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2 Impact of Predisposing Conditions in a Retrospective Cohort”

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1 **ABSTRACT.**

2 Hypoglossal nerve stimulation (HNS) is an emerging therapy for obstructive sleep apnea (OSA), and recent
3 research has explored the influence of comorbidities on treatment outcomes. While these findings offer
4 valuable insights, several methodological limitations should be considered. The reliance on non-standardized
5 clinician documentation for conditions such as depression and insomnia may introduce diagnostic variability,
6 particularly given symptom overlap with OSA. Use of self-reported device adherence, without objective usage
7 data, may further limit accuracy. Additionally, the absence of validated patient-reported outcome measures
8 reduces comparability across studies. A high attrition rate raises concerns about potential selection bias, and
9 unaddressed confounders—including medication use, socioeconomic factors, and variability in treatment
10 protocols—may influence results. Methodological concerns also include single-reviewer data extraction and a
11 short follow-up period, limiting assessment of long-term efficacy. Addressing these issues in future studies will
12 improve the reliability and generalizability of findings related to HNS outcomes.

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14 **Key Words:** Obstructive Sleep Apnea, Hypoglossal Nerve Stimulation, Methodological Limitations, Sleep
15 Comorbidities, Patient-Reported Outcomes

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1 **To the Editor,**

2 We read with great interest the article by Adwer et al.¹ evaluating hypoglossal nerve stimulation (HNS)
3 outcomes in obstructive sleep apnea (OSA). While the study provides valuable insights into the impact of
4 comorbidities on treatment response, We would like to highlight several methodological considerations that
5 could enhance future research.

6 First, the assessment of comorbidities such as depression and insomnia relied on clinician documentation
7 without standardized tools like the PHQ-9 or Insomnia Severity Index.^{2,3} This approach may introduce
8 diagnostic variability, especially given the symptom overlap between OSA and these psychiatric conditions.

9 Second, the pathway classification incorporated self-reported device usage data. Although patient-reported
10 outcomes are valuable, previous research has shown discrepancies between subjective and objective
11 adherence in sleep therapies.⁴ Incorporating device-recorded usage metrics could enhance future analyses by
12 reducing reliance on subjective reporting. In addition, the study did not use validated patient-reported outcome
13 measures (PROMs) such as the Epworth Sleepiness Scale (ESS) or the Functional Outcomes of Sleep
14 Questionnaire (FOSQ), which are widely used to quantify sleepiness and quality of life in OSA populations.
15 Utilizing such tools would improve the consistency, sensitivity, and comparability of subjective benefit
16 assessments. The 75.7% attrition rate warrants particular attention. While acknowledged by the authors,¹ a
17 comparison of baseline characteristics between included and excluded patients could reveal selection bias
18 affecting generalizability. Such attrition analysis is particularly important given the study's retrospective design.
19 Several potentially significant confounders were not addressed, including:

- 20 • Medication use (e.g., sedatives affecting sleep architecture)
- 21 • Socioeconomic factors influencing treatment access
- 22 • Variability in titration protocols across patients

23 Moreover, all chart data were extracted by a single investigator. Although this was done using a standardized
24 abstraction template, single-reviewer extraction may introduce reviewer bias or inconsistency. Best practices
25 in retrospective chart reviews recommend dual, independent abstraction to enhance data reliability.

26 Additionally, the two-month follow-up period¹ provides limited insight into long-term treatment efficacy. Given
27 that OSA management typically requires sustained therapy, longer observation would help establish treatment
28 durability, especially in patients with comorbidities.⁵

29 By highlighting these methodological considerations, we aim to support future research in developing more
30 robust and generalizable findings regarding HNS outcomes. These considerations notwithstanding, the study
31 contributes meaningfully to understanding predictors of HNS response. The findings emphasize the
32 importance of comprehensive pre-implantation assessment and suggest valuable directions for optimizing
33 treatment approaches in comorbid populations.

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