MAKING WEIGHT: Wrestling with the Challenges of Obesity

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Faculty Disclosures

• Shannon Hillier, DO, MPH
  – No financial support or personal connections to disclose that could be perceived to bias this work

• Kelly Murray, PharmD, BCACP
  – No financial support or personal connections to disclose that could be perceived to bias this work
Objectives

- As a result of participating in this activity, learners will be able to:
  - Discuss the epidemiology of obesity and Oklahoma’s role in the epidemic.
  - Understand different classifications for obesity.
  - Recall neurobiological mechanism of obesity.
  - List specific treatment strategies for obesity, with a focus pharmacotherapy options.
  - Address specific challenges associated with patients with obesity within the primary care setting.
Obesity: Epidemiology

- No state has a prevalence of obesity less than 20%.
- 6 states and the District of Columbia have a prevalence of obesity between 20% and 25%.
- 19 states and Puerto Rico have a prevalence of obesity between 25% and 30%.
- 21 states and Guam have a prevalence of obesity between 30% and 35%.
- 4 states (Alabama, Louisiana, Mississippi, and West Virginia) have a prevalence of obesity of 35% or greater.
Obesity: Epidemiology

Oklahoma Obesity Fact Sheet

Adult Obesity Facts:

- Obesity affects more than 33.9% of Oklahomans.
- Oklahoma is ranked 8th/51 in states impacted by obesity.
- The age group most affected by obesity in Oklahoma is 45-64 (36.7%).
- More than 33.1% of male Oklahomans are affected by obesity.
- More than 31.4% of female Oklahomans are affected by obesity.
- Oklahoma ranks 9th in adults with Type 2 Diabetes (11.7%).

Oklahomaans Affected by Obesity by Race:

- Caucasian: 32.5%
- African American: 35.4%
- Hispanic: 33.9%

References:
- Centers for Disease Control
- Trust for America's Health
- Obesity Action Coalition

Obesity Action Coalition; www.obesityaction.org  Accessed Aug 2018
Obesity: Classical Definition

<table>
<thead>
<tr>
<th>Body Mass Index (BMI)</th>
<th>18.5-24.9 kg/m²</th>
<th>25.0-29.9 kg/m²</th>
<th>≥30 kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent Body Fat</td>
<td>Male: &lt;25%</td>
<td>Male: &gt;25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female: &lt;32%</td>
<td>Female: &gt;32%</td>
<td></td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>Male: &lt;40 in.</td>
<td>Male: &gt;40 in.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female: &lt;35 in.</td>
<td>Female: &gt;35 in.</td>
<td></td>
</tr>
</tbody>
</table>

Weight Categories

<table>
<thead>
<tr>
<th>Weight Categories</th>
<th>BMI, kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Healthy Weight</td>
<td>&gt;18.5 and &lt;25</td>
</tr>
<tr>
<td>Overweight</td>
<td>&gt;25 and &lt;30</td>
</tr>
<tr>
<td>Obesity Class I</td>
<td>&gt;30 and &lt;35</td>
</tr>
<tr>
<td>Obesity Class II</td>
<td>&gt;35 and &lt;40</td>
</tr>
<tr>
<td>Obesity Class III</td>
<td>&gt;40</td>
</tr>
</tbody>
</table>
Obesity: Is Not Simple

• Major Driver:
  – Over consumption of food
  – Energy dense meals
  – In greater excess than is needed by the body

• FOOD CONSUMPTION IS NOT SIMPLY A BIOLOGICAL BEHAVIOR TO MEET BODY ENERGY NEEDS:
  – Cognitive, emotional, sensory, economic and environmental factors influence motivation to eat
Obesity: Disease Definition

“Obesity is defined as a chronic, relapsing, multi-factorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences.”

The adverse health consequences of increased body fat are not simply “co-morbidities” or “associated risk factors”
Obesity: Recognized as a Disease

“...obesity is a serious chronic disease with extensive and well-defined pathologies, including illness and death”

“Recognizing obesity as a disease will help change the way the medical community tackles this complex issue that affects approximately one in three Americans”

“Obesity is a chronic disease, prevalent in both developed and developing countries, and affecting children as well as adults”

“Obesity is a complex, multifactorial condition characterized by excess body fat. It must be viewed as a chronic disorder that essentially requires perpetual care, support, and followup. Obesity causes many other diseases, and it warrants recognition by health-care providers and payers.”

Obesity: Recognized as a Disease

“Obesity is a complex, multifactorial disease that develops from the interaction between genotype and the environment. Our understanding of how and why obesity occurs is incomplete; however, it involves the integration of social, behavioral, cultural, and physiological, metabolic, and genetic factors” - 1998

“Overweight and obesity are chronic diseases with behavioral origins that can be traced back to childhood” - 2013

“E66.9 Overweight or Obesity … conditions that my be a focus of clinical attention, affect the diagnosis, course, prognosis, or treatment of a patient’s mental disorder” - 2013

Diagnostic And Statistical Manual Of Mental Disorders, Fifth Edition (2013);
Obesity: Algorithm

1. Obesity as a Disease
2. Data Collection
3. Evaluation and Assessment
4. Management Decisions
5. Motivational Interviewing
   - Nutritional Intervention
   - Physical Activity
   - Behavior Therapy
   - Pharmacotherapy
   - Bariatric Procedures
Comprehensive Evaluation of the Patient with Overweight/Obesity

<table>
<thead>
<tr>
<th>History</th>
<th>Weight history, past medical history, family history, social history, screening for weight-promoting medications, food intake, activity, review of systems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Examination</td>
<td>Height, weight, blood pressure, body composition analysis, waist measurement, complete physical examination</td>
</tr>
<tr>
<td>Laboratory Tests*</td>
<td>Complete blood count, electrolytes, liver function, kidney function, fasting lipid profile, thyroid tests, hemoglobin A1c, uric acid, vitamin D</td>
</tr>
<tr>
<td>Diagnostic Testing*</td>
<td>EKG, echocardiogram, exercise stress test, sleep study, barium swallow or esophagoduodenoscopy</td>
</tr>
<tr>
<td>Psychiatric Examination</td>
<td>Rule out impulse control disorders, eating disorders, depression, anxiety etc.</td>
</tr>
</tbody>
</table>
Obesity: Appetite Complexities

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. Apovian CM, Aronne LJ, Bessesen D et al. / Clin Endocrinol Metab. 2015;100:342-362.
Obesity: Neurobiology

- I’m Satisfied 😊
- LEPTIN
- CHOLECYSTOKININ
- PANCREATIC POLYPEPTIDE
- PP
- PEPTIDE TYROSINE-TYROSINE
- PYY
- OXYNTOMODULIN
- OXM
- GLP-1
- CCK

I’M HANGRY!
- GHRELIN
- OREXIN

I’M HANGRY!

- Low blood glucose levels (or other signals) excite the **ARCULATE NUCLEUS** in the hypothalamus

- **OREXIN**
  - Stimulates hunger / food consumption behaviors / fat storage
  - Decreases fat oxidation / energy expenditure
  - Elevates DA in VTA / nucleus accumbens

- **GHRELIN**

I’m Satisfied 😊
via my hypothalamus

- ADIPOSE tissues produce LEPTIN which signals the ARCULATE NUCLEUS in the hypothalamus

  - Reduces hunger / food intake
  - Increases fat oxidation / energy expenditure
  - Decreases 35% DA in VTA / nucleus accumbens
    - Reduced amount and duration of food intake

I’m Satisfied 😊 via my brainstem

- Food in the GI track triggers enteroendocrine cells to produce **CHOLECYSTOKININ (CCK)**
- Afferent VAGAL NERVES innervating the stomach and duodenum signal **NUCLEUS TRACTUS SOLITARIUS (NTS)** in the brainstem
  - Aids in digestion
  - Increases the sensation of fullness DURING a meal

I’m Satisfied 😊
via my brainstem

• After a meal, **GLUCAGON-LIKE PEPTIDE-1 (GLP-1)** produced by enteroendocrine cells (intestine) and by the NTS (brainstem), which then encourages the release of **INSULIN** (pancreas)

• increases the feeling of fullness during and between meals by acting on appetite centers in the brain and by slowing the emptying of the stomach

Obesity: Positive Feedback

High-fat/High-carb food

Increased endocannabinoids and resistance to leptin and insulin

1. Increased food intake
   2. Weight gain

Hypothalamic injury - CNS insulin and leptin resistance

"Brain can’t tell how much fat is stored, how much food is eaten"

1. Reduced sense of satiety
   2. Craving

Slide courtesy of Louis J. Aronne, MD. Wang J, Diabetes, 2001
DiMarzo V pers comm; Ozcan L, et al, Cell Metabolism; 2009
Obesity: Stress Cycle

1. Obesity, Adiposopathy, and Metabolic Disease
2. Chronic Stress
3. Behavior Changes, Endocrinopathies, and Immunopathies
4. Increasing Body Fat
5. Worsening Adipose Tissue Function

Reference/s: [1]
Obesity: Algorithm

- Obesity as a Disease
- Data Collection
- Evaluation and Assessment
- Management Decisions
- Motivational Interviewing
  - Nutritional Intervention
  - Physical Activity
  - Behavior Therapy
  - Pharmacotherapy
  - Bariatric Procedures
Obesity: Assessing RISK

Edmonton Obesity Staging System (EOSS)

Obesity: Assessing RISK

• Edmonton Obesity Staging System

0  No apparent risk factors (e.g., blood pressure, serum lipid and fasting glucose levels within normal range), physical symptoms, psychopathology, functional limitations and/or impairment of well-being related to obesity
1  Presence of obesity-related subclinical risk factors (e.g., borderline hypertension, impaired fasting glucose levels, elevated levels of liver enzymes), mild physical symptoms (e.g. dyspnea on moderate exertion, occasional aches and pains, fatigue), mild psychopathology, mild functional limitations and/or mild impairment of well-being
2  Presence of established obesity-related chronic disease (e.g., hypertension, type 2 diabetes, sleep apnea, osteoarthritis), moderate limitations in activities of daily living and/or well-being
3  Established end-organ damage such as myocardial infarction, heart failure, stroke, significant psychopathology, significant functional limitations and/or impairment of well-being
4  Severe (potentially end-stage) disabilities from obesity-related chronic diseases, severe disabling psychopathology, severe functional limitations and/or severe impairment of well-being
Obesity: Assessing RISK

- Edmonton Obesity Staging System

Obesity: Comprehensive Treatment

- Nutrition
- Physical Activity
- Behavior
- Medication
Individualized Treatment Plans*

<table>
<thead>
<tr>
<th>Diet</th>
<th>Use calorie restriction, carbohydrate restriction, food journaling, very low-calorie diet programs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity</td>
<td>Give exercise prescription, use pedometers, limit TV and computer time, decrease sedentary time, initial goal of 150 minutes per week of moderate-intensity physical activity</td>
</tr>
<tr>
<td>Counseling</td>
<td>Eliminate provider bias and stigma, identify self-sabotage, develop strong support, address stress management, sleep optimization, other psychological support as needed</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>Use pharmacotherapy as part of a comprehensive program</td>
</tr>
<tr>
<td>Referral</td>
<td>Consider referral to an obesity medicine specialist</td>
</tr>
</tbody>
</table>

* Lab and diagnostic testing should be individualized.

*If ineffective, consider referral to a metabolic and bariatric surgeon. Optimal pre- and post-operative care includes an obesity medicine specialist.

Obesity medicine specialists, certified by the American Board of Obesity Medicine, dedicate a portion or all of their practice to the treatment of obesity. They perform a medical evaluation (history, physical, laboratory, body composition) and provide medical supervision for lifestyle change (nutrition, activity, behavior change), medications, or very low-calorie diets. Obesity is a chronic medical disease and often requires lifelong treatment.
*Potency includes many factors, such as the amount, rate, and sustainability of weight loss, and the long-term resolution of adiposopathy and fat mass disease. Potency varies greatly for each individual (i.e., long-term adherence to a lifestyle program can be as potent as gastric bypass surgery).
Obesity: Algorithm

1. Obesity as a Disease
2. Data Collection
3. Evaluation and Assessment
4. Management Decisions
5. Motivational Interviewing

- Nutritional Intervention
- Physical Activity
- Behavior Therapy
- Pharmacotherapy
- Bariatric Procedures
Motivational Interviewing: Stages

- Pre-contemplation: Unawareness of the problem
- Contemplation: Thinking of change in the next 6 months
- Preparation: Making plans to change now
- Action: Implementation of change
- Relapse: Restart of unfavorable behavior

Reference/s: [204] [205]
MI: Principles

- Express empathy
- Avoid argumentation
- Develop discrepancy
- Resolve ambivalence
- Support self-efficacy
<table>
<thead>
<tr>
<th>MI Techniques: 5A’s</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ask</strong></td>
</tr>
<tr>
<td>• Ask for permission to discuss body weight.</td>
</tr>
<tr>
<td>• Explore readiness for change.</td>
</tr>
<tr>
<td><strong>Assess</strong></td>
</tr>
<tr>
<td>• Assess BMI, waist circumference, and obesity stage.</td>
</tr>
<tr>
<td>• Explore drivers and complications of excess weight.</td>
</tr>
<tr>
<td><strong>Advise</strong></td>
</tr>
<tr>
<td>• Advise the patient about the health risks of obesity, the benefits of modest weight loss (i.e., 5-10 percent), the need for long-term strategy, and treatment options.</td>
</tr>
<tr>
<td><strong>Agree</strong></td>
</tr>
<tr>
<td>• Agree on realistic weight-loss expectations, targets, behavioral changes, and specific details of the treatment plan.</td>
</tr>
<tr>
<td><strong>Arrange/Assist</strong></td>
</tr>
<tr>
<td>• Assist in identifying and addressing barriers; provide resources; assist in finding and consulting with appropriate providers; arrange regular follow up.</td>
</tr>
</tbody>
</table>

Reference(s): [226] [227]
MI Techniques: FRAMES

- Feedback about Personal Risk
- Responsibility of Patient
- Advice to Change
- Menu of Strategies
- Empathetic Style
- Self-efficacy

Reference/s: [228] [229]
Obesity: Behavioral Modification

Thoughts
- I can’t cope
- I must please others
- I’m not in control
- I’m worried about the future
- I can’t concentrate
- What if x, y, z happens?

Physical Feelings
- Heart Races
- Dizzy
- Upset Stomach
- Perspiration
- Tense
- Rapid Breathing
- Panicky

Behaviors
- Social avoidance
- Tap fingers
- Bite nails
- Eat
- Leave situations
Obesity: Behavioral Modification

EVENT
I didn’t get the raise at work.

THOUGHT
“I’m not appreciated. I’ll never move up.”

FEELING
Depressed

CONSEQUENCES/BEHAVIOR
Repeated Automatic Thought: “What’s the point in trying? I don’t get anywhere anyway?”
-Eat, Drink, Give up.
Obesity: Behavioral Modification

**EVENT**
Going out to dinner with a group of friends.

**THOUGHT**
“I’ll never be able to manage this. Screw it - I’m going to overeat.

**FEELING**
Hopeless, Discouraged

**CONSEQUENCES**
Overeat at the restaurant
Not go out.
Repeated Automatic Thought: “I knew I'd blow it. I never succeed at weight loss. Why bother. I might as well just take the whole weekend off my plan.”
Obesity: Behavioral Modification

Challenging Cognitive Distortions:
1. What evidence supports this thought?
2. What evidence is against this thought?
3. What other thoughts, feelings, and behaviors does this thought provoke?
4. What kind of automatic thought is this?
5. Can you think of a more rationale thought?
Obesity: Barriers to Care

- Misaligned perceptions of success
- Past failures
- Prescription coverage
- Clinician competence and confusion
- Patient engagement
- Limited advocacy
- Few effective treatment options
- Time constraints
- Cultural stigma and bias
- Lack of clear guidelines
- Difficult, emotional conversations
- Obesity as a disease vs. condition
- Rx market history of withdrawals
- Competing clinician priorities

**Obesity: Evolution of Reimbursement**

**Prior to 2012:**
Behavioral therapy often outright excluded by most payers, as well as most other services. Bariatric surgery intermittently covered.

**As of 2012:**
Medicare and most private payers cover USPSTF-recommended screening and behavioral counseling when delivered by a primary care provider (not a specialist).

**Going Forward:**
Affordable Care Act (ACA) mandates coverage of screening and counseling. Coverage remains inconsistent in terms of number of visits and insurer guidelines.

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References

- Obesity Algorithm®. ©2017-2018 Obesity Medicine Association
Endocrine Society: Indications for Medication

1. Patients with obesity (e.g., BMI ≥ 30kg/m2)

2. Patients who are overweight (e.g., BMI ≥ 27kg/m2) with presence of increased adiposity complications (e.g., type 2 diabetes mellitus, hypertension, dyslipidemia)

If no clinical improvement (≥5% loss) after 12 weeks with one anti-obesity medication, consider alternative anti-obesity medication or increasing anti-obesity medication dose (if applicable).

Medication Therapy Options

Older options (≤1999):
- Phentermine (‘59)
- Diethylpropion (‘59)
- Benzphetamine (‘60)
- Phendimetrazine (‘76)
- Orlistat (‘99)

Newer options (≥2007):
- Orlistat OTC (‘07)
- Lorcaserin (‘12)
- Phentermine / topiramate ER (‘12)
- Naltrexone / bupropion ER (‘14)
- Liraglutide (‘14)

# FDA Approvals

<table>
<thead>
<tr>
<th>Medication</th>
<th>Short term weight loss (adults)</th>
<th>Obesity mgmt (adults)</th>
<th>Obesity mgmt (peds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine (and others)</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orlistat</td>
<td></td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td></td>
<td>x</td>
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<tr>
<td>Phentermine/topiramate ER</td>
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<td>x</td>
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<tr>
<td>Naltrexone/bupropion ER</td>
<td></td>
<td>x</td>
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<tr>
<td>Liraglutide</td>
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</tbody>
</table>
Sympathomimetic Amines

- **Phentermine**, diethylpropion, phendimetrazine, benzphetamine
  - MOA: *Sympathomimetic*; stimulate the release of norepinephrine; reduce food intake causing early satiety; anorexiant
  - FDA Approved for **SHORT TERM** treatment of obesity (12 weeks)

- Efficacy (Phentermine): average loss is 6.4 - 7.4 kg

- Safety:
  - Palpitation, tachycardia, HTN, overstimulation, tremor, dizziness, insomnia, dysphoria, headache, dry mouth, dysgeusia, diarrhea, constipation, preg category X
  - DEA schedule: CIII or CIV

Orlistat

- Orlistat (Alli, Xenical) or Cetilistat (Phase 2 in US)
  - MOA: reversible inhibitor of gastric and pancreatic lipases; fat is not completely hydrolyzed and fecal fat excretion is increased; inhibits absorption by 30%
  - FDA approved for obesity management in adults AND children ≥ 12

- Efficacy: Absolute reduction = 3 kg after 1 year, 3.26 kg after 2 years
Orlistat

• Safety
  – CI: pregnancy, chronic malabsorption syndrome, cholestasis
  – AE:
    • GI in 15-30% (intestinal borborygmi and cramps, flatus, fecal incontinence, oily spotting, flatus with discharge)
      – Avoid high-fat diets (no more than 30% fat)
    • Reduced absorption of vitamins A, D, E, K and beta-carotene
      – Give vitamin supplements to patients on orlistat
      – Separate dose by at least 2 hours from vitamins
    • Severe liver injury
    • Oxalate-induced kidney injury

Lorcaserin

• Belviq, Belviq XR
  – MOA: Activates the 5-HT$_{2c}$ receptors, stimulating POMC neurons, leading to increased alpha-melanocortin stimulating hormone release at melanocortin-4 receptors and resulting in satiety and reduced food intake

• Efficacy: 4.7-5.0 kg loss
  – Other benefits: improves TC, triglycerides, A1c
  – BLOOM and BLOSSOM studies

• Safety:
  – CI: pregnancy (category X)
  – AE: HA, URI, nasopharyngitis, dizziness, nausea, hypoglycemia (in DM pts); serotonin syndrome risk
  – DEA Schedule IV

Phentermine / Topiramate ER

- **Qsymia**
  - MOA: sympathomimetic amine + appetite suppression/satiety
- **Efficacy**
  - ≥ 1 year = 10.2 kg (also improves TC, BP, LDL, TG, HDL, A1c)
- **Safety**
  - CI: pts with CVD, pregnancy, glaucoma, hyperthyroidism, MAO-I
  - AE (>10%): dry mouth, constipation, paresthesia, psych/cognitive AE, tachycardia, renal calculi, HA, insomnia, dysgeusia, dizziness
  - Drug Interactions: Oral contraceptives (irreg. bleeding), CNS depressants, non-potassium sparing diuretics (hypokalemia)
  - DEA Schedule IV
Naltrexone / Bupropion ER

- **Contrave** 8mg/90mg (titrate up)
  - MOA: unknown; opioid antagonist + dopamine/norepinephrine reuptake inhibitor
  - Efficacious for patients with food addictions

- **Efficacy**: 4-5% weight loss (6.1 kg)

- **Safety**:
  - CI: chronic opioid use, uncontrolled HTN, SZ, bulimia/anorexia, MAO-I, linezolid, methylene blue, pregnancy
  - AE: HA, sleep disorder, nausea, vomiting, constipation, dry mouth, cardiovascular events (tachycardia, HTN), liver dysfunction, neuro/psych events
  - Pregnancy Category: X
  - Do not administer with a high-fat meal (increased levels)

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Liraglutide

• Saxenda: SubQ; D/C if <4% loss at 16 weeks
  – MOA: glucagon-like peptide-1 receptor agonist, delays gastric emptying, promotes satiety

• Efficacy: 2 – 4 kg (DM) and 4.8 – 8 kg (weight loss)

• Safety:
  – CI: pregnancy, thyroid tumor (hx or FH)
  – AE: nausea (37-47%), vomiting (12-16%), diarrhea, low blood sugar, anorexia, pancreatitis, gallbladder disease, renal impairment, suicidal thoughts, thyroid tumors
  – Delayed absorption of drugs requiring rapid absorption (i.e. pain meds, oral contraceptives)

Efficacy and Safety

<table>
<thead>
<tr>
<th>Less Weight Loss (2-3%)</th>
<th>Greater Weight Loss (&gt;3-5%)</th>
<th>Robust Weight Loss (&gt;5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td>Phentermine</td>
<td>Topiramate/ phentermine</td>
</tr>
<tr>
<td></td>
<td>Naltrexone/ bupropion</td>
<td></td>
</tr>
</tbody>
</table>

- Discontinuation of therapy leads to weight re-gain
- Long-term data (1-2 years)
  - Topiramate/phentermine
  - Lorcaserin
  - Orlistat
  - Naltrexone/bupropion
  - Liraglutide
- All are pregnancy category X

Patient Selection

• **Phentermine:**
  – **Good Candidate:** need appetite suppression
  – **Poor Candidate:** uncontrolled HTN, CAD, hyperthyroidism, glaucoma, anxiety, insomnia, sensitive to stimulants, drug abuse, on MAO-Is

• **Orlistat:**
  – **Good Candidate:** patients able to comply with low fat diets, hypercholesterolemia, constipation
  – **Poor Candidate:** malabsorption, GI upset/diarrhea, unable to modify fat content of diet

• **Lorcaserin:**
  – **Good Candidate:** patients who describe inadequate meal satiety
  – **Poor Candidate:** on concomitant serotonin modulating medications, known cardiac valvular disease

Patient Selection

- **Phentermine/topiramate:**
  - **Good Candidates:** patients who would benefit from appetite suppression without cardiovascular history
  - **Poor Candidates:** uncontrolled HTN, CAD, hyperthyroidism, glaucoma, anxiety, insomnia, sensitive to stimulants, drug abuse, on MAO-Is, hx of nephrolithiasis

- **Naltrexone/bupropion:**
  - **Good Candidate:** concomitant depression, tobacco/alcohol use, food cravings
  - **Poor Candidate:** uncontrolled HTN, uncontrolled pain, recent MAO-I use, hx of seizures/predisposition to seizures

- **Liraglutide:**
  - **Good Candidate:** inadequate meal satiety and/or have Type 2 DM, prediabetes, or impaired glucose tolerance, psych patients
  - **Poor Candidate:** aversion to needles, hx of pancreatitis, hx or FH of medullary thyroid carcinoma, or multiple endocrine neoplasia syndrome type 2

Therapeutic Challenge:

COST OF MEDICATIONS
# Brand or Generic?

<table>
<thead>
<tr>
<th>Medication Name</th>
<th>Available as:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>Brand and Generic, Rx</td>
</tr>
<tr>
<td>Orlistat</td>
<td>Brand only, Rx and OTC</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>Brand only, Rx only</td>
</tr>
<tr>
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<tr>
<td>Liraglutide</td>
<td>Brand only, Rx only</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Generic, Rx only</td>
</tr>
<tr>
<td>Bupropion ER</td>
<td>Generic, Rx only</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Generic, Rx only</td>
</tr>
</tbody>
</table>

Prescription Resources

• Medication discount cards and apps
  – GoodRx

• Patient Assistance Programs
  – http://www.needymeds.org

• Rx for Oklahoma
  – 1-800-879-6552
Therapeutic Challenge:

WEIGHT EFFECTS OF MEDICATIONS
# Antihyperglycemics

<table>
<thead>
<tr>
<th>Weight Gain</th>
<th>Weight Loss/Neutral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>Metformin</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>SGLT-2 inhibitors</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>GLP-1 receptor agonists</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Alpha-glucosidase inhibitors</td>
</tr>
<tr>
<td></td>
<td>Amylin analogs</td>
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<tr>
<td></td>
<td>DPP-4 inhibitors</td>
</tr>
</tbody>
</table>

If insulin is started in a patient with Type 2 DM, a weight loss/neutral medication should be added to mitigate weight gain.

Glucocorticoids

• Mechanisms
  – Cause increased appetite
  – Reduce leptin-modulated suppression of food intake through HPA axis and metabolism regulation
  – Dose related effects on glucose, protein and lipid metabolism

• How to minimize gain =
  – Use lowest dose for shortest time
  – Consider alternate day steroid therapy for those in need of long term treatment

Antipsychotics

- Exact pathophysiology unknown
- Likely due to multiple neurotransmitters:
  - $5\text{-HT}_{2a}$, $5\text{-HT}_{2c}$, Histamine H1, $\alpha_1$ and $\alpha_2$ adrenergic receptors
- Significant increase in appetite for nutrient dense foods
  - Potential impact on central feedback system
- Potential hyperprolactinemia induced weight gain

Weight gain:
- Olanzapine
- Clozapine
- Quetiapine
- Risperidone
- Iloperidone
- Aripiprazole
- Ziprasidone

# Antidepressants

<table>
<thead>
<tr>
<th>High Gain</th>
<th>Medium Gain</th>
<th>Low Gain/Neutral</th>
<th>Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirtazapine</td>
<td>Nortriptyline</td>
<td>Citalopram</td>
<td>Fluoxetine</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>Imipramine</td>
<td>Escitalopram</td>
<td>Bupropion</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Clomipramine</td>
<td>Sertraline</td>
<td></td>
</tr>
<tr>
<td>Trimiopramine</td>
<td>Paroxetine</td>
<td>Fluvoxamine</td>
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<tr>
<td></td>
<td></td>
<td>Vortioxetine</td>
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<tr>
<td></td>
<td></td>
<td>Tranylcypromine</td>
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</tr>
</tbody>
</table>

Not enough information: venlafaxine, duloxetine

## Antiepileptic Drugs (AEDs)

<table>
<thead>
<tr>
<th>Effect on Weight</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gain</td>
<td>Valproate, Gabapentin, Pregabalin, Carbamazepine</td>
</tr>
<tr>
<td>Neutral</td>
<td>Lamotrigine, Levetiracetam, Phenytoin</td>
</tr>
<tr>
<td>Loss</td>
<td>Felbamate, Topiramate, Zonisamide</td>
</tr>
</tbody>
</table>

Antihistamines

• Most weight gain with first generation
  – Diphenhydramine, chlorpheniramine, doxylamine
• MOA: Potentially due to reduced energy expenditure secondary to mild sedative effect, increased appetite
• Alternatives for:
  – Motion sickness: scopolamine
  – N/V: meclizine
  – Allergies: montelukast, nasal corticosteroids
  – Insomnia: melatonin, zolpidem


Hormonal Therapies

• Oral Contraceptives
  – No difference in weight gain vs. placebo
    • Gain: 0.5 kg
  – Systematic Review ruled out potential for higher degree of weight gain (small amount of gain not ruled out)
  – Risk of VTE increased in obese patient taking OCPs

• Others: Progestin, megestrol acetate

Maveda ER. J Womens Health (Larchmt) 2014;23(1):38–43.
Gallo MF. Cochrane Database Syst Rev. 2014.
Other Medication Effects

Weight Gain Potential

- Lithium
- Beta-blockers
- Alpha-blockers
- Cannabinoids
- Antiretroviral therapy

Weight Loss Potential

- Levothyroxine
- Stimulants
- Testosterone
Surgery

• Indicated as adjunct in patients with:

1. BMI ≥ 35 kg/m² with comorbidity or

2. BMI > 40 kg/m²

Pharmacotherapy should always be used as an adjunct to nutritional, behavioral, and exercise therapy.

Be cognizant of weight effects of medications. Consider therapy modification if patient is obese.

Discontinuation of therapy will result in weight regain.

Early response to medications is predictive of overall response.
References