

Tomorrow's Wish: We Should Have Started Treating Obesity Today

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Pharmacist Objectives

1. Describe behavioral skills and techniques used in cognitive behavior therapy (CBT) to help clients modify eating and activity habits.
2. Understand the current criteria for anti-obesity pharmacotherapy use.
3. Given a patient case identify the appropriate anti-obesity pharmacotherapy option(s)

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Pharmacy Technician Objectives

1. Identify the multiple factors that contribute to obesity
2. Identify resources available to help patients with weight loss
3. Differentiate patients who are potential candidates for anti-obesity pharmacotherapy.

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Patient Case

- Wanda is a 30-year-old female who is 5' 4" and weighs 180 lbs (BMI 30.9 kg/m²). She has struggled with her weight throughout her life. About 10 years ago she injured herself during a college track meet. Unfortunately, she could not maintain her previous lifestyle after the injury and is now the heaviest she has ever been. She wants to try a pharmacologic agent to assist with weight loss before pursuing bariatric surgery. Her main motivation for losing weight is to help with ongoing fertility issues.
 - PMH: pancreatitis in 2019, type 2 diabetes
 - Medications: metformin 1000mg BID, glimepiride 4mg daily
1. Does Wanda qualify for pharmacologic weight loss medications?
 - A. Yes
 - B. No

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Patient Case

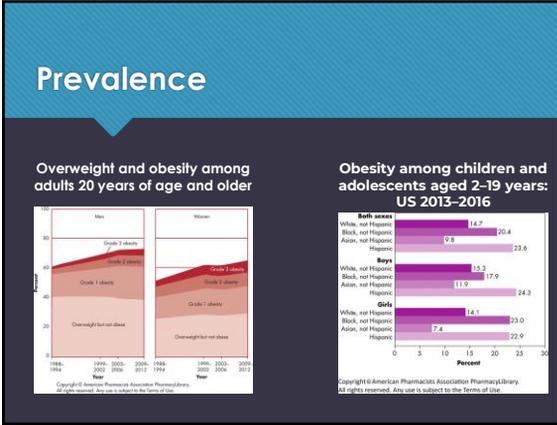
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 - PMH: pancreatitis in 2003, type 2 diabetes
 - Medications: metformin 1000mg BID, glimepiride 4mg daily
2. Which agent would you start to assist with Wanda's weight loss journey?
 - A. Liraglutide
 - B. Orlistat
 - C. Phentermine/topiramate
 - D. Naltrexone/bupropion

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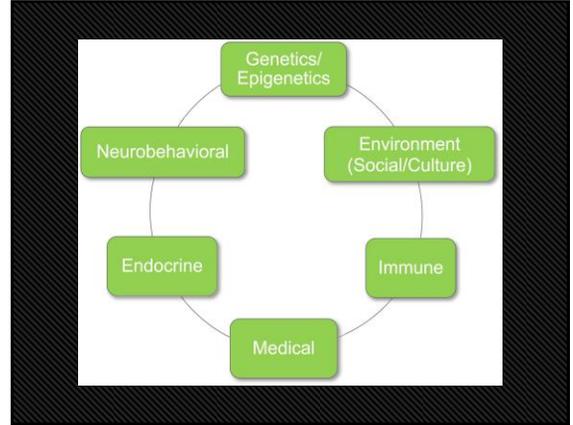
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 - PMH: pancreatitis in 2003, type 2 diabetes
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3. What is Wanda's goal weight after 6 months?
 - A. 144 lbs
 - B. 153 lbs
 - C. 167 lbs
 - D. 173 lbs

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Complications of Obesity

- Associated with cardiovascular disease
 - HTN, dyslipidemia, coronary artery disease, arrhythmias
- Increased risk of cerebrovascular disease
 - Hemorrhagic and ischemic stroke
- Obesity increases risk of DM, gallbladder dx, sleep apnea, osteoarthritis, cancer, disorders of female reproduction, ESRD and psoriasis

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Clinical Indicators

- Overweight = BMI 25-29.9
- Obese = BMI 30 or >
- Metabolic syndrome (3 or more of the following)
 - Waist circumference >40" (men), >35" (women)
 - TG >150 mg/dl
 - HDL <40 mg/dl (men), <50 mg/dl (women)
 - BP >130/85 mm Hg
 - Fasting glucose >100 mg/dl

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Is BMI an accurate measurement?

A. Yes

B. No

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Guidelines

- VA/DoD Management of Adult Overweight and Obesity Practice Guideline - 2020
- The Endocrine Society Guidelines - 2015
- 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults
- National Heart, Lung, and Blood Institute (NHLBI) Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults - 2000
- Obesity Medicine Association - updated annually

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Management

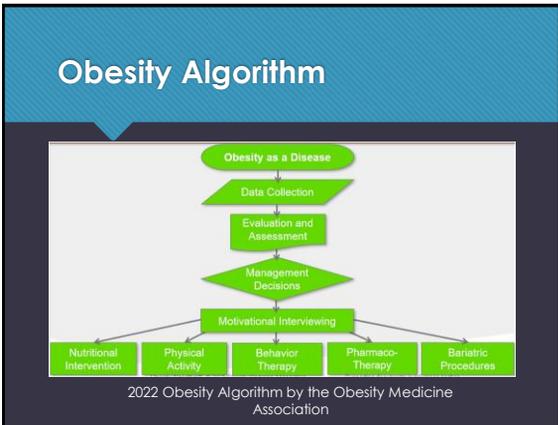
- Weight loss of 5-10% has been shown to have positive benefits for individuals with HTN and DM
- Guidelines encourage 10% weight loss in 6 months
 - If this is achieved, further weight loss can be attempted
 - The 10% loss carries the most health benefit and is easiest to attain
- Weight loss is indicated for patients with health problems (i.e., HTN, sleep apnea, OA, type 2 DM)

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Approaches to Obesity

- Adoption of a healthy lifestyle (i.e., diet and exercise habits)
- Pharmacologic therapy (nonprescription and prescription medications, dietary supplements)
- Bariatric surgery

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What are some reasons to lose weight?

What are some reasons not to lose weight?

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Goals

5-10% weight loss may improve both metabolic and fat mass disease.

Reduce body weight by about 5%-10% over 6 months

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Nonpharmacologic Therapy (Lifestyle Modification)

- Dietary Change**
 - Most used strategy
 - Changes in proportions of fat, protein and carbohydrates
 - Use of macronutrient substitutes (sugar and fat substitutes)
 - Changes in timing or frequency of meals
- Physical activity**
 - Less effective in producing weight loss initially but is important in maintaining weight loss and improving overall fitness

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Caloric Restriction

- Allowances for moderately active adults vary with age, gender and body weight
- U.S. suffers from "portion distortion" - need to relearn appropriate portion sizes based on age and activity levels
- **Calorie deficit of 500 kcal/day or more**
- Low calorie diet (LCD) of about 1200-1800 kcal/day usually results in a weight loss of 1-2 lbs per week
- Very low-calorie diet (VLCD) of 800 calories or less should be conducted under supervision of physician
 - Faster initial weight loss but **long term results no better**

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Have you tried to lose weight before?

- Yes, with a food tracker
- Yes, with a specific diet (keto, Atkins, paleo, etc)
- Yes, with exercise only
- Yes, with multiple methods!
- No

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Altered Proportions of Food Groups

- Dietary Guidelines for Americans recommend a diet with no more than 35% of total calories come from fat
 - No more than 10% from saturated fat
- Low fat diet alone is inadequate
 - Must also reduce total calories
- Very low-fat vegetarian diets
 - Dietary fat must be chosen carefully to prevent essential fatty acid deficiency
 - These diets can increase TG levels and lower HDLs in the short term because of the high carbohydrate content
- Many popular high-protein, higher-fat, and low-carb diets

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Very-low Carbohydrate Diets

- 1 Prevent elevated insulin levels that promote storage of body fat
- 2 Weight loss likely due to caloric decrease
- 3 Initial weight loss partially due to diuretic effect and glycogen depletion

Type of Low-Carb Diets

- Atkins/Keto - Very low carb → 5%-15% of total calories from carbohydrates
- Keto focuses on high fat content as well
- Zone diet - Moderate carb → 35%-50% of calories from carbohydrates

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Meal Replacement Therapy

- Typically geared toward replacing up to two meals a day with a:
 - Liquid drink
 - Snack bar
 - Measured frozen meal
- Dieter is encouraged to eat a "reasonable" third meal each day
- One advantage is portion control
- Typically contain 200-300 kcal per serving
- Caution use of protein bars
 - If only protein bars, can lead to ↑ in protein levels
- Early weight loss from these products can give a psychological boost to dieter

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Commercial Weight Loss Programs

- Structured programs popular in U.S.
- More women than men enroll in these programs
- Systematic review showed that results are suboptimal
- Controlled trials are needed before efficacy and cost-effectiveness can be touted
- Large component of success is support groups and periodic meetings of groups of dieters
- Good short-term results, but...
 - limited long-term efficacy
 - patients typically lose 5% of body weight over first 6 months, then return to baseline weight by 12-24 months.
- High dropout rates

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Physical Activity

Physical Activity Recommendations and Caloric Expenditure Rates	
Children and Adolescents	60 min most days of the week
Adults (for reduction of chronic disease)	Aerobic: 150 minutes of moderate aerobic activity or 75 minutes of vigorous physical activity a week, performed in ≥10-minute episodes
Adults (for prevention of body weight gain over time)	60 minutes of moderate-vigorous activities most days of the week
Adults (for sustaining weight loss)	60-90 minutes of moderate intensity exercise daily

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Food Rules – Do you have them?

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Behavioral Therapy

- Environmental modification**
 - Do not have high-calorie foods readily available
- Modifying thinking patterns**
 - Set reasonable, specific, proximate goals; identify and plan for potential obstacles to the goals
- Self-efficacy**
 - Maintain an optimistic and positive approach
- Social support**
 - Rely on family, friends and health care practitioners

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Pharmacologic Therapy

- If used, should be used concomitantly with lifestyle modifications
- Usually started at BMIs ≥ 30 or ≥ 27 with comorbidities

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Alli® (Orlistat)

Most Common Adverse Reactions

- Oil discharge from the rectum
- Fat in stool
- Feces with discharge
- Fat in stool (stool)

- Only FDA approved over-the-counter weight loss aid
- Encourage patients to take multivitamin
- Efficacy
 - Modestly effective in helping mildly to moderately overweight patients lose weight
 - 391 mildly to moderately overweight patients were randomized to orlistat 60 mg TID vs. placebo x 16 weeks
 - mean weight loss from baseline 3.05 kg (6.7 lbs) with orlistat vs. 1.9 kg (4.2 lbs) with placebo (p < 0.001)
 - Cost - \$50-70

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Phentermine - Schedule IV

Mechanism of action: sympathomimetic amine and stimulates hypothalamus to release norepinephrine

Efficacy	Dosing	Most common Adverse Reactions	Contraindications
<ul style="list-style-type: none"> • 3% body weight in 12 weeks 	<ul style="list-style-type: none"> • Phentermine HCl = 37.5 mg (or 18.75 mg) once per morning • Phentermine resin = 30 mg (or 15 mg) once per morning • Phentermine HCl = 8 mg (or 4 mg) three times a day before meal 	<ul style="list-style-type: none"> • Headache • High blood pressure • Rapid/irregular HR • Insomnia • Tremor 	<ul style="list-style-type: none"> • Hypersensitivity & Pregnancy / Nursing • History of cardiovascular disease (coronary artery disease, stroke, arrhythmias, congestive heart failure, uncontrolled hypertension) • Administration during or within 14 days following the administration of MAOIs • Hypertthyroidism • Glaucoma • Agitated states • History of drug abuse

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Phentermine/topiramate (Qsymia)

Mechanism of action of topiramate: appetite suppression and satiety enhancement through blocking neuronal voltage-dependent sodium channels, enhances GABA(A) activity, antagonizes AMPA/ kainate glutamate receptors

Efficacy	Dosing	Side Effects	Contraindications
<ul style="list-style-type: none"> • 5-10% of body weight 	<ul style="list-style-type: none"> • Starting = 3.75 mg/23 mg (phentermine/topiramate ER) • After 14 day intervals, and as clinically indicated, escalate doses to: • Recommended dose = 7.5 mg/46 mg • Titration dose = 11.25 mg/69 mg • Max dose = 15 mg/92 mg • Gradually wean dose from the top dose (15 mg/92 mg) to help avoid potential seizures 	<ul style="list-style-type: none"> • Anorexia, diarrhea, constipation, dysgeusia (taste distortion), dry mouth, insomnia • Monitor: Metabolic acidosis, Elevated creatinine, Lowering of glucose levels 	<ul style="list-style-type: none"> • Pregnancy • Glaucoma • Hypertthyroidism • During or within 14 days of taking MAOIs

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Naltrexone/bupropion (Contrave)

MOA of Contrave: exact neurochemical effects leading to weight loss are not fully understood. May be due to the regulation of food intake: the hypothalamus (appetite regulatory center) and the mesolimbic dopamine circuit (reward system).

Efficacy	Dosing	Side Effects	Contraindications
<ul style="list-style-type: none"> • ~5-10% of body weight 	<ul style="list-style-type: none"> • Week 1 = 1 tablet in AM • Week 2 = 1 tablet in AM + 1 tablet in PM • Week 3 = 2 tablets in AM, 1 tablet in PM • Week 4 and beyond = 2 tablets in AM, 2 tablets in PM 	<ul style="list-style-type: none"> • Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea, and acute closure glaucoma 	<ul style="list-style-type: none"> • Uncontrolled hypertension • Seizure disorders, anorexia nervosa or bulimia, or undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs • Chronic opioid use

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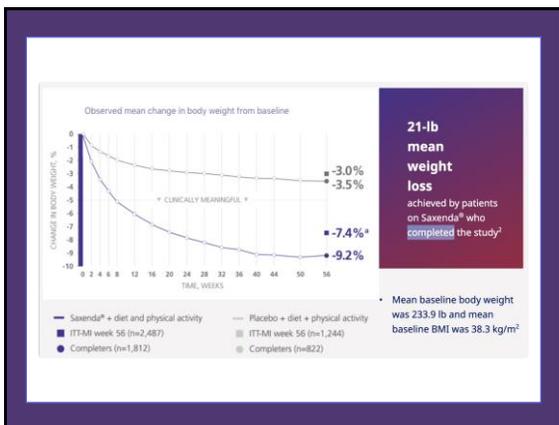
Liraglutide (Saxenda)

Mechanism of action: GLP-1 receptor agonist

Efficacy	Dosing	Side Effects	Contraindications
<ul style="list-style-type: none"> • 5-10% of body weight 	<ul style="list-style-type: none"> • Week 1 = 0.6 mg per day • Week 2 = 1.2 mg per day • Week 3 = 1.8 mg per day • Week 4 = 2.4 mg per day • Week 5 on = 3.0 mg per day 	<ul style="list-style-type: none"> • Nausea/vomiting, decreased appetite, diarrhea, constipation, abdominal pain, headache, fatigue, increased lipase 	<ul style="list-style-type: none"> • Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type 2 • Pancreatitis • Pregnancy



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Semaglutide (Wegovy)

Mechanism of action: GLP-1 receptor agonist

Efficacy	Dosing	Side Effects	Contraindications
<ul style="list-style-type: none"> • 5-15% of body weight 	<ul style="list-style-type: none"> • Week 1-4 = 0.625 mg weekly • Week 5-8 = 0.5mg weekly • Week 9-12 = 1 mg weekly • Week 13-16 = 1.7mg weekly • Week 17 on = 2.4 mg weekly 	<ul style="list-style-type: none"> • Nausea/vomiting, decreased appetite, diarrhea, constipation, abdominal pain, headache, fatigue, increased lipase 	<ul style="list-style-type: none"> • Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type 2 • Pancreatitis • Pregnancy

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Once weekly
Since Wegovy™ comes in a single-use pen, you'll use a new pen every time you dose

Hidden needle
You won't see or handle the needle

Preset dose
The dose is already set on your pen



From week 0 to 68, patients taking Wegovy™ achieved

~15% WEIGHT LOSS

-35 lb

vs -12.5lb (-4.3% weight loss) with a reduced-calorie diet and increased physical activity alone*

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Complementary Therapy

- ~15% of adults attempting weight loss report using a dietary supplement
- Women aged 18-34 years
- Stimulant-containing product, i.e., caffeine and/or bitter orange, country mallow
 - All can have dangerous side effects (like ephedrine)

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Complementary Therapy

- Stimulants, Energy Boosters, Thermogenic Aids
 - Bitter orange →HTN, MI, seizure, stroke
 - Caffeine, cola nut →GI issues, nausea, anxiety, insomnia
- Fat and Carbohydrate Modulators
 - Chromium →well tolerated
 - Green Tea →increased heart rate, GI issues, headache
 - Licorice →pseudoaldosteronism, HTN, hypokalemia
 - Garcinia, brindleberry →GI issues, not rec. in patients with DM or dementia

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Complementary Therapy

- Appetite suppressants
 - Plantain or psyllium →flatulence, GI probs, N/V
 - Hoodia → no risks reported yet
- Fat absorption blockers
 - Chitosan → GI upset, flatulence, N/V, constipation
- Carbohydrate Absorption Blockers
 - Ginseng →nervousness, excitation, inability to concentrate, Stevens-Johnson syndrome, multiple drug interactions
- Pre/Probiotics → may promote microbiome conducive to weight loss

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Complementary Therapy

- Laxatives and Diuretics
 - Safety/efficacy not proven for long-term weight loss
- Cascara sagrada →abdominal pain, diarrhea, muscle weakness
- Dandelion →contraindicated in pts with gallbladder or bile duct obstruction

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Management of Overweight and Obesity

Cornerstones of Weight Loss and Management

- All three must occur for long term success

The diagram consists of three overlapping circles. The top circle is labeled 'Lifestyle Changes', the bottom-left circle is 'Increased exercise', and the bottom-right circle is 'Dietary modifications'. The central area where all three circles overlap is shaded darker blue.

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- Does Wanda qualify for pharmacologic weight loss medications?
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 - No

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 - Phentermine/topiramate
 - Naltrexone/bupropion

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Questions?

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