An Overview of Obesity
for Healthcare Practitioners

June 17, 2019

Preventive Medicine
Task Force
American Medical Women’s Association
Empowering Women & Improving Health Care Since 1915

www.amwa-doc.org
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Introduction

• Overweight and obesity affect two-thirds of U.S. adults, and one-third of children, and are associated with many chronic illnesses.

• We now understand that obesity itself is a disease with abnormalities in CNS pathways and peripheral hormones, which make it difficult for people to lose weight and maintain weight loss.

• Weight management requires a comprehensive approach including lifestyle and behavioral modifications, potential pharmacotherapy to control appetite, and in severe cases, bariatric surgery.

• This presentation aims to increase knowledge about obesity as a disease, its complications and pathophysiology, and approaches to treatment.
Learning Objectives

• Definitions, etiology, prevalence, co-morbidities
• Regulation of food intake and energy expenditure
• Talking about weight
• Assessment and development of a treatment plan
• Lifestyle management
• Pharmacotherapy
• Bariatric surgery
• Minimally invasive procedures
SECTION 1
DEFINITIONS, ETIOLOGY, PREVALENCE, CO-MORBIDITIES
Definitions

• **Obesity**: Body Mass Index (BMI) of 30 or higher.

• **Body mass index (BMI)** – the weight in kilograms divided by the square of the height in meters (kg/m\(^2\)) – is a commonly used index to classify overweight and obesity in adults.

• WHO defines overweight as a BMI equal to or more than 25, and **obesity** as a BMI equal to or more than 30.\(^1\)

• American Medical Association **recognized obesity as a disease** in 2013\(^2\)

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### BMI classification

<table>
<thead>
<tr>
<th>Category</th>
<th>BMI Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5</td>
</tr>
<tr>
<td>Normal range</td>
<td>18.5 - 24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>≥ 25.0</td>
</tr>
<tr>
<td>Preobese</td>
<td>25.0 - 29.9</td>
</tr>
<tr>
<td>Obese</td>
<td>≥ 30.0</td>
</tr>
<tr>
<td>Obese class I</td>
<td>30.0 - 34.9</td>
</tr>
<tr>
<td>Obese class II</td>
<td>35.0 - 39.9</td>
</tr>
<tr>
<td>Obese class III</td>
<td>≥ 40.0</td>
</tr>
</tbody>
</table>
Obesity is Complex

• Obesity is a multifactorial condition

• Recognizing obesity as a complex medical condition can **facilitate a honest and respectful open conversation between the provider and patient**

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Obesity (BMI ≥30 kg/m²)

1994

2000

2015

Diabetes

1994

2000

2015

Obesity and Diabetes 2015
age adjusted percentage of U.S. adults

Maps of Trends in Diagnosed Diabetes and obesity April 2017. CDC’s Division of Diabetes Translation. United States. 
Prevalence of obesity age 20 yrs and older by sex and age in U.S

Total 39.8%, M 38%, F 41.5%

*Significantly different from those aged 20–39.
NOTES: Estimates for adults aged 20 and over were age adjusted by the direct method to the 2000 U.S. census population using the age groups 20–39, 40–59, and 60 and over. Crude estimates are 39.8% for total, 38.0% for men, and 41.5% for women.
Access data table for Figure 1 at: https://www.cdc.gov/nchs/data/databriefs/db288_table.pdf#1.
Prevalence of obesity in U.S. adults by sex and race and Hispanic origin

Age adjusted prevalence of obesity, age 20 and over
2015-2016

Source: Hales CM, et.al. 2017
Medical Complications of Obesity


- Pulmonary disease
  - asthma
  - obstructive sleep apnea
  - hypoventilation syndrome

- Nonalcoholic fatty liver disease
  - steatosis
  - steatohepatitis
  - cirrhosis

- Gall bladder disease

- Reproductive abnormalities
  - abnormal menses
  - infertility
  - polycystic ovarian syndrome

- Osteoarthritis

- Skin

- Gout

- Phlebitis
  - venous stasis

- Idiopathic intracranial hypertension

- Stroke

- Cataracts

- Coronary heart disease

- Diabetes

- Dyslipidemia

- Hypertension

- Severe pancreatitis

- Cancer
  - breast, uterus, cervix
  - colon, esophagus, pancreas
  - kidney, prostate
Obesity associated with 4-5 fold increased risk of osteoarthritis

- 38% of people with obesity have arthritis and 33% are overweight \(^1\)
- 1 extra pound of weight increases force on knee by 4 pounds
- Osteoarthritis may make it difficult for exercise/physical activity, and exercise is helpful for weight loss and essential for maintenance of lost weight
- Weight loss improves knee and hip pain and mobility \(^2,3\)

Relationship of BMI and risk of DM2


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Relationship of BMI and Mortality

Pooled data from 57 prospective studies, 2218 men, 3295 women \(^1\)

- Relative risk for mortality for ages 35-89 adjusted for age and smoking
- First 5 years of follow-up excluded
- This data demonstrates that an *increase in BMI is associated with higher rates of mortality in both males and females* \(^1\)

Relationship of BMI and SBP¹

SECTION 2
PATHOPHYSIOLOGY
REGULATION OF FOOD INTAKE AND ENERGY EXPENDITURE
Appetite is regulated by peripheral hormones and the brain\textsuperscript{1}: Weight loss ↑ appetite stimulating hormones (ghrelin) & ↓ appetite suppressing hormones (leptin, PYY, CCK, amylin) & thermogenesis, thus causing weight regain.

NPY, AGRP ↑ appetite

POMC and α MSH ↑ satiety & energy expenditure

AGRP: agouti-related peptide; α-MSH: α-melanocyte-stimulating hormone; GHSR: growth hormone secretagogue receptor; INSR: insulin receptor; LepR: leptin receptor; MC4R: melanocortin-4 receptor; NPY: neuropeptide Y; POMC: proopiomelanocortin; PYY: peptide YY; Y1R: neuropeptide Y1 receptor; Y2R: neuropeptide Y2 receptor.

Obesity and Hypothalamic Injury

Fattening Foods Cause Dropout of POMC Neurons and Glial Ensheathment of Arcuate Neurons

- In rats, a high fat diet rapidly induced neuron injury in the hypothalamus, a brain area critical for energy homeostasis.
- This occurred in a few days, before substantial weight gain.
- Extending these findings is MRI evidence for gliosis in the hypothalamus of humans with obesity.

The Challenges to Losing Weight

50 obese men and women
Men 233 lbs/average; Women 200 lbs/average
Very low-calorie diet
  - Optifast shakes + 2 cups of low-starch vegetables
Total 500 to 550 calories a day for eight weeks
Body fights against weight loss long after dieting has stopped

Mean change in weight from baseline to week 62

34 participants completed the study

ITT = intention to treat

10 wk weight-loss program 30 lb wt loss

1 yr, 11 lb weight regain
Patients more hungry & preoccupied with food


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High Rate of Relapse After Weight Loss in People with Obesity has a Physiological Basis

14% weight loss in 34 healthy adults with obesity led to changes in appetite stimulating and appetite suppressing hormones that encouraged weight regain.

<table>
<thead>
<tr>
<th>Changes at week 62 compared to baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced appetite suppressing hormones</td>
</tr>
<tr>
<td>Leptin - 36% ↓ at wk 62</td>
</tr>
<tr>
<td>Peptide YY</td>
</tr>
<tr>
<td>Cholecystokinin</td>
</tr>
<tr>
<td>Insulin</td>
</tr>
<tr>
<td>Amylin</td>
</tr>
</tbody>
</table>


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Biological Adaptations to Body Weight

**Question:** How long do these biological adaptations persist with calorie restriction?

**Answer:** Evidence suggests often indefinitely

- Biological pressure to restore bodyweight to the highest-sustained lifetime level gets stronger as weight loss increases.

**Question:** Then is a patient ever truly “recovered” from obesity?

**Answer:**
- Few individuals ever fully recover from obesity
- Individuals with obesity who lose weight are in “remission” and biologically very different than their counterparts

Obesity is a Disease

American Medical Association (AMA) recognized obesity as a disease in 2013\(^1\)

Defined as:

“A multi-metabolic and hormonal disease state with characteristic signs and symptoms; and increase in fat mass associated with obesity is directly related to comorbidities such as type 2 diabetes mellitus, cardiovascular disease, and cancer.”

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Obesity Medicine Certification through ABOM

- The American Board of Obesity Medicine (ABOM) offers a certification exam for physicians annually.
- As of 2019, more than 3,000 ABOM diplomates throughout the U.S. and Canada.
- Learn more at www.abom.org.
SECTION 3
TALKING ABOUT WEIGHT
Assessing Readiness to Change

- Appreciating patient readiness to change, the barriers to change and helping patients to anticipate relapse can improve patient satisfaction and decrease physician frustration during the process.²

- If patient is ready to change, *agree with patient on reasonable weight and activity goals and write them down.*³

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Guidelines for Obesity Screening

Screening for Obesity in Adults:
The US Preventive Services Task Force recommends that clinicians screen all adult patients for obesity and offer intensive counseling and behavioral interventions to promote sustained weight loss for obese adults (Grade B recommendation).

Talk to Your Patients About Weight

• USPSTF screening recommendation is based on 2012 systematic review that showed: *Intensive counseling led to an average 6% body weight loss, along with improved comorbidities and CV risk factors*¹

• Weight-related discussions w/ healthcare providers can affect a patient’s participation in attempting weight loss²

• There is no clearly established method for telling patients that they are overweight or obese³

³. Baron RB. Telling patients they are overweight or obese: an insult or an effective intervention? Arch Intern Med. 2011;171:312–322.
Avoid Weight Bias

- Ask permission to bring up the topic of obesity
- Weight bias, or negative attitudes about one’s weight, often lead the patient to avoid seeking care.¹
- Patients with weight bias are predisposed to more weight gain.²
- Healthcare professionals can help overcome this barrier by being aware of one’s own implicit bias of obesity.¹
- Use “people-first” language:
  - Example: addressing the patient as having obesity instead of addressing him or her as obese¹
- Preferred terms: weight, then excess weight, unhealthy body weight³
- Disliked terms: excess fat, large size, obesity, heaviness

Motivational Interviewing (MI)

- MI is a therapeutic approach to help individuals work through ambivalence about behavior\(^1\)
- Numerous studies have shown MI can help individuals improve diet and physical activity \(^2,3\)
- The goal is to help patients think about their reasons for and against changing behavior
- It is crucial to use reflective listening skills and positive affirmations

SECTION 4
ASSESSMENT AND DEVELOPMENT OF A TREATMENT PLAN
Assessment of the Patient

- Medical history
- Height, weight, BMI
- Waist circumference
- Assessment of comorbidities
- Evaluate causes of obesity
  - Medications, metabolic abnormalities, genetics, stages of life (i.e. post-menopausal), environmental factors, psychological and social factors
- Assess diet and physical activity
- Determine readiness and motivation to lose weight

Metabolic Syndrome and Obesity

- Being overweight or obese is a risk factor for metabolic syndrome
- Metabolic syndrome increases risk for CVD and Type 2 diabetes

Laboratory tests\(^1\)

- Fasting glucose (Insulin resistance and Beta cell failure)
- Fasting lipid studies (typically high TG & high to normal LDL-C and low HDL-C)

# Weight Promoting Drugs and Alternative Options to Consider

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug Class</th>
<th>Weight Gain</th>
<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric</td>
<td>Antipsychotic</td>
<td>Clozapine, risperidone, olanzapine, quetiapine, haloperidol, perphenazine</td>
<td>Ziprasidone, aripiprazole</td>
</tr>
<tr>
<td></td>
<td>Antidepressant/ mood stabilizers: tricyclic antidepressants</td>
<td>Amytriptyline, doxepin, imipramine, nortriptyline, trimipramine, mirtazapine</td>
<td>Bupropion, nefazodone, fluoxetine (short term), sertraline (&lt; 1 year)</td>
</tr>
<tr>
<td></td>
<td>Antidepressant/ mood stabilizers: SSRIs</td>
<td>Fluoxetine ?, sertraline ?, paroxetine, fluvoxamine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Antidepressant/ mood stabilizers: MAOis</td>
<td>Phenylzine, tranylcypromine</td>
<td></td>
</tr>
<tr>
<td>Manic depressive illness</td>
<td></td>
<td>Lithium</td>
<td></td>
</tr>
<tr>
<td>Neurologic</td>
<td>Antiepileptic drugs</td>
<td>Carbamazepine, gabapentin, valproate</td>
<td>Lamotrigine ?, topiramate*, zonisamide*</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Diabetes- glucose lowering</td>
<td>Insulin, sulfonylureas, thiazolidinediones, ? Sitagliptin, metiglinide</td>
<td>Metformin*, acarbose*, miglitol*, pramlintide*, exenatide*, liraglutide*</td>
</tr>
</tbody>
</table>

*Weight reducing

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<th>Category</th>
<th>Drug Class</th>
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<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gynecologic</td>
<td>Oral Contraceptives</td>
<td>Progestational sterods, Progestins, IUD containing hormones</td>
<td>Barrier methods, combination oral contraceptive pills</td>
</tr>
<tr>
<td></td>
<td>Endometriosis</td>
<td>Depot leuprolide acetate</td>
<td>Surgical methods</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Anti-hypertensives</td>
<td>Alpha blocker?, beta blocker?</td>
<td>ACE inhibitors ?, calcium channel blockers ?, angiotensin-2 receptor blockers?</td>
</tr>
<tr>
<td>Infectious Disease</td>
<td>Antiretroviral</td>
<td>Protease inhibitors</td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>Steroid hormones</td>
<td>Corticosteroids, progestational agents</td>
<td>NSAIDs</td>
</tr>
<tr>
<td></td>
<td>Antihistamines, anticholinergics</td>
<td>Diphenhydramine, ? Doxepin?, cyproheptadine?</td>
<td>Decongestants, steroid inhalers</td>
</tr>
</tbody>
</table>

*Weight reducing

Development of a Treatment Plan

- Set realistic weight loss goals
- Establish health goals
- Review patient’s medication list and change or discontinue any weight-promoting drugs
- Intervention strategies
  - Lifestyle interventions: healthy eating, reducing caloric intake, avoiding meal skipping, monitoring portion sizes, ensuring adequate sleep, managing mental illness/stress and increasing physical activity
  - Pharmacotherapy to increase satiety and decrease appetite
  - Consider bariatric surgery when indicated
## Treatment Recommendations

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Treatment Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 25</td>
<td>Reduced calorie diet, physical activity, behavioral modification</td>
</tr>
<tr>
<td>≥27-30 + co-morbidity</td>
<td><strong>Consider adding pharmacotherapy</strong> to decrease food intake</td>
</tr>
<tr>
<td>≥ 30</td>
<td><strong>Consider adding pharmacotherapy</strong> to decrease food intake</td>
</tr>
<tr>
<td>≥35-40 + co-morbidity</td>
<td><strong>Consider bariatric surgery</strong></td>
</tr>
<tr>
<td>≥ 40</td>
<td><strong>Consider bariatric surgery</strong></td>
</tr>
</tbody>
</table>

*5% weight loss is considered clinically important by the FDA; discontinue a weight loss medication if weight loss < 5% at 3 mo.¹

**Bariatric surgery options includes: Laparoscopic Adjustable Gastric Banding (LAGB), Vertical Sleeve Gastrectomy (VSG), or Roux-en-Y bypass (RYGB)**

SECTION 5
LIFESTYLE MANAGEMENT
Adherence to the Diet and Not The Diet Predicts Success

“The best diet is the one you like best”

Diet type does not predict weight loss
Adherence score predicts weight loss

Diet Recommendations

• Low Calorie Diet
  o 1200-1500 kcal/day for women
  o 1500-1800 kcal/day for men
  o Achieves weight loss approximately 1-2 pounds/week
  o Most marketed diets are low calorie

• Medically supervised Very Low Calorie Diet (VLCD)
  o < 800 kcal/day for up to 16 weeks, followed by a refeeding diet
  o May consist of 4 to 5 high protein shakes daily plus vitamins and minerals
  o Not successful long-term

• Meal replacements may be useful

Effectiveness of Commercial Weight Loss Programs

- Randomized controlled trials of weight loss programs versus control/education & counseling

- Data of 12 months or more
  - Weight Watchers: > 2.6% weight loss vs control
  - Jenny Craig: > 4.9% weight loss vs control

- Other programs had only short term data
  - Nutrisystem (>3.8% weight loss vs control), Health Management Resources, Medifast, Optifast

Images: www.weightwatchers.com; www.jennycraig.com
Exercise Recommendations

• **Maintain health:**
  • 150 min/week of *moderate* aerobic exercise
  OR 75min/week of *vigorous* aerobic exercise\(^1\)
  • **AND** resistance exercise on 2 or more days of week\(^1\)

• **Weight loss:** 150-250 min/week of moderate aerobic exercise\(^2\)

• **Prevent weight re-gain:** 150-250 min/week of moderate aerobic exercise

• Minimum of 10 min bouts in duration for activity\(^3\)

Remember to encourage gradual, incremental changes to physical activity

Examples of Exercise

**Moderate Intensity Exercise**
- Walking moderate or brisk pace
- Water aerobics
- Swimming
- Yoga
- Bicycling 5-9 mph
- Stationary bicycling - moderate effort
- Weight training w/ free weight

**Vigorous Intensity Exercises**
- Jogging or running
- Aerobic dancing – high impact
- Step aerobics
- Water jogging
- Most competitive sports

Diet + Exercise = The Most Weight Loss

24 men with obesity

Non-exercise BCDD group lost significantly less weight than the other groups p < 0.01

BCDD  Balanced caloric deficit diet
PSMF   Protein-sparing modified fast

Food and Activity Monitoring

Food and activity tracking is one of the best predictors of weight loss success

• Nearly all extended treatment studies promote recording of food intake and weight

• There is conflicting data about smart-phones improving self-monitoring and weight control\(^1,2,3\)

• Per the National Weight Control Registry, patients should weigh themselves at least weekly


Behavioral interventions are essential\textsuperscript{1,2}

- Comprehensive and high intensity sessions most effective
  - 12 to 26 sessions a year
  - Group or individual sessions
- Setting weight loss goals
- Improving diet, nutrition
- Physical activity sessions
- Addressing barriers to change
- Self monitoring
- Strategies for maintaining lifestyle changes

\textsuperscript{1} Ann Intern Med. 2012;157:373-378.
\textsuperscript{2} http://www.uspreventiveservicestaskforce.org/uspstf11/obeseadult/obesers.htm
SECTION 6
PHARMACOTHERAPY
Indications and Use of Pharmacotherapy

**Indication**

- **Adjunct to low calorie diet & ↑ physical activity**
- BMI ≥ 30 kg/m\(^2\), or BMI ≥ 27 kg/m\(^2\) in the presence of at least one weight related comorbid condition (e.g., HTN, Type 2 DM)

**Efficacy Criteria**

- A weight loss of ≥ 5% of body weight at 3 months is considered effective, and safety and efficacy should be assessed at least every 3 mo. thereafter

- If a patient does not respond to one medication, discontinue it and try another

- Medication should be initiated with dose escalation based on efficacy and tolerability to the recommended dose, not exceeding the upper approved dose limits.\(^1\)

\(^1\) Apovian C et al J Clin Endocrinol Metab 2015; 100:342-362.
## Medications for Weight Loss

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA</th>
<th>Wt Loss*</th>
<th>Contra-indications/ Precautions</th>
<th>Safety and tolerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine*</td>
<td>Norepinephrine-releasing agent</td>
<td>3.6 kg</td>
<td>Pregnancy, nursing, CVD, with MAOIs, hyperthyroidism, glaucoma, agitated states, hx drug abuse, hypersensitivity</td>
<td>Dizziness, dry mouth, difficulty sleeping, constipation, irritability</td>
</tr>
<tr>
<td>Orlistat/Xenical®</td>
<td>Inhibits GI lipases, blocks fat absorption</td>
<td>2.9-3.4%</td>
<td>Chronic malabsorption; gall bladder disease; Pregnancy</td>
<td>GI side effects, rare liver injury, ↓ cyclosporine exposure</td>
</tr>
<tr>
<td>Phentermine/topiramate Qsymia®</td>
<td>Norepinephrine-releasing agent/GABA receptor modulator; ↓ appetite, prolongs satiety</td>
<td>6.6%; 8-9% at high dose</td>
<td>Glaucoma; hyperthyroidism; MAOIs; Pregnancy</td>
<td>Birth defect risk, minor elevation in heart rate; metabolic acidosis; increased creatinine; glaucoma</td>
</tr>
</tbody>
</table>

Notably, Mean placebo-adjusted weight loss demonstrated in clinical studies; all 1 year except for phentermine 2-24 weeks
**Lomaira, a low-dose version of phentermine hydrochloride, in 8-milligram tablets, approved fall 2016, can be taken 8mg PO TID or tablets are scored to be cut in half for 4mg doses if desired. Only approved for short term use of a couple of weeks. More info at [www.lomaira.com](http://www.lomaira.com)

Apovian C et al J Clin Endocrinol Metab 2015; 100:342-362
<table>
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<tr>
<th>Drug</th>
<th>MOA</th>
<th>Wt Loss*</th>
<th>Contra-indications/ Precautions</th>
<th>Safety and tolerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorcaserin</td>
<td>Selective serotonin 2C receptor agonist; ↑ satiety</td>
<td>3.6%</td>
<td>CI pregnancy; Use with extreme caution with serotonergic or antidopaminergic drugs</td>
<td>Possible risk of valvulopathy in obese patients with type 2 diabetes; serotonin syndrome</td>
</tr>
<tr>
<td>Belviq®</td>
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</tr>
<tr>
<td>Naltrexone/</td>
<td>Opioid receptor antagonist/ Dopamine and nor-epinephrine reuptake inhibitor; ↓ appetite, acts on reward pathways</td>
<td>4.8%</td>
<td>Seizure disorder; uncontrolled HTN; chronic opioid use; MAOIs; Pregnancy</td>
<td>Minor increase in heart rate and blood pressure; seizure risk; hepatotoxicity; suicidal thoughts &amp; behaviors</td>
</tr>
<tr>
<td>Bupropion ER</td>
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<tr>
<td>Contrave®</td>
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<tr>
<td>Liraglutide</td>
<td>Glucagon-like peptide 1 analogue, decreases appetite</td>
<td>5–6%</td>
<td>Patients with a personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia type 2; Pregnancy</td>
<td>Nausea, hypoglycemia, risk for pancreatitis; rodent thyroid C cell tumors</td>
</tr>
<tr>
<td>3 mg</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Saxenda®</td>
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</tbody>
</table>

*Mean placebo-adjusted weight loss demonstrated in clinical studies, all 1 year
## Long-Term Medications for Weight Loss

<table>
<thead>
<tr>
<th>Drug</th>
<th>US FDA approval</th>
<th>Drug Frequency &amp; route of administration</th>
<th>Mechanism of action</th>
<th>Weight loss in clinical trials, 1 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat®/Xenical®</td>
<td>1999</td>
<td>120mg PO with meals</td>
<td>GI lipase inhibitor, blocks fat absorption</td>
<td>2.9-3.4%</td>
</tr>
<tr>
<td>Phentermine/Topiramate</td>
<td>July 2012</td>
<td>3.75 mg/23 mg PO QD × 14 d; Then, 7.5/46 mg × 14 d (Schedule IV)</td>
<td>Noradrenergic agent/ GABA receptor modulation; ↑ Satiety</td>
<td>6.6%; 8–9% at high dose</td>
</tr>
<tr>
<td>Lorcaserin/Belviq®</td>
<td>June 2012</td>
<td>10 mg PO BID (Schedule IV)</td>
<td>Serotonin 2C receptor agonist, stimulates α MSH, ↑ Satiety</td>
<td>3.6%</td>
</tr>
<tr>
<td>Naltrexone/Bupropion ER</td>
<td>Sept 2014</td>
<td>Oral BID; 8 mg/90 mg Escalate dose from 1 tab Q am to 2 tabs BID over 4 weeks,</td>
<td>Opioid antagonist/ Dopamine and norepinephrine reuptake inhibitor , ↓ Appetite, reward system</td>
<td>4.8%</td>
</tr>
<tr>
<td>Liraglutide 3.0 mg Saxenda®</td>
<td>Dec 2014</td>
<td>Once-daily SC; start 0.6 mg QD, increase by 0.6 mg weekly to 3.0 mg QD</td>
<td>Glucagon-like peptide 1 analogue ↓ Appetite</td>
<td>5-6%</td>
</tr>
</tbody>
</table>

*Orlistat 60mg (alli®) is the only over-the-counter FDA approved weight-loss drug.

*Liraglutide 0.6-1.8 mg was approved in the United States in 2010, as a treatment for type 2 diabetes.

Ref: US Prescribing Information for each medication
When choosing a medication, consider concomitant diseases.

<table>
<thead>
<tr>
<th>Comorbid Disease</th>
<th>Avoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncontrolled Hypertension / Cardiovascular Disease</td>
<td>Phentermine, phentermine/topiramate; naltrexone/bupropion</td>
</tr>
<tr>
<td>Depression on sertraline</td>
<td>Lorcaserin (risk of serotonin syndrome)</td>
</tr>
<tr>
<td>History of seizure</td>
<td>Naltrexone/bupropion</td>
</tr>
<tr>
<td>History of pancreatitis</td>
<td>Liraglutide</td>
</tr>
<tr>
<td>History of kidney stones</td>
<td>Phentermine/topiramate</td>
</tr>
</tbody>
</table>

1. Apovian C et al J Clin Endocrinol Metab 2015; 100:342-362
Metformin and Weight Loss

- Not approved for weight loss or pre-diabetes.
- Commonly used off-label at academic weight management centers for patients with pre-diabetes and overweight or obesity.
- Diabetes prevention trial: mean weight loss 2.1 kg (4.6lbs).
- Potential mechanisms: increased insulin sensitivity; decreased intestinal glucose absorption; decreased gluconeogenesis.


www.healthybloodsugars.com
CONQUER Trial

Weight loss at 56 weeks with Phentermine/Topiramate ER:

BMI 27-45 and ≥2 obesity-related comorbidities (HTN, DLD, DM2, Pre-DM2, Abdominal Obesity)

<table>
<thead>
<tr>
<th>Weight Loss</th>
<th>Phentermine/Topiramate 7.5 mg/46 mg Daily (n = 1,538)</th>
<th>Phentermine/Topiramate 15 mg/92 mg Daily (n = 981)</th>
<th>Placebo (n = 979)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5%</td>
<td>62%</td>
<td>70%</td>
<td>21%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≥10%</td>
<td>37%</td>
<td>48%</td>
<td>7%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mean weight loss</td>
<td>8.1 kg</td>
<td>10.2 kg</td>
<td>1.4 kg</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

- Dose-related AEs: dry mouth, constipation, dysgeusia, paresthesia, insomnia, dizziness, anxiety, irritability, disturbance in attention
- Endpoint assessments were not available for 31% of participants

Liraglutide: Weight Loss Over 2 Years


All patients on liraglutide/placebo switched to liraglutide 2.4 mg at week 52, and then to 3.0 mg between weeks 70 and 96.
Effects of Discontinuing Pharmacotherapy

BLOOM Study: Body weight increases after lorcaserin is switched to placebo

Pharmacotherapy: Key points

- Medications used for weight loss are adjunctive to lifestyle changes, and are indicated in people with a BMI ≥ 30 or BMI ≥ 27, with at least one comorbidity.

- A medication is considered effective when a 5% or greater reduction in weight is achieved within 3 months.

- Selection of the appropriate medication for a patient involves consideration of the patient’s other diseases so that adverse effects can be avoided.

- Before prescribing, it is important to understand the safety profile of the medication, including contraindications and adverse effects.
SECTION 7
BARIATRIC SURGERY
Assessing Candidacy for Bariatric Surgery

A patient is a good candidate for bariatric surgery if he/she has a:

- BMI 40 or greater OR
- BMI 35 to 40 and at least one obesity related comorbidity (i.e. HTN, T2DM, CAD, etc)

AND:

- Failed to lose and maintain weight loss with non surgical methods
- Well informed about the surgical procedure (i.e. benefits and risks)
- Ready to commit ~6 months of time to prepare for surgery
  - Educational group classes, series of blood tests, multiple visits with physicians and often a psychologist
  - Achieve ~5-10% weight loss of total body weight (to reduce size of liver and complications of surgery)
- Not planning to get pregnant for at least the next 1-2 years
- Ready to quit smoking (if applies)

Bariatric Surgery Procedures

• Mixed Surgery
  • Roux-en-Y gastric bypass (RYGB) also called gastric bypass
  • Restriction of stomach and bypass of small bowel (shortened much less than BPD)
• Vertical Sleeve Gastrectomy (VSG)
  • Removing approximately 80% of stomach
• Restrictive
  • Adjustable gastric banding (LAGB)
  • Induce early satiety during meals by decreasing stomach volume
• Malabsorbtive
  • Bilio-pancreatic diversion (BPD) with duodenal switch
  • Divert bile into terminal segment of ileum so it is only mixed in final segment of small bowel → drastically reducing nutrient absorption
  • Used rarely in U.S. - in patients with very high BMI

Commonly used bariatric surgery procedures

- Roux-en-Y Gastric Bypass
- Vertical sleeve gastrectomy
- Adjustable lap band
Safety of Bariatric Surgery

• Operative mortality (up to 30 days) 0.1-2%, lowest with adjustable gastric band
  • Higher mortality with visceral obesity, BMI ≥ 50, older age, sleep apnea, diabetes mellitus
• Early complications include: venous thromboembolism (1%), respiratory insufficiency (<1%), hemorrhage (1%), peritonitis (1%), wound infection (2%)
• Most common long term complication is GI obstruction
• Meta-analysis of 64 studies found overall 17% complication rate

Data for Weight Loss Success
Swedish Obesity Study\(^1\)

- Swedish subjects with obesity
- \(N=4047\)
- Prospective Matched Cohort Study
- Follow up > 16 yrs

Type 2 Diabetes Remission in the Swedish Obesity Study*

* Prospective, matched surgical intervention study


**blood glucose <110 mg/dL and no diabetes medication**

<table>
<thead>
<tr>
<th></th>
<th>Control Group N=2037</th>
<th>Surgery Group N=2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 2 years</td>
<td>16.4%</td>
<td>72.3%</td>
</tr>
<tr>
<td>At 15 years</td>
<td>6.5%</td>
<td>30.4%</td>
</tr>
</tbody>
</table>

- All types of bariatric surgery were associated with higher remission rates vs. usual care
- This includes adjustable/nonadjustable banding, VBG, or gastric bypass¹

¹ Prospective, matched surgical intervention study
Long term Follow-up Data for Mortality: Swedish Obese Subjects (SOS) Study


Preventive Medicine
Task Force
American Medical Women’s Association
SECTION 8: MINIMALLY INVASIVE PROCEDURES
Minimally Invasive Procedures

- Vagal Blocking Therapy
- Duodenal jejunal bypass liner Device
  EndobARRIER®
- Gelesis100 Polymer
- Intragastric Balloon
- Aspiration Device
**Intragastric Balloons**

- BMI 30-40 kg/m$^2$
- Placed endoscopically; removed 6 mo.
- **ReShape™ Integrated Dual Balloon System**
  - 14.3 lbs (6.8% TBWL at 6 mos; n=187)
- **ORBERA™ Intragastric Balloon System**
  - 11.27% TBWL at 12 months (n=1683)$^1$

**Aspiration Device**

- Age ≥ 22 yrs with BMI 35-55, failed non surgical treatment
- Removes ~30% of food from stomach
- Aspiration process ~20 min after meal is consumed, 5-10 minutes to complete, 3x/day
- At 1 yr, 12.1 % weight loss vs 3.6 % in controls
- Nutritional monitoring$^{1,2}$

TBWL = total body weight loss

2. www.fda.gov/MedicalDevices *Slide adapted from Dr. Dong Kim, BMC Hospital
Summary and Key points

• **Obesity is a disease** associated with changes in adipose and GI hormones, and defective signaling in hypothalamic pathways responsible for appetite regulation and energy balance.

• Obesity contributes to **type 2 diabetes, hypertension, dyslipidemia, atherosclerotic cardiovascular disease, arthritis, & cancer.**

• Effective treatment of obesity **reduces HbA1C, type 2 diabetes, BP, TGs, episodes of sleep apnea, etc.**
Key points Cont’d

• First line treatment includes diet, ↑ physical activity, behavioral interventions, and adjusting medications that cause weight gain.

• Medications that control appetite help patients adhere to dietary recommendations and lose weight.

• Benefits & risks of pharmacological & surgical therapies should be carefully considered in each patient.
Conclusions

• Obesity is a complex disease associated with multiple comorbidities.

• We have the tools and skills to treat obesity.

• It is time for us to begin the conversation about weight and work with our patients to develop a plan that will help them lose it.
Acknowledgments

American Medical Women’s Association
AMWA Preventive Medicine Task Force
#AMWAprevention

www.amwa-doc.org