# When sleep improves but AHI does not: comments on mepolizumab ± FESS in severe CRSwNP

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**Rhinology 64: 4,** 0 - 0, 2026
https://doi.org/10.4193/Rhin26.159

**Received for publication:**
March 1, 2026
**Accepted:** March 30, 2026

**Associate Editor:**
Michael Soyka

**Dear Editor:**

We read with great interest the randomized trial by Homoe et al. evaluating mepolizumab with or without functional endoscopic sinus surgery (FESS) for severe uncontrolled CRSwNP [1], integrating patient-reported sleep outcomes (ESS, FOSQ-10, SNOT-22 sleep items) with WatchPAT-derived indices of sleep-disordered breathing (AHI/ODI). The study addresses a clinically frequent scenario in which patients report prominent fatigue and "poor sleep", while OSA may coexist and require independent management.

The authors report substantial and clinically meaningful improvements in symptom burden and perceived sleep/function over six months in both arms, yet no significant group-level change in AHI or ODI. We agree this apparent dissociation is important; however, several analytic and interpretive refinements—feasible within the existing dataset—could reduce the risk that readers over-interpret a null AHI finding as proof of "no effect on OSA."

First, event-frequency indices (AHI/ODI) may be poorly aligned with the mechanisms most plausibly modified by CRSwNP therapy. Biologics and surgery robustly improve nasal obstruction and inflammatory symptoms, which can affect awakenings, sleep continuity, and daytime functioning without necessarily reducing pharyngeal collapsibility enough to shift AHI—particularly in moderate-to-severe OSA. In CRSwNP trials, improvements in sleep/function domains of SNOT-22 have been consistently observed with biologics (e.g., dupilumab) [2], and patient-reported sleep quality improvement has been reported in real-world cohorts [3]. In this context, it may be more accurate to conclude that mepolizumab ± FESS improves sleep-related quality of life while not demonstrably reducing respiratory event burden on HSAT in this cohort, rather than implying these outcomes should move in tandem [4].

Second, the presentation of objective outcomes could be strengthened by emphasizing estimation over hypothesis testing. With small samples, skewed AHI distributions, and single-night HSAT variability, p-values can be uninformative. Reporting Hodges–Lehmann between-arm estimates with 95% confidence intervals for AHI/ODI change would allow clinicians to gauge what magnitude of improvement is reasonably excluded (or not) by the data. AASM guidance highlights the need to interpret sleep testing results in clinical context and acknowledges limitations of home testing pathways. Confidence intervals would therefore materially improve interpretability without requiring additional data collection.

Third, clinically interpretable "responder" and severity-transition analyses could better capture heterogeneous benefit. The manuscript already shows individual movement across OSA severity categories. Formalizing this as (i) the proportion achieving AHI <5, and/or (ii) ≥1-category improvement, with exact confidence intervals and stratification by baseline severity (mild vs moderate-to-severe), would clarify whether benefit is concentrated in those with milder disease—where nasal and inflammatory factors may contribute more proportionally. Such analyses would also align with the broader evidence base that mepolizumab improves CRSwNP outcomes [5] with sustained efficacy after treatment periods [6], while not presuming parallel improvement in OSA physiology.

## Conclusion

Homøe et al. provide valuable randomized evidence supporting meaningful improvement in patient-centered sleep and fatigue outcomes in severe CRSwNP treated with mepolizumab, with or without FESS. We suggest that estimation-focused reporting and responder/transition analyses—using existing HSAT and PROM data—would sharpen the clinical message: symptom-related sleep benefit is expected, but objective OSA burden may persist and should be assessed and treated on its own track.

## Authorship contribution

WZH drafted and revised the letter.

## Funding

None

## Conflict of interest

The author declares that he has no conflict of interest.

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