30 Suboptimal Weight Loss and Weight Regain: Is it Prime Time for Pharmacotherapy?

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30.1 Introduction

Bariatric surgery is undoubtfully the most effective weight loss intervention in severe obesity and leads to significant improvement of obesity associated health conditions, health-related quality of life and reduction in overall mortality and morbidity [1, 2].

However the variability in weight loss outcome and the longer-term durability of weight loss and control of comorbidity after bariatric procedures are a new concern.

In this chapter we will briefly review the prevalence and possible etiology of suboptimal weight loss (SWL) and weight regain (WR) as complications of bariatric surgery. We will then discuss the evaluation and treatment of these conditions, with a more specific focus on the possible role of weight loss medications as a rescue therapy in patients who experience these complications.

30.2 Search Strategy

A literature search was conducted between November 2019 and January 2020 and aimed to find published clinical trials and systematic reviews. The databases searched was PubMed (January 1921 to January 2020). The key terms used were suboptimal weight loss, weight regain, bariatric surgery, anti-obesity medication, obesity pharmacotherapy, re-operative bariatric surgery, re-operative intervention, conversional procedures, endoscopic procedures.

Laparoscopic Roux-en-Y gastric bypass (RYGB) and vertical sleeve gastrectomy (SG) are the two most common weight reduction surgeries in the world,

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therefore most attention was given in this chapter to these two procedures. Additionally, seen that the SG has been available in the US only since 2010, a larger number of the studies available and discussed here are in RYGB patients.

30.3 Suboptimal Weight Loss after Bariatric Surgery

There is consensus that some patients experience SWL after bariatric surgery [3]. SWL is often defined as never achieving more than 50% excess weight loss (EWL) [4]. Depending on the report, 5–20% of patients do not lose weight successfully, despite perceived optimal surgical technique and regular follow-up [5–7]. Interestingly a retrospective review of 375 post RYGB, showed that an early prediction of insufficient weight loss can be made at 6 months: patients who lost <30% of their initial excess weight were unlikely to loose ≥50% at 24 months [8]. A large retrospective review on approximately 1450 patients who underwent either RYGB (n=918) or SG (n=538) showed that weight loss at 3–6 months was an independent predictor of maximal % weight loss in both SG and RYGB patients [9], ultimately suggesting that early identification and treatment of suboptimal weight loss post bariatric surgery may not be unreasonable when utilizing lifestyle and medical interventions as an initial approach.

30.4 Weight Regain after Bariatric Surgery

There is also growing recognition that post bariatric surgery patients may experience WR which can be associated with diminished health benefits, including recurrence of type 2 diabetes and other comorbidities, which had seen an initial remission [10, 11].

So far there isn't an univocal definition of WR after bariatric surgery. With lack of uniform reporting the prevalence of this condition cannot be conclusively estimated. A systematic review identified nine heterogeneous studies which reported weight regain of 5.7% at 2 years all the way to 75.6% at 6 years [4]. But the majority of the studies were small, in different populations, and the methodology of definition and report was different. There has been a handful of larger longitudinal studies looking at the long term weight loss outcomes after bariatric surgery [2, 3, 12], which show consistently that patients generally regain 5 to 10% of their TWL within the first decade. In a study of 55 patients post SG, Lauti et al. demonstrated the importance of using standardized definitions of weight regain and found that when in their cohort they selected 3 best definitions of weight regain, 40 to 64% of patients regained some weight at 5 years after SG [13]. Across the board the studies show that the susceptibility to weight regain increases as time from surgery increases. However, while some weight regain needs to be expected after bariatric surgery, and patients accept it, there is a subgroup of patient who may regain a significant amount of weight and that is associated with decreased quality of life and possibly recurrence of comorbidities as well as emotional impact and dissatisfaction from the procedure [3, 14]. In a large study which included 1406 RYGB patients, weight

regain quantified as percentage of maximum weight lost correlated best with most clinical outcomes. Utilizing this definition, at 5 years 67.3% of post RYGB patients had regained ≥20% of maximum weight loss [15]. In this study instead the rate of weight regain was largest during the first year after reaching nadir weight and decreased over time, but continued throughout the 5 year follow-up.

Additionally the finding from this study in RYGB [15] combined with the data of Jirapinyo et al. [16] as well as those reported by Lauti et al. in SG [13] suggest a dose-response relationship between weight regain and some bariatric surgery outcomes such as diabetes, hypertension, and physical health–related quality of life, highlighting the importance of effectively intervene to limit or correct the weight regain.

A 5 years prospective weight loss study suggests that super obesity [Body Mass Index (BMI) >50 kg/m^2] puts patients at higher risk of SWL and WR after gastric bypass [17]. In 782 patients post gastric bypass weight loss was completed by 24 months and WR become significant at 48 months. Some WR was observed in approximately 50% of the patients (46% within 24 months and 63.6% within 48 months) who had received gastric bypass. Patients with WR experienced a mean gain of 8.8 kg within 60 months, which represented a 8% increase from the lowest weight after surgery. Again, WR was higher in the patients with super obesity (BMI >50 kg/m^2) with a BMI increase from 34.2 kg/m^2 at 18 months after surgery to 39.4 kg/m^2 at 60 months. SWL was defined as excess weight loss less than 50%, and was highest in the group with super obesity at all times studied, reaching 18.8% at 48 months after surgery.

30.5 Evaluation of Suboptimal Weight Loss and Weight Regain after Weight Loss Surgery

The recommended approach is to perform a multidisciplinary evaluation to determine the potential causes of the poor weight loss response. It should include a nutritional evaluation, a behavioral assessment and an evaluation of the anatomy when indicated. Lifestyle and behavioral modification should be optimized before considering other therapy or revisional endoscopic or surgical procedure. Iatrogenic weight gain due to obesogenic medications should be excluded as it will be discussed in more detail in the coming section.

Nevertheless, even with the most diligent evaluation, the cause of SWL and WR is not always identified and often life style and behavioral interventions alone do not improve the outcome.

30.6 Etiology of SWL and WR Post Bariatric Surgery

Besides cases where obvious anatomic abnormalities exist which may explain a suboptimal weight loss outcome, such as pouch or stoma dilation and gastro-gastric fistula in RYGB or dilated sleeve in SG [18], the mechanisms of SWL and WR after bariatric surgery remains poorly understood, and are likely to be distinct at least in

part, and to involve physiologic processes as well as behavioral and psychological factors. In general, the choice of weight loss surgery is still often empirical, therefore individual factors such as the anatomy of the gastrointestinal tract in relationship to the hormonal function and the CNS response to peripheral hunger and satiety signals are all factors which could affect behavior and determine individual responses to the different weight loss bariatric surgery procedures and ultimately explain both SWL and WR. At this stage there isn't a valid approach to study the unique physiology of each patient after surgery but factors such as the limb length are regarded as important in determining the post-bariatric surgery physiology [19].

A publication studying 49 patients with SWL or WR after 1 year post RYGB compared with 38 matched controls with acceptable weight loss, indicated that lower levels of physical activity, disordered eating behavior and lower quality of life were associated with the unsuccessful weigh loss outcome [20]. While association does not imply causation, it is conceivable that those behaviors may have contributed, at least in part, to the poorer weight loss outcome. In fact, previous studies have shown the importance of physical activity in weight maintenance and prevention of weight regain after RYGB [21–23].

A systematic review of 115 selected articles published between 1998 and 2010 found that the predictors of weight loss outcomes post bariatric surgery (RYGB or laparoscopic adjustable gastric banding (LAGB)) are quite heterogenous across the studies but factors such as the preoperative mandatory weight loss, the initial BMI, the presence of super obesity, eating disorders/maladaptive eating habits and psychiatric disorders/substance abuse may be more often implicated [6]. Similarly, a recent review by Sarwer et al. discusses that the presence of impulsivity, which is an element of overeating, disinhibited eating, substance abuse and mood regulation, is a predictor of weight loss outcomes of bariatric surgery [24]. A prospective observational study in 2365 patients undergoing RYGB found that higher baseline BMI, preoperative use of any diabetes medications, non-use of buproprion medications, no history of smoking, age > 50 years and the presence of fibrosis at liver biopsy were associated with lower % EBWL at 36 months [25]. In a multivariate analysis of 310 RYGB patients with a mean presurgical BMI of 52 kg/m^2 followed up to 12 months, only the presence of diabetes (odds ratio [OR], 3.09; 95% confidence interval [CI], 1.35–7.09 [P =.007]) and larger pouch size (OR, 2.77; 95% CI, 1.81–4.22 [$P < .001$]) were independently associated with poor weight loss (defined in this study as $\leq$ 40% excess weight loss) [26]. Similarly, a previous review published in 2012, which included only RYGB and gastric banding (GB) (as SG was only approved in 2010) identified nutritional non-compliance, hormonal/metabolic imbalance, mental health, physical inactivity and anatomical/surgical factors as possible mechanisms [10]. Specifically, the hormonal factors refer to a blunting of the changes in the appetite regulating hormone levels which have been called to explain in part the satiety, the decreased food intake and consequently the weight loss after bariatric procedures [27–29].

A review of the studies looking at possible causes of post SG weight regain pointed to initial sleeve size, sleeve dilatation, increased ghrelin levels,

inadequate follow-up support and maladaptive lifestyle behaviors as proposed mechanisms [4]. Finally, prescription of one or more medication from a list of 32 obesogenic medications has shown to lead to decreased weight loss at one year in a group of 150 patient versus 173 patients who were not prescribed such medications [30], suggesting that scrutiny of the patients' medication list should be included in the evaluation of insufficient weight loss and weight regain post bariatric surgery.

In general, several classes of medications are known to be associated with weight gain, including steroids, contraceptives, and other hormonal agents as well as some antidiabetic, antihypertensive, antidepressant, antipsychotic, anti-epileptic, and antihistamine agents [31]. Therefore, it is necessary to make a careful review of a patient's medications to identify those which may be limit weight loss and possibly contribute to weight regain. Consideration of alternatives which are weight-neutral and weight-loss promoting [31] should be part of an initial intervention (together with diet and exercise counseling) when assisting patients with an unsatisfactory response to weight loss surgery. Finally, post-bariatric surgery hypoglycemia may represent a rare risk factor for weight regain [32].

In conclusion the patients who present with insufficient weight loss, continued co-morbidities or weight regain present a challenge to the surgeons which may warrant re-assessment and additional therapy. Re-operative interventions and more recently pharmacotherapy are potential treatments.

30.7 Re-Operative Bariatric Surgery and Procedures

Beyond life style interventions, re-operative interventions (correction of an anatomical abnormality or conversation to a different procedure) have been the traditional treatment approach to SWL and WR after bariatric surgery.

In 2014 a task force reviewed the data on re-operative bariatric surgery [18]. They included 175 articles in a systematic review and analysis. The analysis of re-operative surgery for unsuccessful bariatric surgery highlights that the majority of studies available so far are single center retrospective reviews, and/or the outcomes are inconsistently reported in the literature and vary based on the population studied. Conversely one large study reports the outcomes of 449,753 bariatric operations from a large data base, the Bariatric Outcomes Longitudinal Database (BOLD) [33]: a rate of reoperation of 6.3% was observed and the overall complication rate was low. The general sense is that the outcome after re-operative interventions (correction of an anatomical abnormality or conversation to a different procedure) are favorable and demonstrate additional weight loss, but the risk is higher than the initial bariatric surgery [33]. Therefore the decision to proceed for an invasive reintervention needs to be carefully weighted, especially in cases in which an anatomical abnormality suitable for a correction procedure is not identified or the surgical risk of a conversion is high or finally the patient‘s preference is for a non-invasive approach.

30.8 Adjuvant Medical Therapy

In this chapter we suggest that weight loss medications should be considered as a rescue therapy in patients with SWL or significant WR after bariatric surgery. Currently there aren't weight loss medications approved for use post bariatric surgery but weight loss medications could be a currently underutilized strategy in SWL and WR.

Additionally, even when patients have attained the expected weight loss with a bariatric surgery procedure, they are likely to have residual obesity and therefore in principle they still meet eligibility criteria for weight loss medications. Weight loss medication are in fact indicated for a BMI ≥27 kg/m^2 with at least one comorbid condition, including diabetes mellitus (DM), medication-controlled hypertension (blood pressures consistently <140/80), hypercholesterolemia, and/or obstructive sleep apnea; or a BMI ≥30 kg/m^2 without co-morbidities [31, 34].

Table 30.1 reviews the currently approved weight loss medications, their efficacy, safety and dosing [31, 34].

For the most part in the current obesity medicine practice the choice of weight loss medications is still empirical and often driven by the efficacy (tested in non-post bariatric surgery patients), coverage, cost, patients preferences (injectable versus oral) and potential dual benefit, meaning potential amelioration of coexisting conditions, such as diabetes, migraines, depression, addiction, tobacco abuse [36].

At this stage there is a limited number of studies looking at the efficacy of weight loss medications after weight loss surgery. These studies are summarized in Table 30.2.

One important limitation of these studies is that for the most part these are retrospective chart reviews [39–43] or not strictly controlled prospective studies [37, 38]. Additionally, some studies utilize the older and less effective off label drugs which have approved indications outside weight loss such as for depression, migraines, seizure and mood stabilization [38–40]. Of note in most of the studies the medications were given on a background of diet and exercise intervention: this is worth underscoring as generally in obesity a larger weight loss can be achieved when more than on approach is utilized simultaneously, as it is the case when pharmacotherapy is added to lifestyle modifications and more so to intensive behavioral therapy [44]. Therefore, even with the limited evidence available, we recommend that diet and exercise counseling and, when possible, behavioral therapy are adopted as the background to any intervention in SWL and WR after bariatric surgery.

The largest study of pharmacotherapy after bariatric surgery is retrospective and enrolled 319 patients (RYGB = 258; sleeve gastrectomy = 61) treated in two medical centers [40]. More than one medication was trialed in the course of the treatment and the average number of medication trialed was two. More than half of the patients in treatment with a weight loss medication post-surgery lost ≥5% of their weight, 30.1% lost ≥10% and 16% of patients lost ≥15%. The authors describe even one case where the weight loss with pharmacotherapy lead to a BMI decrease from 36 to 26 kg/m^2, surpassing the nadir weight loss of BMI of 33 kg/m^2 achieved with surgery alone.

Table 30.1 Drugs currently approved for weight loss: efficacy, safety and dosing. Data reported are from the RCT in overweight and obese patients without history of bariatric surgery [31, 34, 35]. These drugs have not been evaluated in post-bariatric surgery

Agent	Mechanism of action	Weight loss (% from baseline) in completers vs. placebo	Dosing	Most common side effects
Phentermine	Sympathomimetic; suppresses appetite, possibly increases resting energy expenditure.	7.38% vs 2.28% (15 mg)	8 mg TID orally before meals, 15 mg QD or BID, 30 mg QD	Headache, dry mouth, insomnia, dizziness, irritability, constipation.
Orlistat 120 TID (or OTC Alli 60 TID)	Pancreatic lipase inhibitor, decreases the absorption of 30% of dietary fat.	8.8% vs 5.8%	120 (or 60) mg orally TID before meals	Loose stools, flatulence, fecal urgency, oily stool, fecal incontinence small but significant decreases in fat-soluble vitamins.
Phentermine/ Topiramate ER 7.5/46 mg	Sympathomimetic; possible modulation of gamma-aminobutyric acid receptors, inhibition of carbonic anhydrase, and glutamate antagonism, suppresses appetite.	9.6% vs 1.2%	Orally qAM: 3.75/23 mg for 14 days then 7.5/46 mg	Paresthesias, dizziness, dysgeusia, insomnia, constipation, dry mouth.
Phentermine/ Topiramate ER 15/92 mg	See above.	12.4% vs 1.2%	At 12 weeks on 7.5/46 qAM, option to titrate to 11.25/69 for 2 weeks, then 15/92 mg	Paresthesias, dizziness, dysgeusia, insomnia, constipation, dry mouth.
Lorcarserin 20 mg	5HT-2C receptor agonist, suppresses appetite.	7.9% vs 4.0%	10 mg BID orally or 20 mg QD, no titration needed	Headache, dizziness, fatigue, nausea, dry mouth, constipation. **Withdrawn from the market on February 13 2020 because of potential increased cancer risk.**

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Table 30.1 (continued)

Agent	Mechanism of action	Weight loss (% from baseline) in completers vs. placebo	Dosing	Most common side effects
Naltrexone ER/bupropion ER 32/360	Dopamine/ noradrenaline reuptake inhibitor; opioid receptor antagonist, suppresses appetite	8.1% vs 1.8%	Orally Wk 1–1 table (8/90 mg) in am	Nausea, vomiting, constipation, headache, dizziness, insomnia, dry mouth.
			Wk 2–1 in am and 1 in pm	
			Wk 3–2 in am and 1 in pm	
			Wk 4–2 in am and 2 in pm, titrate slower if side effects	
Liraglutide 3 mg	GLP-1 receptor agonist Suppresses appetite Decreases gastric emptying Has additional independent effects on insulin and glucagon secretion	9.2% vs 3.5%	Inject SQ Wk 1–0.6 daily, increase weekly by 0.6 until 3 mg daily, titrate slower if side effects	Nausea, vomiting, diarrhea, constipation, dyspepsia, abdominal pain.

Abbreviations/symbols: *TID* 3 times per day; *QD* once per day; *BID* 2 times per day, typically before breakfast and before dinner; *OTC* over the counter; *Wk* week; *qAM* once per day in the morning

In this study the most frequent medications prescribed for weight loss were topiramate, phentermine, metformin, buproprion and zonisamide. All except for phentermine are off label for the treatment of obesity. The mean added weight loss was 7.6% (17.8 lbs) of total postsurgical weight. When looking at predictors for weight loss with medication use after weight loss surgery, the authors had some interesting findings. The type of surgery (RYGB over SG) regardless of the postoperative BMI, as well as female gender, history of psychiatric conditions fared better while the presence of one comorbidity or of obstructive sleep apnea were associated with less weight loss [40].

Interestingly, those patients prescribed the medication at weight plateau rather than after some weight regain, experienced the larger percent weight loss from preoperative weigh. While the difference was not statistically significant it suggests that early intervention at weight loss plateau, rather than waiting for weight regain, may lead to a better response.

In a subgroup analysis of 37 young adults from the same data set, predominantly female, of which 75.7% had a RYGB, 54.1% of patients experienced ≥5% weight

Table 30.2 Studies utilizing obesity drugs after bariatric surgery

Author	Sample size	Study design	Surgery	Medication	Summary of findings	Side effects
Zoss et al. [37]	N = 38 Gender non reported	Prospective randomized, unblinded, non-placebo controlled 8 ± 6 months after laparoscopic SAGB 8 months Group A = 19 dietary counseling Group B = 19 orlistat + dietary counseling	SAGB	Orlistat 120 before each meal	Weight loss 8 ± 2 kg ($p < 0.01$) vs 3 ± 2 kg (NS) ($p < 0.02$ between groups)	Increased gas-bloating and increased stool frequency (to a maximum of double frequency).
Zilberstein et al. 2004 [38]	N = 16 2 ♂, 14 ♀ 10/16 patients diagnosed with binge eating disorder or episodes	Prospective, non-controlled 3 months	SAGB	Topiramate 25 mg (2 pts at 12.5 mg, 2 pts at 50 mg, 2 pts discontinued)	Additional mean EWL 14.8% (from 20.9% to 34.1%)	2 patients discontinued due to drug side effects, the nature of the side effects is not reported
Pajecki et al. 2012 [39]	N = 15 4 ♂, 11 ♀ <50% EWL ≥ 2 years (mean 5.6 years) or regained 15% of lowest weight	Retrospective 12.5 ± 4.7 weeks (range 8 to 28 weeks)	4 GB, 9 RYGB,1 DS, 1 longitudinal gastrectomy.	Liraglutide 1.2 to 1.8 mg daily (53.3% received 1.8 mg)	Mean weight loss −7.5 ± 4.3 kg (range 2 to 18 kg)	40% experienced nausea (3 pts post GB and 3 pts post RYGB). No discontinuation of the drug due to side effects

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Table 30.2 (continued)

Author	Sample size	Study design	Surgery	Medication	Summary of findings	Side effects
Cody Stanford et al. 2017 [40]	N = 319 72 ♂, 247 ♀	Retrospective 3 and 12 months	258 RYGB, 61 SG 78.5% had medications prescribed at weight regain, 21.5% at plateau	Topiramate Phentermine Metformin Buproprion Zonisamide	At 12 months mean added weight loss 7.6% (17.8 lbs) ≥5% TWL = 56%, ≥10% TWL = 30.1%, ≥15% TWL = 16% Predictors of better response: Topiramate; RYGB (vs sleeve gastrectomy); Female gender; Psychiatric co-morbidity; Higher preoperative BMI;	Not reported
Schwartz et al. 2016 [41]	N = 65 11 ♂, 47 ♀	Retrospective 90 days	51 RYGB 14 LAGB	Phentermine Phentermine–topiramate ER	Data at 90 days available for 30 pts Phentermine group (N = 24): mean weight loss 6.3 kg (12.8% EWL) Phentermine–Topiramate ER group (N = 6): mean weight loss 3.8 kg (12.9% EWL)	No patients required cessation of medical therapy due to hypertension, cardiac arrhythmias, or insomnia. One patient stopped phentermine due to headaches and one patient due to nausea.

Hanipah et al. 2018 [42]	N = 209 ♂, 14 ♀195	Retrospective 12 months	126 RYGB, 52 SG, 21 LAGB, 4 gastric plication, 6 revisional bariatric surgery	Phentermine N = 156 Phentermine - topiramate ER N = 25 Lorcaserin N = 18 Naltrexone SR/ buproprion SR N = 10	5% TWL: 37% of pts >10% TWL: 19% of pts Mean % weight loss 2.2% Predictors of weight loss: Type of procedure: (4.6% in LAGB pts, 2.8% in RYGB pts, 0 .3% in SG pts); BMI at the start of pharmacotherapy	Not reported
Wharton et al. 2019 [43]	N = 117 ♀ 87.2%	Retrospective chart review 7.6 ± 7.1 months	50 GB, 53 RYGB, 14 SG	Liraglutide 3 mg	Weight loss 6.3 ± 7.7 kg, $p < 0.05$	Nausea 29.1%

Abbreviations/symbols: *SAGB* Swedish adjustable gastric band; *GB* Gastric banding *LAGB* laparoscopic adjustable gastric banding; *RYGB* Roux-en-Y gastric bypass; *DS*: duodenal switch; *pt*: patient; *pts*: patients; *EWL* excess weight loss; *TWL* total weight loss
♂: male; ♀: female

loss, 34.5% and 22% experienced ≥10% and ≥15% weight loss, respectively [45]. The RYGB group achieved larger weight loss on the medication (compared with the SG group) with the difference near statistical significant (P=.051).

Since 2012 we have 4 new medications approved for weight loss, phentermine-topiramate ER, lorcaserine, naltrexone SR/buproprion SR, liraglutide 3 mg [31, 34] (Table 30.1). The efficacy of the newer approved medication options is generally 6%–13% baseline-weight loss, but weight losses of 15% and even 20% of baseline weight are not uncommonly observed with these drugs. Of note, most of the medications utilized in the studies post bariatric surgery, with the exception of two studies, are old obesity drugs or do not have a label for weight loss and are indeed less effective than the newer medications specifically designed for weight loss. Therefore it is conceivable but not yet demonstrated that the newer FDA approved weight loss medication will fare better also in post bariatric surgery patients.

30.9 Conclusions

The small set of uncontrolled data from the studies listed in Table 30.2 suggest that the addition of a medication may give an additional weight loss benefit in patients post bariatric surgery. Additionally, while conclusions cannot be derived, there are limited data suggesting that the optimal time to initiate post-bariatric surgery pharmacotherapy is at weight loss plateau [40], rather than after weight regain.

Given the low risk profile of the medications compared to revisional therapy, we suggest that a trial of pharmacotherapy in weight loss failure after bariatric surgery is warranted in appropriate cases. Larger studies and randomized controlled trials are necessary to determine the optimal medications and the timing of adjuvant medical therapy. At this time the data is insufficient to provide evidence based recommendations and a proven practical guidance on how medical therapy should be utilized as adjuvant to bariatric surgery. Therefore, based on the current knowledge, we suggest that when prescribing pharmacotherapy in post bariatric surgery we adopt the practice utilized in non-bariatric surgery patients. In general pharmacotherapy should be recommended on a background of behavioral counseling focusing on diet, physical activity, and lifestyle modifications, which also in post bariatric surgery should be regarded as the cornerstones of weight management [31, 34]. The efficacy and safety of a prescribed weight loss medication should be assessed monthly for the first three months and every three months thereafter and the medication should be discontinued if at anytime it is determined to be poorly effective or does not meet acceptable tolerability or safety. In that case a different medications with a different mechanism of action or an alternative treatment approach should be considered. A weight loss medication, when effective, should be prescribed long term to promote weight loss maintenance. A practical guideline on the use of medications in suboptimal weight loss outcome after weight loss surgery has been published in the last couple of years but is based on uncontrolled data and mostly on the practical experience of two US medical centers [46].

30.10 A Personal View of the Data

In conclusion, weight regain and even suboptimal weight loss after bariatric surgery are not infrequent and are likely multifactorial. The usefulness of adding obesity medications for SWL or WR after bariatric surgery appears promising and deserves further investigation with larger randomized trials, including controlled studies looking at the best time to add the pharmacotherapy and the most effective medication or combination of medications.

The experience available so far from small, non-randomized studies or retrospective chart reviews cannot support an evidence based standard of care but does suggest that pharmacotherapy after bariatric surgery is safe and that patients who are prescribed a weight loss medication after bariatric surgery are likely to experienced additional weight loss. Therefore pharmacotherapy could be attempted as adjuvant to bariatric surgery in combination with lifestyle modifications to counteract suboptimal weight loss, weight recidivism and to enhance weight maintenance.

Recommendations

- In SWL and/or WR after bariatric surgery a systematic approach including a nutritional evaluation, a behavioral assessment and an evaluation of the anatomy is essential. With the lack of an obvious anatomic abnormality, lifestyle and behavioral modification should be optimized before considering revisional endoscopic or surgical procedure.
- Limited data suggest that anti-obesity medications as adjuvant therapy give an additional weight loss benefit to patients post bariatric surgery. The optimal time to initiate post-bariatric surgery pharmacotherapy may be at weight loss plateau rather than after weight regain. Similarly to what non infrequently we see in patients without history of weight loss surgery, often more than one weight loss medication need to be trialed in each individual patient before finding the effective one.

References

1. Gloy VL, Briel M, Bhatt DL, Kashyap SR, Schauer PR, Mingrone G, Bucher HC, Nordmann AJ. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. BMJ. 2013;347:f5934. Epub 2013/10/24; PubMed PMID: 24149519; PMCID: PMC3806364. https://doi.org/10.1136/bmj.f5934.
2. Sjostrom L. Review of the key results from the Swedish obese subjects (SOS) trial - a prospective controlled intervention study of bariatric surgery. J Intern Med. 2013;273(3):219–34. Epub 2012/11/21; PubMed PMID: 23163728. https://doi.org/10.1111/joim.12012.
3. Courcoulas AP, King WC, Belle SH, Berk P, Flum DR, Garcia L, Gourash W, Horlick M, Mitchell JE, Pomp A, Pories WJ, Purnell JQ, Singh A, Spaniolas K, Thirlby R, Wolfe BM, Yanovski SZ. Seven-year weight trajectories and health outcomes in the longitudinal assessment of bariatric surgery (LABS) study. JAMA Surg. 2018;153(5):427–34. . Epub 2017/12/08.; PubMed PMID: 29214306; PMCID: PMC6584318. https://doi.org/10.1001/jamasurg.2017.5025.

4. Lauti M, Kularatna M, Hill AG, MacCormick AD. Weight regain following sleeve gastrectomy-a systematic review. Obes Surg. 2016;26(6):1326–34. Epub 2016/04/07; PubMed PMID: 27048439. https://doi.org/10.1007/s11695-016-2152-x.
5. de Raaff CA, Coblijn UK, de Vries N, Heymans MW, van den Berg BT, van Tets WF, van Wagensveld BA. Predictive factors for insufficient weight loss after bariatric surgery: does obstructive sleep apnea influence weight loss? Obes Surg. 2016;26(5):1048–56. Epub 2015/07/30; PubMed PMID: 26220241. https://doi.org/10.1007/s11695-015-1830-4.
6. Livhits M, Mercado C, Yermilov I, Parikh JA, Dutson E, Mehran A, Ko CY, Gibbons MM. Preoperative predictors of weight loss following bariatric surgery: systematic review. Obes Surg. 2012;22(1):70–89. Epub 2011/08/13; PubMed PMID: 21833817. https://doi.org/10.1007/s11695-011-0472-4.
7. Perugini RA, Mason R, Czerniach DR, Novitsky YW, Baker S, Litwin DE, Kelly JJ. Predictors of complication and suboptimal weight loss after laparoscopic roux-en-Y gastric bypass: a series of 188 patients. Arch Surg. 2003;138(5):541–5; discussion 5-6. Epub 2003/05/14; PubMed PMID: 12742960. https://doi.org/10.1001/archsurg.138.5.541.
8. Ritz P, Caiazzo R, Becouarn G, Arnalsteen L, Andrieu S, Topart P, Pattou F. Early prediction of failure to lose weight after obesity surgery. Surg Obes Relat Dis. 2013;9(1):118–21. Epub 2012/01/10; . PubMed PMID: 22222302. https://doi.org/10.1016/j.soard.2011.10.022.
9. Manning S, Pucci A, Carter NC, Elkalaawy M, Querci G, Magno S, Tamberi A, Finer N, Fiennes AG, Hashemi M, Jenkinson AD, Anselmino M, Santini F, Adamo M, Batterham RL. Early postoperative weight loss predicts maximal weight loss after sleeve gastrectomy and roux-en-Y gastric bypass. Surg Endosc. 2015;29(6):1484–91. Epub 2014/09/23; PubMed PMID: 25239175; PMCID: PMC4422859. https://doi.org/10.1007/s00464-014-3829-7.
10. Karmali S, Brar B, Shi X, Sharma AM, de Gara C, Birch DW. Weight recidivism post-bariatric surgery: a systematic review. Obes Surg. 2013;23(11):1922–33. Epub 2013/09/03;. PubMed PMID: 23996349. https://doi.org/10.1007/s11695-013-1070-4.
11. Laurino Neto RM, Herbella FA, Tauil RM, Silva FS, de Lima SE Jr. Comorbidities remission after roux-en-Y gastric bypass for morbid obesity is sustained in a long-term follow-up and correlates with weight regain. Obes Surg. 2012;22(10):1580–5. Epub 2012/08/22; PubMed PMID: 22907795. https://doi.org/10.1007/s11695-012-0731-z.
12. Adams TD, Davidson LE, Litwin SE, Kim J, Kolotkin RL, Nanjee MN, Gutierrez JM, Frogley SJ, Ibele AR, Brinton EA, Hopkins PN, McKinlay R, Simper SC, Hunt SC. Weight and metabolic outcomes 12 years after gastric bypass. N Engl J Med. 2017;377(12):1143–55. Epub 2017/09/21; PubMed PMID: 28930514; PMCID: PMC5737957. https://doi.org/10.1056/NEJMoa1700459.
13. Lauti M, Lemanu D, Zeng ISL, Su'a B, Hill AG, MacCormick AD. Definition determines weight regain outcomes after sleeve gastrectomy. Surg Obes Relat Dis. 2017;13(7):1123–9. Epub 2017/04/26; . PubMed PMID: 28438493. https://doi.org/10.1016/j.soard.2017.02.029.
14. Jones L, Cleator J, Yorke J. Maintaining weight loss after bariatric surgery: when the spectator role is no longer enough. Clin Obes. 2016;6(4):249–58. Epub 2016/06/09; PubMed PMID: 27273813. https://doi.org/10.1111/cob.12152.
15. King WC, Hinerman AS, Belle SH, Wahed AS, Courcoulas AP. Comparison of the performance of common measures of weight regain after bariatric surgery for association with clinical outcomes. JAMA. 2018;320(15):1560–9. Epub 2018/10/17; PubMed PMID: 30326125; PMCID: PMC6233795. https://doi.org/10.1001/jama.2018.14433.
16. Jirapinyo P, Abu Dayyeh BK, Thompson CC. Weight regain after roux-en-Y gastric bypass has a large negative impact on the bariatric quality of life index. BMJ Open Gastroenterol. 2017;4(1):e000153. Epub 2017/09/26; PubMed PMID: 28944069; PMCID: PMC5596836. https://doi.org/10.1136/bmjgast-2017-000153.
17. Magro DO, Geloneze B, Delfini R, Pareja BC, Callejas F, Pareja JC. Long-term weight regain after gastric bypass: a 5-year prospective study. Obes Surg. 2008;18(6):648–51. Epub 2008/04/09; . PubMed PMID: 18392907. https://doi.org/10.1007/s11695-007-9265-1.
18. Brethauer SA, Kothari S, Sudan R, Williams B, English WJ, Brengman M, Kurian M, Hutter M, Stegemann L, Kallies K, Nguyen NT, Ponce J, Morton JM. Systematic review on reoperative bariatric surgery: American Society for Metabolic and Bariatric Surgery Revision

Task Force. Surg Obes Relat Dis. 2014;10(5):952–72. Epub 2014/04/30; PubMed PMID: 24776071. https://doi.org/10.1016/j.soard.2014.02.014.
19. Zorrilla-Nunez LF, Campbell A, Giambartolomei G, Lo Menzo E, Szomstein S, Rosenthal RJ. The importance of the biliopancreatic limb length in gastric bypass: a systematic review. Surg Obes Relat Dis. 2019;15(1):43–9. Epub 2018/12/07; PubMed PMID: 30501957. https://doi.org/10.1016/j.soard.2018.10.013.
20. Amundsen T, Strommen M, Martins C. Suboptimal weight loss and weight regain after gastric bypass surgery-postoperative status of energy intake, eating behavior, physical activity, and psychometrics. Obes Surg. 2017;27(5):1316–23. . Epub 2016/12/04; PubMed PMID: 27914028; PMCID: PMC5403843. https://doi.org/10.1007/s11695-016-2475-7.
21. Freire RH, Borges MC, Alvarez-Leite JI, Toulson Davisson Correia MI. Food quality, physical activity, and nutritional follow-up as determinant of weight regain after roux-en-Y gastric bypass. Nutrition. 2012;28(1):53–8. Epub 2011/09/03; PubMed PMID: 21885246. https://doi.org/10.1016/j.nut.2011.01.011.
22. Faria SL, de Oliveira KE, Lins RD, Faria OP. Nutritional management of weight regain after bariatric surgery. Obes Surg. 2010;20(2):135–9. Epub 2008/06/26; PubMed PMID: 18575942. https://doi.org/10.1007/s11695-008-9610-z.
23. Welch G, Wesolowski C, Piepul B, Kuhn J, Romanelli J, Garb J. Physical activity predicts weight loss following gastric bypass surgery: findings from a support group survey. Obes Surg. 2008;18(5):517–24. Epub 2008/03/28; PubMed PMID: 18365295. https://doi.org/10.1007/s11695-007-9269-x.
24. Sarwer DB, Allison KC, Wadden TA, Ashare R, Spitzer JC, McCuen-Wurst C, LaGrotte C, Williams NN, Edwards M, Tewksbury C, Wu J. Psychopathology, disordered eating, and impulsivity as predictors of outcomes of bariatric surgery. Surg Obes Relat Dis. 2019;15(4):650–5. Epub 2019/03/13; PubMed PMID: 30858009; PMCID: PMC6538470. https://doi.org/10.1016/j.soard.2019.01.029.
25. Still CD, Wood GC, Chu X, Manney C, Strodel W, Petrick A, Gabrielsen J, Mirshahi T, Argyropoulos G, Seiler J, Yung M, Benotti P, Gerhard GS. Clinical factors associated with weight loss outcomes after Roux-en-Y gastric bypass surgery. Obesity (Silver Spring). 2014;22(3):888–94. Epub 2013/06/28; PubMed PMID: 23804287; PMCID: PMC3819407. https://doi.org/10.1002/oby.20529.
26. Campos GM, Rabl C, Mulligan K, Posselt A, Rogers SJ, Westphalen AC, Lin F, Vittinghoff E. Factors associated with weight loss after gastric bypass. Arch Surg. 2008;143(9):877–83.; discussion 84; Epub 2008/09/17; PubMed PMID: 18794426; PMCID: PMC2747804. https://doi.org/10.1001/archsurg.143.9.877.
27. Laferrere B. Bariatric surgery and obesity: influence on the incretins. Int J Obes Suppl. 2016;6(Suppl 1):S32–S6. Epub 2017/07/08; PubMed PMID: 28685028; PMCID: PMC5485883. https://doi.org/10.1038/ijosup.2016.8.
28. Dimitriadis GK, Randeva MS, Miras AD. Potential Hormone Mechanisms of Bariatric Surgery. Curr Obes Rep. 2017;6(3):253–65. Epub 2017/08/07; PubMed PMID: 28780756; PMCID: PMC5585994. https://doi.org/10.1007/s13679-017-0276-5.
29. Meek CL, Lewis HB, Reimann F, Gribble FM, Park AJ. The effect of bariatric surgery on gastrointestinal and pancreatic peptide hormones. Peptides. 2016;77:28–37. Epub 2015/09/08; . PubMed PMID: 26344355. https://doi.org/10.1016/j.peptides.2015.08.013.
30. Leggett CB, Desalermos A, Brown SD, Lee E, Proudfoot JA, Horgan S, Gupta S, Grunvald E, Ho SB, Zarrinpar A. The effects of provider-prescribed obesogenic drugs on post-laparoscopic sleeve gastrectomy outcomes: a retrospective cohort study. Int J Obes (Lond). 2019;43(6):1154–63. Epub 2018/09/23; PubMed PMID: 30242239; PMCID: PMC6428627. https://doi.org/10.1038/s41366-018-0207-x.
31. Apovian CM, Aronne LJ, Bessesen DH, McDonnell ME, Murad MH, Pagotto U, Ryan DH, Still CD, Endocrine S. Pharmacological management of obesity: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2015;100(2):342–62. Epub 2015/01/16; PubMed PMID: 25590212. https://doi.org/10.1210/jc.2014-3415.
32. Varma S, Clark JM, Schweitzer M, Magnuson T, Brown TT, Lee CJ. Weight regain in patients with symptoms of post-bariatric surgery hypoglycemia. Surg Obes Relat Dis.

2017;13(10):1728–34. Epub 2017/08/29; PubMed PMID: 28844575; PMCID: PMC5657438. https://doi.org/10.1016/j.soard.2017.06.004.
33. Sudan R, Nguyen NT, Hutter MM, Brethauer SA, Ponce J, Morton JM. Morbidity, mortality, and weight loss outcomes after reoperative bariatric surgery in the USA. J Gastrointest Surg. 2015;19(1):171–178; discussion 8-9. Epub 2014/09/05; PubMed PMID: 25186073. doi: https://doi.org/10.1007/s11605-014-2639-5
34. Igel LI, Kumar RB, Saunders KH, Aronne LJ. Practical use of pharmacotherapy for obesity. Gastroenterology. 2017;152(7):1765–79. Epub 2017/02/14; . PubMed PMID: 28192104. https://doi.org/10.1053/j.gastro.2016.12.049.
35. Saunders KH, Shukla AP, Igel LI, Kumar RB, Aronne LJ. Pharmacotherapy for obesity. Endocrinol Metab Clin N Am. 2016;45(3):521–38. Epub 2016/08/16; PubMed PMID: 27519128. https://doi.org/10.1016/j.ecl.2016.04.005.
36. Saunders KH, Umashanker D, Igel LI, Kumar RB, Aronne LJ. Obesity pharmacotherapy. Med Clin N Am. 2018;102(1):135–48. Epub 2017/11/21; PubMed PMID: 29156182. https://doi.org/10.1016/j.mcna.2017.08.010.
37. Zoss I, Piec G, Horber FF. Impact of or list at therapy on weight reduction in morbidly obese patients after implantation of the Swedish adjustable gastric band. Obes Surg. 2002;12(1):113–7. Epub 2002/03/01; PubMed PMID: 11868286. https://doi.org/10.1381/096089202321144685.
38. Zilberstein B, Pajecki D, Garcia de Brito AC, Gallafrio ST, Eshkenazy R, Andrade CG. Topiramate after adjustable gastric banding in patients with binge eating and difficulty losing weight. Obes Surg. 2004;14(6):802–5. Epub 2004/08/21; PubMed PMID: 15318986. https://doi.org/10.1381/0960892041590926.
39. Pajecki D, Halpern A, Cercato C, Mancini M, de Cleva R, Santo MA. Short-term use of liraglutide in the management of patients with weight regain after bariatric surgery. Rev Col Bras Cir. 2013;40(3):191–5. Epub 2013/08/06; PubMed PMID: 23912365. https://doi.org/10.1590/s0100-69912013000300005.
40. Stanford FC, Alfaris N, Gomez G, Ricks ET, Shukla AP, Corey KE, Pratt JS, Pomp A, Rubino F, Aronne LJ. The utility of weight loss medications after bariatric surgery for weight regain or inadequate weight loss: A multi-center study. Surg Obes Relat Dis. 2017;13(3):491–500. Epub 2016/12/18; PubMed PMID: 27986587; PMCID: PMC6114136. https://doi.org/10.1016/j.soard.2016.10.018.
41. Schwartz J, Chaudhry UI, Suzo A, Durkin N, Wehr AM, Foreman KS, Tychonievich K, Mikami DJ, Needleman BJ, Noria SF. Pharmacotherapy in conjunction with a diet and exercise program for the treatment of weight recidivism or weight loss plateau post-bariatric surgery: a retrospective review. Obes Surg. 2016;26(2):452–8. Epub 2015/11/30; PubMed PMID: 26615406. https://doi.org/10.1007/s11695-015-1979-x.
42. Nor Hanipah Z, Nasr EC, Bucak E, Schauer PR, Aminian A, Brethauer SA, Cetin D. Efficacy of adjuvant weight loss medication after bariatric surgery. Surg Obes Relat Dis. 2018;14(1):93–8. Epub 2017/12/31; PubMed PMID: 29287757. https://doi.org/10.1016/j.soard.2017.10.002.
43. Wharton S, Kuk JL, Luszczynski M, Kamran E, Christensen RAG. Liraglutide 3.0 mg for the management of insufficient weight loss or excessive weight regain post-bariatric surgery. Clin Obes. 2019;9(4):e12323. Epub 2019/06/12; PubMed PMID: 31183988; PMCID: PMC6771702. https://doi.org/10.1111/cob.12323.
44. Phelan S, Wadden TA. Combining behavioral and pharmacological treatments for obesity. Obes Res. 2002;10(6):560–74. Epub 2002/06/11; PubMed PMID: 12055334. https://doi.org/10.1038/oby.2002.77.
45. Toth AT, Gomez G, Shukla AP, Pratt JS, Cena H, Biino G, Aronne LJ, Stanford FC. Weight loss medications in young adults after bariatric surgery for weight regain or inadequate weight loss: A multi-center study. Children (Basel). 2018;5(9) Epub 2018/08/31; PubMed PMID: 30158481; PMCID: PMC6162731 https://doi.org/10.3390/children5090116.
46. Stanford FC. Controversial issues: A practical guide to the use of weight loss medications after bariatric surgery for weight regain or inadequate weight loss. Surg Obes Relat Dis. 2019;15(1):128–32. Epub 2018/12/12; PubMed PMID: 30527889; PMCID: PMC6441616. https://doi.org/10.1016/j.soard.2018.10.020.