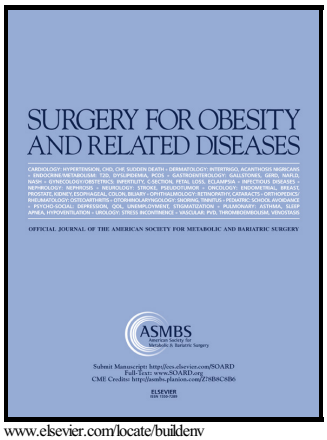

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The utility of weight loss medications after bariatric surgery for weight regain or inadequate weight loss: A multi-center study

Running Head: The utility of weight loss medications after weight loss surgery

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Abstract

Background

Patients who undergo bariatric surgery often have inadequate weight loss or weight regain.

Objective

We sought to discern the utility of weight loss pharmacotherapy as an adjunct to bariatric surgery in patients with inadequate weight loss or weight regain.

Setting

Two academic medical centers

Methods

We completed a retrospective study to identify patients who had undergone bariatric surgery in the form of a Roux-en-Y gastric bypass (RYGB) or a sleeve gastrectomy (SG) from 2000-2014. From this cohort, we identified patients who were placed on weight loss pharmacotherapy post-operatively for inadequate weight loss or weight regain. We extracted key demographic data, medical history, and examined weight loss in response to surgery and after the initiation of weight loss pharmacotherapy.

Results

319 patients (RYGB= 258 and SG= 61) met inclusion criteria for analysis. More than half (54%, n=172) of all study patients lost ≥ 5% (7.2 to 195.2 lbs) of their total body weight with medications after surgery. There were several high responders with 30.3% of patients (n=96) and 15% (n=49) losing ≥ 10% (16.7 to 195.2 lbs) and ≥15% (25 to 195.2 lbs) of their total body weight, respectively, Topiramate was the only medication which demonstrated a statistically significant response for weight loss with patients being twice as likely to lose at least 10% of their weight when placed on this medication (OR=1.9, p=0.018). Regardless of the postoperative

BMI, patients who underwent RYGB were significantly more likely to lose ≥ 5% of their total body weight with the aid of weight loss medications.

Conclusions

Weight loss pharmacotherapy serves as a useful adjunct to bariatric surgery in patients with inadequate weight loss or weight regain.

Key words: obesity, bariatric surgery, weight regain, inadequate weight loss, obesity co-morbidities

Introduction

Obesity is the most prevalent chronic disease in the United States. Over 91 million children and adults meet criteria for obesity denoted by a body mass index (BMI) at or above the 95th percentile of the sex-specific Centers for Disease Control and Prevention (CDC) BMI-for-age growth charts for children and adolescents (aged 2 to 20 years old) and a BMI ≥ 30 (kg/m^2) in adults.[1] Due to the pronounced disease burden, linkage to several co-morbidities including type 2 diabetes mellitus, hypertension, obstructive sleep apnea (OSA), non-alcoholic fatty liver disease (NAFLD), several cancers, a host of other diseases, and its subsequent impact on quality of life, morbidity, and mortality, there is a need for both prevention and treatment.[2]

To date, bariatric surgery has been the most effective treatment for persons with moderate (BMI 35- 39.9) and severe obesity (BMI ≥ 40).[3-5] Patients often experience complete resolution or improvement of obesity related co-morbidities, and there is a dramatic reduction in health care costs.[6] Unfortunately, there is often inadequate weight loss or weight regain after bariatric surgery, and inadequate weight loss is generally defined as an initial loss of <50% of excess body weight loss (EWL) in bariatric surgery. [7, 8]

Weight regain is multi-factorial and categorized as patient specific (i.e. psychiatric, physical inactivity, endocrinopathies/metabolic, genetic, gender, race/ethnicity, and dietary non-

compliance) and operation specific.[9-18] Concomitantly, there is often a re-emergence of co-morbidities that initially improved after bariatric surgery.[19, 20] While revisional bariatric surgery has been employed in this patient population[21], these often fail, require re-operation, and are associated with complications.[22-24] Endoscopic pouch plications, stoma reductions and sclerotherapy have been utilized to treat inadequate weight loss and weight regain in bariatric surgery patients[25, 26], but this too has proven ineffective long term.[27, 28]

Studies that have been conducted in the bariatric surgery population show that significant weight regain (≥15% gain of initial weight loss post bariatric surgery) occurs in 25-35% of persons who undergo surgery 2-5 years after their initial surgical date.[18, 29, 30] There have been a few small studies (<15 patients) conducted on patients who have undergone bariatric surgery that demonstrate the utility of weight loss medications for inadequate weight loss or weight regain,[31, 32] but this practice has been subjected to minimal investigation at this time. In our current study, we performed a retrospective analysis to discern the utility of weight loss medications as an adjunct to bariatric surgery. To our knowledge, our multi-center study is the largest study to date to investigate this practice. Since weight regain and inadequate weight loss are common in patients who undergo bariatric surgery, there is a need for a range of therapeutic options to treat this patient population. We hypothesize that weight loss medications are a useful tool to confer additional weight loss after weight loss surgery. We seek to determine the utility of weight loss medications and determine which medication(s) have the highest efficacy after weight loss surgery.

Methods

Study Sample and Data Collection

Our study sample consisted of patients who had undergone a roux-en-y gastric bypass (RYGB) or sleeve gastrectomy (SG) from November 2000-June 2014 at two academic centers and received subsequent weight loss medications. All patients who underwent the aforementioned procedures and were placed on medication were considered. Eligible patients had a primary weight loss surgery at two major academic medical centers with at least 12 months of documented post-op follow up. Patients were excluded if they underwent surgery for complications within 6 months of their primary weight loss surgery, had a revision surgery, or had insufficient follow up. The clinical data was extracted from the medical record by two research groups. The Institutional Review Boards at both academic centers approved the study.

Measures

Demographic and Clinical Factors

We extracted the following data from the patient record: 1) type of surgery (RYGB or SG), 2) date of operation, 3) date of birth, 4) gender, 5) race/ ethnicity (Caucasian, Hispanic, African-American, Asian, or Other), 6) pre-operative obesity co-morbidities (hypertension, type 2 diabetes mellitus, obstructive sleep apnea (OSA), dyslipidemia, and non-alcoholic fatty liver disease (NAFLD)), 7) pre-operative use of weight loss medications, 8) body mass index (based on initial height and weight at following time points): a) pre-surgery, b) at plateau post-surgery, c) at the start of weight loss medication, d) at plateau post-weight loss medication, and e) current, 9) time to achieve plateau weight post-surgery, 10) post-operative resolution of obesity co-morbidities, 11) continued use of weight loss medication(s), 12) psychiatric co-morbidity

(anxiety, depression, bipolar disorder), 13) use of psychotropic medications pre-surgery, and 14) use of psychotropic medications post-surgery.

Weight Loss Medications

We evaluated 15 medications that are prescribed by obesity medicine physicians within our centers which include: 1) phentermine, 2) topiramate, 3) zonisamide, 4) metformin, 5) bupropion, 6) orlistat, 7) sibutramine, 8) liraglutide, 9) exenatide, 10) pramlinitide, 11) naltrexone, 12) lorcaserin, 13) phentermine/topiramate, 14) canagliflozin, and 15) bupropion/naltrexone. Of the medications evaluated, some have received FDA approval for short term (i.e. phentermine) or long term use (i.e. phentermine/topiramate, lorcaserin, bupropion/naltrexone, liraglutide, and orlistat) for weight loss while others were used off-label (i.e. topiramate, zonisamide, metformin, bupropion, exenatide, pramlinitide, naltrexone, and canagliflozin). While sibutramine was withdrawn from the market in October 2010, we included this drug in our study as its approval corresponded with a portion of our study period.

Lifestyle Factors

All patients who were prescribed medications in this retrospective study were encouraged to engage in healthy lifestyle behaviors such as consuming foods with high nutritional value, complying with post-operative vitamin and mineral supplementation, and engaging in purposeful physical activity as recommended in the 2013 American Association of Clinical Endocrinologists (AACE)/ The Obesity Society (TOS)/ American Society for Metabolic and Bariatric Surgery (ASMBS) guidelines.[33]

Primary End Points

Four co-primary end points were evaluated at the weight plateau after medication administration: (1) relative change in body weight; (2) the proportion of patients losing at least

5% of post surgical body weight; (3) proportion losing at least 10% of post surgical weight, and patients losing at least 15% of post surgical weight. Secondary efficacy end points included changes in BMI and resolution of obesity related co-morbidities (hypertension, type 2 diabetes mellitus, OSA, dyslipidemia, and NAFLD). We defined resolution of obesity related co-morbidities as: 1) hypertension: no longer requiring medication to maintain a normal blood pressure of <120/80, 2) type 2 diabetes mellitus- hemoglobin A1C of <6.5, 3) OSA- no longer requiring CPAP as assessed by overnight polysomnography, 4) dyslipidemia- normalization of lipid values without lipid lowering therapy, and 5) NAFLD- normalization of liver function tests (LFTs).

Statistical Analysis

Data collected from electronic medical records were converted into variables for analysis. Patient demographics, preoperative baseline characteristics, and patient weight histories at three distinct time periods (nadir weight after surgery before medical treatment, at initiation of medical therapy with weight loss medications, and at nadir weight post medical treatment) were summarized with descriptive statistics overall and by surgical cohort Roux en Y gastric bypass (RYGB) and sleeve gastrectomy (SG). We defined the treatment period as time between date weight loss medical therapy was initiated to the date when nadir weight is achieved with therapy. We stratified patients who started weight loss medication treatment at their plateau weight versus those who started medication after weight regain occurred. Plateau weight was defined as within 3% of nadir weight achieved after bariatric surgery.

Logistic regression analyses were performed to build a model with medications used over the treatment period as our candidate predictor variables for our three binary outcomes of 5%, 10%, and 15% weight loss. We adjusted for the type of surgery performed and their BMI at start

of medication by including them as covariates in our model.We then performed logistic regression analyses with candidate predictor variables based on our demographic and baseline characteristics. Odds ratios and corresponding p-values were estimated. All analyses were performed in Stata software (Version 14.1 of the Stata/IC System for Windows, StataCorp LP, College Station, TX, USA 77845).

Results

Participants

Baseline characteristics of study patients are denoted in Table 1. Of the 5110 patient records that were reviewed, 319 (6.2%) met criteria for inclusion. Patients were predominantly female (n=247, 77%), Caucasian (n=231, 72.4%), and had an age from 20-73 years (mean= 45). At the time of surgery, RYGB patients had higher mean BMI, (49.1 kg/m^2, SD=9.0) vs. (45.0 kg/m^2, SD=7.8), higher percentage of obesity related co-morbidities, took longer to reach their weight plateau after surgery, and were less likely than SG patients to have been prescribed weight loss medications prior to surgery. At the start of medication as denoted in Table 2, the mean weight and BMI of RYGB (BMI=36.8, SD=6.3) and SG (BMI= 37.5 kg/m^2, SD=7.4) were similar, but RYGB patients had a longer time elapse between surgery (59.3 months, SD=36.7) and the start of medication when compared to patients who had a SG (23.2 months, SD=15.3). At the nadir weight post weight loss medication, the mean BMI was similar between the RYGB (BMI=35.2 kg/m^2, SD=6.2) and SG (BMI=34.3 kg/m^2, SD=6.96).

Weight Loss Medications and Response

A majority of study patients underwent RYGB (80.9%, n=258), but patients in both groups were often trialed on several medications over the course of treatment (Supplemental Table 1). The average number of medications for study patients was 2. Patients were more likely

to be prescribed medications after weight regain (78.5%, n=249) had occurred than at their plateau (21.5%, n=68) (Table 3). However, patients that were prescribed medications at their plateau had a higher cumulative total body weight loss (32.3%) than those who were prescribed medication after weight regain (26.8%) (p=0.486). More than half (56%, n=178) of all study patients lost ≥ 5% of their post-surgical total body weight with treatment. There were also several high responders to medication after surgery with 30.1% of patients (n=96) and 16% (n=51) losing ≥ 10% and ≥15% of their post- surgical total body weight, respectively (Table 3). Figure 1, shows an example of a patient who achieved 26% of total body weight loss (TBWL) 12 months after a RYGB. The patient achieved a nadir BMI of 33 and had weight regain of >6.5% of her total body weight lost with an increase in BMI to 36. With the use of weight loss medications (topiramate and phentermine), she has surpassed her nadir weight loss achieved with weight loss surgery and has a current BMI of 26.

The most frequently prescribed medications were topiramate, phentermine, metformin, bupropion, and zonisamide (Supplemental Table 2). In our model which was adjusted for type of surgery (RYGB versus SG) and BMI at the start of medications, topiramate was the only medication which demonstrated a statistically significant response for weight loss with patients being twice as likely to lose at least 10% of their post- surgical weight when placed on this medication (OR=1.9, p=0.018) (Table 4). The mean weight loss in patients who were prescribed topiramate was 20.2 lbs (SD=24.5) whereas patients who were not prescribed topiramate had a mean weight loss of 13.99 lbs (SD=13.6). We did not find that the number of medications prescribed over the treatment course to be a significant factor in the percentage of total body weight loss (Supplemental Tables 3 and 4)

Predictors of Weight Loss Medication Response

We evaluated predictors of response to weight loss medications, and we found that patients who underwent RYGB were more likely to lose weight compared to those who underwent SG (Table 5). Regardless of the postoperative BMI, patients who underwent RYGB were significantly more likely to lose ≥ 5% of their post- surgical total body weight with the aid of weight loss medications (OR=2.86, p=0.001). Females were also more likely to lose ≥ 5% (OR=1.81, p=0.031). For every unit increase in BMI based upon preoperative weight, there was a higher likelihood of postoperative response to weight loss medication. Patients who had one obesity co-morbidity at the time of surgery were significantly less likely to lose ≥ 15% of their post-surgical total body weight with the use of medications after surgery (OR=0.16, p=0.014). Persons who had obstructive sleep apnea (OSA) were significantly less likely to lose ≥10% of their post-surgical total body weight (OR=0.45, p=0.005). Persons who had a history of psychiatric co-morbidity were more likely to lose ≥15% of their post- surgical total body weight (OR=1.4, p=0.002). Of note, type 2 diabetes was not a predictor of weight loss response with medications after surgery.

Discussion

The principal finding in our study is that many subjects who received weight loss medication after bariatric surgery had an additional weight loss benefit. The mean of this added weight loss was -7.6% (17.8 lbs) of total post-surgical body weight. After further stratification, we found that subjects who were prescribed medication at weight plateau lost a similar amount of weight compared to those who were prescribed medication after weight regain, (-6.9% or 16.1 lbs and - 7.7% or 18.2 lbs) consistent with findings reported in previous literature.[27, 34-36] Consequently, total body weight loss percentage from pre-operatively was higher in patients who were prescribed medications at their plateau than in those subjects who were prescribed

medication after weight regain had occurred (32.3% vs 26.8% P=0.486). This suggests that the optimal time to initiate weight loss medication after bariatric surgery is once the patient has reached their weight plateau. Of the 317 study subjects included in our analysis, more than half achieved meaningful weight loss with treatment with weight loss medication. In particular, after starting weight loss medications, 56% of study subjects achieved ≥5% additional weight loss, 30% achieved ≥ 10%, and 16% of study subjects achieved ≥ 15% additional weight loss. Losses of this magnitude are considered clinically significant because of their reduction of CVD risk factors, including triglycerides levels, blood pressure, and blood glucose levels.[37, 38]

Weight loss medications assist patients with obesity (BMI ≥ 30 kg/m^2) and patients who are overweight (i.e, BMI ≥ 27 kg/m^2) with obesity associated co-morbidities to achieve long term weight loss.[39] To date, there is a paucity of published literature on utilizing weight loss medication as an adjunct to bariatric surgery for individuals who have had inadequate weight loss or for individuals who have regained weight after undergoing bariatric surgery. We are aware of only a few studies that have examined this issue. [32, 34-36]

In a prospective study examining the use of phentermine and fenfluramine in combination in individuals who regained weight 18 months after RYGB or biliopancreatic diversion (BPD), Jester et al. reported that weight loss ranged from 4.5 to 22.7 kg, over a 12-week course of treatment, corresponding to 8-65% of excess body weight (EWL).[34] Another retrospective study by Schwartz et al., examined the use of phentermine and combination phentermine/topiramate in individuals who underwent RYGB or laparoscopic gastric banding (LAGB) who desired additional weight loss one year after their surgical procedure.[35] In their study, the group reported that at 90 days, weight loss was 6.35 kg (12.8% EWL) and 3.81 kg (12.9% EWL) in the phentermine and phentermine/topiramate groups

respectively.[35] Furthermore, in a retrospective study, Pajecki et al. examined the use of GLP-1 agonist liraglutide over a period of 12.5±4 weeks in 15 individuals who had >15 % of weight regain 2 years after bariatric surgery. The group reported weight losses of 2-18 kg (-7.5±4.3 kg).[27] Finally, Zilberstein et al, in a prospective study using topiramate for 3 months after LAGB in 16 patients with binge eating disorder reported a mean increase in EWL from 20.4% to 34.1% without the need for band readjustment.[36]

In our multi-center retrospective study, we examined subjects that underwent either a RYGB or sleeve gastrectomy (SG) - a group that has not been studied before. Additionally, in our cohort, subjects were prescribed several weight loss medications which helped us further delve into the efficacy of the different anti-obesity pharmacotherapy available. We found that the use of topiramate, the most commonly prescribed medication in our cohort, was often associated with additional weight loss of ≥ 10 % of total body weight. We cannot directly compare these findings to the reported outcomes from Schwartz et al. or Zilberstein et al. since the first group only compared combination phentermine/topiramate to phentermine and did not use topiramate as a monotherapy.[35, 36] Further, the second group used topiramate only in patients with binge eating disorder after undergoing LAGB.[36] While a number of patients in our cohort did suffer from binge eating disorder, we did not look at that subgroup specifically. In addition, we did not include any patients that have underwent LAGB.[36] The EQUATE trial,[40] a RCT that compared the use of topiramate and phentermine monotherapy to combination phentermine/topiramate over a period of 28 weeks, found that combination therapy produced significantly greater weight loss than either component as a monotherapy. However, it is important to point out that the subjects in the EQUATE trial were individuals with obesity who did not undergo bariatric surgery.[40] The physiological changes that occur with bariatric

surgery may have an influence on how subjects respond to different weight loss pharmacological agents.[41]

When we evaluated predictors for weight loss, we found that subjects who have undergone RYGB were more likely to achieve greater weight loss when compared to subjects who have undergone a SG. These findings are similar to previously published data.[42] Other positive predictors for greater response to weight loss medications after bariatric surgery were a higher BMI prior to surgery and the history of a psychiatric comorbidity. It is well known that a number of antidepressants and antipsychotics are associated with significant weight gain.[43-46] Studies have reported associated improvements in mood following weight loss.[47-50] Therefore, we hypothesize that the need for these potential weight promoting medications was decreased in our cohort.

Due to the retrospective nature of our study, there are several limitations which include missing patient data, the lack of a control group for comparison, and the inability to account for the length of time that patients were placed on weight loss medications as longer medication duration may have accounted for greater weight loss. Additionally, interpretation of weight loss in our cohort should be approached cautiously due to the presence of confounding factors including concurrent treatment with weight promoting medications, co-morbidities which might predispose to weight gain such as obstructive sleep apnea, and there are multiple indications for which many of the medications we evaluated for their weight loss potential may have been prescribed which may have lead to potential inferiority of one medication versus another in our analysis. Furthermore, in our analysis we were not able to take into account the effect of diet and exercise on weight, since our subjects were not following a predefined structured program.

Finally, there were significant differences in the frequency of prescriptions of weight loss medications where some medications were prescribed more than others.

Despite our limitations, our study had several strengths which include a large sample size from two academic study sites. Other strengths include our inclusion of patients who had undergone the two most common procedures in the US, RYGB and SG, and our long duration of follow up. This long follow up has helped us further asses the long term efficacy of weight loss medication after bariatric surgery. Finally, the patients in our cohort received several anti-obesity medication which was beneficial in helping us to determine the potential efficacy of weight loss medications and the individual variability in response to the different agents.

Conclusion

Our study demonstrates that weight loss medications are a useful tool for patients with inadequate weight loss or weight regain after bariatric surgery. While patients who underwent RYGB were more likely to have more weight loss with the use of weight loss medications, both groups demonstrate benefit from their use. Our data also suggest that prescribing weight loss medication before weight regain occurs (at weight plateau) may result in greater amount of total weight loss from pre-operatively. Further prospective studies should be performed to detect the optimal time at which to start medications after bariatric surgery.

Disclosures/ Conflicts of Interest

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements, or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Figure 1: Demonstration of the utility of weight loss mediation after bariatric surgery in a RYGB patient

Table 1: Demographic Data and Baseline Characteristics

Table 2: Weight History at Postoperative Nadir Weight, at Start of Medical Weight Loss Treatment, and Nadir Weight after Treatment

Table 3: Mean Weight Change after Treatment by Subgroup

Table 4: Logistic Regression Analysis with Most Commonly Used Medication as Predictor

Table 5: Logistic Regression by Predictor Variable

Table 1. Demographic Data and Baseline Characteristics

Variable	All Patients	Surgery Type	
		Sleeve Gastrectomy	Roux – En – Y Gastric Bypass
	n=319	n= 61 (19.1%)	n=258 (80.9%)
Gender			
Female	247 (77%)	46 (75%)	201 (78%)
Male	72 (23%)	15 (25%)	57 (22%)
Age at Surgery (Years)			
Mean	45	47	45
Median	47	49	46
Range	20-73	20-72	20-73
Race/Ethnicity			
White	231 (72.4%)	42 (68.9%)	189 (73.2%)
Hispanic	34 (10.7%)	4 (6.6%)	30 (11.6%)
African-American	30% (9.4%)	10 (16.4%)	20 (7.8%)
Asian	1 (0.3%)	1 (1.6%)	0
Other/Declined to state	23 (7.2%)	4 (6.6%)	19 (7.4%)
Preoperative Characteristics			
Mean Weight (lbs)	296 (SD=66)	274 (SD=57)	301 (SD=67)
Mean BMI (lbs/inches^2)	48.3 (SD=8.9)	45 (SD=7.8)	49.1 (SD=9.02)
Obesity Class –			
Class I (BMI 30-34.9)	4 (1%)	0	4 (2%)
Class II (BMI 35-39.9)	53 (17%)	19 (31%)	34 (13%)
Class III (BMI >/= 40)	262 (82%)	42 (69%)	220 (85%)
Comorbid Conditions (Individual)			
Hypertension	177 (43.3%)	31 (50.8%)	146 (56.6%)
Type II Diabetes	116 (36.4%)	20 (32.8%)	96 (37.2%)
OSA	106 (33.2%)	20 (32.8%)	86 (33.3%)
Dyslipidemia	184 (56.7%)	34 (55.7%)	150 (58.1%)
NAFLD	235 (73.7%)	33 (54.1%)	202 (78.3%)
Mental Illness	164 (51.4%)	23 (37%)	141 (54.7%)

**n=306, missing data

***n=318, missing data

^n=317

Abbreviations- OSA- obstructive sleep apnea; NAFLD- non-alcoholic fatty liver disease

Table 2. Post Operative Patient Characteristics and Weight History after Surgery, before Medications, and after Treatment

Comorbid Conditions (Individual)	All Patients n=319	Surgery Type: Sleeve Gastrectomy n= 61 (19.1%)	Surgery Type: Roux – En – Y Gastric Bypass n=258 (80.9%)
Hypertension	68 (21.3%)	11 (18.0%)	54 (20.9%)
Preop patients (n=177) who achieved resolution (%)	112 (63.3%)	20 (64.5%)	92 (63%)
Type II Diabetes	54 (16.9%)	12 (19.7%)	42 (16.3%)
Preop patients (n=116) who achieved resolution (%)	62 (53.4%)	8 (40.0%)	54 (56.3%)
OSA[a] (n=318)	47 (14.8%)	4 (6.6%)	43 (16.7%)
Preop patients (n=106) who achieved resolution (%)[a]	59 (55.7%)	16 (80.0%)	43 (50.6%)
Dyslipidemia	104 (32.6%)	17(27.9 %)	87 (33.7%)
Preop patients (n=184) who achieved resolution (%)	88 (47.8%)	18 (52.9%)	70 (46.7%)
NAFLD	187 (58.6%)	24 (39.3%)	163 (63.2%)
Preop patients (n=235) who achieved resolution (%)	51 (21.7%)	9 (27.3%)	42 (20.8%)
Mental Illness[b] (n=314)	152 (48.4%)	18 (29.5%)	134 (51.9%)
Preop patients (n=164) who achieved resolution (%)[b]	9 (5.5%)	3 (13.0%)	6 (4.3%)
PostOp Nadir Weight Before Medication	**All Patients n=319**	**Surgery Type: Sleeve Gastrectomy n= 61 (19.1%)**	**Surgery Type: Roux – En – Y Gastric Bypass n=258 (80.9%)**
Mean BMI (lbs/inches^2) ***	33.3 (SD=6.5)	35.1 (SD=6.2)	32.9 (SD=6.5)
Mean Time to Achieve Nadir (Months)**	15.7 (SD=10.8)	10.8 (SD=6.6)	16.8 (SD=11.3)
Average Wt. Loss at Nadir Weight (lbs)***	91.9 (SD=39.7)	60 (SD=26.5)	100 (SD=38.5)
At Start of Medication			
Mean weight (lbs.)^	229.4 (SD=53.3)	225.3 (SD=49.2)	230.3 (SD=54.3)
Mean BMI (lbs/inches^2)	37.4 (SD=7.2)	36.8 (SD=6.3)	37.5 (SD=7.4)
Time elapsed between surgery and start of medication (months)			
Mean (SD)	52.4 (SD=36.7)	23.2 (SD=15.3)	59.3 (SD=36.7)
Min	2.1	2.3	2.1
Max	167	88.7	167
Post Medication Treatment – At Nadir Weight			

Mean weight (lbs.)	211. 6 (SD=50.4)	215. 5 (SD=48.9)	210.7 (SD=50.8)
Mean BMI (lbs/inches^2)	34.5 (SD=6.8)	35.2 (SD=6.2)	34.3 (SD=6.96)

**n=306, missing data

***n=318, missing data

^n=317

[a] Missing data for 1 patient

[b] Missing data for 5 patients

Abbreviations: BMI- Body Mass Index

Table 3. Mean Weight Change after Treatment by Subgroup

Subgroup	Weight Change		P-value	95 % CI
	(lbs)	(%)^		
All patients (n=317)*	-17.8 (SD=21.1)	-7.6 (SD=7.8)		
Patients prescribed medication at weight plateau (n=68, 21.5%)~	-15.8 (SD=27.8)	-6.9 (SD=8.8)	0.3901[a]	(-20.1, -15.4)
Patients prescribed medication at weight regain (n=249, 78.5%)~	-18.3 (SD=19.0)	-7.7 (SD=7.6)		
Surgery Type				
Sleeve Gastrectomy (n=61)	-9.8 (SD=13.5)	-4.3 (SD=5.7)	0.001[a]	(-20.1, -15.4)
Roux-En-Y Gastric Bypass (n=256)	-19.7 (SD=22.2)	-8.3 (SD=8.1)		
Patients who lost ≥ 5% total body weight with treatment (n=172, 54%)	-29.7 (SD=21.9)	-12.6 (SD=7.2)		
Patients who lost ≥ 10% total body weight with treatment (n=96, 30.3%)	-40.7 (SD=23.7)	-17.1 (SD=6.7)		
Patients who lost ≥ 15% total body weight with treatment (n=49, 15.4%)	-52.9 (SD= 27.7)	-22.02(SD= 6.2)		

*Missing data for 2 patients

~ Plateau defined as weight that is within 3% above or below nadir weight postoperatively before medication. If above 3%

patient defined as starting medication at weight regain

^Calculated this number as [(weight at nadir post medications) – (weight at start of medication)]/ (weight at start of medication)

[a] Two-sample t-test of means conducted for post-treatment weight change (lbs.)

Abbreviations: SD- standard deviation

Table 4. Logistic Regression Analysis with Most Commonly Used Medication as Predictor

Medication	Number of Patients (%)	Treatment Period Weight Loss >=5% OR	P value	95%CI	>=10% OR	P value	95%CI	>=15% OR	P value	95%CI
Topiramate	194 (60.8%)	1.03	0.901	(.65, 1.64)	1.9	0.018	(1.1, 3.2)	2.08	0.041	(1.03, 4.2)
Phentermine	121 (37.9%)	1.18	0.504	(.73, 1.89)	1.09	0.729	(.66, 1.82)	1.42	0.27	(.63, 1.77)
Metformin	123 (38.6)	1.01	0.98	(.63, 1.61)	1.15	0.583	(.70, 1.90)	0.96	0.91	(.51, 1.8)
Bupropion	75 (23.5%)	0.92	0.776	(.54, 1.58)	1.1	0.753	(.62, 1.93)	1.23	0.55	(.62, 2.46)
Zonisamide	65 (20.4%)	1.15	0.643	(.64, 2.04)	1.03	0.914	(.57, 1.89)	0.97	0.94	(.46, 2.07)

** Model is adjusted for type of surgery and BMI at start of medications

Abbreviations: OR- Odds Ratio

Table 5. Logistic Regression By Predictor Variable

Predictor	Treatment Period Weight Loss >=5% OR	P Value	95% CI	R^2	>=10% OR	P value	95% CI	R^2	>=15% OR	P value	95% CI	R^2
Surgery Type												
Gastrectomy (Reference)												
RYGB	2.96	0.0001	(.44, 1.97)	0.0323	3.47	0.002	(1.58, 7.62)	0.0307	4.23	0.019	(1.27, 14.1)	0.0291
RYGB[a]	2.97	0.0001	(1.64, 5.37)	0.0404	3.4	0.002	(1.55, 7.54)	0.0307	4.18	0.02	(1.25, 13.9)	0.0323
RYGB[b]	2.92	0.001	(1.54, 5.51)	0.0324	3.5	0.003	(1.53, 8.0)	0.0307	4.6	0.016	(1.33, 15.9)	0.0301
Gender[c]												
Male (Reference)												
Female	1.79	0.031	(1.05, 3.05)	0.0108	1.7	0.093	(0.92, 3.14)	0.0077	1.37	0.431	(.63, 2.97)	0.0024
Female[C]	1.75	0.04	(1.03, 2.98)	0.0427	1.8	0.034	(1.05, 3.1)	0.0427	1.35	0.457	(.61, 2.9)	0.0312

Age												
20 – 30 (Reference)												
31 - 50	1.28	0.28	(0.82, 1.99)	0.0027	0.97	0.894	(0.6, 1.56)	0.0000	1.08	0.817	(.55, 2.12)	0.0023
51 +	0.82	0.406	(0.52, 1.3)	0.0016	0.94	0.793	(0.57, 1.54)	0.0002	0.92	0.817	(.47, 1.81)	0.0023
Weight when Medications Prescribed												
At Plateau (Reference)												
At Regain	1.44	0.18	(.84, 2.5)	0.0041	1.15	0.635	(0.64, 2.09	0.0006	1.08	0.847	(.51, 2.29)	0.0001
At Regain[a,d]	0.98	0.948	(.54, 1.78)	0.0527	0.76	0.412	(.39, 1.46)	0.0463	0.71	0.409	(.32, 1.6)	0.0372
Race/Ethnicity												
Caucasian (Reference)												
All Other	1.59	0.069	(0.96, 2.64)	0.0077	0.95	0.859	(0.56, 1.63)	0.0001	1.18	0.628	(.61, 2.29)	0.0008
BMI Class – At baseline preoperatively												
For 1 unit increase	1.02	0.1	(1.0, 1.05)	0.0063	1.03	0.052	(1.0, 1.05)	0.0096	1.03	0.097	(1.0, 1.06)	0.0097
Class I (Reference)												
Class II	0.54	0.043	(0.30, .98)	0.0095	0.55	0.102	(0.27, 1.12)	0.0075	0.52	0.19	(.19, 1.38)	0.0072
Class III	1.53	0.15	(0.86, 2.72)	0.0048	1.79	0.097	(0.9, 3.56)	0.0076	1.68	0.26	(.68, 4.17)	0.0051

Table 5. (Continued) Logistic Regression By Predictor Variable

	Treatment Period Weight Loss											
	>=5%				**>=10%**				**>=15%**			
Predictor	**OR**	**P Value**	**95% CI**	**R^2**	**OR**	**P Value**	**95% CI**	**R^2**	**OR**	**P Value**	**95% CI**	**R^2**
Comorbities – Number present at Preop[d]												
0 (Reference)												
1	1.03	0.929	(0.55, 1.91)	0.0428	0.9	0.761	(0.46, 1.77)	0.0383	0.29	0.045	(.08, .97)	0.0510
2	1.14	0.66	(0.65, 2.0)	0.0432	1.19	0.566	(0.66, 2.14)	0.0388	1.38	0.38	(.67, 2.81)	0.0339
3	0.70	0.19	(0.41, 1.19)	0.0467	0.62	0.116	(0.34, 1.13)	0.0447	0.87	0.721	(.42, 1.82)	0.0317
4	0.8	0.65	(0.51,	0.04	0.7	0.453	(0.44,	0.03	0.9	0.78	(.43,	0.03

	8		1.52)	32	9		1.45)	95		5	1.91)	15
5	2.01	0.208	(0.68, 5.99)	0.0466	2.06	0.159	(0.75, 5.6)	0.043	1.61	0.431	(.49, 5.23)	0.0333
Type of Comorbidity[d]												
HTN	0.86	0.526	(0.54, 1.37)	0.0437	0.79	0.347	(0.48, 1.3)	0.0403	0.8	0.494	(.42, 1.5)	0.0329
Diabetes	1.36	0.212	(0.84, 2.2)	0.0463	0.9	0.692	(0.54, 1.51)	0.0384	1.02	0.944	(.54, 1.95)	0.0312
OSA	0.77	0.302	(.47, 1.26)	0.0452	0.47	0.01	(0.27, 0.84)	0.0559	0.81	0.541	(.40, 1.6)	0.0326
Dyslipidemia	0.83	0.434	(0.52, 1.32)	0.0441	1.16	0.56	(0.7, 1.9)	0.0389	1.22	0.543	(.64, 2.3)	0.0326
NAFLD	0.98	0.946	(0.58, 1.67)	0.0428	1.21	0.53	(0.67, 2.17)	0.039	1.25	0.573	(.58, 2.7)	0.0324
Mental Illness	1.04	0.878	(0.65, 1.64)	0.0428	1.41	0.177	(0.86, 2.32)	0.0427	1.3	0.019	(1.05, 1.62)	0.0526
Time to achieve nadir weight Post-Op before meds[d]~												
<=12 months (Reference)												
13-36 months	0.97	0.91	(0.61, 1.56)	0.0428	1.31	0.29	(0.80, 2.15)	0.0409	1.93	0.041	(1.03, 3.61)	0.0467
>36 months	0.84	0.756	(0.29, 2.45)	0.0430	0.73	0.601	(0.22, 2.39)	0.0387	0.33	0.292	(.04, 2.59)	0.0467
BMI at start of medications (every 1 unit increase)	1.03	0.052	(1.0, 1.07)	0.0089	1.02	0.111	(.99, 1.06)	0.0065	1.02	0.291	(.98, 1.06)	0.0040

[a]Adjusted for BMI at Start of Meds

[b]Adjusted time elapse between surg date and start of meds

[c]Adjusted for type of surgery by including as covariate

[d]Adjusted for type of surgery and gender

~n=306, missing this data for 13 patients

Abbreviations: HTN- hypertension, OSA- obstructive sleep apnea, NAFLD- non-alcoholic fatty liver disease

Figure 1 Demonstration of the utility of weight loss mediation after bariatric surgery in a RYGB patient