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Peer-Review Report

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# Peer Review of “Interpreting the Estimand Framework From a Causal Inference Perspective”

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Hao Wu

Michigan State University, East Lansing, MI, United States

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## Related Articles:

Preprint (JMIR Preprints): <http://preprints.jmir.org/preprint/88813>

Author's Response to Peer-Review Reports: <https://med.jmirx.org/2026/1/e98121>

Published Article: <https://med.jmirx.org/2026/1/e88813>

*JMIRx Med* 2026;7:e98126; doi: [10.2196/98126](https://doi.org/10.2196/98126)

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**Keywords:** causal inference; clinical trial; estimand; intercurrent event; treatment effect

*This is a peer review report for “Interpreting the Estimand Framework From a Causal Inference Perspective.”*

short of expectations for novelty, depth, or rigor in a specialist statistics or causal inference journal.

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## Round 1 Review

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This manuscript [1] provides a pedagogical interpretation of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E9 framework through the lens of the potential outcomes causal inference framework. The author translates the 5 attributes and intercurrent event strategies into formal statistical notation, primarily using simple randomized trial settings and linear models. The paper is largely conceptual and expository in nature, aiming to improve methodological clarity rather than introduce new causal methodology.

Within the context of *JMIRx Med* as an overlay journal for preprints, the manuscript is generally coherent, technically correct at a basic level, and suitable as an educational or perspective-style contribution, though it would likely fall

## Major Comments

1. The manuscript repeatedly states that it “interprets” the ICH E9 framework, but in practice, it mostly rephrases ICH E9 concepts using potential outcomes notation. Readers would more likely expect to see discussions on limitations, ambiguities, or contested aspects.
2. While pedagogical simplicity may be intentional, several aspects risk being misleading if read uncritically. For example, conditioning on posttreatment variables (section 3.6) is introduced without adequate warning about collider bias or causal ordering issues, and the discussion of principal stratification glosses over identification challenges, relying on brief mentions of Bayesian methods without clarifying assumptions. These are not fatal flaws, but the author should be more explicit about what is heuristic versus formally justified.

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## Conflicts of Interest

None declared.

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## References

1. Zeng J. Interpreting the estimand framework from a causal inference perspective. *JMIRx Med*. 2026;7:e88813. [doi: [10.2196/88813](https://doi.org/10.2196/88813)]

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## Abbreviations

**ICH:** International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

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*Edited by Amy Schwartz; This is a non-peer-reviewed article; submitted 13.Apr.2026; accepted 13.Apr.2026; published 22.May.2026*

Please cite as:

Wu H

Peer Review of “Interpreting the Estimand Framework From a Causal Inference Perspective”

*JMIRx Med* 2026;7:e98126

URL: <https://med.jmirx.org/2026/1/e98126>

doi: [10.2196/98126](https://doi.org/10.2196/98126)

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