Letters to the Editor

Letter to the Editor: The Relative Risk Index: A Complementary Metric for Assessing Statistical Fragility in Orthopaedic Surgery Research

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o the Editor: I read with great interest the article by Brown et al¹ addressing the statistical fragility of research on tranexamic acid (TXA) use in orthopaedic surgery. The authors used the fragility index (FI) and its derivatives to evaluate fragility. They concluded that research on TXA is fragile and recommended routine reporting of FI and related measures in future trials.

Although I commend the authors for their thorough analysis, I respectfully propose that the relative risk index (RRI) may be a viable alternative or complementary metric to assess statistical fragility. The FI and fragility quotient (FQ) strongly correlate with statistically significant *P*-values, providing mainly redundant information.³ By contrast, the RRI and its risk quotient are only weakly correlated with notable *P*-values, offering unique, nonredundant information.

Using the example provided by Brown et al in Figure 2, the FI of 3 suggests fragility because changing outcomes for 3 TXA subjects (6%) flips the *P*-value to nonnotable. However, this represents a 30% increase in overall transfusions, suggesting the research findings are robust. By contrast, the RRI for this table is 4.5, indicating that a 16.5% change per cell, on average, is required to reach therapeutic equivalence.

Although the FI's strength lies in identifying the minimal change to alter statistical significance, it has the weakness of relying on population-level *P*-values, with an arbitrary 0.05 cutoff value.⁴ The RRI's focus on global changes across study groups and outcomes provides a more comprehensive assessment. Its emphasis on therapeutic equivalence aligns with clinical decision making, offering an intuitive, clinically relevant metric. Incorporating the RRI in future research could provide a more nuanced understanding of fragility and its clinical effect.

As Brown et al acknowledge, the lack of standardized FI and fragility quotient values leaves statistical fragility poorly defined. Given this and the RRI's relative independence from *P*-value changes, the RRI warrants consideration as a complementary metric focusing on therapeutic equivalence and aligning with clinical decision making.

I appreciate the authors' valuable contribution to this important topic and hope that future research will further explore the utility of the RRI alongside more established fragility measures. This broader perspective could lead to more nuanced and clinically relevant assessments of statistical fragility, ultimately improving evidence-based practice and patient outcomes.

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Neither Heston nor any immediate family member has received anything of value from or has stock or stock options held in a commercial company or institution related directly or indirectly to the subject of this article.

J Am Acad Orthop Surg 2025;33:e412-e413 DOI: 10.5435/JAAOS-D-24-00473

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References

- 1. Brown AN, Yendluri A, Lawrence KW, et al: The statistical fragility of tranexamic acid use in the orthopaedic surgery literature: A systematic review of randomized controlled trials. *J Am Acad Orthop Surg* 2024;32:508-515.
- 2. Walsh M, Srinathan SK, McAuley DF, et al: The statistical significance of randomized controlled trial results is frequently fragile: A case for a Fragility Index. *J Clin Epidemiol* 2014;67:622-628.

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- 3. Heston TF: Statistical significance versus clinical relevance: A head-to-head comparison of the fragility index and relative risk index. *Cureus* 2023; 15:e47741.
- 4. Kennedy-Shaffer L: When the Alpha is the Omega: P-values. "Substantial evidence," and the 0.05 Standard at FDA. *Food Drug Law J* 2017;72:595-635.