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INNOVATIONS IN OBESITY TREATMENT – GLP – 1 PHARMACOTHERAPY AND BARIATRIC SURGERY

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ABSTRACT

Background: Obesity is a growing global health challenge requiring effective, long - term treatment strategies. This paper focus on two leading innovations: GLP - 1 receptor agonists and bariatric surgery. GLP - 1 - based pharmacotherapy, including agents like semaglutide and tirzepatide, has shown impressive weight loss outcomes by regulating appetite and glucose metabolism. Meanwhile, bariatric procedures such as sleeve gastrectomy and gastric bypass remain the most effective interventions for severe obesity, offering sustained weight reduction and improvement of metabolic comorbidities. By comparing the efficiency, safety, and indications of both approaches, this paper show how pharmacological and surgical treatments can work synergistically to improve patient outcomes in obesity management.
Aim: The aim of this article is to highlight the challenges involved in treating obesity especially using GLP - 1 receptor agonists and bariatric surgery.
Methods: A review of scientific articles published on ResearchGate and PubMed from 2013 to 2025.
Results: Both GLP - 1 receptor agonists and metabolic surgery were found to be effective in reducing body weight and improving metabolic health in obese patients. Treatment with GLP - 1 analogs such as liraglutide or semaglutide led to moderate weight loss, typically between 5–15% of initial body weight. These medications also improved blood sugar control and lipid levels. Metabolic surgery, including sleeve gastrectomy and gastric bypass, resulted in greater weight reduction - often 25 - 35%, and more significant improvement in conditions like type 2 diabetes and hypertension. Interestingly, GLP - 1 levels tend to rise after surgery, suggesting that hormonal changes may partly explain the effectiveness of surgical interventions. In summary, both approaches show clear benefits, with surgery providing stronger effects, while GLP - 1 therapy offers a less invasive option.
Conclusion: GLP - 1 receptor agonists and metabolic surgery are methods to cure obesity and both of these methods are effective. GLP - 1 therapies offer a non - invasive option with metabolic benefits, while surgery provides greater and more sustained weight loss. The rise in GLP - 1 levels after surgery suggests shared mechanisms. Choosing the right approach should be based on individual patient needs and clinical factors.

KEYWORDS

Obesity, Bariatric Surgery, GLP – 1 Receptor Agonist, Bariatric Procedures, BMI

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1. Introduction

Obesity and overweight has emerged as a critical health crisis worldwide. Since 1990, its prevalence has more that doubled, reaching over 890 milion adults by 2022, and forecasts indicate a continued upward trend.[1] Obesity is not only a chronic disease but also a major risk factor of comorbidities, including type 2 diabetes mellitus (T2DM), cardiovascular diseases, obstructive sleep apnea, osteoarthritis and several types of cancer. Obesity is a condition characterized by increasing body weight cause by accumulation of fat tissue (men above 25%, women above 30% of body mass), caused by hypertrophy and/or hyperplasia of adipocytes. [2]

Measuring body weight is the simplest procedure that we can perform on a patient but it's not ideal because it doesn't show the actual amount of fat tissue. The most common used index for diagnosing and assessing obesity is the Body Mass Index (BMI), also known as the Quetelet index. We can measure it by dividing body weight (at kilograms) by height (at metres) squared . According to the World Health Organization (WHO), in adults, obesity is diagnosed when BMI is ≥ 30.0 kg/m².

Table 1. Types of obesity

Criterium		BMI amount [kg/m²]
BMI	Overweight	25.0-29.9
	Obesity I°	30.0-34.9
	Obesity II°	35.0-39.9
	Obesity III°	≥40.0

Source: [3]

Non - pharmacological obesity treatment are life style modification - diet and physical activity. However, the long-term success of these interventions is limited. We observe weak effect of weight loss and high rates of weight fluctuations (yo-yo effect). Pharmacotherapy and bariatric surgery have emerged as adjunctive or alternative options in cases where conservative therapy is uneffective.

GLP - 1 receptor agonists (e.g. semaglutide, liraglutide) were originally developed for glycemic control in type 2 diabetes. Subsequent clinical trials revealed their significant potential for reducing weight in non - diabetic patients. Their benefits are for example slower gastric emptying, enhanced satiety signals, and appetite suppression - effects that in some studies approximate those seen after bariatric surgery. They have demonstrated weight loss effects which make them attractive therapeutic options even for patients not only with diabetes but with obesity too.[4] Their mechanisms include delaying gastric emptying, promoting satiety and reducing appetite through central pathways with recent trials showing outcomes rivaling those of bariatric procedures in selected populations.[5].

On the other hand, bariatric surgery remains the most effective intervention for achieving significant and sustained weight loss, particularly among patients with severe obesity or obesity - related complications [6]. Bariatric surgery procedures for example Roux – en – Y gastrin bypass (RYGB) and sleeve gastrectomy (SG) have shown metabolic benefits for people for example with diabetes and obesity, including the remission of T2DM and hypertension.

With both GLP – 1 - based pharmacotherapy and bariatric surgery showing strong clinical evidence, the obesity treatment landscape is undergoing significant transformation. The purpose of this article is to critically evaluate these two major innovations, summarizing findings from recent meta - analyses and systematic reviews regarding their efficiency, safety, and long - term outcomes. By comparing pharmacological and surgical approaches, this review aims to provide a comprehensive perspective for clinicians, researchers, and policymakers on the evolving standards of overweight and obesity care.

2. Methods:

A review of scientific articles published on Google Scholar and PubMed from 2013 to 2025

2.1 GLP – 1 Pharmacotherapy

GLP - 1 receptor agonists - such as liraglutide, semaglutide, and tirzepatide - act by mimicking the endogenous incretin GLP - 1. They produce appetite suppression, delay gastric emptying, and promote satiety via both peripheral and central nervous system pathways [7]. Originally approved for type 2 diabetes, these agents have shown striking weight loss efficiency even in non - diabetic individuals [8].

Efficiency In Obesity

A meta - analysis of 47 randomized controlled trials involving 23,244 adults (with or without diabetes) found average weight loss of - 4.57 kg, BMI reduction of - 2.07 kg/m², and waist circumference reduction of - 4.55 cm compared with placebo. These effects were consistent across GLP - 1 RA types and demographic subgroups [9]. For individuals without diabetes, another meta - analysis of 24 RCTs (5,867 participants) showed that GLP - 1 RAs produced significantly more weight loss compared to placebo or metformin - weighted mean difference approximately - 5.4 kg - with semaglutide demonstrating the strongest efficiency and lower gastrointestinal adverse events [10].

Performance of GLP 1 Agents

A Bayesian network meta - analysis including over 12,300 non - diabetic adults found that weekly tirzepatide at 10 mg or 15 mg doses and semaglutide 2.4 mg achieved the greatest weight loss, with patients more likely to lose between 5% and 20% of baseline weight compared to other GLP - 1 receptor agonists such as liraglutide.[11] Another systematic review focusing on about 5,800 participants observed that tirzepatide led to an average weight reduction of approximately 12.5 kg (i.e. 12 - 15%), outperforming semaglutide by about 1.9 kg in head – to - head comparisons. [12]

Body Composition Effects

A network meta - analysis including 22 randomized controlled trials with approximately 2,258 participants revealed that GLP - 1 receptor agonists reduced fat mass by about 2.95 kg and lean mass by approximately 0.86 kg, accounting for roughly 25% of total weight loss. Notably, tirzepatide (15 mg/week) and semaglutide (2.4 mg/week) achieved the greatest reductions in fat but also led to the greatest reductions in lean tissue compared to liraglutide, which preserved more lean mass in certain dosage regiment.[13]

Safety and Tolerability

The majority of clinical trials involving GLP - 1 receptor agonists consistently reported gastrointestinal symptoms - such as nausea, vomiting, diarrhea, and appetite suppression - affecting up to 85% of patients in some studies, compared with lower incidence in placebo groups. Tirzepatide was generally well tolerated, but had slightly higher rates of GI adverse effects than semaglutide or liraglutide.[14] Additionally, pooled data from cardiovascular outcome trials involving over 60,000 individuals with type 2 diabetes showed that GLP - 1 RAs were associated with a 14% reduction in major adverse cardiovascular events (MACE), roughly 12% lower all - cause mortality, and improvements in heart failure hospitalizations and renal outcomes, supporting substantial cardioprotective and renoprotective effects.[14]

Emerging Co-Agonists

The combination of GLP - 1 receptor agonists with other gut hormones, such as tirzepatide - which targets both GLP - 1 and GIP receptors - and investigational triple agonists like retatrutide, has demonstrated enhanced effectiveness in weight reduction. In clinical trials involving individuals with obesity, weekly administration of tirzepatide at 15 mg resulted in weight loss of up to 17.8% after 72 weeks. Meanwhile, retatrutide showed an even greater reduction, achieving approximately 22.1% weight loss after 48 weeks in early - phase studies [15,16].

2.2 Bariatric Surgery

Bariatric surgery remains the most effective long - term treatment for severe obesity. Meta - analyses indicate that Roux – en - Y gastric bypass (RYGB) results in greater weight loss compared to sleeve gastrectomy (SG), with approximately 65.7% versus 57.3% weight loss at 5 years, as well as better improvement of comorbid conditions such as dyslipidemia and gastroesophageal reflux disease [17]. A broader meta - analysis comparing SG and RYGB found that long - term weight loss at 3 to 5 years favors RYGB, although mid - term outcomes were comparable [18,19]. In a real - world cohort study involving 122,567 bariatric patients in Australia, total body weight loss after 5 years was about 30.7% for RYGB, 26.5% for SG, and 34.9% for one-anastomosis gastric bypass, with a low overall complication rate (~3.6%) [20].

Safety and Risks

Although Roux – en - Y gastric bypass (RYGB) typically results in more pronounced metabolic improvements compared to sleeve gastrectomy (SG), it is accompanied by a higher risk of complications, such as increased need for reoperation and longer surgical duration. The safety and outcomes of these procedures depend heavily on appropriate patient selection, surgeon experience, and thorough postoperative management.[21]

Long – Term Challenges

Up to one - third of patients experience inadequate weight loss or significant weight regain following bariatric surgery, underscoring the chronic and relapsing nature of obesity. Long - term studies indicate that sleeve gastrectomy (SG) may increase the risk of gastroesophageal reflux disease (GERD), while Roux – en - Y gastric bypass (RYGB) is associated with nutritional deficiencies over time. These findings emphasize the importance of ongoing postoperative surveillance and, when necessary, revisional surgery [22,23].

Special Populations

Recent findings indicate that bariatric surgery remains safe and effective even in individuals with extreme obesity (BMI ≥ 70 kg/m²), resulting in substantial weight loss while maintaining low rates of serious complications [24]. Moreover, these surgical interventions have shown significant improvements in non-alcoholic fatty liver disease (NAFLD) and obstructive sleep apnea (OSA); up to 92% of patients experienced resolution of hepatic steatosis, and substantial reductions in cardiovascular and all - cause mortality risk were observed following surgery [25,26].

Efficiency

Bariatric surgery remains the most effective long-term method for achieving substantial weight reduction, often resulting in a total body weight loss (TBWL) of 25 - 35% over the course of 1 to 5 years, depending on the procedure type and quality of postoperative support[27]. In contrast, pharmacologic agents such as semaglutide (2.4 mg weekly) result in average weight loss of 12 - 15%, while tirzepatide (15 mg weekly) can lead to a reduction of 17–21% over 72 weeks, approaching the effectiveness of surgery in certain patients with lower BMI and fewer metabolic complications[28].

However, the success of these medications depends on patient adherence, tolerance of the drug (especially gastrointestinal side effects), and continued access to treatment, which is often impacted by high costs or insurance limitations. Real-world outcomes may therefore be less impressive than clinical trial data suggest[29,30]. Bariatric surgery tends to produce more consistent and durable results, particularly in individuals with BMI ≥40 kg/m² or those suffering from obesity-related comorbidities[31].

2. Discussions

GLP - 1 receptor agonists are generally well tolerated, with adverse effects primarily limited to transient gastrointestinal symptoms such as nausea or diarrhea. Severe adverse events are uncommon. In contrast, while bariatric surgery is associated with low perioperative mortality (typically below 0.5%), it involves a greater risk of complications including anastomotic leaks, micronutrient deficiencies, the need for revision procedures, and long-term gastrointestinal issues. These risks can be significantly reduced when procedures are performed in specialized, high-volume centers with structured postoperative monitoring and care protocols.[32,33]

Cardiometabolic and mortality outcomes

Both pharmacological therapies using GLP - 1 receptor agonists and bariatric surgical procedures lead to significant improvements in glycemic control, blood pressure, and lipid metabolism. However, surgical approaches typically result in more rapid and sustained remission of type 2 diabetes and hypertension, particularly in individuals with advanced or long-standing disease.[34] Long-term data indicate that bariatric procedures are associated with considerable reductions in all-cause mortality (ranging from 30% to 59%), as well as lower rates of cardiovascular mortality and obesity-related cancers.[35] On the other hand, GLP - 1 receptor agonists - especially liraglutide, semaglutide, and tirzepatide - have demonstrated cardiovascular and renal benefits. Meta-analyses show these agents reduce the incidence of major adverse cardiovascular events (MACE) and slow the progression of chronic kidney disease.[36,37]

Cost - Effectiveness and Accessibility

From a public health standpoint, both bariatric surgery and GLP - 1 receptor agonist therapy involve significant initial costs. Surgical treatment typically includes substantial procedural and hospitalization expenses, whereas chronic use of GLP - 1 Ras - often costing between $1,000 and $1,400 per month in certain countries - can impose a heavy economic burden on patients and health systems.[38] Despite these expenses, pharmacotherapy may be more practical in settings with limited surgical infrastructure or insurance coverage, especially since dosage can be adjusted or discontinued as needed. Furthermore, several cost - effectiveness analyses indicate that GLP - 1 RAs can be a justifiable investment for individuals at high cardiometabolic risk, particularly when compared to no treatment or unsuccessful lifestyle interventions.[39]

Patient Preferences and Final Clinical Decision

The selection of treatment should be tailored to individual patient characteristics such as BMI, age, existing comorbidities, tolerance to medications, psychological readiness, and willingness to maintain long-term therapy. Patients with a BMI between 30 and 35 kg/m² and early metabolic disturbances might find GLP-

1 receptor agonists more suitable, whereas those with a BMI over 40 kg/m² or poorly managed diabetes could achieve better results with surgical options.

Patient preferences are pivotal: some favor pharmacological treatments due to their reversible and less invasive nature, while others opt for surgery despite its inherent risks because it typically involves a single procedure. To maximize treatment success, shared decision-making, thorough counseling, and ongoing follow-up are crucial components regardless of the chosen intervention.[40, 41, 42]

4. Conclusion

Table 2. Comparison of obesity treatment

Factor	**GLP-1-Based Pharmacotherapy**	**Bariatric Surgery**
Weight Loss (avg.)	10–21%	25–35%
Onset of Effect	Gradual (weeks to months)	Rapid (weeks)
Invasiveness	Non-invasive	Invasive (surgery)
Risk Profile	Mild-moderate (GI side effects)	Moderate (operative risks, long-term complications)
Durability	Requires ongoing use	Long-lasting; some weight regain possible
Cardiometabolic Benefits	Moderate to high	High
Mortality Reduction	Yes (modest)	Yes (significant)
Accessibility	Broad (with insurance)	Limited by cost, surgical access
Cost-Effectiveness	Variable	Generally favorable long-term

Source: [43,44,45]

The management of obesity is rapidly evolving. Bariatric surgery remains the most effective method for achieving long-term, significant weight loss and reducing mortality and related health risks.[46] However, GLP - 1 receptor agonists like semaglutide and tirzepatide have emerged as effective non-surgical alternatives, particularly for patients ineligible for surgery or preferring less invasive treatments.[47] These medications not only promote weight loss comparable to surgery but also improve blood sugar control, cardiovascular health, and kidney function.[47] Despite their benefits and relatively favorable safety profiles, issues such as long - term adherence and high costs may limit their widespread use.[48]

Effective obesity care requires personalized treatment plans that balance effectiveness, safety, patient preferences, comorbidities, accessibility, and goals.[49] Both surgery and pharmacotherapy are valuable and complementary components of a comprehensive approach. With ongoing advancements, especially in dual and triple agonists, pharmacological treatments may further narrow the gap with surgical outcomes.[47] Nonetheless, bariatric surgery remains crucial for patients with severe obesity or when medications alone are insufficient.[46] Combining these strategies offers the best chance for sustainable health improvements in individuals with obesity.

Disclosure

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Conceptualization: Piotr Bartnik, Jarosław Baran
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