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# Weight Regain and Insufficient Weight Loss after Bariatric Surgery: A Call for Action

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## Abstract

Despite successful weight loss after bariatric surgery (BS), weight regain (WR) may occur on long term following most bariatric procedures, with 20–30% of patients either failing to reach their target weight goals or failing to maintain the achieved weight loss. Significant WR has important health consequences, including the reversal of the improved obesity-related comorbidities and psychological function leading to decreased quality of life. Given the challenges faced by these patients, there is a need for multidisciplinary approaches to deal with WR. This chapter addresses the issue of WR among bariatric patients. It starts with the various definitions of insufficient weight loss and WR and the prevalence of weight regain by type of bariatric procedure. The chapter then explores the underlying causes as well as the predictors of WR. It will also outline the behavioral and psychotherapeutic, dietary and exercise strategies employed in the prevention of post-surgery WR. The chapter will then highlight the non-surgical and surgical approaches used in the management of WR. The chapter will conclude with a summary of the findings emphasizing that WR is complex and multifactorial, requiring multidisciplinary and multimodal dietary, behavioral, pharmacological, and surgical management strategies tailored to meet the individual needs of each patient.

**Keywords:** bariatric surgery, weight regain, insufficient weight loss, causes, predictors, management

## 1. Introduction

Bariatric surgery (BS) can achieve weight loss (WL), treat obesity-related metabolic disease and enhance the metabolic status by improving hypertension, type 2 diabetes mellitus (T2DM) and lipid profile, thereby decreasing the cardiovascular risk [1, 2]. Despite effective WL after BS, some patients do not achieve their target weight goals, and others regain a significant portion of their weight at long-term follow-up. Weight regain (WR) has a range of undesirable medical and psychological impacts [3, 4].

WR might occur after common BS procedures e.g. gastric bypass, adjustable gastric banding (LAGB), and sleeve gastrectomy (LSG), to different extents and at variable interval times [5]. The causes for WR are multifactorial, including patient- and procedure-specific factors [6, 7]. Interestingly, WR might occur despite the

patients' stated adherence to advised behavioral measures and absence of surgical anatomic causes. This suggests that various pre or post-operative demographic, physiologic or metabolic features could play a role. Given the complexity of the factors involved in WR, multimodal management strategies tailored to meet the individual needs of patients are essential.

## **2. Definitions of insufficient weight loss and weight regain**

There is a distinction between two types of WL failure post BS: insufficient WL (IWL); and WR. The grouping of these two categories together should be discouraged. IWL is defined as excess weight loss (EWL%) of <50% at 18 months after BS [8], while WR is defined as regain of weight that occurs after achievement of an initial successful weight loss (defined as EWL% > 50%).

A range of definitions describe WR post BS [9, 10]. The lack of standard definition, consensus statements and guidelines leads to poor reporting and understanding of the significance of WR [3, 8, 10]. Moreover, clearer definitions will help to recognize when intervention is required and guide the intervention [8]. Available definitions include: regaining weight reaching a body mass index (BMI) >35 after successful WL [11]; an increase in BMI of  $\geq 5 \text{ kg/m}^2$  above the nadir weight [12]; > 25% EWL% regain from nadir [13, 14]; increase in weight of >10 kg from nadir [15, 16]; any WR [17]; any WR after type 2 diabetes mellitus (T2DM) remission [18]; or an increase of >15% of total body weight from nadir [19, 20]. The most common definition, an increase of  $\geq 10 \text{ kg}$  of nadir weight [15, 21], does little to define the clinical significance of the amount of WR in the affected individual. Therefore, a WR definition needs to be meaningful rather than arbitrary. It is important to note that multiple definitions affect the reporting of the prevalence of WR, and considerably change the reported outcomes. For instance, applying 6 different WR definitions to 55 patients 5 years after LSG led to WR rates ranging from 9–91% [10]. Similarly, the use of 5 continuous and 8 dichotomous measures among 1406 Roux en Y gastric bypass (RYGB) patients followed up for 5 years resulted in WR rates ranging from 44–87% [9]; and others reported rates between 16–37% WR 5 years post LAGB, LSG, and RYGB [19]. Therefore, more research is needed to define WR after BS in order to standardize its measurement.

## **3. Prevalence of WR and IWL after bariatric procedures**

WR following BS varies by the type of BS performed, whether restrictive or malabsorptive as outlined below.

### **3.1 Laparoscopic gastric band (LAGB)**

A large prospective multicenter study in Sweden found that 10 years post LAGB, patients regained 38% of the maximal weight they lost post surgery [1]. Likewise, research at 10 US hospitals that assessed weight trajectories among 2348 participants including 610 LAGB patients reported 1.4% WR 3 to 7 years after surgery [22] (**Table 1**).

### **3.2 Laparoscopic sleeve gastrectomy (LSG)**

A systematic review of 21 studies reported WR rates post LSG ranging from 5.7% at 2 years to 76% over variable follow-up periods from (2 to 6 years) [3].

Type of BS	Prevalence of WR
LAGB	1.4% between years 3 and 7 years [22] 38% at 10 years [1]
LSG	5.7% at 2 years [3] 39.5% at 5 years [23] 76% over variable follow-up periods ranging from 2 to 6 years [3]
RYGB	17.1% at 2 years [24] 22.5% at 3 years [9] 14.6%–26.8% at 5 years [9, 25] 3.9% between 3 and 7 years [22]

*LAGB: Laparoscopic gastric band; LSG: Laparoscopic sleeve gastrectomy; RYGB: Roux en Y gastric bypass.*

**Table 1.**  
Prevalence of WR by type of BS.

Other studies found that WR started three years after LSG [23]. At 5 years, WR (>10 kg) was observed in 39.5% of patients, where the EWL% decreased from 84.8% at one year to 57.3% after 5 years [23].

### 3.3 Roux en Y gastric bypass (RYGB)

Research among 1426 patients found that at 2 years, 17.1% regained >15% of their 1-year post-operative weight [24]. Others reported a 22.5% WR at 3 years and 26.8% at 5 years [9]. The Longitudinal Assessment of Bariatric Surgery (LABS) study observed 3.9% WR between 3 and 7 years post RYGB [22]. Others found that among 2965 patients, WR was 14.6% at 5 years post-surgery [25].

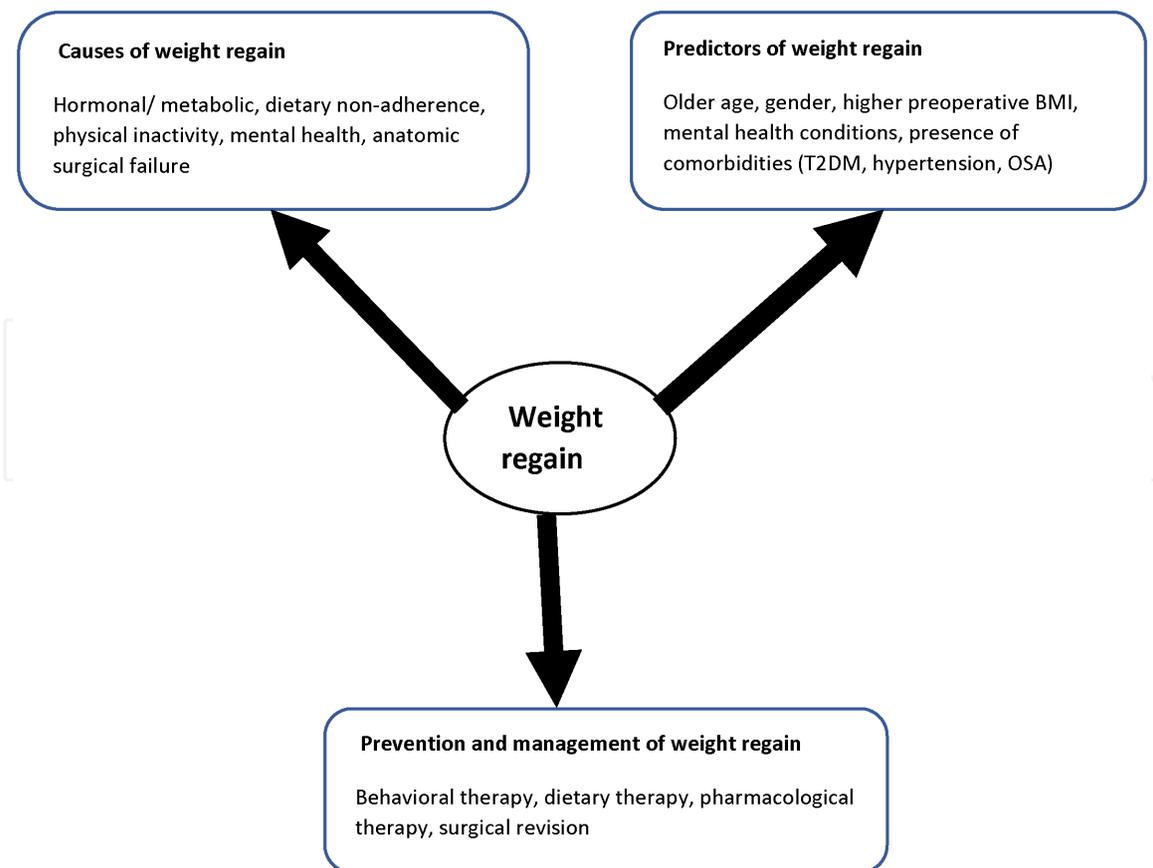
## 4. Causes of WR

Causes of WR following BS are multifactorial, and can be categorized into patient- and surgical-specific causes. The former includes hormonal causes and maladaptive lifestyle behaviors (e.g. dietary non-compliance and physical inactivity) [3, 7]. Other factors include the lack of follow-up support and mental health causes such as psychiatric conditions and maladaptive eating [3, 7]. Surgical-specific factors include e.g., enlargement of the gastric pouch or gastro-gastric fistula. Recognizing such underlying etiologies is key to develop appropriate management strategies [26]. **Figure 1** depicts the causes of WR.

### 4.1 Hormonal

Weight reduction following BS may be dependent to some extent on the ‘normalization’ of hormonal inputs. Furthermore, patients who fail to achieve WL post-BS or experience WR may have persistent hormonal ‘imbalances’ (e.g. high ghrelin, low peptide YY) which need to be addressed in order to accomplish WL.

Ghrelin is a hormone that is important in regulating food intake and energy balance. BS has a positive effect on ghrelin, where a significant decrease in both fasting and post prandial ghrelin is observed early after BS leading to decreased appetite and food intake [27]. However, research have found that among RYGB patients, subjects with WR had significantly higher pre and postoperative ghrelin levels compared to those who maintained or lost weight ( $722 \pm 29$  vs.  $540 \pm 156$  pg/ml) [28]. Similarly, patients with WR 5 years post LSG had higher plasma ghrelin levels than their level at 1 year post surgery [16].



**Figure 1.** Summary of the causes, predictors and prevention and management strategies of weight regain.

Peptide YY (PYY) is a 36 amino acid hormone that is released by the L-cells of the gastrointestinal tract after food intake to suppress appetite. Likewise, Glucagon-like protein-1 (GLP-1) is released after meals by L cells in the small intestine to stimulate insulin secretion, inhibit glucagon release, and delay gastric emptying [29]. Both these anorexigenic hormones display enhanced nutrient-stimulated secretion after BS, more so after RYGB than LSG [29]. However, the level of these hormones was noticed to be lower in patients with WR. For instance, meal-stimulated gastric inhibitory polypeptide and glucagon-like peptide-1 (GLP-1) levels at 30 min were lower in 10 patients who had WR compared with 14 patients who successfully maintained WL post RYGB [30]. Whilst hormonal adaptation as a biological response to non-surgical WL has been examined [31], its influence on WR post BS is less documented in humans. For example, rodent studies showed that postsurgical WR was associated with failure to maintain elevated plasma PYY concentrations [32].

#### 4.2 Nutritional non-adherence

Immediately following BS, caloric intake is reduced due to a smaller gastric capacity, diminished hunger, and increased satiety brought about by the anatomical and metabolic changes. Nevertheless, for some patients, caloric intake gradually increases over time which contributes to postoperative WR. In the Swedish Obesity Study, mean daily intakes of 2900, 1500, 1700, 1800, 1900, and 2000 kcal/day were observed at baseline, 6 months, 12 months, 2 years, 3 years, and 4–10 years postsurgery respectively [1]. Such increase in food intake often begins in the second post-operative year, likely causing WR [1]. In addition, dietary non-adherence and the consumption of high-calorie foods and beverages contribute to the higher caloric intake leading to WR. A postoperative behavioral survey of 203 patients observed

positive correlations between the magnitude of WR and evening or night consumption of large quantities of food, eating large amounts of high-fat foods, and eating out more frequently [33]. Equally, among 289 RYGB patients, 23% demonstrated dietary non-adherence and a continuation of pre-surgical eating patterns, leading to suboptimal weight loss and WR [34]. Such evidence substantiate the importance of diet quality and caloric intake as causative factors for WR after BS, and also highlight the importance of measuring and documenting the diet quality after BS [35].

Grazing behavior is the repeated episodes of consumption of smaller quantities of food over a long period of time accompanied by feelings of loss of control [36]. Those engaging in grazing nibbled continuously  $\geq 2$  days per week for a 6-month period, with an inability to stop or control their eating while nibbling [36]. Grazing contributes to poor weight outcomes post BS [37]. Although grazing and binge eating are similar as they involve subjective episodes of food consumption accompanied by a loss of control; however, grazing is physiologically more possible post BS than large binges. In 80% of patients with preoperative binge eating or grazing with loss of control, these behaviors returned 6 months post-surgery [36]. This suggests that preoperative binge eating may reemerge as postsurgical grazing in the context of a reduced stomach capacity [36].

Food indiscretion also contributed to WR. For instance, the follow up of 100 patients for 85 months after surgery revealed that poor dietary habits including consumption of excessive calories, snacks, sweets oils and fatty foods were statistically higher in WR patients [6]. This highlights the importance of appropriate nutritional counselling for long-term weight maintenance. Lack of appropriate nutritional follow-up was also significantly associated with WR post BS [6]. For example, studies have found that among those with WR post-RYGB, 60% never maintained follow-up with appropriate nutritional consultants [38].

### **4.3 Physical Inactivity**

Inadequate physical activity contributes to WR. Only 10–24% of BS patients met the guidelines regarding minimal physical activity for health promotion (i.e.,  $\geq 150$  min/week or moderate-to-vigorous physical activity in bouts of  $\geq 10$  min) [39]. A meta-analysis of 14 studies and a literature review of 19 studies concluded that post-BS physical activity was significantly associated with greater WL [40]. Amongst 100 obese patients post-RYGB, those who performed physical activity had the lowest incidence of WR compared to those who were relatively inactive [6]. Barriers to exercise among bariatric patients such as health concerns, lack of proximity to a gym/park, or feeling self-conscious should be identified and addressed [40]. Such findings highlight the importance of measuring and documenting physical activity levels after BS [35].

Similarly, sedentary behavior, defined as 'any waking behavior performed while in a sitting or reclining posture that requires very low energy expenditure'. The represents a risk factor for WR Sedentary behavior is associated with increased risk of obesity and related comorbidities [40]. Research have found that severely obese BS candidates are at high risk for SB [41]. In this study they found that BS candidates spent about 30% of their sedentary time watching television, suggesting that this is an important cause of sedentary behavior and should be a target for patient counseling [41].

### **4.4 Mental health**

Mental health status prior to surgery is linked to WL following BS. Therefore, pre-operative psychological evaluation is important. Psychological factors might interfere with successful WL by undermining motivation, diet and exercise compliance, and other health behaviors critical to maintaining WL [42]. Among

60 adults who underwent RYGB or LAGB, 40% and 33.4% had single or multiple psychiatric diagnoses respectively, 47.5% stopped losing weight after 1 year, and 29.5% regained weight [43]. Furthermore, patients with  $\geq 2$  psychiatric conditions were 6 times more likely to either stop losing weight or regain weight relative to those with no or single psychiatric diagnosis [43]. Evidence supports the association between post-operative depressive disorders and poorer WL; however, the directionality of the relationship remains unknown [44]. More research is required to assess the long-term associations and directionality of depression and weight loss post BS.

#### **4.5 Maladaptive eating: Binge eating (BE) disorder**

Maladaptive eating patterns after BS have impact on weight and psychological outcomes [45]. One of these abnormal eating patterns is BE disorder which is defined as 'the consumption of large quantities of food during a short amount of time without being in control of this behavior', and is strongly associated with psychological distress [26]. BE disorder predicts poorer weight outcomes post BS, resulting in smaller BMI reductions as well as more WR [46, 47]. Despite the physical limitations of BS on stomach capacity, BE is not always abolished and many of those who had BE before BS still had feelings of loss of control when eating even small amounts of food post BS [37, 47]. Following RYGB, patients who regained  $>10\%$  of their EWL% had significantly higher frequencies of BE and loss of control [46], and these maladaptive eating behaviors were significantly correlated with greater WR [46]. Follow up of 96 patients post RYGB two to seven years after surgery showed that binge eaters increased their BMI by  $5.3 \text{ kg/m}^2$  compared with  $2.4 \text{ kg/m}^2$  increase in non-binge eaters [48]. Likewise, among LAGB patients, the prevalence of eating disorder increased from 26.3% to 38.0% over one year post surgery, an increase that correlated with poorer WL outcomes [37].

#### **4.6 Anatomic surgical failure**

Each type of BS has its own potential mechanism/s of surgical failure that can lead to WR as outlined below.

##### *4.6.1 Laparoscopic gastric band*

LAGB success is correlated with appropriate follow-up, as saline adjustment of the band is essential for proper restriction and WL. Therefore, it is important to assess patients with WR after LAGB for potential pouch distension. Pouch distension is managed conservatively by complete band deflation, low calorie diet, reinforcement of portion size, and follow-up contrast study in 4–6 weeks, with success in more than 70% of patients [49]. On the other hand, premature removal of LAGB also causes WR. Studies have found that only 12% of patients with early band removal maintained their current weight [50]. Long term, LAGB removal rate is high, reaching 12% [51]. Moreover, after 14 years, the reoperation rate was as high as 30.5% with an average reoperation rate of 2.2% for every year of follow-up [51]. The main reason for LAGB removal was intolerance secondary to increased reflux type symptoms [52].

##### *4.6.2 Laparoscopic sleeve gastrectomy*

There are surgical causes of WR post LSG. The gastric sleeve may dilate over time leading to reduced restrictive effect and increase in gastric capacity, both

associated with reduced satiety response and increased food intake resulting in WR [23]. For instance, among the 15.7% patients who had WR, CT scan volumetry showed that the mean gastric volume increased from 120 mL early after surgery to a mean of 240 mL at 3 years and to 524 mL at 5 years follow-up [23]. Several theories have been proposed as to the relationship of increased gastric volume and WR. One theory is that the physiologic dilation of the remnant stomach over time and the size of the gastric sleeve are linearly correlated with post-operative BMI [53, 54]. Another theory is the incomplete removal of the gastric fundus [55, 56], where in many cases, the dissection over the fundus, especially on the posterior aspect, may be difficult and technically demanding, notably in patients with the extreme obesity. Therefore, the success of LSG depends on the surgeon's learning curve [55].

#### 4.6.3 Roux-en-Y gastric bypass

RYGB produces WL through restriction of intake and malabsorption. In assessing WR post-RYGB, anatomical abnormalities are proposed to play a role. Dilatation of the gastric pouch or gastrojejunostomy (GJ) stoma outlet have been associated with loss of satiety with subsequent increase in food intake and WR [57, 58]. Among 205 RYGB patients who had upper endoscopy as workup for WR, dilation of the GJ was identified in 58.9%, enlarged gastric pouch in 28.8%, and both abnormalities in 12.3% of patients [57]. Multivariate analysis found that stoma diameter (>2 cm) was independently associated with WR [58], where among 28 patients following RYGB, WR was associated with dilated gastric stoma [59]. In this group, successful reduction in anastomotic size (<12 mm) with a sclerotic agent resulted in a mean 26-kg WL at 18 months [59].

Another anatomic change that reduces RYGB'S effectiveness is gastro-gastric fistula, an abnormal communication between the gastric pouch and the excluded stomach. This is thought to develop as a result of the breakdown of the surgical staple line. Although gastro-gastric fistulas are uncommon, with a 1.5–6% incidence rate [60]. Gastro-gastric fistulas have potentially significant effects as a complication after RYGB [60] as they may diminish the restrictive and malabsorptive components of RYGB leading WR [61].

## 5. Predictors of WR post BS

Knowledge of the preoperative predictors of WR post-BS can assist in identifying patients at risk for WR. The bariatric team can then offer such patients appropriate resources and counseling. **Figure 1** depicts the predictors of WR.

### 5.1 Age

Age seems to be a predictor of WR, however, findings are inconsistent. Some smaller studies identified older age as a potential preoperative predictor of WR [62, 63]. Among 227 patients who underwent RYGB, older age (>60 years) predicted inadequate EWL% at 12 months [62]. While others found that younger individuals were more likely to have WR after RYGB [24].

### 5.2 Gender

Among post RYGB patients, male sex was associated with a worse weight trajectory [22] and suboptimal WL at 1 year after surgery [64]. Others found no effect of gender on weight loss outcomes [62].

### **5.3 Duration since surgery**

Longer duration after BS predicted WR [24]. One study reported significant longer time since RYGB surgery in patients with WR (6 years) compared with patients who sustained their weight loss (3.3 years) [24]. Longer durations after surgery are probably associated with resolution of food intolerances, return to preoperative eating and other lifestyle patterns, anatomic surgical failure, or poor attendance of postoperative appointments [7, 65].

### **5.4 Preoperative BMI**

Greater preoperative BMI was significantly associated with IWL [64]. A meta-analysis found that preoperative BMI and super-obesity were negatively associated with WL, where super-obese patients had 10.1 EWL% decrease [66]. Others observed that at 12 months post RYGB or LAGB, patients with baseline BMI  $\geq 50$  kg/m<sup>2</sup> were more likely to have significant WR, but those with BMI  $< 50$  kg/m<sup>2</sup> were likely to continue losing weight [67]. Similarly, 80–100% of LSG patients with pre-surgery BMI  $> 40$  kg/m<sup>2</sup> had WR to BMI  $> 30$  kg/m<sup>2</sup> two years after surgery; but only 3.6–38% of patients with lower pre-operative BMI (32.1–39.9 kg/m<sup>2</sup>) had BMI  $> 30$  kg/m<sup>2</sup> during the same time period [68].

### **5.5 Mental health**

A presurgical BE disorder diagnosis predicted higher BMI. For example, studies found that among post-RYGB patients with 28.1 months mean follow-up, 79% reported WR and 15% regained  $\geq 15\%$  of their total weight loss [65]. The independent predictors of significant WR were lack of control of food urges (odds ratio, OR = 5.1), alcohol/drug use (OR = 12.74), lowest self-reported well-being scores (OR = 21.5), and lack of follow-up visits [65].

### **5.6 Presence of Comorbidities**

Presence of T2DM predicts WR [22, 62, 63]. An assessment of 2348 bariatric participants in the Longitudinal Assessment of Bariatric Surgery (LABS) Study found that low HDL cholesterol and hypertension were also associated with an inferior weight trajectory [22].

## **6. Implications of weight regain**

WR has important health consequences including recurrence of obesity related co-morbidities such as T2DM and deterioration in quality of life (QoL), thus contributing to socioeconomic and direct health care costs. This range of implications of WR is highlighted below.

### **6.1 Relapse of comorbidities**

WR following BS is associated with and significantly predicted relapse of T2DM [12, 70]. At 10 year follow up, T2DM relapse was dependent on the extent of WR [70]. Patients with no WR had no relapse of their diabetes [70]. While, patients with mild regain (increase body weight  $> 5$  kg from nadir) and severe regain ( $> 10$  kg from nadir) had 5% and 17% relapse rates respectively [70]. Among 1406 RYGB patients with WR during the first year after reaching nadir weight, 25.8% and

46.2% of participants experienced progression of hyperlipidemia and hypertension respectively [9].

## 6.2 Quality of life

WR is significantly associated with deterioration in QoL [3, 9]. A study found that WR at 5 years after LSG was associated with a lower odds of satisfaction with surgery as measured by the Bariatric Analysis Reporting Outcome System (BAROS) score (incorporates weight loss, changes in medical conditions, health-related QoL, and reoperations) [3]. Others reported declines of physical and mental health-related QoL among 20.2% and 27.7% of patients with WR respectively [9]. Moreover, satisfaction with surgery also declined among 12.4% of patients with WR [9]. This decline was observed when the rate of WR was the highest, supporting a dose-response relationship (i.e., the less WR, the better) for physical health-related QoL [9].

## 7. Prevention of weight regain

**Figure 1** summarizes the prevention strategies of WR. The foundation of prevention of WR after BS is aggressive behavioral interventions, similar to those utilized for medical weight management patients [33]. Behavioral modification components include commitment to regular structured physical activity, dietary control, nutritional optimization with substantive changes in eating practices and lifestyle habits [33, 71]. Other modulators include stress management, realistic goal setting, environmental control strategies, support systems, and cognitive restructuring [33, 71]. Close regular follow-up should start shortly after BS to reinforce nutritional and lifestyle instructions provided at discharge. Monitoring, education, and support should continue on the long term as the effectiveness of behavioral changes diminishes with time [33]. Self-monitoring with regular weight measurement, food records, and exercise diaries are essential tools for avoiding WR. These strategies increase patient's awareness of eating patterns, and allow the bariatric dietitian to identify high-risk areas, such as nutritional inadequacy, food intolerances, poor food choices, or food dislikes that compromise weight loss and nutritional status [72]. In-person dietary counseling by a registered dietitian has an important role in prevention of WR post BS [73]. Structured physical activity is vital for weight prevention. An RCT demonstrated that a 5-month supervised exercise program post LSG resulted in reduction total body weight (TBW) and waist circumference with an increase in EWL% compared with the control group [74]. Conversely, stopping of the exercise program led to weight regain, with increased fat mass and decreased EWL% [74].

## 8. Management of WR

**Figure 1** illustrates the management strategies of WR. WR after BS is complex and multifactorial [7]. Hence, management requires a holistic strategy addressing patient- and surgery-related factors that might contribute to WR. Dietary patterns, psychological disorders and physical activity levels should all be reviewed, as diet (25.3%), physical activity (21%) and motivational issues (19.7%) were the most common reasons among patients with WR [75]. Patients seeking BS often present with a range of mental health issues including mood, anxiety, addiction and personality disorders [7, 26]. Diagnosis and management of these conditions may improve outcomes following BS. As the patient undergoes psychological, dietary and physical activity counselling, it is critical to address the hormonal causes, and any

anatomic/post-surgical changes that cause WR. Baseline anatomic studies include esophagogastroduodenoscopy or an upper gastrointestinal contrast to evaluate the GI tract [76]. These modalities provide essential data about the gastric remnant size, size of the gastrojejunal anastomosis, presence of gastro-gastric fistula, and location/integrity of the bands. Available treatment options include behavior interventions, WL-approved medications, endoscopic interventions and revision surgery to counter some of the factors that resulted in WR.

### **8.1 Behavioral**

Psychological and behavioral factors that have negative impact on long term WL outcomes include life stressors that derail weight maintenance and decreased adherence to the recommended postoperative diet. This is likely due to lack of psychological skills to engage in long term healthy eating behaviors. This is particularly important as the effects of surgery on appetite, hunger, and desire for food decrease. The aim is to address such challenges by behavioral therapy that is tailored to each patient's need [77, 78]. Many patients with WR are lost to follow up; therefore, open, non-judgmental strategies that support the actions that patients are doing well are critical to motivate and involve patients in management [76].

A 6-week intervention of cognitive and dialectical behavior therapies among 29 RYGB patients (93% female) with WR of 37% of the initial WL, found that treatment completers had  $1.6 \pm 2.38$  kg mean weight decrease compared with non-completers [79]. Moreover, patients who completed behavior therapy treatment had improvement in their depressive symptoms with decreased grazing patterns ( $p \leq 0.01$ ), as well as subjective binge eating episodes ( $p \leq 0.03$ ) compared to non-completers [79]. Likewise, a 10-week behavioral intervention of psychological skills to mitigate WR among 11 patients after BS was feasible, acceptable (72% retention), and with high satisfaction among completers (4.25 out of 5.00) [80]. WR was stopped or reversed, with a mean  $3.58 \pm 3.02\%$  total body WL% [80]. Similarly, the use of acceptance-based strategies and online or phone intervention delivery modes to enhance outcomes and reach more patients showed feasibility, acceptability (70% retention), efficacy, high satisfaction score of (4.7 out of 5.0), and reversal of WR with a mean  $5.1 \pm 5.5\%$  total WL% at 3-month follow-up [81].

### **8.2 Dietary**

Structured dietary interventions assist patients to improve WL. A randomized controlled trial (RCT) assigned post RYGB patients into two groups: a structured dietary intervention incorporating portion-controlled foods vs. a control group [77]. Both groups received behavioral WL instructions (one 60-min session followed by 4 coaching telephone calls at monthly intervals). The intervention group had significantly reduced calorie intake at 4 months ( $-108$  vs.  $116$  Kcal) and increased WL% at 4 and 6 months compared to the control group ( $-4.56\%$  vs.  $-0.13\%$ ,  $-4.07\%$  vs.  $-0.14\%$ , respectively) [77]. Another 16-week RCT among women who regained  $\geq 5\%$  of their lowest post-RYGB weight found that whey protein supplementation promoted WL and fat mass loss, with preserved muscle mass, compared to controls who gained weight (0.42 kg) and fat mass [82].

### **8.3 Pharmacological**

Prior to 2012, the only FDA-approved WL drugs were orlistat, a modestly effective pancreatic lipase inhibitor with some side effects and phentermine, a sympathomimetic appetite suppressant approved for short-term use [83]. Since 2012, 4

other WL medications were approved [83]: phentermine-topiramate, bupropion hydrochloride-naltrexone hydrochloride, liraglutide and lorcaserin hydrochloride (withdrawn due to cancer risk [84]). Since then, anti-obesity medications have been increasingly used to manage WR post-BS. In an assessment of anti-obesity medications for WR/IWL among 319 patients (258 RYGB, 61 LSG), 54% lost  $\geq 5\%$  of their TBW, with many high responders (30.3% of patients lost  $\geq 10\%$ , and 15% lost  $\geq 15\%$  of their TBW) [85]. Of the 14 FDA approved and off-label anti-obesity medications, only topiramate showed statistically significant WL, where patients were 1.9 times more likely to lose  $\geq 10\%$  of their TBW [85]. Regardless of the postoperative BMI, RYGB patients were significantly more likely to lose  $\geq 5\%$  of their TBW with anti-obesity medications [85]. Another study of individual and combined anti-obesity medications for WR post RYGB reported that patients who received medications achieved significantly more WL compared to those not using anti-obesity medications [86]. Additionally, there was slower overall WR in the anti-obesity medications group during long term (11 year) follow up [86].

Among young adults post RYGB and LSG, topiramate, phentermine, and/or metformin led to 54.1%, 34.3% and 22.9% of patients losing  $\geq 5\%$ ,  $\geq 10\%$  and  $\geq 15\%$ , of their weight respectively [87]. Again, RYGB had higher median WL% than LSG ( $-8.1\%$  vs.  $-3.3\%$ ), with no differences whether the anti-obesity medications were started at weight plateau or after WR [87]. In another study, phentermine was compared to phentermine-topiramate combination among RYGB or LAGB patients with WR and WL plateau [88]. The study showed that phentermine and phentermine-topiramate patients lost 6.35 kg (12.8% EWL%) and 3.81 kg (12.9% EWL%) respectively at 90 days post treatment [88].

Liraglutide, a GLP-1 analogue with central and peripheral actions, inhibits glucagon secretion, increases insulin secretion, decreases the gastric emptying rate, and promotes satiety [89]. In a recently published study, among 117 patients with WR after RYGB, LAGB and LSG, the use of liraglutide 3 mg over a 7 month period resulted in statistically significant WL ( $-6.3 \pm 7.7$  kg,  $P < .05$ ) compared to baseline regardless of the type of surgery [90]. Moreover, the decrease in weight remained significant even after one year of liraglutide use [30]. In this study, nausea was the most prevalent side effect (29.1% patients) [90].

## 8.4 Surgical

Revision of a previous BS are carried out due to surgical complications e.g., development of intractable marginal ulcer, gastro-gastric fistula, severe gastro-esophageal reflux, and malnutrition [91]. Recently, revisional surgery is increasingly utilized for the management of WR [91, 92].

### 8.4.1 After failed LAGB

In patients with WR or IWL after gastric band, the surgical options include band removal and revisional BS. A retrospective study evaluated the outcomes of revision of LAGB for inadequate weight loss to LSG or single anastomosis duodenal switch and found that patients who underwent single anastomosis duodenal switch had significantly greater weight loss than LSG in the first year post surgery, with excess BMI loss percentage of 66.7% versus 51.5% [93]. In the same study, at  $>12$  months post revision, both single anastomosis duodenal switch patients and LSG patients had adequate WL (79% for single anastomosis duodenal switch versus 67.8% for LSG) [93]. A systematic review compared the WL outcomes of conversion gastric band to LSG or RYGB and showed significant increase in EWL% in RYGB and patients than LSG patients at 12 and 24 months after revision [94].

However, no statistically significant change was observed in terms of EWL% after 3, 6, or 36 months post revision [94]. RYGB was also associated with a higher rate of complications, readmission and longer operative time [94].

#### *8.4.2 After failed LSG*

Several surgical interventions can be considered for failed LSG including conversion to RYGB, biliopancreatic diversion with duodenal switch (BPD/DS), one anastomosis gastric bypass (OAGB) or single anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S). Among 43 post LSG patients who had revisional surgery for IWL/WR (25 patients converted to BPD/DS, 18 to RYGB), the median EWL% after 34 months was significantly greater for BPD/DS compared to RYGB (59% vs. 23%) [14]. However, short-term complications and vitamin deficiencies were higher in BPD/DS compared with RYGB [14].

Conversions of LSG to OAGB or RYGB are also utilized to manage WR. At 12 months, mean total WL percentage was significantly higher in OAGB compared to RYGB ( $15.8 \pm 7.8\%$  vs.  $10.3 \pm 7.6\%$ ), with no differences in readmission and complications between the two procedures, suggesting that OAGB is safe after failed LSG [95]. However, long-term follow up including the risk of malnutrition is needed for a complete evaluation of OAGB as a revisional BS. Another study evaluating the conversion of LSG to four different gastric bypass procedures including proximal RYGB, type 2 distal RYGB, long biliopancreatic limb RYGB and OAGB showed that the long biliopancreatic limb RYGB and OAGB resulted in significant EWL% at 3 years (33.8% and 33.2% respectively). However, the effect lasted only for 2 years in the proximal RYGB (EWL% of 23.1%) [96].

SADI-S is a relatively new procedure utilized as an alternative to the current duodenal switch (DS) [97]. Outcomes of SADI-S as a revision after LSG showed 20.5% weight loss and 9.4 units BMI change two years post revision with 93.7% T2DM remission rate [98]. Additionally, there were no mortality or conversions to open surgery, and postoperative early and late complication rates were low (5.3% and 6.4% respectively) [98].

#### *8.4.3 After failed RYGB*

There seems no standardized approach to revisional surgery after failed RYGB. A systemic review of revision of RYGB for WR (799 studies, 866 patients) assessed 5 revisions: conversion to distal RYGB or BPD/DS, or revision of gastric pouch and anastomosis, revision with gastric band or endoluminal procedures [92]. At 3-years after revision, mean excess body mass index loss percentage for distal RYGB was 52.2%, for BPD/DS was 76%, for gastric pouch or anastomosis revision was 14%, for gastric banding revision was 47.3%, and for endoluminal procedures was 32.1% [92]. Amongst these revisions, gastric pouch or anastomosis revision had the lowest rates for major complications (3.5%), while DRYGB had the highest rate for major complications (11.9%) and mortality (0.6%) [92]. A recently published study showed promising short and long term results as regards to the conversion of RYGB to long biliopancreatic limb RYGB for the management of IWL, where patients achieved an additional excess EWL% ranging from 40.0% at 1 year to 45.3% at 6 years [99].

## **9. Conclusions**

Although BS is an effective treatment for weight loss and comorbidities resolution, however WR may occur on the long term. The lack of a standard definition

and consensus on what constitutes clinically significance WR leads to poor reporting of this entity which requires further research. The underlying factors that contribute to WR are multifactorial, including hormonal and surgical causes, nutritional noncompliance, physical inactivity, and mental health issues. Therefore, patients with significant WR following BS should undergo comprehensive evaluations to determine the underlying etiology. Management should focus on preventive and treatment strategies delivered in a multidisciplinary approach to include dietary intervention, behavioral counseling, lifestyle modifications, pharmacotherapy and, if indicated, surgical revision. Future research should focus to identify the etiological factors and effective intervention strategies.

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### **Conflict of interest**

None.

### **Abbreviations**

BMI	body mass index
BPD/DS	laparoscopic biliopancreatic diversion with duodenal switch
BS	Bariatric surgery
EWL	excess weight loss
FDA	food and drug administration
GI	gastrointestinal
GLP-1	polypeptide and glucagon-like peptide-1
IWL	insufficient weight loss
LAGB	Laparoscopic gastric band
LSG	Laparoscopic sleeve gastrectomy
OAGB	one anastomosis gastric bypass
QoL	quality of life
RCT	randomized controlled trial
RYGB	Roux en Y gastric bypass
SADI-S	single anastomosis duodeno-ileal bypass with sleeve gastrectomy
T2DM	type 2 diabetes mellitus
TBW	total body weight
WL	weight loss
WR	weight regain

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