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Mini Review

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# Tirzepatide (Mounjaro®) For Insufficient Weight Loss and Weight Regain After Bariatric Surgery: A Mini Review

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## Abstract

A substantial proportion of patients undergoing Metabolic/Bariatric Surgery (MBS) experience Insufficient Weight Loss (IWL) or significant Weight Regain (WR), which may reach 20-35% of operated patients and can attenuate the metabolic benefits of surgery and prompt consideration of revisional procedures [1,2]. Anti-obesity medications have therefore emerged as an important adjunct to post-bariatric care. Tirzepatide, a once-weekly dual Glucose-Dependent Insulinotropic Polypeptide (GIP) and Glucagon-Like Peptide-1 (GLP-1) receptor agonist, produces approximately 20% mean weight loss and robust cardiometabolic benefit in non-surgical obesity trials [3]. Emerging observational data suggest that tirzepatide is also effective and generally well tolerated in patients with IWL or WR after Sleeve Gastrectomy (SG) and Roux-En-Y Gastric Bypass (RYGB). A retrospective cohort of 115 patients with weight recurrence after SG showed clinically meaningful weight loss with both semaglutide and tirzepatide and significantly greater Total Weight Loss (TWL) with tirzepatide (~15.5% vs ~10.3% at 6 months) [4]. A separate single-centre series of 21 post-MBS patients with IWL/WR treated with tirzepatide reported ~12% TWL at 6 months, with 76.5% of patients achieving ≥10% weight loss and concurrent improvements in body composition and glycaemia [5]. A recent systematic review and meta-analysis of 964 post-bariatric patients found mean TWL of -13.6% with tirzepatide, numerically greater than with semaglutide [6]. Safety findings in these surgical cohorts mirror those seen in non-surgical obesity, dominated by dose-dependent gastrointestinal adverse events, with few serious events reported. However, current evidence is limited to small, retrospective observational studies with short follow-up, and discontinuation of tirzepatide in non-surgical trials is associated with substantial weight regain [7,8]. Tirzepatide appears to be a promising pharmacologic option for patients with IWL or WR after bariatric surgery, but high-quality prospective and randomized studies are needed to define optimal timing, duration, and long-term safety in this population.

**Keywords:** Tirzepatide, Mounjaro, Zepbound, Weight Regain, Insufficient Weight Loss, Bariatric Surgery, Sleeve Gastrectomy, Roux-En-Y Gastric Bypass, GLP-1, GIP

**Abbreviations:** AOM: Anti-Obesity Medication, FBM: Fat Body Mass, FFM: Fat-Free Mass, GIP: Glucose-Dependent, Insulinotropic Polypeptide, GLP-1: Glucagon-Like Peptide-1, IWL: Insufficient Weight Loss, MBS: Metabolic/Bariatric Surgery, RYGB: Roux-En-Y Gastric Bypass, SG: Sleeve Gastrectomy, T2D: Type 2 Diabetes, TWL: Total Weight Loss, WR: Weight Regain

## Introduction

Metabolic/Bariatric Surgery (MBS) is currently the most effective intervention for achieving substantial and durable weight loss in patients with severe obesity, with associated improvements or remission in type 2 diabetes, hypertension, dyslipidaemia and obstructive sleep apnoea [1]. Nevertheless, up to 20-35% of patients experience clinically significant Weight Regain (WR) after an initial nadir, and a substantial proportion have Insufficient Weight Loss (IWL), commonly defined as <50% excess weight loss [1,2,9]. These patterns may lead to recurrence of comorbidities and are a major indication for revisional surgery [2]. WR/IWL after MBS is multifactorial, involving anatomical factors (e.g. dilated gastric sleeve or pouch, large gastrojejunal anastomosis), behavioural and psychosocial influences, and complex physiological adaptations in appetite, energy expenditure and gut hormones [2,9,10]. Management traditionally centers on re-intensified lifestyle intervention, psychological support and, in selected cases, endoscopic or surgical revision [10]. However, revisional procedures are technically challenging, costly and associated with higher peri-operative risk than primary surgery.

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Over the past decade, Anti-Obesity Medications (AOMs) have emerged as an intermediate step between lifestyle therapy and revisional surgery. GLP-1 receptor agonists (GLP-1 RAs) such as liraglutide 3.0 mg and semaglutide 2.4 mg have demonstrated additional weight loss of around 7-12% TWL in patients with WR/IWL after bariatric surgery [11-14]. Tirzepatide, a dual GIP/GLP-1 receptor agonist, has shown even greater efficacy in non-surgical obesity and is now being used off-label in post-bariatric populations. This mini review summarizes current evidence regarding tirzepatide in patients who have undergone MBS and subsequently present with IWL or WR.

## Materials and Methods

This mini review is a narrative synthesis of published evidence on tirzepatide for patients with IWL or WR after bariatric surgery. A non-systematic literature search of PubMed and major publishers (up to December 2025) was conducted using combinations of the following keywords: "tirzepatide", "Mounjaro", "Zepbound", "bariatric surgery", "sleeve gastrectomy", "gastric bypass", "weight regain", and "insufficient weight loss". Additional relevant articles were identified from reference lists of retrieved papers and recent reviews on post-bariatric pharmacotherapy. Priority was given to original studies specifically evaluating tirzepatide in post-bariatric cohorts, meta-analyses including tirzepatide, and key randomized controlled trials of tirzepatide in non-surgical obesity. Because of the limited number of studies and heterogeneity of designs, no formal meta-analysis was performed.

## Results and Discussion

### Tirzepatide in Non-Surgical Obesity: Rationale for Post-Bariatric Use

Tirzepatide is a once-weekly peptide that acts as an agonist at both the GIP and GLP-1 receptors. In the SURMOUNT-1 trial, which enrolled adults with obesity or overweight without diabetes, tirzepatide at doses of 5, 10 and 15 mg achieved mean weight reductions of approximately -15.0%, -19.5% and -20.9% at 72 weeks, compared with -3.1% in the placebo group [3]. Up to 57% of participants on 15 mg lost ≥20% of their baseline weight [3]. Tirzepatide also improved glycaemic control, blood pressure and lipid profiles.

SURMOUNT-4 further demonstrated the chronic-disease nature of pharmacologic obesity management. After an open-label lead-in with tirzepatide, participants who were randomized to continue tirzepatide maintained or augmented their weight loss, whereas those switched to placebo experienced substantial weight regain and partial reversal of cardiometabolic improvements [7,8]. These robust trial data provide a strong rationale for using tirzepatide as an adjunct in post-bariatric patients who continue to live with obesity. Mechanistically, tirzepatide may enhance the gut-hormone changes already induced by MBS, further suppressing appetite, reducing energy intake, slowing gastric emptying and improving insulin sensitivity.

### Observational Data After Sleeve Gastrectomy

The largest available dataset specifically examining tirzepatide after bariatric surgery comes from Jamal et al., who reported a retrospective cohort of 115 patients with WR after Laparoscopic Sleeve Gastrectomy (LSG) treated in a single bariatric centre [4]. Patients received either semaglutide (n=70) or tirzepatide (n=45) as adjunctive pharmacotherapy. Baseline mean BMI at initiation was approximately 35 kg/m$^2$, and most patients were female. After 6 months of treatment, both groups achieved clinically meaningful weight loss: semaglutide was associated with a mean TWL of 10.3% (±5.9), while tirzepatide yielded a mean TWL of 15.5% (±6.3), a statistically significant difference favouring tirzepatide ($p<0.02$) [4]. No severe treatment-related adverse events were reported, and the side-effect profile was dominated by transient gastrointestinal symptoms. These findings indicate that both semaglutide and tirzepatide are effective pharmacologic strategies for WR after LSG, with tirzepatide providing greater short-term weight loss.

Limitations of this study include its retrospective design, potential selection bias, lack of randomization, absence of standardized dosing/titration and relatively short follow-up. Nonetheless, it provides real-world evidence supporting the use of tirzepatide in this setting.

### Mixed-Procedure Post-Bariatric Cohort

Stoll et al. examined tirzepatide in a mixed cohort of 21 patients who had undergone SG or RYGB and subsequently developed IWL or WR [5]. All patients were free of type 2 diabetes at baseline and received tirzepatide for approximately 6 months. The mean TWL at 6 months was 12.0% ± 3.4%, and the proportions of patients achieving ≥5%, ≥10% and ≥15% weight loss were 100%, 76.5% and 23.5%, respectively [5]. Significant reductions in BMI, waist circumference, body fat percentage and HbA1c were observed, indicating both weight and metabolic benefits. The study also reported that patterns of fat-free mass loss differed between IWL and WR subgroups, suggesting potential phenotype-specific responses. No serious adverse events were noted, and the safety profile appeared consistent with that reported in non-surgical tirzepatide trials [3,7,8]. Although limited by small sample size and retrospective design, this study supports the concept that tirzepatide can provide clinically meaningful additional weight loss across different bariatric procedures.

### Meta-Analytic Evidence

Manyari et al. performed a systematic review and meta-analysis of eight retrospective studies, including a total of 964 post-bariatric patients with recurrent weight gain treated with semaglutide or tirzepatide [6]. Pooled mean TWL was -10.97% (95% CI -13.41 to -8.53) for semaglutide and -13.63% (95% CI -22.59 to -4.67) for tirzepatide [6]. Both agents thus produced clinically relevant additional weight loss, with numerically greater reductions in body weight observed for tirzepatide. The meta-analysis also found improvements in cardiometabolic parameters such as

glycaemia and blood pressure. Heterogeneity among studies and the observational design of all included cohorts were important limitations. Nevertheless, this synthesis reinforces the role of GLP-1-based therapies, including tirzepatide, as effective non-surgical options for managing recurrent weight gain after MBS.

### GLP-1 Receptor Agonists as Precedent Therapy

Prior to tirzepatide, several observational studies demonstrated that GLP-1 RAs can be used successfully for post-bariatric WR or IWL. Jensen et al. found that liraglutide and semaglutide produced additional weight loss in patients with WR after various bariatric procedures [11]. Wharton et al. reported efficacy of liraglutide 3.0 mg for IWL/WR post-surgery [14], and Margvelashvili et al. observed that semaglutide was more effective than liraglutide in this setting [12]. Stanford et al. showed that various weight-loss medications, including GLP-1 RAs, phentermine/topiramate and others, could help treat post-bariatric WR [13]. These data provide the therapeutic context into which tirzepatide has been introduced, suggesting that agents targeting the incretin axis are particularly suitable for patients after bariatric surgery.

### Safety and Tolerability in Post-Bariatric Patients

Across the available post-bariatric tirzepatide studies, adverse events have largely mirrored those seen in the general obesity population [3,6,7,4,5]. The most commonly reported events are gastrointestinal (nausea, vomiting, diarrhoea, constipation, dyspepsia). These are usually mild to moderate in severity and occur mainly during dose escalation. In the Jamal and Stoll cohorts, no increase in surgical complications such as anastomotic problems, strictures or obstruction was reported [4,5]. However, the follow-up periods were relatively short and sample sizes small, so rare events cannot be excluded.

**Specific Considerations in Post-Bariatric Patients Include:**

a. Nutritional Status: Additional weight loss after MBS may increase the risk of micronutrient deficiencies and sarcopenia; adequate protein intake, vitamin/mineral supplementation and resistance exercise should be emphasized [2,10,15].

b. Gastro-Oesophageal Reflux and Dumping Symptoms: GLP-1-based therapies can alter gastric emptying; in some patients they may improve dumping and reactive hypoglycaemia, while in others they may worsen reflux or dyspeptic symptoms.

c. Hypoglycaemia Risk: In patients receiving insulin or insulin secretagogues, particularly RYGB patients, close monitoring and dose reduction of concomitant glucose-lowering agents may be required.

Long-term safety data for tirzepatide in post-bariatric populations are currently lacking. Extrapolation from obesity trials suggests a generally favourable profile, but specific concerns such as gallbladder disease, pancreatitis and thyroid C-cell tumours (as for GLP-1 RAs) should be considered and discussed with patients [3,6,8,15].

### Clinical Positioning and Practical Approach

a. Based on current evidence and expert opinion, tirzepatide can be considered for adults with prior SG or RYGB who:

b. Have IWL (e.g. <50% excess weight loss) or clinically significant WR (e.g. ≥10-15% regain from weight nadir) with persistent obesity-related comorbidities [1,2,9].

c. Have already undergone optimization of lifestyle measures (nutrition, physical activity, behavioural support).

d. Are not immediate candidates for revisional surgery, or prefer pharmacotherapy as a less invasive option.

### A practical Approach Includes:

1. Comprehensive assessment of anatomical, behavioural and psychosocial contributors to WR/IWL, with imaging and endoscopy when structural abnormalities are suspected.

2. Initiation of tirzepatide at the lowest dose (e.g. 2.5 mg once weekly) with careful titration according to tolerability, especially in patients with significant gastrointestinal sensitivity.

3. Regular monitoring of weight, body composition (where possible), glycaemic control, blood pressure, lipids and nutritional status.

4. Long-term management plan, explaining that continued treatment is likely necessary to maintain benefits, analogous to other chronic disease therapies, as suggested by SURMOUNT-4 [7,8].

## Conclusion

IWL and WR after bariatric surgery are common and clinically important phenomena that can attenuate the benefits of MBS and prompt consideration of revisional surgery. Anti-obesity pharmacotherapy has emerged as an important adjunct in this setting. Tirzepatide, a dual GIP/GLP-1 receptor agonist, has shown unprecedented weight-loss efficacy in non-surgical obesity trials and is now supported by early real-world evidence in post-bariatric patients. Retrospective cohorts and a recent meta-analysis suggest that tirzepatide can achieve approximately 12-16% additional TWL over 6 months in patients with IWL or WR after SG or RYGB, with a safety profile similar to that observed in non-surgical trials [6,3,5]. These findings position tirzepatide as a promising pharmacologic option that may delay or reduce the need for revisional surgery in selected patients. However, current evidence is limited by small sample sizes, retrospective design and short follow-up. Randomized controlled trials and longer-term observational studies are needed to define optimal timing, duration and combination strategies (with other AOMs or revisional procedures), as well as to clarify the effects of tirzepatide on nutritional status, bone health and quality of life in post-bariatric populations. Until such data are available, tirzepatide should be used as part of a multidisciplinary, long-term obesity management strategy, with careful attention to nutritional

monitoring, gastrointestinal symptoms and patient education regarding the chronic nature of pharmacotherapy.

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## Conflict of Interest

The author(s) declare no conflict of interest related to this manuscript.

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