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More on Causal Inference Studies

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Dear Dr. Karp,

Thank you for highlighting the literature distinguishing etiologic and intervention conceptual approaches to the study of causation. Emulating a clinical trial in the design of observational studies, however, remains a powerful tool to understand causation. We disagree that this recommendation is a "failure."

In writing for a clinical journal (1), we aimed to maximize comprehension at the expense of specificity on a few occasions. For example, we chose to use the term "casual association" to convey the idea that the associations we are interested in are causal in nature – that a causal model must underlie one's thinking. Although not in common usage, authors may wish to use this term to describe the purpose of their study. We agree that it should not be used to justify claims of causality. We also used the word "confounding" to describe the effect of conditioning on a collider. While not technically accurate, we conveyed the correct message.

The confidence interval is a measure of the precision of an estimate or measure. Imprecision is a reasonable term when confidence intervals are large. Confidence intervals that include the null value too often lead to claims of "no association," even when they contain clinically or biologically meaningful effect sizes. This is particularly true when the point estimate is meaningfully large. We encourage authors to thoughtfully interpret effect estimates and confidence intervals rather than adhering to an alpha "litmus test" of 0.05.

A few of the points made in the letter suggest we are implying something we are not. We do not state that a single study can prove causality, nor that confidence intervals exclude effects outside of their boundaries, nor that causal factors should be ignored in prediction models. Indeed, an important point of the paper was to instruct authors not to read things into

their data that aren't there. Equally, we encourage readers not to read things into our

recommendations that weren't there.

On behalf of the writing committee,

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Alan R Smyth, MD

James D Chalmers, MD, PhD

Reference

1) Lederer DJ, Bell SC, Branson RD, et al. Control of confounding and reporting of results in causal inference studies. Guidance for authors from editors of respiratory, sleep, and critical care journals. *Ann Am Thorac Soc* 2019;16(1):22-28.