

Ahsan Ahmed, B.S¹, Shaynie Segal, B.A¹, Marc Gibber, MD^{1,2}

¹Albert Einstein College of Medicine; ²Department of Otorhinolaryngology – Head and Neck Surgery, Montefiore Medical Center

Introduction

- Obstructive sleep apnea (OSA) is a highly prevalent disorder, affecting nearly 1 billion people worldwide.¹
- OSA is strongly linked to type 2 diabetes, a comorbidity observed in nearly 30% of patients with OSA.^{2,3}
- OSA has been shown to worsen diabetes control through multiple mechanisms, including intermittent hypoxia and sympathetic activation.⁴
- Hypoglossal Nerve Stimulation (HNS) is a novel therapeutic modality that offers an alternative to CPAP and improves OSA by stimulating the hypoglossal nerve to improve airway patency (Figure 1).
- We theorize that by mitigating OSA, HNS might confer metabolic benefits, including improved glycemic control and reduced reliance on diabetes medications.
- Understanding the impact of HNS on diabetes regulation has significant implications for the management of both conditions.

Figure 1. HNS Device Implantation

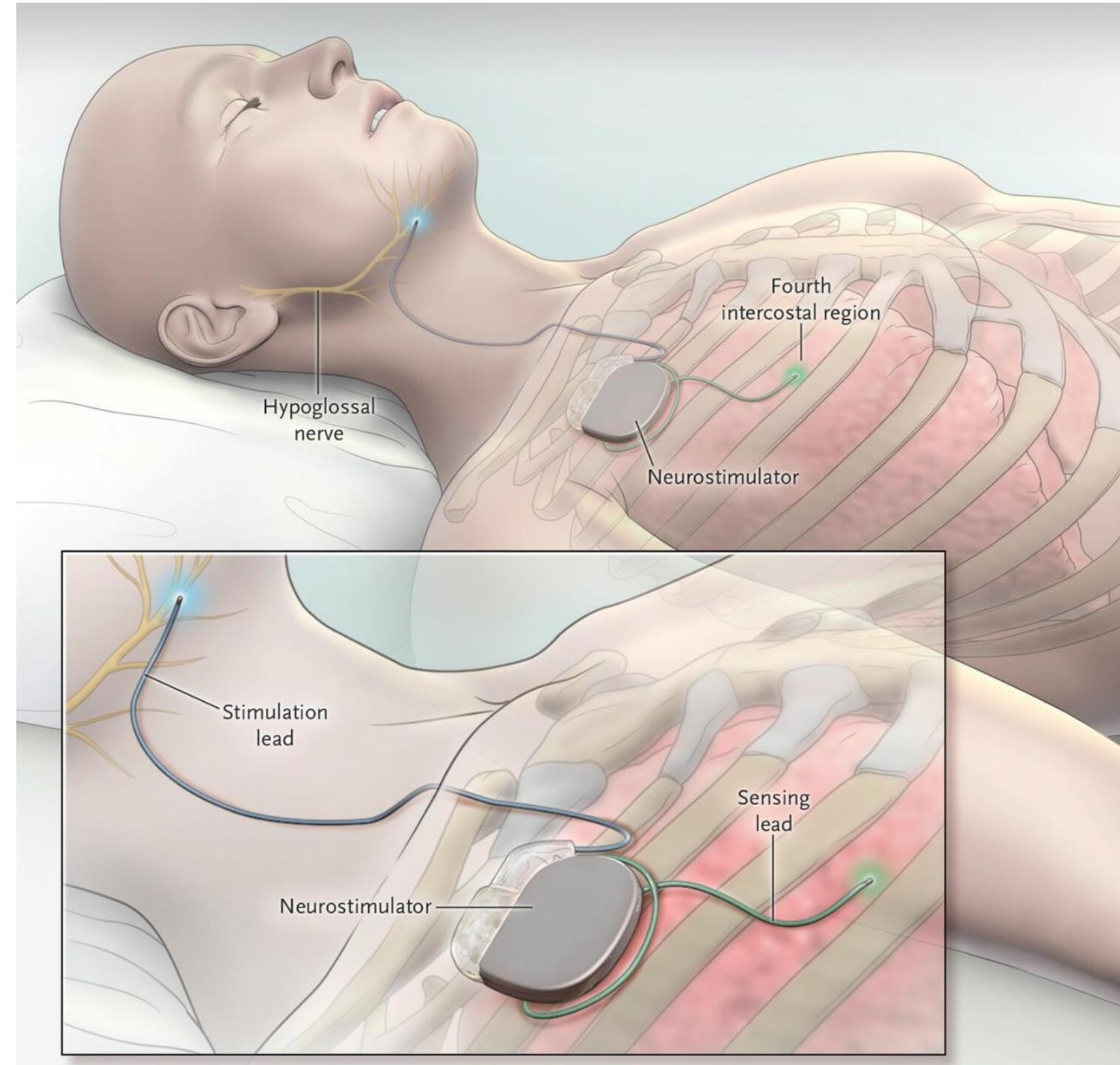


Image Citation: Strollo PJ Jr, Soose RJ, Maurer JT, et al. Upper-airway stimulation for obstructive sleep apnea. *N Engl J Med*. 2014;370(2):139-149.

Methods

- Design: A retrospective cohort study of patients who underwent HNS therapy between June 2020 and October 2024 at an academic institution.
- Inclusion criteria: Patients with type II diabetes with moderate-to-severe OSA who underwent HNS therapy.
- Exclusion criteria: Patients who did not acquire pre- and post-operative polysomnography (PSG) and did not have follow-up of diabetes status.
- Population: Out of 80 charts reviewed, 17 adults met the criteria for the study and were included.
- Outcome Measures:
 - Apnea-hypopnea index (AHI) from full-night PSGs.
 - Hemoglobin A1c (HbA1c), insulin dependence, number and type of diabetes medications, assessed before and at-least 3 months after HNS implantation.
- Statistics Analysis: Paired t-tests and correlation analysis using Microsoft Excel ($P<0.05$ significant).

Results

- The study cohort included 17 patients, 52.9% male, with a mean age of 65.3 years and mean BMI of 30.4.
- OSA Outcomes:
 - Mean AHI decreased from 32.4 to 8.8 events/hour ($\Delta-24.0$, $P<0.001$).
 - Device adherence was high, with an average usage of 6.7h/night.
- Diabetes Control:
 - Average HbA1c decreased from 6.60 to 6.26 ($\Delta -0.31$, $P=0.27$) (Table 1).
 - Of the 6 patients who were insulin-dependent prior to HNS therapy, 50% were able to discontinue insulin following implantation (Table 2).
 - There was no significant reduction in diabetes medication regimen after HNS therapy. However, GLP-1 agonists saw an increase during follow-up (3 → 4 patients).
- Correlation analysis: Greater reductions in AHI were significantly associated with improvements in HbA1c ($r= -0.69$, $P=0.027$) (Figure 4).

Table 1: Primary results of HNS Stimulation

	Pre-HNS	Post-HNS	Average Change	P value
AHI	33.47	8.71	-23.98	$P<0.001$
A1C	6.60	6.26	-0.31	$P=0.27$
BMI	30.35	29.72	-0.63	$P=0.59$

Figure 2a: Pre and Post AHI

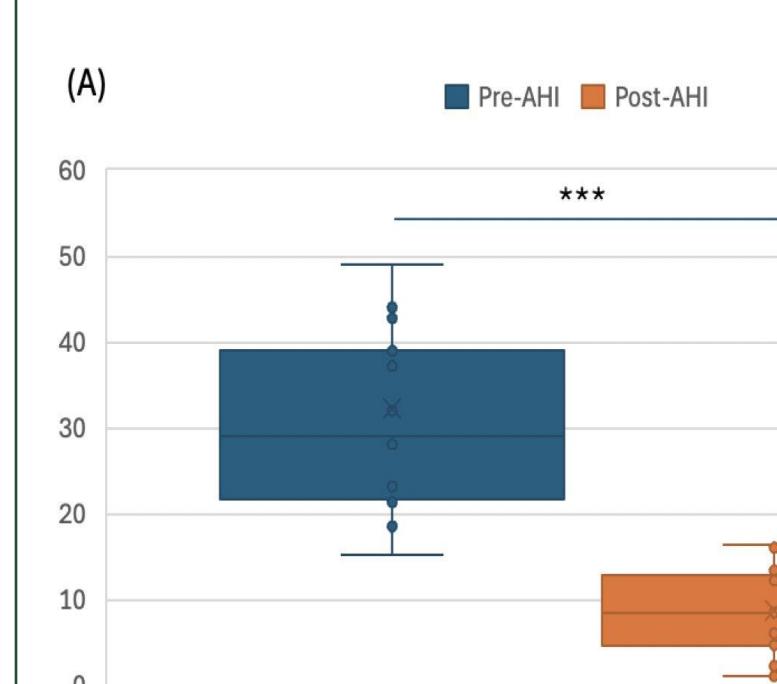


Figure 2b: Pre and Post BMI

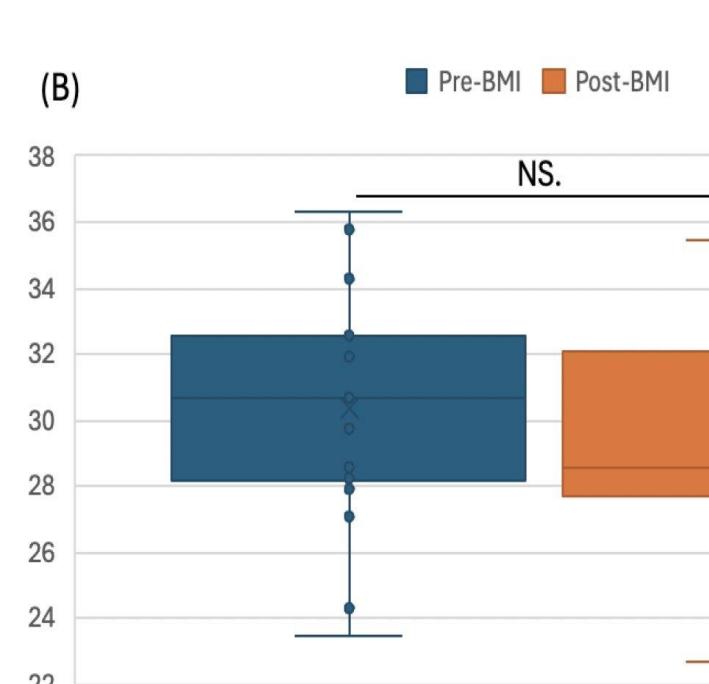


Figure 2c: Pre and Post A1C

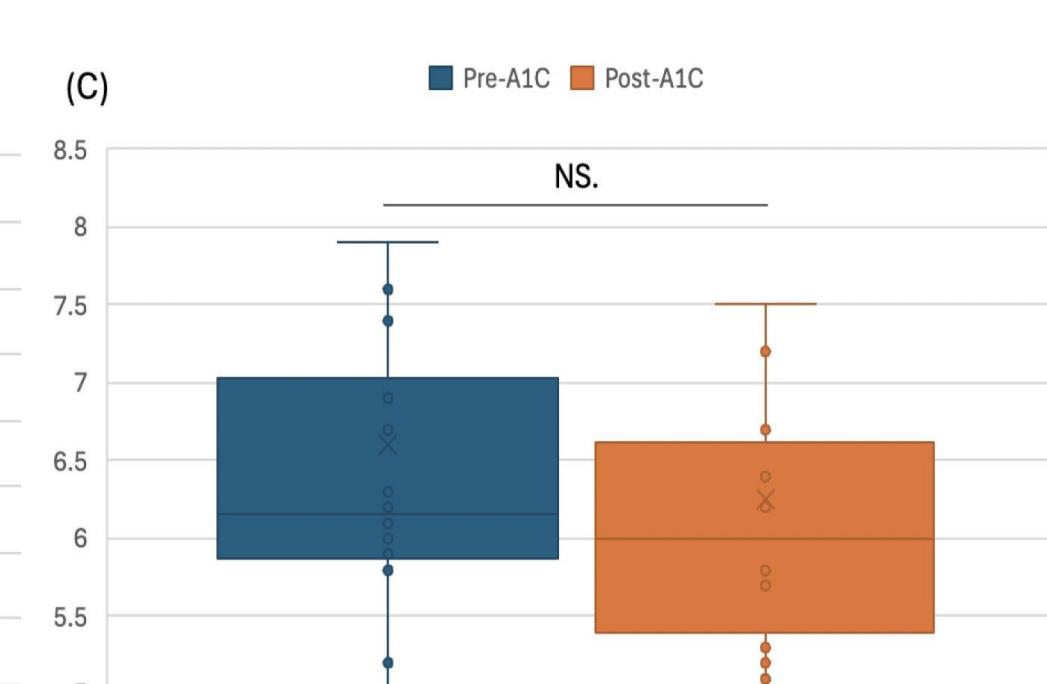
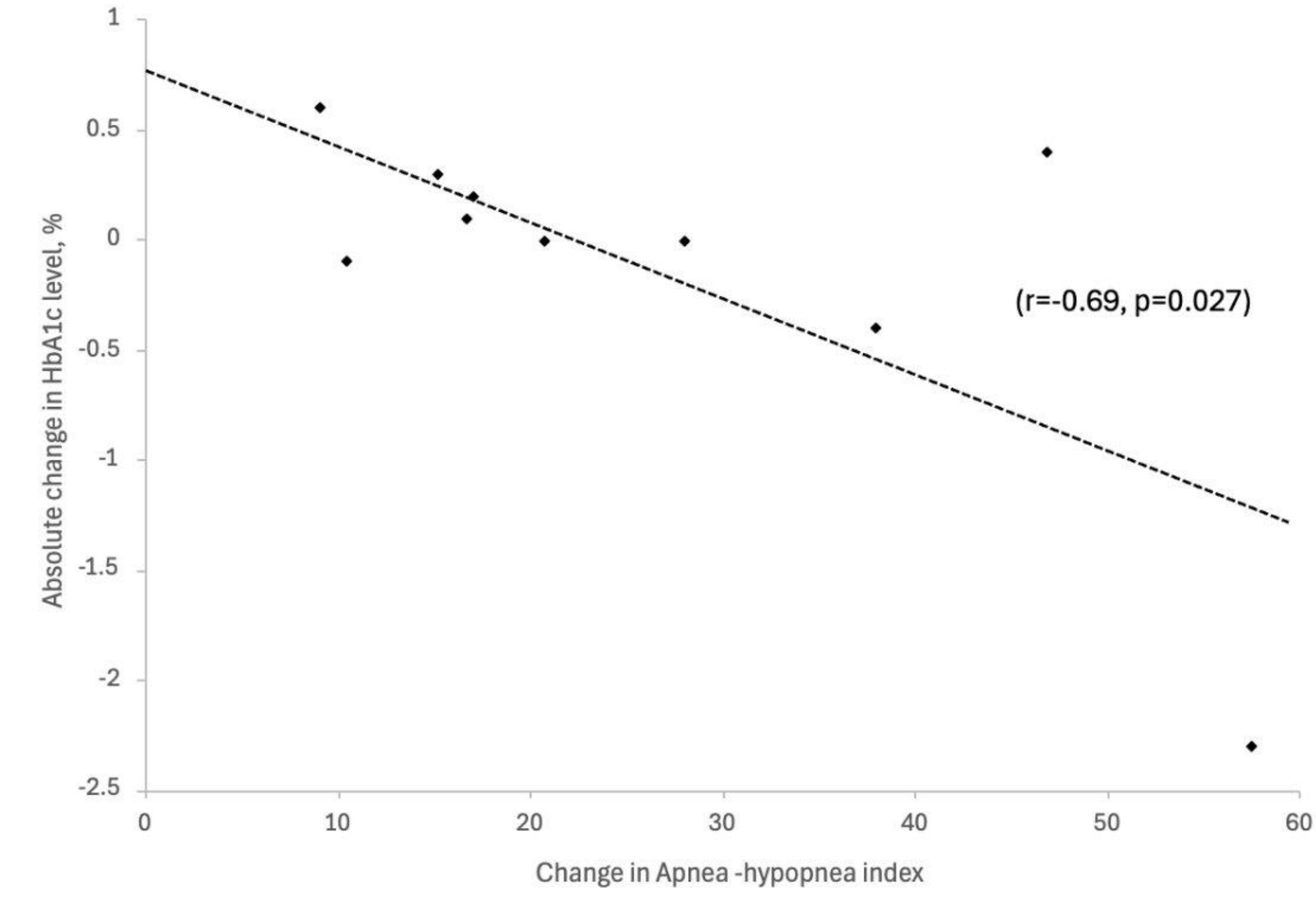


Table 2: Insulin Dependence

	Pre-HNS	Post-HNS	Pre-HNS	Post-HNS
Insulin	6	3	35.3%	17.6%

Figure 3: Correlation between AHI Reduction and HbA1c Improvement



Discussion

- HNS significantly reduced OSA severity and was associated with moderate improvements in glycemic control, reflected by a decline in HbA1c and a 50% reduction in insulin dependence.
- On average, HbA1c decreased by 0.31% (Figure 2). While not statistically significant, prior meta-analyses show that decreases in HbA1c of $\geq 0.3\%$ are associated with significantly lower rates of adverse cardiovascular events, underscoring the clinical relevance of our findings.⁵
- While overall medication usage did not show significant reduction, the use of GLP-1 receptor agonists increased during follow-up, demonstrating a shift in current medical practice. As GLP-1 therapy is now FDA-approved for OSA, its potential contribution highlights an important confounding factor.
- Our study also observed a significant correlation between improvements in AHI and reduction in HbA1c (Figure 3). These findings are consistent with randomized CPAP trials that demonstrate AHI improvements with HbA1c decline.⁶

Limitations

- Small cohort size ($n=17$) which may limit generalizability.
- Potential confounders could include diabetes treatment modification, weight loss, or lifestyle changes.

Future Directions

- Our study remains one of the first to assess the impact of HNS therapy on diabetes control, and studies with larger populations will provide greater insight.
- Conduct randomized controlled trials with standardized follow-up to determine the impact of HNS therapy on different measures of glycemic control.
- Assess the potential role of GLP-1/GIP agonists in improving type 2 diabetes and OSA outcomes.

References

- Abbasi A, Gupta SS, Sabharwal N, et al. A comprehensive review of obstructive sleep apnea. *Sleep Sci*. 2021;14(2):142-154. doi:10.5935/1984-0063.20200056
- Qian Y, Dharmage SC, Hamilton GS, et al. Longitudinal risk factors for obstructive sleep apnea: A systematic review. *Sleep Med Rev*. 2023;71:101838. doi:10.1016/j.smrv.2023.101838
- Mahmood K, Akhter N, Eldeirawi K, et al. Prevalence of type 2 diabetes in patients with obstructive sleep apnea in a multi-ethnic sample. *J Clin Sleep Med*. 2009;5(3):215-221.
- Cantley J, Grey ST, Maxwell PH, Withers DJ. The hypoxia response pathway and β -cell function. *Diabetes Obes Metab*. 2010 Oct;12 Suppl 2:159-67. doi: 10.1111/j.1463-1326.2010.01276.x. PMID: 21029313.
- Giugliano D, Chiodini P, Maiorino MI, Bellastella G, Esposito K. Cardiovascular outcome trials and major cardiovascular events: does glucose matter? A systematic review with meta-analysis. *J Endocrinol Invest*. 2019 Oct;42(10):1165-1169. doi: 10.1007/s40618-019-01047-0. Epub 2019 Apr 6. PMID: 30955180.
- Martínez-Cerón E, Barquiel B, Bezos AM, Casitas R, Galera R, García-Benito C, Hernanz A, Alonso-Fernández A, García-Rio F. Effect of Continuous Positive Airway Pressure on Glycemic Control in Patients with Obstructive Sleep Apnea and Type 2 Diabetes. A Randomized Clinical Trial. *Am J Respir Crit Care Med*. 2016 Aug 15;194(4):476-85. doi: 10.1164/rccm.201510-1942OC. PMID: 26910598.