

GLP-1 Receptor Agonists in Idiopathic Intracranial Hypertension

- [GLP-1 Receptor Agonists in Idiopathic Intracranial Hypertension](#)
- [An eye on long-duration spaceflight: Controversies, countermeasures and challenges](#)
- [Effectiveness and tolerability of liraglutide as add-on treatment in patients with obesity and high-frequency or chronic migraine: A prospective pilot study](#)
- [Impact of GLP-1 receptor agonists on idiopathic intracranial hypertension clinical and neurosurgical outcomes: a propensity-matched multi-institutional cohort study](#)
- [The effect of glucagon-like peptide-1 agonists on ocular parameters in idiopathic intracranial hypertension patients: a retrospective study](#)
- [Glucagon-like peptide-1 receptor agonists and the eye](#)
- [Liraglutide for idiopathic intracranial hypertension: a real-world propensity score-matched study](#)
- [Efficacy of Tirzepatide Dual GIP/GLP-1 Receptor Agonist in Patients With Idiopathic Intracranial Hypertension. A Real-World Propensity Score-Matched Study](#)

Source: Sioutas GS, Mualem W, Reavey-Cantwell J, Rivet DJ. Published in JAMA Neurology, 2025.
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Study Design: Retrospective cohort study using the TriNetX national EHR database.

Objective: To assess whether GLP-1 receptor agonist (GLP-1 RA) therapy is associated with improved clinical outcomes in patients with [idiopathic intracranial hypertension](#) (IIH) compared with standard treatments or [bariatric surgery](#).

Population: Patients diagnosed with IIH, matched cohorts based on demographics and baseline characteristics.

Outcomes:

↓ [Headache](#), ↓ [papilledema](#), ↓ [visual disturbances](#)

↓ Medication burden

↓ Need for surgical interventions (e.g., shunt, optic nerve sheath fenestration)

↓ 1-year all-cause mortality

Interestingly, no significant reduction in BMI was observed in the GLP-1 RA group compared to controls, despite symptomatic improvement. This suggests mechanisms beyond weight loss, possibly involving [central GLP-1 pathways](#) or modulation of cerebrospinal fluid dynamics.

Bariatric surgery, although more effective in weight reduction, was associated with worse clinical outcomes than GLP-1 RAs.

Critical Appraisal

Strengths:

Large national dataset with broad geographic and demographic representation.

Matched cohort analysis reduces bias from confounders.

Comprehensive assessment of both symptomatology and healthcare utilization.

Limitations:

Retrospective design → risk of [confounding by indication](#).

No data on IIH severity scales (e.g., opening pressure, OCT metrics).

Mechanistic pathways not explored — no imaging, biomarker, or CSF analysis.

Weight and BMI changes were not clearly correlated with outcomes.

Clinical Significance:

Suggests potential off-label utility of GLP-1 RAs in IIH, even in non-obese or moderately obese patients.

Opens the door to weight-independent neuroprotective effects of GLP-1 agonists.

Could shift therapeutic paradigms in IIH away from purely weight-centric approaches.

Caveats:

Causality cannot be established — prospective randomized trials are required.

Selection bias may favor patients more engaged with healthcare (and possibly more adherent).

Potential overestimation of benefits due to residual confounding and lack of data on disease duration or prior therapies.

Bottom Line

GLP-1 RAs are associated with clinically meaningful improvements in IIH-related symptoms and outcomes, potentially through mechanisms beyond weight loss. While promising, these findings remain hypothesis-generating. High-quality RCTs are essential before routine adoption.

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