Response to the letter "Critical appraisal of methodological rigor in a systematic review on post-COVID-19 vaccination-associated olfactory dysfunction"

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Dear Editor:

We appreciate the thoughtful comments by Dr. Gupta et al. [1] regarding our systematic review [2]. Their commitment to this rare, but emerging clinical topic is welcome, and we would like to address the methodological points raised.

1. Inclusion of institutional cases

Reports addressing the olfactory disorder following COVID-19 vaccination remains exceedingly scarce worldwide. To provide a more comprehensive overview of this rare presentation, we aggregated the published cases with those encountered in our institution, all of which met the same eligibility criteria defined for the review. Adding institutional cases in the context of limited global evidence is a commonly accepted approach in systematic reviews of rare conditions and does not conflict with PRISMA methodology. We believe that it enhances, rather than diminishes, the descriptive value of the review.

2. Comorbidities and baseline assessment

All cases, including those from our institution, demonstrated normal nasal endoscopy findings. For the institutional cases, additional evaluation with paranasal sinus CT and clinical history allowed us to exclude chronic rhinosinusitis, neurodegenerative disorders, autoimmune disease, and metabolic disorders. Similarly, the original reports included in the review provided their own diagnostic assessments prior to publication. Because post-vaccination olfactory dysfunction is inherently a diagnosis of exclusion, the review necessarily relied on the clinical evaluation presented in each primary report. While this is an inherent limitation, it does not fundamentally affect the interpretation of our findings.

3. Heterogeneity of diagnostic tools (Sniffin' Sticks and T&T)

Although the two tests utilize different scoring systems, both have well-established severity thresholds. For clarity and clinical relevance, we summarized the outcomes categorically rather than attempting to directly compare them numerically. Given the small number of past cases and the aims of the review, we consider that this approach is appropriate and may be methodologically justified. A more granular comparison would likely introduce unnecessary complexity without improving interpretability.

4. Absence of a comparator cohort

A comparator group is not required for a systematic review of case reports, and our aim was not to establish causality but to synthesize available evidence. As noted in our article, past undiagnosed COVID-19 infection remains a possible confounder, an issue we had explicitly discussed. We agree that this limitation underscores the need for future controlled studies. Regarding the female predominance, we agree that both biological factors and reporting bias may contribute to this distribution, as noted in the prior olfactory research. However, given the very small number of reported cases, the observed sex distribution should be interpreted descriptively rather than conclusively, and it does not alter the overall interpretation of our review.

Conclusion

Although available evidence is constrained by the rarity of reported cases and heterogeneity of diagnostic approaches, our principal conclusion remains unchanged: olfactory disorders after COVID-19 vaccination are rare but have been documented across multiple settings. We hope that our review helps to raise awareness of this uncommon clinical presentation and supports the development of more robust future investigations.

Authorship contribution

MK, EM, MT, NY, NO have made significant contributions to conception and design and drafting of this work.

Conflict of interest

No conflict of interest to declare.

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References

1. Gupta T, Verma JK. Critical appraisal of methodological rigor in a systematic review on post-COVID-19 vaccination-associated olfactory dysfunction. Rhinology. 2026;64(2):x-x.
2. Kawabata M, Mori E, Yanagi N, Tei M, Otori N. Olfactory disorder after COVID-19 vaccination. Rhinology. 2025;63(4):441-447.

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