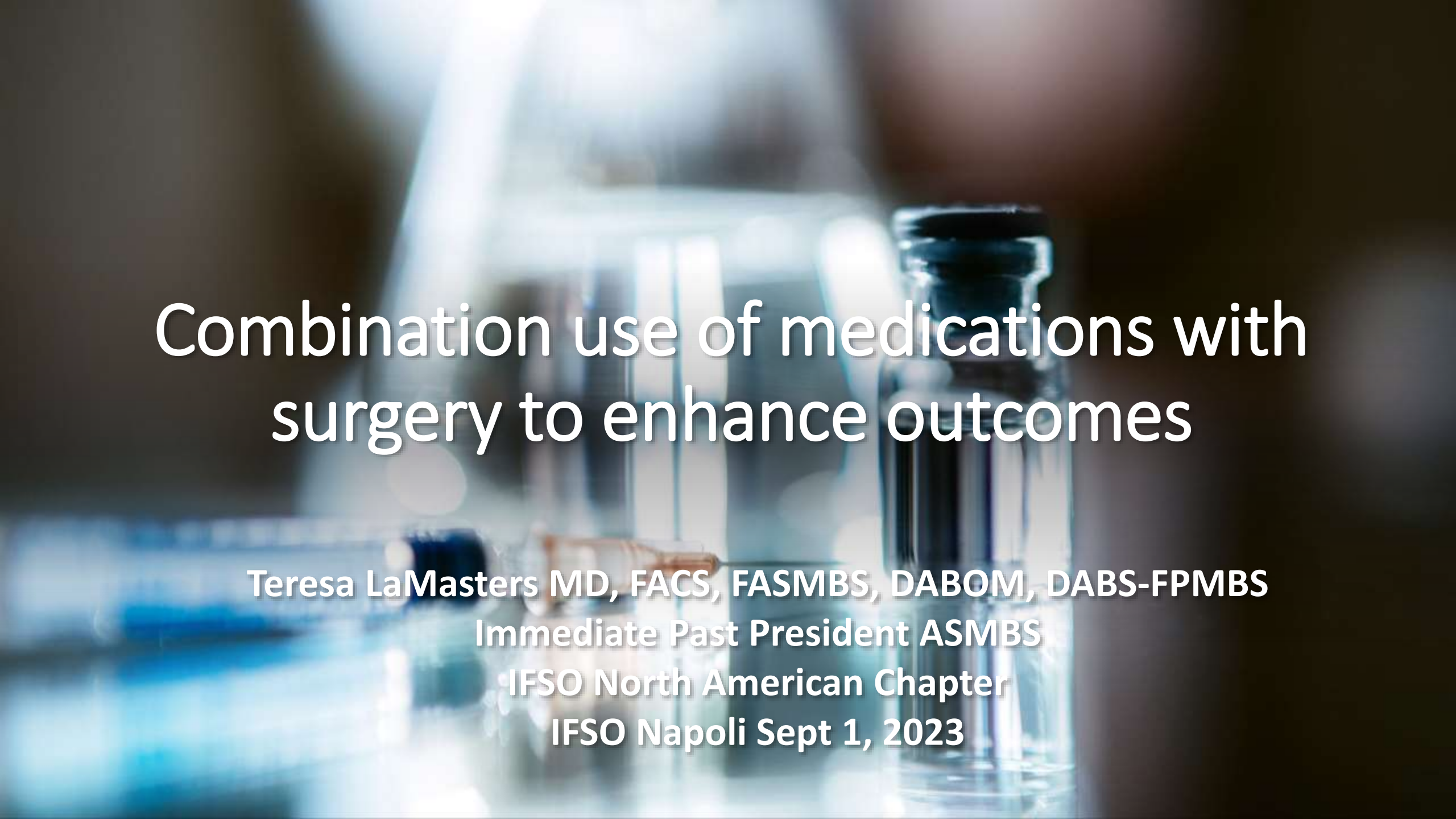

Combination use of medications with surgery to enhance outcomes

Teresa LaMasters MD, FACS, FASMBS, DABOM, DABS-FPMBS
Immediate Past President ASMBS
IFSO North American Chapter
IFSO Napoli Sept 1, 2023

CONFLICT OF INTEREST DISCLOSURE

In accordance with «EACCME criteria for the Accreditation of Live Educational Events», please disclose whether you have or you have not any conflict of interest with the companies:

I have the following potential conflict(s) of interest to report:

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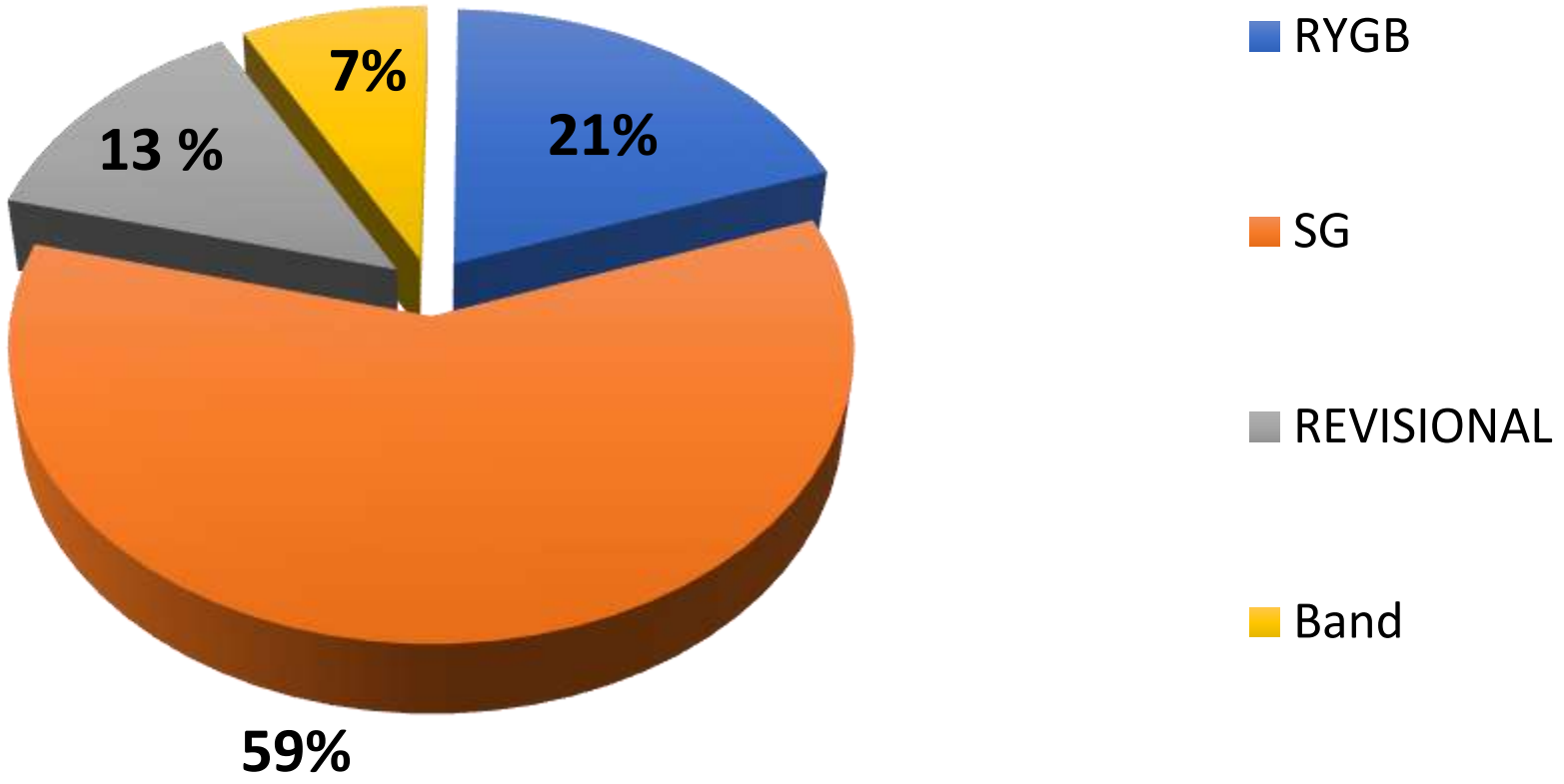
CAREER CASE MIX DISCLOSURE



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Objectives

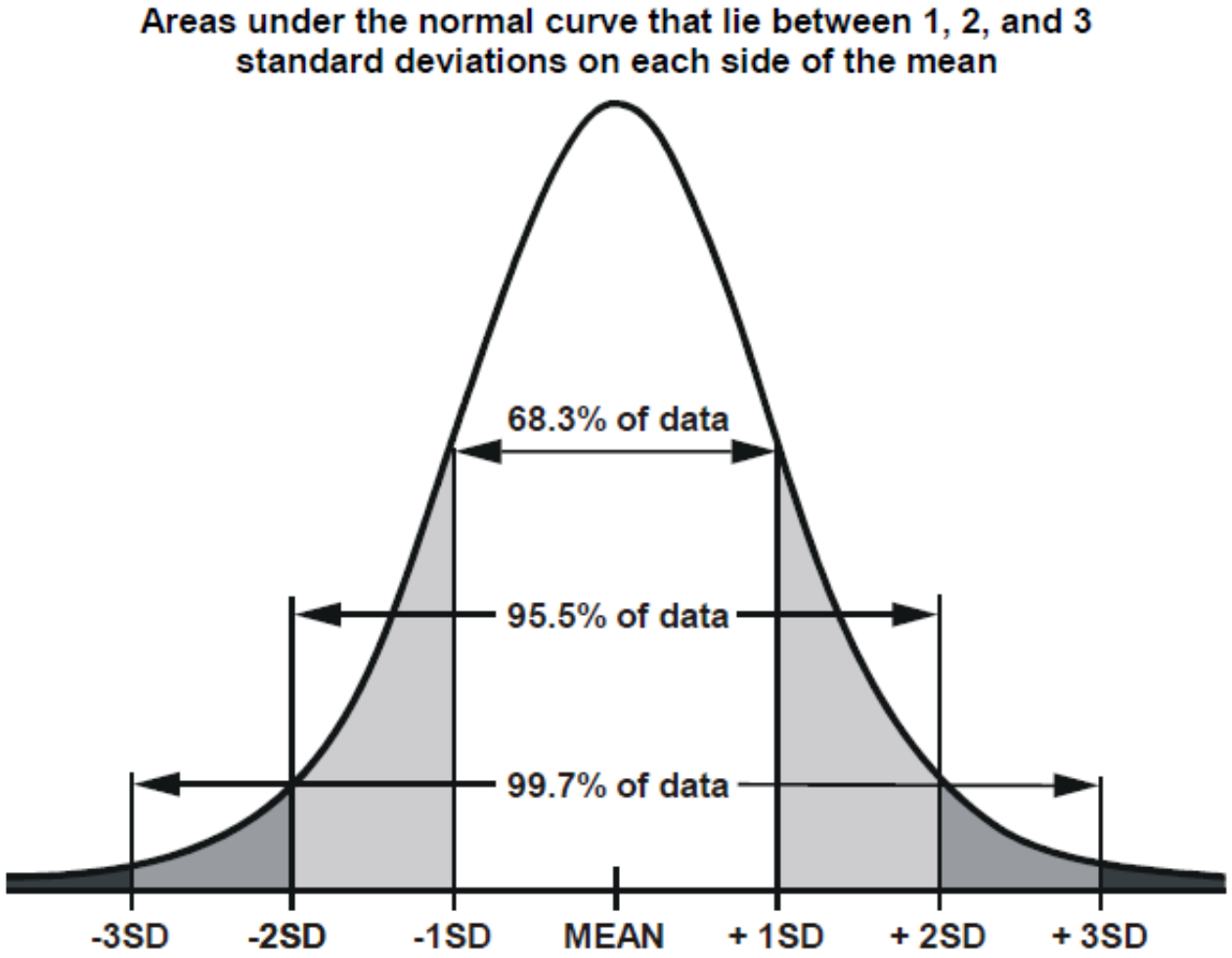
- Understand bariatric surgery works through neurohormonal pathways
- There is a variable response to surgical treatment of obesity
- Medications can be used to enhance the outcomes of surgery

Metabolic Bariatric Surgery is VERY Effective

- Excellent weight loss and treatment of metabolic disease
- Variable response to treatment modalities we are only beginning to understand
- There is a limit in the weight loss we can achieve with surgery = New set point
- Can we push it further?

Variable response

- All treatments have variation of response within individuals
- This includes response to metabolic bariatric surgical procedures.
- There is a bell shaped curve distribution



https://medium.com/@rishisharma2628/why-is-normal-distribution-bell-shaped-80a784955e92

Van de Lar et al.

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Surgery for Obesity and Related Diseases 15 (2019) 200–210

SURGERY FOR OBESITY AND RELATED DISEASES

Original article

The Dutch bariatric weight loss chart: A multicenter tool to assess weight outcome up to 7 years after sleeve gastrectomy and laparoscopic Roux-en-Y gastric bypass

Arnold W. van de Laar, M.D.[a,*], Simon W. Nienhuijs, Ph.D.[b], Jan A. Apers, M.D.[c], Anne-Sophie van Rijswijk, M.D.[a], Jean-Paul de Zoete, M.D.[b], Ralph P. Gadiot, Ph.D.[c]

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Received 4 June 2018; received in revised form 7 October 2018; accepted 20 November 2018

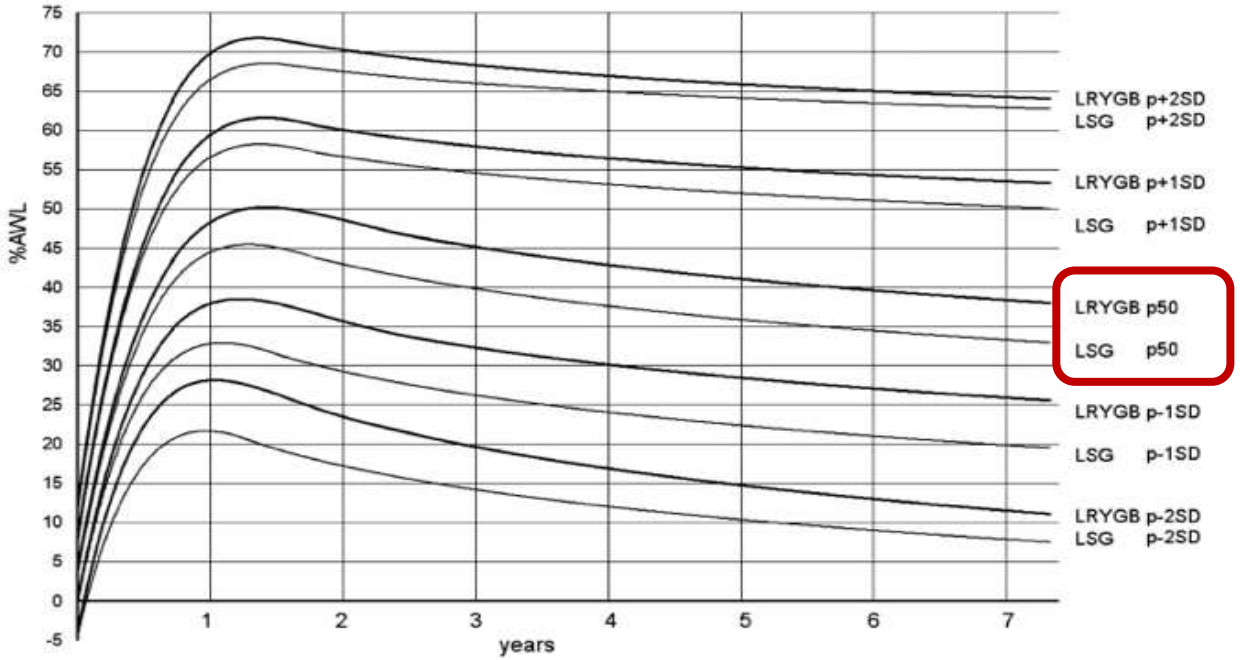

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Fig. 2. Standard deviation (SD) percentile (p) curves, based on the last measured weight loss results of multicenter 5516 primary laparoscopic Roux-en-Y gastric-bypass (LRYGB) patients and 3877 primary laparoscopic sleeve gastrectomy (LSG) patients, are expressed as percentage alterable weight loss (%AWL) and calculated as (BMI at first preoperative visit minus the last

Found 16% of RYGB patients would fit into "poor responder" from initial surgery

All patients will have a weight change over the nadir as part of the **natural history** of the chronic disease of obesity

Weight change over nadir is not abnormal or unexpected

Need to define when it is pathologic

Van de Laar AW , Acherman YI . Weight loss percentile charts of large representative series: a benchmark defining sufficient weight loss challenging current criteria for success of bariatric surgery. Obes Surg 2014;24(5):727–34 .

What are the Expected Outcomes?

- Bariatric Outcomes Longitudinal Database (BOLD) data

- More than **three quarters of all LRYGB patients never reach BMI < 25 kg/m 2 and more than one quarter never even BMI < 30 kg/m 2**

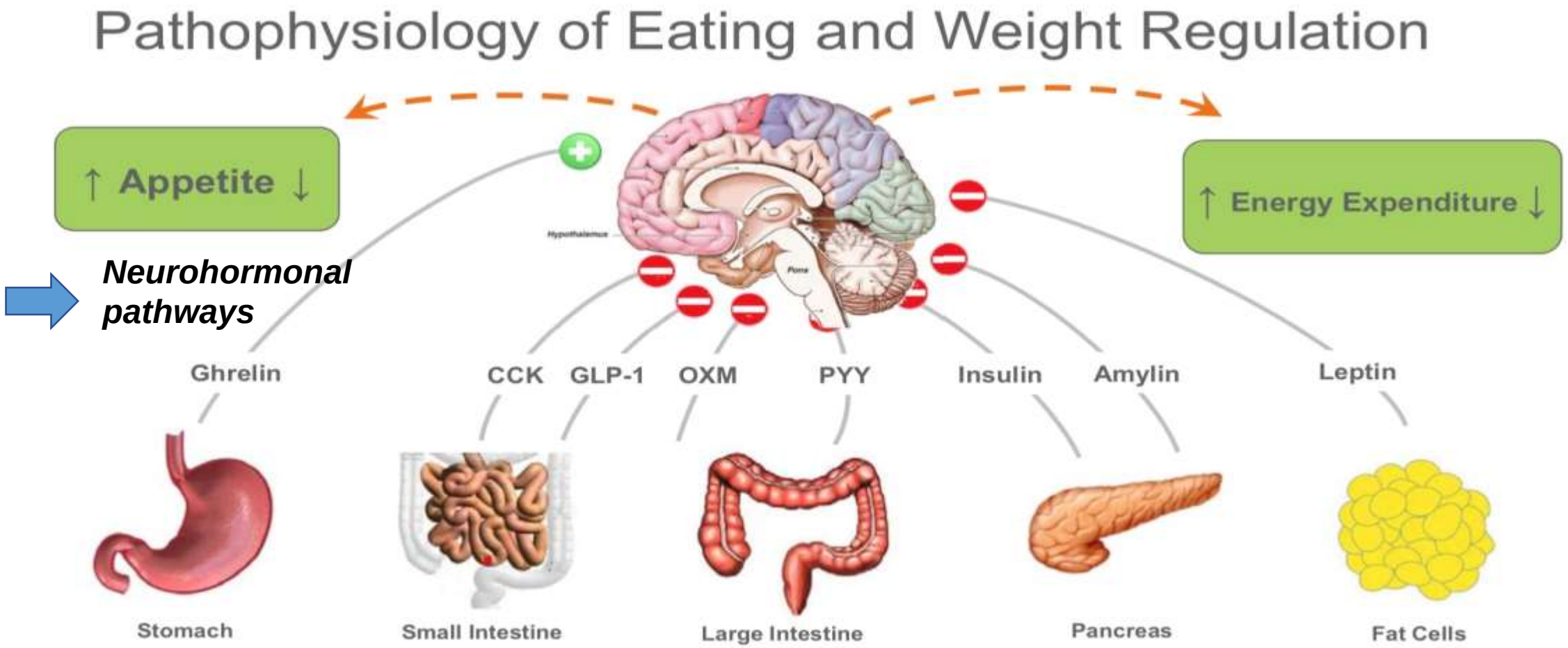
Instead of looking at results that patients should achieve, it would be better to look at results that patients do achieve - compared with results of peers

Realistic NOT “Dream” Outcomes

Obesity
A Disease of the Brain

Regulate weight using Hunger, Feeling Satisfied, and Burning Calories =Metabolism

Obesity is a disease of the brain and regulation pathways



Metabolic Surgery

Works through alteration of biochemistry and gut hormones

Different procedures impact hormones differently and can have different mechanisms of action.

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SURGERY FOR OBESITY AND RELATED DISEASES

Surgery for Obesity and Related Diseases ■ (2019) 1–11

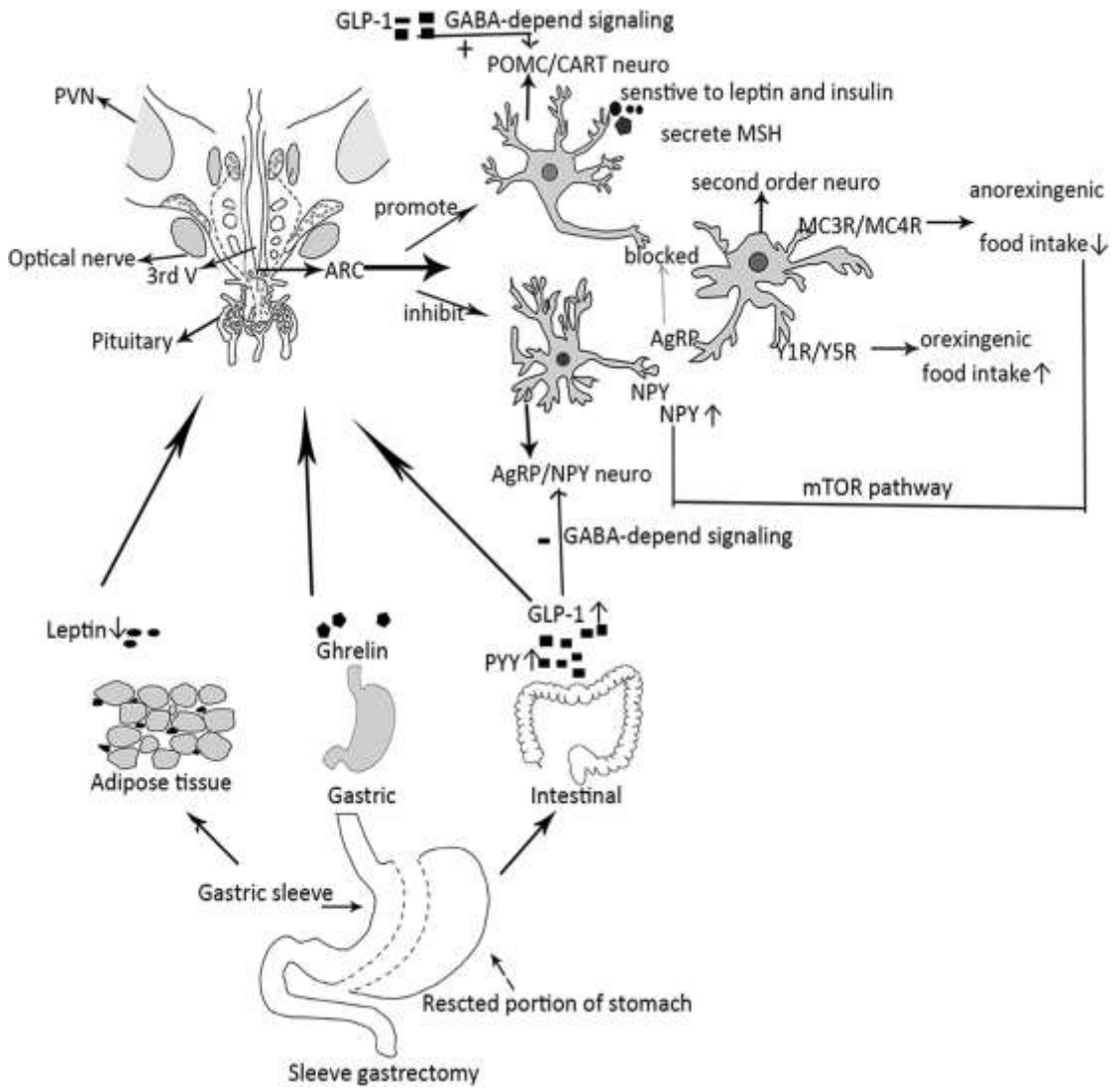
Review article

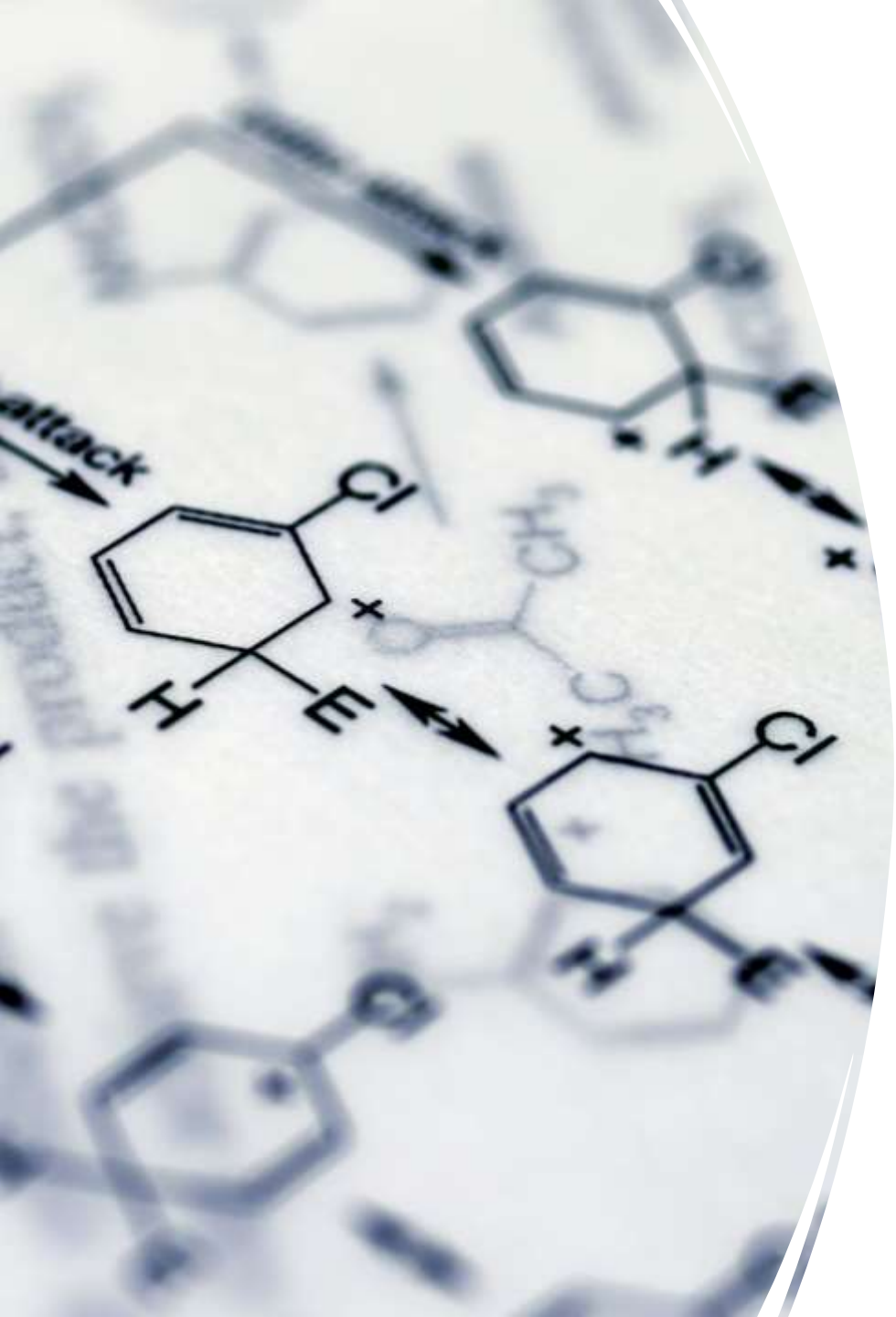
Potential mechanisms of sleeve gastrectomy for reducing weight and improving metabolism in patients with obesity

Renhong Huang, M.Sc., M.D., Xusheng Ding, M.Sc., M.D., Hongbing Fu, M.D., Ph.D.*, Qingping Cai, M.D., Ph.D.*

Department of General Surgery of Changzheng Hospital affiliated to Naval Military Medical University, Shanghai, China

Received 7 May 2019; accepted 19 June 2019





GLP-1 (Glucagon Like Peptide -1)

- Restore first phase insulin secretion and response – improves **blood sugar control**
- Suppresses Glucagon – Reduces extra production of sugar
- Delayed Gastric emptying – improved satiety
- Reduce appetite – CNS signaling

Sleeve has very powerful effect on Ghrelin, lesser effect on GLP -1

	Ghrelin	GLP-1	Insulin	Leptin	PYY	OXM
Dieting	↑ ↑		↓	↓		
Lap Band	↑ ↑	↔	↓	↓	↑	↔
Sleeve	↓ ↓ ↓	↑	↓	↓	↑	?
RYGB	↑ ↔ ↓	↑ ↑	↓	↓	↑	↑

Ochner et al. Changes in neurohormonal gut peptides following bariatric surgery. Int J Obesity 2011; 35:153-166.

OBES SURG (2016) 26:919–925
DOI 10.1007/s11695-015-1908-z

ORIGINAL CONTRIBUTIONS

Weight Regain After Gastric Bypass: Influence of Gut Hormones

Marco Aurelio Santo[1] · Daniel Riccioppo[1] · Denis Pajecki[1] · Flavio Kawamoto[1] · Roberto de Cleva[1] · Leila Antonangelo[1,2] · Lia Marçal[1,2] · Ivan Cecconello[1]

Hormone impact is different in those with weight regain

Less increase in GLP 1 for weight regain group

Can we alter the patient response to surgery?

- YES
- How?
- With addition of medications
- Medications can be used to fine tune the patient response to surgery

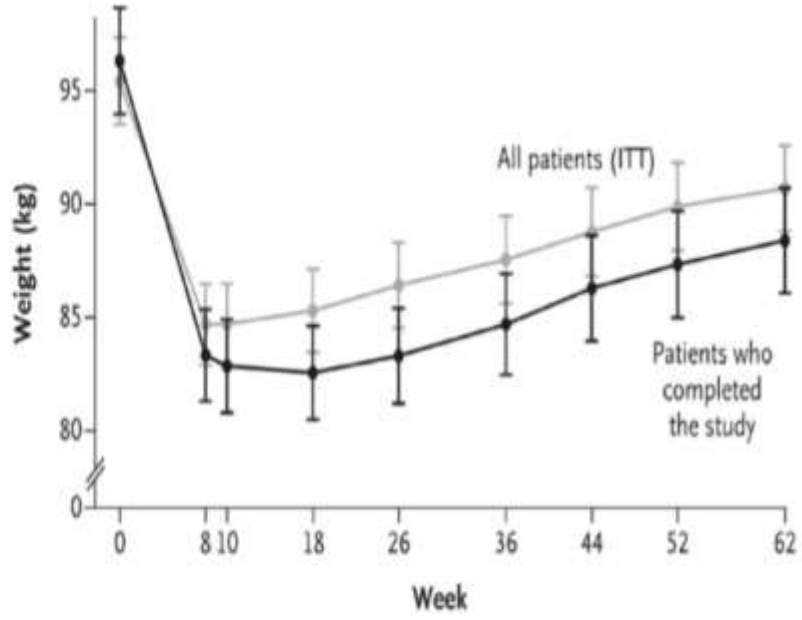

Physiology drives behavior
Controlling abnormal physiology supports good behavior

Physiology drives behavior

Controlling abnormal physiology supports good behavior

Hormonal Adaptations to Weight Loss

- Weight regain is common due to hormonal counter regulatory adaptations
- 10 weeks of weight loss
- Followed for another 1 year
- Measurement of regulating hormones over the year



Weight Loss Medications

TOOLS

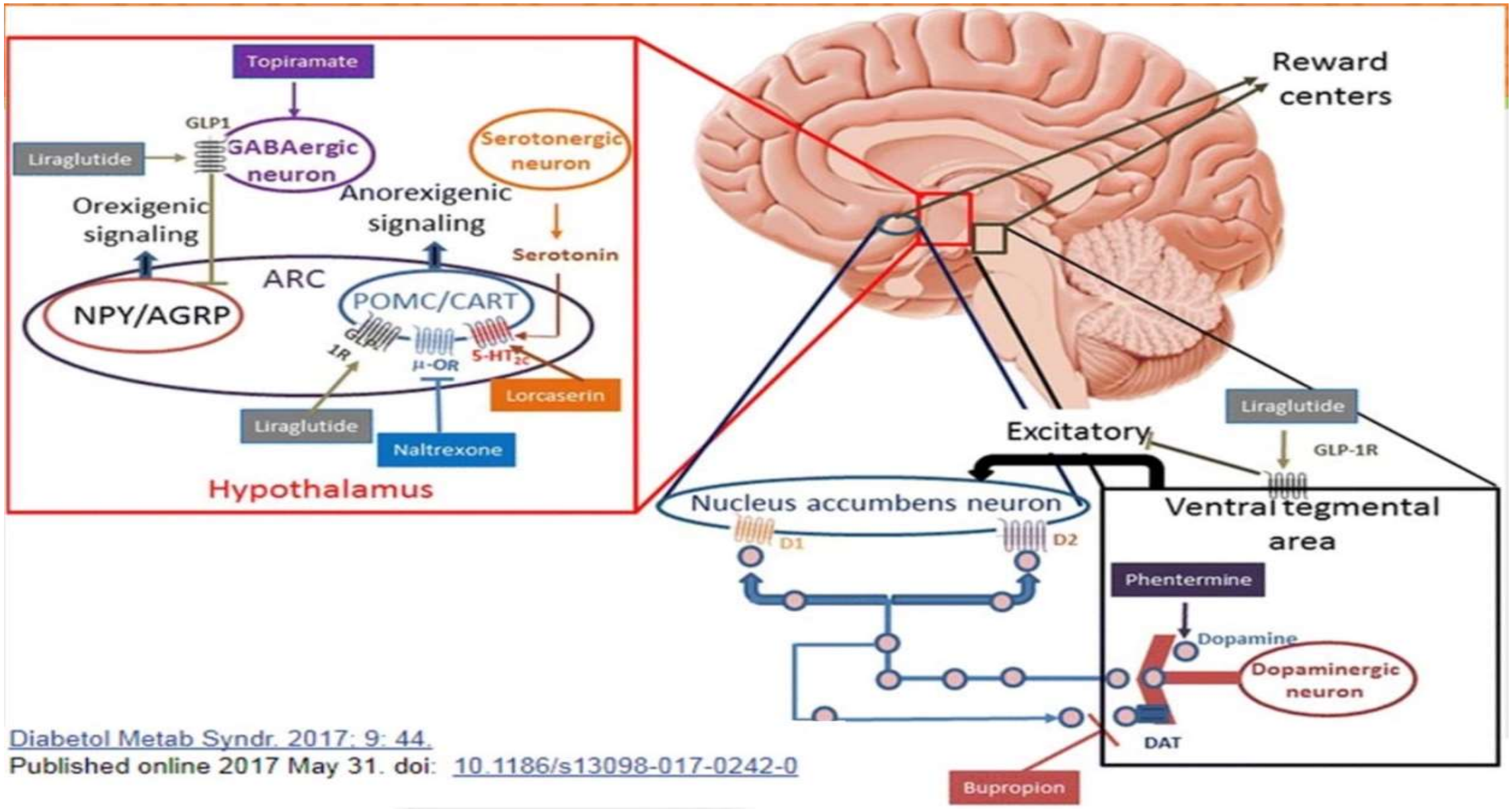
- **Can be used to augment the neurohormonal effects of surgery**
- **Help fine tune or adjust variable physiologic response**

Can use pre-surgery optimization

inadequate initial weight loss

early post surgery weight gain

later post surgery weight gain



Diabetol Metab Syndr. 2017; 9: 44.
Published online 2017 May 31. doi: 10.1186/s13098-017-0242-0

Adapted from Kim et al. and Wang et al. Obesity Medicine Association Pharmacotherapy 2018

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

Fatima Cody Stanford, M.D., M.P.H., M.P.A.[a,b,c,*], Nasreen Alfaris, M.D., M.P.H.[a,c,d], Gricelda Gomez, B.S.[c,e], Elizabeth T. Ricks, M.S.[f,g,h], Alpana P. Shukla, M.D.[f], Kathleen E. Corey, M.D., M.P.H., M.M.Sc.[c,i], Janey S. Pratt, M.D.[c,j], Alfons Pomp, M.D.[k], Francesco Rubino, M.D.[l], Louis J. Aronne, M.D.[g]

Post RYGB nadir BMI 33

Weight regain to BMI 36 (6.5%)

Medications Topiramate and Phentermine added and reduced BMI to 26

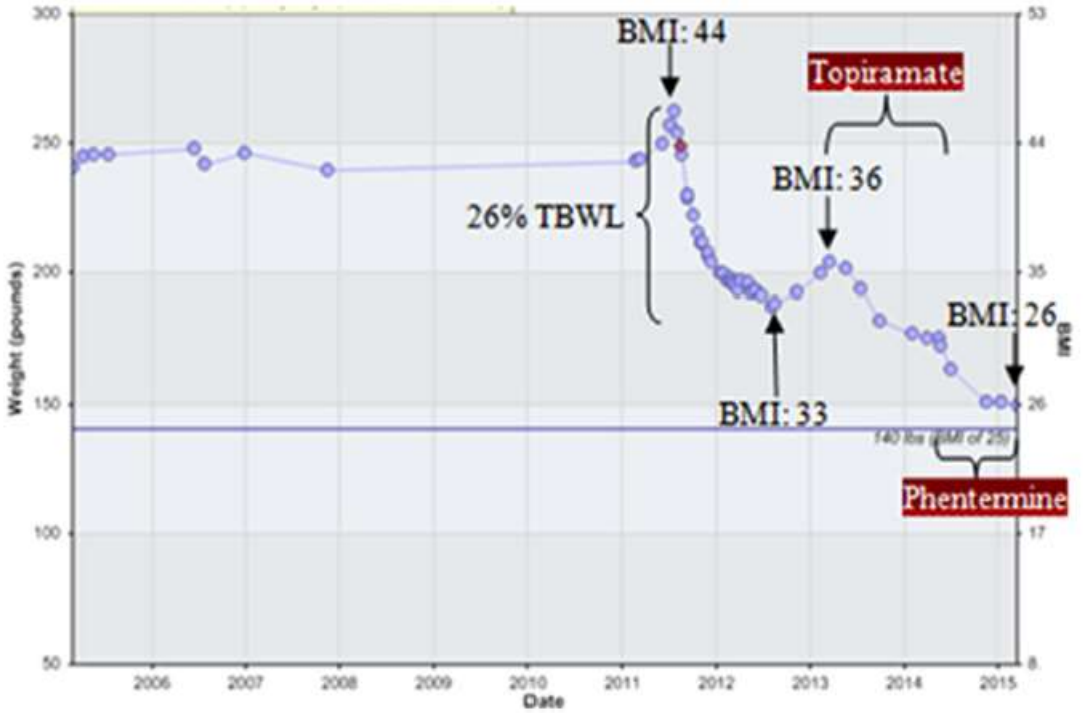


Fig. 1. Demonstration of the utility of weight loss mediation after bariatric surgery in an RYGB patient. RYGB = Roux-en-Y gastric bypass; BMI = body mass index; TBWL = total body weight loss.

Surg Obes Relat Dis. 2017 Mar;13(3):491-500. doi: 10.1016/j.soard.2016.10.018. Epub 2016 Oct 27.

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Surgery for Obesity and Related Diseases 13 (2017) 491–501
SURGERY FOR OBESITY AND RELATED DISEASES

Original article

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

Fatima C[illegible],[c,d],
Gricel[illegible],
Kathleen E.[illegible] M.D.[k],

Additional weight loss 5-30 pounds (20 pounds)

Weight loss %	All med com after				n altrexone without
> 5%	54%	62%	67%	47%	42%
> 10%	30%	34%	47%	22%	21%
> 15%	15%				10%

Using medications to optimize pre-surgical weight loss, prevent and/or treat weight regain and produce greater weight loss is important

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SURGERY FOR OBESITY AND RELATED DISEASES

Surgery for Obesity and Related Diseases 15 (2019) 1039–1043

Original article

Use of phentermine-topiramate extended release in combination with sleeve gastrectomy in patients with BMI 50 kg/m^2 or more

Jamy D. Ard, M.D.[a,b,*], Daniel P. Beavers, Ph.D.[c], Erica Hale, M.S.[b], Gary Miller, Ph.D.[b,d], Stephen McNatt, M.D.[b,e], Adolfo Fernandez, M.D.[b,e]

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Received 21 January 2019; accepted 16 April 2019

Conclusions

- **Starting BMI near 60**
- **62% on phen/top combo + LSG reached BMI <40**
- **47.5% LSG alone reached BMI <40**
- **Odds ratio of reaching bmi <40 with medication was 4.1 compared with LSG alone in high bmi group**
- **Additional weight loss started before surgery and continued for 2 years after**

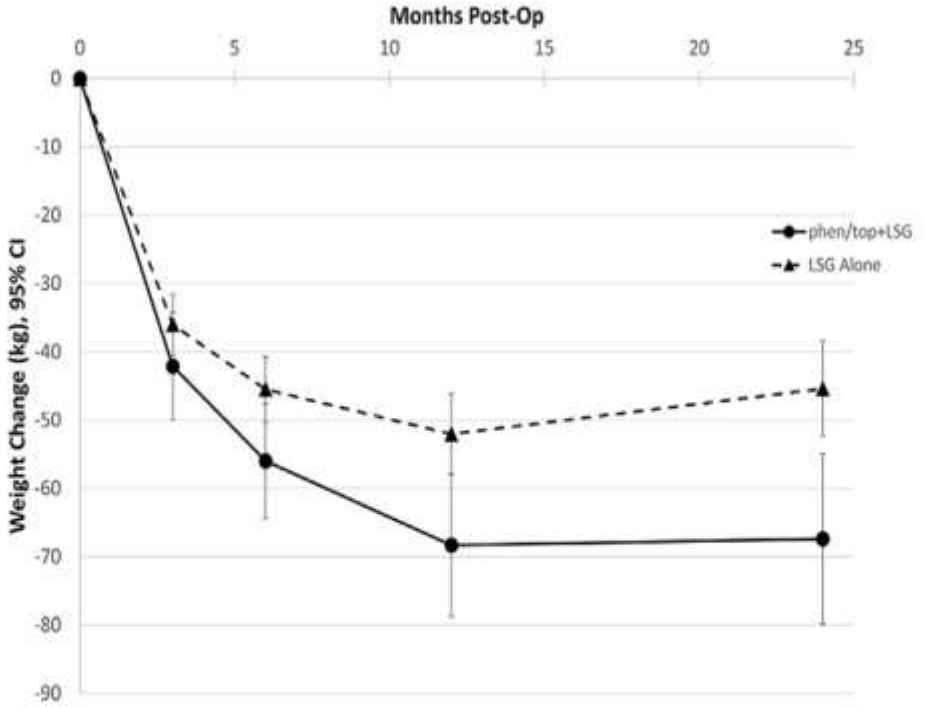


Fig. 1. Change in weight (kg) after laparoscopic sleeve gastrectomy (LSG) for those treated with phentermine and topiramate extended release (phen/top) + LSG versus LSG alone

Jamy D. Ard et al/ SOARD 15 (2019) 1039-1043

Preoperative and early adjuvant weight loss medications in bariatric surgery patients with body mass index over 60 or suboptimal initial response to surgery

Jessica G. Cunningham, M.D., Ph.D. • Nova Szoka, M.D., F.A.S.M.B.S., F.A.C.S. • Lawrence E. Tabone, M.D., M.B.A., F.A.S.M.B.S., F.A.C.S., D.A.B.O.M. • Stephanie Cox, Ph.D. • Laura Aylward, Ph.D. • Salim Abunnaja, M.D., F.A.C.S., F.A.S.M.B.S., D.A.B.O.M.

Published: February 14, 2023 • DOI: https://doi.org/10.1016/j.soard.2023.01.021

SURGERY FOR OBESITY AND RELATED DISEASES ASMBS

HIGH BMI>60 starting

Meds preop = 31.3% TBWL

Meds for suboptimal weight loss in year 1 = 25.3% TBWL

No meds just surgery = 20.8% TBWL

Methods

A retrospective chart review of patients receiving adjuvant pharmacotherapy for obesity treatment and bariatric surgery. Patients received pharmacotherapy either preoperatively if their body mass index was >60, or in the first or second postoperative years for suboptimal weight loss. Outcome measures included percentage of total body weight loss as well as comparison with the expected weight loss curve as determined by the Metabolic and Bariatric Surgery Risk/Benefit Calculator.

Results

A total of 98 patients were included in the study, with 93 (94.9%) undergoing sleeve gastrectomy and 5 (5.1%) undergoing Roux-en-Y gastric bypass surgery. During the study period, patients were prescribed phentermine and/or topiramate. At postoperative year 1, patients who received pharmacotherapy preoperatively lost 31.3% of their total body weight (TBW) compared with 25.3% TBW for patients with suboptimal weight loss who received medication in the first postoperative year, and 20.8% TBW for patients who did not receive any antiobesity medication in the first postoperative year. Using the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) curve for comparison, patients receiving medication preoperatively weighed 2.4% less than expected, whereas patients receiving medication during the first postoperative year weighed 4.8% higher than expected.

Considerations to guide therapy

1. Clinical Presentation
2. Initial procedure
3. Comorbidities
4. Insurance Coverage/Cost/Samples
5. Guide changes in therapy – Response, Side Effects
6. Layering therapy

Fine tuning treatment

Layering therapy	Many medications can be layered and are frequently more effective when used in that fashion	Adjust dose based on response – may lower dose or space throughout the day
GLP-1 agonists can have increased nausea, reflux, constipation, hypoglycemia	Phentermine- palpitations, insomnia, anxiety (low dose 2 or 3 times a day, intermittent)	Topamax- brain fog, combination with Phentermine can offset side effects

Emerging data

- Data is still emerging to give us guidance
- Some art with this science

Case: Pre-surgery Optimization High BMI

- 42 yo female **starting weight 341#, Height 5’8”, BMI 51.8**
- Co-morbidities – Metabolic syndrome with pre-dm, hyperlipidemia, centralized obesity, GERD controlled PPI daily, chronic back pain, history of DVT, history of kidney stones, OSA-CPAP, mild asthma, Depression- significant now controlled (Wellbutrin, Lexapro, Lamictal, Lyrica)
- Started **Metformin** 1000 mg daily and lifestyle management
- **Lost 22 pounds over 6 months (Wt 319# BMI 48.5, 6.5%TBWL)**

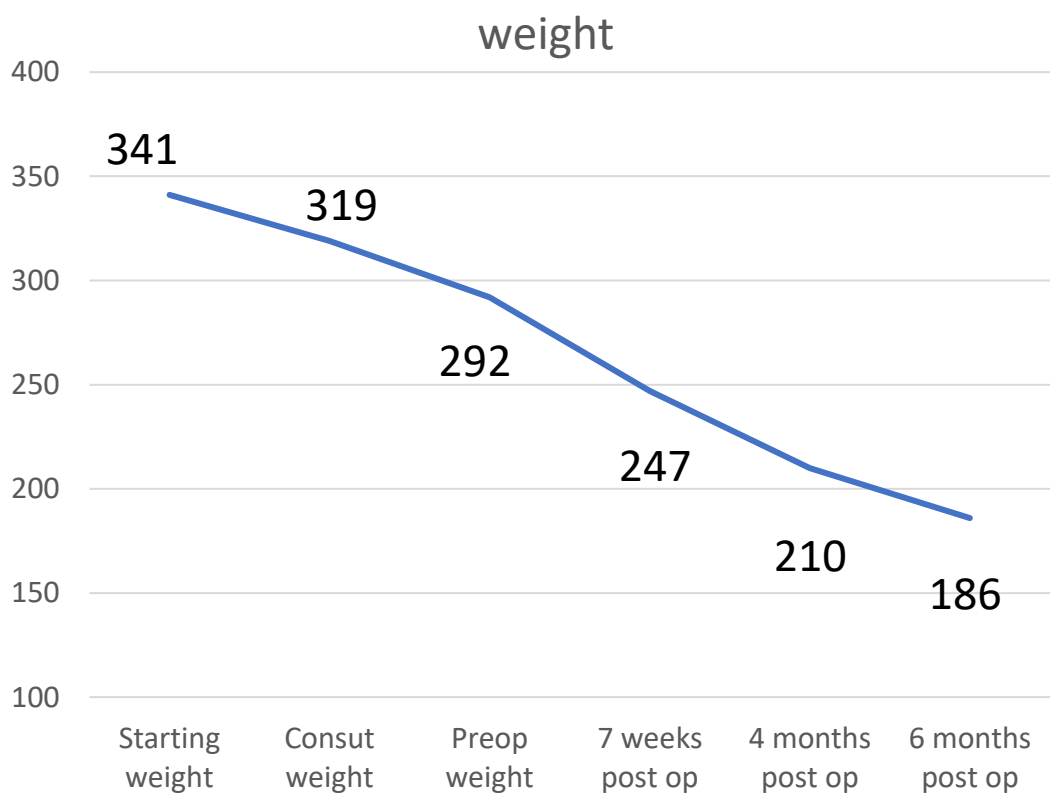
Case: Pre-surgery Optimization

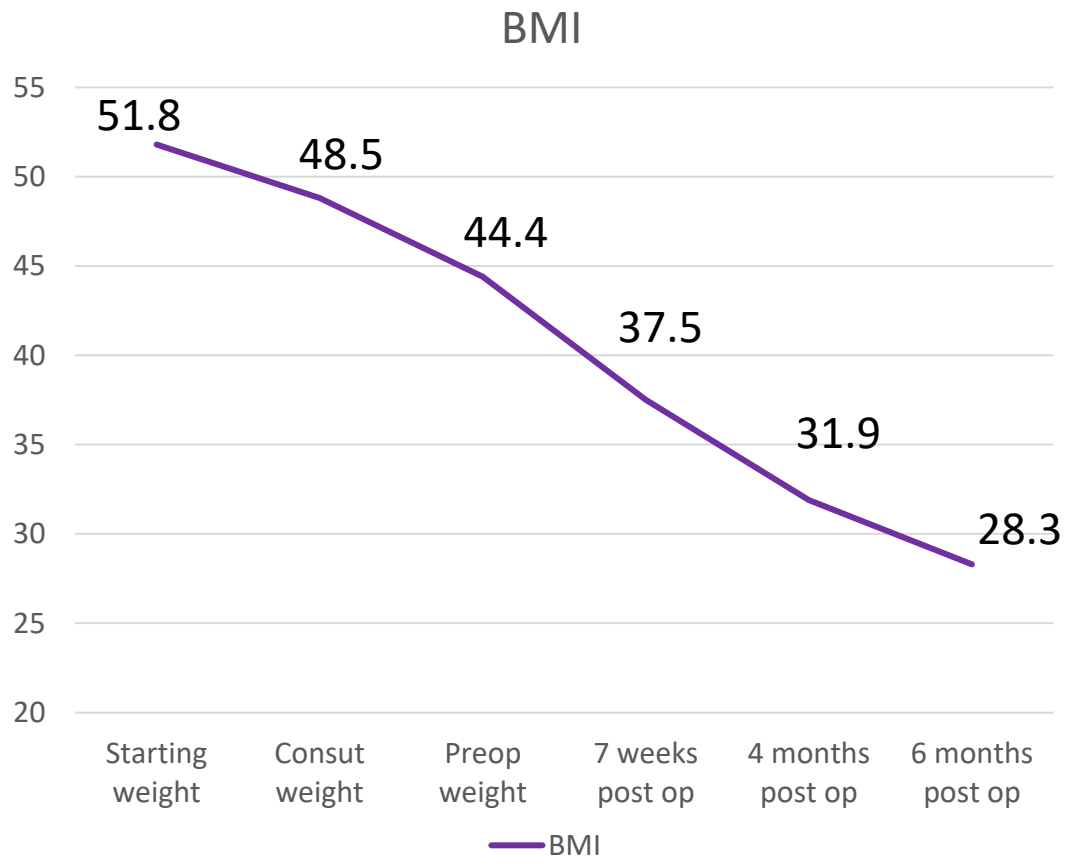
- At time of surgery consultation **weight 319# BMI 48.5** – desires sleeve gastrectomy (171 # EBW – target lose 103# (216# BMI 32.8) to achieve 60%EBWL, patient stated goal is to reach 190# = lose 129# BMI 28.9 or 75% EBWL)
- Further lifestyle modification and start **Semaglutide** (Ozempic) 0.25 mg weekly – taper up dose q 4 weeks
- At **pre-op schedule visit weight 292# BMI 44.4 (144# EBW at surgery)**
- **Lost 27# additional starting Semaglutide (8% TBWL),**
- **lost 49# total in pre-surgery optimization (14% TBWL)**
- Did report increased reflux and nausea with Semaglutide dose at 1 mg weekly – decreased to 0.5 mg weekly well tolerated

Case #: Pre-surgery Optimization- post surgery

- Patient had LSG with HHR no complications, noted gastritis on EGD increased PPI to BID
- At **7 weeks post-op Weight 247# and BMI 37.5 (lost 45# since surgery and 94# since start=27% TBWL)**
- Restart **Semaglutide**/Ozempic and gradually increased dose
- At 3 months Patient reported epigastric pain and gastritis symptoms with nausea
- Stopped Semaglutide/Ozempic, treated with PPI BID and H2 - Abd pain and nausea resolved
- At 4 months post surgery weight 210#, lost 82# since surgery 57% EBWL, and 131# total since start (76.6% EBWL since consult), BMI 31.9
- Restarted **Semaglutide**/Ozempic at lowest dose 0.25 mg at 5 months post surgery
- **6 months post surgery weight 186#, BMI 28.3, lost 106# since surgery 73% EBWL, and lost 155# total since start TBWL 45.5%**

Pre surgical optimize with continue treatment. Started at 341# lost 22# Metformin 6mon, sematglutide lost additional 27# total of 49# lost presurgery, (14%TBWL), surgery + medication (Metformin/Semaglutide)
6 months post surgery weight 186#, lost 106# since surgery 73% EBWL, and **lost 155# total since start TBWL 45.5%**
(lost 133 # 77.7% EBWL since consult), BMI 28.3





UnityPoint Clinic

Case #: LSG Initial expected weight loss with regain Post-op Rescue

- 41 yo female with consultation weight 260 pounds, height 5’7”, BMI 40.7.
- **Preop 260# BMI 40.7, lowest weight 185# (loss 75#) BMI 29, EBWL 65.8%, 28.9%TBWL**
- 3 years postop LSG started to have weight regain- weight 221 pounds (regained 36#), BMI 34.6, maintained 39# weight loss; 34.2% EBWL, 15% TBWL.
- Problem List:
  - PCOS- no meds
  - Elevated Vitamin A- from face cream. Liver evaluation normal.
  - Migraines- no meds
- Intervention????

Case #: Post-op Rescue

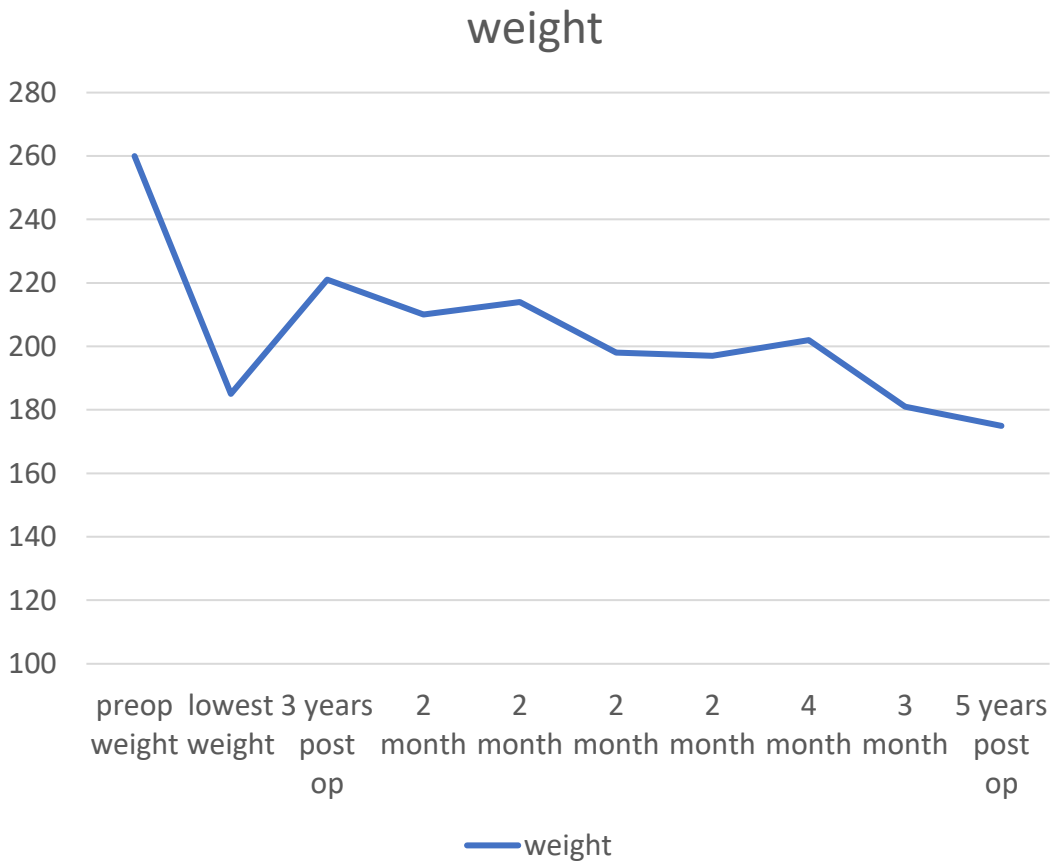
- **Start metformin** 500 mg bid. Weight 221.
- 2 month follow up- lost 11 pounds (5%TBW). Increase metformin 1000 mg bid. Weight 210
- 2 month follow up- gained 4 pounds. Continue metformin, **start phentermine** 18.75 mg. Weight 214.
- 2 month follow up- lost 16 pounds. Continue current meds. Weight 198.
- 2 month follow up- lost 1 pound. Continue same plan. Weight 197.
- 4 month follow up- gained 5 pounds. Continue same meds, **add topiramate** 25 mg qhs. Weight 202. (lost net 20 pounds from starting med management-4 years post surgery)

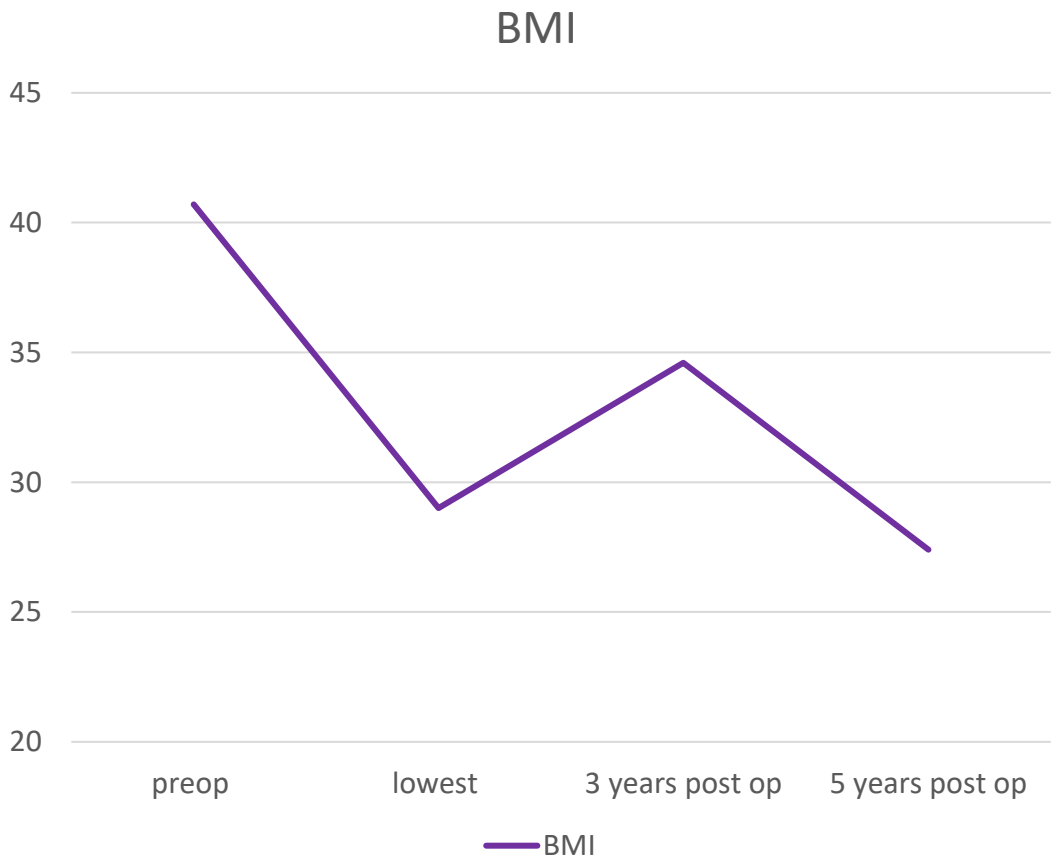
Update: now 5 years postop. Weight 175, BMI 27.4; (maintains loss of 75% EBW, 32.7% TBWL).

Lost 46 pounds with addition of medications reached below initial post-surgery Nadir

LSG Initial expected weight loss with regain Post-op Rescue –

Preop 260# BMI 40.7, lowest weight 185# (loss 75#) BMI 29, EBWL 65.8%, 28.9%TBWL,
3 yrs post op gained 36#, wt 221 BMI 34.6, maintained 39# weight loss; 34.2% EBWL, 15% TBWL
5 years postop LSG. Weight 175, BMI 27.4; (maintains loss of 75% EBW, 32.7% TBWL).
Lost 46 pounds with addition of medications (metformin, phentermine, topiramate) reached below initial post-surgery Nadir





Case #: Post-op LSG Rescue, late regain

- 63 yo female with consultation weight 226, Height 5’5”, BMI 37.0.
- EBW 118, EBWL: 50% 167 60% 153 75% 138
- Lowest weight achieved post LSG surgery prior to intervention 150 pound, (76# weight loss) **BMI 24.6; 64.4% EBWL, 33.6% TBWL**
- Lost to follow up x 9 years. Had weight regain (+32#) when returned at 10 years postop. Weight 182, BMI 29.8 (at 37.3%EBWL and 19.4% TBWL).
- Intervention????

Case #: Post-op Rescue

Problem List:

- Type 2 Diabetes- on amaryl and metformin. Recent a1c 8.2.
- OSA
- Asthma
- Glaucoma
- Depression- well controlled without medications.

- Intervention????

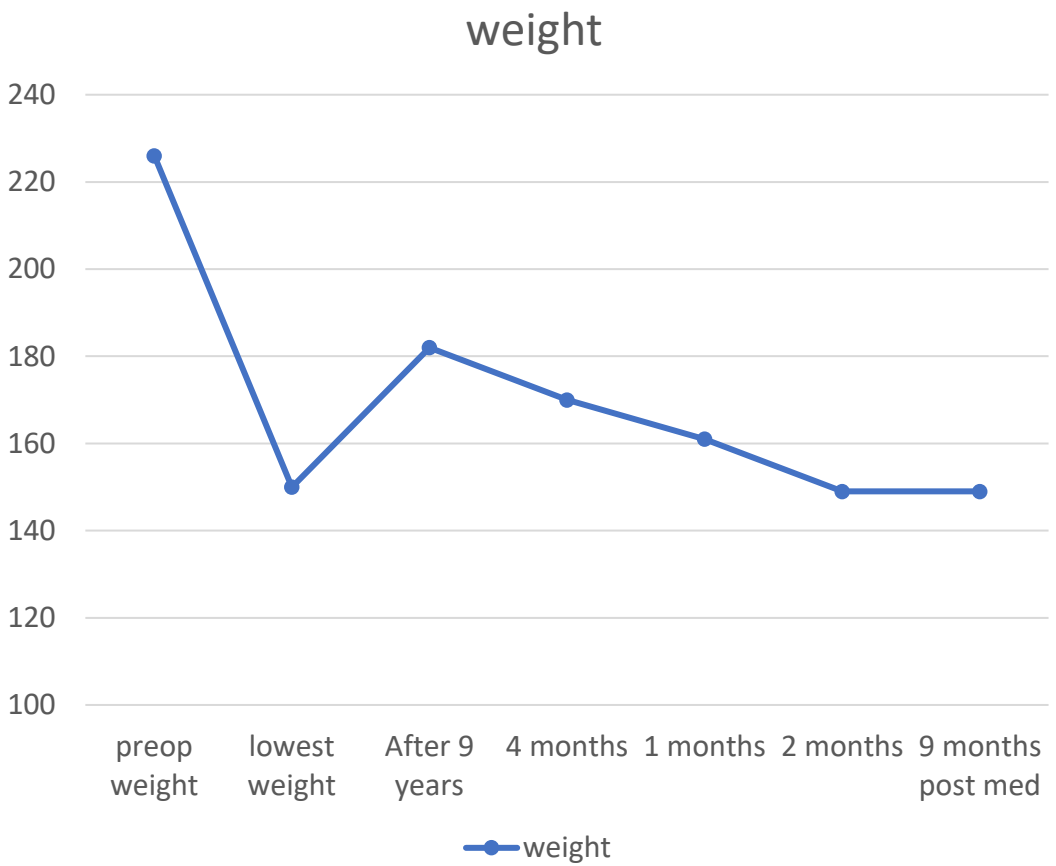
- Problem List (continued):
  - GERD- no medication. Denies symptoms.
  - Hyperlipidemia
  - HTN

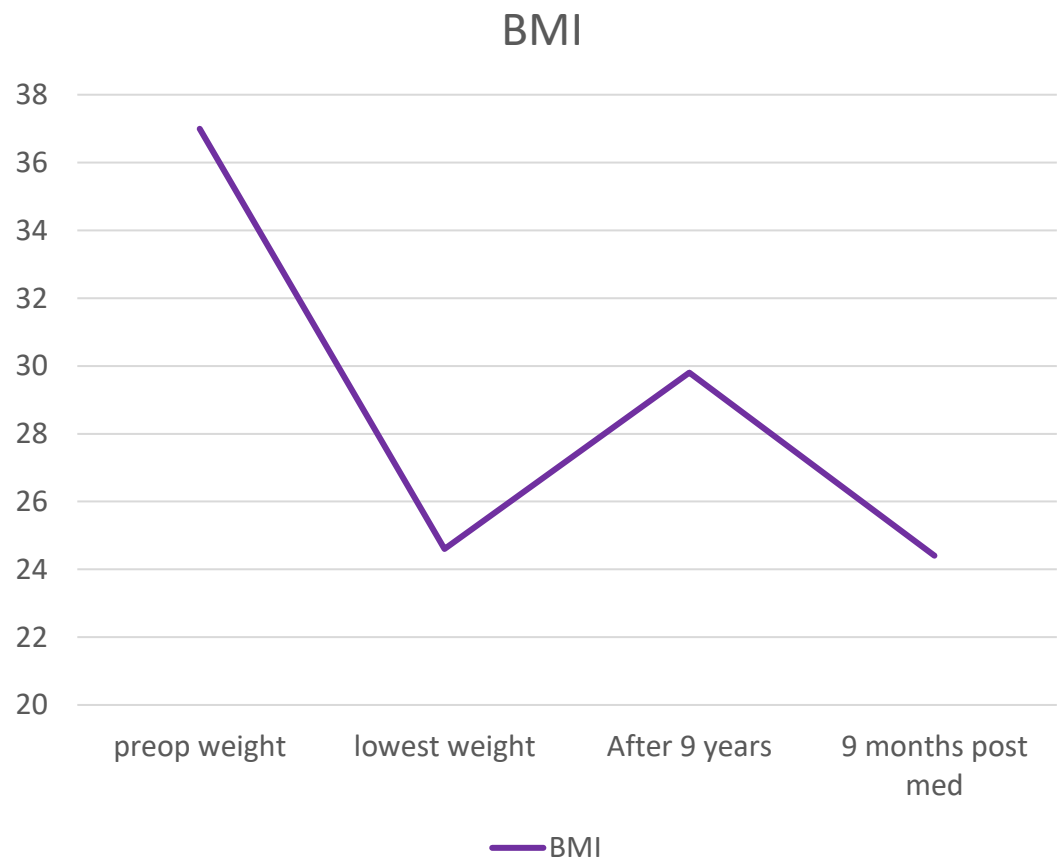
Case #: Post-op Rescue

- Started on Semaglutide/Ozempic a GLP-1. Advised to monitor sugars. Weight 182 pounds. A1c 8.2.
- 4 month follow up- lost 12 pounds. Weight 170. A1c now 5.9. Stopped amaryl. Continue metformin and ozempic. Having some fatigue so added phentermine.
- 1 month follow up- lost 9 pounds. Weight 161. Continue metformin, ozempic, and phentermine.
- 2 month follow up- lost 12 pounds. Weight 149. Continue metformin and ozempic. Moved phentermine to prn use.
- **Update**: now 11 years postop, 9 months post medication intervention. Taking Semaglutide/Ozempic and metformin. **Weight 149, BMI 24.4. (lost 77 pounds since pre-surgery, lost 33# after medication intervention, 65.2% EBWL, 34% TBWL)**

Post-op LSG Rescue, late regain

preop weight 226, BMI 37.0, 150 pound, (76# weight loss) BMI 24.6; 64.4% EBWL, 33.6% TBWL
11 years postop LSG, weight regain (+32#), Weight 182, BMI 29.8 (37.3%EBWL and 19.4% TBWL).
9 months post medication intervention. Taking Semaglutide and metformin Weight 149, BMI 24.4. (lost 77 pounds since pre-surgery, lost 33# after medication intervention, 65.2% EBWL, 34% TBWL)





UnityPoint Clinic

Case: Post RYGB Initial good response with weight regain

- 59 yo female prior lap band removed and converted to LRYGB
- Weight pre LRYGB 249 lbs, Height 5’5.5”, BMI 40.8
- LRYGB –Lowest weight 143#. Initially lost 106# (96%EBWL, BMI 23.4, 42.6% TBWL)
- After 7 years weight 202 lbs. Regained 59 pounds from lowest weight 143#, now maintained weight loss is 47 pounds (42.7%EBWL, BMI 33.1, 18.8% TBWL)
- OSA-CPAP, HTN- 1 med, hypothyroidism, Depression/anxiety (3 meds)
- Intervention???

Case # Post RYGB weight regain

- C/o Hunger, fatigue. Treated gastritis PPI and started phentermine.
- 3 mon later- lost 1 pound, had only taken phentermine 2 weeks, side effects. Restarted phentermine at ½ dose
- 2 mon later – gained 8 pounds, full dose phentermine, started low dose Topiramate 25 mg
- 2 mon later – lost 2 pounds (207), start liraglutide/Victoza, Continue topiramate, stop phentermine
- 2 mon later – lost 5 pounds (202), Continue liraglutide/Victoza, Increased topiramate to 50 mg nightly
- 3 mon later –lost 14 pounds (188), Continue same meds – helping with cravings

Case # Post RYGB weight regain

- 3 mon later –lost 8 pounds (180), down total of 69 pounds since bypass
- At 9 years post LRYGB –Initially lost 106 (96%EBWL, BMI 23.4), After 7 years regained 59 pounds (42.7% EBWL, BMI 33.1, 18.8% TBWL)
- **With medication intervention re-engage with program = lost 27 pounds additional**
- Weight 180 pounds, BMI 29.5, 63% EWL, 27.8% TBWL

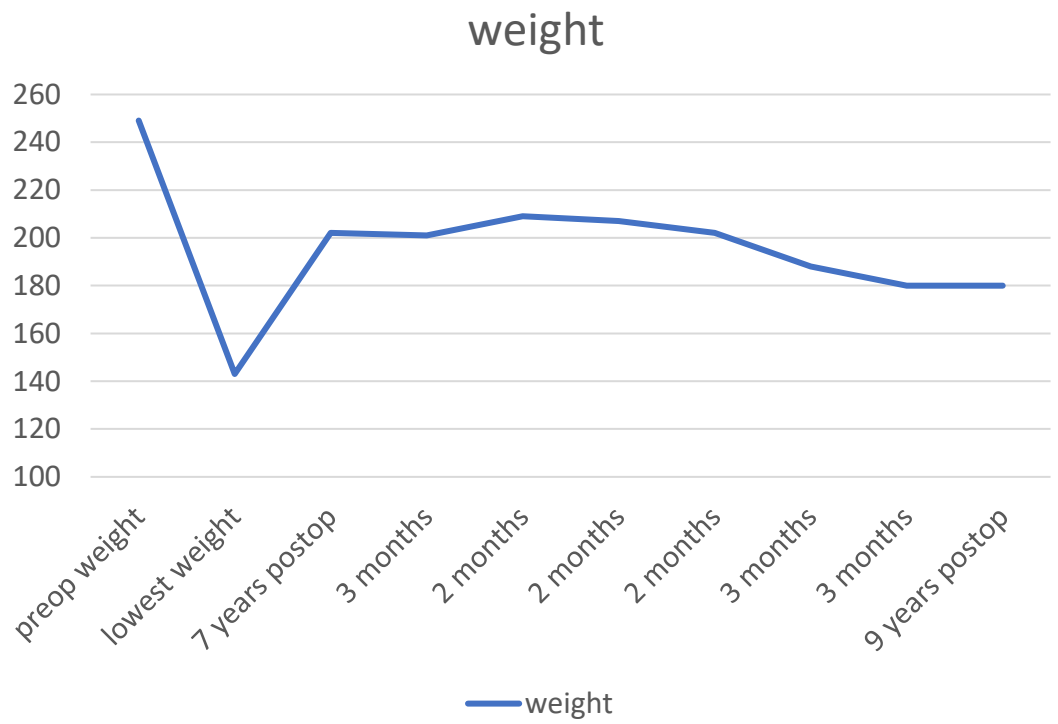
- Other changes including change of metoprolol to diltiazem with good control BP and less fatigue, liraglutide and topiramate helped most with soda cravings taste changes and improved fatigue

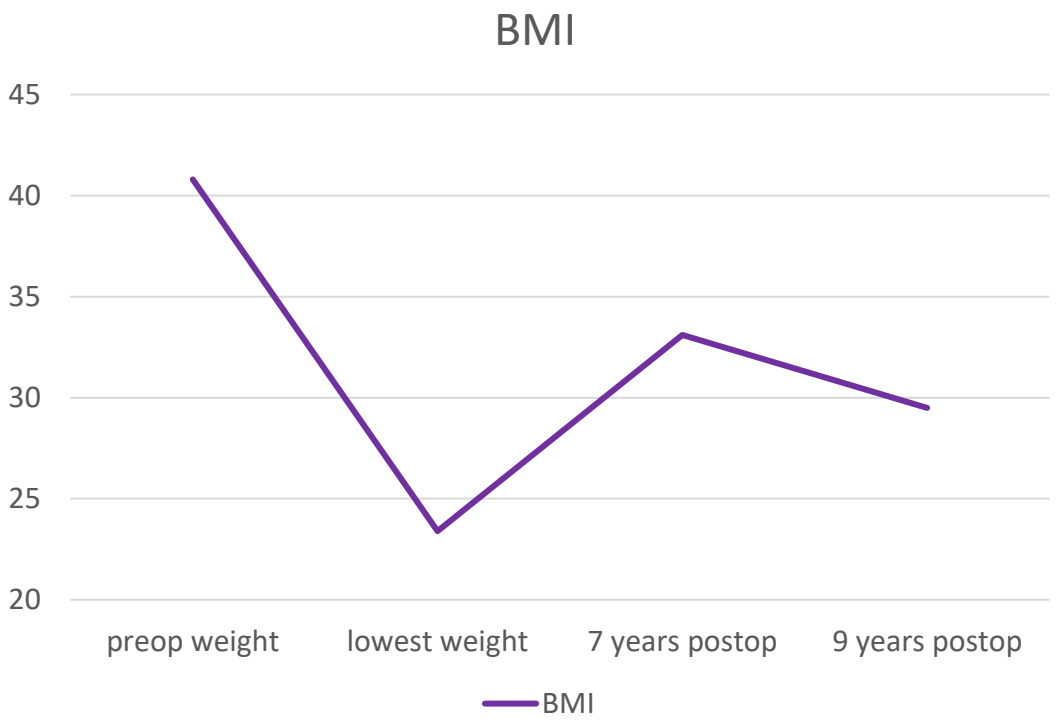
Post RYGB Initial good response with weight regain

At 9 years post LRYGB –Initially lost 106 (96%EBWL, BMI 23.4), After 7 years regained 59 pounds (42.7% EBWL, BMI 33.1, 18.8% TBWL)

With medication intervention (Phentermine/Topiramate – Topiramate/Liraglutide)re-engage with program = lost 27 pounds additional

Weight 180 pounds, BMI 29.5, 63% EWL, 27.8% TBWL





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YIKES!! Where do I begin?

Can you learn to do it? ***YES!!***

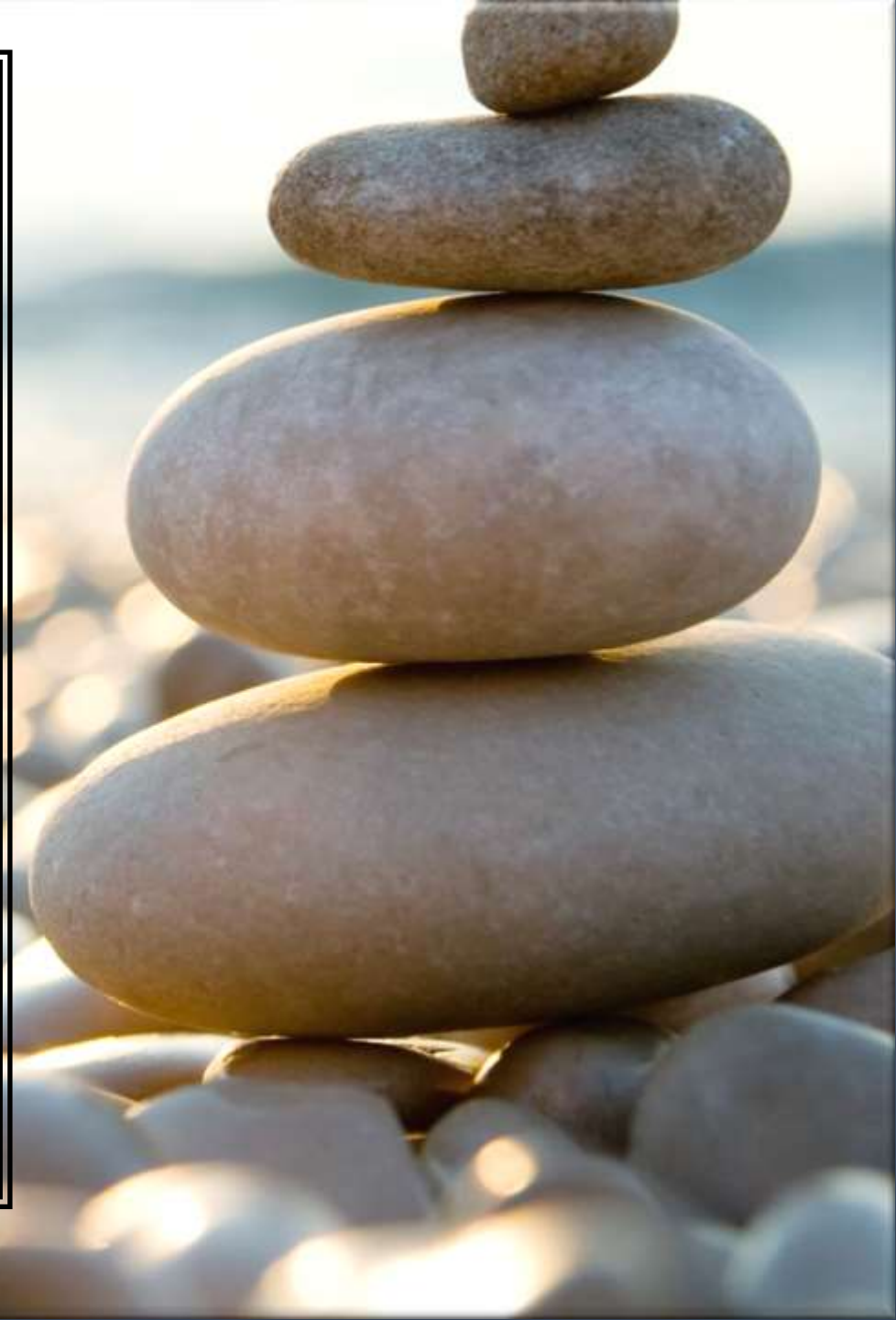
I don’t feel comfortable prescribing medications for weight loss and metabolic hormone alteration

Now What?

Get someone to help you

Future of Obesity Treatment

- Oncology model: “What would the oncologist do?”
- Access to the full spectrum of therapy
- Least invasive to most invasive
- Neoadjuvant therapy
- Surgical treatment
- Adjuvant Therapy
- Repeat Therapy
- Combination Therapy
- Re-operative Therapy



What does this mean for surgeons?

- To operate or not to operate, that is the question

- Additional surgery
- Risks, benefits, goals (patient, surgeon, payors?)
- Treat complications or for weight loss

Conclusions

- *Understanding the physiology of the disease of obesity can help us better understand mechanisms of Metabolic Bariatric Surgery*
- *Medication can be used to augment the effects of surgery and fine tune the patient response*
- *Multi-modal therapy can enhance outcomes*

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