Engaging Pharmacotherapy and Behavioral Interventions to **Maximize Post-Procedure Weight Loss**

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September 28, 2017






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Disclosures

I will discuss off-label use of medications

I am a consultant, speaker, advisor, or receive research support from:

Aspire Bariatrics

Eisai Inc.

Ethicon Endo-Surgery Inc.

GlaxoSmithKline Consumer Healthcare LP

GI Dynamics

Novo Nordisk

Pfizer

USGI

VIVUS Inc.

Zafgen Inc.

Ownership Interest:

BMIQ

Myos Corporation

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Trends in Weight Regain Following Roux-en-Y Gastric Bypass Surgery.

- The primary purpose of this study was to assess weight loss and occurrence of weight regain among patients who underwent Roux-en-Y gastric bypass (RYGB) using categorical analysis.

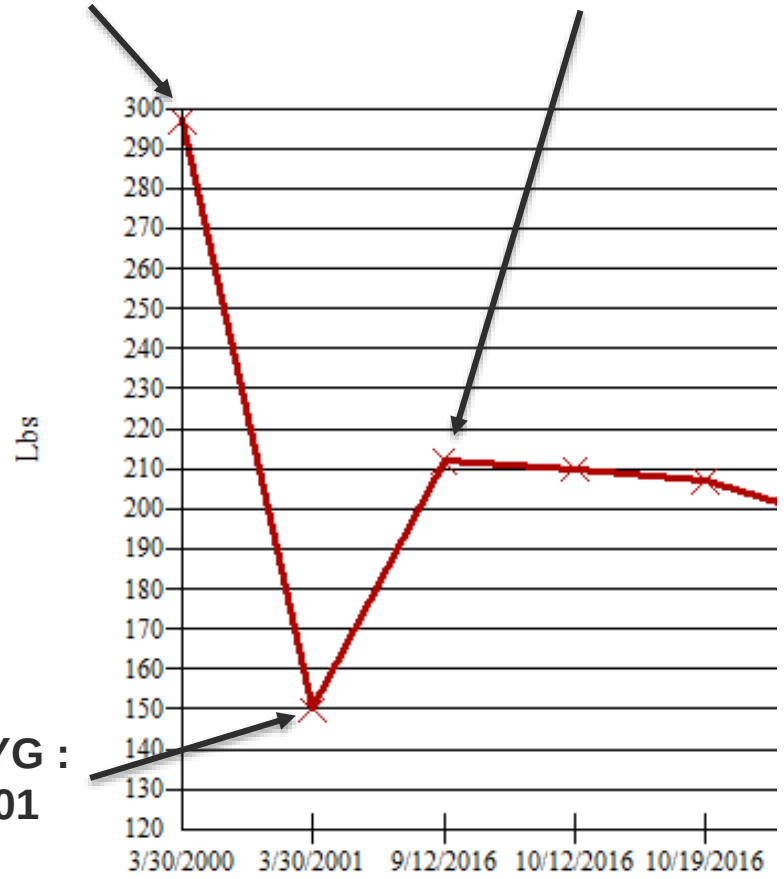
- Study subjects were mostly Caucasian (56.7 %) and female (80.3 %). Participants were stratified a priori into four cohorts based on percent of weight loss at 1 year, <25 % (n = 39), 25-30 % (n = 51), 30-35 % (n = 73), and >35 % (n = 113).
- **RESULTS:**
- The mean weight regain for all patients was 23.4 % of maximum weight loss. Using categorical analysis, mean weight regain in the <25, 25-30, 30-35, and >35 % weight loss cohorts was 29.1, 21.9, 20.9, and 23.8 %, respectively. Excessive weight regain, defined as ≥25 % of total lost weight, occurred in 37 % of patients.
- **CONCLUSION:**
- **Weight gain is a common complication following RYGB surgery. Despite the percentage of weight loss over the first year, all cohort patient groups regained on average between 21 and 29 % of lost weight. Excessive weight gain was experienced by over one third of patients. Greater initial absolute weight loss leads to more successful long-term weight outcomes.**

Cooper TC1, Simmons EB, Webb K, Burns JL, Kushner RF.
Obes Surg. 2015 Aug;25(8):1474-81. doi: 10.1007/s11695-014-1560-z.

Patient AS: RNYGB in 2001 at 134 kg, low 68kg, regained to 94 kg with increased glucose in 2016

RNYG :
295 lbs - 134kg 2001

Regain post - RNYG : 2016
207 lbs - 94 kg , A1c 8.4



Minimum post - RNYG :
150 lbs – 68 kg - 2001

Approach to patient who gains

- "Congratulate them for having the courage to come in".
- Is the weight gain:
  - **Anatomical**
  - **Medical, drug-induced**
  - **Behavioral / Dietary.**
- It is extremely helpful if the patient brings a food journal to the visit.

Lloyd Stegemann, MD, at obesityaction.org

Trends in Weight Regain Following Roux-en-Y Gastric Bypass (RYGB) Bariatric Surgery.

- The primary purpose of this study was to assess weight loss and occurrence of weight regain among patients who underwent Roux-en-Y gastric bypass (RYGB) using categorical analysis.

CONCLUSION:

- **Weight gain is a common complication following RYGB surgery. Despite the percentage of weight loss over the first year, all cohort patient groups regained on average between 21 and 29 % of lost weight. Excessive weight gain was experienced by over one third of patients. Greater initial absolute weight loss leads to more successful long-term weight outcomes.**

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Mean percent weight regain of weight lost among four cohorts stratified by year one weight loss

One year percent weight loss cohorts	*N* (%)	Mean weight regain in kilograms (%)	Standard deviation (kg)	Standard error (kg)	95 % CI
<25 %	39 (14.1 %)	11.0 (29.1)	11.4	1.8	7.3–14.7
25–30 %	51 (18.5 %)	9.7 (21.9)	7.7	1.1	7.5–11.9
30–35 %	73 (26.4 %)	10.8 (20.9)	8.9	1.0	8.7–12.9
>35 %	113 (40.9 %)	15.2 (23.8)	13.1	1.2	12.8–17.6
Total	276	12.4 (23.4)	11.2	0.7	11.1–13.8

Postoperative Behavioral Variables and Weight Change 3 Years After Bariatric Surgery LABS-2

- **Question** What are the postoperative predictors of the amount of subsequent weight loss following bariatric surgery in severely obese adults?
- **Findings** In a cohort study of 2022 post–bariatric surgery patients from 10 US hospitals in the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) study, those patients who adopted healthier eating and weight control behaviors after surgery experienced significantly greater weight loss than other patients.
- **Meaning** Addressing problematic eating and weight control behaviors, many of which are potentially modifiable, may improve weight loss substantially following bariatric surgery.

Mitchell JE et al JAMA Surg. 2016 Aug 1;151(8):752-7. doi: 10.1001/jamasurg.2016.0395.

Conclusions

- Certain weight control practices and eating behaviors can significantly influence the amount of weight loss after bariatric surgery.
- This suggests that structured programs to modify problematic eating behaviors and eating patterns following bariatric surgery should be evaluated as a method to improve weight outcomes among patients undergoing bariatric surgery.
- The results also underscore the need for health care professionals to target these behaviors in the postoperative period.

Mitchell JE et al JAMA Surg. 2016 Aug 1;151(8):752-7. doi: 10.1001/jamasurg.2016.0395.

Table 1. Modifiable Practices and Behaviors

Category	Practice or Behavior
Weight loss practices	Self-weigh at least weekly
	See nutritionist or dietitian
	See personal trainer or exercise specialist
	Keep a food diary
	Count fat grams
	Decrease fat intake
	Reduce number of calories eaten
	Use a very low-calorie diet
	Cut out between-meal snacking
	Eat fewer high-carbohydrate foods
	Eat special low-calorie diet foods
	Eat or drink meal replacements
	Increase fruits and vegetables
	Cut out sugar-sweetened beverages
Alcohol, smoking, and illegal drugs	Alcohol use disorder
	Current smoker
	Illegal drug use
Eating behaviors and problems	Eat breakfast regularly
	Eat breakfast, lunch, and dinner regularly
	Eat when feeling full, more than once a week
	Eat when not hungry, more than once a week
	Eat continuously during the day or part of the day
	Binge-eating disorder
	Loss-of-control eating
	Night eating syndrome
	Evening hyperphagia
	Night eating

- "This suggests that structured programs to modify problematic eating behaviors and eating patterns following bariatric surgery should be evaluated as a method to improve weight outcomes among patients undergoing bariatric surgery. "

JAMA Surg. 2016;151(8):752-757. doi:10.1001/jamasurg.2016.0395

How Do You Deliver a Program?

- A comprehensive delivery system for large scale implementation of an evidence based diabetes prevention and weight management intervention
- We use our own program, BMIQ
- Very low cost, can be implemented in any medical setting or online via HIPAA compliant telehealth. It is easy to implement, flexible to use, and supports patients outside of the office setting.
- Several pilots and projects, and now being used by Brigham and Women's Hospital to remotely implement a 24 site PCORI-funded, 840 subject trial using population health managers.

How BMIQ Works

Two Users

Healthcare Professional

Patient

Four Core Functions

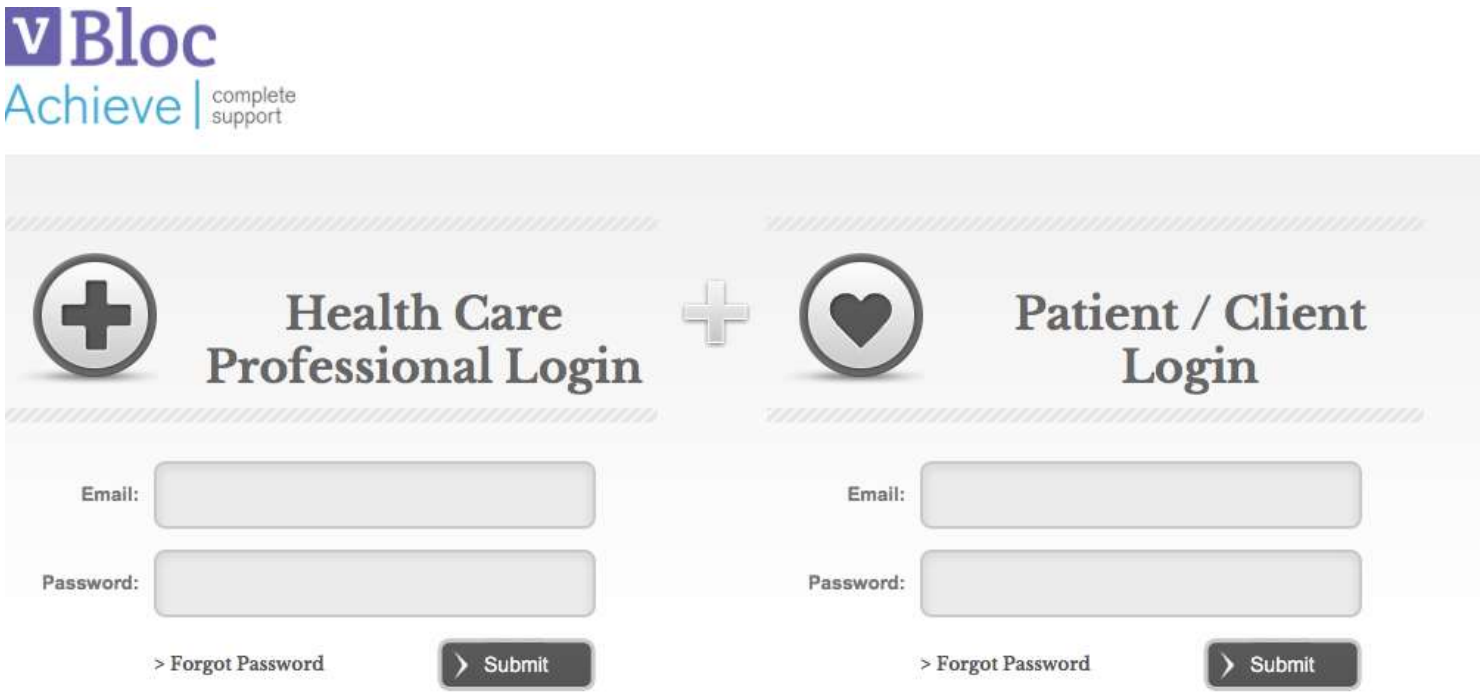
Proprietary Online Patient Assessment
Generates medical recommendation for Professional

Educational Material for Patients and Professionals
30 treatment sessions include: meal plans, patient lessons and videos in English and Spanish, professional tutorial videos, treatment guides, references, and more

Progress Monitoring Tools
Both users can track patient progress

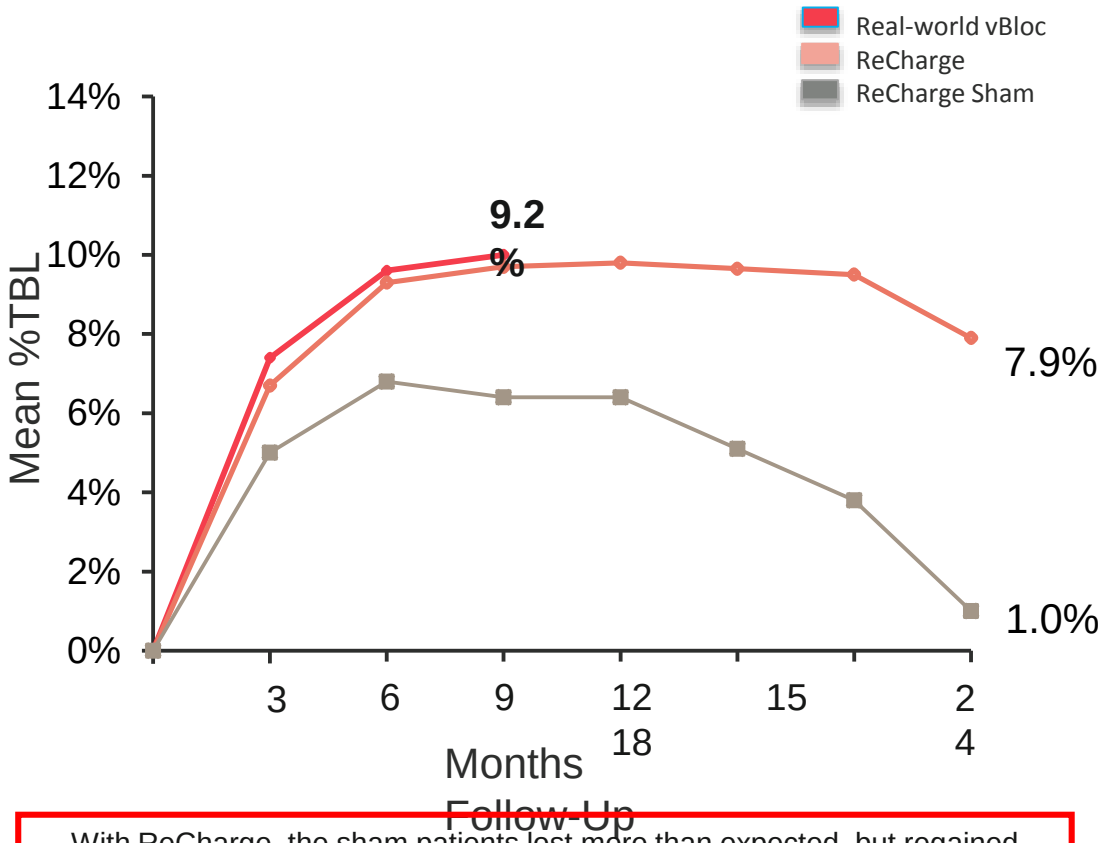
Direct Communication
Both users can directly communicate within BMIQ

User Login


vBloc
Achieve | complete support
Health Care Professional Login
Email:
Password:
> Forgot Password
Submit
Patient / Client Login
Email:
Password:
> Forgot Password
Submit

vBloc Clinical Data

Results of vBloc ReCharge FDA Trial
% Total Body Weight Loss (%TBL)



With ReCharge, the sham patients lost more than expected, but regained nearly all weight by 24 months.

Efficacious

- Achieves meaningful and sustainable weight loss

Safe

- Low complication rate (3.7%) is significantly safer than any other surgical treatment.

8. Caroline M. Apovian & Sajani N. Shah & Bruce M. Wolfe & Sayeed Ikramuddin & Christopher J. Miller & Katherine S. Tweden & Charles J. Billington & Scott A. Shikora., *Two-Year Outcomes of Vagal Nerve Blocking (vBloc) for the Treatment of Obesity in the ReCharge Trial*, OBES SURG, DOI 10.1007/s11695-016-2325-7

9. Short-Term Results for Intermittent Vagal Nerve Blocking (vBloc) in the Real World, Nonresearch Environment, ASMBS Abstract, Accepted for 2017 Fall Meeting

EnteroMedics

The Problem

- **How do you manage patients who have inadequate weight loss (<20% of total body weight loss) or weight regain (≥15% gain of initial weight loss) post bariatric surgery but don't respond to diet and behavior alone?**

Question

- Does anti-obesity pharmacotherapy work as an adjunct to bariatric surgery?

Result

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

- **Fatima C Stanford, MD, MPH, MPA,** Nasreen Alfaris, MD, MPH; Gricelda Gomez, BS; et al
- Surg Obes Relat Dis. 2017 Mar;13(3):491-500.

Demonstration of the utility of weight loss medication after bariatric surgery in a RYGB patient

Stanford, FC, et al Surg Obes Relat Dis. 2017 Mar;13(3):491-500.

Case 1:Patient AC

- 69-year-old M w obesity (BMI 35.7 kg/m^2), T2DM (HA1c 6.2) and HTN

- S/p lap band 10 years ago – lost 36 lbs, then regained all weight

- Medications :
  - Actos 45 mg daily,
  - Metformin 500 mg daily,
  - Lisinopril 40 mg daily,
  - Tricor 145 mg daily,
  - Vytorin 10-10 mg daily

- Rx:
  What would you do for AC ?

Case 1:Patient AC

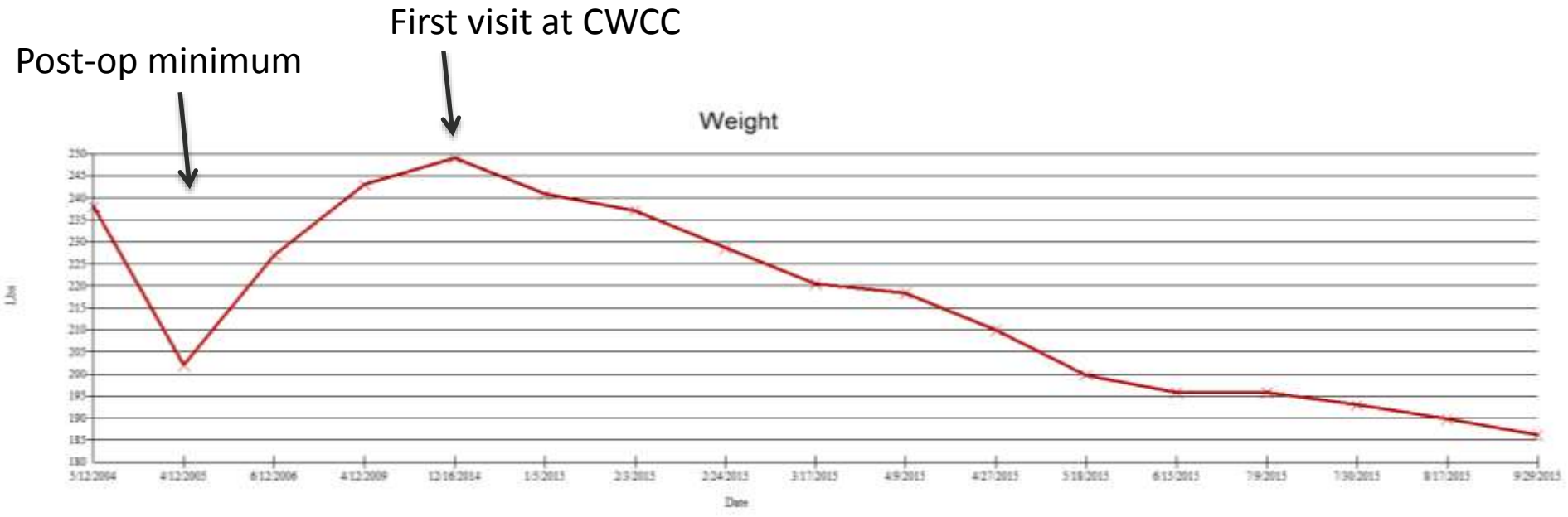
- 69-year-old M w obesity (BMI 35.7 kg/m^2), T2DM (HA1c 6.2) and HTN

- S/p lap band 10 years ago – lost 36 lbs, then regained all weight

- Medications 12/2014:
  - Pioglitazone 45 mg daily,
  - Metformin 500 mg daily,
  - Lisinopril 40 mg daily,
  - Fenofibrate 145 mg daily,
  - simva/ezetemibe 10-10 mg daily

- Rx:
  - Low glycemic index diet,
  - d/c'd Pioglitazone
  - Increased metformin to 1000 mg BID,
  - Added Liraglutide 0.6 mg daily – titrated up to 1.8 mg daily

Case 1:Patient AC



238 lbs
5/2004

Lap band

249 lbs
12/2014

Initial visit

Pioglitazone 45 mg
Metformin 500 mg

186 lbs
9/2015

Metformin 2000 mg
Liraglutide 1.8 mg

Drug-Associated Weight Change Reference

Therapeutic Category	Drug Class	May Cause Weight Gain	Alternatives That Cause Less Weight Gain, Weight Loss, or are Weight Neutral
Psychiatry	Antipsychotic	• Clozapine • Risperidone • Olanzapine • Quetiapine • Other	• Ziprasidone • Aripiprazole
	Antidepressants and Mood Stabilizers	• Citalopram • Escitalopram • Fluvoxamine • Lithium • MAOIs	• Bupropion • Nefazodone • Fluoxetine (short term: <1 year) • Sertraline (short term: <1 year)
Neurology	Anticonvulsants	• Carbamazepine • Gabapentin • Valproate	• Lamotrigine • Topiramate • Zonisamide
Endocrinology	Diabetes Treatments	• Insulin • Sulfonylureas • Thiazolidinedione	• Metformin • Acarbose • Miglitol
Obstetrics & Gynecology	Oral Contraceptives	• Progestational steroids • Hormonal contraceptives containing progestational steroids	• Barrier methods • IUDs
	Endometriosis Treatment	• Depot leuprolide acetate	• Surgical methods
Cardiology	Antihypertensives	• α-blocker • β-blocker	• ACE inhibitors • Calcium channel blockers
Infectious Disease	Antiretroviral Therapy	• Protease inhibitors	• None
General	Steroid Hormones	• Corticosteroids • Progestational steroids	• NSAIDs
	Antihistamines/ Anticholinergics	• Diphenhydramine • Doxepin • Cyproheptadine • Other potent antihistamines	• Decongestants • Steroid inhalers

Slide: Louis J. Aronne, MD, FACP

Case 2:Patient GF

- 56-year-old F w obesity, HTN, OSA, RA and asthma

- Medications: Abatacept, MTX, valsartan, theophylline, h/o steroid use

- S/p lap band 5 years ago – lost 12 lbs and then regained all weight; now lap band loosened

Case 2:Patient GF

- 56-year-old F w obesity, HTN, OSA, RA and asthma

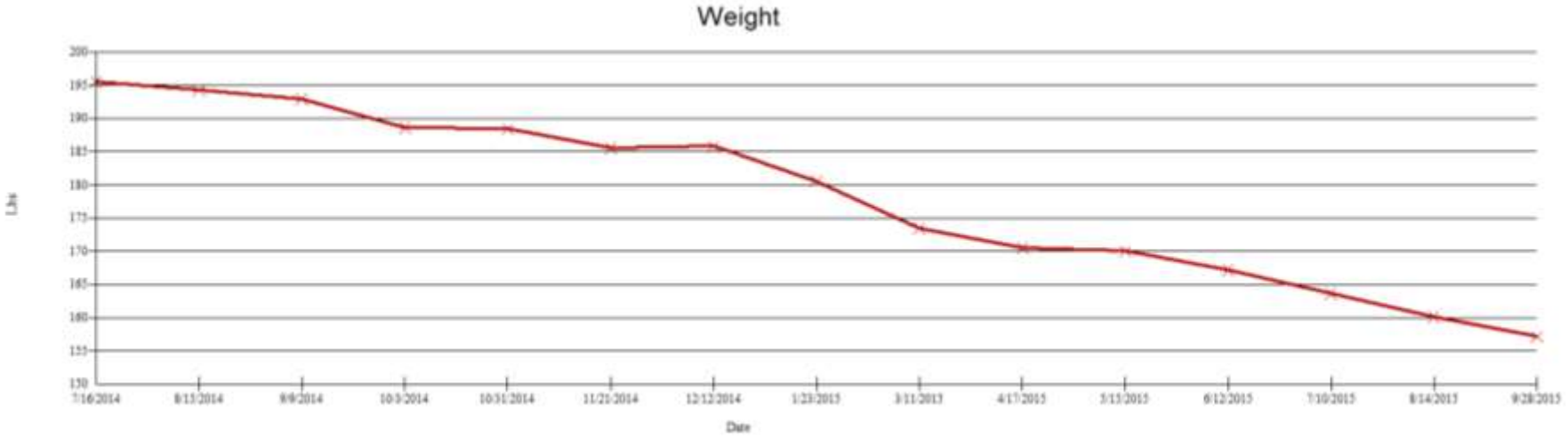
- Medications: Abatacept, MTX, valsartan, theophylline, h/o steroid use

- S/p lap band 5 years ago – lost 12 lbs and then regained all weight; now lap band loosened

- Rx: low glycemic index diet and metformin, added phentermine/topiramate 2 months later and liraglutide 5 months later

- 14 months later: lost 38 lbs, doing well on metformin 500 mg BID, phentermine/topiramate 7.5/46 mg and liraglutide up to 1.8 mg daily

Case 2:Patient GF



195 lbs
7/2014

157 lbs
9/2015

Metformin 500 mg BID
phentermine/topiramate 7.5/46 mg
liraglutide1.8 mg daily

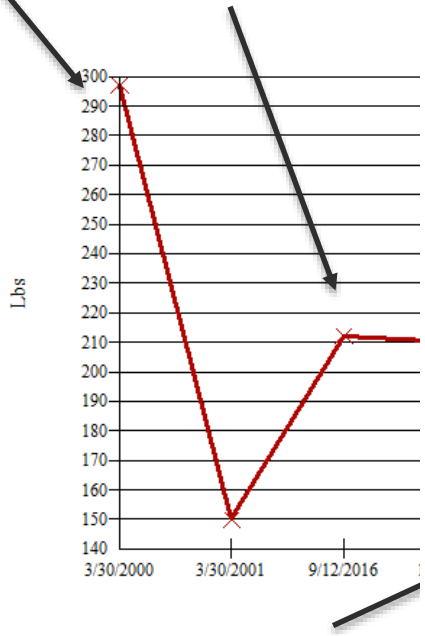
Patient AS: RNYGB in 2001 at 134 kg, low 68kg, regained to 94 kg with increased glucose in 2016

RNYG : 295 lbs

1st visit: 207 lbs
BMI 38.8 kg/m^2
Rx: metformin
titrate to 1000 mg BID

3rd visit: 174 lbs
Down 33 lbs
BMI 32.9 kg/m^2

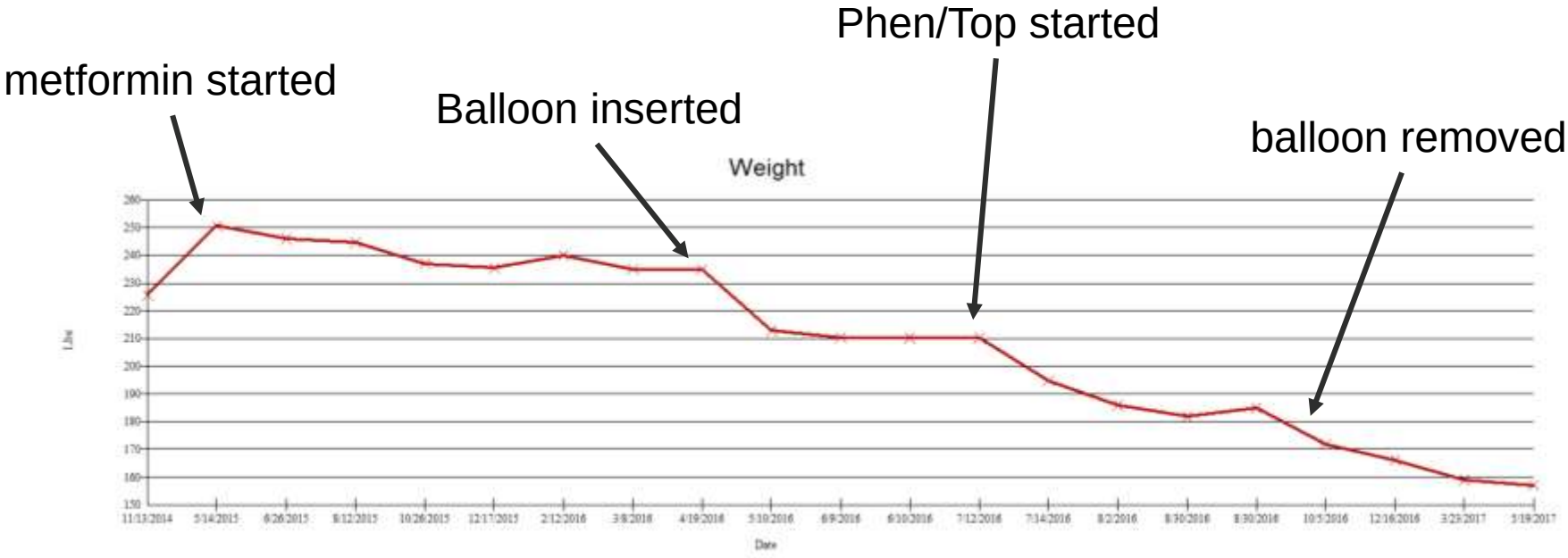
4th visit: 159 lbs
Down 48 lbs
BMI 30.1 kg/m^2



2nd visit: 192 lbs
Down 15 lbs
BMI 35.9 kg/m^2

Phone call
Stopped losing weight
Rx: Belviq 10 mg BID

Device + Medication:
17 year old woman with PCOS and NASH



Utility of Weight Loss Medications After Weight Loss Surgery

Design

- Retrospective study 2000-2014

Setting

- 2 Academic Institutional Practices

Patients and Other Participants

- Patients who had undergone Roux-en-Y gastric bypass (RYGB) or a vertical sleeve gastrectomy (VSG) who were subsequently placed on weight loss pharmacotherapy post-operatively
- Of the 5110 charts reviewed, 319 met inclusion criteria

Interventions

- Weight loss pharmacotherapy:15 FDA and non-FDA approved medications

Weight loss medications after bariatric surgery
Review of patients treated at MGH and WCMC

Mean Weight Change after Treatment by Subgroup			
Subgroup	Weight Change		P-value
	(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)	0.486[a]
Patients prescribed medication at weight regain (n=249, 78.5%)~	-18.3 (SD=19.0)	-7.7 (SD=7.6)	

~ 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)

Same amount of weight loss if medications started at plateau vs. regain, but TBW higher if started at regain –

The best time to treat is at plateau, with slight regain

Stanford, FC, et al. The utility of weight loss medications after weight loss surgery. Surg Obes Relat Dis. 2017 Mar;13(3):491-500.

Review of patients treated at MGH and WCMC

Surgery Type	Weight Change		P-value
Sleeve Gastrectomy (n=61)	-9.8 (SD=13.5)	-4.3 (SD=5.7)	0.0001[a]
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)	

- RNYGB weight loss > Gastric Sleeve
  - 54% lost ≥ 5%,
  - 30% lost ≥ 10%,
  - 15% lost ≥ 15%

Stanford, FC, et al. The utility of weight loss medications after weight loss surgery. Surg Obes Relat Dis. 2017 Mar;13(3):491-500.

Different Medications Can Work. Many Are Widely Available.

Medication	Number of Patients (%)
Topiramate	194 (60.8%)
Phentermine	121 (37.9%)
Metformin	123 (38.6)
Bupropion	75 (23.5%)
Zonisamide	65 (20.4%)
Lorcaserin	39 (12.2%)
Liraglutide	38 (11.91%)
Naltrexone	13 (4.1%)
Exenatide	7 (2.2%)
Orlistat	4 (1.3%)
Canagliflozin	3 (0.94%)
Sibutramine	3 (0.94%)

Number of Medications Used~	Number of Patients (%)
1	126 (39.5%)
2	93 (29.2%)
3	52 (16.3%)
4	22 (6.9%)
5	11 (3.5%)
6	7 (2.19%)
7	4 (1.3%)
8	4 (1.3%)

Table 6A ~Over course of treatment period, from start of medication to date when nadir weight is achieved

Conclusion: Weight loss pharmacotherapy is a useful adjunct to bariatric surgery in patients with inadequate weight loss and weight regain

Stanford, FC, et al. The utility of weight loss medications after weight loss surgery. Surg Obes Relat Dis. 2017 Mar;13(3):491-500.

Conclusion

- Bariatric surgery is the most effective treatment for obesity
- Weight regain can occur following bariatric surgery
- Once anatomical causes have been excluded, behavioral and medical management can improve outcomes

Conclusion

- Our review of medical treatment demonstrates efficacy for a variety of available medical therapies
- Weight loss plateau may be the optimal time to use medication
- More research is necessary to continue to improve results and make these treatments more widely available