International Journal of Community Medicine and Public Health
Naseem S et al. Int J Community Med Public Health. 2025 Aug;12(8):3805-3812
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20252496

Review Article

Tirzepatide: a dual approach to combat obesity and obstructive sleep apnea

Sadia Naseem*, Summaiya Afreen, Sayed Fareha, Chinthoju Pushpa, Mirza H. Reja

Department of Pharmacy Practice, St. Pauls College of Pharmacy, Turkayamjal, Telangana, India

Received: 02 May 2025
Revised: 23 June 2025
Accepted: 01 July 2025

***Correspondence:**
Dr. Sadia Naseem,
E-mail: khansadia395@gmail.com

ABSTRACT

Obesity and obstructive sleep apnea (OSA) are strongly connected conditions that significantly affect morbidity and mortality worldwide. Recurrent airway blockage during sleep is a hallmark of OSA, which is frequently made worse by being overweight, especially by fat deposits around the neck that constrict the airway. This syndrome is associated with a higher risk of heart disease, daytime weariness, and fragmented sleep. The potential option for treating obese conditions and its related problems, such as OSA, is tirzepatide, a new bivalent agonist that targets the glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors. Tirzepatide has been shown in clinical trials to greatly aid in weight loss; over a 72-week period, reports show reductions in body weight of up to 22.4%. Improved metabolic parameters, such as increased insulin sensitivity and decreased inflammatory markers, are correlated with this significant weight loss. According to research, the apnea-hypopnea index (AHI), a crucial indicator of the severity of OSA, might significantly decline with even modest weight loss. Tirzepatide has been proven in studies to significantly lower AHI; one research found that the drug reduced AHI by an average of -29.3 occurrences per hour when compared to a placebo. In addition to increasing insulin secretion, which improves glycemic control, tirzepatide also reduces hunger through pathways in the central nervous system, which makes weight management easier. Tirzepatide's mode of action is especially pertinent to obesity and OSA since it targets weight gain and metabolic dysregulation, two important contributors in the onset and aggravation of sleep apnea. Tirzepatide's novel mechanism, clinical effectiveness in encouraging weight reduction and reducing the severity of OSA, and the close connection between obesity and OSA are all highlighted in this review, indicating that it may be a game-changing treatment for this dual health issue.

Keywords: Tirzepatide, Obesity, Obstructive sleep apnea, GLP-1 and GIP agonist, Apnea-hypopnea index

INTRODUCTION

Obesity

Obesity is defined by an excessive buildup of body fat, which frequently happens when the body consumes more calories than it can use. The surplus calories are stored as fat, orose tissue.[1] Among the most dangerous medical conditions in existence today, this condition is categorized as a chronic disease and represents a growing global concern.[2] Numerous health and psychological issues are associated with it, which raises mortality and disability rates.[3,4] Obesity and a sedentary lifestyle are strongly and directly related, especially in Western countries; a recent meta-analysis found that among obese people, the prevalence rates of sedentary behavior and physical inactivity were 31% and 43%, respectively.[5] Consequently, a comprehensive lifestyle intervention is typically regarded as the primary approach for managing obesity, encompassing calorie reduction, regular physical exercise, and regular check-ins with healthcare providers.[6] Behavioral treatment methods play a vital role for these individuals, having proven effective in enhancing adherence to lifestyle modification programs.[7]

Obstructive sleep apnea

In OSA, the airway collapses during sleep, causing recurrent episodes of obstruction. This leads to recurring instances of low oxygen levels and reoxygenation, resulting in nighttime awakenings, fragmented sleep, and heightened sympathetic activity. Ultimately, these factors contribute to unrefreshing sleep, which is linked to daytime drowsiness, diminished quality of life, and increased risk of metabolic and cardiovascular diseases.[8] OSA is notably prevalent among middle-aged adults, with studies indicating that 34% of males and 17% of females in this demographic fulfils the diagnostic criteria for the disorder.[9] Given the close relationship between obesity and OSA, coupled with the rising obesity rates in developed countries, it is likely that more individuals will begin to experience this condition.[10]

The connection between obstructive sleep apnea and obesity

There exists a direct correlation between OSA and obesity. Obesity peoples may have fat deposits in their upper respiratory tracts, which can narrow their airways and reduce their muscle activity. Sleep apnea is the result of hypoxic and apneic episodes brought on by this condition. Such episodes result in a reduced oxygen supply to body tissues and blood vessels, which can cause tissue hypoxia— a significant contributor to atherosclerosis and a primary risk factor for cardiovascular diseases.[11]

HOW OBESITY CONTRIBUTES TO OSA PATHOPHYSIOLOGY

Obesity significantly increases the risk of developing OSA through various interconnected mechanisms. One of the primary factors is the accumulation of fat around the upper airway; this excess fat around the neck and pharyngeal area narrows the airway, raising the chances of airway collapse during sleep.[12] This issue worsens when there is fat buildup in the parapharyngeal region, which mechanically compresses the airway. Additionally, obesity diminishes the muscle tone that helps keep the airway open, particularly during REM sleep when muscle tone is naturally reduced, making the airway more susceptible to collapse. People with obesity may also experience impaired neuromuscular responses, which further hinder the airway's ability to stay open, leading to apneic events.[13]

Furthermore, increased abdominal fat elevates intra-abdominal pressure, pushing the diaphragm upwards and lowering lung volumes, which heightens the risk of airway collapse. This additional abdominal fat can also hinder effective diaphragm movement, affecting respiratory function and making it more difficult to breathe during sleep. Chronic low-grade systemic inflammation associated with obesity can influence the muscles and tissues of the upper respiratory tract, leads to collapse. Inflammatory substances released from excess adipose tissue can exacerbate the severity of OSA.[14] Obesity is also closely linked to metabolic disorders like insulin resistance and metabolic syndrome, which can disrupt respiratory function, leading to further complications. Hormonal imbalances, particularly fluctuating leptin levels, may interfere with breathing regulation, increasing the likelihood of apneic episodes.[15]

Fat infiltration in respiratory muscles weakens their function, raising the chances of airway collapse.[16] In some instances, OSA may occur alongside obesity hypoventilation syndrome (OHS) characterized by chronic carbon dioxide retention from impaired ventilation, which worsens hypoxemia and hypercapnia. Leptin resistance, commonly seen in obesity, complicates appetite and respiration regulation, contributing to ventilatory instability and more severe apneas. Lastly, excess fat around the thoracic region can reduce chest wall compliance, making lung expansion more challenging and resulting in shallow, ineffective breathing. Together, these mechanisms reveal how obesity crucially impacts the onset and worsening of obstructive sleep apnea.[17]

The pathophysiology of OSAS involves mechanisms that impact upper airway collapse and the interaction of many variables (Figure 1). One major contributing reason to upper airway collapse is the decrease in upper airway volume brought on by obesity or anomalies of the craniofacial structure and soft tissue. The degree of damage to the upper airway's anatomical structure varies across OSAS patients. An increase in peripheral pressure is known as a nocturnal rostral fluid shift, which occurs when fluid that has accumulated in the legs during the day re-distributes to the upper body when the person is lying down at night. Furthermore, the mechanism is unclear, and the majority of patients have mucosal edema. Additionally, OSAS may be involved in a number of processes linked to low respiratory arousal threshold, poor pharyngeal neuromuscular muscle response, excessive loop gain, and high passive Pcrit. When awake, the dilated throat's muscles are kept active by neural activity, which keeps the throat from collapsing. The airway may collapse if this muscle (chemosensitivity, central respiratory neurons, and ventilatory drive) stops being activated during rapid eye movement (REM) sleep. Multiple pathogenic mechanisms interacting to induce cyclical OSAS development are shown schematically in Figure 1b. Furthermore, these pathways may serve as targets for treatment.

TIRZEPATIDE

The US FDA has endorsed tirzepatide, a novel drug, to treat type 2 diabetic mellitus (T2DM). This drug also shows effectiveness in promoting weight loss, which has led to its alternative use for treating obesity. Tirzepatide is a long-acting stimulating agent that efficiently activates both the glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors. Its amino acid structure features a C20 fatty acid moiety that allows for binding to albumin, extending its half-life.[18] Treatment of obstructive sleep apnea with tirzepatide has

resulted in notable reductions in excessive weight, improvements in cardiovascular health, and reductions in indicators of vascular endothelial dysfunction and inflammation.[19,20]

Adults who are overweight (BMI of 27 kg/m² or higher) or obese (BMI of 30 kg/m² or higher) and who suffer from obesity-related medical conditions such as cardiovascular disease, type 2 diabetes mellitus, hypertension, dyslipidemia, or obstructive sleep apnea are prescribed Zepbound (Tirzepatide) to aid in weight loss and maintenance. It should be taken alongside increased activity and a low-calorie diet. Patients with a history of severe gastrointestinal disorders, such as severe gastroparesis, or pancreatitis have not had the safety of Zepbound examined. It is not recommended to be used with any GLP-1 receptor agonists or tirzepatide preparations.[21]

MECHANISM OF ACTION OF TIRZEPATIDE

Dual GLP-1 and GIP receptor agonist activity

All around the body, but especially in the gastrointestinal tract and pancreatic beta cells, are GLP-1 receptors (GLP-1R). Because GLP-1R signalling is involved in controlling glucose levels by increasing insulin secretion in response to glucose, slowing stomach emptying, lowering plasma glucagon levels, and lowering body weight by activating appetite-suppressing brain pathways, they contribute to the pathophysiology of type II diabetes. The peptide hormones GIP and GLP-1 are essential for preserving glucose homeostasis and inducing the release of insulin from beta cells in the pancreas. However, when food is consumed, the main incretin hormone that has insulinotropic effects is GIP.[22,23]

Although tirzepatide's exact mode of action is yet unknown, the drug's benefits on weight management and glycemic control may be due to the combined activation of GIP and GLP-1R.[24] Studies have demonstrated that when GIP and a GLP-1R agonist are administered together, the insulin response is markedly increased and glucagon release is decreased in comparison to when either hormone is administered alone.[24] Tirzepatide has a high affinity for both GIP and GLP-1R; it is five times less effective at binding GLP-1R than native GLP-1, but it is comparable to native GIP in binding GIP receptors.[24] *In vitro*, tirzepatide strongly stimulates the GLP-1R signaling pathway to promote glucose-dependent insulin secretion, whether through GIPR or GLP-1R activation. More research is necessary to clarify the part that GIPR activation plays in the drug's overall mechanism, as preclinical and clinical studies have produced contradictory findings about the impact of GIPR agonism on glycemic and obesity management.[24]

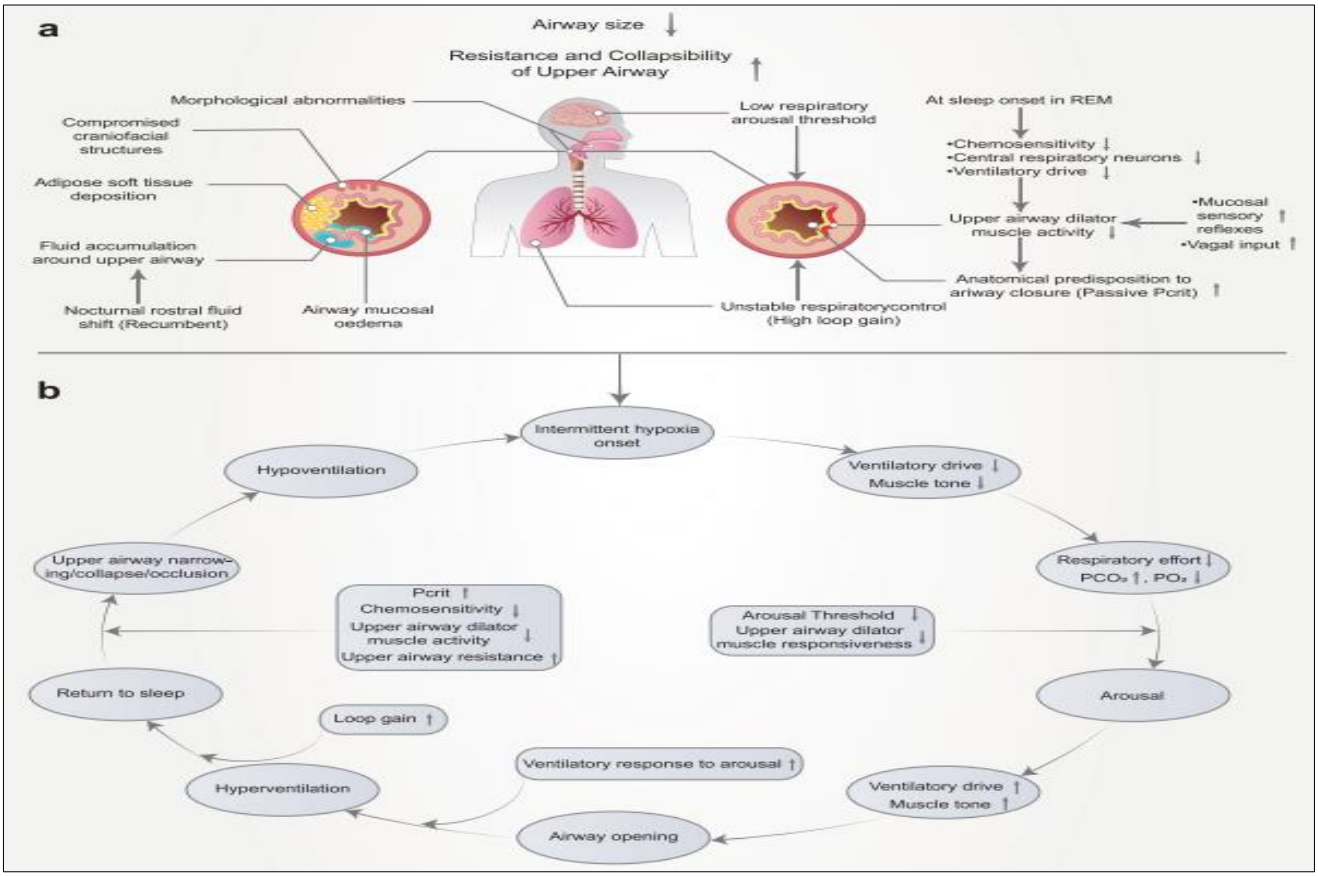

Figure 1: The pathophysiology of OSAS involves mechanisms that (a) impact upper airway collapse, and (b) interaction of many variables.

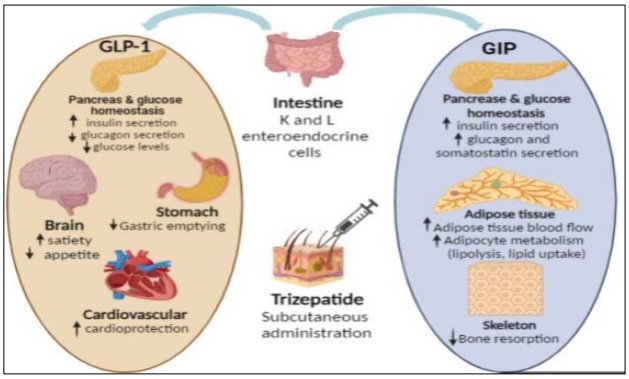

Figure 2: GLP-1 and GIP have important physiological functions. The GLP-1 and GIP receptors are being agonistically acted upon by tirzepatide.

Role in appetite regulation and weight loss

Tirzepatide activates hormone receptors from the intestine, namely GLP-1 and GIP, which helps to reduce hunger and lower food intake. This action prompts the pancreas to release insulin while suppressing agon— a hormone that increases blood sugar levels. As a result, sugar management improves after meals.[25] Moreover, tirzepatide affects certain brain chemicals, leading to a reduced appetite, heightened energy expenditure, and the limitation of unusual fat buildup in areas typically low in fat, which significantly aids in weight loss (Figure 3).[26]

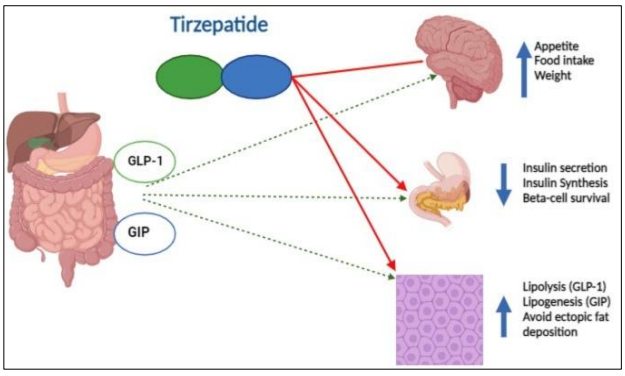

Figure 3: Tirzepatide functions by triggering your body's GLP-1 and GIP receptors.

THE IMPACT OF WEIGHT LOSS CAUSED BY TIRZEPATIDE ON OSA MANAGEMENT

The most modifiable causes for OSA is obesity, and the AHA scientific statement on OSA and heart health emphasizes that OSA is associated with BMI.[28] This claim is supported by a population-based study that found that even modest weight control can successfully prevent the onset of new OSA cases or lessen the severity of AHI, while a 10% increase in body mass is related with a 32% increase in AHI.[29] Reduces of 10%, 20%, and 30% in body mass or BMI were linked to decreases in AHI of 36%, 57%, and 69%, respectively, according to a recent meta-analysis.[30] Therefore, for all OSA patients, weight loss and lifestyle modifications should be given first priority.[30]

The estimated treatment difference in weight in SURMOUNT trial 1 was -16.1% (95% CI -18.0, -14.2), whereas the AHI change was -47.7% (-65.8, -29.6). Trial 2 also showed a treatment difference in weight of -17.3% (-19.3, -15.3) and a change in AHI of -56.2% (-73.7, -38.7), which is similar to what would be anticipated from a 20% weight loss.[30] AHI alterations and weight loss have not yet been thoroughly examined, indicating the need for more research on this topic. AHI and BMI were found to have a non-linear relationship in a cross-sectional research, with steady AHI levels up to 35 kg/m² as BMI increased.[31] The need for weight loss in obese people with OSA was reinforced by Malhotra et al.'s meta-analysis, which comprised weight reduction research in persons with a baseline BMI of 35 kg/m². Consistent reductions in AHI were found.[32]

TIRZEPATIDE'S EFFECT ON DIABETES MANAGEMENT

Tirzepatide is an artificial double agonist targeting glucagon like peptide-1 and gastric inhibitory peptide. Known as "twincretin," it has unique features that differentiate it from standard GLP-1 receptor agonists.[33] With a composition of 39 amino acids, it serves as an analog of GIP.[34] Functionally, tirzepatide drives insulin production from the pancreas and alleviates hyperglycemia. Additionally, it raises levels of adiponectin.[35]

Tirzepatide's dual agonism substantially lowers hyperglycemia when compared to standalone GLP-1 agonist medications and also curbs appetite.[36,37] In non-diabetic patients, weekly doses of tirzepatide between 5 to 15 mg for obesity management resulted in significant weight reductions, between 16.5% and 22.4%, over 72 weeks. Post hoc studies revealed that tirzepatide led to marked improvements in insulin sensitivity and β-cell function.[38,39]

CLINICAL RESEARCH ADVANCEMENTS

Under the supervision of Malhotra et al, two phase 3, double-blind, randomized controlled trials were carried out. Trial 2's mean AHI was 49.5 occurrences per hour, compared to trial 1's initial mean of 51.5 incidents per hour. The average BMI for each experiment was 39.1 and 38.7. Study 1's mean reduction in AHI after 52 weeks was -25.3 events per hour (95% CI, -29.3 to -21.2) for tirzepatide and -5.3 events per hour (95% CI, -9.4 to -1.1) for placebo, with an estimated treatment difference of -20.0 events per hour (95% CI, -25.8 to -14.2) ($p<0.001$). The results of trial 2 indicated that tirzepatide caused a mean reduction in AHI after 52 weeks of -29.3 events per hour (95% CI, -33.2 to -25.4) and the control group caused -5.5 occurrences per hour (95% CI, -9.9 to -1.2). The estimated treatment difference was -23.8 occurrences per

hour (95% CI, -29.6 to -17.9) (p<0.001). Tirzepatide significantly improved all pre-specified critical secondary endpoint metrics when compared to a placebo. Gastrointestinal side effects were most frequently recorded, and they were usually mild to moderate in intensity.[40]

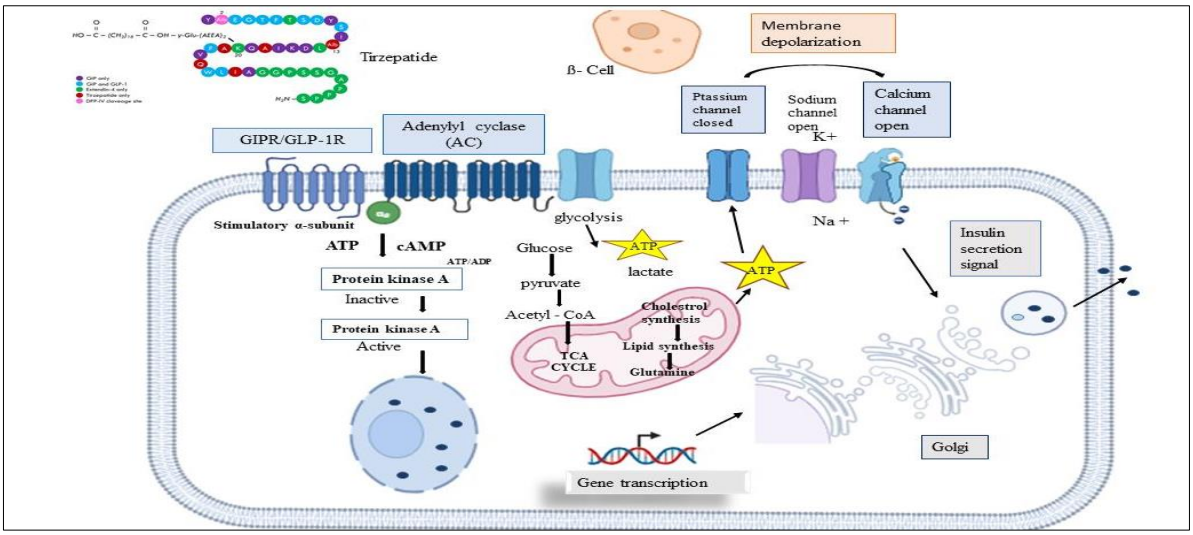

Figure 4: Tirzepatide stimulates the adenylyl cyclase-cAMP-PKA pathway, which in turn increases glucose metabolism through its receptor. This results in elevated ATP levels, which delay K+ channel closing and depolarize β-cells. Depolarization causes voltage-gated Ca2+ channels to open, which improves Ca2+ entry and causes the endoplasmic reticulum to release calcium, which leads to the production of insulin. PKA also stimulates the transcription of the insulin gene, which increases the production of insulin even more. PKA, cAMP, ATP, GIP-R/GLP-1R, and calcium signaling are important elements.

Another large multinational RCT, headed by Jastreboff et al, involved 2,539 obese people who were given TZP at doses of 5, 10, or 15 mg per week for 72 weeks, or a placebo. Participants were examined for waist circumference (WC), and results indicated greater reductions in WC for all TZP doses compared to placebo at week 72: -14.0 cm, -17.7 cm, -18.5 cm for 5, 10, and 15 mg TZP, respectively, versus -4.0 cm in the placebo group. A subset of 255 participants underwent DXA scans to evaluate body composition, but data was only available at the 72-week mark for 160 participants. In the TZP groups, the change in total fat mass from baseline to week 72 was -33.9%, while in the placebo group, it was -8.2%, representing a 25.7% treatment difference. Additionally, the TZP groups experienced a greater decrease in total fat-free mass, with values of -10.9% for TZP and -2.6% for the placebo. In the TZP group, the ratio of fat mass to fat-free mass increased from 0.93 to 0.70, whereas in the placebo group, it changed from 0.95 to 0.88.[41]

In an 84-week multicenter experiment, Wadden et al evaluated the effectiveness of TZP in helping overweight or obese adults lose 5% of their initial weight over the course of a 12-week behavior modification phase. Following that, at random, 579 subjects were given either a control group or the highest tolerable dose of TZP (10 or 15 mg) once a week. 86.4% of the TZP cohort received the maximal dose of 15 mg. The TZP group experienced a more substantial decrease in WC at week 72 (-14.6±0.7 cm) than the placebo group (+0.2±1.0 cm).[42]

Zhao et al started the SURMOUNTCN study in 2024 with patients who were overweight or obese in China. A lifestyle modification and weekly subcutaneous doses of 10 mg or 15 mg TZP or a placebo were administered to 210 individuals over a 52-week period. When compared to the placebo group, those on TZP consistently lost weight, as evidenced by a dose-dependent drop in WC. Their mean age was 36.1 years, and their mean BMI was 32.3 kg/m^2.[43]

The 52-week SURMOUNT-OSA study is a randomized, placebo-controlled experiment designed to assess tirzepatide's safety and effectiveness in treating moderate-to-severe OSA in obese patients.[44] The primary endpoint is the difference in AHI change as determined via polysomnography at the 52-week mark between the tirzepatide and placebo groups.[45] Secondary targets include functional outcomes, cardiometabolic markers, and sleep apnea-specific hypoxic load.[46] The trial incorporates acceleration measurements to evaluate daily activities and devices for at-home sleep testing to follow time till improvement.[47]

Grunstein explored data from SURMOUNT-1, including 197 participants with OSA who met baseline criteria and were divided by tirzepatide dose (5 mg, 10 mg, and 15 mg) or placebo.[48] The average age ranged from 48 to 53 years, with body weights between 110-122 kg and BMIs from 39 to 43 kg/m^2. The mean weight change at week 72 between tirzepatide and placebo was calculated to be -11.2% for 5 mg, -18.2% for 10 mg, and -20.7% for 15 mg, all of which were statistically significant (p<0.001). An additional

substantial percentage of those receiving tirzepatide achieved weight loss of 5% (83-98% versus 25% on placebo) and 10% (46-93% versus 15% on placebo). Notably, 27-62% of participants on tirzepatide reached a 20% weight loss milestone, opposed to 0% in the placebo group.[49]

After propensity score matching, Rodriguez et al recruited 18,386 participants from a cohort study of more than 41,000 adults who met the criteria (semaglutide, 32,029; tirzepatide, 9,193). 52.0% of the population had a T2D diagnosis, while 70.5% of the population was female.[50,51] Their mean age was 52 years. The average starting weight was 110 kg. Discontinuation led to 5,140 (55.9%) of tirzepatide and 4,823 (52.5%) of semaglutide patients dropping out. Patients on tirzepatide had significantly higher chances of achieving specified weight loss percentages (5%; HR, 1.76; 10%; HR, 2.54; 15%; HR, 3.24). Weight changes after 3, 6, and 12 months were notably larger in those taking tirzepatide. Rates of gastrointestinal adverse events were comparable between both groups.[52,53]

Yabe et al's SURPASS J-mono study in Japan involved 48 T2D individuals who were randomly assigned to receive either 0.75 mg of dulaglutide or 5, 10, or 15 mg of TZP for a 52-week period. The initial BMI and mean age were 27.5 kg/m² and 58.6, respectively. All TZP groups showed a reduction in total fat mass from baseline after 52 weeks, however the groups taking 10 and 15 mg of tirzepatide demonstrated a greater reduction in fat mass than the dulaglutide group.[54]

In a 2023 study, Heise et al analyzed the impact of TZP on body composition in T2D patients.[55] For 28 weeks, 117 participants were given either 15 mg tirzepatide, 1 mg semaglutide, or a placebo once a week. Plethysmography was used to measure their body composition. Only those on TZP or semaglutide showed significant total fat mass and fat-free mass reductions. Furthermore, TZP users saw a significantly greater reduction of FM% than semaglutide users.[56]

CONCLUSION

Clinical studies on tirzepatide show that it is a very effective treatment for OSA and obesity. The AHI and waist circumference (WC) consistently decrease with different dosages, according to several phase 3 randomized controlled trials. According to the results, tirzepatide not only lowers AHI but also significantly improves body composition, resulting in a favorable shift in the ratios of fat mass to fat-free mass (FFM) and a notable drop in fat mass (FM).

Notably, compared to placebo groups, those who received tirzepatide was more prevalent to reach weight loss goals, highlighting the medication's promise as a treatment for obesity and related disorders. Most adverse occurrences were mild to moderately severe, indicating a manageable side effect profile, even if gastrointestinal adverse events were the most frequent.

New research on tirzepatide's wider effects in treating OSA, like the SURMOUNT-OSA trial, highlights the need for more research on the drug's long-term effects and safety. All things considered, tirzepatide is a promising dual strategy for treating obesity and OSA, with the potential to enhance metabolic health and quality of life for those who are impacted.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Britannica, The Editors of Encyclopaedia. "Obesity". 2024. Available at: https://www.britannica.com/science/obesity. Accessed on 16 May 2025.
2. Tiwari A, Balasundaram P. Public Health Considerations Regarding Obesity. In StatPearls. StatPearls Publishing: Treasure Island, FL, USA. 2024.
3. El Ghoch M, Fakhoury R. Challenges and New Directions in Obesity Management: Lifestyle Modification Programmes, Pharmacotherapy and Bariatric Surgery. J Popul Ther Clin Pharmacol. 2019;26:1-4.
4. Abdelaal M, le Roux CW, Docherty NG. Morbidity and mortality associated with obesity. Ann Transl Med. 2017;5:161.
5. Silveira EA, Mendonça CR, Delpino FM, Elias Souza GV, Pereira de Souza Rosa L, de Oliveira C, et al. Sedentary behavior, physical inactivity, abdominal obesity and obesity in adults and older adults: A systematic review and meta-analysis. Clin Nutr ESPEN. 2022;50:63-73.
6. Franz MJ, Boucher JL, Rutten-Ramos S, VanWormer JJ. Lifestyle weight-loss intervention outcomes in overweight and obese adults with type 2 diabetes: a systematic review and meta-analysis of randomized clinical trials. J Acad Nutr Diet. 2015;115(9):1447-63.
7. Burgess E, Hassmén P, Welvaert M, Pumpa KL. Behavioural treatment strategies improve adherence to lifestyle intervention programmes in adults with obesity: a systematic review and meta-analysis. Clin Obes. 2017;105-14.
8. Sánchez-de-la-Torre M, Campos-Rodriguez F, Barbé F. Obstructive sleep apnoea and cardiovascular disease. Lancet Respir Med. 2013;1(1):61-72.
9. Romero-Corral A, Caples SM, Lopez-Jimenez F, Somers VK. Interactions between obesity and obstructive sleep apnea: implications for treatment. Chest. 2010;137(3):711-9.
10. Mediano O, González Mangado N, Montserrat JM, Alonso-Álvarez ML, Almendros I, Alonso-Fernández A, et al; el Spanish Sleep Network. International Consensus Document on Obstructive

Sleep Apnea. Arch Bronconeumol. 2022;58(1):52-68.
11. Chen X, Pensuksan WC, Lohsoonthorn V, Lertmaharit S, Gelaye B, et al. Obstructive sleep apnea and multiple anthropometric indices of general obesity and abdominal obesity among young adults. Int J Soc Sci Stud. 2014;2(3):89-99.
12. Ding Q, Qin L, Wojeck B, Inzucchi SE, Ibrahim A, Bravata DM, et al. Polysomnographic Phenotypes of Obstructive Sleep Apnea and Incident Type 2 Diabetes: Results from the DREAM Study. Ann Am Thorac Soc. 2021;18(12):2067-78.
13. Grimaldi D, Beccuti G, Touma C, Van Cauter E, Mokhlesi B. Association of obstructive sleep apnea in rapid eye movement sleep with reduced glycemic control in type 2 diabetes: therapeutic implications. Diabetes Care. 2014;37(2):355-63.
14. Guo J, Dai L, Luo J, Huang R, Xiao Y. Shorter respiratory event duration is related to prevalence of type 2 diabetes. Front Endocrinol (Lausanne). 2023;14:1105781.
15. Li X, Liu X, Meng Q, Wu X, Bing X, Guo N, et al. Circadian clock disruptions link oxidative stress and systemic inflammation to metabolic syndrome in obstructive sleep apnea patients. Front Physiol. 2022;13:932596.
16. Alterki A, Abu-Farha M, Al Shawaf E, Al-Mulla F, Abubaker J. Investigating the relationship between obstructive sleep apnoea, inflammation and cardio-metabolic diseases. Int J Mol Sci. 2023;24(7):6807.
17. Tamisier R, Pepin JL, Remy J, Baguet JP, Taylor JA, Weiss JW, et al. 14 Nights of intermittent hypoxia elevate daytime blood pressure and sympathetic activity in healthy humans. Eur Respir J. 2011;37(1):119-28.
18. Trinh MD, Plihalova A, Gojda J, Westlake K, Spicka J, Lattova Z, et al. Obstructive sleep apnoea increases lipolysis and deteriorates glucose homeostasis in patients with type 2 diabetes mellitus. Sci Rep. 2021;11(1):3567.
19. Coskun T, Sloop KW, Loghin C, Alsina-Fernandez J, Urva S, Bokvist KB, et al. LY3298176, a novel dual GIP and GLP-1 receptor agonist for the treatment of type 2 diabetes mellitus: from discovery to clinical proof of concept. Mol Metab. 2018;18:3-14.
20. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al. Tirzepatide once weekly for the treatment of obesity. N Engl J Med. 2022;387:205-16.
21. Wilson JM, Lin Y, Luo MJ, Considine G, Cox AL, Bowsman LM, et al. The dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist tirzepatide improves cardiovascular risk biomarkers in patients with type 2 diabetes: a post hoc analysis. Diabetes Obes Metab. 2022;24:148-53.
22. Lilly Investors. FDA Approves Lilly's Zepbound™ (tirzepatide) for Chronic Weight Management, a Powerful New Option for the Treatment of Obesity or Overweight with Weight-Related Medical Problems. 2023. Available at: https://investor.lilly.com/news-releases/news-release-details/fda-approves-lillys-zepboundtm-tirzepatide-chronic-weight. Accessed on 18 May 2025.
23. Frias JP. Tirzepatide: a glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) dual agonist in development for the treatment of type 2 diabetes. Expert Rev Endocrinol Metab. 2020;15(6):379-94.
24. Coskun T, Sloop KW, Loghin C, Alsina-Fernandez J, Urva S, Bokvist KB, et al. LY3298176, a novel dual GIP and GLP-1 receptor agonist for the treatment of type 2 diabetes mellitus: From discovery to clinical proof of concept. Mol Metab. 2018;18:3-14.
25. Sinha R, Papamargaritis D, Sargeant JA, Davies MJ. Efficacy and safety of tirzepatide in type 2 diabetes and obesity management. J Obes Metab Syndr. 2023;32:25-45.
26. Min T, Bain SC. The Role of Tirzepatide, Dual GIP and GLP-1 Receptor Agonist, in the Management of Type 2 Diabetes: The SURPASS Clinical Trials. Diabetes Ther. 2021;12(1):143-57.
27. Sallam M, Snygg J, Allam D, Kassem R. Shifting the Scales: Tirzepatide's Breakthrough in Obesity Management. Cureus. 2024;16(5):e60545.
28. Beccuti G, Bioletto F, Parasiliti-Caprino M, Benso A, Ghigo E, Cicolin A, et al. Estimating Cardiovascular Benefits of Tirzepatide in Sleep Apnea and Obesity: Insight from the SURMOUNT-OSA Trials. Curr Obesity Rep. 2024;8:1-4.
29. Yeghiazarians Y, Jneid H, Tietjens JR, Redline S, Brown DL, El-Sherif N, et al. Obstructive sleep apnea and cardiovasculardisease: a scientifc statement from the American heart association. Circulation. 2021;144(3):e56-67.
30. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA. 2000;284(23):3015-21.
31. Malhotra A, Heilmann CR, Banerjee KK, Dunn JP, Bunck MC, Bednarik J. Weight reduction and the impact on apnea-hypopneaindex: A systematic meta-analysis. Sleep Med. 2024;121:26-31.
32. Bucca C, Brussino L, Maule MM, Baldi I, Guida G, Culla B, et al. Clinical and functional prediction of moderate to severe obstructive sleep apnoea. Clin Respir J. 2011;5(4):219-26.
33. Dutta D, Surana V, Singla R, Aggarwal S, Sharma M. Efficacy and safety of novel twincretin tirzepatide a dual GIP and GLP-1 receptor agonist in the management of type-2 diabetes: A Cochrane meta-analysis. Indian J Endocrinol Metab. 2021;25(6):475-89.
34. Sun B, Willard FS, Feng D, Alsina-Fernandez J, Chen Q, Vieth M, et al. Structural determinants of dual incretin receptor agonism by tirzepatide. Proc Natl Acad Sci U S A. 2022;119(13):e2116506119.
35. Thomas MK, Nikooienejad A, Bray R, Cui X, Wilson J, Duffin K, et al. Dual GIP and GLP-1 Receptor Agonist Tirzepatide Improves Beta-cell Function and

Insulin Sensitivity in Type 2 Diabetes. J Clin Endocrinol Metab. 2021;106(2):388-96.
36. Collins L, Costello RA. Glucagon-Like Peptide-1 Receptor Agonists. StatPearls. StatPearls Publishing. Treasure Island (FL). 2023.
37. Dahl D, Onishi Y, Norwood P, Huh R, Bray R, Patel H, et al. Effect of Subcutaneous Tirzepatide vs Placebo Added to Titrated Insulin Glargine on Glycemic Control in Patients With Type 2 Diabetes: The SURPASS-5 Randomized Clinical Trial. JAMA. 2022;327(6):534-45.
38. Gao L, Lee BW, Chawla M, Kim J, Huo L, Du L, et al. Tirzepatide versus insulin glargine as second-line or third-line therapy in type 2 diabetes in the Asia-Pacific region: the SURPASS-AP-Combo trial. Nat Med. 2023;29(6):1500-10.
39. Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2022;45(11):2753-86.
40. Malhotra A, Grunstein RR, Fietze I, Weaver TE, Redline S, Azarbarzin A, et al; SURMOUNT-OSA Investigators. Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity. N Engl J Med. 2024;391(13):1193-205.
41. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al; SURMOUNT-1 Investigators. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022;387(3):205-16.
42. Rochira V, Greco C, Boni S, Costantino F, Dalla Valentina L, Zanni E, et al. The Effect of Tirzepatide on Body Composition in People with Overweight and Obesity: A Systematic Review of Randomized, Controlled Studies. Diseases. 2024;12(9):204.
43. Wadden TA, Chao AM, Machineni S, Kushner R, Ard J, Srivastava G, et al. Tirzepatide after intensive lifestyle intervention in adults with overweight or obesity: the SURMOUNT-3 phase 3 trial. Nat Med. 2024;30(6):1784.
44. Zhao L, Cheng Z, Lu Y, Liu M, Chen H, Zhang M, et al. Tirzepatide for Weight Reduction in Chinese Adults With Obesity: The SURMOUNT-CN Randomized Clinical Trial. JAMA. 2024;332(7):551-60.
45. Human Energy Requirements. Report of a Joint FAO/WHO/UNU Expert Consultation. 2001. Available at: https://www.fao.org/3/y5686e/y5686e00.html. Accessed on 18 April 2025.
46. Jang MS, Kim HY, Dhong HJ, Chung SK, Hong SD, Cho HJ, et al. Effect of parapharyngeal fat on dynamic obstruction of the upper airway in patients with obstructive sleep apnea. Am J Respir Crit Care Med. 2014;190(11):1318-21.
47. Dempsey JA, Veasey SC, Morgan BJ, O'Donnell CP. Pathophysiology of sleep apnea. Physiol Rev. 2010;90(1):47-112.
48. Kim AM, Keenan BT, Jackson N, Chan EL, Staley B, Poptani H, et al. Tongue fat and its relationship to obstructive sleep apnea. Sleep. 2014;37(10):1639-48.
49. Malhotra A, Bednarik J, Chakladar S, Dunn JP, Weaver T, Grunstein R, et al. Tirzepatide for the treatment of obstructive sleep apnea: Rationale, design, and sample baseline characteristics of the SURMOUNT -OSA phase 3 trial. Contemp Clin Trials. 2024;141:107516.
50. Grunstein RR, Taylor R, Shinde S, Dunn JP, Bednarik J, Stefanski A, et al. Effect of Tirzepatide on Weight Loss in Patients with Obstructive Sleep Apnea and Obesity from SURMOUNT-1. Sleep. 2024;47(1):A264-5.
51. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al; STEP 1 Study Group. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med. 2021;384(11):989-1002.
52. Davies M, Færch L, Jeppesen OK, Pakseresht A, Pedersen SD, Perreault L, et al; STEP 2 Study Group. Semaglutide 2·4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. Lancet. 2021;397(10278):971-84.
53. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al; SURMOUNT-1 Investigators. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022;387(3):205-16.
54. Rodriguez PJ, Cartwright BM, Gratzl S, Brar R, Baker C, Gluckman TJ, et al. Semaglutide vs tirzepatide for weight loss in adults with overweight or obesity. JAMA Int Med. 2024;184(9):1056-64.
55. Yabe D, Kawamori D, Seino Y, Oura T, Takeuchi M. Change in pharmacodynamic variables following once-weekly tirzepatide treatment versus dulaglutide in Japanese patients with type 2 diabetes (SURPASS J-mono substudy). Diabetes Obes Metab. 2023;25(2):398-406.
56. Heise T, DeVries JH, Urva S, Li J, Pratt EJ, Thomas MK, et al. Tirzepatide Reduces Appetite, Energy Intake, and Fat Mass in People With Type 2 Diabetes. Diabetes Care. 2023;46(5):998-1004.

Cite this article as: Naseem S, Afreen S, Fareha S, Pushpa C, Reja MH. Tirzepatide: a dual approach to combat obesity and obstructive sleep apnea. Int J Community Med Public Health 2025;12:3805-12.