STASIAK, Michał, ŻYRO, Wiktor, WOŹNIAK, Karolina, ŻYRO, Katarzyna, GLAPIŃSKI, Franciszek and WOŹNIAK, Adam. Glucagon-Like Peptide-1 Receptor Agonists in Obesity Management: Mechanisms, Efficacy, and Safety. Quality in Sport. 2025;42:60634. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.42.60634
https://apcz.umk.pl/QS/article/view/60634

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).
The authors declare that there is no conflict of interest regarding the publication of this paper.
Received: 29.04.2025. Revised: 10.06.2025. Accepted: 16.06.2025. Published: 17.06.2025.

Glucagon-Like Peptide-1 Receptor Agonists in Obesity Management: Mechanisms, Efficacy, and Safety

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ABSTRACT

Obesity remains a major global health challenge with limited pharmacological options that combine efficacy and long-term safety. Traditional anti-obesity drugs, targeting energy expenditure and appetite, often present significant cardiovascular and neuropsychiatric risks. In contrast, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have emerged as promising agents due to their dual benefits of glycemic control and weight reduction. GLP-1, an enteroendocrine hormone, enhances insulin secretion, suppresses glucagon release, and modulates appetite via central pathways. By binding to receptors in the hypothalamus and brainstem, GLP-1 RAs promote satiety, delay gastric emptying, and modulate reward-related eating behaviors, thereby reducing caloric intake. Meta-analyses of randomized controlled trials have demonstrated significant body weight reductions in both diabetic and non-diabetic individuals, with semaglutide showing particularly robust outcomes compared to liraglutide and exenatide. Beyond weight loss, GLP-1 RAs improve insulin sensitivity, lipid profiles, and cardiovascular risk factors. However, their use is associated with gastrointestinal side effects

such as nausea, vomiting, and diarrhea, which can affect treatment adherence. While concerns about potential impacts on pancreatic and thyroid tissues have been raised, current large-scale studies do not confirm a causal relationship. Overall, GLP-1 RAs represent a significant advancement in obesity pharmacotherapy by integrating appetite suppression, delayed gastric emptying, and metabolic improvements. Continued research is needed to further optimize their clinical application and ensure long-term safety in obesity management.

Key words: GLP-1 receptor agonists, obesity pharmacotherapy, appetite regulation, weight loss

INTRODUCTION

The majority of pharmacological agents developed to date for the treatment of obesity have not demonstrated sufficient clinical efficacy nor an acceptable safety profile to support their long-term use in routine medical practice. In particular, compounds that act by increasing energy expenditure—such as thyroid hormones, sympathoadrenergic agents, or sibutramine—exhibit limitations primarily due to their lack of cardiovascular safety, thereby constraining their therapeutic application in chronic obesity management. Moreover, the potential for serious adverse events related to increased sympathetic activity has further discouraged their widespread adoption.

Centrally acting appetite suppressants have also proven suboptimal: while some, such as serotonin reuptake inhibitors, exhibit limited long-term effectiveness, others, including amphetamine derivatives and cannabinoid receptor antagonists, have been associated with significant neuropsychiatric adverse effects, thus raising concerns regarding their long-term tolerability and safety (1). These safety limitations underscore the urgent need for safer, more effective pharmacological alternatives for long-term obesity management. Glucagon-like peptide-1 (GLP-1) is an incretin hormone of enteroendocrine origin, primarily secreted in the

postprandial state in response to nutrient intake. It plays a pivotal role in the regulation of glucose homeostasis by stimulating insulin secretion in a glucose-dependent manner and concurrently inhibiting glucagon release from pancreatic α-cells, also in a dose-dependent fashion (2) . As a consequence of these pharmacodynamic properties, GLP-1 effectively contributes to the reduction of hyperglycemia without eliciting hypoglycemic episodes, a characteristic particularly advantageous in the management of type 2 diabetes mellitus (3) . In light of these physiological attributes, long-acting GLP-1 receptor agonists (GLP-1 RAs) have been developed and introduced as therapeutic agents intended to improve glycemic control in individuals diagnosed with type 2 diabetes. These agents are administered via subcutaneous injection, either on a daily (once or twice) or weekly basis, thus offering enhanced flexibility and adherence potential in clinical settings (4). Their dosing regimens are designed to accommodate a wide range of patient lifestyles and therapeutic needs, making them an increasingly practical option in routine endocrinological practice. Notably, beyond their glucose-lowering effects, a growing body of clinical evidence has demonstrated that GLP-1 RAs induce significant and sustained weight reduction, thereby positioning them as promising pharmacological interventions in the context of obesity treatment and long-term weight management strategies (5) .

Mechanism of action

The effect of GLP-1 and its receptor agonists on body weight regulation is predominantly attributed to a reduction in caloric intake, which is primarily mediated through the peptide's direct influence on central nervous system structures involved in the regulation of appetite and satiety. Specifically, GLP-1 exerts its central anorexigenic actions by binding to GLP-1 receptors that are widely expressed in critical regions of the brain responsible for energy homeostasis, such as the hypothalamic arcuate nucleus and specific areas within the brainstem. Within these regions, GLP-1 enhances satiety signaling and concurrently suppresses hunger-driven behaviors, thereby contributing to decreased food consumption (6). In addition to modulating appetite through central mechanisms, activation of the GLP-1 receptor also results in a deceleration of gastric emptying. This gastrointestinal effect is at least partially mediated through central pathways involving the autonomic nervous system, which in turn leads to an extension of postprandial gastric distension and the subjective sensation of fullness, thereby facilitating a reduction in overall caloric intake(7) . Beyond its well-documented effects on satiety regulation and gastric motility, GLP-1 also influences reward-driven eating behaviors.

This is achieved through modulation of mesolimbic dopaminergic pathways, which play a key role in hedonic aspects of food intake. By attenuating dopaminergic activity associated with food-related reward signaling, GLP-1 reduces the motivational drive to consume palatable, high-calorie foods, thus further contributing to its weight-lowering effects (8). Among the most frequently reported adverse effects of GLP-1 receptor agonist therapy is nausea, which may occasionally be accompanied by vomiting. These gastrointestinal symptoms have been hypothesized to contribute, at least in part, to the observed weight loss in patients receiving these agents. Nevertheless, substantial weight reduction has also been observed in individuals who do not experience such side effects, indicating that the anti-obesity efficacy of GLP-1 receptor agonists cannot be solely attributed to treatment-related nausea. Rather, these findings suggest that the weight-reducing effects are primarily the result of direct neuroendocrine mechanisms that modulate appetite, satiety, and energy balance through central and peripheral pathways (9).

Results

A meta-analysis conducted in 2012, encompassing data from randomized clinical trials, systematically evaluated the effects of GLP-1 RAs on body weight reduction. This comprehensive analysis included 22 trials (n = 7,859) with outcomes assessed at six months, as well as seven trials (n = 2,416) reporting 12-month results. The average baseline body mass index (BMI) among participants was approximately 32.4 kg/m², indicating a population with overweight or class I obesity. After six months of treatment, GLP-1 RAs were associated with a statistically significant reduction in BMI compared to placebo (weighted mean difference [WMD]: –1.0 kg/m²; 95% confidence interval [CI]: –1.3 to –0.6), corresponding to an approximate 3% decrease in total body weight. Notably, greater reductions in BMI were observed among non-diabetic individuals, suggesting a potentially more pronounced effect of GLP-1 RAs in populations without metabolic dysregulation. Exenatide demonstrated a BMI reduction of 1.6 kg/m² in a placebo-controlled trial of six months' duration ($p = 0.002$), whereas liraglutide induced a decrease of 1.2 kg/m² over a 52-week period ($p = 0.04$). At the 12-month follow-up, BMI reduction reached –1.9 kg/m² (95% CI: –3.0 to –0.8, $p < 0.001$), further substantiating the sustained efficacy of GLP-1 RAs. The observed weight loss appeared to be independent of the presence or severity of nausea, and was predominantly attributed to central appetite suppression, delayed gastric emptying, and modulation of reward-related neural pathways influencing food intake behavior. These findings collectively underscore the therapeutic utility of GLP-1 RAs as effective weight-lowering agents in both diabetic and non-

diabetic populations, thereby supporting their integration into obesity management strategies (10). A more recent and methodologically rigorous meta-analysis assessed the effectiveness of GLP-1 receptor agonists in promoting weight loss among adults with obesity who did not have concomitant diabetes mellitus. This systematic review incorporated data from randomized controlled trials published up to September 30, 2021, and included a total of 12 high-quality studies with a cumulative sample size of 11,459 participants. The pooled analysis revealed a statistically significant and clinically meaningful reduction in body weight among individuals receiving GLP-1 RAs compared to those in control groups, with a mean difference of −7.1 kg (95% CI: −9.2 to −5.0; $I^2 = 99\%$), reflecting a robust and consistent therapeutic effect despite inter-study heterogeneity. In addition to weight reduction, treatment with GLP-1 RAs was associated with improved glycemic control, notably without an elevated risk of hypoglycemia. Moreover, beneficial effects were observed across multiple cardiovascular risk markers, including reductions in systolic blood pressure, plasma low-density lipoprotein (LDL) cholesterol, and triglyceride concentrations, as well as an increase in high-density lipoprotein (HDL) cholesterol levels. Subgroup analyses revealed that semaglutide exerted a more substantial weight-lowering effect in comparison to liraglutide, highlighting differential pharmacodynamic efficacy among agents within the GLP-1 RA class. However, it is important to note that the treatment was frequently accompanied by gastrointestinal adverse effects, such as nausea, vomiting, dyspepsia, diarrhea, constipation, and abdominal discomfort, which may impact tolerability and adherence in certain patients. These cumulative findings reinforce the potential of GLP-1 receptor agonists as effective pharmacotherapeutic options for obesity management, particularly in non-diabetic individuals, and warrant their consideration in evidence-based clinical guidelines (11). A direct comparison of the effects of GLP-1 receptor agonists on body weight is presented in Table 1.

Table 1. Summary of GLP-1 RA Effects on Body Weight

Study	Findings
Monami et al., 2012	**Participants**: 22 trials (n = 7,859); 7 trials (n = 2,416)
	Duration: 6 and 12 months
	Effect: BMI ↓ 1.0 kg/m² at 6 months (~3% body weight), ↓ 1.9 kg/m² at 12 months
	Population: Overweight / class I obese (mean BMI ~32.4 kg/m²)
	Benefits: Appetite suppression, delayed gastric emptying, central appetite regulation
	Side effects: Effect independent of nausea
Iqbal et al., 2022	**Participants**: 12 trials (n = 11,459)
	Duration: Various (studies up to 2021)
	Effect: Weight ↓ 7.1 kg (95% CI: −9.2 to −5.0)
	Population: Obese, non-diabetic adults
	Benefits: Improved glycemic control, ↓ SBP, ↓ LDL/TG, ↑ HDL
	Side effects: Nausea, vomiting, diarrhea, constipation, dyspepsia

Discussion

The relatively limited number of clinical trials that have been specifically designed to investigate weight loss as the primary endpoint in individuals with obesity who do not have coexisting type 2 diabetes have consistently provided evidence supporting the efficacy of GLP-1 RAs as pharmacological agents with significant weight-reducing potential (12). These findings underscore the relevance of GLP-1 RAs not only in glycemic control but also in the broader context of weight management in metabolically healthy individuals with obesity. Their mechanism of action, which includes modulation of appetite, satiety, and reward pathways, further strengthens the rationale for their clinical application in obesity pharmacotherapy. Furthermore, it is essential to recognize that the benefits of GLP-1 receptor agonist therapy in individuals with obesity likely extend beyond weight reduction alone. These agents have demonstrated the capacity to improve various metabolic parameters, including enhancement of insulin sensitivity, reduction in systemic inflammation, and a potential lowering of the risk of progression to type 2 diabetes mellitus. This multifactorial impact is particularly valuable in addressing the complex pathophysiology of obesity-related disorders. In addition, GLP-1 RAs may exert favorable effects on cardiovascular health by contributing to reductions in arterial blood pressure and improvements in lipid profiles. Such pleiotropic actions suggest that GLP-1 RAs could serve as valuable components of comprehensive obesity treatment strategies, particularly for individuals at elevated cardiometabolic risk. Despite their clinical promise, the use of GLP-1 receptor agonists is associated with a number of adverse effects, most of which pertain to the gastrointestinal (GI) system. The most frequently reported GI symptoms include nausea, vomiting, diarrhea, constipation, and abdominal discomfort, with nausea being the most prevalent, reportedly affecting up to 50% of patients undergoing treatment (13). These adverse events are generally transient and dose-dependent, typically diminishing in severity and frequency over time as patients continue therapy (14). Patient education and gradual dose titration have been shown to improve tolerability and adherence during the initiation phase of treatment. Nevertheless, for a subset of individuals—particularly those receiving higher therapeutic doses of exenatide or liraglutide—these symptoms may result in reduced adherence or even treatment discontinuation, thereby potentially compromising therapeutic outcomes. Beyond gastrointestinal tolerability, several safety concerns have emerged regarding the long-term use of GLP-1 RAs, particularly in relation to the pancreas and thyroid gland. Preclinical studies and select observational investigations have suggested a possible association between

GLP-1 RA exposure and increased risks of pancreatic and thyroid neoplasia (15). Specifically, concerns have been raised about a potential link to pancreatic ductal hyperplasia, pancreatitis, and, more controversially, pancreatic cancer. However, large-scale, high-quality meta-analyses have not established a causal relationship between GLP-1 RA therapy and increased malignancy risk. Similarly, while rodent studies have indicated an association between long-term administration of GLP-1 RAs and the development of medullary thyroid carcinoma, such findings have not been substantiated in human clinical trials, suggesting a species-specific effect rather than a generalizable human risk. GLP-1 RAs have also been linked to an elevated incidence of gallbladder-related complications, including cholelithiasis and cholecystitis. These effects are thought to arise from the agents' impact on delayed gastric emptying and alterations in bile acid metabolism, both of which may predispose susceptible individuals to biliary stasis. Although these events are relatively infrequent, they should be considered in the risk-benefit assessment for long-term therapy. Moreover, isolated case reports have implicated exenatide in the development of acute kidney injury, primarily due to volume depletion resulting from persistent gastrointestinal side effects such as vomiting and diarrhea (16). However, clinical trial data to date have not demonstrated a statistically significant increase in the risk of renal impairment with GLP-1 RA therapy (17). In summary, while GLP-1 receptor agonists represent a promising class of agents for obesity treatment—with demonstrated efficacy in promoting weight loss and improving metabolic and cardiovascular parameters—their use must be carefully tailored to individual patient profiles, balancing the substantial benefits against potential adverse effects and safety considerations (18).

CONCLUSION

GLP-1 RAs and their co-agonists represent a highly promising and increasingly utilized class of pharmacological agents that facilitate significant weight loss through a multitude of complex, multifactorial, and interconnected physiological mechanisms. By modulating intricate neural circuits within central nervous system pathways, these agents exert their effects by suppressing appetite and enhancing satiety signaling, which together contribute to a meaningful and sustained reduction in caloric intake (19). This neuroregulatory modulation plays a crucial role in altering feeding behavior, especially in individuals with dysregulated appetite control. In addition to their central actions on appetite control, GLP-1 RAs and co-agonists exert peripheral effects by slowing the process of gastric emptying, thereby prolonging the sensation of postprandial fullness, reducing overall hunger between meals, and decreasing the frequency

and volume of food intake. These actions not only improve subjective feelings of satiety but also modulate gastrointestinal motility and nutrient absorption in ways that support long-term weight regulation. Beyond their well-documented impact on appetite suppression and gastric motility, these pharmacological agents also contribute to the maintenance of energy homeostasis through several important metabolic mechanisms. Notably, they improve glycemic control by enhancing insulin secretion and reducing glucagon levels, stimulate thermogenesis, and increase overall energy expenditure, thereby promoting a more favorable energy balance that facilitates fat loss and weight maintenance(20). Such mechanisms are particularly relevant in the treatment of obesity accompanied by insulin resistance or metabolic syndrome. Furthermore, GLP-1 RAs and their co-agonists demonstrate additional metabolic benefits by exerting favorable effects on lipid metabolism. These include the optimization of fat storage, enhancement of lipid oxidation processes, and more efficient utilization of lipids as an energy source, all of which contribute to reductions in adipose tissue mass and improvements in metabolic flexibility (21). Taken together, these diverse and synergistic physiological mechanisms underscore the clinical utility of GLP-1 RAs and co-agonists as highly effective therapeutic agents for promoting sustained and clinically meaningful weight reduction. This outcome remains a central therapeutic objective in the comprehensive management of obesity and its numerous associated metabolic disorders, including type 2 diabetes mellitus, dyslipidemia, and cardiovascular disease (22). However, despite the significant progress achieved thus far, continued and rigorous scientific investigation is essential to fully elucidate the underlying molecular and systemic mechanisms of action. Additionally, future research should aim to refine and personalize treatment approaches, optimize dosing strategies, and minimize potential adverse effects in order to maximize the long-term safety, efficacy, and accessibility of these agents for diverse patient populations.

DISCLOSURE

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The authors have read and agreed with the published version of the manuscript.

Funding Statement:

The Study Did Not Receive Special Funding.

Institutional Review Board Statement:

Not Applicable.

Informed Consent Statement:

Not Applicable.

Data Availability Statement:

Not Applicable.

Conflict Of Interest:

The authors declare no conflict of interest.

REFERENCES

1. Vetter ML, Faulconbridge LF, Webb VL, Wadden TA. Behavioral and pharmacologic therapies for obesity. Nat Rev Endocrinol [Internet]. 2010 Oct 3 [cited 2025 Mar 20];6(10):578. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3031864/
2. Doyle ME, Egan JM. Mechanisms of Action of GLP-1 in the Pancreas. Pharmacol Ther [Internet]. 2006 Mar [cited 2025 Mar 20];113(3):546. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC1934514/
3. Ahrén B. GLP-1 for type 2 diabetes. Exp Cell Res [Internet]. 2011 [cited 2025 Mar 20];317(9):1239–45. Available from: https://pubmed.ncbi.nlm.nih.gov/21237153/
4. Garber AJ. Long-acting glucagon-like peptide 1 receptor agonists: A review of their efficacy and tolerability. Diabetes Care [Internet]. 2011 May [cited 2025 Mar 20];34(SUPPL. 2):S279. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3632193/
5. Gallwitz B. Glucagon-like peptide-1 analogues for Type 2 diabetes mellitus: current and emerging agents. Drugs [Internet]. 2011 [cited 2025 Mar 20];71(13):1675–88. Available from: https://pubmed.ncbi.nlm.nih.gov/21902291/
6. Hayes MR, De Jonghe BC, Kanoski SE. Role of the Glucagon-Like-Peptide-1 Receptor in the Control of Energy Balance. Physiol Behav [Internet]. 2010 Jul [cited 2025 Mar 20];100(5):503. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC2886183/
7. Kanoski SE, Rupprecht LE, Fortin SM, De Jonghe BC, Hayes MR. The role of nausea in food intake and body weight suppression by peripheral GLP-1 receptor agonists, exendin-4 and liraglutide. Neuropharmacology [Internet]. 2011 Apr [cited 2025 Mar 20];62(0):1916. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4183930/
8. Lutter M, Nestler EJ. Homeostatic and hedonic signals interact in the regulation of food intake. J Nutr [Internet]. 2009 Mar [cited 2025 Mar 20];139(3):629–32. Available from: https://pubmed.ncbi.nlm.nih.gov/19176746/
9. Moiz A, Filion KB, Tsoukas MA, Yu OH, Peters TM, Eisenberg MJ. Mechanisms of GLP-1 Receptor Agonist-Induced Weight Loss: A Review of Central and Peripheral Pathways in Appetite and Energy Regulation. Am J Med [Internet]. 2025 [cited 2025 Mar 20]; Available from: https://pubmed.ncbi.nlm.nih.gov/39892489/

10. Monami M, Dicembrini I, Marchionni N, Rotella CM, Mannucci E. Effects of Glucagon-Like Peptide-1 Receptor Agonists on Body Weight: A Meta-Analysis. Exp Diabetes Res [Internet]. 2012 [cited 2025 Mar 20];2012:672658. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3362858/
11. Iqbal J, Wu HX, Hu N, Zhou YH, Li L, Xiao F, et al. Effect of glucagon-like peptide-1 receptor agonists on body weight in adults with obesity without diabetes mellitus—a systematic review and meta-analysis of randomized control trials. Obesity Reviews [Internet]. 2022 Jun 1 [cited 2025 Mar 20];23(6):e13435. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/obr.13435
12. Rosenstock J, Klaff LJ, Schwartz S, Northrup J, Holcombe JH, Wilhelm K, et al. Effects of Exenatide and Lifestyle Modification on Body Weight and Glucose Tolerance in Obese Subjects With and Without Pre-Diabetes. Diabetes Care [Internet]. 2010 Jun [cited 2025 Mar 20];33(6):1173. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC2875418/
13. Wysham C, Blevins T, Arakaki R, Colon G, Garcia P, Atisso C, et al. Efficacy and safety of dulaglutide added onto pioglitazone and metformin versus exenatide in type 2 diabetes in a randomized controlled trial (AWARD-1). Diabetes Care [Internet]. 2014 [cited 2025 Mar 20];37(8):2159–67. Available from: https://pubmed.ncbi.nlm.nih.gov/24879836/
14. Sun F, Yu K, Yang Z, Wu S, Zhang Y, Shi L, et al. Impact of GLP-1 receptor agonists on major gastrointestinal disorders for type 2 diabetes mellitus: a mixed treatment comparison meta-analysis. Exp Diabetes Res [Internet]. 2012 [cited 2025 Mar 20];2012. Available from: https://pubmed.ncbi.nlm.nih.gov/23365557/
15. Elashoff M, Matveyenko A V., Gier B, Elashoff R, Butler PC. Pancreatitis, Pancreatic, and Thyroid Cancer With Glucagon-Like Peptide-1–Based Therapies. Gastroenterology [Internet]. 2011 [cited 2025 Mar 20];141(1):150. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4404515/
16. Kaakeh Y, Kanjee S, Boone K, Sutton J. Liraglutide-induced acute kidney injury. Pharmacotherapy [Internet]. 2012 Jan [cited 2025 Mar 20];32(1). Available from: https://pubmed.ncbi.nlm.nih.gov/22392833/
17. Filippatos TD, Panagiotopoulou T V., Elisaf MS. Adverse Effects of GLP-1 Receptor Agonists. Rev Diabet Stud [Internet]. 2015 Sep 1 [cited 2025 Mar 20];11(3):202. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5397288/

18. Huang YN, Liao WL, Huang JY, Lin YJ, Yang SF, Huang CC, et al. Long-term safety and efficacy of glucagon-like peptide-1 receptor agonists in individuals with obesity and without type 2 diabetes: A global retrospective cohort study. Diabetes Obes Metab [Internet]. 2024 Nov 1 [cited 2025 Mar 22];26(11). Available from: https://pubmed.ncbi.nlm.nih.gov/39171569/
19. van Bloemendaal L, ten Kulve JS, La Fleur SE, Ijzerman RG, Diamant M. Effects of glucagon-like peptide 1 on appetite and body weight: focus on the CNS. J Endocrinol [Internet]. 2014 Apr [cited 2025 Mar 20];221(1). Available from: https://pubmed.ncbi.nlm.nih.gov/24323912/
20. Ronveaux CC, Tomé D, Raybould HE. Glucagon-like peptide 1 interacts with ghrelin and leptin to regulate glucose metabolism and food intake through vagal afferent neuron signaling. J Nutr [Internet]. 2015 [cited 2025 Mar 20];145(4):672–80. Available from: https://pubmed.ncbi.nlm.nih.gov/25833771/
21. Lecis D, Prandi FR, Barone L, Belli M, Sergi D, Longo S, et al. Beyond the Cardiovascular Effects of Glucagon-like Peptide-1 Receptor Agonists: Body Slimming and Plaque Stabilization. Are New Statins Born? Biomolecules [Internet]. 2023 Dec 1 [cited 2025 Mar 20];13(12). Available from: https://pubmed.ncbi.nlm.nih.gov/38136567/
22. Alkhezi OS, Alahmed AA, Alfayez OM, Alzuman OA, Almutairi AR, Almohammed OA. Comparative effectiveness of glucagon-like peptide-1 receptor agonists for the management of obesity in adults without diabetes: A network meta-analysis of randomized clinical trials. Obes Rev [Internet]. 2023 Mar 1 [cited 2025 Mar 22];24(3). Available from: https://pubmed.ncbi.nlm.nih.gov/36579723/