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Authors' Affiliation:

¹Faculty of Medicine, Collegium Medicum, University of Rzeszów, Poland

²Clinical Provincial Hospital No. 2, Rzeszów, Poland

*Corresponding author:

Sylwia Lepak,
Faculty of Medicine, Collegium Medicum, University of Rzeszów, Poland,
E-mail: szylwia42@gmail.com

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Glucagon-like peptide 1 receptor agonists in obesity treatment: efficacy, safety and clinical implications

Sylwia Lepak^{1*}, Zuzanna Irzyk¹, Dominika Ruszel¹, Emilia Goc¹, Julia Rogala¹, Katarzyna Markuszka¹, Kinga Polityńska¹, Klaudia Samuła¹, Martyna Sarzyńska¹, Mateusz Szabat²

ABSTRACT

Background: Obesity is one of the leading causes of morbidity and mortality nowadays, with prevalence tripling since the 1970s. Lifestyle modification remains the cornerstone of treatment, but pharmacotherapy has emerged as a critical adjunct, including GLP-1R (glucagon-like peptide-1 receptor) agonists. **Objective:** To present the efficacy, safety, and clinical implications of GLP-1 receptor agonists in the treatment of obesity. **Methods:** A narrative review was based on articles available in PubMed, NIH, Wiley, The Lancet, and NEJM databases. **Keywords** included “obesity”, “GLP-1R agonists”, “semaglutide”, “liraglutide”, “tirzepatide”. Inclusion criteria encompassed randomized clinical trials, observational studies, meta-analyses, and review articles published in English between October 2018 and December 2025. **Results:** GLP-1 receptor agonists demonstrate significant weight loss efficacy. Semaglutide achieves weight loss of 11.4–13.9% at 68 weeks, and liraglutide produces 5.3–5.8% weight loss at 52–56 weeks. Tirzepatide, a dual GIP/GLP-1 agonist, demonstrates efficacy with even 17.8% weight loss at 72 weeks. Furthermore, these agents improve cardiometabolic parameters, such as blood pressure, lipid profiles, and glycemic control. Gastrointestinal adverse events, such as nausea, vomiting, diarrhea, and constipation, are common but generally mild. More serious adverse events are rare. **Conclusions:** GLP-1 receptor agonists are among the most effective options for the treatment of obesity. They help achieve clinically significant weight loss and improvements in metabolic parameters. There is a need for further research to investigate long-term safety and optimal treatment strategies.

Keywords: obesity, GLP-1R agonists, semaglutide, liraglutide, tirzepatide

1. INTRODUCTION

Obesity is becoming an increasingly significant challenge for modern medicine, representing one of the main causes of morbidity and mortality worldwide. Although the progression is modifiable and it is treatable, the number of patients

facing its consequences continues to rise. In 2024, 3.7 million people worldwide died as a result of obesity. Particularly worrying is the increase in obesity among children and adolescents, which brings the occurrence of accompanying diseases that have not occurred before with such high frequency in this age group. Since the 1970s, the prevalence of obesity worldwide has tripled, reaching more than 650 million obese adults in 2016 (Alcaino et al., 2025). Among children and adolescents aged 5-19, the number of overweight or obese individuals was 340 million, with the highest concentration of the problem in the United States, and according to estimates, the number of obese individuals will double by 2030. It estimates that by the same year, the global financial cost will increase to \$3 trillion per year (Banerjee et al., 2025; WHO, 2025).

In the pathogenesis of obesity, the fundamental role is played by exceeding caloric requirements, which is not balanced by adequate physical activity that would allow the excess to be burned off. In a healthy, properly nourished body, adipocytes produce adipokines (e.g., adiponectin), which increase insulin sensitivity and have anti-inflammatory effects. After the increased calorie supply, adipocytes accumulate excess energy as triglycerides and undergo hypertrophy. That leads to a restructuration, chronic hypoxia, and cytokine imbalance, where pro-inflammatory cytokines begin to predominate. That leads to chronic inflammation and increased macrophage mobilization, as well as impaired insulin signaling in peripheral tissues. Hyperinsulinemia and abnormal central leptin secretion occur, disturbing the hunger and satiety signaling pathway, leading to further hyperphagia (Banerjee et al., 2025; Salehi and Purnell, 2019).

The basis for treating obesity, which must be included in every treatment plan, is lifestyle modification and changing existing habits related to nutrition, physical activity, and the patient's functioning. Health education and verification of the patient's awareness of the impact of their habits on their body weight and health, as well as the consequences of obesity, are also very important. In addition, psychological support and emotional regulation are important throughout the therapeutic process. However, lifestyle modification usually leads to an average weight loss of 3-5%. Even the most intensive programs — involving partial meal replacement with a modified diet or a total meal replacement diet — achieve an average weight loss of about 10% after 12 months. However, maintaining significant long-term weight loss remains a major challenge.

A weight loss of 5–10% contributes to a partial reduction in risk factors for cardiovascular and metabolic diseases. However, this often proves insufficient to reverse obesity-related complications such as sleep apnea or type 2 diabetes. Bariatric surgery is often necessary for patients with a BMI ≥ 40 kg/m², ≥ 35 kg/m² with comorbidities, or ≥ 30 kg/m² with type 2 diabetes (Papamargaritis et al., 2024; Kushner and Shapiro, 2025). Pharmacotherapy has recently played a key role, which combined with lifestyle modifications, has shown promising results. Pharmaceuticals used in the treatment of obesity worldwide include: Orlistat, 1999; Bupropion/Naltrexone, 2018; Liraglutide 3.0 mg, 2018; Phentermine/Topiramate, 2019; Semaglutide 2.4 mg, 2021; Tirzepatide, 2023 (Son and Lim, 2024).

GLP-1 (glucagon-like peptide 1), as one of the anorexigenic peptides (along with cholecystokinin, peptide YY, and oxyntomodulin), is responsible for the feeling of satiety. It is secreted by L cells in the ileum after a meal. Its mechanism of action primarily involves stimulating insulin secretion, and it also regulates (inhibits or stimulates) glucagon secretion by pancreatic α cells. In addition, it suppresses appetite and gastric emptying, which best explains the mechanism of action of GLP-1 receptor agonist drugs (Son and Lim, 2024). Elevated plasma GLP-1 concentrations are detectable within 5 minutes after oral glucose administration, and their level usually peaks 30-60 minutes after a meal, depending on the nutrients contained in the food. The early, rapid increase in GLP-1 is due to the small number of L cells located in the duodenum and jejunum. In contrast, the largest number of L cells is found in the ileum and colon. L cells located in the distal sections of the intestine do not usually come into direct contact with rapidly absorbed nutrients. However, it is believed that L cells in the ileum are responsible for prolonged postprandial GLP-1 secretion after the consumption of more slowly digested foods.

2. REVIEW METHODS

A review was conducted of selected articles available in databases such as PubMed, NIH, Wiley, The Lancet, and NEJM. The keywords used to search for the articles were: “obesity”, “obesity treatment”, “GLP-1R agonists”, “semaglutide”, and “GLP-1R”. The criteria included randomized clinical trials, prospective and retrospective observational studies, meta-analyses, and review articles published in English between October 2018 and December 2025. The selection of articles included aspects such as the Patho mechanism of obesity and its associated consequences, treatment methods, the mechanism of action of GLP-1 and GLP-1R agonists, as well as their efficacy and adverse effects. The process of study identification and selection is presented in Figure 1.

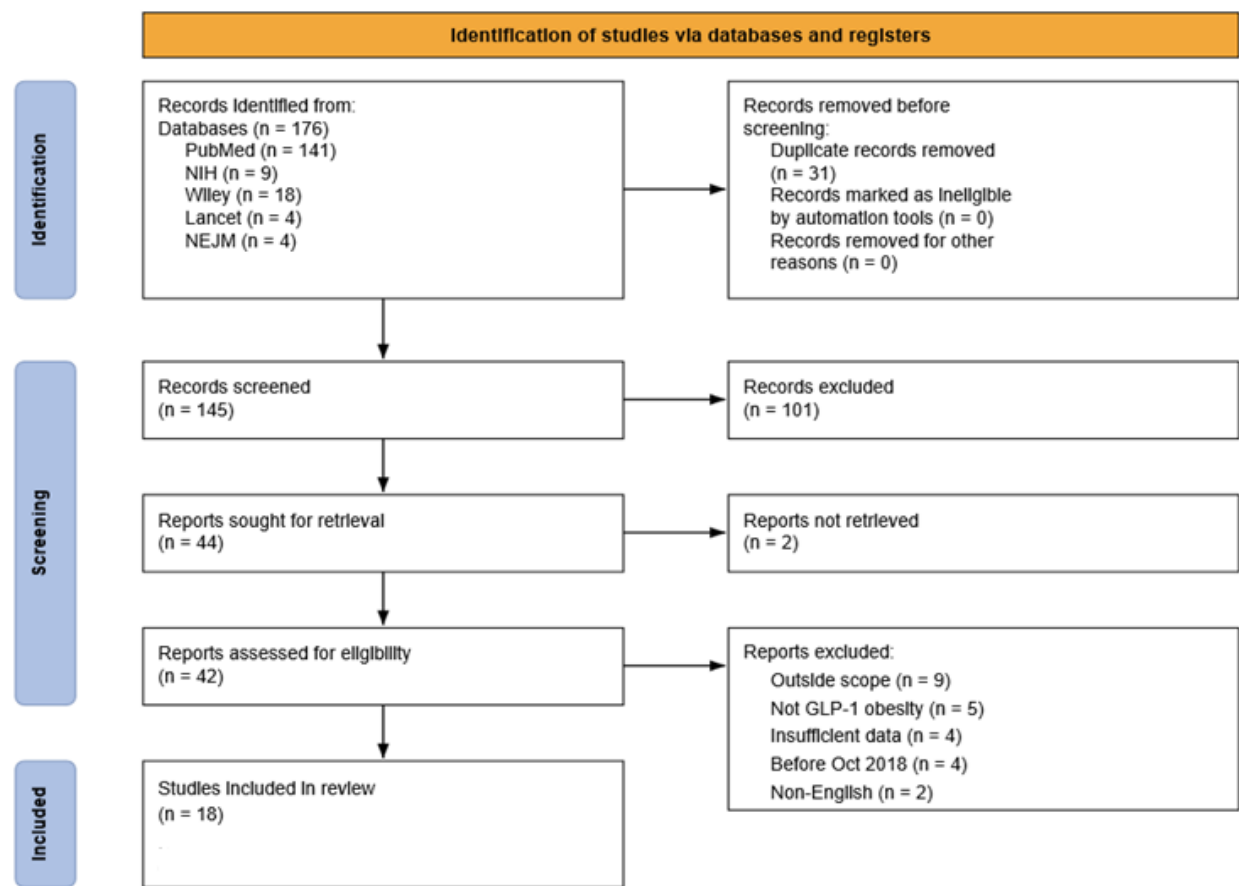


Figure 1. PRISMA flow diagram.

3. RESULTS AND DISCUSSION

Among GLP-1 receptor agonists, we distinguish between pharmaceuticals with different durations of action and is shown in Table 1.

Table 1. Different duration of action among GLP-1 receptors agonists.

GLP-1R agonists with a shorter duration of action	GLP-1R agonists with a longer duration of action
Exenatide	Dulaglutide
	Exenatide SR
Lixisenatide	Liraglutide
	Semaglutide

Liraglutide and lixisenatide are administered once daily, while exenatide is administered twice daily. GLP-1 receptor agonists are highly effective at reducing glucose levels, but there are differences within the drug class. Studies show that semaglutide administered once a week may have the greatest effect, followed by dulaglutide and liraglutide, exenatide administered once a week, then exenatide administered twice daily, and lixisenatide has a greater postprandial effect. All GLP-1 receptor agonists cause weight loss ranging from 1.5 kg to 6.0 kg during one month of therapy. In addition, agonists with a shorter duration of action increase insulin release and reduce glucagon secretion without causing hypoglycemia. They slow gastric emptying, contributing to increased satiety. Long-acting GLP-1R agonists also cause increased insulin release and reduced glucagon secretion without hypoglycemia, but they are more effective at lowering fasting blood glucose and are characterized by reduced postprandial blood glucose fluctuations (Davies et al., 2018).

Semaglutide

Semaglutide is commonly available as Ozempic and Wegovy. Ozempic is started at a dose of 0.25 mg once weekly and increased to 0.5 mg once weekly after 4 weeks of use. The dose can become enhanced to 1 mg once weekly if there is no effect. Wegovy starts at a dose of 0.25 mg and is gradually increased over 4 weeks until a dose of 2.4 mg per week is reached.

A study was conducted involving 3,962 patients from six trials who were obese or overweight. 2,562 participants received a weekly subcutaneous dose of 2.4 mg of semaglutide, and 1,400 received a placebo. All participants were over 18 years of age, with a BMI of 30 kg/m² and higher or a BMI equal to or greater than 27 kg/m² with at least one weight-related comorbidity, and none of them had diabetes.

Currently, a widely used criterion for weight reduction that is clinically relevant in the context of response to anti-obesity therapy is weight loss $\geq 5\%$ of initial weight. As demonstrated, subcutaneous administration of 2.4 mg of semaglutide once a week contributed to a weight loss of 11.80%, resulting in an average absolute weight loss of 12.2 kg. In five of six studies ($n = 3588$), there were cases of individuals who achieved weight loss exceeding 5%, 10%, 15%, and 20%. These results showed a significant numerical advantage for individuals taking semaglutide compared to those taking a placebo. A decrease in waist circumference was also observed in five studies ($n = 3890$) and in BMI in four studies ($n = 3679$) by 4.5 kg/m², a significant reduction in systolic blood pressure and, less significantly, diastolic blood pressure in five studies ($n = 3890$). Five studies ($n = 3890$) also showed a significant effect of semaglutide on lipid metabolism, associated with a reduction in total cholesterol, LDL, vLDL, FFA, triglycerides, and an increase in HDL. Reductions in CRP levels were also observed in four studies ($n = 3087$) and improvements in physical functioning in three studies ($n = 3375$) (on the SF-36 scale) (Qin et al., 2024). Another study also showed reduced postprandial apoB-48 (Raza et al., 2024).

The SELECT study, conducted between October 2018 and March 2021, involved 17,604 patients (72.3% male) from 41 countries, with a mean (SD) age of 61.6 (8.9) years and a BMI of 33.3 (5.0) kg m⁻². At week 208 of the study, the mean weight loss in the analyzed group of patients receiving semaglutide was -11.7%, and in the placebo group, up to -1.5%. At week 104, weight loss of $\geq 5\%$, $\geq 10\%$, $\geq 15\%$, $\geq 20\%$, and $\geq 25\%$ was achieved by 67.8%, 44.2%, 22.9%, 11.0%, and 4.9% of patients taking semaglutide, and 21.3%, 6.9%, 1.7%, 0.6%, and 0.1% of patients receiving placebo, respectively. At week 208, the reduction in waist circumference in people taking semaglutide was -7.7 cm, and in the placebo group it was -1.3 cm. At week 104, 52.4% of patients treated with semaglutide had a decrease in BMI compared to a decrease in BMI in 15.7% of patients receiving placebo (Ryan et al., 2024).

A study involving patients with diabetes was also conducted. The Semaglutide Treatment Effect in People with Obesity (STEP) 2 study compared the efficacy and safety of semaglutide at a dose of 2.4 mg s.c. with semaglutide at a dose of 1.0 mg and placebo in adults with obesity or overweight and type 2 diabetes. The study involved 1,210 participants who were randomly assigned to three equal groups. Participants received the appropriate dose of semaglutide or placebo once a week (depending on the group) for 68 weeks, with appropriate lifestyle and dietary modifications. At week 68, the mean weight reduction was 9.64% in the 2.4 mg semaglutide group and 3.42% in the placebo group ($P < 0.001$). Weight loss $\geq 5\%$ was more common in the 2.4 mg semaglutide group (68.8%) compared to the placebo group (28.5%; $P < 0.001$). What's more, semaglutide group also saw a 1.6% reduction in an HbA1c, which helped most patients achieve HbA1c of 6.5% or below. Cardiovascular and metabolic risk factors, lipid profile, inflammatory markers, and systolic blood pressure also improved (Raza et al., 2024).

Another study showed in a DXA examination, that semaglutide not only led to weight loss, but also contributed to a change in body composition, reducing the proportion of total and visceral fat. In this way, it increased the percentage of lean body mass in total body weight (Wilding et al., 2021).

Side effects

The most serious side effects of semaglutide include: cardiac disorders, infections, nervous system disorders, surgical procedures, tumors of varying degrees of malignancy, gallbladder disorders, and gastrointestinal disorders. The most common side effects are nausea, vomiting, diarrhea, and constipation. Several studies have shown that the incidence of side effects was similar or even lower in people taking semaglutide compared to placebo. However, indigestion symptoms were more common in patients using semaglutide, which more often led to discontinuation of the drug and withdrawal from treatment. No correlation was found between the occurrence and severity of adverse effects and belonging to a specific BMI class, but more patients with a lower BMI discontinued semaglutide due to persistent symptoms. This could be due to greater exposure to the drug in this group of patients, but also to cultural conditions, motivation, and individual factors. The association between GLP-1RA (glucagon-like peptide receptor agonists) and the occurrence of

non-inflammatory anterior ischemic optic neuropathy (NAION) is also being investigated (Qin et al., 2024; Raza et al., 2024; Ryan et al., 2024; Lincoff et al., 2023; Thomsen et al., 2025).

As it turns out, semaglutide is very similar in its action to liraglutide, which means that these drugs have the same eligibility criteria for treatment and similar side effects, although nausea is more commonly observed in patients taking semaglutide. Despite this, it remains more effective in the process of weight reduction compared to liraglutide. Its advantage is also that it is available in two effective forms of administration – oral and injection (Raza et al., 2024).

Liraglutide

Liraglutide is available as a subcutaneous injection under the trade name Saxenda. Treatment is started with a dose of 0.6 mg of liraglutide per day, taken independently of meals. After that, the dose increases by 0.6 mg each week until a total daily dose of 3 mg is reached. If the patient responds well to the 3 mg dose, treatment is continued as before. In people who do not tolerate the therapy well and in those who have not achieved a 4% reduction in their initial body weight within 4 months of treatment, treatment is usually discontinued. It is intended for adults with a BMI ≥ 30 kg/m² or ≥ 27 kg/m² with existing comorbidities such as hypertension, type 2 diabetes, or dyslipidemia. It can also be used in children over 12 years of age with a BMI ≥ 30 kg/m² and a minimum body weight of 60 kg.

A large, 104-week, multicenter STRIVE study was conducted to evaluate the clinical efficacy of liraglutide 3 mg. According to the criteria, adults aged 18–75 years referred to SWMS, with stable body weight over 12 weeks and a BMI ≥ 35 kg/m², and at least one of the following comorbidities: prediabetes, type 2 diabetes, hypertension, or obstructive sleep apnea (OSA). A total of 392 individuals were enrolled in the study and randomly assigned to receive liraglutide 3 mg (n = 260) or placebo (n = 132). After 52 weeks of the study, 25.4% (51 of 201) of participants in the liraglutide group achieved $\geq 15\%$ weight loss compared to 6.5% (6 of 93) in the control group (OR = 5.2; 95% CI = 2.1, 12.9; $p < 0.0001$). The mean weight reduction at 52 weeks was 8.1% in the liraglutide group and 2.7% in the control group [estimated treatment difference -5.4 (95% CI -7.0, -3.7), $p < 0.0001$], while at week 104, the mean weight reduction was -5.2% in the liraglutide group and -1.2% in the control group [estimated treatment difference -4.1 (95% CI, -6.4 to -1.8), $p < 0.0001$]. A decrease in HbA1c levels of 6.6 mmol/mol (-0.6%) and 6.0 mmol/mol (-0.6%) was observed at weeks 52 and 104 in the liraglutide group, while no significant changes were noted in the control group. This change also included patients with previously diagnosed prediabetes. Mild gastrointestinal symptoms (nausea, vomiting, constipation, diarrhea, abdominal pain) were also observed in over 40% of patients in the liraglutide group (Cerrillo and Parmar, 2024; Raza et al., 2024; Papamargaritis et al., 2024).

The LEADER study (n= 9340) showed lower mortality in the liraglutide group compared to placebo and a lower incidence of cardiometabolic disorders. A weight loss of 2.3 kg was reported compared to placebo, a decrease in systolic blood pressure of 1.2 mm Hg, and a lower HbA1c concentration of -0.40 percentage points. Promising results were also obtained in the SCALE obesity and prediabetes study. Due to the reduction of adipose tissue around the upper respiratory tract, reduction of inflammation, endothelial dysfunction, and cardiovascular diseases, a positive effect has been observed on reducing the incidence of obstructive sleep apnea and reducing the AHI index, which describes the incidence of apneas and hypopneas while sleeping, which correlates with better regeneration, and prevents chronic fatigue, leading to an improved quality of life (Yang et al., 2025; Raza et al., 2024). Liraglutide has similar side effects to semaglutide.

Safety Profile and Clinical Implications

A cohort study was conducted to evaluate the safety profile of GLP-1R agonists in patients being treated for obesity and type 2 diabetes. The safety analysis of obesity compared the use of GLP-1R agonists with naltrexone/bupropion and GLP-1R agonists with phentermine/topiramate. As a result, an increased incidence of hospitalizations due to gallbladder and biliary tract diseases was observed in the group receiving the GLP-1R agonist. No increased or decreased trend in the incidence of cardiovascular events (heart attack, stroke) was observed. The drug also had no effect on the incidence of suicidal thoughts and behaviors. In this study, a reduced incidence of liver disease was observed in the GLP-1R group.

Based on numerous studies, the most common clinical issue associated with GLP-1RA treatment has been gastrointestinal symptoms, which do not pose a significant risk to the patient and resolve over the course of therapy. More serious complications include intestinal obstruction and gastroparesis. The occurrence of these conditions under the influence of the drug has been reported; however, due to methodological shortcomings in the studies, it appears that GLP-1RAs do not commonly cause these conditions. Nevertheless, particular caution is exercised when using the drug prior to surgical procedures. The complication of pancreatitis

remains controversial. This complication may occur; however, studies have not demonstrated a direct effect of GLP-1RAs on the more common occurrence of pancreatitis in the patient population. One can also draw conclusions regarding the indirect protective effect of these drugs in the context of pancreatic cancer, which is one of the consequences of obesity.

A lack of association between these drugs and thyroid diseases or cancer has also been demonstrated. A new observation, which has sparked considerable controversy and conflicting views, is the effect of semaglutide on an increased risk of diabetic retinopathy, due to a rapid decrease in HbA1c levels. An increased risk of a rare condition—non-inflammatory anterior ischemic optic neuropathy (NAION)—which leads to blindness, has also been observed (Hurwitz et al., 2025; Thomsen et al., 2025).

Another drug with a mechanism of action similar to what is described above is tirzepatide, which has garnered interest due to its dual action. It is a glucose-dependent insulinotropic polypeptide and a GLP-1R agonist. In a randomized trial, tirzepatide resulted in body weight reductions of 19.5% (10 mg) and 20.9% (15 mg) at week 72 of treatment, demonstrating its high efficacy. In addition to changes in body weight, common features shared with GLP-1R agonists include changes in body composition, a reduction in waist circumference, a decrease in fasting insulin and lipid levels, and a positive impact on systolic and diastolic blood pressure. In this case, the most common adverse effects are also gastrointestinal complaints. The impact of tirzepatide on the treatment of obesity is still being studied (Jastreboff et al., 2022). The principal studies on GLP-1 receptor agonists in obesity included in this review are summarized in Table 2.

Table 2. Summary of key studies on GLP-1 receptor agonists in the treatment of obesity.

Study (year)	Drug and dose	Population (n)	Duration	Main efficacy outcome	Main adverse effects
Qin et al., 2024	Semaglutide 2.4 mg s.c. weekly	Meta-analysis of 6 RCTs; adults with overweight/obesity without diabetes (n = 3,962)	Up to 68 weeks	Mean weight loss 11.8% (–12.2 kg); lower blood pressure, improved lipid profile and CRP	Mostly mild gastrointestinal effects (nausea, vomiting, diarrhoea)
SELECT – Lincoff et al., 2023; Ryan et al., 2024	Semaglutide 2.4 mg s.c. weekly	RCT; adults with overweight/obesity and cardiovascular disease, without diabetes (n = 17,604)	Up to 208 weeks	Weight loss –11.7% vs –1.5% (placebo); reduced cardiovascular events	Gastrointestinal effects; serious events not increased vs placebo
STEP 2	Semaglutide 2.4 mg s.c. weekly	RCT; adults with overweight/obesity and type 2 diabetes (n = 1,210)	68 weeks	Weight loss 9.6% vs 3.4% (placebo); HbA1c –1.6%	Mild gastrointestinal effects
STRIVE – Papamargaritis et al., 2024	Liraglutide 3.0 mg s.c. daily	RCT; adults with BMI ≥35 and ≥1 comorbidity (n = 392)	104 weeks	Weight loss 8.1% at 52 weeks and 5.2% at 104 weeks; HbA1c –0.6%	Mild gastrointestinal symptoms in >40%
LEADER	Liraglutide s.c. daily	RCT; type 2 diabetes at high cardiovascular risk (n = 9,340)	—	Weight –2.3 kg vs placebo; lower mortality and cardiovascular events; HbA1c –0.4%	Gastrointestinal effects
SURMOUNT-1 – Jastreboff et al., 2022	Tirzepatide 10–15 mg s.c. weekly	RCT; adults with overweight/obesity without diabetes	72 weeks	Weight loss 19.5% (10 mg) and 20.9% (15 mg)	Mostly mild gastrointestinal effects

4. CONCLUSION

Among GLP-1 agonists, semaglutide is particularly effective, enabling significant and sustained weight loss, as well as improvements in lipid profile, blood pressure, and levels of inflammatory markers. Liraglutide has a similar effect in the treatment of obesity, helping patients achieve a better quality of life. Both drugs have a similar safety profile, and the most common side effects involve the digestive system, presenting as mild symptoms. The same applies to tirzepatide, which has an additional effect as a glucose-dependent insulinotropic polypeptide (GIP).

GLP-1 receptor agonists currently represent one of the most promising pharmacotherapeutic options for obesity. Combined with lifestyle modifications, the process can lead to significant improvements in metabolic parameters and patients' quality of life. At the same time, further studies are needed to evaluate the long-term safety and optimal strategies for using these drugs in the treatment of obesity.

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Authors' Contributions

Sylwia Lepak - contributed to the study conception and design, conducted the literature search and data analysis, wrote the manuscript, and approved the final version for publication.

Klaudia Samuła - conducted the literature search and data analysis.

Dominika Ruszel - conducted the literature search and data analysis.

Emilia Goc - conducted the literature search and data analysis.

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Katarzyna Markuszka - conducted the literature search and data analysis.

Kinga Polityńska - conducted the literature search and data analysis.

Martyna Sarzyńska - conducted the literature search and data analysis.

Mateusz Szabat - conducted the literature search and data analysis.

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Informed consent

Not applicable.

Ethical approval

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

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Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

REFERENCES

1. Alcaïno C, Reimann F, Gribble FM. Incretin hormones and obesity. *J Physiol* 2025;603:7645-7659.
2. Banerjee D, Mani A. Obesity's systemic impact: exploring molecular and physiological links to diabetes, cardiovascular

- disease, and heart failure. *Front Endocrinol (Lausanne)* 2025;16:1681766. doi: 10.3389/fendo.2025.1681766.
3. Cerillo JL, Parmar M. Liraglutide. In: *StatPearls. Treasure Island (FL): StatPearls Publishing; 2024.*
4. Davies MJ, D'Alessio DA, Fradkin J, Kernan WN, Mathieu C, Mingrone G, Rossing P, Tsapas A, Wexler DJ, Buse JB. Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2018;41(12):2669-2701. doi: 10.2337/dci18-0033.
5. Hurwitz SR, Lanes S, Quimbo T, Papazian A, White J, Fisher V, Cziraky MJ, Crowley MJ, Willey VJ. Comparative safety of glucagon-like peptide 1 receptor agonists (GLP-1-RAs) in type 2 diabetes and chronic weight management: a real-world data study. *Pharmacoepidemiol Drug Saf* 2025;34(9):e70214.
6. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, Kiyosue A, Zhang S, Liu B, Bunck MC, Stefanski A; SURMOUNT-1 Investigators. Tirzepatide Once Weekly for the Treatment of Obesity. *N Engl J Med* 2022;387(3):205-216. doi: 10.1056/NEJMoa2206038.
7. Kushner RF, Shapiro M. Obesity: assessment and treatment across the care continuum. *Ann Med* 2025;57(1):2521433. doi: 10.1080/07853890.2025.2521433.
8. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, Hardt-Lindberg S, Hovingh GK, Kahn SE, Kushner RF, Lingvay I, Oral TK, Michelsen MM, Plutzky J, Tornøe CW, Ryan DH; SELECT Trial Investigators. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. *N Engl J Med* 2023;389(24):2221-2232. doi: 10.1056/NEJMoa2307563.
9. Papamargaritis D, Al-Najim W, Lim JZM, Crane J, Bodicoat DH, Barber S, Lean M, McGowan B, O'Shea D, Webb DR, Wilding JPH, le Roux CW, Davies MJ. Effectiveness of integrating a pragmatic pathway for prescribing liraglutide 3.0 mg in weight management services (STRIVE study): a multicentre, open-label, parallel-group, randomized controlled trial. *Lancet Reg Health Eur* 2024;39:100853. doi: 10.1016/j.lanepe.2024.100853.
10. Qin W, Yang J, Deng C, Ruan Q, Duan K. Efficacy and safety of semaglutide 2.4 mg for weight loss in overweight or obese adults without diabetes: An updated systematic review and meta-analysis including the 2-year STEP 5 trial. *Diabetes Obes Metab* 2024;26(3):911-923. doi:10.1111/dom.15386
11. Raza FA, Altaf R, Bashir T, Asghar F, Altaf R, Tousif S, Goyal A, Mohammed A, Mohammad MF, Anan M, Ali S. Effect of GLP-1 receptor agonists on weight and cardiovascular outcomes: A review. *Medicine (Baltimore)* 2024;103(44):e40364. doi: 10.1097/MD.00000000000040364.
12. Ryan DH, Lingvay I, Deanfield J, Kahn SE, Barros E, Burguera B, Colhoun HM, Cercato C, Dicker D, Horn DB, Hovingh GK, Jeppesen OK, Kokkinos A, Lincoff AM, Meyhöfer SM, Oral TK, Plutzky J, van Beek AP, Wilding JPH, Kushner RF. Long-term weight loss effects of semaglutide in obesity without diabetes in the SELECT trial. *Nat Med* 2024;30:2049-2057. doi: 10.1038/s41591-024-02996-7.
13. Salehi M, Purnell JQ. The Role of Glucagon-Like Peptide-1 in Energy Homeostasis. *Metab Syndr Relat Disord* 2019;17(4):183-191. doi: 10.1089/met.2018.0088.
14. Son JW, Lim S. Glucagon-Like Peptide-1 Based Therapies: A New Horizon in Obesity Management. *Endocrinol Metab* 2024;39(2):206-221.
15. Thomsen RW, Mailhac A, Løhde JB, Pottegård A. Real-world evidence on the utilization, clinical and comparative effectiveness, and adverse effects of newer GLP-1RA-based weight-loss therapies. *Diabetes Obes Metab* 2025;27(Suppl. 2):66-88. doi:10.1111/dom.16364
16. WHO. WHO issues global guideline on the use of GLP-1 medicines in treating obesity. Geneva: World Health Organization; 2025.
17. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, McGowan BM, Rosenstock J, Tran MTD, Wadden TA, Wharton S, Yokote K, Zeuthen N, Kushner RF; STEP 1 Study Group. Once-Weekly Semaglutide in Adults with Overweight or Obesity. *N Engl J Med* 2021;384(11):989-1002. doi: 10.1056/NEJMoa2032183.
18. Yang R, Zhang L, Guo J, Wang N, Zhang Q, Qi Z, Wu L, Qin L, Liu T. Glucagon-like Peptide-1 receptor agonists for obstructive sleep apnea in patients with obesity and type 2 diabetes mellitus: a systematic review and meta-analysis. *J Transl Med* 2025;23(1):389. doi: 10.1186/s12967-025-06302-y.