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Obstructive Sleep Apnea in Obesity: The Role of Tirzepatide and Incretin Therapies

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Abstract

Background. Obesity is one of the most important modifiable contributors to obstructive sleep apnea (OSA). Recurrent upper-airway obstruction during sleep produces intermittent hypoxemia, sleep fragmentation, sympathetic activation, and clinically relevant daytime and cardiometabolic consequences.

Aim. This review evaluates tirzepatide and other incretin-based therapies in the management of obesity-related OSA, with emphasis on randomized evidence, clinically relevant endpoints, safety, and integration with positive airway pressure (PAP) therapy.

Material and methods. A narrative review with a structured literature search was conducted. PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials were searched for publications from January 2014 to April 2026, with older foundational studies included when required for mechanistic or historical context. Priority was given to randomized

trials, prespecified secondary analyses, regulatory documents, clinical guidelines, and recent meta-analyses.

Results. The SURMOUNT-OSA phase 3 program enrolled 469 adults with obesity and moderate-to-severe OSA. Tirzepatide reduced AHI by 25.3 events/hour versus 5.3 with placebo in participants not using PAP, and by 29.3 events/hour versus 5.5 with placebo in established PAP users after temporary PAP withdrawal. Treatment also produced substantial weight loss, lower sleep-apnea-specific hypoxic burden, and favorable changes in systolic blood pressure, systemic inflammation, triglycerides, fasting insulin, and insulin resistance.

Conclusions. Among incretin-based therapies, tirzepatide has the strongest direct randomized evidence for adults with obesity-related moderate-to-severe OSA. Its role is best framed as phenotype-directed obesity treatment integrated with, rather than automatically replacing, PAP. Objective reassessment of OSA remains necessary before any reduction or discontinuation of device therapy.

Keywords: obstructive sleep apnea; obesity; tirzepatide; GLP-1 receptor agonists; positive airway pressure; weight loss.

1. Introduction

Obstructive sleep apnea (OSA) results from repeated sleep-related narrowing or closure of the upper airway despite continued respiratory effort. These episodes produce intermittent hypoxemia, arousals, sleep fragmentation, and sympathetic surges. Clinical consequences include excessive daytime sleepiness, impaired function, reduced quality of life, and increased cardiometabolic risk. Severity is usually categorized by the apnea-hypopnea index (AHI): 5-14 events/hour indicates mild OSA, 15-29 events/hour indicates moderate OSA, and 30 or more events/hour indicates severe OSA. Population analyses suggest that OSA affects a very large number of adults worldwide and remains substantially underdiagnosed. [1]

Obesity is one of the most important modifiable contributors to OSA. Excess adiposity promotes airway collapsibility through parapharyngeal and tongue fat deposition, reduced lung volumes, impaired caudal traction on the upper airway, and obesity-related inflammation. These mechanisms explain why weight management has long been recommended in OSA care, although durable weight loss is difficult to achieve with lifestyle intervention alone.[2,3] Recent literature published in the Journal of Education, Health and Sport has likewise emphasized the

bidirectional relationship between OSA and obesity and the need for integrated management rather than isolated treatment of each condition.[4]

Positive airway pressure (PAP) remains the standard intervention for many adults with symptomatic moderate-to-severe OSA.[5] PAP mechanically stabilizes the upper airway during sleep, but its real-world effectiveness depends on adherence. In cardiovascular populations, benefit appears most evident among adherent users, commonly defined as those using PAP for at least four hours per night.[6] PAP also does not directly treat excess adiposity. This separation between airway stabilization and metabolic disease creates a clinical rationale for therapies that address obesity and OSA simultaneously.

Tirzepatide is a once-weekly subcutaneous peptide that activates both glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors. It reduces appetite and energy intake, delays gastric emptying, and improves glycemic and cardiometabolic markers. In adults with obesity without diabetes, tirzepatide produced weight loss approaching 20% at higher doses in SURMOUNT-1.[7] The phase 3 SURMOUNT-OSA program then tested whether this degree of pharmacological weight reduction could improve obesity-related OSA directly.[8]

Regulatory interpretation has differed between jurisdictions. In December 2024, the U.S. Food and Drug Administration approved tirzepatide for moderate-to-severe OSA in adults with obesity, in combination with a reduced-calorie diet and increased physical activity.[9] The European Medicines Agency reviewed the same OSA evidence and concluded that the data should be reflected in product information, while a separate OSA indication was not required because the use was considered covered by the weight-management indication.[10]

This review evaluates current evidence for tirzepatide and incretin-based therapy in obesity-related OSA. It focuses on efficacy, cardiometabolic outcomes, safety, comparison with earlier incretin therapy, regulatory interpretation, and practical integration with PAP within phenotype-directed care.

2. Material and methods

This narrative review was developed through a targeted literature search of PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials. Publications from January 2014 to April 2026 were considered, and the last search was conducted on April 30, 2026. Search concepts combined terms for OSA (obstructive sleep

apnea, sleep-disordered breathing, apnea-hypopnea index, AHI, hypoxic burden) with terms for incretin-based and obesity-directed therapy (tirzepatide, GLP-1 receptor agonist, GIP/GLP-1, semaglutide, liraglutide, anti-obesity medication, bariatric surgery, weight loss). Reference lists of key trials, guidelines, regulatory documents, and meta-analyses were also reviewed. Seminal references prior to 2014 were incorporated as historical background.

Evidence was prioritized in the following order: phase 3 randomized trials directly evaluating OSA, prespecified secondary analyses, randomized studies of other incretin-based therapies in OSA, meta-analyses of GLP-1 receptor agonists or incretin therapies in OSA, relevant clinical guidelines, and official FDA or EMA documents.

Outcomes of interest were AHI, body weight, sleep-apnea-specific hypoxic burden, patient-reported symptoms, blood pressure, inflammatory and metabolic biomarkers, adverse events, discontinuation considerations, and implications for PAP use. Evidence strength was considered according to study design, population relevance, directness, effect size, follow-up duration, and risk of overinterpretation.

3. Results

Mechanistic rationale and endpoint interpretation

Weight reduction can improve OSA through several converging mechanisms. Reduced parapharyngeal and tongue fat may increase upper-airway caliber and reduce collapsibility. Lower abdominal and visceral adiposity may improve lung volume and caudal traction on the upper airway. Reduced systemic inflammation and improved insulin sensitivity may also modify vascular and neuromuscular pathways involved in sleep-disordered breathing.[2,3,11]

Older observational and randomized lifestyle-intervention studies support this relationship. In the Wisconsin Sleep Cohort, weight change tracked with sleep-disordered breathing severity; a 10% weight loss predicted a substantial decrease in AHI, while weight gain had the opposite effect.[12] In the Sleep AHEAD trial, intensive lifestyle intervention improved OSA in adults with obesity and type 2 diabetes.[13]

OSA is nevertheless heterogeneous. Endotype studies show interindividual differences in anatomical compromise, upper-airway muscle responsiveness, loop gain, and arousal threshold.[14] A patient whose OSA is primarily driven by obesity-related anatomical loading is more likely to respond to major weight reduction than a patient whose dominant mechanism is

non-anatomical. Therefore, large mean effects in a trial do not imply universal remission or universal PAP discontinuation.

AHI remains the standard endpoint in most OSA trials, but it counts event frequency and incompletely captures event depth, duration, arousal burden, and oxygen stress. Sleep-apnea-specific hypoxic burden is clinically relevant because it quantifies the desaturation burden attributable to respiratory events and has been associated with cardiovascular mortality more strongly than AHI in cohort analyses.[15] Patient-reported sleepiness, commonly assessed by the Epworth Sleepiness Scale (ESS), adds patient-centered context but cannot replace objective reassessment when considering changes in device therapy.

Outcome	What it measures	Clinical value	Main caveat
AHI	Number of apneas and hypopneas per hour of sleep.	Standard severity metric and primary endpoint in most OSA trials.	Does not capture depth and duration of desaturation or symptom burden.
Hypoxic burden	Area under the oxygen-desaturation curve attributable to respiratory events.	More physiologically linked to nocturnal oxygen stress and cardiovascular risk.	Not yet routinely used in all sleep laboratories.
ESS	Subjective daytime sleepiness on a 0-24 scale.	Useful patient-centered measure and part of some remission definitions.	Symptoms may improve despite residual OSA or nocturnal hypoxemia.
Body weight and BMI	Magnitude of obesity modification.	Mechanistic driver of improvement in obesity-related OSA.	Does not specify whether residual OSA is anatomical or non-anatomical.
Blood pressure, hsCRP, triglycerides, insulin resistance	Cardiometabolic response to therapy.	Links OSA treatment with broader metabolic and vascular risk.	Biomarkers are not substitutes for hard cardiovascular outcomes.

Table 1. Interpretation of clinically relevant outcomes in obesity-related OSA trials.

Pivotal evidence: SURMOUNT-OSA

SURMOUNT-OSA consisted of two parallel, 52-week, double-blind, randomized, placebo-controlled phase 3 trials within a master protocol.[8] The program enrolled 469 adults with

obesity and moderate-to-severe OSA. Trial 1 included participants unwilling or unable to use PAP, and trial 2 included established PAP users. This design is clinically relevant because it separates two common real-world populations: patients without effective device use and patients whose airway is supported during sleep but whose obesity phenotype remains untreated.

Participants were assigned to tirzepatide, titrated to the maximum tolerated dose of 10 mg or 15 mg once weekly, or placebo. Lifestyle counseling was provided in both groups. In trial 2, PAP was suspended for 7 days before endpoint assessment to measure AHI under natural-airway conditions. Baseline mean AHI was approximately 50 events/hour and mean BMI was close to 39 kg/m², indicating severe OSA and substantial obesity burden.[8]

After 52 weeks, AHI decreased markedly with tirzepatide. In trial 1, the mean AHI change was -25.3 events/hour with tirzepatide and -5.3 with placebo, yielding an estimated treatment difference of -20.0 events/hour. [8]

In trial 2, the corresponding changes were -29.3 and -5.5 events/hour, with an estimated treatment difference of -23.8 events/hour.[8] These effects are larger than those reported with earlier pharmacological strategies directed at OSA.

Responder outcomes make the findings more clinically interpretable. At least 50% AHI reduction occurred in most tirzepatide-treated participants, and remission or mild non-symptomatic OSA was achieved in 42.2% of tirzepatide-treated participants in trial 1 and 50.2% in trial 2.[8,16] These outcomes show that tirzepatide can change disease category in a substantial subset, but also that many patients have residual disease and require continued monitoring.

Body-weight reduction paralleled the sleep-study effects. Placebo-adjusted weight differences were approximately 16 to 17 percentage points across the two trials.[8] Sleep-apnea-specific hypoxic burden also improved substantially, with estimated treatment differences of approximately -70.1 percentage points in trial 1 and -61.3 percentage points in trial 2.[8] The concordant improvements in AHI, body weight, and hypoxic burden support a coherent effect on obesity-related airway physiology rather than an isolated numerical change in one sleep-study measure. A comparative summary of the two SURMOUNT-OSA trials is provided in Table 2.

Parameter	Trial 1: participants not using PAP	Trial 2: established PAP users
Population	Adults with obesity and moderate-to-severe OSA who were unwilling or unable to use PAP.	Adults with obesity and moderate-to-severe OSA using PAP for at least 3 months and planning to continue.
Sample	n=234; tirzepatide n=114, placebo n=120.	n=235; tirzepatide n=120, placebo n=115.
Endpoint assessment	AHI assessed under natural-airway conditions without PAP.	PAP was suspended for 7 days before endpoint assessment to measure natural-airway AHI.
AHI change at week 52	-25.3 vs -5.3 events/hour; estimated treatment difference -20.0 events/hour (95% CI -25.8 to -14.2).	-29.3 vs -5.5 events/hour; estimated treatment difference -23.8 events/hour (95% CI -29.6 to -17.9).
Body-weight effect	Estimated treatment difference in percent change: -16.1% (95% CI -18.0 to -14.2).	Estimated treatment difference in percent change: -17.3% (95% CI -19.3 to -15.3).
OSA-specific hypoxic burden	Estimated treatment difference in percent change: -70.1% (95% CI -90.9 to -49.3).	Estimated treatment difference in percent change: -61.3% (95% CI -84.7 to -37.9).
Remission or mild non-symptomatic OSA endpoint	42.2% of tirzepatide-treated participants met criteria for remission or mild non-symptomatic OSA in the treatment-regimen estimand.	50.2% of tirzepatide-treated participants met criteria for remission or mild non-symptomatic OSA in the treatment-regimen estimand.
Clinical interpretation	Supports tirzepatide as an evidence-based option when effective PAP use is absent or not feasible.	Shows improvement in obesity-related OSA physiology despite established PAP background, but does not prove that PAP can be safely discontinued.

Table 2. Comparative summary of the pivotal SURMOUNT-OSA trials. AHI, apnea-hypopnea index; CI, confidence interval; OSA, obstructive sleep apnea; PAP, positive airway pressure. Source: Malhotra et al.[8] and Zepbound prescribing information.[16]

Cardiometabolic and patient-centered outcomes

The clinical argument for tirzepatide would be narrower if it improved only AHI. A prespecified secondary analysis of SURMOUNT-OSA broadened the interpretation by showing favorable changes in cardiometabolic risk markers.[17] Compared with placebo, tirzepatide improved systolic blood pressure, high-sensitivity C-reactive protein (hsCRP), triglycerides, fasting insulin, and homeostatic model assessment of insulin resistance (HOMA-IR).

The mediation analysis suggested that improvements in AHI and hypoxic burden explained part of the treatment effect on selected metabolic markers.[17] This does not prove reduction in cardiovascular events, but it supports the biological plausibility that treating obesity-related OSA may improve metabolic risk through both weight-dependent and sleep-disordered-breathing-related pathways.

Patient-reported outcomes in SURMOUNT-OSA generally moved in the same direction as objective outcomes, but symptom improvement should be interpreted cautiously. Some patients with severe OSA report little sleepiness, while others may feel better despite persistent nocturnal hypoxemia. Clinical decisions about PAP pressure reduction, oral appliance adjustment, or device discontinuation should therefore be based on repeat objective testing rather than symptoms alone.

Marker	Trial 1: estimated treatment difference	Trial 2: estimated treatment difference	Interpretation
Systolic blood pressure	-7.9 mm Hg	-4.3 mm Hg	Clinically relevant direction of vascular risk change.
hsCRP	-28.9%	-45.1%	Reduction in systemic inflammatory activity.
Triglycerides	-32.2%	-31.5%	Improvement in atherogenic lipid profile.
Fasting insulin	-41.4%	-45.4%	Improvement in insulin exposure.
HOMA-IR	-48.0%	-54.5%	Improvement in insulin resistance.

Table 3. Selected cardiometabolic estimated treatment differences for tirzepatide versus placebo in SURMOUNT-OSA secondary analyses. Abbreviations: hsCRP, high-sensitivity C-reactive protein; HOMA-IR, homeostatic model assessment of insulin resistance. Source: prespecified secondary analysis of SURMOUNT-OSA.[17]

Other incretin-based therapies

Tirzepatide currently has the strongest direct evidence, but it is not the only incretin-based therapy studied in OSA. Liraglutide 3.0 mg was evaluated in the SCALE Sleep Apnea randomized trial in adults with obesity and moderate or severe OSA who were unwilling or unable to use CPAP. After 32 weeks, AHI decreased more with liraglutide than placebo, with an estimated treatment difference of -6.1 events/hour.[18] The effect was statistically significant but much smaller than that observed in SURMOUNT-OSA, consistent with the smaller weight loss produced by liraglutide.

Recent meta-analyses support a class-related signal but also highlight heterogeneity. One meta-analysis of GLP-1 receptor agonist therapy in OSA estimated an overall AHI reduction of 9.48 events/hour, with subgroup estimates favoring tirzepatide over liraglutide.[19] A separate placebo-controlled meta-analysis focused on individuals without diabetes found clinically meaningful AHI reduction but a higher overall adverse-event burden versus placebo.[20]

No phase 3 OSA-specific trial of semaglutide comparable to SURMOUNT-OSA was identified in the present literature search. In STEP 1, semaglutide produced a mean body-weight reduction of 14.9% at 68 weeks in adults with overweight or obesity without diabetes.[21] It is biologically plausible that semaglutide may improve obesity-related OSA through weight loss, but direct OSA efficacy, hypoxic-burden effects, and PAP-related strategies require dedicated trials.

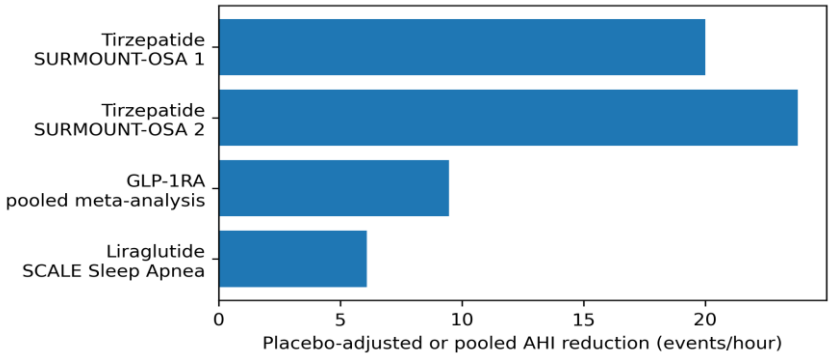

Figure 1. Comparative magnitude of placebo-adjusted or pooled AHI reduction across selected incretin-based therapy evidence. Values are not from head-to-head trials and should be interpreted as contextual, not comparative efficacy claims. AHI, apnea-hypopnea index; GLP-1RA, glucagon-like peptide-1 receptor agonist. Sources: SURMOUNT-OSA,[8] SCALE Sleep Apnea,[18] and meta-analysis.[19]

Safety and tolerability

The safety profile observed in the SURMOUNT-OSA trial aligned with that from previous tirzepatide studies and other incretin-based obesity trials. The most common adverse events were gastrointestinal, including nausea, diarrhea, vomiting, constipation, abdominal pain, and dyspepsia, usually mild to moderate and more frequent during dose escalation.[8,16] The current U.S. prescribing information includes a boxed warning about the risk of thyroid C-cell tumors observed in rodents. Tirzepatide is contraindicated in patients with a personal or family history of medullary thyroid carcinoma and in patients with multiple endocrine neoplasia syndrome type 2.[16] According to the current U.S. prescribing information, other recognized warnings and precautions include severe gastrointestinal adverse reactions, acute kidney injury due to volume depletion, acute gallbladder disease, acute pancreatitis, hypersensitivity reactions, hypoglycemia, diabetic retinopathy complications in patients with type 2 diabetes, pulmonary aspiration during general anesthesia or deep sedation, and the instruction never to share a ZEPBOUND KwikPen between patients.[16] Discontinuation is also clinically relevant because SURMOUNT-4 showed substantial weight regain after tirzepatide withdrawal and maintenance of weight reduction with continued treatment.[22]

Relationship to positive airway pressure therapy and clinical placement

The central implementation question is whether tirzepatide can replace PAP. Current evidence does not support a universal replacement approach. SURMOUNT-OSA demonstrated improvement in natural-airway AHI in both non-PAP participants and PAP users after protocol-defined temporary PAP withdrawal for endpoint assessment, but it did not randomize responders to stop PAP and did not establish long-term criteria for safe device discontinuation.[8,16]

For patients with marked sleepiness, severe baseline OSA, cardiovascular disease, professional driving responsibilities, high accident risk, or persistent nocturnal hypoxemia, PAP should usually continue while pharmacological weight-loss therapy is initiated.[5,24,25] After substantial weight loss, repeat home sleep apnea testing or polysomnography should guide PAP pressure adjustment, oral appliance adjustment, or supervised discontinuation.[24,25]

For patients who cannot or will not use PAP, tirzepatide provides an evidence-based option when obesity is present and there are no contraindications.

It should still be used with lifestyle intervention and, where appropriate, positional therapy, oral appliance therapy, treatment of nasal obstruction, and cardiometabolic risk management. The most defensible clinical framing is additive rather than substitutive: tirzepatide targets the obesity phenotype, while PAP stabilizes the sleeping airway.

Clinical scenario	**Reasonable role of tirzepatide**	**What should not be assumed**
Moderate-to-severe OSA with obesity and poor PAP tolerance	Evidence-based pharmacological option targeting the obesity phenotype, alongside lifestyle and non-PAP OSA strategies.	That medication alone will normalize OSA in every patient.
Established PAP user with obesity	Adjunctive therapy to reduce adiposity, AHI, and hypoxic burden; may later permit pressure adjustment after testing.	That PAP can be stopped without repeat objective sleep assessment.
Severe OSA, marked sleepiness, cardiovascular disease, or safety-critical occupation	Potential addition to PAP and risk-factor management.	That symptom improvement is sufficient proof of safety.
Patient considering bariatric surgery	Non-surgical alternative, bridge to surgery, or adjunct depending on BMI, comorbidities, and preference.	That pharmacotherapy and surgery are interchangeable in all patients.

Table 4. Practical placement of tirzepatide in obesity-related OSA management.

Comparison with bariatric surgery

Bariatric surgery remains a highly effective intervention for severe obesity and can substantially reduce OSA severity. Its advantages include large and often durable weight loss, improvement in type 2 diabetes and other obesity-related disease, and a long evidence history.[3,29] Its disadvantages include perioperative risk, altered anatomy for many procedures, nutritional surveillance, and variable OSA remission.[3]

Tirzepatide creates a non-surgical alternative whose weight-loss magnitude can approach surgical ranges in some patients.[7,22] The comparison should not be framed as simple competition. Surgery may be preferable for selected patients with severe obesity, metabolic complications, and willingness to undergo an operation. Pharmacotherapy may be preferable for patients who decline surgery, are not surgical candidates, need reversible treatment, or require a bridge to surgery.[2,3,29] Comparative-effectiveness studies in OSA-specific populations are still needed.[29,30]

4. Discussion

SURMOUNT-OSA is a phase 3 program with two adequately powered placebo-controlled trials, prespecified endpoints, and converging evidence across the primary endpoint, responder analyses, hypoxic burden, and body weight.[8] A 50% reduction in AHI in most tirzepatide-treated participants, and conversion to remission or mild non-symptomatic OSA in roughly four to five out of every ten treated patients support the clinical relevance of the observed treatment effect. In the historical context of OSA pharmacology, where most non-PAP attempts have not produced reliable AHI reductions of 10 events/hour, this is a different magnitude of result.[18-20] Despite these numbers, the most defensible reading of the current evidence is that tirzepatide is an adjunct to, not a substitute for, PAP. Three reasons matter. First, OSA is biologically heterogeneous. Endotype-level work has shown that anatomical loading from obesity is one driver among several: pharyngeal muscle responsiveness, arousal threshold, and loop gain also vary substantially across patients, and not all of these are weight-modifiable.[14] Reducing parapharyngeal fat does not necessarily restore dilator-muscle responsiveness in a patient whose dominant endotype is neuromuscular. Second, SURMOUNT-OSA did not test long-term PAP withdrawal as a clinical strategy.[8,16] Third, AASM guidance still positions PAP as the standard of care for symptomatic adult OSA.[5] A guideline change of that magnitude typically

follows hard-outcome data, and tirzepatide does not yet have OSA-specific evidence for reduction in myocardial infarction, stroke, heart failure hospitalization, or mortality.

The cardiometabolic mediation result is one of the most consequential findings for how combined obesity-OSA disease should be interpreted.[17] It is consistent with older mechanistic work suggesting that recurrent intermittent hypoxemia drives oxidative stress, sympathetic activation, and endothelial dysfunction, while sleep fragmentation contributes to insulin resistance independently of weight.[11] The mediation analysis quantifies what was previously a plausible clinical assumption: treating sleep-disordered breathing and excess adiposity together may be better than treating either domain in isolation.

A natural question is how tirzepatide compares with semaglutide, the other incretin-based therapy now widely used for obesity. In the STEP 1 trial, semaglutide 2.4 mg once weekly produced a mean weight loss of 14.9% from baseline at 68 weeks in adults with obesity or overweight but without diabetes.[21] This is meaningful but smaller than the approximately 20% achieved with higher-dose tirzepatide in SURMOUNT-1.[7] No phase 3 trial has yet tested semaglutide specifically in OSA, so direct comparisons of AHI outcomes are not possible. Any expectation that semaglutide would improve obesity-related OSA should therefore be framed as a biologically plausible inference from weight loss, not as established OSA-specific efficacy.

Several limitations of the evidence base deserve acknowledgement. SURMOUNT-OSA enrolled adults with BMI ≥30 kg/m² and did not establish outcomes for mild OSA or for patients whose OSA is not primarily obesity-related.[8,30] Long-term durability beyond the pivotal trial period remains incompletely defined, and the hard cardiovascular endpoints clinicians most want to see specifically in OSA with obesity are not yet available. SURPASS-CVOT provides important cardiovascular outcome information for tirzepatide compared with dulaglutide in patients with type 2 diabetes and atherosclerotic cardiovascular disease,[23] but those data should not be overextended to OSA-specific populations. Finally, the pivotal OSA dataset was sponsored by the drug manufacturer; although the trial methodology is rigorous and the secondary analyses are peer-reviewed, this should be transparently noted.

Additional complementary evidence supports this cautious, integrated framing. Contemporary diagnostic reviews and international consensus documents emphasize OSA heterogeneity and multimodal management.[24,25] A recent weight-reduction meta-analysis, long-term Sleep AHEAD data, and CPAP/weight-loss trials support a dose-response link between weight reduction and AHI improvement while also showing that airway stabilization and obesity treatment are complementary rather than interchangeable.[26-28]

Observational metabolic-surgery data and SURMOUNT-OSA design work further support the need to study long-term cardiometabolic outcomes, predictors of remission, and objective criteria for PAP de-escalation.[29,30]

5. Conclusion

Tirzepatide currently has the strongest direct pharmacological evidence base for adults with obesity-related moderate-to-severe OSA. In SURMOUNT-OSA, it produced large reductions in AHI, body weight, and sleep-apnea-specific hypoxic burden in participants not using PAP and in established PAP users.

Secondary analyses show favorable changes in blood pressure, inflammation, triglycerides, and insulin resistance, with evidence that improvement in sleep-disordered breathing may contribute independently to part of the metabolic benefit. These findings support viewing obesity-related OSA as an integrated sleep, metabolic, and cardiovascular risk phenotype.

Tirzepatide should be implemented as part of phenotype-directed care, not as an automatic substitute for PAP. PAP remains the principal airway-stabilizing therapy for many symptomatic or high-risk patients. Before PAP pressure reduction or discontinuation, objective reassessment with home sleep apnea testing or polysomnography is recommended. Future studies should define long-term durability, safety in broader populations, comparative effectiveness against other obesity therapies, cost-effectiveness, predictors of remission, and criteria for supervised PAP withdrawal after pharmacological weight loss.

Disclosure

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