Fragility of Assumptions: Letter to the Editor

Dear Editor:

We read with interest the recent article entitled "Statistical Fragility of Randomized Controlled Trials Evaluating Platelet-Rich Plasma Use for Knee Osteoarthritis: A Systematic Review" by Chan et al.[1] We appreciate the authors' work but the article raises key issues concerning fragility—its definition, assumptions, and clinical relevance. The fragility index, for example, assumes that fragility appears in the group with fewer events, not necessarily in the treatment group.[2] This assumption can significantly skew the fragility estimate. In the authors' table, altering treatment A instead of treatment B results in a fragility index of 2. Had treatment B been modified, the index would be 1. An alternative approach is unit fragility, defined as the result when "the smallest possible alteration is made to the data, subject to both sets of table margins remaining constant."[3] This definition mitigates the assumption that one group is inherently more fragile, although it still poses issues when outcomes in one group approach zero.

A viable alternative is moving from P value fragility to evaluating relative risk deviation. In a standard 2×2 contingency table, the residual is defined as the difference between expected and observed values. This quantity signifies the adjustment needed in each cell to normalize the relative risk to 1. Using conventional cell labels, the residual is determined by the formula $(ad - bc)/(a + b + c + d)$. Dividing this residual by the mean cell value produces a relative risk index (RRI). In the example provided by the authors, the residual calculates to 5.3, leading to an RRI of 23.6% (=5.3/22.5). This percentage represents the required change to achieve treatment neutrality.

Clinical practice frequently requires treatment choices based on a favorable relative risk rather than P values. By anchoring fragility assessments in relative risk metrics, we reduce underlying assumptions and better align statistical evaluations with clinical judgment.

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