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Comparative Effectiveness of GLP-1 Agonists Versus Continuous Positive Airway Pressure in Reducing Symptoms and Improving Outcomes for Adults with Obstructive Sleep Apnoea: A Literature Review

Dr Sanjin Bajgoric[1*], Dr Habiba Amraoui[2]

[1]Family Medicine Consultant, Primary Healthcare Corporation, Qatar
[2]Family Medicine Consultant, Primary Healthcare Corporation, Qatar

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***Corresponding author:** Dr Sanjin Bajgoric
Family Medicine Consultant, Primary Healthcare Corporation, Qatar

Abstract **Review Article**

Obstructive sleep apnoea (OSA) is a common condition associated with significant cardiometabolic morbidity. Continuous positive airway pressure (CPAP) remains the gold-standard therapy, providing immediate and reliable suppression of apnoea–hypopnoea events through mechanical airway stabilization. Adherence challenges and residual cardiovascular risk have prompted exploration of adjunctive and alternative therapies. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), originally developed for type 2 diabetes and obesity, have recently demonstrated promise in OSA management, particularly among obese patients. This literature review synthesizes evidence from randomized controlled trials, meta-analyses, and narrative reviews comparing CPAP and GLP-1 agonists. CPAP consistently reduces apnoea–hypopnoea index (AHI), improves oxygen saturation, and alleviates daytime sleepiness, though long-term cardiovascular outcomes remain debated. GLP-1 agonists, including liraglutide and tirzepatide, achieve substantial weight loss and modest reductions in AHI, with additional benefits in improving glycaemic control and reducing systemic inflammation. Current data comparing CPAP to GLP1-agonists is limited by the absence of head-to-head randomized trials and heterogeneity in study populations. Furthermore, GLP-1 agonist trials have tended to be weight-centric, which contrasts with airway-centric CPAP, complicating direct comparison. Current data suggest GLP-1 agonists should be considered adjuncts to CPAP, enhancing long-term disease modification and cardiometabolic risk reduction, rather than substitutes. In CPAP-intolerant patients, GLP-1 agonists may serve as alternatives, though they do not replicate CPAP's immediate efficacy in airway stabilization. Future research should prioritize combined and personalized therapeutic strategies, integrating CPAP's mechanical benefits with GLP-1–mediated metabolic improvements. Such approaches may optimize both symptom control and long-term outcomes, particularly in obese patients at heightened cardiometabolic risk.

Keywords: Obstructive sleep apnoea; CPAP; GLP-1 receptor agonists; semaglutide; liraglutide; tirzepatide; obesity; personalised therapy; adjunctive treatment.

INTRODUCTION

OSA is a prevalent and underdiagnosed sleep-related breathing disorder characterized by recurrent episodes of upper airway obstruction during sleep, leading to intermittent hypoxia, sleep fragmentation, and significant cardiovascular and metabolic consequences. Affecting an estimated 1 in 4 adults globally, OSA has been strongly associated with obesity, insulin resistance, hypertension, and increased cardiovascular morbidity, positioning it as a critical public health concern (Dragonieri *et al.,* 2024). The current gold-standard treatment for moderate to severe OSA is CPAP therapy, which maintains airway patency by delivering pressurized air through a nasal or oronasal mask during sleep. Numerous randomized controlled trials and meta-analyses have demonstrated CPAP's efficacy in reducing the apnea-hypopnea index (AHI), improving daytime sleepiness, and mitigating cardiovascular risk factors (Batool-Anwar *et al.,* 2016; Gottlieb *et al.,* 2014). However, despite its clinical effectiveness, CPAP adherence remains suboptimal, with many patients discontinuing use due to discomfort, inconvenience or perceived lack of benefit (Pogach, 2020). This has prompted exploration into alternative and adjunctive

therapies that address both the mechanical and metabolic underpinnings of OSA.

In recent years, glucagon-like peptide-1 receptor agonists, originally developed for the treatment of type 2 diabetes and obesity, have emerged as promising pharmacological agents in the management of OSA. GLP-1 RAs such as semaglutide and tirzepatide have demonstrated significant weight loss and anti-inflammatory effects, which may directly impact the pathophysiology of OSA by reducing upper airway adiposity and improving ventilatory control (Yang *et al.,* 2025; Aljazeeri *et al.,* 2025). Preliminary clinical trials suggest that GLP-1 therapy may reduce AHI and improve sleep quality, either as monotherapy or in combination with CPAP, offering a novel therapeutic avenue for patients with obesity-related OSA (Dragonieri *et al.,* 2024). This literature review aims to critically compare the effectiveness of GLP-1 receptor agonists versus continuous positive airway pressure (CPAP) in the management of obstructive sleep apnoea. While CPAP remains the cornerstone of treatment, emerging evidence suggests that GLP-1 agonists may offer a novel therapeutic pathway, particularly for patients with obesity-related OSA. By synthesizing current clinical data, mechanistic insights, and evolving treatment paradigms, this review seeks to contribute to the growing body of literature supporting the potential role of GLP-1 agonists in OSA management. Furthermore, it aims to clarify existing gaps in knowledge and highlight key areas for future research.

Mechanisms of action: CPAP and GLP-1 receptor agonists in obstructive sleep apnoea

The pathophysiology of OSA is multifactorial, involving anatomical susceptibility, impaired neuromuscular control, and metabolic dysfunction. Two therapeutic modalities, CPAP and GLP-1 RAs, target distinct aspects of this complex condition.

Continuous Positive Airway Pressure (CPAP)

CPAP is the first-line treatment for moderate to severe OSA. It functions by delivering a constant stream of pressurized air through a nasal or oronasal mask, which acts as a pneumatic splint to maintain upper airway patency during sleep (Jordan *et al.,* 2014). This pressure counteracts the collapsing forces of the pharyngeal soft tissues, particularly during REM sleep when muscle tone is reduced (Eckert *et al.,* 2013). The upper airway, lacking rigid support, is highly susceptible to collapse. CPAP increases intraluminal pressure, stabilizing the airway and significantly reducing the apnea-hypopnea index (AHI), thereby improving oxygenation, sleep architecture, and reducing cardiovascular risk (Marin *et al.,* 2005). Long-term CPAP use has also been associated with improvements in insulin sensitivity and reductions in systemic inflammation (Sharma *et al.,* 2018).

GLP-1 receptor agonists

GLP-1 receptor agonists, originally developed for type 2 diabetes and obesity, have shown promise in OSA management due to their metabolic effects. These agents promote weight loss by enhancing satiety, delaying gastric emptying, and reducing caloric intake (Pi-Sunyer *et al.,* 2015). Given the strong correlation between obesity and OSA, particularly due to fat deposition around the neck and upper airway, weight reduction can decrease pharyngeal collapsibility and improve airway patency (Schwartz *et al.,* 2008). Beyond weight loss, GLP-1 RAs exhibit anti-inflammatory and neuroprotective properties that may influence ventilatory control and upper airway neuromuscular function (Müller *et al.,* 2019). Emerging evidence suggests that GLP-1 RAs may reduce systemic inflammation and improve insulin sensitivity, both implicated in OSA pathogenesis (Polotsky *et al.,* 2012). Recent trials have demonstrated that agents such as semaglutide and liraglutide can reduce AHI and improve sleep quality, even in the absence of CPAP therapy (Blackman *et al.,* 2023). These findings suggest that GLP-1 RAs may serve as a complementary or alternative therapy, particularly for patients with obesity-related OSA or poor CPAP adherence.

Clinical effectiveness of GLP-1 receptor agonists and CPAP in OSA

GLP-1 receptor agonists

Recent literature has explored the therapeutic potential of GLP-1 RAs in the management of OSA, particularly in populations with obesity and type 2 diabetes mellitus (T2DM). Given the strong association between excess adiposity and upper airway collapsibility, GLP-1 RAs, originally developed for glycemic control and weight reduction, have emerged as promising adjuncts in OSA treatment. A systematic review and meta-analysis by Wong et al. (2025) synthesized data from six randomized controlled trials (RCTs) involving 1,023 participants with moderate to severe OSA. The analysis revealed that GLP-1 RA therapy significantly reduced apnea-hypopnea index (AHI) compared to placebo, with a standardized mean difference (SMD) of –0.601 (95% CI: –0.969 to –0.233, $p = 0.001$). However, when compared to continuous positive airway pressure (CPAP), no significant difference in AHI reduction was observed, suggesting that GLP-1 RAs may serve as a complementary rather than replacement therapy. Yang et al. (2025) conducted a broader meta-analysis including eight RCTs and two non-RCTs, focusing on patients with obesity and/or T2DM. Their findings indicated a mean AHI reduction of –5.68 events/hour (95% CI: –7.97 to –3.38, $p < 0.00001$) in the GLP-1 RA group among patients with T2DM. While similar trends were noted in obese patients without diabetes, the evidence was less consistent, highlighting the need for stratified analyses based on metabolic profiles. Mechanistically, GLP-1 RAs may exert beneficial effects on OSA through multiple pathways: reduction of upper airway fat deposition,

improvement in insulin sensitivity, and attenuation of systemic inflammation. Dragonieri *et al*. (2024) emphasized these pleiotropic effects in their narrative review, noting improvements in sleep architecture and reductions in intermittent hypoxia with GLP-1 RA therapy. Despite encouraging results, limitations persist across studies, including small sample sizes, short follow-up durations, and heterogeneity in outcome measures. Moreover, long-term safety and efficacy data remain sparse, particularly in non-diabetic populations. Future research should aim to delineate the optimal patient subgroups, explore combination therapies, and assess durability of treatment effects.

Continuous Positive Airway Pressure

CPAP remains the most effective first-line therapy for moderate–severe OSA, offering robust reductions in apnea–hypopnea index (AHI), symptom relief (daytime sleepiness, snoring), and meaningful cardiometabolic benefits when adherence is adequate. A 2025 landmark meta-analysis published in The Lancet Respiratory Medicine reported that CPAP use was associated with a 37% reduction in all-cause mortality and a 55% reduction in cardiovascular mortality across more than one million patients, underscoring the therapy's long-term survival benefit beyond symptomatic control (The Lancet Respiratory Medicine, 2025). CPAP consistently outperforms alternative modalities (e.g., positional therapy, oral appliances) on physiologic endpoints like AHI and oxygen desaturation, although patient preference and tolerance may guide individualized choices. OSA also delivers success with patient-centered outcomes: improvements in sleep-related quality of life and daytime functioning are well documented, with broader public health relevance given OSA's high global prevalence and associated cardiovascular risk.

Comparative barriers and practical issues: CPAP vs GLP-1 agonists

CPAP

CPAP therapy conveys a significant adherence burden in that it requires nightly use. Furthermore, real-world effectiveness is constrained by mask/interface discomfort, aerophagia, nasal congestion/dryness, machine noise, and travel/logistical burdens, making structured support (education, mask fitting, humidification, behavioral follow-up) critical to achieve sustained nightly use. Additionally, logistical hurdles and perceived stigma surround the use or CPAP e.g. equipment maintenance, travel convenience. Device costs vary, though CPAP is often covered by health insurance and is widely accessible. One of the benefits of CPAP are its immediate onset of action: improvements in AHI and subjective sleep scores begin immediately upon effective use and apply across phenotypes, including non-obese OSA, craniofacial/upper-airway anatomic contributors, and positional OSA.

GLP-1 receptor agonists

The eligibility and indications for use of GLP-1 RAs in OSA are unclear; evidence is strongest in patients with obesity/T2DM. Generalizability to non-obese OSA is limited and regulatory pathways for OSA-specific indications are evolving. Side effects and discontinuation are important to note: gastrointestinal adverse effects (e.g. nausea and vomiting) leading to potential treatment discontinuation, and weight regain after cessation can attenuate the sustained benefits of OSA. Access and cost remain an ongoing concern: high costs, insurance variability, supply constraints, and injection burden present barriers. Furthermore, clinical monitoring is needed for metabolic and safety considerations. Lastly, a delayed onset of action presents a further barrier to GLP1-RA adoption in OSA management: AHI improvements are indirect and gradual via weight loss and airway collapsibility may persist despite weight reduction, particularly in anatomically driven OSA phenotypes.

Therapeutic positioning of GLP-1 receptor agonists relative to CPAP

Research to date suggests GLP-1 receptor agonists should be considered adjunctive to continuous positive airway pressure (CPAP) for adults with obstructive sleep apnoea (OSA), particularly in those with obesity, rather than wholesale alternatives. CPAP provides rapid, reliable suppression of apnoea–hypopnoea events and symptom relief, while GLP-1 agonists contribute longer-term disease modification through weight reduction and cardiometabolic improvements (Chirinos *et al.,* 2014). Recent randomized trials of tirzepatide demonstrate clinically meaningful reductions in OSA severity both in patients using CPAP and in those not using CPAP, supporting an adjunctive role and, in CPAP-intolerant individuals, a potential alternative pathway for mitigation of disease burden (Malhotra *et al.,* 2024).

Rationale for using GLP-1 RA as an adjunct in the management of OSA

Mechanistic complementarity:

CPAP mechanically splints the airway, providing immediate control of apnoeas and hypopnoeas; GLP-1 agonists act systemically to reduce weight, improve insulin sensitivity, and lower inflammation, thereby decreasing pharyngeal collapsibility over time.

Cardiometabolic synergy:

GLP-1 agonists address obesity and metabolic dysfunction which are major OSA drivers, potentially enhancing the overall impact of CPAP on blood pressure, glycaemic control, and hypoxic burden.

Adherence considerations:

CPAP effectiveness is adherence-dependent. GLP-1 agonists can reduce OSA severity and symptom load, which may improve CPAP tolerability, reduce

required pressures, or mitigate residual disease in sub optimally adherent patients.

Rationale for using GLP-1 RAs as an alternative to CPAP in the management of OSA

CPAP intolerance or refusal:

For patients who cannot tolerate CPAP, GLP-1 agonists (especially those with robust weight-loss efficacy) offer a non-mechanical pathway to meaningful reductions in OSA severity and cardiometabolic risk (O'Donnell *et al.,* 2023).

Limits of substitution:

Even with substantial weight loss, many patients retain residual OSA; GLP-1 therapy does not immediately abolish apnoeas during sleep and may not achieve the degree of nocturnal event control seen with CPAP. As such, GLP-1 agonists are best positioned as alternatives only when CPAP is not feasible, with close monitoring and consideration of combination approaches if residual disease persists.

Limitations of the evidence comparing GLP-1 Receptor Agonists and CPAP in OSA

The biggest barrier to the adoption of GLP 1 RAs in OSA patients stem from methodological and conceptual limitations that limit direct comparison of two these treatment modalities. These are summarized below:

Lack of head-to-head trials

One of the most significant limitations is the absence of randomized controlled trials directly comparing GLP-1 agonists with CPAP. Most studies evaluate CPAP against placebo or sham interventions (McEvoy *et al.,* 2016; Bratton *et al.,* 2015), while GLP-1 agonists are tested against placebo in populations with obesity and OSA (Blackman *et al.,* 2016; Wadden *et al.,* 2024). Without head-to-head data, conclusions about relative efficacy remain speculative and rely on indirect comparisons across heterogeneous populations and study designs.

Weight-centric vs airway-centric outcomes

Another limitation lies in the differing outcome measures emphasized in GLP-1 and CPAP studies. GLP-1 agonist trials primarily focus on weight reduction, metabolic parameters, and secondary improvements in apnoea–hypopnoea index (AHI). The improvements in OSA severity are often interpreted as downstream effects of weight loss rather than direct airway stabilization (Blackman *et al.,* 2016; Malhotra *et al.,* 2024). CPAP trials, by contrast, are airway-centric, measuring immediate reductions in AHI, oxygen desaturation, and sleep fragmentation (McEvoy *et al.,* 2016; Bratton *et al.,* 2015). These outcomes reflect direct mechanical resolution of airway collapse, independent of weight or metabolic status.This divergence in endpoints complicates comparative interpretation, as GLP-1 agonists may improve long-term risk factors without replicating CPAP's immediate airway stabilization.

Heterogeneity of study populations

GLP-1 agonist studies often recruit patients with obesity and metabolic comorbidities, while CPAP trials include broader OSA populations regardless of body mass index. This heterogeneity limits generalizability and makes it difficult to determine whether GLP-1 agonists could benefit non-obese OSA patients or whether CPAP's effects differ in obese versus non-obese cohorts.

Duration and sustainability of effects

CPAP studies typically assess short- to medium-term outcomes (weeks to months), focusing on immediate symptom relief and cardiovascular risk markers. GLP-1 agonist studies, however, emphasize sustained weight loss and metabolic improvements over longer periods. The mismatch in study duration and endpoints further complicates comparative evaluation, as CPAP's benefits may diminish with poor adherence, while GLP-1 agonists require ongoing pharmacological support to maintain weight loss.

CONCLUSION

The current body of literature highlights the distinct yet complementary roles of GLP-1 receptor agonists and continuous positive airway pressure in the management of obstructive sleep apnoea. CPAP remains the gold-standard intervention, offering immediate and reliable suppression of apnoea–hypopnoea events through direct mechanical stabilization of the airway. Its efficacy in reducing symptom burden and improving sleep quality is well established, though adherence challenges continue to limit its long-term effectiveness. By contrast, GLP-1 receptor agonists show considerable promise, particularly in patients with obesity-related OSA. Their capacity to induce significant weight loss and improve metabolic parameters translates into meaningful reductions in disease severity and cardiometabolic risk. However, these benefits are gradual and mediated primarily through systemic pathways rather than direct airway control, underscoring their role as disease-modifying agents rather than substitutes for CPAP. Taken together, the evidence suggests that the future of OSA management lies not in positioning GLP-1 agonists as alternatives to CPAP, but in exploring combined or personalized therapeutic strategies. Integrating CPAP's immediate airway stabilization with GLP-1–mediated long-term metabolic improvements may offer synergistic benefits, particularly for obese patients at heightened cardiometabolic risk. Personalized approaches that tailor therapy to patient phenotype, adherence capacity, and comorbidity profile will be essential to optimize outcomes. In this context, future research should prioritize head-to-head and combination trials, harmonizing airway-centric and weight-centric outcome measures to clarify the relative and additive benefits of

these therapies. Such work will be critical to advancing a more nuanced, individualized model of OSA care.

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