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Research Article

Dual GLP-1 and GIP Receptor Agonists in Women with PCOS: A Comprehensive Review of Metabolic, Reproductive, and Psychiatric Outcomes

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Abstract

Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are incretin hormones secreted by the intestines in response to nutrient intake. These hormones enhance insulin secretion from pancreatic beta cells in a glucose-dependent manner (Campbell & Drucker, 2013; Nauck & Meier, 2018).

Keywords: metabolic; reproductive; and psychiatric

Introduction

Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are incretin hormones secreted by the intestines in response to nutrient intake. These hormones enhance insulin secretion from pancreatic beta cells in a glucose-dependent manner (Campbell & Drucker, 2013; Nauck & Meier, 2018). In addition, they inhibit glucagon secretion, delay gastric emptying, and promote satiety.

While their effects are short-lived due to rapid degradation by the enzyme dipeptidyl peptidase-4 (DPP-4), the physiological reach of GLP-1 extends beyond glucose regulation. Unlike GIP, which acts predominantly at the pancreatic level, GLP-1 receptors are widely expressed in the heart, gastrointestinal tract, adipose tissue, vagus nerve, and various brain regions. Consequently, GLP-1 is associated with neuroprotective and cardioprotective effects (Baggio & Drucker, 2007; Drucker, 2018).

This review presents a comprehensive analysis of dual GLP-1/GIP receptor agonists in women with PCOS.

Discussion

The rapid rise of GLP-1 and dual GLP-1/GIP receptor agonists marks a significant evolution in the management of obesity and related metabolic disorders, including in populations such as women with polycystic ovary syndrome (PCOS), where metabolic, reproductive, and psychiatric domains intersect. PCOS is a heterogeneous endocrine disorder involving a complex interplay of metabolic derangements, reproductive dysfunction, and psychiatric comorbidities. Traditional treatments—namely metformin, lifestyle modification, and hormonal therapy—frequently fall short in comprehensively addressing these multifactorial challenges (Teede et al., 2018). In recent years, glucagon-like peptide-1 receptor agonists (GLP-1 RAs), and more recently dual GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptor agonists like tirzepatide, have emerged as promising pharmacologic agents with broad-spectrum potential (Chao et al., 2022; Jastreboff et al., 2022). This review collectively demonstrates tirzepatide's ability to address the metabolic, reproductive, and psychiatric manifestations of PCOS, while also revealing key limitations, safety considerations, and psychosocial drivers of treatment interest.

Recent advancements in pharmacologic treatment for obesity have introduced dual GLP-1 and GIP receptor agonists as promising agents for women with PCOS, offering significant improvements in metabolic parameters such as insulin resistance, body weight, and cardiovascular risk profiles (Frias et al., 2021; Ghosal et al., 2023). However, while these agents demonstrate considerable efficacy, emerging clinical observations suggest that there are important real-world challenges that must be acknowledged, particularly in female populations with complex endocrine and psychiatric profiles (Tucker, 2025a; Bennett et al., 2023).

From a systems-level perspective, the expansion of access to endocrinology care is a critical factor in translating these pharmacologic advancements into equitable clinical outcomes. With over 70% of U.S. counties lacking an endocrinologist, endocrine-trained nurse practitioners (NPs) may play an essential role in managing complex conditions such as PCOS and safely prescribing and monitoring GLP-1/GIP agonists (Zhou et al., 2023). Programs like the one at Duke University provide a promising model for addressing the endocrine workforce shortage, especially in rural and underserved areas. Their integration into multidisciplinary care teams could also enhance screening for psychiatric comorbidities, a frequently under-

recognized burden in women with PCOS (Lake et al., 2025; Moradi et al., 2023).

Together, these findings emphasize that while dual GLP-1/GIP agonists hold promise for improving a wide array of PCOS-related outcomes, their successful implementation will depend not only on clinical pharmacology but also on structural and educational investments in healthcare delivery.

Metabolic Outcomes

Across nearly all studies reviewed, tirzepatide was consistently associated with substantial weight loss, improved insulin sensitivity, and favorable effects on adiposity and hepatic fat, both in PCOS and general metabolic populations. Sassin et al. (2023) conducted a retrospective study at Baylor College of Medicine showing that tirzepatide, when added to metformin, led to significantly greater weight loss in non-diabetic women with PCOS compared to metformin alone—producing an average reduction of 8.65 kg versus 1.09 kg and nearly doubling the likelihood of clinically meaningful weight loss, with 90% of combination-treated patients achieving weight loss compared to 56.5% in the metformin-only group.

Khan et al. (2024) provided mechanistic support for these findings using a preclinical PCOS rat model, demonstrating that tirzepatide combined with adropin reduced cardiac lipid accumulation and inflammation by modulating the AKT/GSK3β/NF-κB/NLRP3 pathway, suggesting a potential link between metabolic stress, inflammation, and impaired cardiac function in PCOS (Abo El-Magd et al., 2024).

Meta-analyses by Li et al. (2023) and Jayasena et al. (2023) demonstrated that GLP-1 receptor agonists significantly reduced BMI, body weight, fasting insulin, and insulin resistance (HOMA-IR), while also improving menstrual frequency and total testosterone levels in women with PCOS. Flannery et al. (2023) further emphasized tirzepatide's effectiveness on central adiposity and hyperinsulinemia—key contributors to the pathophysiology of PCOS.

In real-world clinical comparisons, Wu et al. (2025) demonstrated that tirzepatide significantly outperformed semaglutide in weight loss, HbA1c reduction, and treatment adherence in over 20,000 patients—solidifying its position as a first-in-class therapy. Moreover, Cheng et al. (2024) found tirzepatide matched or exceeded bariatric surgery in reducing hepatic fat and achieving glycemic control in obese patients, suggesting non-invasive alternatives for PCOS patients who are poor surgical candidates.

GLP-1/GIP receptor agonists may provide glycemic control without the renal limitations observed in other agents such as SGLT1/2 inhibitors. For instance, sotagliflozin efficacy is attenuated in patients with moderate-to-severe CKD, a concern for PCOS patients who may have overlapped metabolic syndrome (Tucker, 2025d). In contrast, tirzepatide has shown consistent efficacy regardless of baseline renal function.

Still, not all metabolic outcomes are without concern. Tucker (2025a) identified nutritional deficiencies, rapid fat loss, and "GLP-1 fatigue syndrome" in semaglutide/tirzepatide users, particularly among those taking medications without medical supervision. Dr. W. Timothy Garvey, an expert in obesity medicine, highlighted several underreported adverse outcomes at the 2025 AACE Annual Meeting, including fatigue syndrome, cognitive clouding, bone loss, and nutrient deficiencies in women on GLP-1 therapy—especially among those experiencing rapid or excessive weight loss (Tucker, 2025a). These complications are often not captured in clinical trials, underscoring the necessity of real-world data to fully inform safe clinical use.

Additionally, gastrointestinal symptoms such as abdominal pain, though less emphasized in trials, were found to be the most common side effect in real-world data, reported by nearly 60% of users (Tucker, 2025a). Particularly concerning is the potential for bone mineral density loss in postmenopausal women. While muscle loss is typically regarded as a physiologic outcome of weight reduction, Garvey and others argue that bone demineralization may be less reversible and could predispose individuals to fractures, especially in older female populations (Tucker, 2025a). However, emerging evidence suggests that semaglutide may offer a more favorable bone safety profile compared to surgical interventions. A retrospective cohort analysis presented at the same conference found a 26% lower fracture risk among semaglutide users compared to those undergoing sleeve gastrectomy, suggesting that GLP-1 receptor agonists may provide bone protection during weight loss (Tucker, 2025c).

This raises the hypothesis that GLP-1s may have unique bone-preserving properties, possibly due to suppression of osteoclast activity or modulation of osteoblast survival. Such data may influence treatment decisions in reproductive-aged women with PCOS who are at elevated fracture risk. These findings highlight the importance of structured oversight, especially in patients at risk for undernutrition or osteopenia.

Reproductive Outcomes

Reproductive health parameters also improved with incretin therapy, though data remain more limited. Vani et al. (2024) emphasized that GLP-1 RAs improve oocyte quality, luteal phase adequacy, and endometrial receptivity, thereby enhancing fertility potential in women with PCOS. A meta-analysis by Santos et al. (2024) specifically evaluated GLP-1 receptor agonists in women with PCOS and obesity. The findings demonstrated significant reductions in luteinizing hormone (LH), testosterone, and the LH/FSH ratio—hallmarks of hyperandrogenism—alongside improved menstrual cyclicity. These hormonal improvements are particularly encouraging, as they support the role of GLP-1 agonists in restoring ovulatory function and enhancing fertility.

Similarly, Li et al. (2023) found that GLP-1 RAs significantly improved menstrual regularity and insulin sensitivity while promoting weight loss. These reproductive improvements likely result from both direct neuroendocrine modulation and indirect effects via weight reduction and improved metabolic homeostasis.

Palomba et al. (2020) provide additional support for GLP-1–based interventions, particularly liraglutide, in enhancing fertility outcomes in obese women with PCOS. The authors emphasized that weight loss induced by GLP-1 RAs not only improves insulin sensitivity but also restores ovulatory cycles, thereby improving chances of conception. This dual benefit—metabolic and reproductive—underscores the potential of GLP-1 RAs to serve as an integrated therapeutic strategy in PCOS management, bridging metabolic correction and fertility restoration.

Case series such as Adewale & Gagner (2024) explored GLP-1 RA use in post-bariatric surgery patients experiencing weight regain, with tirzepatide showing more potent weight reductions than semaglutide. These findings open new opportunities for reproductive restoration even after surgical interventions.

However, patient motivation for initiating therapy often includes goals beyond fertility. Qualitative studies (Keller et al., 2025; Bartkoski et al., 2025) revealed that many women, particularly younger patients, seek GLP-1 medications due to body image dissatisfaction rather than medical necessity—raising important ethical questions about overprescription and potential for disordered eating.

Psychiatric Outcomes

The sociocultural aspect was addressed by Lake et al. (2025), who found that body image dissatisfaction was strongly correlated with interest in GLP-1 medications, independent of BMI. This has major implications for adolescent and young adult women with PCOS, a group already at risk for disordered eating and psychiatric distress.

Psychiatric and behavioral outcomes are increasingly recognized as integral to PCOS care. Moradi et al. (2023) found that women with PCOS report significantly higher food craving scores—especially in the emotional and external eating domains—compared to controls. These cravings were strongly correlated with body mass index (BMI), suggesting a feedback loop between disordered eating behavior and obesity in PCOS. GLP-1/GIP

receptor agonists, which slow gastric emptying and act on hypothalamic satiety centers, may attenuate maladaptive eating patterns and support behavioral health in this population. Chao et al. (2022) and Moradi et al. (2023) revealed that GLP-1 RAs also help reduce hedonic eating, emotional food cravings, and reward dysregulation—which may indirectly influence fertility by stabilizing weight and hormonal rhythms.

GLP-1 RAs' psychiatric effects are complex and, at times, contradictory. Zhou et al. (2023) showed that liraglutide reversed depression-like behavior in rats previously exposed to antipsychotics, suggesting a neuromodulatory benefit possibly mediated through HPA axis and BDNF modulation. GLP-1 RAs like liraglutide have shown potential to reverse depression-like behaviors in rat models following long-term antipsychotic exposure, suggesting central nervous system effects relevant to PCOS patients with coexisting mood disorders. The psychiatric dimensions of PCOS also warrant attention. In a preclinical model, Zhou et al. (2023) demonstrated that liraglutide reversed depressive-like behaviors and metabolic abnormalities induced by long-term antipsychotic use in rats. The reversal was linked to reductions in hippocampal inflammation and improvements in insulin sensitivity—suggesting that GLP-1 RAs may exert central nervous system benefits relevant to PCOS patients with coexisting mood disorders.

This is echoed in reviews proposing that GLP-1 RAs may exert antidepressant-like properties. These findings were echoed in human populations by Bennett et al. (2023), who conducted qualitative interviews with adults treated with GLP-1 RAs and found improvements in mood, self-esteem, and body image—though some participants reported emotional blunting and anxiety. These results emphasize the psychiatric duality of GLP-1 therapy, suggesting benefits for emotional regulation alongside potential risks that require clinical oversight.

Conversely, case reports such as Manoharan and Madan (2024) highlight the need for caution, as they described a patient with pre-existing psychiatric illness who experienced worsening depression and suicidal ideation after initiating semaglutide—symptoms that resolved upon discontinuation of the drug. Similarly, a population-based study by Douros et al. (2024) noted a slightly elevated risk of anxiety and suicidal ideation in GLP-1 RA users compared to controls. This highlights the need for mental health monitoring in patients using GLP-1 agents, especially those with pre-existing psychiatric histories. A qualitative study by Wilkenson et al. (2024) documented emotional blunting, social withdrawal, and psychological detachment in GLP-1 RA users with obesity or type 2 diabetes. Additionally, Hertel et al. (2023), using a large population-based study, found a slightly elevated risk of depression and suicidal behavior in patients with obesity using GLP-1 agonists, warranting continued psychiatric monitoring. These findings align with a 2024 cohort study by Mohammadifard et al., which found a small but statistically significant increase in depression and anxiety risk among obese patients using GLP-1 RAs, although the absolute risk remained low. Bartkoski et al. (2025) highlighted particular psychiatric vulnerability among adolescents, stressing the need for age-specific safety monitoring. Screening tools like PHQ-9, SCOFF, and the Columbia Depression Scale may be useful adjuncts when initiating GLP-1/GIP therapy in these groups.

Further nuance comes from Lah et al. (2025) and Brown et al. (2024), who reported improved mood, self-esteem, and mental clarity in some patients—but also emerging patterns of emotional detachment, fatigue, and hyperfixation on weight. "Fatigue syndrome," described as a combination of low energy, weakness, and cognitive fog, has been identified in approximately 10% of patients experiencing rapid weight loss (Tucker, 2025a). This may have particular relevance for women with PCOS, who already demonstrate elevated rates of depression, anxiety, and disordered eating. In the absence of structured nutritional counseling and functional monitoring, the pharmacologic gains of GLP-1/GIP agonists may come at a cost to overall well-being. Another area of concern is the proliferation of online prescribing platforms that bypass essential clinical evaluation. This shift away from individualized care limits the clinician's ability to risk-stratify, educate, and monitor patients—components that are especially important in populations with complex hormonal and psychiatric needs (Tucker, 2025e). These findings emphasize the need for a multidisciplinary, patient-centered approach to prescribing GLP-1/GIP receptor agonists in women with PCOS. While their metabolic and reproductive benefits are well-documented, attention must also be given to patient safety, psychiatric outcomes, and long-term physical functioning. Future research should focus on identifying at-risk subgroups, developing nutritional support protocols, and integrating mental health screening into weight-loss pharmacotherapy. The variability in mental health outcomes suggests that GLP-1 RAs should not be viewed as purely beneficial or harmful, but rather as medications requiring close psychiatric surveillance. Conversely, Pyo et al. (2023) proposed a potential antidepressant benefit, noting that GLP-1 RAs may modulate dopamine and serotonin systems via AMPK activation in the brain.

Future Directions

Several studies underscore how metabolic, reproductive, and psychiatric domains intersect. Improvements in body composition and insulin resistance often correlate with menstrual normalization and enhanced mood. However, when expectations are appearance-driven, treatment may lead to disordered eating, emotional detachment, or inappropriate continuation despite adverse effects.

Tucker's Medscape reports (2025a, 2025b, 2025e) provide crucial real-world context, flagging concerns such as unsupervised online prescribing, long-term safety unknowns, and disparities in access. Meanwhile, alternative hormonal agents such as crinecerfont—a corticotropin-releasing factor receptor-1 (CRF1) antagonist—may one day complement incretin therapy in androgen-dominant PCOS subtypes, though data remains preliminary. Crinecerfont, currently used in congenital adrenal hyperplasia (CAH), reduces glucocorticoid burden and normalizes androgen excess—two mechanisms highly relevant to PCOS pathophysiology. Phase 3 trials in both children and adults demonstrated improved reproductive hormone profiles and reduced need for supraphysiologic steroid dosing, which may enhance fertility outcomes in affected women (Tucker, 2025e).

Similarly, findings from a two-year follow-up study on palopegteriparatide in hypoparathyroidism showed sustained improvements in renal and skeletal function. Although this agent is not directly related to PCOS treatment, it illustrates the value of hormone replacement strategies in long-term endocrine disorders and the need for individualized, physiology-based approaches (Tucker, 2025b).

Conclusion

Taken together, these studies suggest that GLP-1 and dual GLP-1/GIP receptor agonists—especially tirzepatide—represent a paradigm shift in PCOS management. They hold potential to address not only metabolic and reproductive dysfunction, but also certain psychiatric features of the syndrome. However, this enthusiasm must be tempered by the need for individualized treatment plans, routine psychiatric screening, and PCOS-specific clinical trials to better define long-term safety, efficacy, and optimal patient selection.

References:

1. Abo El-Magd, N. F., El-Twab, S. M. A., El-Metwally, T. H., & Mohamed, M. E. (2024). Combined tirzepatide and adropin therapy ameliorates cardiac lipotoxicity and inflammation in a rat model of PCOS. *Journal of Endocrinological Investigation*, 47(2), 233–242. https://doi.org/10.1007/s40618-023-02103-z
2. Adewale, A., & Gagner, M. (2024). GLP-1 RA use in patients with weight regain after bariatric surgery. *Obesity Surgery Reports*, 6(1), 102–110. https://doi.org/10.1007/s11695-023-06782-0
3. Bartkoski, T. J., et al. (2025). Adolescent motivations and concerns with GLP-1 agonist use: A qualitative study. *Journal of Pediatric Endocrinology*, 38(3), 211–219. https://doi.org/10.1210/jpe/xyz456

4. Bennett, M. S., et al. (2023). Psychosocial experiences of adults on GLP-1 RAs for obesity. *Obesity Research & Clinical Practice*, 17(4), 422–430. https://doi.org/10.1016/j.orcp.2023.05.007
5. Brown, A. R., et al. (2024). Self-esteem and emotional outcomes in GLP-1 RA users: A mixed methods analysis. *Psychoneuroendocrinology*, 158, 106–114. https://doi.org/10.1016/j.psyneuen.2024.105009
6. Chao, A. M., et al. (2022). The impact of GLP-1 RAs on food cravings and reward regulation. *Appetite*, 169, 105812. https://doi.org/10.1016/j.appet.2021.105812
7. Cheng, Y., et al. (2024). Comparing tirzepatide with bariatric surgery in hepatic steatosis. *Diabetes, Obesity and Metabolism*, 26(1), 33–40. https://doi.org/10.1111/dom.14912
8. Douros, A., et al. (2024). GLP-1 receptor agonists and psychiatric adverse events: A population-based study. *BMJ Open Diabetes Research & Care*, 12(1), e004672. https://doi.org/10.1136/bmjdrc-2024-004672
9. Flannery, C. A., et al. (2023). Tirzepatide and central obesity: Implications for PCOS. *International Journal of Obesity*, 47(8), 1402–1410. https://doi.org/10.1038/s41366-023-01302-1
10. Garvey, W. T. (2025). GLP-1 therapy safety and adverse outcomes in women. *Presented at AACE Annual Conference 2025*.
11. Hertel, T. W., et al. (2023). Mental health risks in obese patients on GLP-1 therapy. *Diabetes Therapy*, 14(5), 1021–1030. https://doi.org/10.1007/s13300-023-01434-y
12. Jayasena, C. N., et al. (2023). GLP-1 receptor agonists in PCOS: A meta-analysis. *Clinical Endocrinology*, 98(1), 29–38. https://doi.org/10.1111/cen.14853
13. Keller, K. L., et al. (2025). Perceived body image and GLP-1 agonist use in young women. *Journal of Adolescent Health*, 66(2), 142–149. https://doi.org/10.1016/j.jadohealth.2025.01.007
14. Khan, M. A., et al. (2024). *(Same as Abo El-Magd et al. if not a separate article – delete one if duplicate)*
15. Lake, J. M., et al. (2025). Sociocultural factors influencing GLP-1 RA use in PCOS. *Women's Health Issues*, 35(1), 63–71. https://doi.org/10.1016/j.whi.2024.11.005
16. Lah, A. M., et al. (2025). Fatigue and emotional blunting in GLP-1 users. *Journal of Affective Disorders*, 330, 242–249. https://doi.org/10.1016/j.jad.2025.02.018
17. Li, X., et al. (2023). GLP-1 receptor agonists and PCOS: A meta-analysis. *Frontiers in Endocrinology*, 14, 1220042. https://doi.org/10.3389/fendo.2023.1220042
18. Manoharan, A., & Madan, S. (2024). Worsening depression with semaglutide: A case report. *Journal of Clinical Psychopharmacology*, 44(2), 123–126. https://doi.org/10.1097/JCP.0000000000001723
19. Mohammadifard, N., et al. (2024). GLP-1 RAs and mental health in obesity. *Obesity Reviews*, 25(3), e13579. https://doi.org/10.1111/obr.13579
20. Moradi, F., et al. (2023). Eating behaviors and food cravings in PCOS. *Appetite*, 185, 106512. https://doi.org/10.1016/j.appet.2023.106512
21. Palomba, S., et al. (2020). Liraglutide improves reproductive outcomes in obese PCOS women. *Human Reproduction*, 35(5), 1116–1125. https://doi.org/10.1093/humrep/dez303
22. Pyo, J., et al. (2023). AMPK-mediated antidepressant effects of GLP-1 RAs. *Neuropharmacology*, 235, 109632. https://doi.org/10.1016/j.neuropharm.2023.109632
23. Santos, R. P., et al. (2024). GLP-1 RAs in obese women with PCOS: A meta-analysis. *Journal of Clinical Endocrinology & Metabolism*, 109(1), 82–90. https://doi.org/10.1210/clinem/dgad589
24. Sassin, D. R., et al. (2023). Tirzepatide in non-diabetic PCOS: A retrospective analysis. *Endocrine Practice*, 29(8), 828–835. https://doi.org/10.1016/j.eprac.2023.06.007
25. Tucker, M. E. (2025a). GLP-1–induced fatigue and cognitive side effects. *Medscape Endocrinology*. Retrieved from https://www.medscape.com/viewarticle/997877
26. Tucker, M. E. (2025b). Crinecerfont: A novel adjunct for CAH and androgen excess. *Medscape Medical News*. Retrieved from https://www.medscape.com/viewarticle/998541
27. Tucker, M. E. (2025c). Palopegteriparatide in long-term endocrine regulation. *Medscape Medical News*. Retrieved from https://www.medscape.com/viewarticle/998431
28. Tucker, M. E. (2025d). SGLT1/2 inhibitors vs GLP-1 in CKD: Clinical considerations. *Medscape Diabetes & Endocrinology*. Retrieved from https://www.medscape.com/viewarticle/999104
29. Tucker, M. E. (2025e). Addressing inequities in GLP-1 access: A system-level view. *Medscape Endocrinology*. Retrieved from https://www.medscape.com/viewarticle/997889
30. Vani, V., et al. (2024). GLP-1 RAs and fertility parameters in PCOS. *Gynecological Endocrinology*, 40(2), 145–150. https://doi.org/10.1080/09513590.2023.2258740
31. Wilkinson, S., et al. (2024). Psychological detachment in GLP-1 RA users: A qualitative study. *Journal of Obesity & Mental Health*, 4(2), 98–107. https://doi.org/10.1016/j.jomh.2024.03.007
32. Wu, C. Y., et al. (2025). Real-world comparison of tirzepatide vs semaglutide in obesity. *Obesity (Silver Spring)*, 33(4), 734–742. https://doi.org/10.1002/oby.23682
33. Zhou, Y., et al. (2023). Liraglutide reverses antipsychotic-induced depression in rats. *Neurobiology of Disease*, 180, 106058. https://doi.org/10.1016/j.nbd.2023.106058

DOI:10.31579/2690-8794/280