Comment on "Associations Between Headache (Migraine and Tension-Type Headache) and Psychological Symptoms (Depression and Anxiety) in Pediatrics"

To the Editor:

We read with great interest the article by Lee et al (1) titled "Associations between headache and psychological symptoms in pediatrics" published in *Pain Physician*. The authors performed a systematic review and meta-analysis examining associations of migraine and tension-type headaches with depressive and anxiety-related symptoms in children and adolescents. They found that patients with migraines had notably higher scores for depression compared to healthy controls, yet the scores related to anxiety did not show a significant difference between the migraine sufferers and the control group (1). Headaches are very prevalent in kids and teens, affecting up to almost 30% of school-aged children. Understanding factors linked to migraines can help guide treatment and prevention strategies. However, we would like to raise a concern regarding the interpretation of the collective evidence.

The meta-analysis found significantly higher Children's Depression Inventory (CDI) scores in the migraine group compared to controls (1). However, there was substantial heterogeneity (I^2 = 71%) between the included studies for this analysis. Potential reasons for this heterogeneity may include variability in study populations, differences in migraine characteristics, and selection bias. Because of the high heterogeneity, additional analysis may be required to provide more information regarding their finding. To address this concern, the use of prediction interval for this outcome may be informative. The prediction interval estimates the range of effects that might be expected in a new study (2,3). This analysis takes into account both the heterogeneity as well as the uncertainty around the summary effect estimate. The primary benefit of using a prediction interval is that it allows us to establish realistic expectations regarding the potential variability of outcomes in future research.

To further characterize the heterogeneity in the original meta-analysis (1), we calculated a 95% prediction interval for the CDI score comparison between migraine patients and controls. We utilized the raw study data on CDI mean, SD, and subject numbers from the included studies of the original meta-analysis (1) to calculate the prediction interval with Comprehensive Meta-Analysis (Version 4, Biostat, Englewood, NJ, USA). As shown in Fig. 1, this 95% prediction interval ranged from -0.5 to 1.44, demonstrating that the true CDI score difference between migraine and control groups could plausibly range widely. In this way, the prediction interval suggests that findings on this research question remain preliminary. Therefore, we should be cautious about over-interpreting the precise summary estimate without further consistent evidence. In summary, the current finding of the original meta-analysis should be interpreted cautiously. While depressive symptoms appear elevated in pediatric migraines, the wide prediction interval suggests uncertainty regarding the effect size.
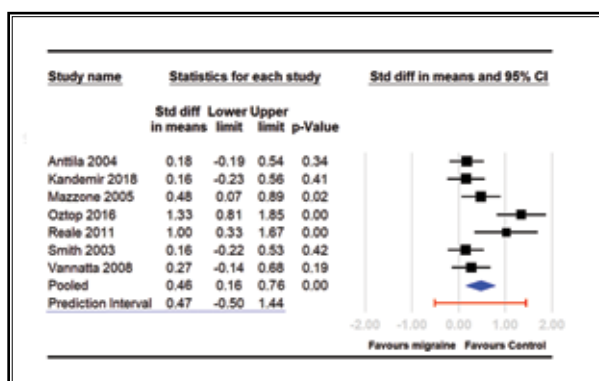

Fig. 1. *Forest plot displaying the standardized difference (std diff) in means for depression scores between patients with migraine and healthy controls. Each line represents the results from a separate study, with the square marker denoting the standardized difference and the horizontal lines representing the 95% confidence interval (CI). The blue diamond marker illustrates the pooled standardized difference in means across all studies. The red lines depict the 95% prediction interval, ranging from -0.50 to 1.44, which suggests that in a new study, the true effect could vary from slightly favoring the migraine group to a much stronger effect favoring the control group.*

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