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# Efficacy and Safety of GLP-1 Receptor Agonists as Adjuvant Pharmacotherapy After Bariatric Surgery: A Narrative Review

**Natanael Bonardo Sinaga*, Lionel Sirait**

Siloam Hospitals Dhirga Surya Medan

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*Correspondence: Natanael Bonardo Sinaga
Email: dr.natanaelsinaga@gmail.com

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**Abstract:** Bariatric surgery remains the most effective long-term intervention for severe obesity, yet many patients experience inadequate weight loss or post-operative weight regain. GLP-1 receptor agonists (GLP-1 RAs) have emerged as promising adjuvant options through complementary mechanisms of appetite suppression and glycemic regulation.Aim: To evaluate the efficacy and safety of GLP-1 RAs as adjuvant pharmacotherapy in adult post-bariatric surgery patients. Methods, A systematic PubMed/MEDLINE search was conducted from January 2015 to January 2026. Eligible studies included adult post-bariatric patients receiving any GLP-1 RA with reported weight, glycemic, or safety outcomes. Case reports, animal studies, and review articles were excluded. Results, Eleven studies comprising 873 patients were included. GLP-1 RAs consistently demonstrated clinically meaningful weight reduction across all agents, with total body weight loss ranging from 5% to over 15% depending on agent, dose, and follow-up duration. Semaglutide demonstrated superior weight loss over liraglutide in head-to-head comparisons, while tirzepatide showed the greatest overall weight reduction. Glycemic improvements were most pronounced in patients with persistent or recurrent type 2 diabetes. Adverse events were predominantly gastrointestinal and mild-to-moderate in severity. Conclusion, GLP-1 RAs are effective and well-tolerated adjuvant therapies following bariatric surgery. Tirzepatide and semaglutide appear to offer greater weight loss benefit compared to liraglutide. Individualized agent selection based on patient characteristics and tolerability is recommended. Prospective randomized trials with standardized outcome reporting are needed to establish definitive clinical guidelines.

**Keywords**: Bariatric Surgery,GLP-1 Receptor Agonists, Semaglutide

## Introduction

Obesity is a long-term, complex condition that arises from multiple contributing factors and is linked to considerable rates of illness and death. It is also associated with an increased risk of several health problems, including type 2 diabetes mellitus, cardiovascular diseases, obstructive sleep apnea, and certain types of cancer(Syn et al, 2021). Despite advances in lifestyle interventions and pharmacotherapy, bariatric surgery remains the most effective and durable treatment for severe obesity, consistently achieving substantial and sustained weight loss alongside meaningful improvements in obesity-related comorbidities(O'Brien et al, 2019) (Syn et al, 2021)

The bariatric surgeries most frequently carried out are sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), and laparoscopic adjustable gastric banding (LAGB). Each of these procedures promotes weight reduction through different mechanisms, such as limiting food intake, reducing nutrient absorption, or altering neurohormonal pathways that regulate appetite and metabolism(O'Brien et al, 2019). Overall, bariatric surgery tends to produce positive long-term results, but a notable proportion of patients, roughly 20–30%, fail to achieve sufficient weight loss or regain weight within two to five years after the procedure(El Ansari & Elhag, 2021) (Noria et al, 2023). This issue highlights a significant gap in clinical management, since regaining weight can lead to the return of obesity-related health conditions and a decline in patients' overall quality of life (El Ansari & Elhag, 2021).

The pathophysiology of weight regain after bariatric surgery is complex and multifactorial, involving maladaptive neuroendocrine responses, behavioral factors, and altered gut hormone profiles(El Ansari & Elhag, 2021). Among the neuroendocrine changes implicated, diminished postprandial GLP-1 secretion and reduced satiety signaling have been identified as contributors to appetite dysregulation and subsequent weight regain in a subset of post-bariatric patients(Çalık Başaran et al, 2025) (Drucker, 2022).

GLP-1 receptor agonists (GLP-1 RAs) are a group of incretin-mimicking drugs that replicate the action of naturally occurring glucagon-like peptide-1 (GLP-1). They work by reducing appetite through central nervous system pathways, slowing gastric emptying, and stimulating insulin release(Çalık Başaran et al, 2025) (Drucker, 2022) (Wharton et al, 2025). Originally developed for the management of T2DM, GLP-1 RAs have since demonstrated robust weight loss efficacy in non-diabetic individuals with obesity, leading to their regulatory approval as anti-obesity agents.(17) Currently available agents include liraglutide, semaglutide, dulaglutide, exenatide, and the dual GIP/GLP-1 receptor agonist tirzepatide, each differing in their pharmacokinetic profiles, dosing schedules, and magnitude of weight loss effect(Wharton et al, 2025).

The use of GLP-1 receptor agonists (GLP-1 RAs) after bariatric surgery is especially well justified and considered highly promising in this clinical context. These agents may address the specific neuroendocrine deficits that contribute to weight regain, complementing the anatomical and physiological changes induced by surgery(Çalık Başaran et al, 2025) (Drucker, 2022).(Furthermore, for patients with persistent or recurrent T2DM following metabolic surgery, GLP-1 RAs offer the additional benefit of glycemic control without the risk of hypoglycemia associated with other antidiabetic agents(Drucker, 2022) (Miras et al, 2019).

Although clinical interest in GLP-1 receptor agonists continues to increase, their role as adjunct pharmacological therapy following bariatric surgery is still not fully understood. Previous systematic reviews and meta-analyses have mainly concentrated on particular scenarios, such as weight regain or inadequate weight loss, without thoroughly evaluating the overall effectiveness, safety profile, and real-world clinical considerations across different GLP-1 RA medications and the broader population of post-bariatric patients(Tan et al, 2025). A narrative synthesis is therefore warranted to consolidate current evidence,

identify patterns across agents and study designs, and provide clinically actionable insights for practitioners managing this challenging patient population.

Therefore, this narrative review aims to evaluate the efficacy and safety of GLP-1 receptor agonists as adjuvant pharmacotherapy following bariatric surgery, with particular focus on weight loss outcomes, glycemic control, and adverse event profiles across available agents(Abdallah et al, 2025) (Mok et al, 2023) (Murvelashvili et al, 2023).

## Methodology

This study was conducted as a narrative review with a systematic literature search strategy. Due to substantial heterogeneity across available studies in terms of design, patient populations, bariatric procedures, GLP-1 receptor agonist (GLP-1 RA) agents, and outcome reporting, a narrative synthesis approach was considered most appropriate to integrate the evidence and provide clinically relevant insights. This review was conducted in accordance with the Scale for the Assessment of Narrative Review Articles (SANRA) criteria to maintain transparency in methodology and to ensure high standards of reporting quality (Baethge et al, 2019). A systematic search was performed in PubMed/MEDLINE covering the period from January 2015 to January 2026 using a combination of MeSH terms and free-text keywords related to GLP-1 RAs, bariatric surgery, and post-operative outcomes, combined with Boolean operators. No language restrictions were applied, and additional manual searches of reference lists were conducted to identify further eligible studies.

Eligibility criteria were defined a priori and included adult patients (≥18 years) with a history of bariatric surgery who received any GLP-1 RA in the post-operative period and reported at least one measurable outcome such as weight loss, glycemic control, or adverse events. Eligible studies were limited to original research designs such as randomized controlled trials, cohort studies, and observational studies. Studies were excluded if they were case reports or small case series involving fewer than ten participants, experimental animal or in vitro research, review papers or other non-original publications, investigations where GLP-1 receptor agonists were started before surgery without a clearly defined post-operative initiation period, or studies that did not provide sufficient quantitative data for extraction. Study selection was conducted independently by two reviewers (N.B.S. and L.S.), with disagreements resolved through consensus, and the process was documented using a PRISMA flow diagram. Data extraction was performed using a standardized template capturing study characteristics, surgical procedures, GLP-1 RA regimens, follow-up duration, weight and glycemic outcomes, and adverse events, with preference given to the longest follow-up data when multiple time points were reported.

Methodological quality was assessed using the Newcastle–Ottawa Scale (NOS) for observational studies, evaluating selection, comparability, and outcome domains, with scores of seven or more stars considered high quality(Wells et al, 2000). The single randomized controlled trial included was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool(Sterne et al, 2019). All assessments were conducted independently by both reviewers. Due to significant clinical and methodological heterogeneity across studies—including differences in surgical techniques, pharmacologic agents, dosing regimens, outcome measures, and follow-up duration—formal meta-analysis was not performed. Instead,

findings were synthesized narratively and organized by outcome domains, including weight loss, glycemic outcomes, and safety/tolerability, with comparative interpretation across GLP-1 RA agents (liraglutide, semaglutide, tirzepatide, and dulaglutide). The study selection process is summarized in Figure 1 in accordance with PRISMA 2020 guidelines.

## Result and Discussion

### Study Selection and Characteristics

A systematic search of PubMed/MEDLINE identified 187 records after restricting the publication period to January 2015 through January 2026. After eliminating 19 duplicate entries and screening titles and abstracts, 34 articles were selected for full-text evaluation. Based on predefined eligibility criteria, 11 studies were finally included in this narrative review, representing a total of 873 patients. The main reasons for exclusion were small case reports or case series with fewer than 10 patients, lack of extractable quantitative outcomes, publication as review articles, or initiation of GLP-1 receptor agonist therapy before the post-operative period.

The 11 included studies were published between 2019 and 2025 and encompassed a range of study designs, including one randomized controlled trial(Miras et al, 2019), one open-label extension of the RCT,(2) six retrospective or prospective observational cohort studies,(Colbourne et al, 2023) (Jamal et al, 2024) (Jensen et al, 2025) (Lautenbach et al, 2023) two prospective longitudinal cohorts(Elhag & El Ansari, 2022) (Lautenbach et al, 2023), and one comparative retrospective study(Abdallah et al, 2025). Sample sizes ranged from 29 to 207 patients. Bariatric procedures represented across studies included sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), laparoscopic adjustable gastric banding (LAGB/AGB), and mixed cohorts incorporating more than one procedure type. GLP-1 RA agents studied included liraglutide (1.8 mg and 3.0 mg daily subcutaneous), semaglutide (0.5–2.4 mg weekly subcutaneous), tirzepatide (weekly subcutaneous), and dulaglutide (weekly subcutaneous). Follow-up durations ranged from a minimum of three months to a maximum of twelve months. A summary of all included study characteristics and extracted outcomes is presented in Table 1.

**Table 1.**
Characteristics and outcomes of included studies (n = 11)

| # | Study | N | Surgery | Agent & Dose | Follow-up | Weight Outcome | Glycemic Outcome | Adverse Events |
|---|---|---|---|---|---|---|---|---|
| **1** | Miras et al. 2019 (GRAVITAS RCT) | 80 | RYGB + SG | Liraglutide 1.8 mg/d | 26 wks | −4.2 kg vs placebo (p<0.01) | ΔHbA1c −1.22% (p=0.0001) | GI 45% vs 41% placebo) (no serious AEs |
| **2** | Mok et al. 2023 (BARI-OPTIMISE RCT) | 70 | SG (93%) | Liraglutide 3.0 mg/d | 24 wks | −8.03% TBWL vs placebo (p<0.001) | Favorable cardiometabolic profile | GI 80% vs 57%) (no serious AEs |
| **3** | Murvelashvili et al. 2023 | 207 | SG / RYGB / AGB | Semaglutide vs Liraglutide | 12 mo | Sema −12.92% vs Lira −8.77% (p<0.001)) (OR 2.34 for ≥10% TBWL | Not reported | Not reported |

| # | Study | N | Surgery | Agent & Dose | Follow-up | Weight Outcome | Glycemic Outcome | Adverse Events |
|---|---|---|---|---|---|---|---|---|
| **4** | Jensen et al. 2023 | 50 | Mixed | Liraglutide → Semaglutide (sequential) | 6 mo | −8.8% TBWL) (67.4% regained weight recovered | HbA1c trend improved | No serious AEs |
| **5** | Jensen et al. 2025 | 40 | Mixed | Liraglutide → Semaglutide (sequential) | 12 mo | −11.2% TBWL) (60% achieved ≥10% TBWL | HbA1c improved in T2DM subgroup | No serious AEs |
| **6** | Lautenbach et al. 2022 | 53 | Mixed | Semaglutide 0.5 mg/wk | 6 mo | −10.3% TBWL (p<0.001)) (61% lost >5% | Not reported | Not reported |
| **7** | Lautenbach et al. 2023 | 29 | SG + RYGB | Semaglutide (variable dose) | 12 mo | −14.7% TBWL (p<0.001)) (89.7% >5%) (62.1% >10% | All 6 prediabetes patients achieved normoglycemia | Not reported |
| **8** | Elhag & El Ansari 2022 | 61 | Mixed | Liraglutide (variable dose) | 12 mo | %TWL 5.97% at 6 mo) (6.93% at 12 mo | No cardiometabolic improvement observed | Nausea) (generally well tolerated) (no severe AEs |
| **9** | Jamal et al. 2024 | 115 | SG | Semaglutide vs Tirzepatide | 6 mo | Sema −10.3%) (Tirz −15.5% (p<0.05)) (Tirz > Sema (p<0.02) | Not reported | No severe AEs in either arm |
| **10** | Colbourne et al. 2023 | 68 | LSG / RYGB / LGB | Liraglutide (variable dose) | ≥3 mo | 89.7% lost weight) (22.1% achieved >10% TBWL | Not reported | 41/68 (60.3%) discontinued — primarily due to cost |
| **11** | Abdallah et al. 2025 | 100 | SG (96%) + RYGB (4%) | Semaglutide + Dulaglutide | 12 mo | %TWL 25.5%) (%EWL 66.3%) (BMI −3.7 kg/m² | ΔHbA1c −0.8% | Nausea) (5% treatment discontinuation rate |

*Abbreviations: TBWL = total body weight loss) (TWL = total weight loss) (EWL = excess weight loss) (AE = adverse event) (GI = gastrointestinal) (T2DM = type 2 diabetes mellitus) (RYGB = Roux-en-Y gastric bypass) (SG/LSG = sleeve gastrectomy) (AGB/LGB = adjustable gastric banding) (mo = months) (wks = weeks.*

## Weight Loss Outcomes

### *Liraglutide*

Four studies evaluated liraglutide as adjuvant pharmacotherapy following bariatric surgery. Miras et al. (GRAVITAS, 2019), the only randomized controlled trial in this review, enrolled 80 patients who had undergone either SG or RYGB and randomized them to liraglutide 1.8 mg daily versus placebo for 26 weeks.(1) Liraglutide-treated patients achieved a significantly greater weight reduction of 4.2 kg compared with placebo ($p < 0.01$), representing a clinically meaningful but

modest absolute weight loss attributable to the relatively conservative dose employed(Miras et al, 2019) Mok et al. (BARI-OPTIMISE, 2023) evaluated a higher liraglutide dose of 3.0 mg daily in 70 patients who had predominantly undergone SG (93% of cohort) and demonstrated a substantially greater mean %TBWL of 8.03% compared with placebo at 24 weeks ($p < 0.001$)(Mok et al, 2023). This dose-dependent enhancement in weight loss underscores the importance of agent dosing in the post-bariatric pharmacotherapy context.

Elhag and El Ansari (2022) reported on 61 patients in a real-world observational cohort receiving variable-dose liraglutide, documenting a %TWL of 5.97% at six months, increasing modestly to 6.93% at twelve months. The authors noted that no significant cardiometabolic improvements were observed alongside the weight change, a finding that may reflect differences in patient selection or baseline comorbidity burden(Elhag & El Ansari, 2022).

(Colbourne et al, 2023)evaluated liraglutide in 68 patients across mixed bariatric procedure types (LSG, RYGB, LGB) for a minimum of three months. A notable finding in this real-world study was that 89.7% of patients lost weight during treatment, yet only 22.1% achieved the clinically meaningful threshold of greater than 10% TBWL. Critically, 41 of 68 patients (60.3%) discontinued liraglutide during the study period, predominantly citing medication cost as the primary barrier, highlighting a significant practical limitation of liraglutide use in routine clinical practice.

***Semaglutide***

Five studies reported weight loss outcomes with semaglutide. Lautenbach et al. (2022) evaluated semaglutide 0.5 mg per week in 53 patients with mixed bariatric procedures and demonstrated a mean %TBWL of 10.3% at six months ($p < 0.001$), with 61% of patients achieving greater than 5% total body weight loss(Lautenbach et al, 2023). In their subsequent longitudinal follow-up cohort (2023), the same research group reported outcomes in 29 patients receiving variable-dose semaglutide across SG and RYGB procedures over twelve months, achieving a mean %TBWL of 14.7% ($p < 0.001$). Notably, 89.7% of patients in this cohort achieved greater than 5% TBWL and 62.1% surpassed the 10% threshold, demonstrating that extended duration of semaglutide therapy is associated with progressively greater and more clinically meaningful weight loss(Lautenbach et al, 2023).

Jensen et al. (2023) prospectively evaluated a combined liraglutide-to-semaglutide sequential treatment protocol in 50 patients over six months, reporting a mean %TBWL of 8.8% with 67.4% of regained weight recovered(Jensen et al, 2023). In their extended twelve-month follow-up cohort (2025), 40 patients treated with sequential liraglutide and semaglutide achieved a mean %TBWL of 11.2%, with 60% of patients reaching the clinically significant threshold of 10% or greater TBWL.(5) These two studies collectively support the notion that transitioning to semaglutide following suboptimal response to liraglutide may yield additional weight loss benefit.

Murvelashvili et al. (2023), in the largest comparative study in this review ($n = 207$), conducted a retrospective head-to-head comparison of semaglutide versus liraglutide across SG, RYGB, and adjustable gastric banding (AGB) patients over twelve months. Semaglutide-treated patients achieved a significantly greater mean %TBWL of 12.92% compared with 8.77% in the liraglutide

group ($p < 0.001$).(3) Furthermore, patients receiving semaglutide were 2.34 times more likely to achieve the clinically meaningful threshold of ≥10% TBWL compared with those receiving liraglutide (OR 2.34) ($p < 0.001$), providing robust comparative evidence supporting semaglutide's superior weight loss efficacy over liraglutide in the post-bariatric setting(Murvelashvili et al, 2023).

### *Tirzepatide*

One study directly evaluated tirzepatide in a post-bariatric population. Jamal et al. (2024) conducted a retrospective comparative study in 115 patients who had undergone SG, comparing semaglutide and tirzepatide over six months (Jamal et al, 2024). Tirzepatide demonstrated a mean %TBWL of 15.5%, significantly surpassing the 10.3% TBWL observed in the semaglutide arm ($p < 0.05$), with the between-group difference reaching statistical significance ($p < 0.02$).(9) This finding positions tirzepatide as the most potent GLP-1–based agent evaluated in the post-bariatric surgery literature to date, consistent with the broader anti-obesity pharmacotherapy literature in which tirzepatide's dual GIP/GLP-1 receptor agonism has demonstrated superior weight loss compared with GLP-1 mono-agonists (Jamal et al, 2024).

### *Dulaglutide*

Abdallah et al. (2025) evaluated both semaglutide and dulaglutide in 100 patients predominantly following SG (96%) and RYGB (4%) over twelve months(Abdallah et al, 2025). Patients achieved a mean %TWL of 25.5%, percent excess weight loss (%EWL) of 66.3%, and a BMI reduction of 3.7 kg/m².(11) The substantial %TWL reported in this study likely reflects the combined effect of continued post-operative weight loss trajectory alongside GLP-1 RA pharmacotherapy, as the study included patients at varying post-operative intervals.

### *Summary of Weight Loss Outcomes*

Across all 11 studies, GLP-1 RAs consistently produced clinically meaningful weight loss in post-bariatric patients, with %TBWL ranging from approximately 4.2 kg absolute (liraglutide 1.8 mg at 26 weeks)(Miras et al, 2019) to 15.5% TBWL (tirzepatide at 6 months)(Jamal et al, 2024). A clear agent hierarchy emerged, with tirzepatide demonstrating the greatest weight loss effect, followed by semaglutide, and liraglutide producing the most modest outcomes. Weight loss magnitude was further modulated by dose and treatment duration, with higher doses and longer follow-up consistently associated with greater %TBWL. These findings are summarized in Table 1.

## Glycemic Outcomes

Glycemic data were reported in five of the eleven included studies.(1,2,4,5,11)

The most robust glycemic efficacy data were derived from the GRAVITAS trial (Miras et al, 2019), in which liraglutide 1.8 mg daily produced a mean reduction in HbA1c of 1.22% ($p = 0.0001$) compared with placebo in post-bariatric patients, the majority of whom had persistent or recurrent type 2 diabetes mellitus (T2DM)(Miras et al, 2019). This HbA1c reduction is clinically significant and comparable to that observed with GLP-1 RA use in non-bariatric T2DM populations, suggesting that the glycemic benefit of these agents is preserved following bariatric surgery.

Mok et al. (BARI-OPTIMISE, 2023) reported favorable cardiometabolic improvements in liraglutide 3.0 mg-treated patients at 24 weeks, though granular HbA1c data were not separately reported in their primary publication(Mok et al, 2023).

Jensen et al. (2023 and 2025) reported trends toward HbA1c improvement in both their six- and twelve-month sequential liraglutide-to-semaglutide cohorts, with more pronounced and statistically quantified glycemic benefit specifically in the subgroup of patients with pre-existing T2DM(Jensen et al, 2023, 2025).

Lautenbach et al. (2023) reported normalization of glycemic parameters in all six patients with pre-existing prediabetes in their semaglutide cohort, with all progressing to normoglycemia by twelve months — a finding of potential significance for secondary prevention of T2DM progression in this population(Lautenbach et al, 2023).

Abdallah et al. (2025) reported a mean HbA1c reduction of 0.8% across the combined semaglutide and dulaglutide cohort at twelve months, predominantly in the subset of patients with residual or recurrent T2DM following SG(Abdallah et al, 2025).

Notably, six of the eleven included studies (Colbourne et al, 2023) (Jamal et al, 2024) (Lautenbach et al, 2022) (Murvelashvili et al, 2023)did not report extractable glycemic outcome data, precluding a comprehensive comparative analysis of glycemic efficacy across agents. This represents a meaningful gap in the current evidence base.

## Adverse Events and Safety Profile

Adverse event data were reported in eight of the eleven included studies. Across all agents, the safety profile of GLP-1 RAs in the post-bariatric setting was consistent with that observed in the general obesity pharmacotherapy literature, with gastrointestinal adverse events constituting the predominant adverse effect class.

In the GRAVITAS trial, gastrointestinal adverse events occurred in 45% of liraglutide-treated patients compared with 41% in the placebo group, a non-significant difference suggesting that the post-bariatric gastrointestinal milieu may independently predispose patients to symptoms that partially overlap with GLP-1 RA–related side effects.(1) No serious adverse events were reported in either arm(Miras et al, 2019).

Mok et al. (BARI-OPTIMISE) reported a higher gastrointestinal adverse event rate of 80% in the liraglutide 3.0 mg group compared with 57% in placebo-treated patients, consistent with the dose-dependent gastrointestinal side effect profile of liraglutide.Despite this higher incidence, no serious adverse events were documented and treatment was generally well tolerated(Mok et al, 2023).

Elhag and El Ansari (2022) noted nausea as the most frequently reported adverse event in their liraglutide cohort, characterizing the overall tolerability as acceptable, with no severe adverse events or treatment-related complications reported (Elhag & El Ansari, 2022).

Abdallah et al. (2025) similarly identified nausea as the predominant adverse event across both semaglutide and dulaglutide-treated patients, with a treatment discontinuation rate of 5%

attributable to adverse events — a low rate consistent with the favorable tolerability profiles of weekly GLP-1 RAs.

Jamal et al. (2024) reported no severe adverse events in either the semaglutide or tirzepatide arms of their comparative study, with both agents demonstrating an acceptable safety profile in the post-SG population.

Jensen et al. (2023 and 2025) reported no serious adverse events in either of their sequential liraglutide-to-semaglutide cohorts across six- and twelve-month follow-up periods respectively.

A clinically important real-world safety-adjacent finding was reported by Colbourne et al. (2023), who documented that 41 of 68 patients (60.3%) discontinued liraglutide during the follow-up period, with medication cost identified as the primary reason for discontinuation rather than adverse events per se.(10) This finding underscores that cost-related non-adherence may significantly attenuate the population-level effectiveness of GLP-1 RA therapy following bariatric surgery.

Three studies — Murvelashvili et al, Lautenbach et al. 2022, and Lautenbach et al. 2023 did not report formal adverse event data, limiting the completeness of the safety synthesis for semaglutide across different doses and follow-up durations.

Overall, no cases of severe hypoglycemia, pancreatitis, thyroid pathology, or other serious GLP-1 RA–associated adverse events were reported in any of the eleven included studies, supporting the general safety of adjuvant GLP-1 RA use in the post-bariatric surgical population.

### Risk of Bias Assessment

Methodological quality was variable across the included studies, reflecting the predominantly observational and retrospective nature of the available evidence. The single included RCT (GRAVITAS) demonstrated low risk of bias across most RoB 2 domains. Among observational studies assessed using the Newcastle–Ottawa Scale, studies by Murvelashvili et al, Mok et al, Lautenbach et al, 2023) and (Abdallah et al) were classified as high quality (NOS ≥7 stars), while Jensen et al. and Lautenbach et al. 2022 were rated as moderate quality, primarily due to the absence of a control group and limited control for confounding variables. Colbourne et al. and Elhag & El Ansari were rated moderate quality owing to retrospective design and heterogeneous patient populations. Jamal et al. was rated moderate quality given its retrospective design and absence of randomization.

## Discussion

### Principal Findings

This narrative review synthesized evidence from 11 studies comprising 873 patients and demonstrated that GLP-1 receptor agonists produce clinically meaningful and consistent weight loss when used as adjuvant pharmacotherapy following bariatric surgery. Across all agents and study designs, %TBWL ranged from approximately 4.2 kg with liraglutide 1.8 mg at 26 weeks to 15.5% TBWL with tirzepatide at six months, establishing a clear agent hierarchy in which tirzepatide outperforms semaglutide, which in turn surpasses liraglutide. Glycemic improvements were

documented in five studies and were most pronounced in patients with persistent or recurrent T2DM, while the adverse event profile across all agents was predominantly mild-to-moderate gastrointestinal in nature, with no severe adverse events reported in the majority of studies. These findings collectively position GLP-1 RAs as a viable, effective, and well-tolerated adjuvant strategy in the post-bariatric surgical setting.

## Weight Loss Efficacy in the Context of the Broader Literature

The weight loss outcomes observed in this review are consistent with and supported by the broader pharmacotherapy literature. In the general obesity population without prior bariatric surgery, semaglutide 2.4 mg weekly has been shown to produce a mean %TBWL of approximately 14.9% over 68 weeks in the STEP 1 trial, while tirzepatide at its highest approved dose has demonstrated %TBWL exceeding 20% in the SURMOUNT-1 trial (Moore et al, 2023) (Wharton et al, 2025). Notably, semaglutide 2.4 mg is also the first obesity pharmacotherapy to demonstrate a statistically significant reduction in major adverse cardiovascular events, achieving a 20% reduction in the composite of cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke in obese non-diabetic patients with pre-existing cardiovascular disease in the SELECT trial — a finding with particular relevance to the post-bariatric population, who carry a disproportionate burden of cardiometabolic risk(Lincoff et al, 2023).The weight loss magnitudes observed in the included post-bariatric studies — particularly those employing semaglutide and tirzepatide — approach and in some cases approximate these benchmarks despite the use of lower doses and shorter follow-up durations, suggesting that the post-bariatric physiological context may enhance or preserve the pharmacodynamic efficacy of GLP-1 RA (Çalık Başaran et al, 2025) (Drucker, 2022).

This observation is biologically plausible. Bariatric surgery, particularly RYGB and SG, induces profound neuroendocrine remodeling that includes enhanced postprandial GLP-1 secretion, accelerated gastric emptying, and altered gut microbiota composition. In patients who subsequently experience weight regain, these favorable adaptations may attenuate over time, with diminishing postprandial GLP-1 responses potentially contributing to appetite dysregulation and progressive weight recovery.(The exogenous administration of GLP-1 RAs in this setting may therefore serve to reinstate and amplify the very neuroendocrine signals that underpinned the initial surgical weight loss response, creating a pharmacological-surgical synergy that is mechanistically distinct from GLP-1 RA use in a non-bariatric population. This complementary mechanism rationale is further supported by the finding of Çalık Başaran et al, who demonstrated that lower endogenous postprandial GLP-1 levels were significantly associated with weight regain after metabolic bariatric surgery, directly implicating GLP-1 deficiency as a modifiable mediator of post-operative weight recurrence.

The agent hierarchy identified in this review — tirzepatide > semaglutide > liraglutide — mirrors patterns observed in the broader anti-obesity pharmacotherapy literature and is consistent with the findings of the recent systematic review and meta-analysis by (Tan et al, 2025), which similarly concluded that tirzepatide demonstrated the greatest weight loss among GLP-1–based

agents used post-bariatric surgery, and that semaglutide outperformed liraglutide in achieving both ≥10% and ≥15% TBWL thresholds(Tan et al, 2025). The superiority of tirzepatide is attributable to its dual agonism at both GLP-1 and GIP receptors, with the additive GIP receptor activation providing incremental effects on adipose tissue lipolysis, hypothalamic appetite regulation, and energy expenditure beyond what GLP-1 mono-agonism achieves(Wharton et al, 2025). This superiority has now been directly confirmed in a head-to-head randomized trial: in the SURMOUNT-5 trial, tirzepatide produced significantly greater weight loss than semaglutide 2.4 mg at 72 weeks in adults with obesity without type 2 diabetes, providing the first phase 3 head-to-head evidence that dual GIP/GLP-1 agonism confers a meaningful clinical advantage over GLP-1 mono-agonism in weight reduction(Aronne et al, 2025).

The dose-response relationship observed across liraglutide studies in this review is also noteworthy. The GRAVITAS trial, employing liraglutide 1.8 mg — the diabetes-approved dose rather than the obesity-approved 3.0 mg dose — achieved only 4.2 kg of absolute weight reduction, whereas the BARI-OPTIMISE trial using liraglutide 3.0 mg demonstrated a significantly greater %TBWL of 8.03%. This dose-dependent difference underscores the practical importance of dose selection in the post-bariatric setting and suggests that studies employing sub-maximal doses may underestimate the true weight loss potential of liraglutide in this population.

## Glycemic Outcomes and the Post-Bariatric Diabetic Population

The glycemic outcomes reported across included studies, while incompletely characterized due to the absence of HbA1c data in six of eleven studies, provide important clinical signals. The most robust glycemic efficacy evidence was derived from the GRAVITAS RCT, in which liraglutide 1.8 mg produced a clinically meaningful mean HbA1c reduction of 1.22% compared with placebo ($p = 0.0001$), a magnitude of glycemic improvement comparable to that observed with GLP-1 RAs as monotherapy in non-bariatric T2DM populations. This finding is particularly significant in the context of the well-established phenomenon of T2DM recurrence following initially successful metabolic surgery, which occurs in an estimated 35–50% of patients within five years of the procedure(Noria et al, 2023).

For patients with persistent or recurrent T2DM, GLP-1 RAs offer a pharmacologically elegant solution that simultaneously addresses both weight and glycemic targets without the hypoglycemia risk associated with insulin secretagogues or exogenous insulin — a critical safety consideration in the post-bariatric milieu where altered gastrointestinal anatomy and glycemic variability may amplify hypoglycemia risk(Drucker, 2022) (Miras et al, 2019). The finding by Lautenbach et al. (2023) of complete normalization of glycemic parameters in all patients with prediabetes within twelve months of semaglutide therapy(Lautenbach et al, 2023) further suggests a potentially preventive role for GLP-1 RAs in halting the progression from prediabetes to frank T2DM in the post-bariatric population — a clinically meaningful secondary prevention opportunity that warrants prospective investigation.

The limited glycemic reporting across the majority of included studies represents a significant gap in the current evidence base. Given that glycemic control is one of the primary stated indications

for GLP-1 RA use in this setting, the absence of standardized HbA1c reporting in six of eleven studies substantially limits the ability to draw comprehensive conclusions regarding comparative glycemic efficacy across agents. Future studies should adopt standardized glycemic outcome reporting as a co-primary endpoint rather than a secondary or exploratory measure.

## Safety, Tolerability, and Real-World Considerations

The safety profile of GLP-1 RAs in the post-bariatric setting observed in this review is reassuring and consistent with the established pharmacological class effects of these agents. Gastrointestinal adverse events — predominantly nausea, vomiting, and diarrhea — were the most commonly reported adverse effects across all agents, with rates ranging from approximately 41% to 80% depending on agent, dose, and comparator group. While the 80% gastrointestinal adverse event rate reported in the BARI-OPTIMISE trial(Mok et al, 2023) may initially appear concerning, it should be interpreted in the context that no serious adverse events were documented and treatment discontinuation for tolerability reasons was uncommon. The naturally altered gastrointestinal anatomy and transit following bariatric procedures may independently predispose patients to symptoms that overlap with GLP-1 RA side effects, partially confounding the attribution of gastrointestinal complaints to pharmacotherapy alone, as suggested by the relatively high 41% gastrointestinal adverse event rate in the GRAVITAS placebo arm(Miras et al, 2019).

The absence of severe adverse events — including pancreatitis, thyroid pathology, or severe hypoglycemia — across all eleven included studies is an important safety signal, albeit one that must be interpreted cautiously given the relatively short follow-up durations (predominantly six to twelve months) and modest sample sizes of the included studies. Long-term post-marketing safety data from larger real-world cohorts will be required before definitive safety conclusions can be drawn for this specific post-bariatric population(Moore et al, 2023).

A critically important real-world finding emerging from this review is the high rate of cost-driven treatment discontinuation documented by Colbourne et al, in which 60.3% of patients discontinued liraglutide primarily due to medication cost rather than adverse effects(Colbourne et al, 2023). This observation highlights a dimension of GLP-1 RA pharmacotherapy that extends beyond clinical pharmacology and into health systems and access equity — namely, that the real-world population-level effectiveness of even a clinically effective and well-tolerated agent may be substantially attenuated if it remains financially inaccessible to the patients who need it most. Clinicians selecting adjuvant pharmacotherapy in this setting should therefore consider not only pharmacological efficacy but also long-term accessibility and patient affordability as determinants of sustained clinical benefit.

## Positioning GLP-1 RAs Within the Post-Bariatric Treatment Algorithm

The findings of this review support the positioning of GLP-1 RAs as a first-line pharmacological adjuvant option for post-bariatric patients experiencing inadequate weight loss or weight regain, as an alternative to revisional bariatric surgery. Revisional surgery, while anatomically definitive, carries substantially higher complication and mortality rates than primary bariatric procedures, and

its outcomes in the setting of prior surgical failure are inconsistent(El Ansari & Elhag, 2021). GLP-1 RAs, by contrast, offer a reversible, non-invasive, and pharmacologically titratable approach to managing weight recurrence that can be initiated and adjusted in outpatient settings without the risks and recovery associated with reoperation.(15) As Tan et al. (2025) concluded in their meta-analysis, GLP-1 RAs have emerged as a promising alternative to revisional surgery for patients with insufficient weight loss or weight regain, with tirzepatide representing the most potent currently available option in this class(Tan et al, 2025).

However, the absence of standardized clinical guidelines for GLP-1 RA use in the post-bariatric setting remains a meaningful barrier to consistent clinical practice. No prospective randomized trial has yet directly compared GLP-1 RA therapy to revisional surgery, and the optimal timing of GLP-1 RA initiation relative to the post-operative period has not been established. Similarly, the optimal duration of therapy, strategies for managing treatment discontinuation-related weight regain, and the role of sequential or combination GLP-1 RA regimens remain areas of active investigation(Drucker, 2022).

Agent selection should currently be guided by individualized clinical factors including the magnitude of weight loss required, the presence and severity of T2DM or prediabetes, patient tolerability, dosing convenience, and crucially, medication accessibility and cost. For patients with concomitant T2DM, GLP-1 RAs offer the dual benefit of weight reduction and glycemic control, making them a particularly compelling option in this subgroup(Miras et al, 2019). For patients requiring maximum weight loss efficacy, tirzepatide appears to offer the greatest benefit based on current evidence(Jamal et al, 2024),though its long-term safety and efficacy data in the post-bariatric population specifically remain limited to short-term observational evidence at this time. Semaglutide represents a well-evidenced intermediate option with a growing post-bariatric evidence base and established long-term tolerability data from non-bariatric populations(Jensen et al, 2025) (Lautenbach et al, 2022) (Murvelashvili et al, 2023).

## Conclusion

This narrative review of 11 studies comprising 873 post-bariatric patients demonstrates that GLP-1 receptor agonists are effective and well-tolerated adjuvant pharmacotherapies following bariatric surgery, consistently producing clinically meaningful weight loss across all agents studied and glycemic improvements most pronounced in patients with persistent or recurrent type 2 diabetes mellitus. A clear efficacy hierarchy was identified — tirzepatide > semaglutide > liraglutide — with weight loss magnitude further modulated by agent dose and treatment duration, and the adverse event profile across all agents predominantly limited to mild-to-moderate gastrointestinal symptoms with no severe adverse events reported in the majority of studies. These findings support the integration of GLP-1 RAs, particularly tirzepatide and semaglutide, into the clinical management algorithm for post-bariatric patients experiencing inadequate weight loss or weight regain, as a safe and less invasive alternative to revisional surgery, with individualized agent selection guided by required weight loss magnitude, glycemic comorbidity burden, tolerability, and medication accessibility. However, the current evidence base remains substantially limited by the

predominance of retrospective observational studies, short follow-up durations not exceeding twelve months, heterogeneous outcome reporting, and small sample sizes, underscoring the critical need for prospective multicenter randomized controlled trials with standardized endpoints and longer follow-up to establish definitive evidence-based clinical guidelines for GLP-1 RA use in this population.

**References**

Abdallah, H., Klink, W. H., Derienne, J., Voican, C., Perlemuter, G., Courie, R., & al., et. (2025). Interest in treatment with GLP-1 receptor agonists for the management of insufficient weight loss or weight regain after bariatric surgery. *Obesity Surgery*, *35*(10), 4286–4291.

Aronne, L. J., Horn, D. B., le Roux, C. W., & al., et. (2025). Tirzepatide as compared with semaglutide for the treatment of obesity. *New England Journal of Medicine*, *393*(1), 1–12. https://doi.org/10.1056/NEJMoa2416394

Baethge, C., Goldbeck-Wood, S., & Mertens, S. (2019). SANRA — a scale for the quality assessment of narrative review articles. In *Research Integrity and Peer Review* (Vol. 4, Issue 5). https://doi.org/10.1186/s41073-019-0064-8

Çalık Başaran, N., Dotan, I., & Dicker, D. (2025). Post metabolic bariatric surgery weight regain: the importance of GLP-1 levels. *International Journal of Obesity*, *49*(3), 412–417. https://doi.org/10.1038/s41366-024-01461-2

Colbourne, J. R. M., Fisher, O. M., Mo, S., & al., et. (2023). The role of adjuvant pharmacotherapy with liraglutide for patients with inadequate weight loss following bariatric surgery. *Langenbeck's Archives of Surgery*, *408*(1), 115.

Drucker, D. J. (2022). GLP-1 physiology informs the pharmacotherapy of obesity. *Molecular Metabolism*, *57*, 101351. https://doi.org/10.1016/j.molmet.2021.101351

El Ansari, W., & Elhag, W. (2021). Weight regain and insufficient weight loss after bariatric surgery: definitions, prevalence, mechanisms, predictors, prevention and management strategies, and knowledge gaps — a scoping review. *Obesity Surgery*, *31*(4), 1755–1766. https://doi.org/10.1007/s11695-020-05160-5

Elhag, W., & El Ansari, W. (2022). Effectiveness and safety of liraglutide in managing inadequate weight loss and weight regain after primary and revisional bariatric surgery: anthropometric and cardiometabolic outcomes. *Obesity Surgery*, *32*(4), 1005–1015.

Jamal, M., Alhashemi, M., Dsouza, C., & al., et. (2024). Semaglutide and tirzepatide for the management of weight recurrence after sleeve gastrectomy: a retrospective cohort study. *Obesity Surgery*, *34*(4), 1324–1332.

Jensen, A. B., Machado, U., Renström, F., & al., et. (2025). Efficacy of 12 months therapy with GLP-1 receptor agonists liraglutide and semaglutide on weight regain after

bariatric surgery: a real-world retrospective observational study. BMC Endocrine Disorders, 25(1), 93. https://doi.org/10.1186/s12902-025-01913-4

Jensen, A. B., Renström, F., Aczél, S., & al., et. (2023). Efficacy of the glucagon-like peptide-1 receptor agonists liraglutide and semaglutide for the treatment of weight regain after bariatric surgery: a retrospective observational study. Obesity Surgery, 33(4), 1017-1025. https://doi.org/10.1007/s11695-023-06484-8

Lautenbach, A., Kantowski, T., Wagner, J., & al., et. (2023). Sustained weight loss with semaglutide once weekly in patients without type 2 diabetes and post-bariatric treatment failure. Clinical Obesity, 13(5), e12593. https://doi.org/10.1111/cob.12593

Lautenbach, A., Wernecke, M., Huber, T. B., & al., et. (2022). The potential of semaglutide once-weekly in patients without type 2 diabetes with weight regain or insufficient weight loss after bariatric surgery - a retrospective analysis. Obesity Surgery, 32(10), 3280-3288. https://doi.org/10.1007/s11695-022-06211-9

Lincoff, A. M., Brown-Frandsen, K., Colhoun, H. M., & al., et. (2023). Semaglutide and cardiovascular outcomes in obesity without diabetes. *New England Journal of Medicine*, *389*(24), 2221–2232. https://doi.org/10.1056/NEJMoa2307563

Miras, A. D., Pérez-Pevida, B., Aldhwayan, M., Mok, J., Adeleke, M. O., Brown, A., Murvelashvili, N., Xie, L., Schellinger, J. N., Jensen, A. B., Renström, F., Aczél, S., Jensen, A. B., Machado, U., Renström, F., Lautenbach, A., Wernecke, M., Huber, T. B., Lautenbach, A., … le Roux, C. W. (2019). Adjunctive liraglutide treatment in patients with persistent or recurrent type 2 diabetes after metabolic surgery (GRAVITAS): a randomised, double-blind, placebo-controlled trial . In Lancet Diabetes Endocrinol https://doi.org/10.1016/S2213-8587(19)30157-3

Mok, J., Adeleke, M. O., Brown, A., & al., et. (2023). Safety and efficacy of liraglutide, 3.0 mg, once daily vs placebo in patients with poor weight loss following metabolic surgery: the BARI-OPTIMISE randomized clinical trial. JAMA Surgery, 158(10), 1003-1011. https://doi.org/10.1001/jamasurg.2023.2930

Moore, P. W., Malone, K., VanValkenburg, D., & al., et. (2023). GLP-1 agonists for weight loss: pharmacology and clinical implications. Advances in Therapy, 40(3), 723-742. https://doi.org/10.1007/s12325-022-02394-w https://doi.org/10.1007/s12325-022-02394-w

Murvelashvili, N., Xie, L., Schellinger, J. N., & al., et. (2023). Effectiveness of semaglutide versus liraglutide for treating post-metabolic and bariatric surgery weight

recurrence. Obesity (Silver Spring), 31(5), 1280-1289. https://doi.org/10.1002/oby.23736

Noria, S. F., Shelby, R. D., Atkins, K. D., & al., et. (2023). Weight regain after bariatric surgery: scope of the problem, causes, prevention, and treatment. *Current Diabetes Reports*, *23*(3), 31–42. https://doi.org/10.1007/s11892-023-01498-z

O'Brien, P. E., Hindle, A., Brennan, L., & al., et. (2019). Long-term outcomes after bariatric surgery: a systematic review and meta-analysis of weight loss at 10 or more years for all bariatric procedures and a single-centre review of 20-year outcomes after adjustable gastric banding. Obesity Surgery, 29(1), 3-14. https://doi.org/10.1007/s11695-018-3525-0

Sterne, J. A. C., Savović, J., Page, M. J., & al., et. (2019). RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ, 366, l4898. https://doi.org/10.1136/bmj.l4898

Syn, N. L., Cummings, D. E., Wang, L. Z., & al., et. (2021). Association of metabolic-bariatric surgery with long-term survival in adults with and without diabetes. The Lancet, 397(10287), 1830-1841. https://doi.org/10.1016/S0140-6736(21)00591-2

Tan, Y. W., Shang, M., Davis, S., & Gananadha, S. (2025). GLP-1 receptor agonists as an adjunct to bariatric surgery for weight loss and metabolic outcome improvement: a systematic review and meta-analysis. Langenbeck's Archives of Surgery, 410(1), 295. https://doi.org/10.1007/s00423-025-03831-4

Wells, G. A., Shea, B., O'Connell, D., & al., et. (2000). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa Hospital Research Institute. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

Wharton, S., Blevins, T., Connery, L., & al., et. (2025). Mechanisms of GLP-1 receptor agonist-induced weight loss: a review of central and peripheral pathways in appetite and energy regulation. American Journal of Medicine. https://doi.org/10.1016/j.amjmed.2025.01.014