



# Overview of Obesity Medicine


Focus on Pharmacotherapy

Lea Grace R. Famularcano, MD, DABOM

CAMC Weight Loss Center



# What is Obesity Medicine?

- Obesity Medicine is the field of medicine dedicated to the comprehensive care of patients with obesity.
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# The Current State of Obesity

- 41.9% people in the US live with or suffer from obesity.
- Increased from 30.5% in 2020.
- The estimated annual cost of obesity in 2019 was nearly \$173 billion
- Medical cost for adults who had obesity were \$1,861 higher than medical cost for people with healthy weight.



Why is it important to treat the disease of obesity?

**Chronic weight management reduces cost of living by reducing:**

1. prescription medications
2. Co-pays
3. Time off work and lost wages
4. Decreased hospitalizations
5. Food cost
6. Accident proneness/injuries
7. Risk for cancer and other chronic diseases
8. Medical visits

# Obesity is a Disease Process



Obesity is defined as a multifactorial, **chronic, relapsing, neurobehavioral** disease.



Wherein an increased body fat promotes adipose tissue dysfunction and mass physical forces resulting in adverse metabolic, biomechanical and psychosocial health consequences.



It needs to be treated like any other diseases – with earnest, compassion and in a judgment-free setting.

# How do you Measure Obesity?

## BMI

- Normal Weight 18.5-24
- Overweight: 25-29.9
- Class 1 Obesity: 30.0-34.9
- Class 2 Obesity: 35.0-39.9
- Class 3 Obesity: >40



# How do you Measure Obesity?

- **Looking Beyond the BMI**

Abdominal Obesity  
Men

>40 in >102 cm

Asians  
>35.4 in >90 cm

Europeans  
>37 in >94 cm

Abdominal Obesity  
Women

>35 in >88 cm

Asians  
>31.5 in >80 cm

Europeans  
>31.5 in >80 cm

\*equivalent prevalence of DM2 in Asians at a lower BMI

# How do you Measure Obesity?

- Looking Beyond the BMI

## Percent Body Fat

Classification	Essential Fat	Athletes	Fitness	Acceptable	Obesity
Male	2-5%	6-13%	14-17%	18-24%	>25%
Female	10-13%	14-20%	21-24%	25-31%	>32%



# How do you Measure Obesity

Looking beyond the BMI


## Edmonton Obesity Staging System (applies the medical, mental and functional limitations)

Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
No obesity related risk factors	Pre-clinical risk factors borderline HTN or DM; minor aches or psychopathology	Established obesity related disease HTN, DM, PCOS, moderate limitation of ADLs	Established organ damage MI, CHF, DM complications; significant limitations of ADLs	Severe disabilities, end-stage disease; Wheelchair use

# Obesity-related Health Conditions

**multisystemic disease  
often the root cause  
of other disease processes**

Neurological	Pseudotumor cerebri, intracranial hypertension
Psychosocial	Depression, eating disorders, poor self-esteem, impaired body image satisfaction, decreased libido, impaired intimacy
Cardiovascular	HLD, HTN, endothelial dysfunction, inflammation, MI, stroke, CHF, PVD
Pulmonary	OSA, asthma, exercise intolerance, hypoventilation syndrome
Gastrointestinal	GERD, NAFLD, hernias
Renal	Glomerulopathy, kidney stones renal CA
Endocrine	DM2, PCOS, hypogonadism, infertility, metabolic syndrome
MSK	OA (knees, hips), back pain, myalgia, impaired balance, gait disturbance
Hematology Oncology	Multiple myeloma, prothrombotic state CA- breast, endometrial, esophageal, colon, pancreatic
Integument	Stasis dermatitis, skin tags, intertrigo, acanthosis



What does  
comprehensive  
Medical Obesity  
Treatment  
Include?



## **Four Pillars of Obesity Treatment**

1. Nutrition
2. Physical activity
3. Recognizing Medical conditions and utilizing Medications
4. Behavioral

# 5 A's of Obesity Management

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ASK – for permission to discuss weight; about readiness for change



ASSESS – BMI, waist and neck circumference, complete PE, obesity stage, drivers and complications of excess weight



ADVISE – health benefits of modest weight loss (5-10%); long-term strategies and treatment options



AGREE – realistic expectations, targets and behavioral changes



ARRANGE/ASSIST – identify their barriers, provide resources, regular follow up

Avoid  
Derogatory  
Language

USE	INSTEAD OF
Overweight	Fat
Unhealthy Weight	Obese
Heavy	Morbidly Obese
Eating Habits	Diet
Physical Activity	Exercise

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# Evaluation of the patient with Obesity

<b>History of weight gain</b>	<b>age of onset, highest/lowest weight, pattern, life events</b>
<b>Previous Weight Loss</b>	<b>What has been tried; what worked, did not work</b>
<b>Nutrition</b>	<b>Eating patterns, triggers, reasons for eating out, household factors</b>
<b>Physical Activity</b>	<b>Current level of activity, favorite activities, activities that they can maintain, barriers</b>
<b>Medical</b>	<b>PMH, current conditions; surgical history, allergies, current medications</b>
<b>Eating Disorders</b>	<b>Prior diagnosis, medical treatment</b>
<b>Family History</b>	<b>Obesity, metabolic diseases, psychiatric disorders</b>
<b>Social Readiness</b>	<b>Readiness, motivators, education, occupation, household, sleeping behavior, life stressors, substance use</b>

# Evaluation of the patient with Obesity

- Perform a Physical Examination
  - Neck circumference
  - Waist circumference
  - EKG
  - Body composition
    - BMR, Fat%
    - Calculate TDEE (total daily energy expenditure)
- PHQ-9, BEDS-7, OSA Screening

# Common Nutritional Approaches

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- **Low Carb Diet**
  - <45% of calories from carbs
  - Health benefit – decreased trigly, increased HDL
- **Mediterranean Diet**
  - Fish, nuts, healthy fats, fruits, veg, whole grains, legumes, dairy
- **DASH Diet**
  - Not intended for weight loss but may promote WL when at a calorie deficit
  - Benefit – decreased blood pressure
- **Low Fat Diet**
  - Benefit – decreased total cholesterol and LDL
- **Vegetarian**
  - Decreased LDL, Decreased CV mortality, improvement and/or prevention of T2DM
- **Meal Replacements**
  - Can be used with any dietary approach
  - Greater weight loss when using 2 meal replacements per day



# Clinical Pearls With Nutrition

- The diet that works is the one the patient can stick with and can incorporate in their lifestyle long term
- Think beyond calories – current evidence suggests that not all calories are created equal
- Meal replacements can be very effective for weight loss and weight maintenance

# How Much Physical Activity?

## General Health Benefit

- Moderate aerobic exercise 150 min/week with strength training 2x/week

## Prevention of Weight Gain

- 150-250 active minutes/week

## Prevention of Weight Regain

- 200-300 minutes/week

# The Exercise Prescription

## FITTE

- Frequency
- Intensity
- Time
- Type
- Enjoyment


Not All  
Physical  
Activity is  
Exercise

- NEAT - Non-exercise Activity Thermogenesis
  - Common Daily Activities such as walking, standing and climbing stairs can result to up to 2000 kcals of energy expenditure per day.
  - Encourage patients/individuals to get up – standing desk, raised computer monitor, frequent breaks from sitting





# Obesity Pharmacotherapy



Who can  
benefit from  
pharmacologic  
therapy?



**Patients who failed to benefit adequately  
from lifestyle modifications alone**

**AND**

**Have health problems because of their weight**

**AND**

**BMI > 30**


**OR**

**BMI > 27 with 1 or more obesity related  
disease**

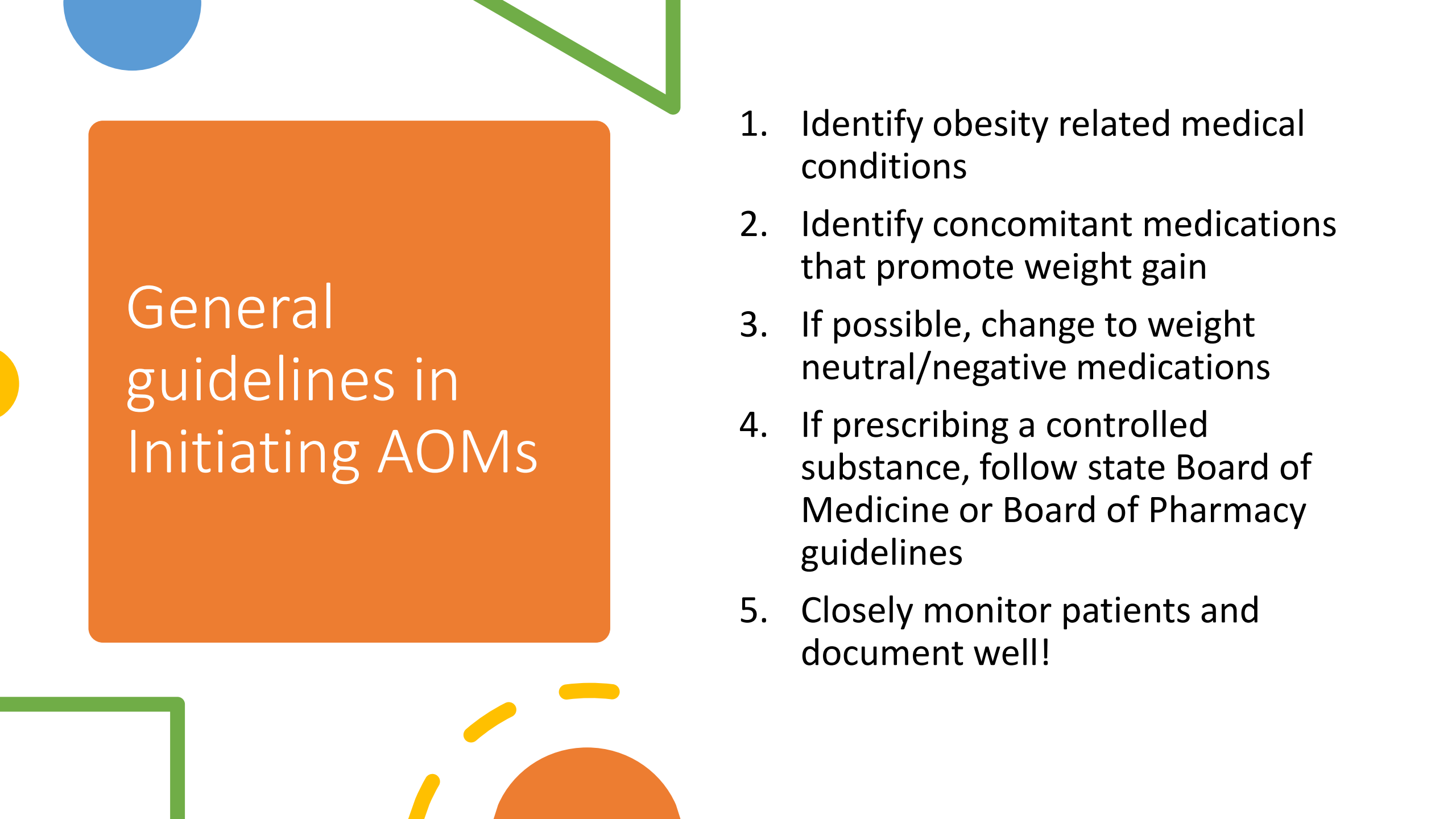
# Guidelines for Selecting Obesity Treatment

Treatment	BMI 25-26.9 (Overweight)	BMI 27-29.9 (Overweight)	BMI 30-34.9 (Obesity class 1)	BMI 35-39.9 (Obesity Class 2)	BMI 40+ (Obesity Class 3)
Nutrition Physical Activity Behavioral therapy	Yes	Yes	Yes	Yes	Yes
Pharmacotherapy	6 months lifestyle mod *If increased abdominal girth/adiposity consider rx	With comorbidities	yes	Yes	Yes
Metabolic and Bariatric Surgery			*recent ASMBS update 2022 – recommend if failed other therapy	With comorbidities	Regardless of comorbidities

# Benefits of anti-obesity medications (AOMs)

- To help patients make or sustain the necessary lifestyle changes ( eating habits, improved activity level)
  - To initiate weight loss in patients to qualify for surgery
  - For maintenance of weight loss and body composition (prevent recurrence of obesity)
  - Maintenance of improved health and remission of associated medical conditions
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## General guidelines in Initiating AOMs

1. Identify obesity related medical conditions
2. Identify concomitant medications that promote weight gain
3. If possible, change to weight neutral/negative medications
4. If prescribing a controlled substance, follow state Board of Medicine or Board of Pharmacy guidelines
5. Closely monitor patients and document well!

FDA  
Approved  
AOMs for  
Long-term  
use

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Orlistat (Xenical, Alli)

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Phentermine/Topiramate ER (Qsymia)

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Bupropion/Naltrexone (Contrave)

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Liraglutide (Saxenda)

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Semaglutide (Wegovy)



FDA  
Approved for  
short-term  
use

- Phentermine
- Diethylpropion
- Benzphetamine
- Phendimetrazine

# Off-label medications used for Obesity

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Sympathomimetics for > 12 weeks  
(Phentermine, diethylpropion, benzphetamine)

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Metformin

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Topiramate

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Generic combination bupropion and naltrexone

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Generic combination phentermine and  
topiramate



## Non-systemic Hydrogel

- **Plenity**
  - Regulated by FDA as a device than medication
  - Not absorbed systemically
  - They are capsules with superabsorbent hydrogen particles that expand in the stomach to induce fullness – when fully hydrated it occupies 25% of the stomach's volume
  - Indicated for BMI 25-40 in conjunction with diet and exercise

## Qsymia (Phentermine/ Topiramate)


- Indicated for chronic weight management
- In clinical trials 5% weight loss achieved by 67% at full dose; and 10% weight loss achieved by 47% at full dose
- Common side effects: paresthesia, dysgeusia, insomnia constipation, dry mouth; makes carbonated drinks taste bad
- Fetal toxicity: pregnancy test monthly (office or in-home) or document 2 forms of contraception
- DC if <5% weight loss at 12 weeks at max dose
- When discontinuing – it's important to titrate down at least 7 days to reduce seizure risk
- Expensive if not covered by insurance

# Contrave (Bupropion/ naltrexone)

- FDA approved in 2014
- Indicated for BMI >30 or BMI >27 with 1 or more weight related comorbidity
- Titrate weekly over the course for 4 weeks:
  - Week 1: 1 tab daily
  - Week 2: 1 tab BID
  - Week 3: 2 tabs in AM 1 tab in PM
  - Week 4: 2 tabs BID



# Contrave (Bupropion/ Naltrexone)

- MOA:
    - Naltrexone – opioid antagonist
    - Bupropion – weak inhibitor of neuronal reuptake of dopamine and NE
    - Both may work in hypothalamus and mesolimbic/dopamine circuit to decrease appetite and reward
    - \*exact MOA is not fully understood
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# Contrave (Bupropion/ naltrexone)

- Contraindicated in uncontrolled HTN, Seizure DSO, anorexia nervosa/bulimia
- AE: nausea, constipation, HA, dizziness, insomnia, dry mouth, diarrhea
- Prescribing practice considerations
  - Do not administer with opioids
  - MAOIs increase BP when administered concomitantly
  - May appear in drug screening as false positive for amphetamines
  - It can decrease digoxin levels
  - Neurotoxicity with dopaminergic drugs (levodopa, amantadine)



## Saxenda (Liraglutide)

- MOA – GLP-1 receptor agonist; slows down gastric emptying; activates areas in the hypothalamus that reduces food intake, increases satiety
- Daily injection; titrate up weekly
- Titration:
  - Week 1: 0.6 mg
  - Week 2: 1.2 mg
  - Week 3: 1.8 mg
  - Week 4: 2.4 mg
  - Week 5 and onward: 3.0 mg



# Saxenda (Liraglutide)

## **Adverse reactions:**

Nausea, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain and increased lipase

## **Precautions:**

Acute pancreatitis, acute gallbladder disease, hypoglycemia when used with insulins/insulin secretagogues

Renal impairment

Increased depression/suicidal behavior





## Saxenda (Liraglutide)

Clinical trial significant weight loss rates:

- 5% WL: 62% at full dose
- 10% WL: 34% at full dose


Contraindications: personal hx of pancreatitis; family history of pancreatic cancer, medullary thyroid cancer, or MEN type 2

Blackbox: counsel patients re: C-cell tumors in rats

(human occurrence is unknown)



## Wegovy (Semaglutide)

- MOA – GLP-1 receptor agonist; slows down gastric emptying; activates areas in the hypothalamus that reduces food intake, increases satiety
  - Weekly injection; titrate every 4 weeks
  - Month 1: 0.25 mg
  - Month 2: 0.5 mg
  - Month 3: 1 mg
  - Maintenance doses 1.7 mg and 2.4 mg
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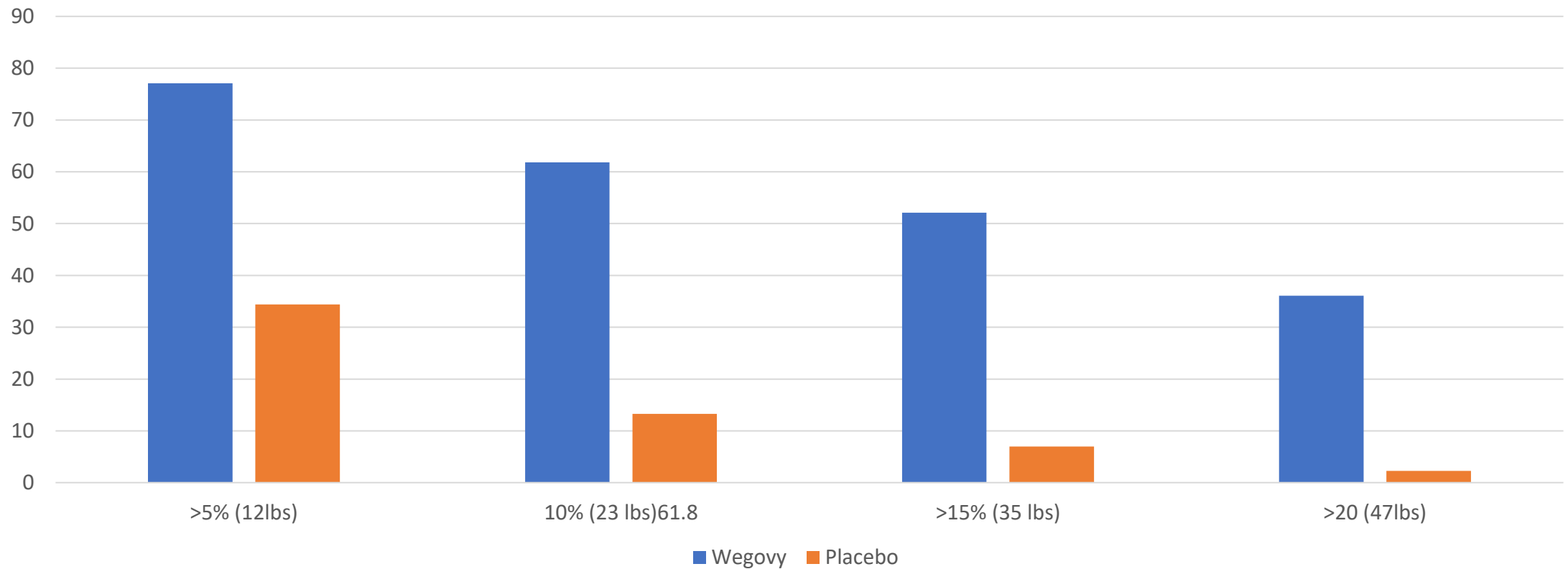


## Wegovy (semaglutide)

- Mean Weight loss 15.2% vs placebo at 2 years when combined with diet and increased physical activity
  - >5% achieved by 77%
  - >10% achieved by 61.8%
  - >15% achieved by 52.1%
  - >20% achieved by 36.1%
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# 77% of patients taking Wegovy (semaglutide) sustained >5% weight loss at 2 years\*

Wegovy 2.4 mg vs Placebo





# Wegovy (Semaglutide)

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# Economic Fun Anecdotes

High demand for Wegovy is changing Denmark's economy

Groceries like Walmart are noticing decline in food sales

Airlines support weight loss medications as it can save them millions in fuel efficiency

SMPs  
(Sympathomimetics)

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Drug class phenethylanines – include amphetamine, methamphetamine, phentermine, diethylpropion, epinephrine, dopamine, etc

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Phentermine is not an amphetamine

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It got FDA approval in 1959, around the time of amphetamine addiction epidemic – presumption then was that all SMPs had addiction potential

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Prescribing these medications are “off-label”, however there is abundant literature demonstrating efficacy of these drugs beyond 12 weeks



# Phentermine

- Doses:
  - 8 mg tablet (Lomaira) ½ tab to 1 tab QD-TID
  - 15 mg cap
  - 30 mg
  - 37.5 mg scored tablets (QD or BID)
  - Daily recommended dose 15-37.5 mg
  - DEA Schedule IV



# Phentermine



## Common misperceptions on Adverse effects

- 1. Addiction
  - No evidence of addiction potential in clinical setting
  - No evidence of amphetamine-like withdrawals
- 2 Adverse Cardiovascular Effects
  - No established relationship related to cardiac valvulopathy or pulmonary hypertension

# Off-label medications used for Obesity

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Metformin

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Topiramate

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Generic combination phentermine and  
topiramate

# Metformin

Prevention of T2DM (JAMA, 2017; 317(11):1784-1792. doi:10.1001/jama.2016.17844)

May help improve adiposopathic disorders

- Insulin resistance
- PCOS
- Fatty Liver
- CVD

May help treat complications of other concurrent drug treatments

- Antipsychotic-related weight gain
- HIV protease inhibitor-associated abnormalities (i.e HIV lipodystrophy)

May help reduce overall cancer rate and help improve the treatment of multiple cancers

- Colon, Ovary, Lung, Breast, Prostate CA

May enhance effects of GI hormones applicable to weight loss (GLP-1, peptide YY)

May alter gut microbiome

# Metformin

Weight Loss	2% in T2DM, insulin resistance or impaired fasting glucose
Dose	500-2000 mg/day
MOA	Activates AMPK; decreases hepatic glucose production, increase muscle glucose uptake
Adverse SE	GI: nausea, abdominal cramping, diarrhea B12 deficiency

# Metformin

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FDA approve ONLY for T2DM treatment in adults and children

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Off-label for obesity management

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May be used and an adjunct in combination with other AOMs in patients with insulin resistance

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Consider ER/XR if GI symptoms intolerable



# Topiramate

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- Approved for seizures in 1996, and migraine prevention in 2004
- Except in Qsymia, not approved for the treatment of obesity
- Several studies have shown encouraging results for the use of topiramate (alone or in combination with SMPs) for BED and obesity
- Typical dosing:
  - epilepsy 400 mg/day
  - Migraine 200 mg /day
  - Obesity 25-100 mg/day
- Start dosing at 25 mg QHS increase dose every 2 weeks by 25 mg

# Coming down the Pipeline

- Tirzepatide (Mounjaro)
  - Dual GIP/GLP-1 receptor co-agonist
  - Currently approved for T2DM
  - Awaiting FDA approval for obesity treatment
  - SURMOUNT 3- and SURMOUNT 4 trial showed 26.6% mean weight loss after 88+ weeks with intensive lifestyle intervention
- Retatrutide
  - Triagonist GIP/GLP-1/GCG
  - Phase II trial showed 24.2% weight loss in 48 weeks

# Practice Pearls

- Depression – bupropion might be first choice in patients with obesity
- Binge eating DSO – lisdexamfetamine (Vyvanse) is FDA approved
- Topiramate 25 mg PM up to 100 mg BID for BED (off-label)
- T2DM with obesity - best choice: Metformin, GLP-1RA, SGLT2 inhibitors, glucosidase inhibitors, DPP4 inhibitors
- Premenstrual carb cravings: spironolactone in latter half of the cycle
- When treating HTN in patients with obesity – avoid BB, reserve for post- MI or CHF patients

# Weight Promoting Medications

## Antipsychotics

- Risperidone, lithium, quetiapine, aripiprazole, olanzapine, valproic acid

## Antidepressants

- Citalopram, duloxetine, venlafaxine

## Sleep Agents

- Zolpidem, eszopiclone, trazodone, zaleplon

## Neuropathic agents

- Gabapentin, pregabalin

## B-blockers

- Least weight promoting among BB is carvedilol

## Steroids

## Insulin

## Insulin secretagogues

# Treatment Strategy for Weight Promoting Medications

Investigate	Investigate whether medications are a likely source of weight gain
Replace or discontinue	Replace or discontinue if possible
Consider	If not possible, consider AOM in conjunction with lifestyle changes



Happy Fall, Y'all!  
Thank you!