Medical Management of the Patient with Obesity:
Using drugs, devices and surgery to improve health

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Disclosures

• **Consulting fee**: Eisai, Inc., Janssen, Merck, Novo Nordisk, Orexigen, Real Appeal, Sanofi

• **Speakers bureau**: Eisai Inc., Novo Nordisk, Orexigen

• **Equity**: Gila Therapeutics, Scientific Intake

• **Other/data monitoring board**: BaroNova
The chronic disease burden challenging public health in the 21st century is largely driven by obesity.²

Objectives

At the end of the presentation attendees will be able to
1. describe, according to AACE Guidelines, steps for assessment and staging to direct medical management of obesity;
2. discuss the safety and efficacy of currently available medications approved for chronic weight management; and
3. describe the efficacy and safety of common bariatric surgery procedures and the long term nutritional support of patients who have these procedures.
Obesity is a Clinical Diagnosis, not a number on a scale

1. Population medicine and epidemiology
   • BMI: on population basis, correlates with body fat and a host of comorbidities, but different populations have different BMI:health-risk relationships

2. Clinical medicine
   • WHO: “Condition where excess of abnormal body fat impairs health”
   • Diagnosis = cut points + health risk assessment + diagnosis

For Europids:¹
Overweight BMI >25 kg/m²
Obese BMI >30 kg/m²
Waist circumference 35 in for women and 40 in for men

For Asians:²
Overweight BMI >23 kg/m²
Obese BMI >25 kg/m²
Waist circumference 31.5 in for women and 35 in for men

Patients Present in Two Ways\textsuperscript{1,2}

AACE/ACE Algorithm for the Medical Care of Patients With Obesity

### Staging Directs Treatment

#### Stage 0
- **Normal Weight (No Obesity)**
- **Goal:** Maintain healthy weight
- **Healthy meal plan, physical activity, health education**

#### Stage 1
- **Overweight BMI 25-29.9**
- **Obesity BMI ≥30**
- **No complications**
- **Goal:** 5%-10% loss
- **Lifestyle/behavioral therapy, consider pharmacotherapy if lifestyle alone not effective**

#### Stage 3
- **≥1 Severe complication or requires more aggressive weight loss for effective treatment**
- **BMI ≥25**
- **Goal:** >10% loss
- **Lifestyle/behavioral therapy, add pharmacotherapy (BMI ≥27), consider bariatric surgery (BMI ≥35)**

Modest Weight Loss Has Benefits—
Greater Weight Loss Is Associated With Greater Benefits

- Progression from prediabetes to diabetes\textsuperscript{1}
- Measures of glycemia\textsuperscript{1}
- Triglycerides and HDL cholesterol\textsuperscript{1}
- Systolic and diastolic blood pressure\textsuperscript{1}
- Hepatic steatosis (measured by MRS)\textsuperscript{2}
- Measures of feeling and function
  - Symptoms of urinary stress incontinence\textsuperscript{1}
  - Measures of sexual function\textsuperscript{3}
  - Quality of life measures (IWQOL)\textsuperscript{4}
- NASH activity score (measured by biopsy)\textsuperscript{1}
- Apnea-hypopnea index\textsuperscript{1}
- Reduction in CV events, mortality, remission of T2DM\textsuperscript{5,6}

Individualizing the Treatment Plan

Key concept: it’s shared disease management

• Consider your patient’s weight history: triggers, and successful and unsuccessful interventions
• Review your therapeutic toolbox
  • Lifestyle change options
  • Enhanced diet and activity plans
  • Drugs
  • Devices
  • Bariatric surgery
• Remember, it’s a chronic disease; you do not need to do it all at once
Identifying Barriers and Roadblocks

- Medications that drive weight gain
- Hypoglycemia risk
- Sleep disorders
- Stress: emotional and financial
- Lack of social support
- Mental health issues: binge eating disorder, bulimia, uncontrolled depression
# Weight Effects of Common Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Weight Gain Associated With Use</th>
<th>Alternatives (Weight Reducing in Parentheses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes medications</td>
<td>Insulin, sulfonylureas, TZDs, mitiglinide, sitagliptin(^a)</td>
<td>(Metformin, acarbose, miglitol, pramlintide, exenatide, liraglutide, SGLT-2 inhibitors)</td>
</tr>
<tr>
<td>Hypertension medications</td>
<td>(\alpha)-Blocker?, (\beta)-blocker?</td>
<td>ACE inhibitors?, calcium channel blockers?, angiotensin-2 RAs</td>
</tr>
<tr>
<td>Antidepressants and mood stabilizers</td>
<td>Amytriptyline, doxepin, imipramine, nortriptyline, trimipramine, mirtazapine, fluoxetine?, sertraline?, paroxetine, fluvoxamine</td>
<td>(Bupropion), nefazodone, fluoxetine (short term, sertraline, &lt;1 year)</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>Depot progesterone</td>
<td>Barrier methods, IUDs</td>
</tr>
</tbody>
</table>

\(^1\) represents uncertain/under investigation.

For Patients with Diabetes: Importance of Hypoglycemia Prevention During Negative Energy Balance

Hypoglycemia is common during weight loss with most diabetes medications, so …

Defend against hypoglycemia by reducing diabetes medications, not by adding food

• Rules of thumb
  • Duration of diabetes may affect outcome (longer duration, less beta cell reserve)
  • Initial glycemic control will affect level of blood-glucose change (better control, higher risk)
  • Some weight loss is good; more weight loss can be better
  • Approximately 50% of changes in FBG will occur in the first 10 days with calorie restriction
  • Reduce it
  • Discontinue it
  • Do not add a new one
  • Do not start one

What Can Be Expected from Lifestyle Change?
from the 2013 ACC/AHA/TOS Obesity Guidelines on Lifestyle Intervention

• Gold standard: trained interventionist; face to face counseling; 14 sessions in 6 months with follow-up for 1 year; comprehensive (diet, physical activity and behavioral therapy); reliably produces 8 kg weight loss at 1 year.
• No difference in individual or group approaches.
• Telephone interventions generally equal to face-to-face.
• Internet or email interventions produce less weight loss.
• Commercial counseling programs (with or without packaged foods) and (in person or telephone counseling) can be effective – Jenny Craig, Nutrisystem, Weight Watchers.

• Approximately 1 in 5 patients will succeed with self-help approaches; most patients (~70%) will succeed with programmatic approaches to lifestyle counseling

### How Do We Intensify Lifestyle Intervention?

<table>
<thead>
<tr>
<th>Face-to-face counseling</th>
<th>More contact time</th>
<th>More structure in the diet (meal replacements)</th>
<th>Liquid diets (low-calorie [&gt;800 kcal/d] or very-low-calorie diets [&lt;800 kcal/d])</th>
<th>Alternate-day fasting</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image of people interacting" /></td>
<td><img src="image2.png" alt="Image of a clock" /></td>
<td><img src="image3.png" alt="Image of a fork and knife" /></td>
<td><img src="image4.png" alt="Image of water" /></td>
<td><img src="image5.png" alt="Image of a calendar" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group support</th>
<th>Medications</th>
<th>Devices</th>
<th>Referral for surgery</th>
<th>Campaigns</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image6.png" alt="Image of a network of people" /></td>
<td><img src="image7.png" alt="Image of a prescription" /></td>
<td><img src="image8.png" alt="Image of a smartwatch" /></td>
<td><img src="image9.png" alt="Image of a phone" /></td>
<td><img src="image10.png" alt="Image of a checklist" /></td>
</tr>
</tbody>
</table>

*We need to be more open to these—sooner—in our patients' struggles*

Rationale for Medications in Obesity Management

• Food intake is biologically determined.
• Weight loss is opposed and regain promoted by physiology of reduced obese state.
• Meds work through biology of appetite regulation to help patients adhere to diet plans.
• Medications help patients lose more weight than lifestyle alone.
• Continuing medications sustains reduced body weight.

Guidance on medications which produce weight loss or are weight neutral

But... within the context of foundational treatment with diet, physical activity and behavior modification

And... recognizing that some patients benefit from bariatric surgery.
Why have medications gotten a bad rap?

Older medications were not safe.

• They weren’t studied properly! Short-term studies, few patients. We thought we could produce weight loss and the patient would be cured.

The science of obesity was not understood.

• We thought patients just needed to be told to eat less and exercise more and try harder.
How are newer medications evaluated?

- FDA requires comparison of >2000 patients treated with medication and a similar number on placebo.
- They evaluate efficacy (average weight loss, percentage who can achieve 5% or more or 10% or more weight loss and improvement in risk factors).
- They evaluate safety – adverse events recorded at every visit, effect on mood recorded at every visit, routing labs and labs of special interest.
- If the drug passes initial testing a large study (~10,000 people) is conducted testing the effect on heart attack and stroke.

Best Practices in Prescribing Medications for Chronic Weight Management

1. Follow the label: indicated for
   • BMI 30+ or 27+ with comorbidity (patients who need to lose weight for health reasons)
   • patients who have history of struggle
   • improving adherence to diet and physical activity (always prescribe as part of a lifestyle regimen).

2. Do no harm: know warnings and contraindications.

3. Consider secondary benefits of medications.

4. Use shared decision making in choosing a medicine.

5. Evaluate efficacy at ~3 months.

6. Continue for long term use, like other meds for chronic disease.

Remember…..

• There is no ideal medication. In the right patient, every medication can be a good medication. In the wrong patient, every medication can be a bad medication.

• Medications don’t work in every patient. The medication profile must be matched to the patient profile.

• They don’t work on their own!
Phentermine: FDA-Approved for Obesity Management: Short-Term Use

• Sympathomimetic agent; Scheduled drug (II or IV)
• Common adverse events\(^1\): insomnia, elevated heart rate, dry mouth, taste alterations, dizziness, tremors, headache, diarrhea, constipation, vomiting, gastrointestinal distress, anxiety, restlessness

ENDO Pharmacotherapy Guidelines\(^2\): “In patients with uncontrolled hypertension or a history of heart disease, we recommend against using sympathomimetic agents phentermine and diethylpropion.

\[\text{1⊗⊗⊗◯ (strong rec, moderately high quality evidence)}\]

1. Yanovski SZ, Yanovski JA. JAMA. 2014;311:74-86
Randomized comparison of weight loss at 28 weeks with lifestyle intervention and placebo, phentermine 7.5 mg or phentermine 15 mg


Data shown are LS mean and all comparisons are statistically significant. Treatment arms not shown are topiramate 46 mg and 92 mg and phentermine/topiramate ER 7.5/46 mg and 15/92 mg.
Randomized Comparision: Phentermine 30 mg continuously vs. Phentermine 6 week intermittent therapy vs. Placebo

Data shown are 64 completers; 44 drop-outs not shown.

Medications approved for chronic weight management and how they work

http://www.accessdata.fda.gov/scripts/cder/drugsatfda/

<table>
<thead>
<tr>
<th>Agent</th>
<th>Action</th>
<th>Approval</th>
<th>Scheduled Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat Xenical®</td>
<td>• Peripheral pancreatic lipase inhibitor - blocks ingested fat absorption</td>
<td>Approved 1997</td>
<td>• No</td>
</tr>
</tbody>
</table>
| Lorcaserin Belviq®     | • 5-HT$_2C$ serotonin agonist  
• Little affinity for other serotonergic receptors                                                                                             | Approved 2012 | • YES          |
| Phentermine/Topiramate ER Qsymia™ | • Sympathomimetic  
• Anticonvulsant (GABA receptor modulator, carbonic anhydrase inhibitor, glutamate antagonist)                                                                 | Approved 2012 | • YES          |
| Naltrexone SR/ Bupropion SR Contrave® | • Opioid receptor antagonist  
• Dopamine/noradrenaline reuptake inhibitor                                                                                                     | Approved 2014 | • No           |
| Liraglutide 3.0 mg Saxenda® | • GLP-1 receptor agonist                                                                                                                                                                                                 | Approved 2014 | • No           |

Orlistat 120 mg tid by prescription
Orlistat 60 mg tid OTC

- Blocks absorption of 30% ingested fat (intestinal lipase inhibitor)
- 120 mg TID with meals (Rx) or 60 mg TID (OTC)
- Available world-wide
- Generally safe; Contraindications: pregnancy, chronic malabsorption syndrome, cholestasis
- Reinforces low fat diet, has efficacy in LDL lowering
- No effect on appetite
- Must counsel patients regarding gastrointestinal side effects and steatorrhea
- Consider using with Metamucil, multivitamin at bedtime

Information from product label
Lorcaserin 10 mg or 20 mg tabs

- 5HT 2c receptor agonist, reduces food intake
- 20 mg/day single dose available
- Scheduled (DEA) in US; though no abuse potential
- Well tolerated
- No evidence of valvulopathy.
- With other serotonergic or SSRIs, prescribe with ‘extreme caution’ because of serotonin syndrome risk

Information from product label
Phentermine/ Topiramate ER
recommended dose 7.5 mg/46 mg

• Two common medications, at low dose
• Acts centrally to reduce food intake
• Scheduled (DEA) in US
• Titrate to 7.5mg/43 mg
• Produces greatest weight loss, on average
• Tolerability issues: taste disturbance (carbonation),
• Safety issues: teratogenicity (topiramate), glaucoma (topiramate)
• Obtain negative pregnancy test before use and monthly in women of childbearing potential

Information from product label
Naltrexone SR/ Bupropion SR 32/360 mg tabs

• Two common medications; reduces food intake centrally & may affect craving
• Not scheduled
• Titrate to 32mg/360 mg
• Tolerability issues: nausea – requires dose escalation from 8 mg/90mg
• Safety issues: opioid antagonist (naltrexone), lowers seizure threshold and can unmask mania and increase suicidality risk (bupropion)
• Has indication for smoking cessation and depression (bupropion)
Liraglutide 3.0 mg:

• Liraglutide is GLP-1 receptor agonist, given by daily injection
• Not scheduled
• Tolerability issues: nausea – requires dose escalation from 0.6 mg
• Safety issues: pancreatitis risk; gall bladder disease risk; contraindicated with history of MEN II or medullary thyroid cancer.
• Has indication for diabetes at 1.8 mg dose, so has secondary benefit on glycemia
Let’s talk about efficacy...

- FDA efficacy benchmarks for approval:
  >5% weight loss than placebo
  at least 35% of those on medications achieve 5% weight loss and twice as many as on placebo

All approved medications have approximated or exceeded these benchmarks.
Individual Weight Loss with Placebo or 2 Doses of Phentermine/Topiramate

Each vertical bar represents a single subject experience in subjects completing 56 weeks on study drug.
<table>
<thead>
<tr>
<th>Agent</th>
<th>Dosing</th>
<th>Response Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td>120 mg orally with each meal</td>
<td>Not addressed in label</td>
</tr>
<tr>
<td>Lorcanerin</td>
<td>10 mg orally twice daily or 20 mg orally daily</td>
<td>Stop if &lt;5% loss at 12 weeks</td>
</tr>
<tr>
<td>Phentermine/Topiramate ER</td>
<td>Orally in am; 3.75 mg/23 mg x 14 days; Then, 7.5/46 mg x 14 days.</td>
<td>At 12 weeks, option to ↑ to 11.25 mg/69 mg x 14 days, then 15 mg/96 mg; Stop if &lt;5% loss at 12 weeks on top dose</td>
</tr>
<tr>
<td>Naltrexone SR/Bupropion SR</td>
<td>Orally; Wk 1 - 1 tab (8 mg/90 mg) in am; Wk 2 - 1 in am 1 in pm; Wk 3 - 2 in am 1 in pm; Wk 4 - 2 in am 2 in pm.</td>
<td>Stop if &lt;5% loss at 12 weeks</td>
</tr>
<tr>
<td>Liraglutide 3 mg</td>
<td>Inject subcutaneously (any time of day); Wk 1 - 0.6 mg; increase dose by 0.6 mg weekly until dose is 3.0 mg (Wk 5)</td>
<td>Stop if &lt;4% weight loss at 16 weeks</td>
</tr>
</tbody>
</table>

All data from product labels
<table>
<thead>
<tr>
<th>Drug</th>
<th>Common AE</th>
<th>Contraindication</th>
<th>Safety Consideration</th>
<th>Tolerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td><strong>Insomnia</strong>&lt;br&gt;Dry mouth&lt;br&gt;Agitation&lt;br&gt;Constipation</td>
<td><strong>CVD, CHF, arrhythmias</strong>&lt;br&gt;Uncontrolled hypertension&lt;br&gt;MAOI use&lt;br&gt;Hyperthyroidism&lt;br&gt;Glaucoma&lt;br&gt;Pregnancy</td>
<td>Primary pulmonary hypertension</td>
<td>Discontinuation (CNS):&lt;br&gt;Phentermine – 17%&lt;br&gt;Placebo – 3%</td>
</tr>
<tr>
<td>Orlistat</td>
<td><strong>GI complaints</strong></td>
<td>Chronic malabsorption&lt;br&gt;Gallbladder disease</td>
<td>May increase cyclosporine exposure; Liver failure&lt;br&gt;Multivitamin administration</td>
<td>Discontinuation:&lt;br&gt;Orlistat – 8.8%&lt;br&gt;Placebo – 5%</td>
</tr>
<tr>
<td>Phentermine/topiramate ER</td>
<td><strong>Dry mouth</strong>&lt;br&gt;Paresthesias&lt;br&gt;Headache&lt;br&gt;Insomnia</td>
<td>Glaucoma&lt;br&gt;Hyperthyroidism&lt;br&gt;MAOI use&lt;br&gt;Pregnancy</td>
<td>Teratogenicity&lt;br&gt;Metabolic acidosis&lt;br&gt;Glaucoma</td>
<td>Discontinuation:&lt;br&gt;Top dose – 17%&lt;br&gt;Low doses – 12%&lt;br&gt;Placebo – 8%</td>
</tr>
<tr>
<td>Lorcarserin</td>
<td><strong>Headache</strong>&lt;br&gt;Dizziness&lt;br&gt;Fatigue&lt;br&gt;Dry mouth</td>
<td>MAOI use&lt;br&gt;&lt;strong&gt;Use with caution with serotonergic drugs&lt;/strong&gt;&lt;br&gt;Pregnancy</td>
<td>Serotonin syndrome&lt;br&gt;Valvular heart disease&lt;br&gt;Depression&lt;br&gt;Priapism</td>
<td>Discontinuation:&lt;br&gt;Lorcaserin – 8.6%&lt;br&gt;Placebo – 6.7%</td>
</tr>
<tr>
<td>Naltrexone/bupropion SR</td>
<td><strong>Nausea</strong>&lt;br&gt;GI complaints&lt;br&gt;Headache&lt;br&gt;Insomnia</td>
<td>Seizure disorder&lt;br&gt;Uncontrolled hypertension&lt;br&gt;&lt;strong&gt;Chronic opioid use&lt;/strong&gt;&lt;br&gt;MAOI use&lt;br&gt;Pregnancy</td>
<td>Suicidality in adolescents&lt;br&gt;Elevated blood pressure, pulse&lt;br&gt;Glaucoma&lt;br&gt;Hepatotoxicity</td>
<td>Discontinuation:&lt;br&gt;Naltrexone/bupropion – 24%&lt;br&gt;Placebo – 12%</td>
</tr>
<tr>
<td>Liraglutide 3.0</td>
<td><strong>Nausea</strong>&lt;br&gt;GI complaints</td>
<td><strong>Personal/family history of medullary thyroid carcinoma or MEN2</strong>&lt;br&gt;History of pancreatitis&lt;br&gt;Pregnancy</td>
<td>Thyroid c-cell tumors (rodents)&lt;br&gt;&lt;strong&gt;Acute pancreatitis&lt;/strong&gt;&lt;br&gt;Gallbladder disease&lt;br&gt;Hypoglycemia&lt;br&gt;Tachycardia&lt;br&gt;Renal impairment&lt;br&gt;Suicidal behavior</td>
<td>Discontinuation:&lt;br&gt;Liraglutide – 9.8%&lt;br&gt;Placebo – 4.3%</td>
</tr>
</tbody>
</table>

All information from product labels
## Contraindications and Cautions

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Avoid/Caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated seizure risk</td>
<td>Naltrexone/bupropion</td>
</tr>
<tr>
<td>History of recurrent kidney stones</td>
<td>Phentermine/topiramate, orlistat</td>
</tr>
<tr>
<td>History of glaucoma</td>
<td>Phentermine/topiramate</td>
</tr>
<tr>
<td>Uncontrolled hypertension</td>
<td>Naltrexone/bupropion</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>Phentermine</td>
</tr>
<tr>
<td>Moderate-to-severe renal impairment</td>
<td>Do not exceed half-dose: phentermine/topiramate, naltrexone/bupropion Caution: liraglutide, lorcaserin</td>
</tr>
<tr>
<td>Moderate-to-severe hepatic impairment</td>
<td>Do not exceed half-dose: phentermine/topiramate</td>
</tr>
<tr>
<td></td>
<td>Do not exceed one-quarter dose: naltrexone/bupropion Caution: liraglutide, lorcaserin</td>
</tr>
<tr>
<td>SSRI use</td>
<td>Caution: lorcaserin</td>
</tr>
</tbody>
</table>

SSRI = selective serotonin reuptake inhibitor.
Choosing Between Options

**Drug factors**
- Contraindications
- Dual benefits
- Studied populations

**Patient factors**
- Patient preferences
- Adverse events
- Prior experiences
- Access

**Physician factors**
- Provider knowledge/comfort
## Dual Benefits

<table>
<thead>
<tr>
<th>If Patient has Obesity and...</th>
<th>Consider (But not Explicitly Approved)...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Naltrexone/bupropion</td>
</tr>
<tr>
<td>Depression</td>
<td>Naltrexone/bupropion</td>
</tr>
<tr>
<td>Migraines</td>
<td>Phentermine/topiramate ER</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Liraglutide 3.0 mg</td>
</tr>
<tr>
<td>Chronic constipation</td>
<td>Orlistat</td>
</tr>
<tr>
<td>Elevated LDL</td>
<td>Orlistat</td>
</tr>
</tbody>
</table>
How do prescribers choose a drug?

1. What are the contraindications? Let’s eliminate those.
3. “Shared decision making”
4. The drugs are new. Prescribers are not knowledgeable about all and tend to go to those they trust. But all can play a role.
5. The ‘stopping rule’ guides pragmatic approach (~5% in 12 weeks).
## Medications Causing Weight Gain

<table>
<thead>
<tr>
<th>Category</th>
<th>Drugs That May Cause Weight Gain</th>
<th>Possible Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroleptics</td>
<td>Thioridazine, haloperidol, olanzapine, quetiapine, risperidone, clozapine</td>
<td>Ziprasidone, aripiprazole</td>
</tr>
<tr>
<td>Antidiabetic agents</td>
<td>Insulin, sulfonylureas, thiazolidinediones</td>
<td>AGIs, DPP-4i, SGLT2i, GLP-1 RAs, metformin</td>
</tr>
<tr>
<td>Steroid hormones</td>
<td>Contraceptives, glucocorticoids, progesterone</td>
<td>Barrier methods, NSAIDs</td>
</tr>
<tr>
<td>Tricyclics (ADs)</td>
<td>Amitriptyline, nortriptyline, imipramine, doxepin</td>
<td>Protriptyline, bupropion, nefazodone</td>
</tr>
<tr>
<td>MAOIs (ADs)</td>
<td>Phenelzine</td>
<td></td>
</tr>
<tr>
<td>SSRIs (ADs)</td>
<td>Paroxetine</td>
<td>Fluoxetine, sertraline</td>
</tr>
<tr>
<td>Other (ADs)</td>
<td>Mirtazapine, duloxetine</td>
<td>Bupropion</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Valproate, carbamazepine, gabapentin, pregabalin, vigabatrin</td>
<td>Topiramate, lamotrigine, zonisamide, felbamate</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Cyproheptadine</td>
<td>Inhalers, decongestants</td>
</tr>
<tr>
<td>β- and α-adrenergic blockers</td>
<td>Propranolol, doxazosin</td>
<td>ACEIs, CCBs</td>
</tr>
</tbody>
</table>

New devices approved by FDA since 2015

- 2 balloons approved – ORBERA and ReShape
- Vagal blocking therapy - VBLOC
- Stomach aspiration device – AspireAssist
- SMART Device
Two Balloon Devices Approved in 2015

ReShape™ Integrated Dual Balloon System
- 11.27% TBWL at 12 months (n=1683)\(^1\)
- Balloons are deflated at removal in 6 months
- BMI of 30-40 kg/m\(^2\)

ORBERA™ Intragastric Balloon System
- 10.2% TBWL at 6 months
- Maximum use of 6 months before removal
- BMI of 30-40 kg/m\(^2\)

2. www.fda.gov/MedicalDevices
Vagal Blocking Therapy

• Pacemaker-like device designed to block the vagus nerve to affect the perception of hunger and fullness.
• Satiation by delaying food processing and gastric emptying.

<table>
<thead>
<tr>
<th>%EWL achieved</th>
<th>VBLOC 12 months (N=147)</th>
<th>VBLOC 24 months (N=103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5.0%</td>
<td>67%</td>
<td>58%</td>
</tr>
<tr>
<td>≥7.5%</td>
<td>56%</td>
<td>45%</td>
</tr>
<tr>
<td>≥10.0%</td>
<td>39%</td>
<td>34%</td>
</tr>
<tr>
<td>≥12.5%</td>
<td>32%</td>
<td>27%</td>
</tr>
<tr>
<td>≥15.0%</td>
<td>22%</td>
<td>21%</td>
</tr>
</tbody>
</table>

Ikramuddin S, et al. JAMA 2014;312(9):915-922
AspireAssist – Stomach Draining Device

- Removable device
- 16 week weight loss 12.4 kg
- Removes ~30% of food from stomach before calories are absorbed, causing weight loss
- Thin tube connects inside of stomach directly to a discreet Skin-Port on outside of abdomen. Valve on port valve controls flow of stomach contents
- Aspiration process is performed ~20 minutes after entire meal is consumed and takes 5 to 10 minutes to complete, 3x/da
- Requires oral processing of food.

http://aspirebariatrics.com/
ACC/AHA/TOS Obesity Guidelines: Recommendation 5 Grade A (Strong)

- Advise your patients with a BMI $\geq 35$ kg/m$^2$ and a co-morbidity or $>40$ kg/m$^2$ that bariatric surgery may be an appropriate option to improve health and offer referral to an experienced bariatric surgeon for consultation and evaluation.

2016 Statement on Metabolic Surgery for Diabetes

- Recommend surgery for patients with BMI $\geq 40$ or for patients with BMI 35–39.9 and poor glycemic control and Consider surgery for patients with BMI 30-34.9.

### Common Bariatric Surgery Procedures

<table>
<thead>
<tr>
<th></th>
<th>Adjustable Gastric Banding</th>
<th>Sleeve Gastrectomy</th>
<th>Gastric Bypass</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pouch Size</strong></td>
<td>Small</td>
<td>Small</td>
<td>Small</td>
</tr>
<tr>
<td><strong>Hormone Effects</strong></td>
<td>None</td>
<td>Ghrelin ↓</td>
<td>GLP-1 ↑, PYY ↑</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td><strong>Weight Loss</strong></td>
<td>+</td>
<td>+++</td>
<td>++++</td>
</tr>
<tr>
<td><strong>Peri-operative Risk</strong></td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
</tbody>
</table>

Bariatric Surgery - Low Mortality

Mortality Rate (%)

- Bariatric Surgery: 0.13%
- Lap Chole: 0.52%
- Hip Replacement: 0.93%
- CABG: 3.30%

CABG = coronary artery bypass grafting; lap chole = laparoscopic cholecystectomy.
Bariatric Surgery Misconceptions. ASMBS. http://asmbs.org/patients/bariatric-surgery-misconceptions
STAMPEDE Trial

218 Patients Screened

150 Randomized

50 Intensive Medical Therapy Alone
- 8 withdrew consent
- 2 lost to follow-up

50 Medical Therapy + Gastric Bypass
- 2 lost to follow-up

50 Medical Therapy + Sleeve Gastrectomy
- 1 withdrew consent prior to surgery

Year 3 Population

40

48

49

91% Retention

STAMPEDE = Surgical Therapy and Medications Potentially Eradicate Diabetes Efficiently.
Weight Change After Bypass and Sleeve vs Medical Tx in Patients with T2DM


**Five-year data** of patients with T2DM and BMI of 27 to 43

- **Medical Therapy**: -5.3 kg
- **Sleeve Gastrectomy**: -18.6 kg
- **Gastric Bypass**: -23.2 kg

**Mean BMI Value at Visit**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
<th>Visit 4</th>
<th>Visit 5</th>
<th>Visit 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical therapy</td>
<td>36.4</td>
<td>34.1</td>
<td>35.0</td>
<td>34.8</td>
<td>35.1</td>
<td>34.0</td>
</tr>
<tr>
<td>Gastric bypass</td>
<td>37.0</td>
<td>26.9</td>
<td>27.4</td>
<td>28.2</td>
<td>28.6</td>
<td>28.9</td>
</tr>
<tr>
<td>Sleeve gastrectomy</td>
<td>36.0</td>
<td>26.9</td>
<td>27.7</td>
<td>28.1</td>
<td>28.2</td>
<td>29.3</td>
</tr>
</tbody>
</table>
Five-year Outcomes for Bariatric Surgery vs Intensive Medical Therapy for Diabetes

A Glycated Hemoglobin

Mean (median) Value at Visit

- Medical therapy: 8.8 (8.6) 7.3 (6.8) 7.5 (7.2) 8.4 (7.7) 8.6 (8.2) 8.5 (8.0)
- Gastric bypass: 9.3 (9.4) 6.4 (6.2) 6.5 (6.4) 6.8 (6.6) 6.8 (6.8) 7.3 (6.9)
- Sleeve gastrectomy: 9.5 (8.9) 6.7 (6.4) 6.8 (6.8) 7.0 (6.7) 7.1 (6.6) 7.4 (7.2)

B Diabetes Medications

* P<0.05 for comparison with medical-therapy group at 60 mo
△ P<0.05 for comparison between surgical groups at 60 mo

SOS and All Cause Mortality

Surgery: 101 deaths
13 MI
29 cancer

Control: 129 deaths
25 MI
47 cancer

Unadjusted Hazard ratio 0.76;
95% CI 0.59-0.99
P=0.04

MOUTH
ESOPHAGUS
STOMACH
DUODENUM
JEJUNUM
ILEUM
COLON

GI TRACT

Amylase
Pepsin
HCl
IF
Pancreatic
bicarb
enzymes
BILE

Nutrient Absorption

- Alcohol
- Niacin (B3)
- $\text{Cl}^-$, $\text{SO}_4^{2-}$
- Iron, Calcium, Magnesium, Zinc
- Glucose, Galactose, Fructose
- Water Soluble Vitamins:
  - Folic acid
  - Thiamine (B1)
  - Riboflavin (B2)
  - Niacin (B3)
  - Pyridoxine (B6)
  - Ascorbic acid (C)

Protein

- Fat-soluble vitamins (A,D,E,K)

Fat

- Cholesterol
- Bile salts
- Vitamin B12

Sodium/potassium

Water

Nutritional and Metabolic Deficiencies After Bariatric Surgery

- Gastric restrictive procedures
  - Iron deficiency 32%
  - Thiamine deficiency
- Roux-en Y gastric bypass (RGB)
  - Calcium (50% to 60%) and vitamin D (20% to 60%)
  - Iron deficiency 15% to 50% (49% to 52% with BMI > 50)
    - Decreased acidification and proximal small bowel absorption
  - B12 deficiency 10% to 70% 1-9 years after* (half-life 400 d)
    - Decreased liberation of B12 from protein foods
    - Decreased intrinsic factor production
    - Decreased ileal absorption
    - Requirement = 2 mcg/day; stores = 3000 to 5000 mcg
- Thiamine deficiency
- Folic acid deficiency 10% to 35% due to low intake and ↓ gastric acid
- Protein deficiency (<1% to 4.7%\(^1\))

* Earlier if B12 deficiency occurs preoperatively.

Recommended Nutritional Screening Pre- and Post-bariatric Surgery

- CBC with differential
- Serum iron, ferritin, and TIBC test
- Serum vitamin B12
- Folate, consider plasma homocysteine
- PTH and 25-hydroxyvitamin D
  - Consider DXA scan

Duodenal switch patients
- Fat-soluble vitamins
- A, D, E, K
- Albumin/pre-albumin

DXA = dual-energy x-ray absorptiometry; PTH = parathyroid hormone; TIBC = total iron binding capacity.

# Routine Vitamin and Mineral Supplementation for RYGB Patients

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin-mineral/prenatal</td>
<td>1 to 2 daily</td>
</tr>
<tr>
<td>Calcium citrate with vitamin D</td>
<td>1200 to 2000 mg/day + 3000 U/day Vitamin D</td>
</tr>
<tr>
<td>Elemental iron</td>
<td>40 to 65 mg/day</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>5000 µg/day orally OR 1000 µg/month IM OR 500 µg weekly intranasal</td>
</tr>
</tbody>
</table>

RYGB = Roux-en-Y gastric bypass.
Thiamine Deficiency

- Stores last 3 to 6 weeks
- Decreased gastric acid production
- Altered GI anatomy
- Decreased food intake
- Frequent vomiting
- Dextrose infusion

- WHEN YOU THINK OF IT: GIVE IT

Developing a Weight Centric Approach in YOUR office

What is YOUR role?

• Raise the issue
• Keep patients engaged, or at least returning
• Wise prescribing: Download (FREE!) ENDO Guidance on Medications
• Refer for lifestyle counseling
  • Office extender as trained interventionist, RD with weight management certificate, Nutrisystem, Jenny Craig, Weight Watchers
• Refer for device or surgical therapy
• or become an expert
**Growth of recognition of obesity as a specialty**

- **Over 200 physicians, nurses, nutritionists, dietitians and educators certified, to date**
- **>50 regional and national obesity associations**

**Mission:** to lead and drive global efforts to reduce, prevent and treat obesity

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Thank You