligence (AI) and machine learning methods in epidemiological research has generated substantial enthusiasm for their ability to analyze large datasets and improve risk prediction. However, this enthusiasm has also been accompanied by an increasing tendency to conflate predictive accuracy with causal inference. This misconception threatens the validity of epidemiological conclusions and their translation into public health policy.

In epidemiology, causality is not an inherent property of statistical associations but an inferential judgment grounded in explicit assumptions about the data-generating process. At minimum, causal inference requires clearly established temporality, exchangeability between exposed and unexposed groups, positivity, and the absence of major sources of bias, including confounding, selection, and information biases (1–3). These conditions are independent of model complexity or predictive performance and cannot be satisfied solely through algorithmic optimization.

AI-based models are primarily designed to maximize prediction rather than estimate causal effects. High discrimination or calibration does not imply that an exposure has a causal impact on an outcome, nor does it guarantee that an intervention on the exposure would alter disease risk. Without an explicit counterfactual framework, many machine learning models could not directly address the question most relevant to epidemiology: what would happen if we intervened? (4, 5). As Hernán has emphasized, prediction and causal inference address fundamentally different scientific questions and require distinct methodological approaches (6).

Moreover, the “black box” nature of many AI algorithms may obscure key epidemiological concepts such as confounding, mediation, and collider stratification. In some cases, complex models may even amplify systematic biases present in the underlying data, producing highly precise but invalid estimates (7, 8). Large sample sizes and high-dimensional data do not alleviate these concerns; rather, they may increase confidence in biased results.

The integration of AI into epidemiology must be accompanied by renewed attention to causal thinking. Explicit specification of causal questions, use of directed acyclic graphs (DAGs), careful study design, and transparent language distinguishing association, prediction, and causation remain essential. AI should be viewed as a complementary analytical tool—not a replacement for epidemiological reasoning.

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Maintaining this distinction between prediction and causal inference is essential, as failing to do so risks reinforcing misleading causal narratives and undermining evidence-based decision-making. As the field continues to evolve, clarity about when an association can legitimately be interpreted as causal is more critical than ever.

Keywords: Association, Causal Inference, Artificial Intelligence

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