The Pitfalls of the Use of Obesity Medications in the Metabolic and Bariatric Surgical Patient

W. Scott Butsch, MD, MSc FTOS

Director of Obesity Medicine | Bariatric and Metabolic Institute | Cleveland Clinic

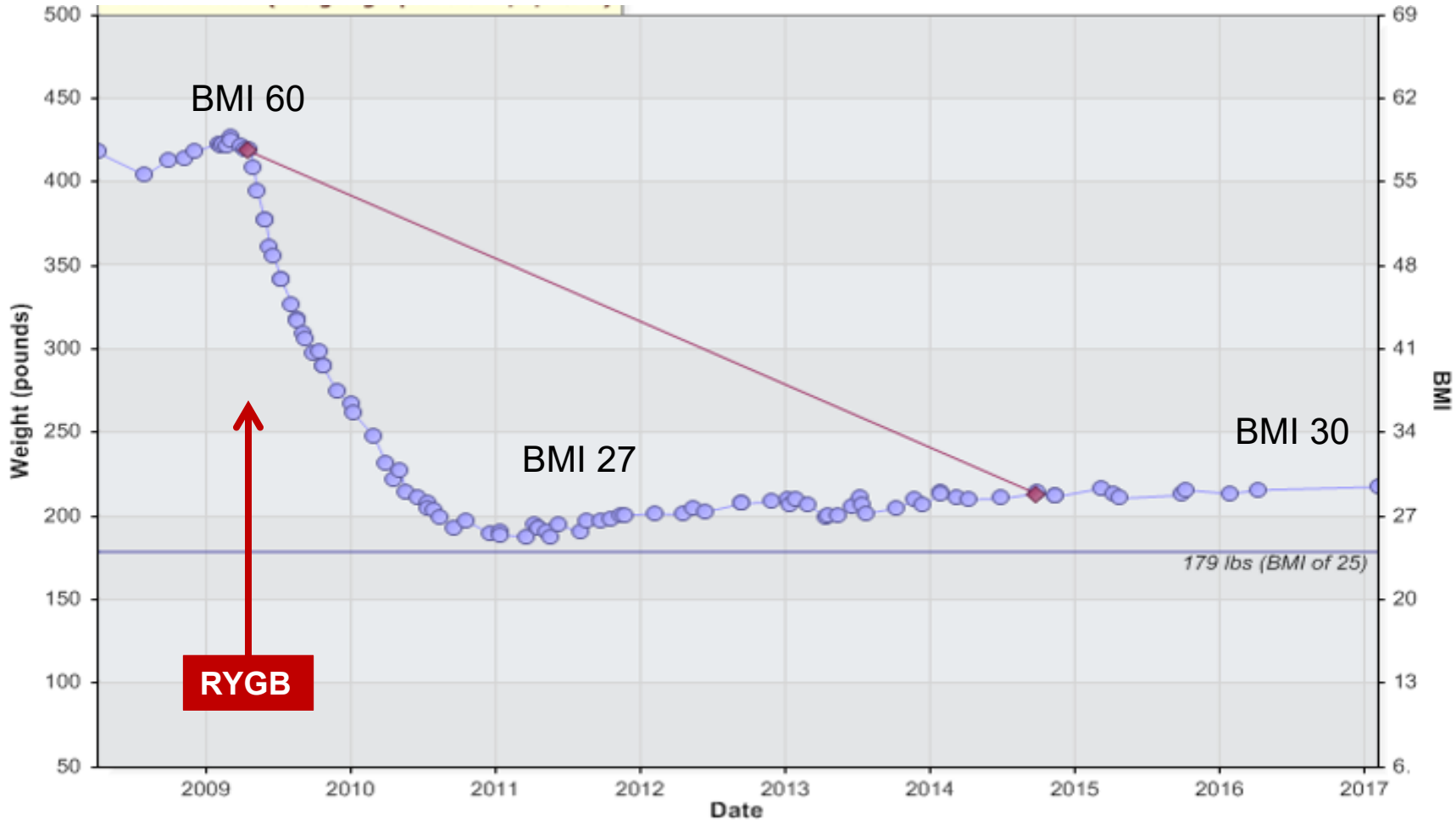
butschw@ccf.org | drbutsch

Disclosures

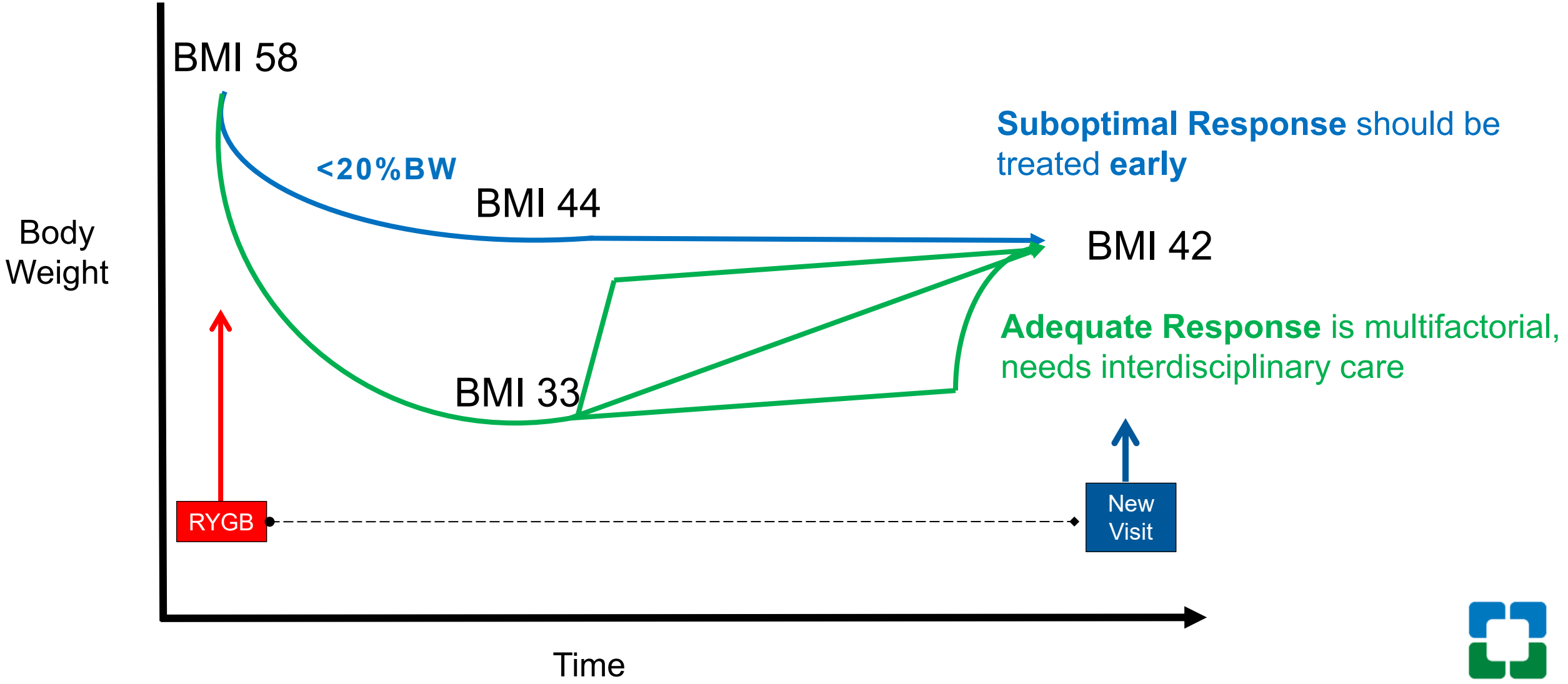
- Abbott
- Boehringer Ingelheim
- Verdiva Bio

These conflicts of interest do not apply to this presentation

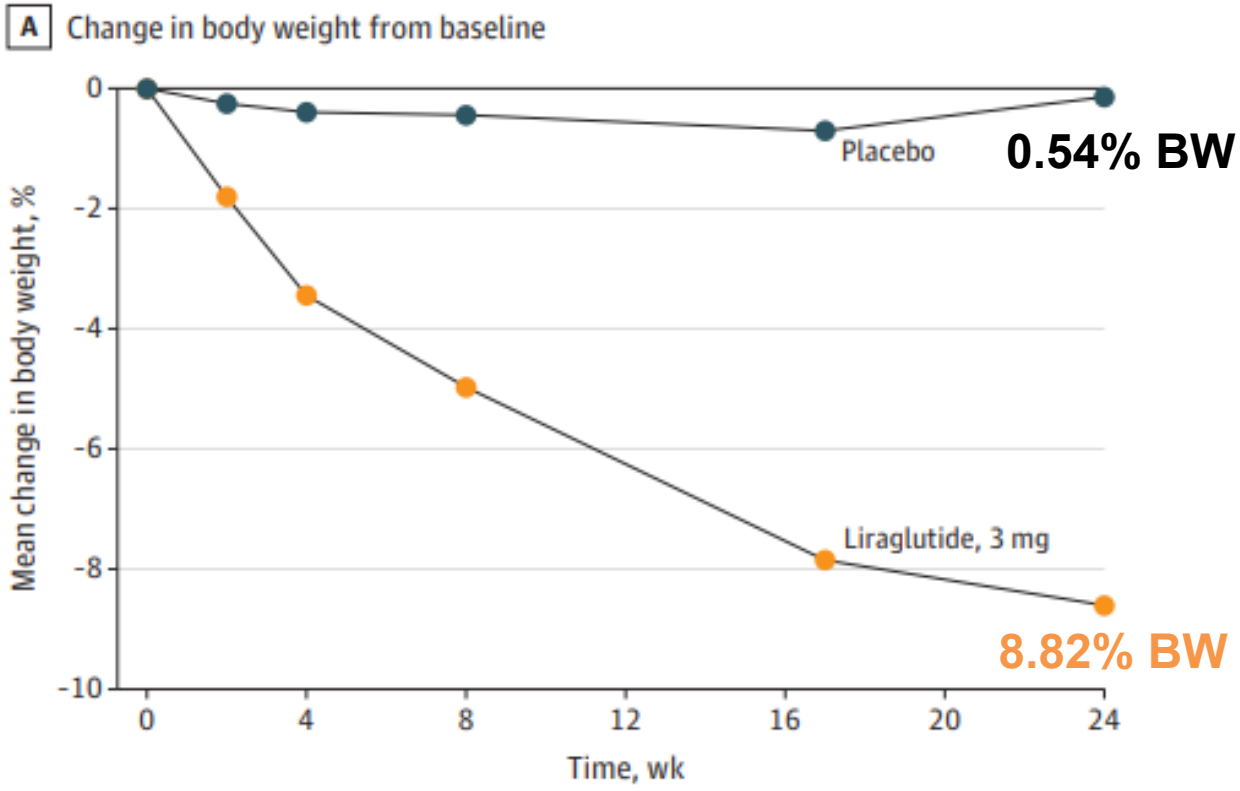
Bariatric and Metabolic Surgery is effective



Understanding Response to Surgery May Help Tailor Medical Treatment Options



Adjunctive use of Obesity Medications for Suboptimal Response to Metabolic and Bariatric Surgery




Research

JAMA Surgery | Original Investigation

Safety and Efficacy of Liraglutide, 3.0 mg, Once Daily vs Placebo in Patients With Poor Weight Loss Following Metabolic Surgery
The BARI-OPTIMISE Randomized Clinical Trial

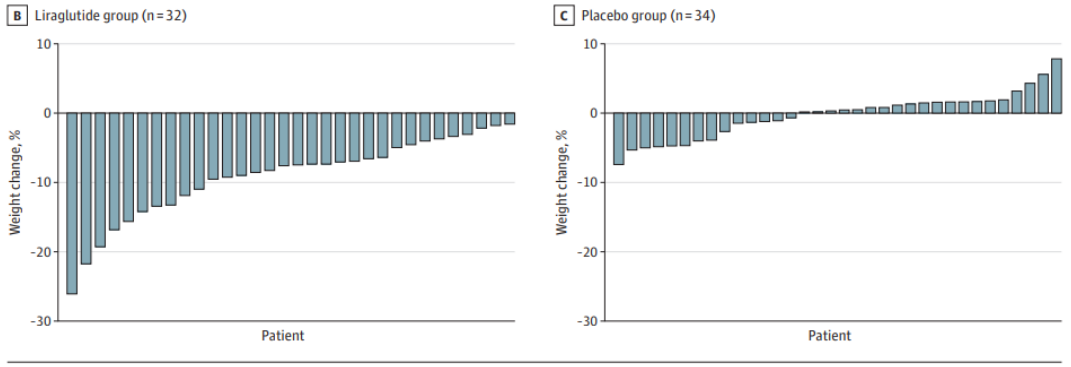
Jessica Mok, BMBS, MPhil; Mariam O. Adeleke, PhD; Adrian Brown, PhD; Cormac G. Magee, MBBChir, MA; Chloe Firman, MRes; Christwishes Makahamadze, MRes; Friedrich C. Jassil, PhD; Parastou Marvasti, PhD; Alisia Carnemolla, PhD; Kalpana Devalia, MBBS, MS; Naim Fakih, MD; Mohamed Elkalaawy, MRCSEd, MS, MD; Andrea Pucci, MD, PhD; Andrew Jenkinson, MBBS, MS; Marco Adamo, MD; Rumana Z. Omar, PhD; Rachel L. Batterham, MBBS, PhD; Janine Makaronidis, MBChB, PhD

IMPORTANCE Metabolic surgery leads to weight loss and improved health, but these outcomes are highly variable. Poor weight loss is associated with lower circulating levels of glucagon-like peptide-1 (GLP-1).

OBJECTIVE To assess the efficacy and safety of the GLP-1 receptor agonist, liraglutide, 3.0 mg, on percentage body weight reduction in patients with poor weight loss and suboptimal GLP-1 response after metabolic surgery.

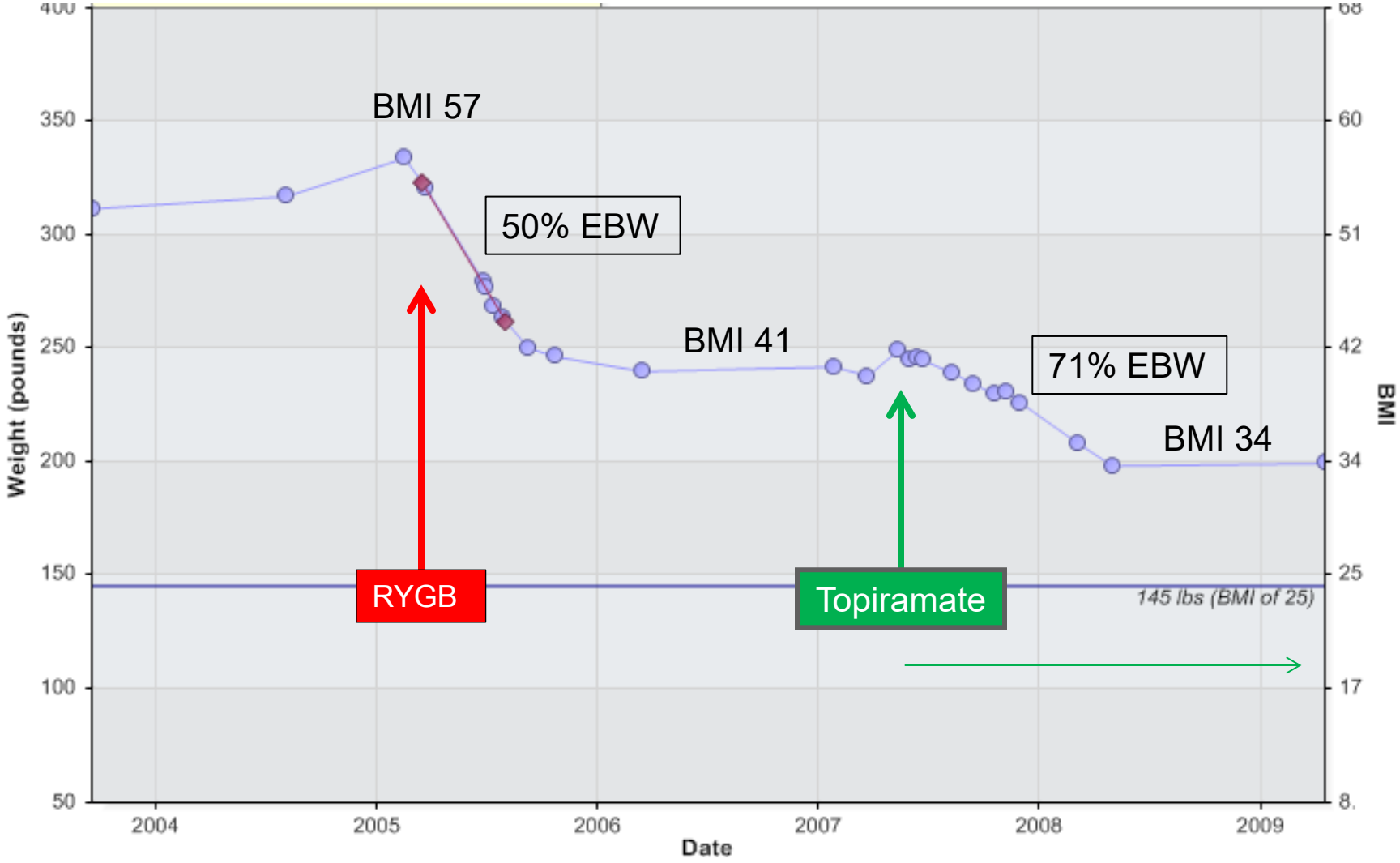
Visual Abstract
Invited Commentary page 1011
Supplemental content

BARI-OPTIMIZE
24 wk RCT n=57(70), BMI 43
>1yr post MBS (- 7.2%BW), 52mo s/p MBS
Liraglutide 3.0mg v Placebo

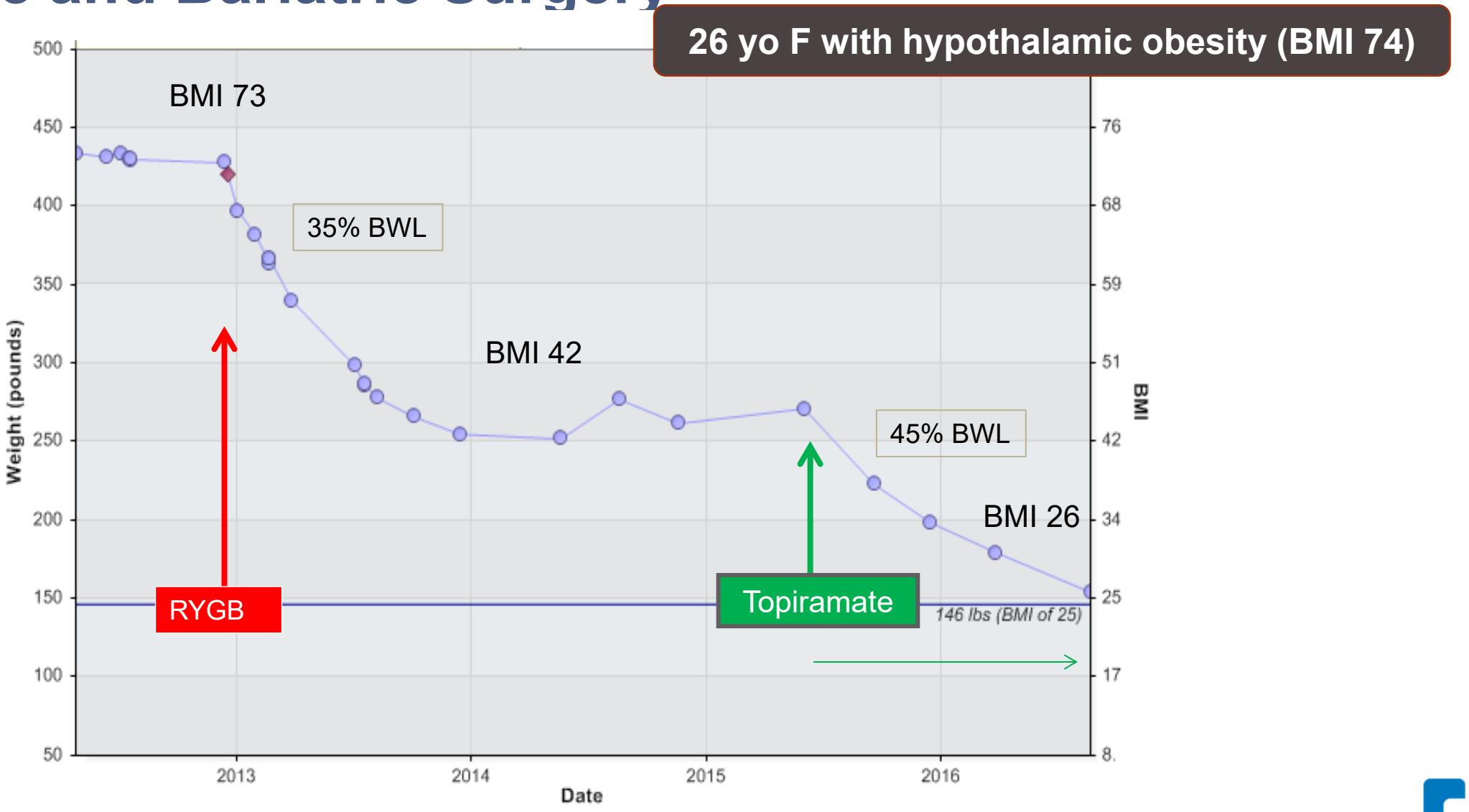


Mok J et al *JAMA Surg* 2023

Use Obesity Medications in Combination for individuals with a **Suboptimal Response** after Surgery



Adjuvant Obesity Therapy for Severe Obesity after Metabolic and Bariatric Surgery



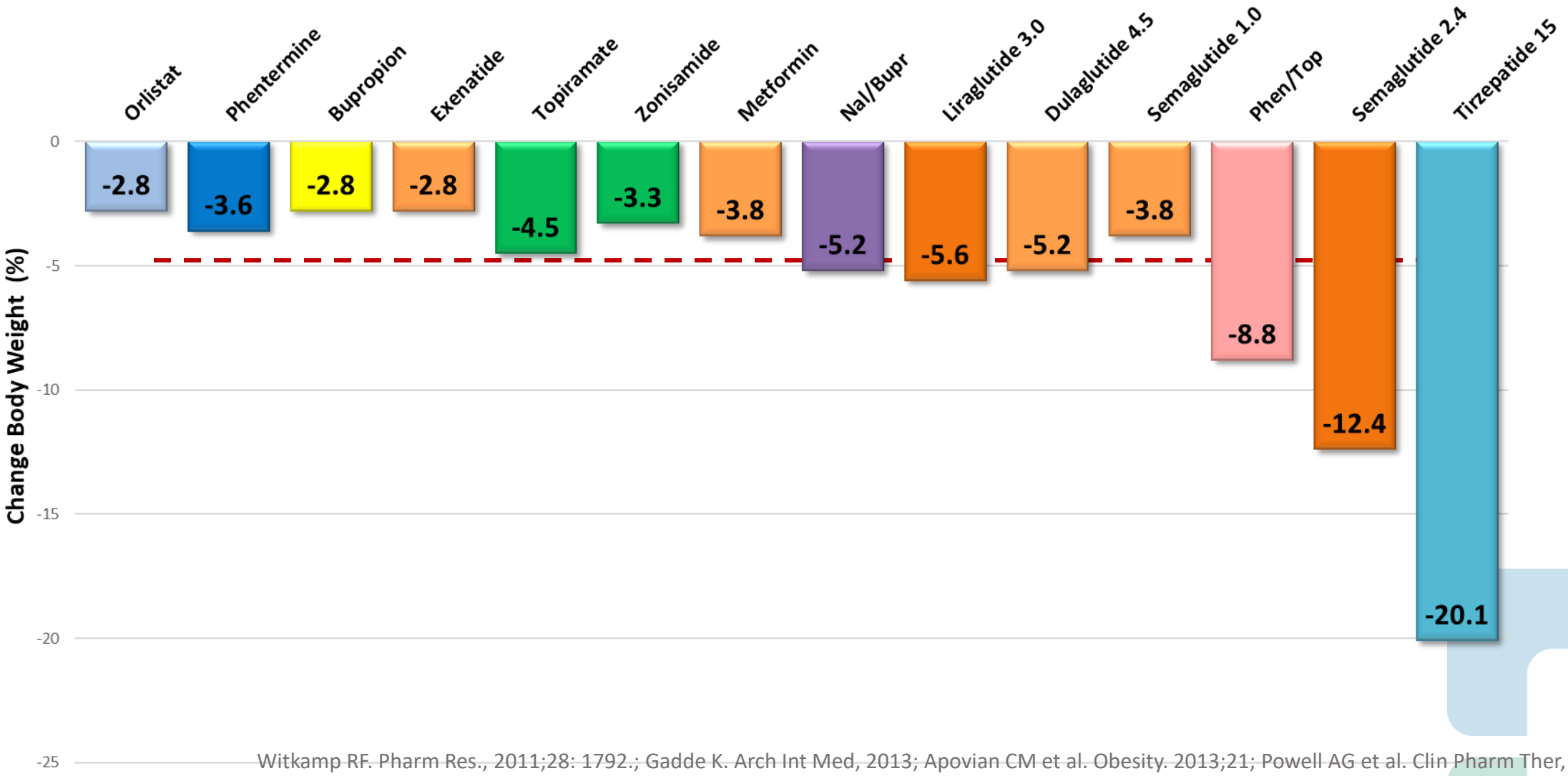
What should I do before starting obesity medications(OMMs) in my metabolic surgical patient?

1. Manage both provider and patient expectations
2. Understand side effect profiles may alter surgical complications
3. Understand the evaluation and preservation of lean mass amid weight loss using GLP-1RAs and other obesity therapies after metabolic surgery
4. Recognize perioperative/periprocedural management of OMMs

Set Expectations of Use of OMMs early
Many Unanswered Questions Remain

- **Understand many OMMs are available, not just GLP1s**
- **Set Weight outcomes in setting of limited evidence**
  - Unclear guidelines to estimate effectiveness
  - Unclear what OMM selection/ dose of medication
  - Unclear timing of initiation (eg 6mo, nadir, plateau)
- **Set Clear outcome measures for OMM benefit**
  - Weight/BMI vs QOL vs body fat%
  - Comorbidity improvement
  - Appetite control (eg decreased Hunger / increased Satiety

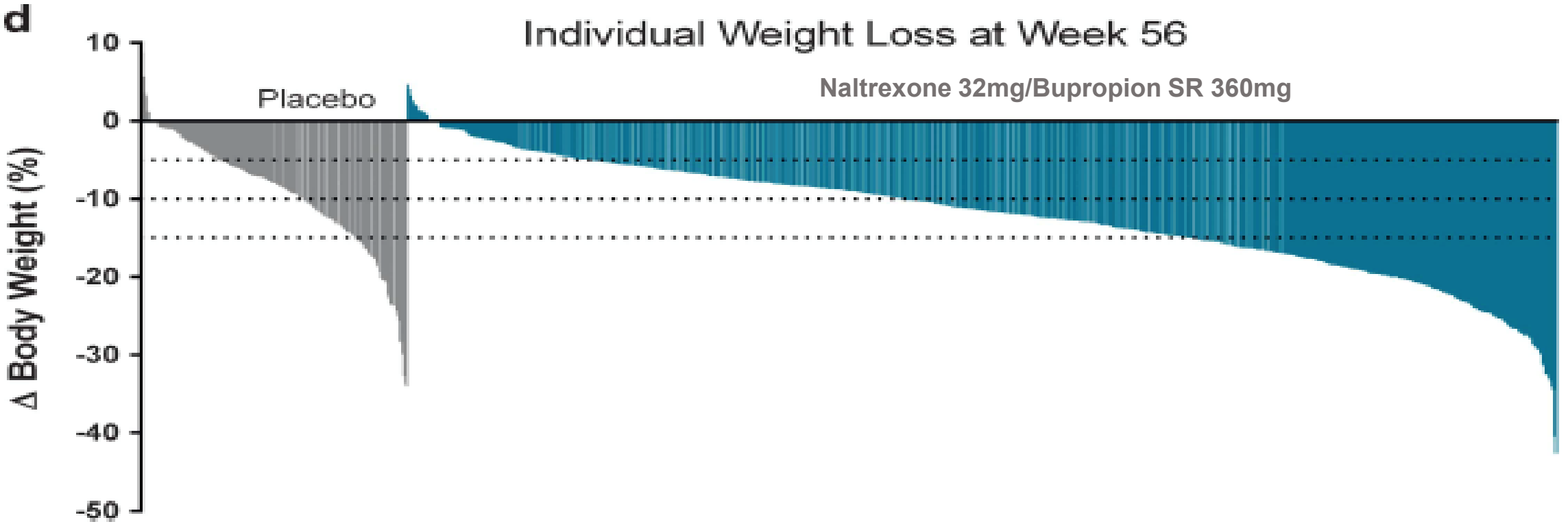
Should we pick the most effective Obesity Medication?



Witkamp RF. Pharm Res., 2011;28: 1792.; Gadde K. Arch Int Med, 2013; Apovian CM et al. Obesity. 2013;21; Powell AG et al. Clin Pharm Ther, 2011;90 ; Torgerson JS . Diab Care, 2004; Smith et al. NEJM, 2010;363.; Garvey WT. AJCN. 2012.; Bonora,E. Diabetes Obes Metab. 2021;23. Wilding JA, et al. NEJM, 2021. Jastreboff A, et al NEJM 2022

Slide: W. Scott Butsch

Individual Responsiveness to **Medication** varies



Fujioka K et al. *IJO* 2016;40:1369

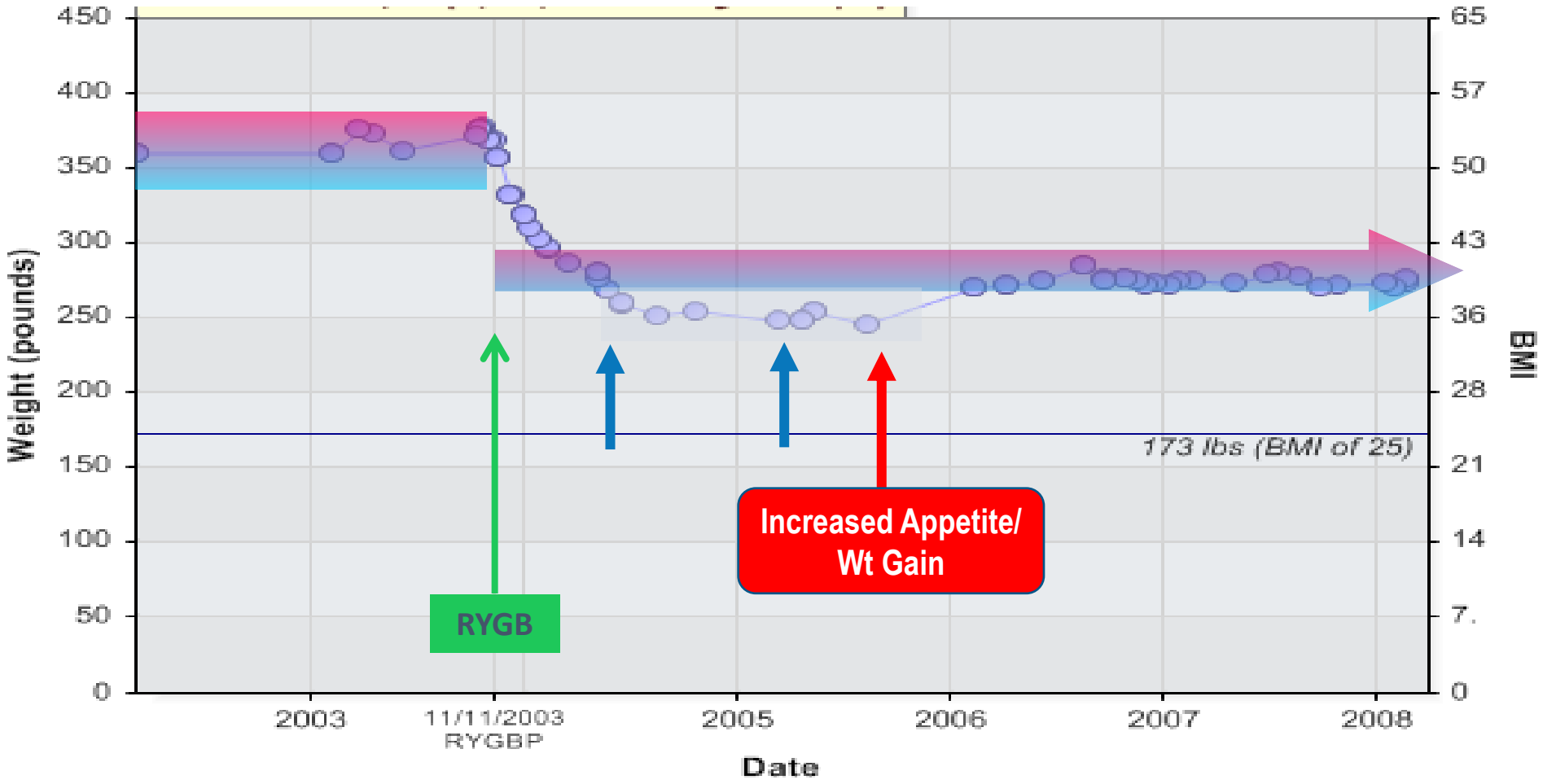
Tailoring OMMs to help other medical conditions

Additional Condition	Medication to Consider
Diabetes	Liraglutide 1.8 mg; Cana-,Empa-, Dapagliflozin, Semaglutide 2.0mg, Tirzepatide
Depression	Bupropion
Migraines	Topiramate, Zonisamide
Bipolar disorder (on psychotropic medications)	Metformin*
Sleep dysfunction	Topiramate*, Zonisamide*
Elevated LDL,TG	Orlistat
Smoking, Cravings	Naltrexone-bupropion, Topiramate*, Bupropion

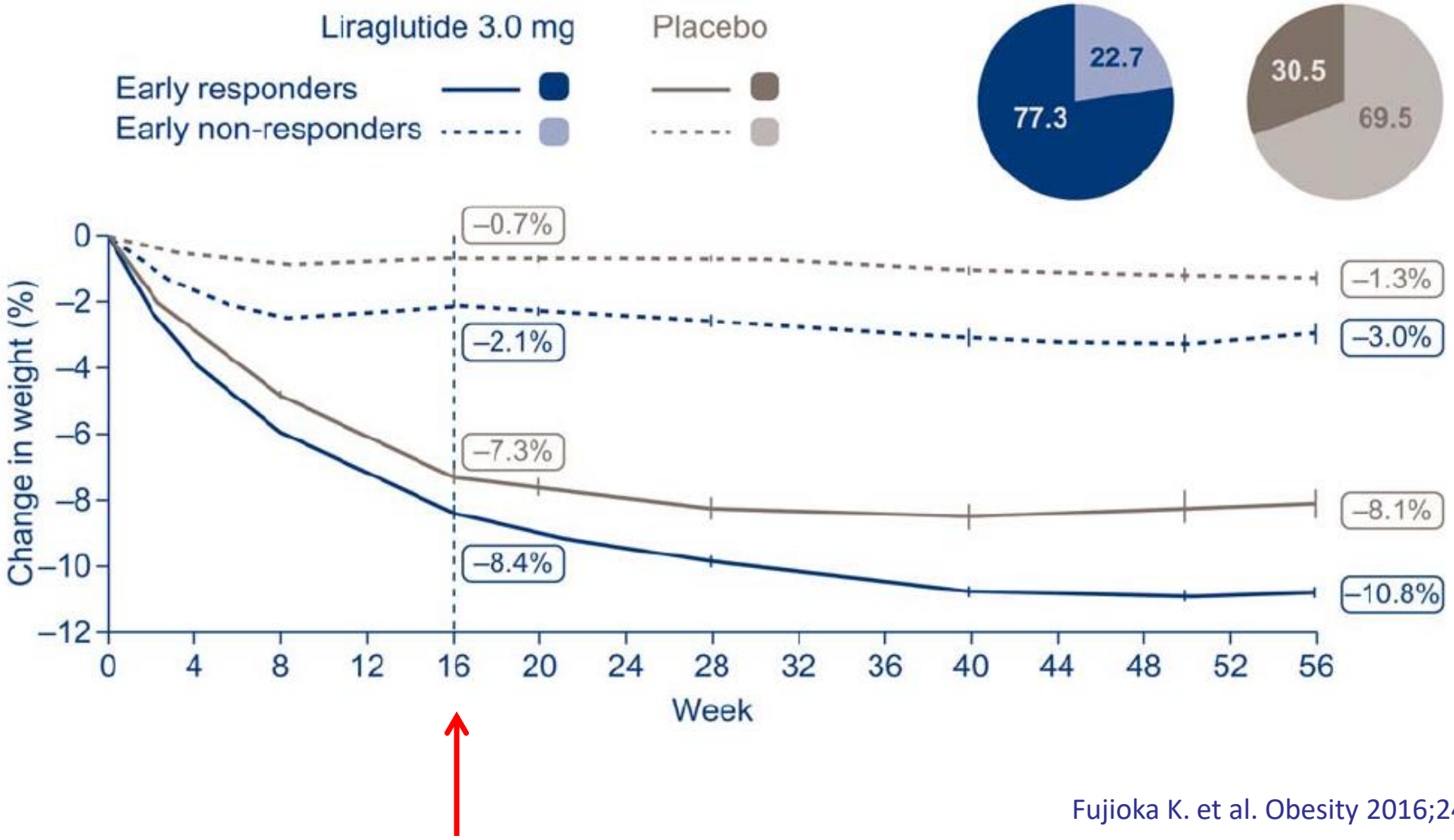
* Off Label Use

Managing Expectations is Critical

Discuss Weight Gain/Hunger in context of weight regulation

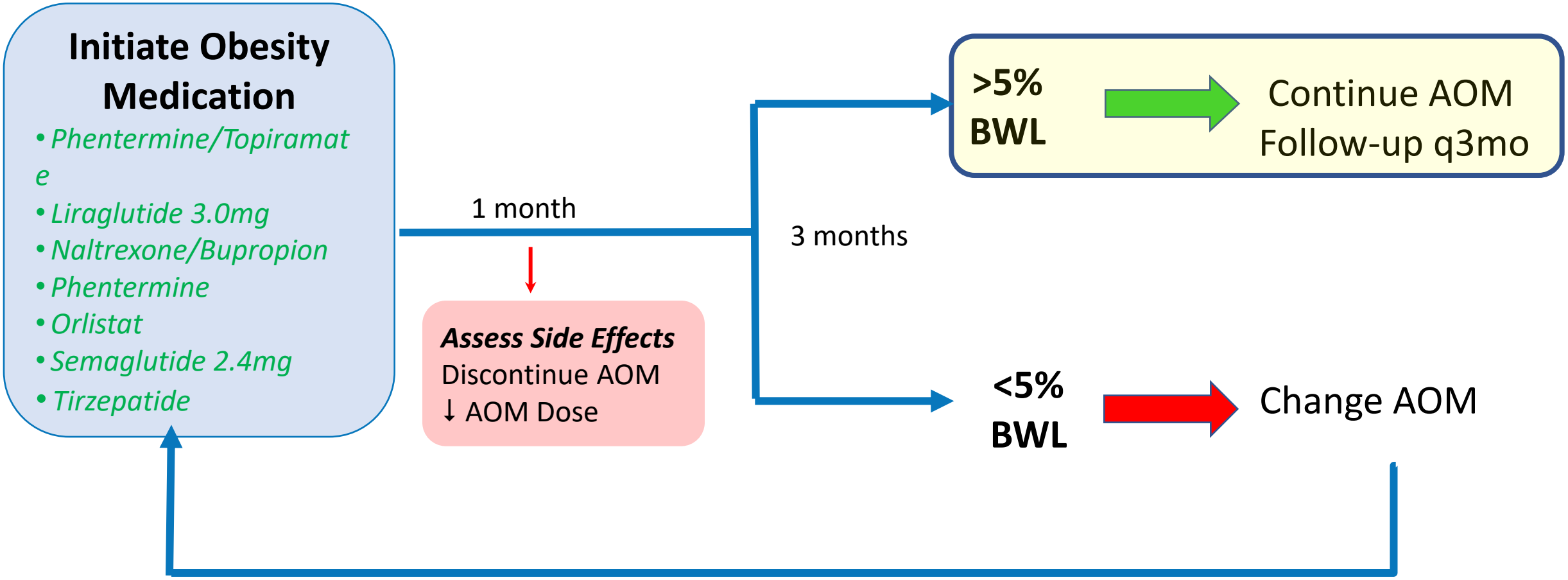


Early Responders to Liraglutide 3.0mg Predicts One Year Outcome



Fujioka K. et al. Obesity 2016;24:

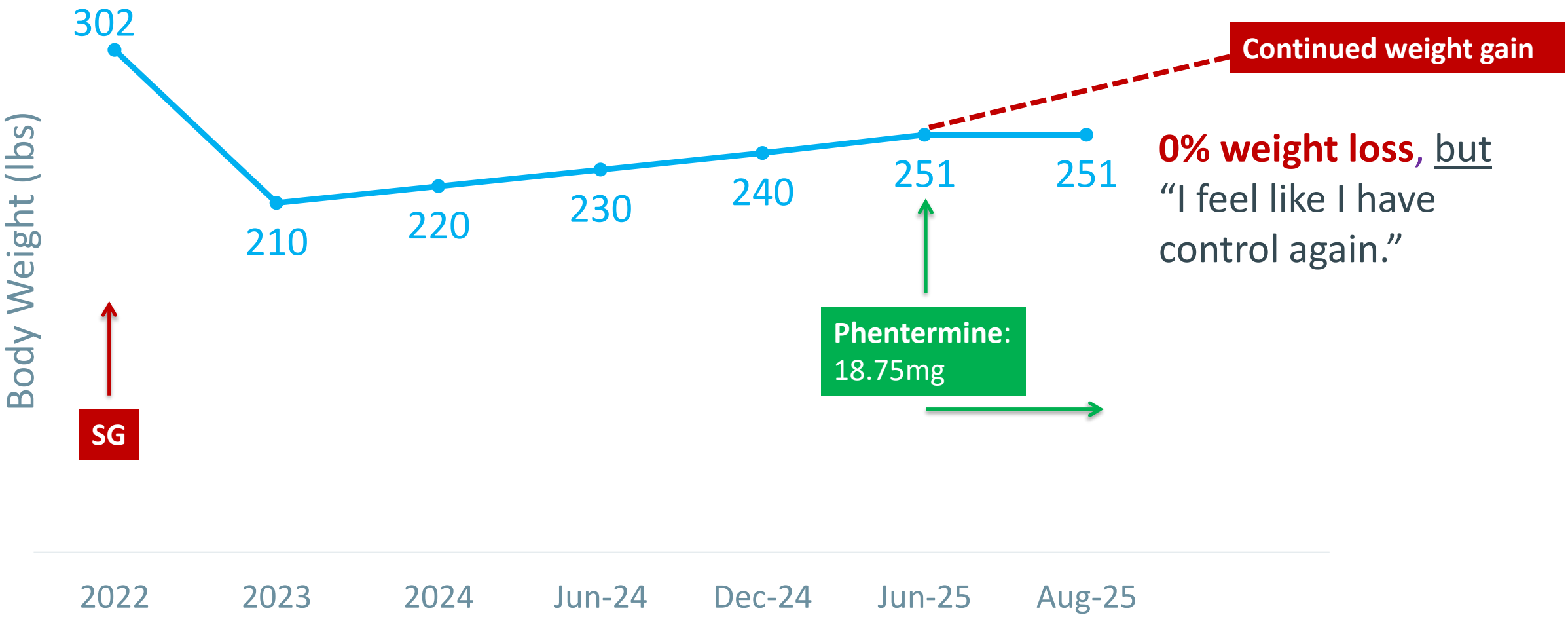
Continue Anti-Obesity Medication in Responders



Gossman A, Butsch WS, Jastroboff AJ. *Med Clin* 2021

Slide: W. Scott Butsch

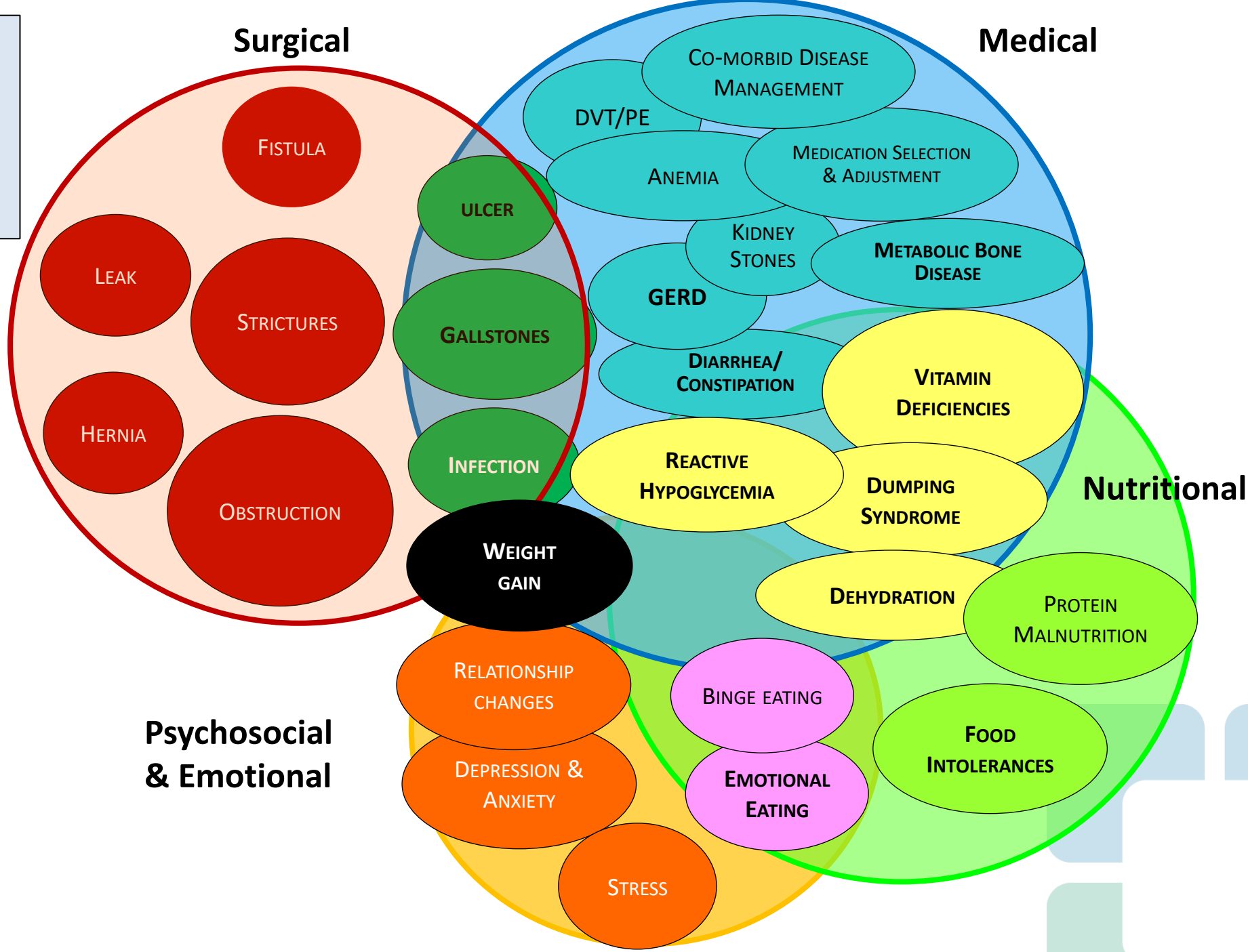
Weight Gain Post MBS: Flattening the Curve



What should I know before starting obesity medications in a bariatric surgical patient?

1. Manage both provider and patient expectations
2. Understand side effect profiles may alter surgical complications
3. Understand the evaluation and preservation of lean mass amid weight loss using GLP-1RAs and other obesity therapies after metabolic surgery
4. Recognize perioperative/periprocedural management of OMMs

Multidisciplinary Management of Surgical Patients is Critical



Overview of available FDA-Approved Obesity Medications

*excluding Orlistat, Setmelanotide

Sympathomimetic amines[1,2]

Phentermine

37.5 mg PO QD

Phentermine/ topiramate

15 mg/92 mg PO QD

Efficacy: 5-10%BWL

Most common AEs
- Dry mouth
- Constipation
- Dysguesia (*Qsymia*)
- Paresthesias (*Qsymia*)
- **CI**: CAD, arrhythmias, kidney stones

Other considerations
- Sched IV controlled substance
- Use birth control (*Qsymia*)
- Monitor renal(*Qsymia*), HR/BP

Reward system modulator[3]

Naltrexone ER/ Bupropion SR

16/180 mg PO BID

Efficacy: 5-7%BWL

Most common AEs
- Headache
- Dizziness
- Insomnia
- GI AEs
- **CI**: seizure, bulimia

Other considerations
- Monitor mood, HR
- Consider if smoking, depression

GLP-1RAs[4-6]

Liraglutide

3 mg SC QD

Semaglutide

2.4 mg SC weekly

Efficacy: 7-15%BWL

Most common AEs
- GI AEs
- Headache
- Fatigue
- Injection site reactions
- **CI**: MTC, MEN2 , acute pancreatitis

Other considerations
- $$$, lack of insurance covg
- **Discontinue before surgery, procedure**

GLP-1/GIP receptor dual agonist[7,8]

Tirzepatide

15 mg SC weekly

Efficacy: 20-22%BWL

Most common AEs
- GI AEs
- Headache
- Fatigue
- Injection site reactions
- **CI**: MTC, MEN2, acute pancreatitis

Other considerations
- $$$, lack of insurance covg
- **Discontinue before surgery, procedure**

Note: Most frequent AEs as listed in the respective product prescribing information. **NOT INDICATED in PREGNANCY or BREASTFEEDING**

AE, adverse event; CI, contraindication; GI, gastrointestinal; MTC, medullary thyroid cancer; MEN2, multiple endocrine neoplasms 2; EGD, endoscopy (also any endoscopic procedure, colonoscopy)

1. Phentermine hydrochloride. Prescribing information. Epic Pharma, LLC; 2019. **2.** Qsymia. Garvey WT et al. *AJCN* 2012. **3.** Contrave: Apovian CM et al.*Obesity* 2013. **4.** Saxenda® Prescribing info. Novo Nordisk; 2023. **5.** Wegovy® Prescribing info. Novo Nordisk; 2023. **6.** Wilding J et al. *NEJM.* 2021. **7.** Jastreboff A et al. *NEJM.* 2022. **8.** Zepbound™ Prescribing info. Eli Lilly and Company; 2023.

If I start a GLP-1 what should I know?

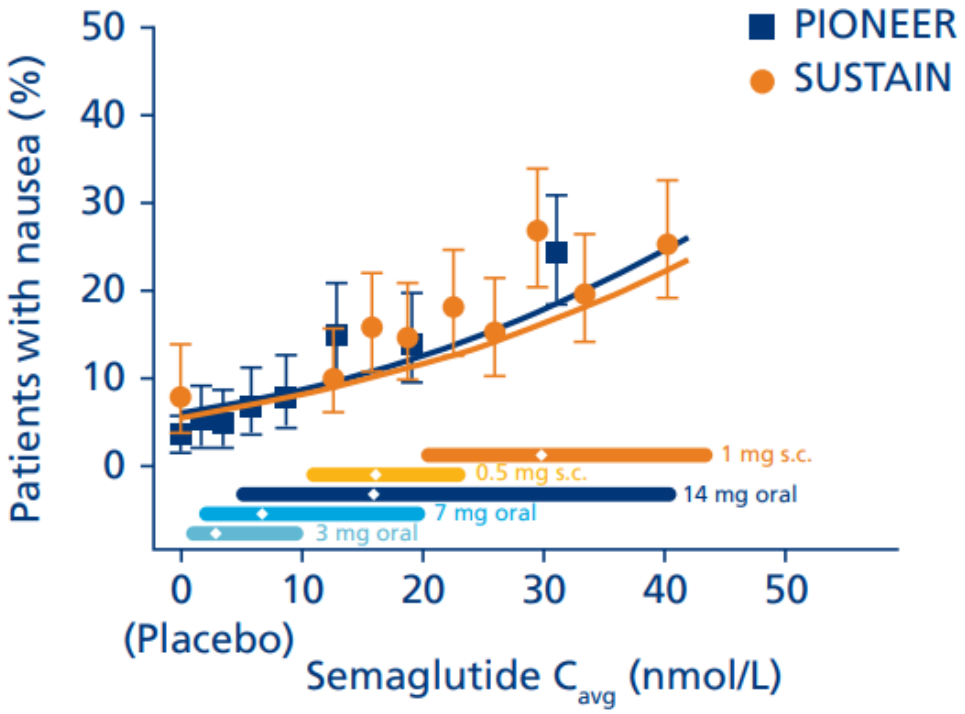
- **Screen** for personal/family h/o **medullary thyroid cancer** or **MEN II**
- **No** influence on thyroid disease, as the thyroid has no GLP1 receptors
- **GI side effects** are common, **mild-moderate** and **dose-dependent**.
  - Mitigate AEs by addressing diet: decrease **Fat**, **Fiber** intake 1-2 days post injection
- **Gallstone** incidence is higher (1.4x), not weight loss effect, not direct (? FGF19, GLP-2, CCK)
- Acute Pancreatitis is rare, equally distributed in RCTs. Chronic pancreatitis was excluded, risk of pancreatic cancer is unknown
- **Visual problems** (worsening progression of *diabetic retinopathy*, *nonarteritic anterior ischemic optic neuropathy-NAION*) are uncommon, conflicting studies, association not causal
- **Lean muscle mass loss** accounts for 35-45% of weight lost.
  - Mitigate by encouraging resistance training; Maintain **Protein** **intake** 1.2-1.5g/kg/day

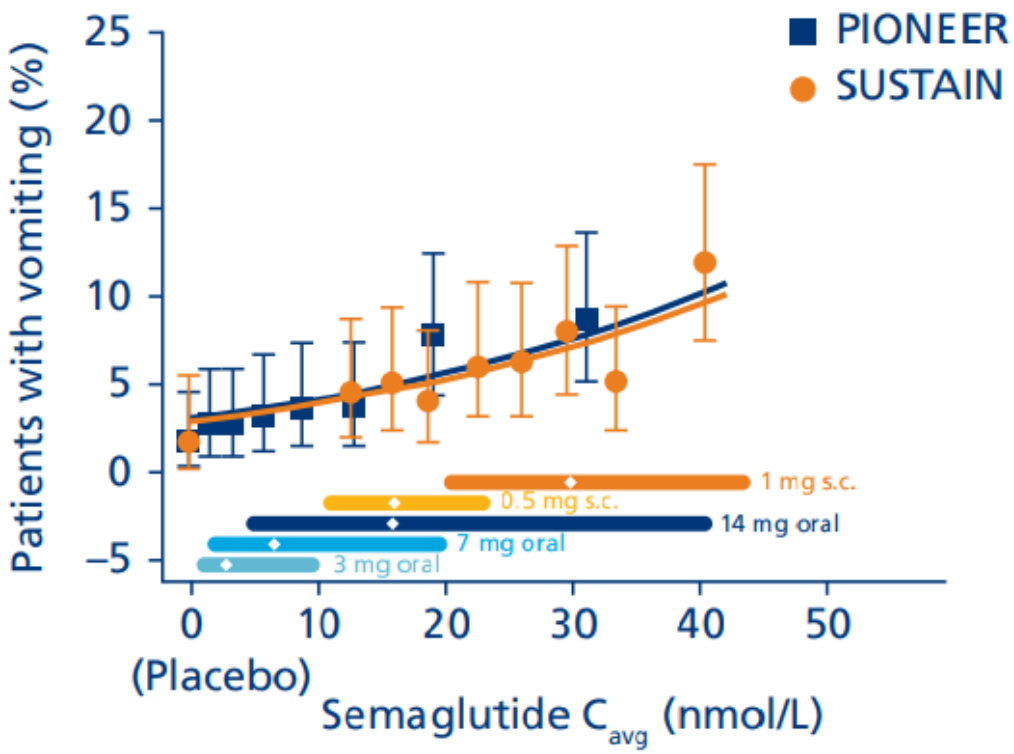
Vidal J et al ***Int J Obes*** **2024**
Zhou J et al. *Endocr* 2025
Hathaway JT, et al. *JAMA Ophthal* 2024

Gastrointestinal adverse effects are Similar in low dose Oral and Subcutaneous Semaglutide

PIONEER – 3,7,14mg

SUSTAIN – 0.5, 1.0mg

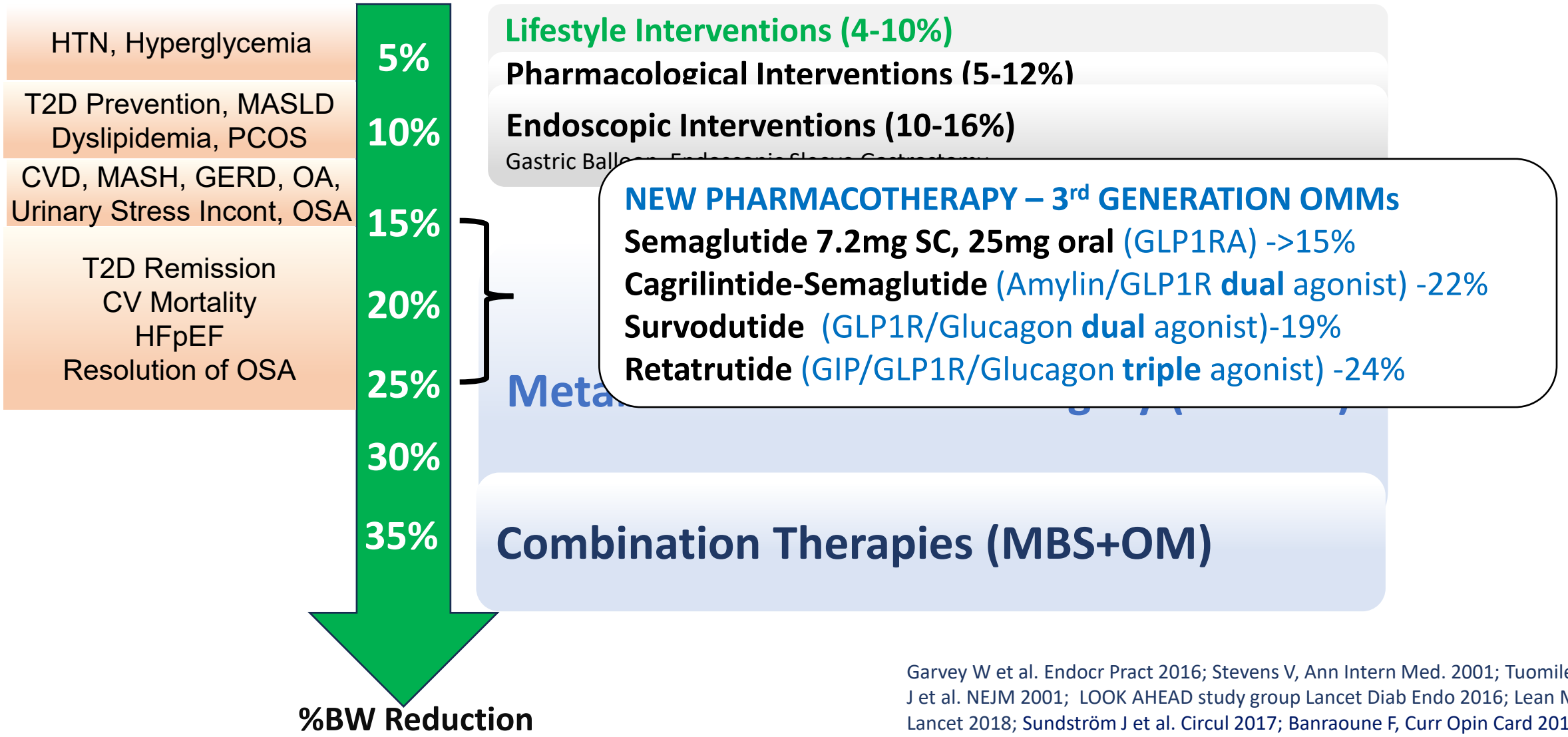




What should I know before starting obesity medications in a bariatric surgical patient?

1. Manage both provider and patient expectations
2. Understand side effect profiles may alter surgical complications
3. Understand the evaluation and preservation of lean mass amid weight loss using GLP-1RAs and other obesity therapies after metabolic surgery
4. Recognize perioperative/periprocedural management of OMMs

Combination of Obesity treatments may produce significant weight reduction



Garvey W et al. Endocr Pract 2016; Stevens V, Ann Intern Med. 2001; Tuomilehto J et al. NEJM 2001; LOOK AHEAD study group Lancet Diab Endo 2016; Lean M Lancet 2018; Sundström J et al. Circul 2017; Banraoune F, Curr Opin Card 2011; Ryan D et al. Curr Obes Rep 2017; Muller TD, et al. Nature Rev 2022:21:201-23

Slide: W. Scott Butsch

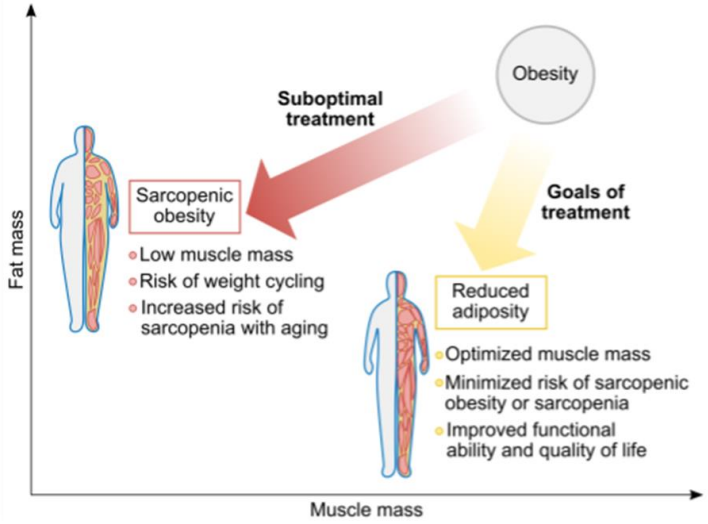
Proposed Management with OMMs requires attention to preservation of muscle mass

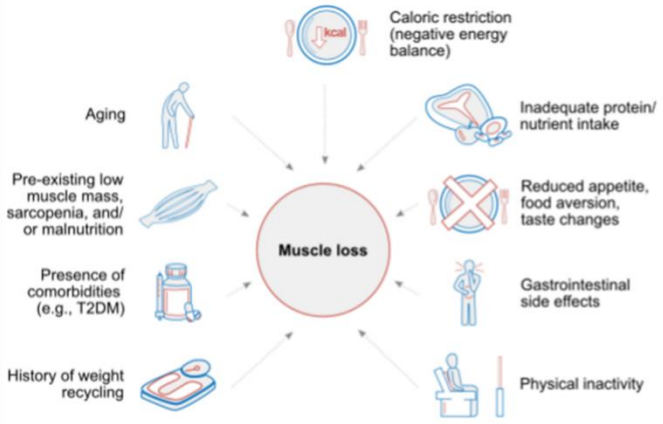
Received: 2 February 2024 | Revised: 16 August 2024 | Accepted: 22 August 2024
DOI: 10.1111/obr.13841
REVIEW
Obesity Management / Intervention
OBESITY Reviews WILEY

Strategies for minimizing muscle loss during use of incretin-mimetic drugs for treatment of obesity

Jeffrey I. Mechanick[1] | W. Scott Butsch[2] | Sandra M. Christensen[3] | Osama Hamdy[4] | Zhaoping Li[5] | Carla M. Prado[6] | Steven B. Heymsfield[7]

Mechanick JI, Butsch WS, Christensen SM et al Obes Rev 2024



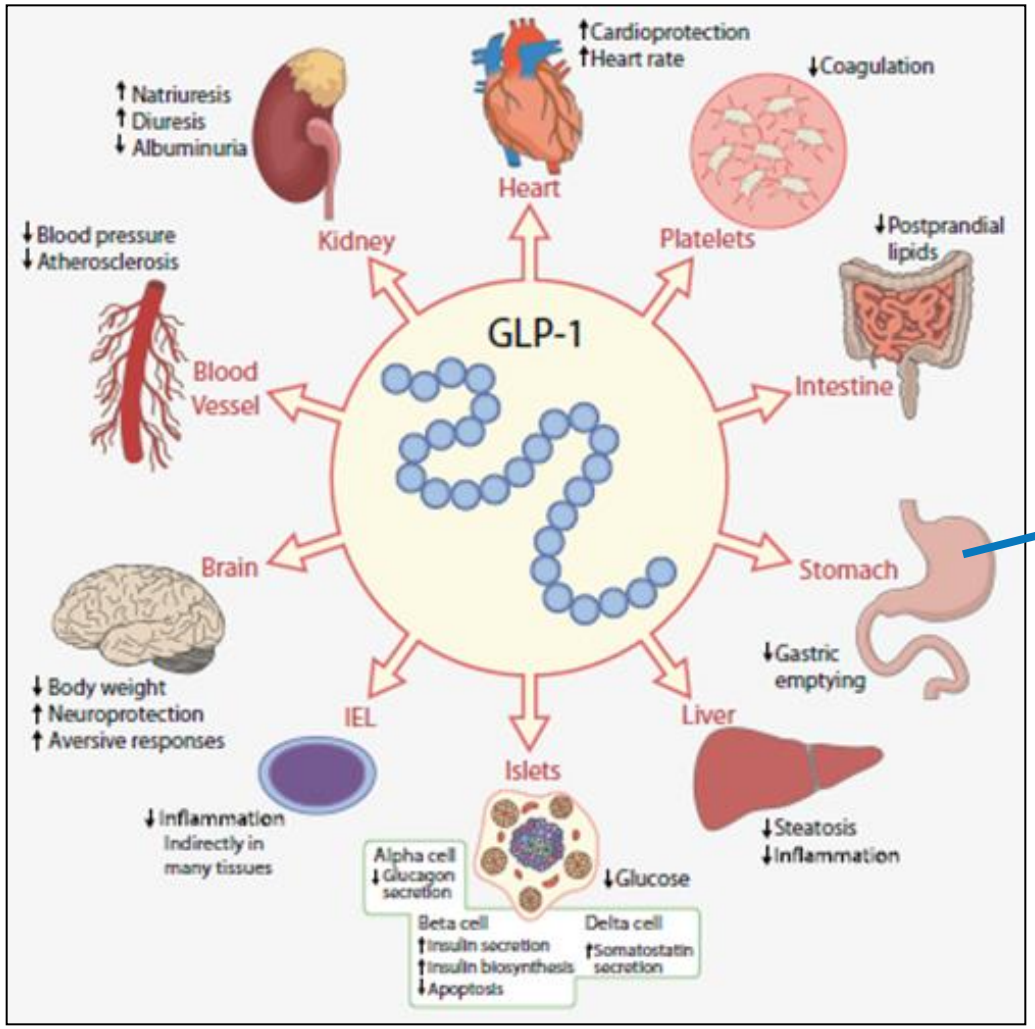


1. Identify Contributing or **Compounding Factors**
2. Consider **Body Composition** (baseline,sequential) to better understand adiposity, muscle mass
3. Sequential testing may help management decisions – OMM dose, OMM choice
4. Consider muscle evaluation (Hand grip, Sit-to-stand) to understand global muscle health
5. Use multimodal approach to minimize Muscle Mass Loss (Nutrition therapy – protein 1.2-1.5g/kg/d) + resistance training
6. Understand GLP1RA and MBS may alter dietary and protein intake

What should I know before starting obesity medications in a bariatric surgical patient?

1. Manage both provider and patient expectations
2. Understand side effect profiles may alter surgical complications
3. Understand the evaluation and preservation of lean mass amid weight loss using GLP-1RAs and other obesity therapies after metabolic surgery
4. Recognize perioperative/periprocedural management of OMMs

Metabolic Actions of GLP-1



Inhibits Gastrointestinal motility and gastric secretion

- Constipation
- Dehydration
- *Unintentional Restrictive Eating Patterns*
- *Exacerbation of Past Eating Disorder*

Drucker DJ. *Diabetologia* 2023;66: 1765-79

Multi-society CPG for GLP1RA (2024)

ELSEVIER

Surgery for Obesity and Related Diseases 20 (2024) 1183–1186

SURGERY FOR OBESITY AND RELATED DISEASES

ASMBS guidelines/statements

Multisociety clinical practice guidance for the safe use of glucagon-like peptide-1 receptor agonists in the perioperative period

Tammy L. Kindel, M.D., Ph.D.[a,*], Andrew Y. Wang, M.D.[b], Anupama Wadhwa, M.D.[c,d], Allison R. Schulman, M.D., M.P.H.[e], Reem Z. Sharaiha, M.D., M.Sc[f], Matthew Kroh, M.D.[g], Omar M. Ghanem, M.D.[h], Shauna Levy, M.D., M.S.[i], Girish P. Joshi, M.D.[c], Teresa L. LaMasters, M.D.[j], representing the American Gastroenterological Association, American Society for Metabolic and Bariatric Surgery, American Society of Anesthesiologists, International Society of Perioperative Care of Patients with Obesity, and the Society of American Gastrointestinal and Endoscopic Surgeons

[a]Department of Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin
[b]Division of Gastroenterology and Hepatology, University of Virginia, Charlottesville, Virginia
[c]Department of Anesthesiology and Pain Management, University of Texas, Southwestern Medical Center, Dallas Texas
[d]Outcomes Research Consortium, University of Texas, Houston, Texas

Table. Multi-Society Guideline Recommendations

Guideline recommendation	Considerations
Recommendation 1: Use of GLP-1s in the perioperative period should be based on shared decision-making of the patient, with procedural, anesthesia and prescribing care teams balancing the metabolic need for the GLP-1 with individual patient risk. This can be achieved by developing multidisciplinary protocols/procedures appropriate for individual practices.	**Providers should consider:** • **Dosing.** The GLP-1 dosing escalation phase usually lasts 4 to 8 weeks and is associated with a higher risk for delayed gastric emptying than the maintenance phase. Higher doses, as well as weekly doses, also increase the risk for GI side effects. • **GI symptoms.** The presence of nausea, vomiting, abdominal pain, dyspepsia and constipation are suggestive of delayed gastric emptying. • **Medical conditions beyond GLP-1 usage.** Patients should be evaluated for medical conditions that increase the risk for delayed gastric emptying, including bowel dysmotility, gastroparesis and Parkinson's disease. Assessment for such risk factors should be done early enough before surgery to allow any necessary adjustments in preoperative care, such as diet modification and medication bridging if GLP-1 discontinuation is appropriate. For patients who do not have an elevated risk for delayed gastric emptying and aspiration based on these considerations, GLP-1 therapy may be continued preoperatively.
Recommendation 2: The safe use of GLP-1s in the perioperative period should include efforts to minimize the aspiration risk of delayed gastric emptying. This can be achieved by preoperative diet modification and/or altering the anesthesia plan to consider rapid sequence induction of general anesthesia for tracheal intubation.	To minimize the aspiration risk of delayed gastric emptying, use a 24-hour liquid diet for patients undergoing colonoscopy and bariatric surgery. A POCUS could be used to assess aspiration risk, if available. If providers decide there is an unacceptable risk for delayed gastric emptying, they should follow the original guidance from the ASA, holding the day of surgery for daily agents and a week before surgery for weekly agents.

GLP-1, glucagon-like peptide-1 receptor agonist; POCUS, point-of-care gastric ultrasound.

Based on Surg Obes Relat Dis 2024 20(12):1183-1186

Recommendation 1

*Use of GLP-1RAs in the perioperative period should be based on **shared decision-making** of the patient with procedural, anesthesia, and prescribing care teams **balancing the metabolic need for the GLP-1RA with individual patient risk**.*

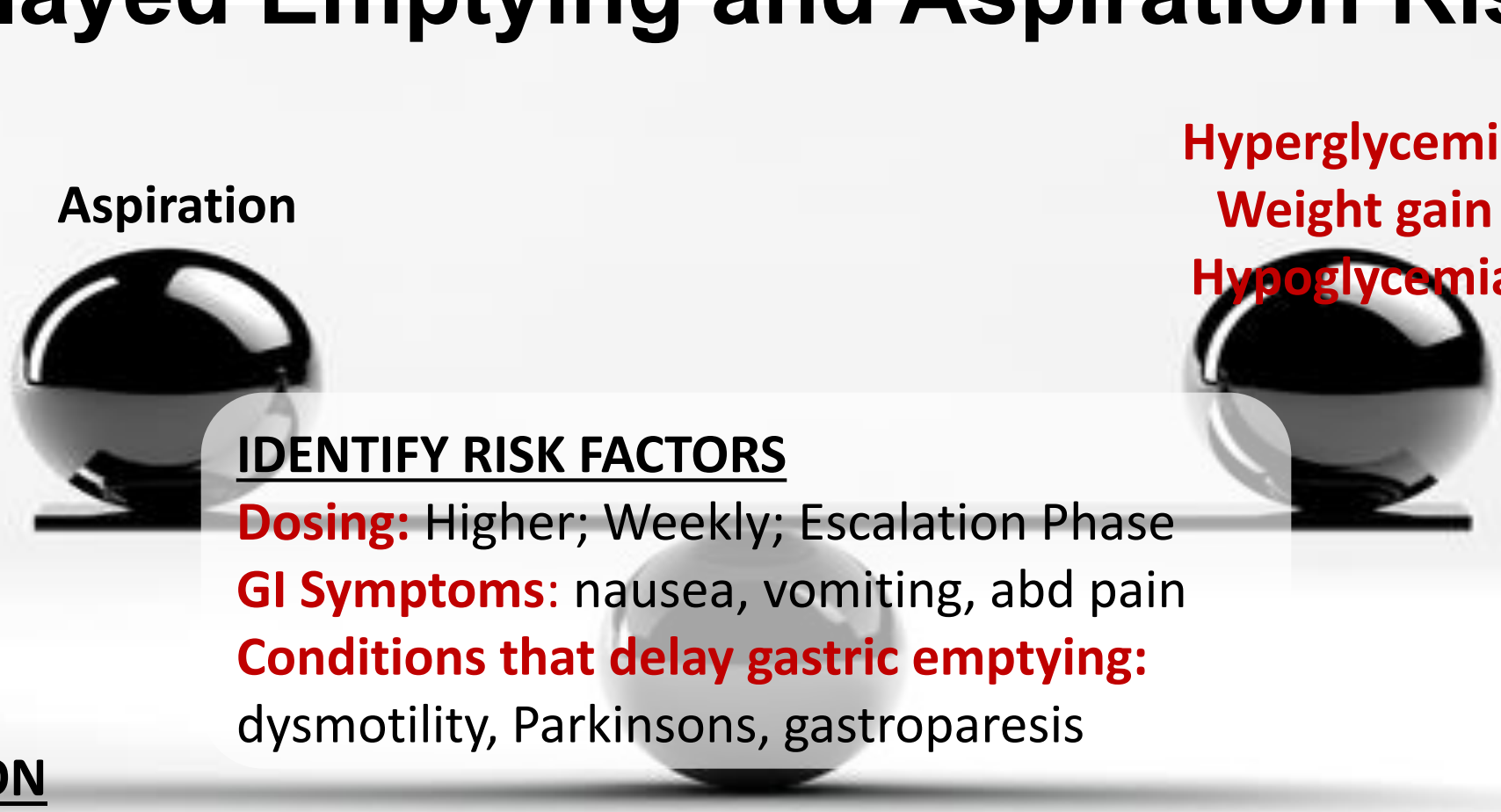
Recommendation 2

*The safe use of GLP-1RAs in the perioperative period should include **efforts to minimize the aspiration risk** of delayed gastric emptying. This can be achieved by preoperative **diet modification** and/or **altering anesthesia plan** to consider rapid sequence induction of general anesthesia for tracheal intubation*

ASMBS American Society for Metabolic & Bariatric Surgery · aga · ASGE American Society for Gastrointestinal Endoscopy · International Society for the Perioperative Care of Patients with Obesity ISPCOP

SORD 2024;20:1183-86

Balance the Variables Elevating the Risk of Delayed Emptying and Aspiration Risk



IDENTIFY RISK FACTORS

Dosing: Higher; Weekly; Escalation Phase

GI Symptoms: nausea, vomiting, abd pain

Conditions that delay gastric emptying:
dysmotility, Parkinsons, gastroparesis

TAKE ACTION

Modify Preoperative Diet – 24hr Liquid Diet: Based on clinical evaluation of GI symptoms

Gastric Ultrasound (POC): concern for retained gastric content ; **Rapid Seq Induction GA**

Follow ASA Guidance(2023): Hold **Lira one day**, Hold **Dula/Sema/Tirz one week before**

Quick Pearls to Avoid the Pitfalls of Obesity Management Medications in MBS Patients

- Understand patients may be bias, balance expectations
- Don’t only focus on weight loss
- Don’t stop the treatment after weight plateau
- Weight history and trajectory BEFORE OMMs is important to best understand the response
- Start with LOW DOSES, you may not need to increase
- Caution of having GLP1 ONLY treatment plan, other OMMs are available and may be effective
- If one medication doesn’t work, try another
- Don’t stop treating obesity, even after bariatric surgery
- Don’t use compounded versions of semaglutide, tirzepatide


drbutsch
@drbutsch
butschw@ccf.org

The Pitfalls of the Use of Obesity Medications in the Metabolic and Bariatric Surgical Patient

W. Scott Butsch, MD, MSc FTOS

Director of Obesity Medicine | Bariatric and Metabolic Institute | Cleveland Clinic

butschw@ccf.org | drbutsch