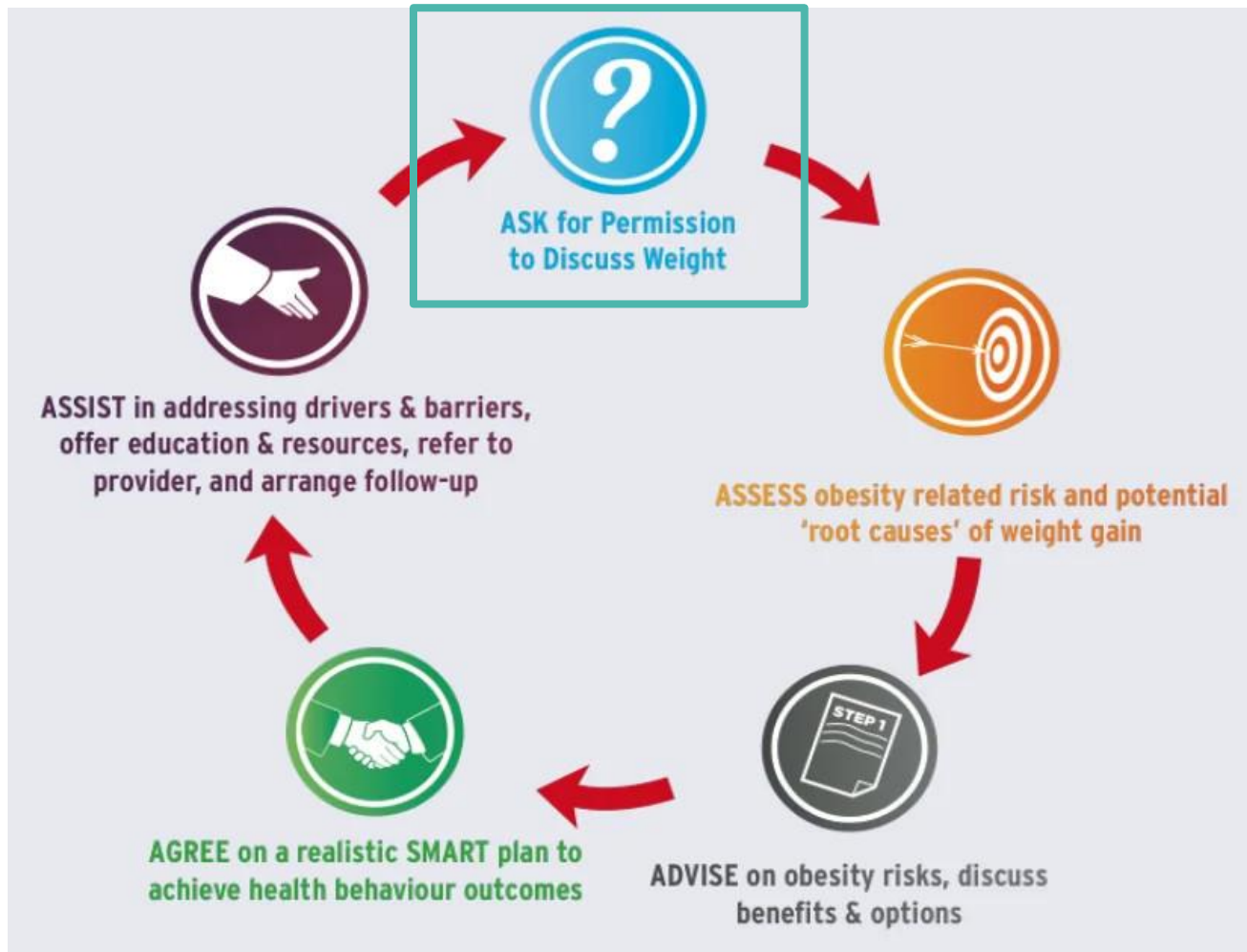

5As Approach to Treatment of Obesity

— Emily O'Dell, DO
ABOM Diplomate —

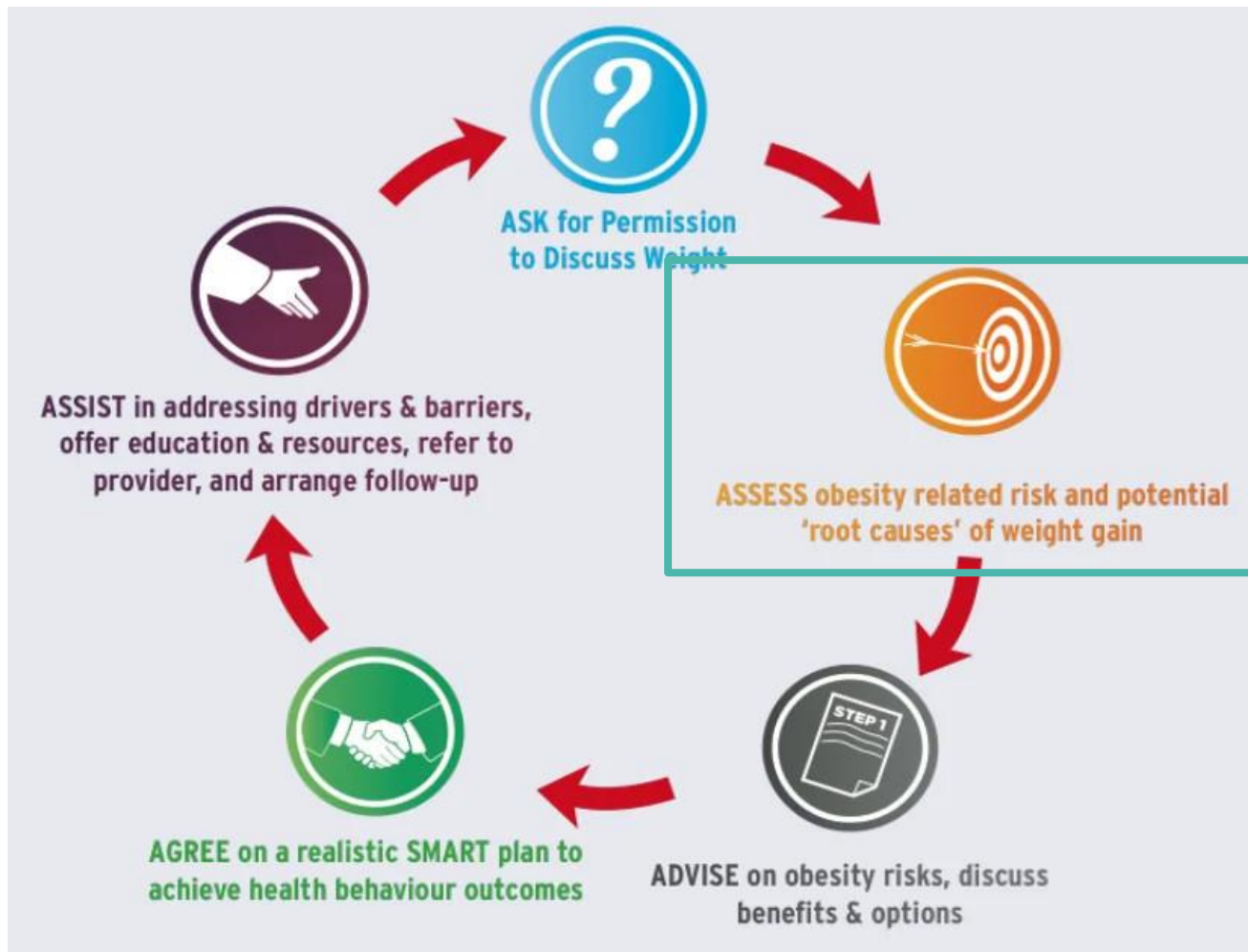
Learning Objectives

- Explain the indications, side-effects, adverse reactions and contraindications for the use of weight loss medications
- Review the 5 As Approach to management of patients with obesity
- Briefly review diagnosis of obesity and basic staging
- Review case of obesity management in primary care



The ASK: Starting the Conversation

- People first language
 - Individual affected by obesity
 - Patient with obesity
 - Person living with obesity
- Avoiding the word “obese”
- Substitute the word “obesity”
- Focus on health
- Use motivational interviewing
 - OARS: open-ended questions, affirmations, reflections, summaries
- Obesity Action Coalition: Provider & Patient Education Study:
- Weight friendly language
 - Weight
 - Unhealthy weight
 - “Your weight may be damaging your health”
 - Physical activity
 - Eating habits
- Avoid
 - Fat
 - Obese
 - Large size
 - Heaviness
 - Morbidly obese
 - Exercise
 - Diet



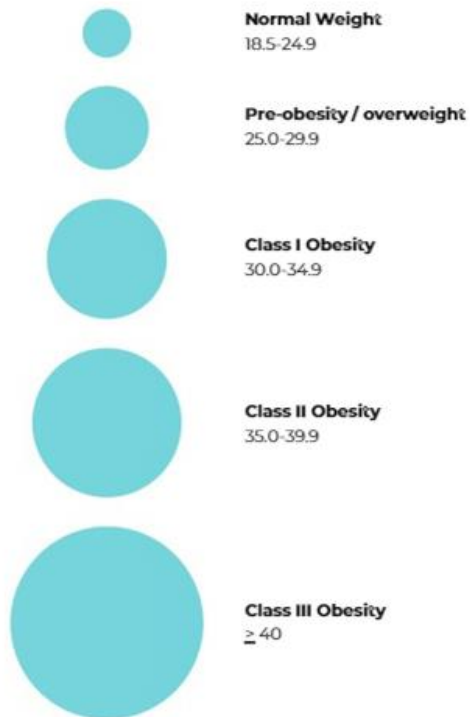
Assess: Diagnosis of Obesity

Definition of Obesity, Obesity Algorithm 2023

“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, result in in adverse metabolic, biomechanical and psychosocial health consequences.”

Body Mass Index: Increased Body Fat (Adiposity)

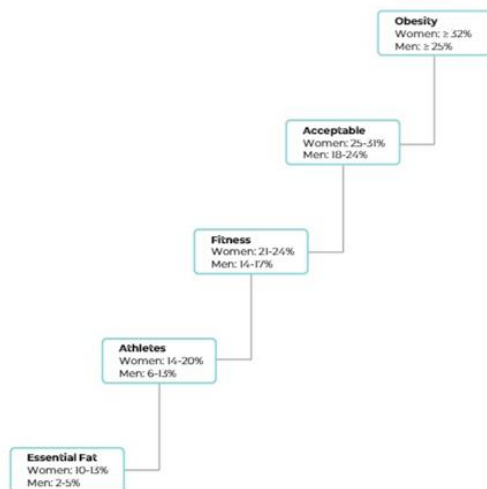
Body Mass Index (BMI) in kilograms per meters squared (kg/m^2)*



*Different BMI cut-off points may be more appropriate based upon gender, race, ethnicity, and menopausal status. For example, among Asians, a BMI $>23 \text{ kg}/\text{m}^2$ may indicate pre-obesity, a BMI $>27.5 \text{ kg}/\text{m}^2$ may indicate class I obesity, a BMI $>32.5 \text{ kg}/\text{m}^2$ may indicate class II obesity, and a BMI $>37.5 \text{ kg}/\text{m}^2$ may indicate class III obesity

Percent Body Fat: American Council on Exercise Classification

American Council on Exercise Classification: Percent body fat*



*Based on "expert opinion," cut-off points not scientifically validated

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Waist Circumference: Increased Body Fat (Adiposity)

Obesity classification: Waist circumference (WC)*

Abdominal Obesity - Men
 ≥ 40 inches
 ≥ 102 centimeters

Abdominal Obesity - Women
 ≥ 35 inches
 ≥ 88 centimeters

*Different WC abdominal obesity cut-off points are appropriate for different races

Waist Circumference: Thresholds for Abdominal Obesity - Ethnic Differences

Population	Men	Women
European	≥ 94 cm	≥ 80 cm
Caucasian	≥ 94 cm (increased risk) ≥ 102 cm (high risk)	≥ 80 cm (increased risk) ≥ 88 cm (high risk)
United States, Canada & European	≥ 102 cm	≥ 88 cm
Asian (including Japanese)	≥ 90 cm	≥ 80 cm
Japanese	≥ 85 cm	≥ 90 cm
China	≥ 85 cm	≥ 80 cm
Middle East, Mediterranean & Sub-Saharan African	≥ 94 cm	≥ 80 cm
Ethnic Central and South American	≥ 90 cm	≥ 80 cm

*A waist to height ratio of 0.5 may be a simplified threshold common to all ethnicities. It may also be a better screening tool for cardiometabolic risk than BMI

Metabolic Syndrome: The NCEP ATP III Definition*

Patient must meet **three or more** of the following five risk factors:

Diagnostic Criteria	Defining Level
Abdominal obesity	Waist circumference
• Men	>102 cm (>40 in)
• Women	>88 cm (>35 in)
Triglycerides*	≥ 150 mg/dL (1.7 mmol/L)
HDL cholesterol*	
• Men	<40 mg/dL (1.04 mmol/L)
• Women	<50 mg/dL (1.29 mmol/L)
Blood pressure*	≥ 150 / ≥ 95 mmHg
Fasting glucose*	≥ 100 mg/dL (5.6 mmol/L)

Metabolic syndrome (MetSyn):

- MetSyn is not a disease; it is a descriptive clustering of atherosclerotic cardiovascular risk factors
- Abdominal obesity is the only diagnostic physical finding
- Diagnostic criteria does NOT include low density lipoprotein cholesterol
- Diagnostic criteria may vary, depending on the organization crafting the diagnostic criteria
- Waist circumference diagnostic criteria may vary, depending upon race and gender
- Central obesity is a clinical marker of adiposity; increased visceral adiposity is a surrogate for global (integrative) fat dysfunction

*Or receiving drug treatment for these diagnostic criteria



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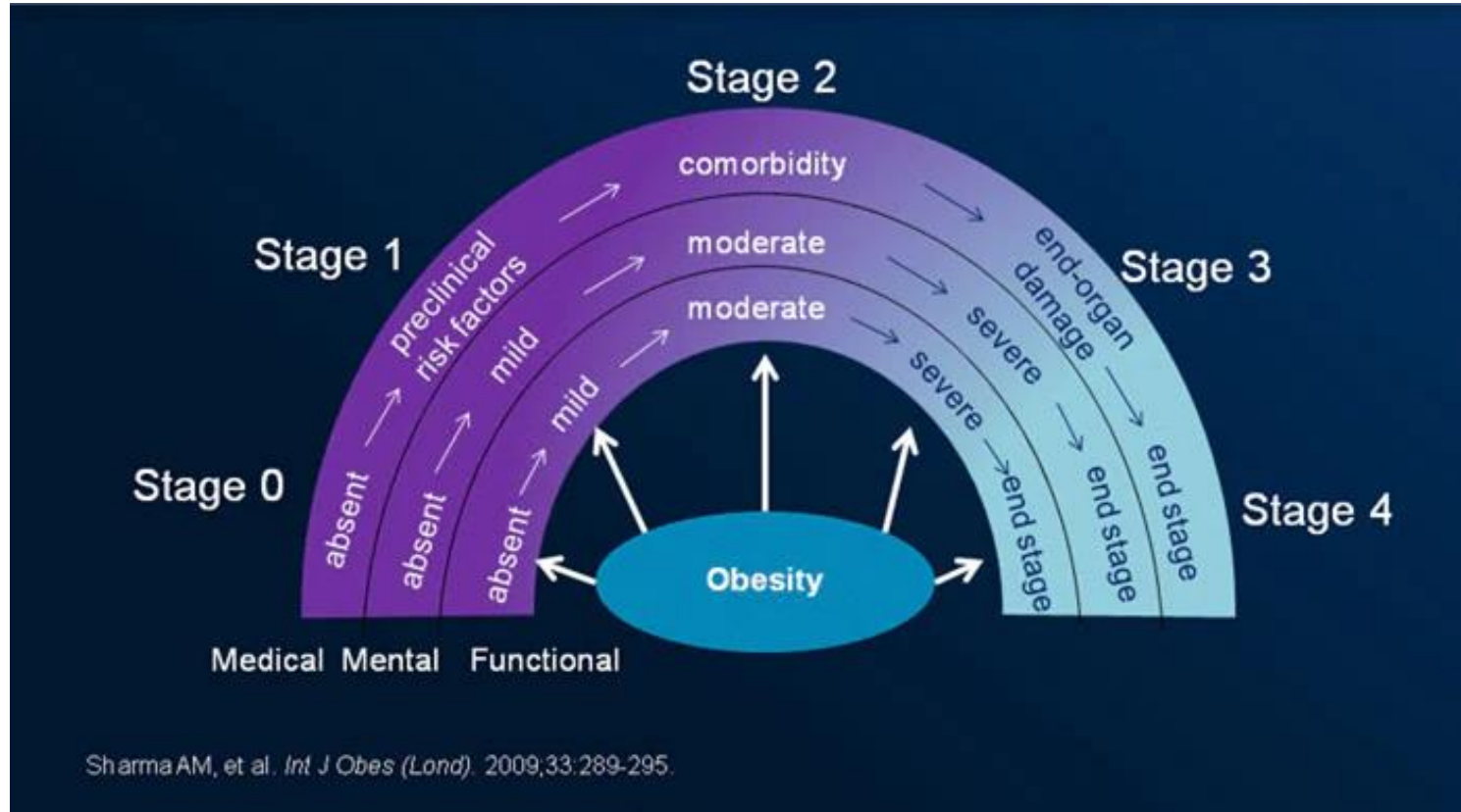
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Edmonton Obesity Staging System:



Initial Obesity Evaluation- Focused History and Physical

- HPI
 - Weight history
 - Age of onset
 - Maximum weight
 - Triggers/ life changes
 - Rate of weight gain
 - Previous weight loss attempts-
 - Current nutrition/physical activity
 - Sleep history
 - Insomnia, Latency, OSA
 - Sleep hygiene
 - Current medications
 - Labs: CMP, A1c, Lipids, Vit D, TSH
- Past Medical/Family Hx + Current Medical Issues
 - Comorbidities: prediabetes, diabetes, CVD, HTN, Thyroid disease, PCOS, OSA, depression/anxiety, eating disorders, gout, alcoholism
 - Medication
contraindication/caution: eating d/o, seizure hx, MEN 2, medullary thyroid cancer, arrhythmias, kidney stones, glaucoma, uncontrolled HTN, primary pulmonary HTN, opioid pain medication use

Evaluation for Comorbid Conditions

Adiposity-Related Disease—Adiposopathy “Sick Fat”

Neurologic Disease

- Cognitive Impairment
- Peripheral neuropathy (DM)
- Hypothalamic Disorder

Psychological

- Depression
- Loss of Libido

Cardiovascular Disease

- CAD
- Stroke
- HTN
- CHF
- Venous Insufficiency/Phlebitis

Pulmonary Disease

- Asthma
- Pulmonary Embolism
- Obstructive Sleep Apnea

GI Disease

- NAFLD
- Gall Bladder disease
- Pancreatitis

Endocrine Disease

- Insulin resistance/MetS
- Adiposopathic dyslipidemias
- Sex Hormone abnormalities
- Pre DM and T2DM
- Gout

Immune

- ↑ Inflammatory markers

GU Disease

- Nephrolithiasis
- Chronic Kidney Disease

MSK Disease

- Osteoarthritis
- Immobility
- Low Back Pain
- Gait Disturbance

Integumentary

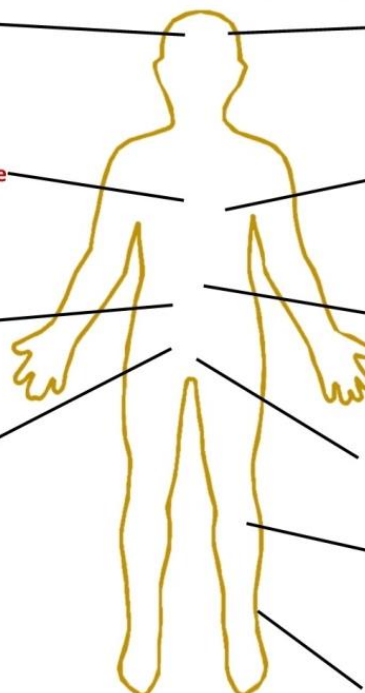
- Acanthosis Nigricans
- Acne
- Hair Abnormalities

Gynecologic

- PCOS
- Infertility
- Menstrual Abnormalities
- Pregnancy complications

Cancer

- Breast
- Colon
- Esophagus
- Kidney
- Liver
- Pancreas
- Uterus



Adiposity-Related Disease—“Fat Mass” Disease

Neurologic Disease

- Intracranial Hypertension
- Peripheral NS (entrapment)

Psychological

- Depression
- Loss of Libido
- Poor Self-Esteem
- Body Image dissatisfaction

Cardiovascular Disease

- HTN (vascular compression)
- CHF
- Venous Insufficiency/Phlebitis

Pulmonary Disease

- Obstructive Sleep apnea
- Hypoventilation Syndrome
- Pulmonary Embolism

GI Disease

- GERD
- Hernias

Gynecologic

- Pregnancy complications

GU Disease

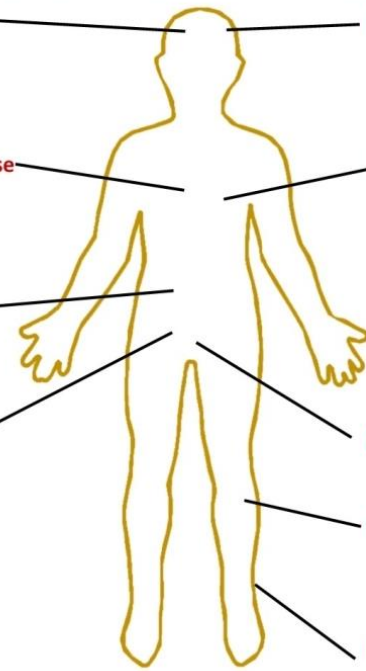
- Chronic Kidney Disease

MSK Disease

- Osteoarthritis

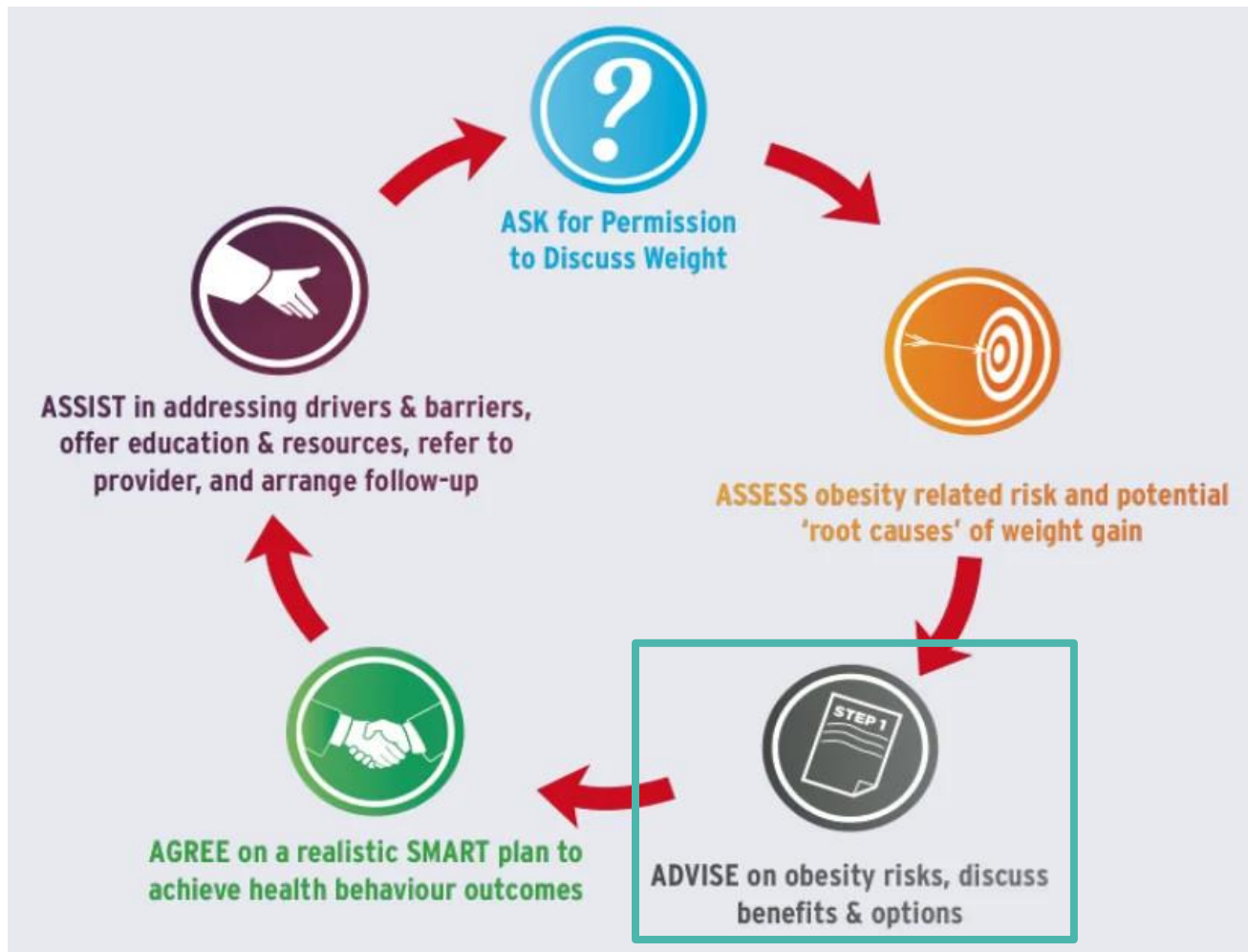
Integumentary

- Intertrigo
- Infections
- Skin tags
- Striae Distensae
- Stasis Pigmentation/Ulcers



Top 10 Weight Positive Medication Categories

1. Anti-hypertensives: beta-blockers like propranolol and metoprolol, calcium channel blockers amlodipine, nifedipine
2. Anti-diabetes medications: insulin, sulfonylureas, TZDs
3. Antidepressants: paroxetine, TCAs, mirtazapine, SNRIs
4. Mood stabilizers- gabapentin, lithium, valproate, carbamazepine
5. Anti-seizure medications- carbamazepine, gabapentin, valproate, pregabalin
6. Migraine medications- amitriptyline, gabapentin, valproate, propranolol
7. Hormone therapies- progestin contraceptives- variable effects on weight gain
8. Antipsychotics and hypnotics- clozapine, olanzapine, lithium, quetiapine, risperidone, diphenhydramine, zolpidem
9. Chemotherapies, HIV and anti-rejection medications: corticosteroids, tamoxifen, methotrexate, 5-fluorouracil, aromatase inhibitors, cyclosporin, tacrolimus
10. Anti-inflammatories and pain treatment: corticosteroids, gabapentin, pregabalin, amitriptyline, doxepin, duloxetine



When to Use Medications:

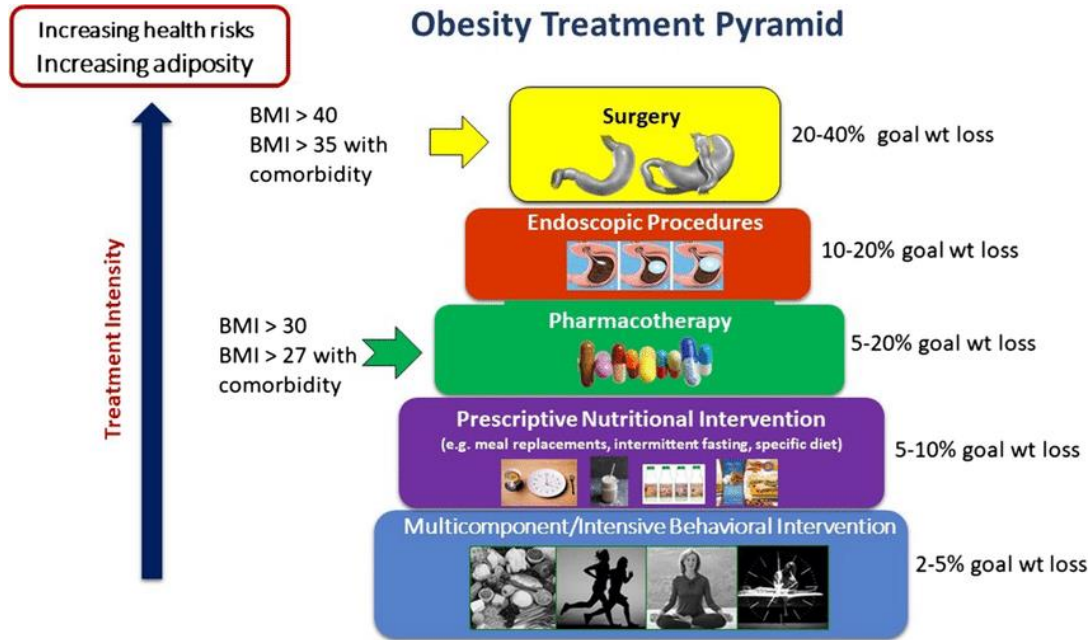
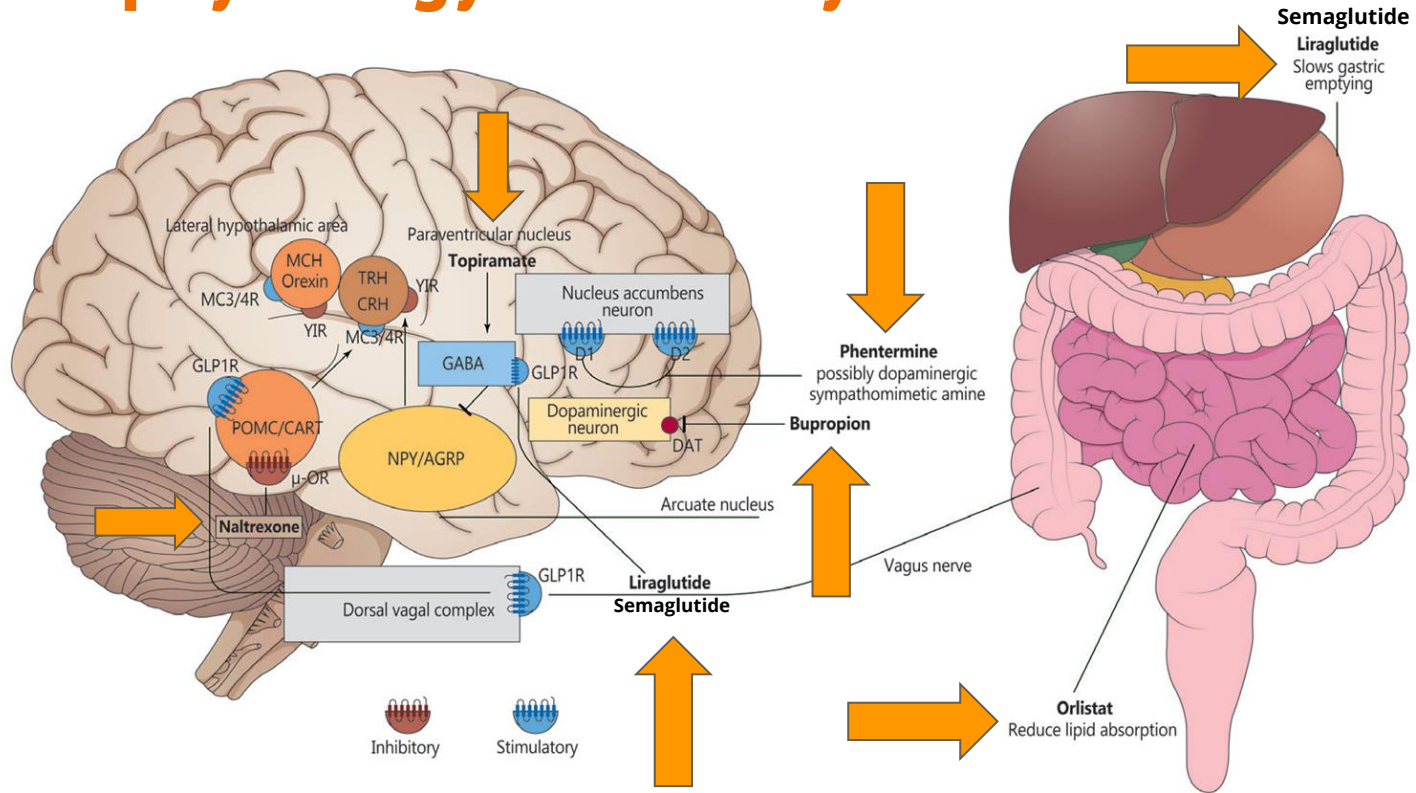


Image courtesy of Angela Finch, MD

Pathophysiology of Obesity



FDA Approved Medications for the Treatment of Obesity

- Phentermine
- Diethylpropion
- Benzphetamine
- Phendimetrazine
- *Lorcaserin (Removed from the market in 2020 due to concerns for cancer risk)*
- Phentermine/ topiramate ER
- Naltrexone SR/ Bupropion SR
- Liraglutide
- Semaglutide
- Orlistat
- Setmelanotide*

Phentermine

- Mechanism: sympathomimetic amine
- Dosage: 15 mg, 30 mg and 37.5 mg once daily
 - Also available 8 mg TID with meals
- Schedule IV controlled substance
- FDA approved for short term usage- 12 weeks
- Some patients may lose 5% of body weight
- Side effects: Headache, elevated BP, rapid or irregular HR, tremor, insomnia
- Contraindicated in glaucoma, agitated states, drug abuse, history of CAD
- Avoid with overactive thyroid, uncontrolled HTN, or uncontrolled seizure disorder
- Most affordable: GoodRx cost \$12.35 at Dillons for 30 tabs of 37.5mg tabs

Phentermine/ Topiramate ER

- Mechanism: sympathomimetic amine and anti-epileptic medication
 - Acts on GABA receptors in hypothalamus
- Schedule IV controlled substance
- Dosages: 3.27mg/23mg, 7.5mg/46mg, 11.25mg/69mg, 15mg/92mg
- Discontinue if wt loss <5% after 12 weeks on max dose
- EQUIP trial: Mean weight loss of 10.9 % at 56 weeks, and 66% of patients achieved >5% wt loss, 47.2% achieved >10% wt loss
- Side effects: paresthesias, dizziness, abnormal taste, insomnia, constipation, dry mouth
- Contraindicated in pregnancy
 - Topiramate can cause birth defects
 - REMS program: need monthly pregnancy test and effective contraception
- Contraindicated in glaucoma, uncontrolled HTN, CAD, hyperthyroidism
- GoodRx cost: \$170.09 for 30 tabs of 15mg/92mg

Naltrexone SR/ Bupropion SR

- Mechanism: Naltrexone inhibits appetite enhancing effects of beta-endorphin; Bupropion is norepinephrine and dopamine reuptake inhibitor- POMC activation and inhibits food intake via reward system
- Dosing: 8mg/ 90 mg
 - Titrate up weekly from 1 tab daily to 2 tabs BID
- Discontinue if wt loss <5% at 12 weeks
- COR-II trial- mean body weight loss was 6.4%
 - 50% of patients able to achieve 5% wt loss
 - 28.3% able to achieve 10% wt loss
- Side effects: Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea and acute angle closure glaucoma
- Contraindicated in seizure disorders, uncontrolled HTN, drug and alcohol withdrawal, pregnancy
- Should not be used in combination with opioid pain medications, anti-seizure medications
- GoodRx: \$515.56 for 120 tabs, 30 day supply

Liraglutide

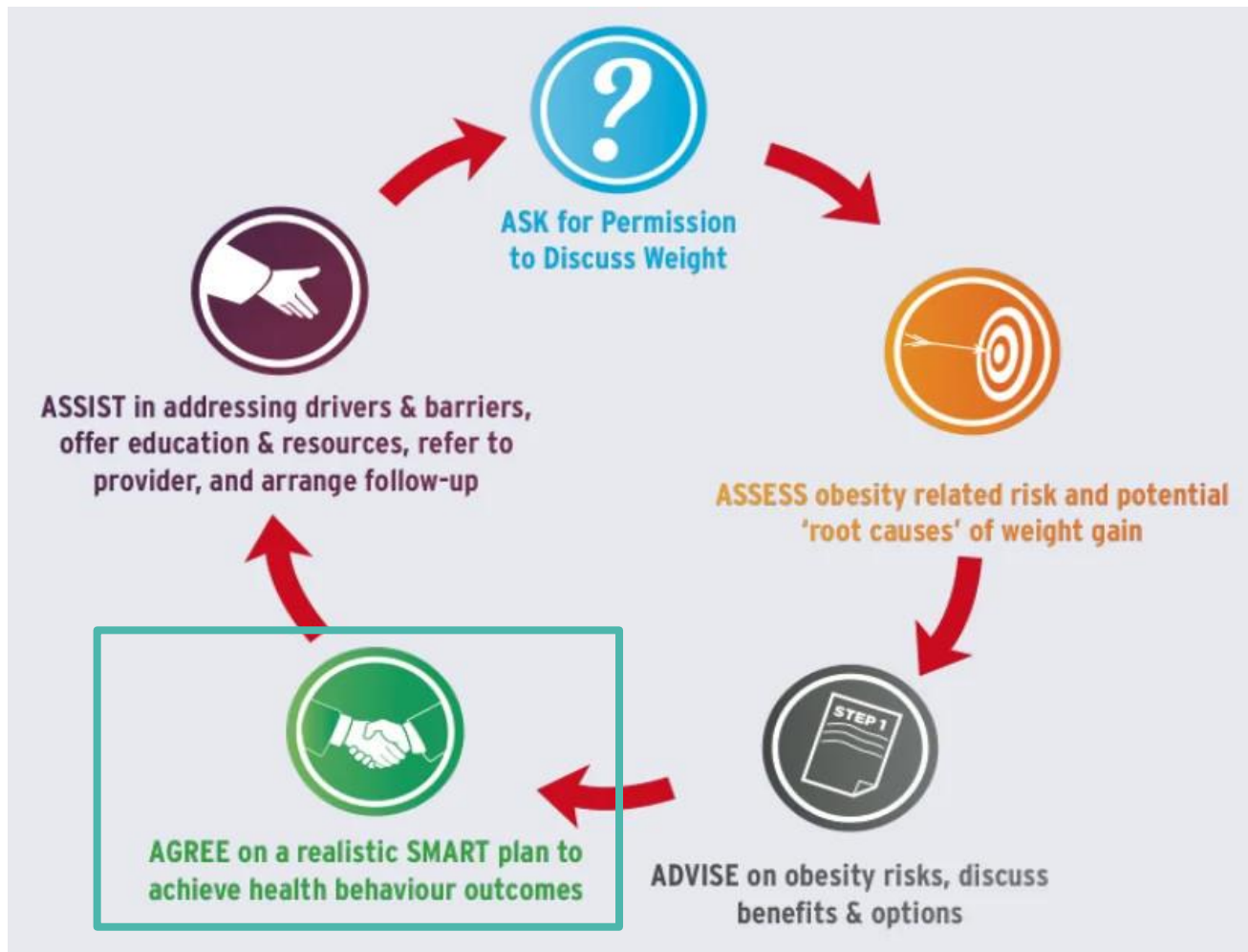
- Mechanism: GLP-1 Receptor agonist
 - SubQ injection
- Dosing: FDA approved for Diabetes at dosages up to 1.8 mg/day; FDA approved for obesity up to 3.0 mg/day; Different branding
- SCALE- Obesity trial- mean wt loss of 8.0%, 63.2% of patients able to achieve 5% wt loss, 33.1% able to achieve 10% wt loss
- Discontinue if wt los <4% after 16 weeks
- Titration weekly, have to restart titration if miss 3 days
- Side effects: nausea, diarrhea, hypoglycemia (when combined with insulin or sulfonylureas), constipation, vomiting, headache, dyspepsia, abdominal pain
- Contraindicated if personal or family hx of medullary thyroid cancer, or MEN type 2
 - Caution if history of pancreatitis, CKD
- Drug interactions due to impaired gastric emptying
- GoodRx: \$1,382 for 1 mo/supply at 3.0 mg

Semaglutide

- Mechanism: GLP-1 Receptor agonist
 - Weekly SubQ injection
- Dosing: FDA approved for diabetes at doses up to 2 mg
 - FDA approved for wt loss up to 2.4 mg. Pens come in 0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg and 2.4 mg doses
- 16% weight loss from baseline at 52 weeks, 86% of patients able to lose 5%, 69% of patients able to lose 10%, and 50% of patients able to lose 15%
- Side effects: nausea, diarrhea, hypoglycemia (when combined with insulin or sulfonylureas), constipation, vomiting, headache, dyspepsia, abdominal pain
- Contraindicated if personal or family hx of medullary thyroid cancer, or MEN type 2
 - Caution if history of pancreatitis, CKD
- Drug interactions due to impaired gastric emptying
- GoodRx: \$1,382 for 4 pens of 2.4 mg dose

Orlistat

- Mechanism: Gastrointestinal Lipase inhibitor
- Only AOM that does not affect appetite
- Dosage 120 mg TID before meals (lower doses available over the counter)
- Mean weight loss: 2.8 kg
- XENDOS study showed 10.6 kg loss after 1 yr compared to 6.2 kg in the placebo group.
 - 52% of pts achieved at least 5% wt loss
- Side effects: oily discharge, flatus from rectum, fecal incontinence
- Decreases absorption of fat soluble vitamins, patient should take multivitamin nightly
- Contraindications: chronic malabsorption syndromes, cholestasis, pregnancy, lactation
- GoodRx: \$555.91 for 90 tabs of 120 mg
- OTC price: \$68 for 120 tabs of 60 mg



How to choose which one?

The 5Cs of Choosing an AOM

Coverage/Cost

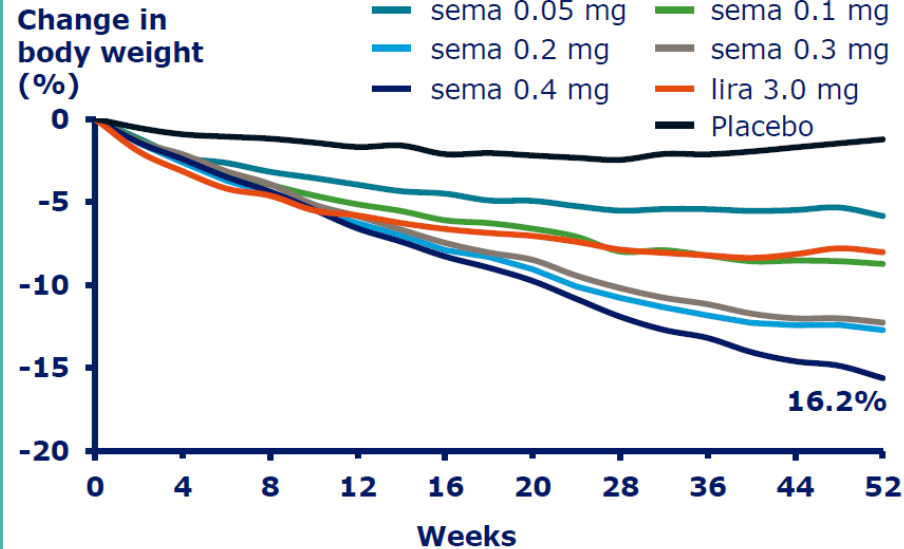
Contraindications/ Cautions

Comorbidities/Co- Indications

Cues

Combinations

16.2% weight reduction with the highest semaglutide dose in phase 2 obesity trial



Note: All treatment arms are adjunct to diet and exercise
QD: Once-daily; sema: Semaglutide; lira: Liraglutide

Source: Novo Nordisk investor presentations

Medication (Schedule)	Mechanism of Action	Mean weight loss	Oral/ TID AC	Contraindications/Precautions (Allergy/Pregnancy/Lactation for all)	Side Effects	Cost (month)
Orlistat	Gastrointestinal lipase inhibitor (Decreases fat absorption in intestines)	5% (2.8 kg)	Oral/ TID	Severe malabsorptive state, deficiencies of certain fat- soluble vitamins, cholestasis	Flatulence, Oily stools, fecal incontinence, diarrhea, rare-severe liver disease	OTC: \$68, Rx: \$556
Phentermine (IV) Diethylpropion (IV) Phendimetrazine (III)	Works on Hunger and satiety in the brain (Norepinephrine/ Sympathomimetic amine)	5%	Oral/ Daily or BID	Uncontrolled Blood pressure, CAD, Arrhythmia, Glaucoma, Seizures, Agitated states	Dry mouth, insomnia, constipation, Jittery feeling, nervousness	\$12.35
Phentermine/ Topiramate (IV)	Works on hunger and satiety in the brain by decreasing appetite and increasing feeling of fullness (topiramate acts on GABA)	10%	Oral/ Daily	Uncontrolled BP, CAD, Arrhythmia, Glaucoma, Seizures, hyperthyroidism, kidney stones. Contraception/ monthly pregnancy tests in women of childbearing age, requires taper	Dry mouth, insomnia, constipation, Jittery feeling, nervousness, Tingling, headache, brain fog (memory issues)	\$170.09
Naltrexone ER /Bupropion ER	Works on hunger and satiety in the brain as well as cravings (opiate antagonist and Dopamine/NE reuptake inhibitor)	5-10%	Oral/ BID	Seizures, Uncontrolled BP, Narcotic pain meds, Alcohol abuse/ Withdrawal, Glaucoma	Nausea, vomiting, diarrhea, constipation, headache, dizziness, insomnia	\$515.56
Liraglutide	Works on hunger and satiety by slowing stomach emptying and increasing feeling of fullness (GLP 1 receptor agonist)	5-10%	Sub Q/ Daily	Personal or family history of medullary thyroid cancer/MEN2, Pancreatitis, Gastroparesis, CKD	Nausea, vomiting, Diarrhea, constipation, hypoglycemia, dyspepsia, abdominal pain	\$1,382
Semaglutide	Works on hunger and satiety by slowing stomach emptying and increasing feeling of fullness (GLP 1 receptor agonist)	10-15%	Sub Q/ Weekly	Personal or family history of medullary thyroid cancer/MEN2, Pancreatitis, Gastroparesis, CKD	Nausea, vomiting, Diarrhea, constipation, hypoglycemia, dyspepsia, abdominal pain	\$1,382

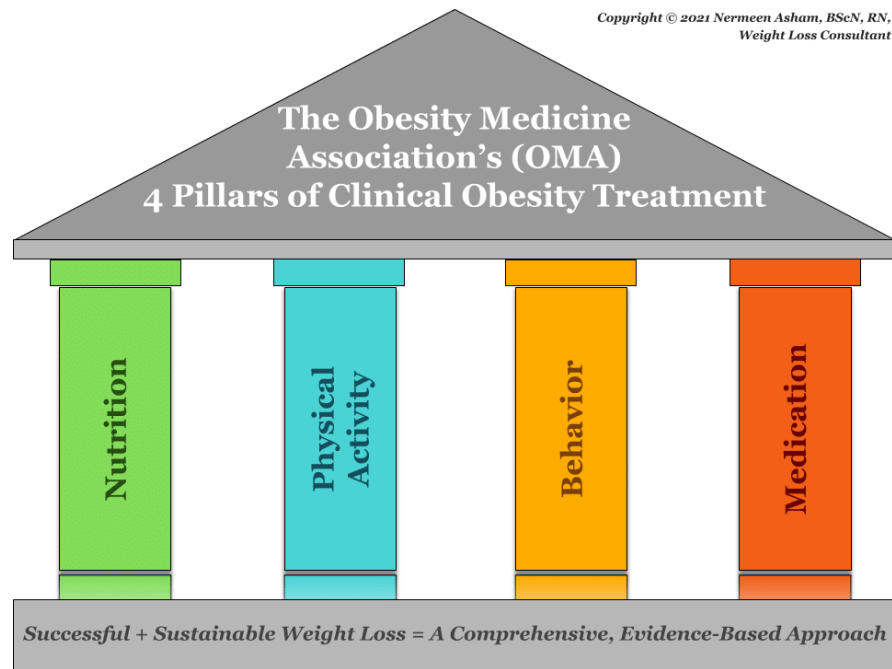
Provider Reference- Included in Additional materials

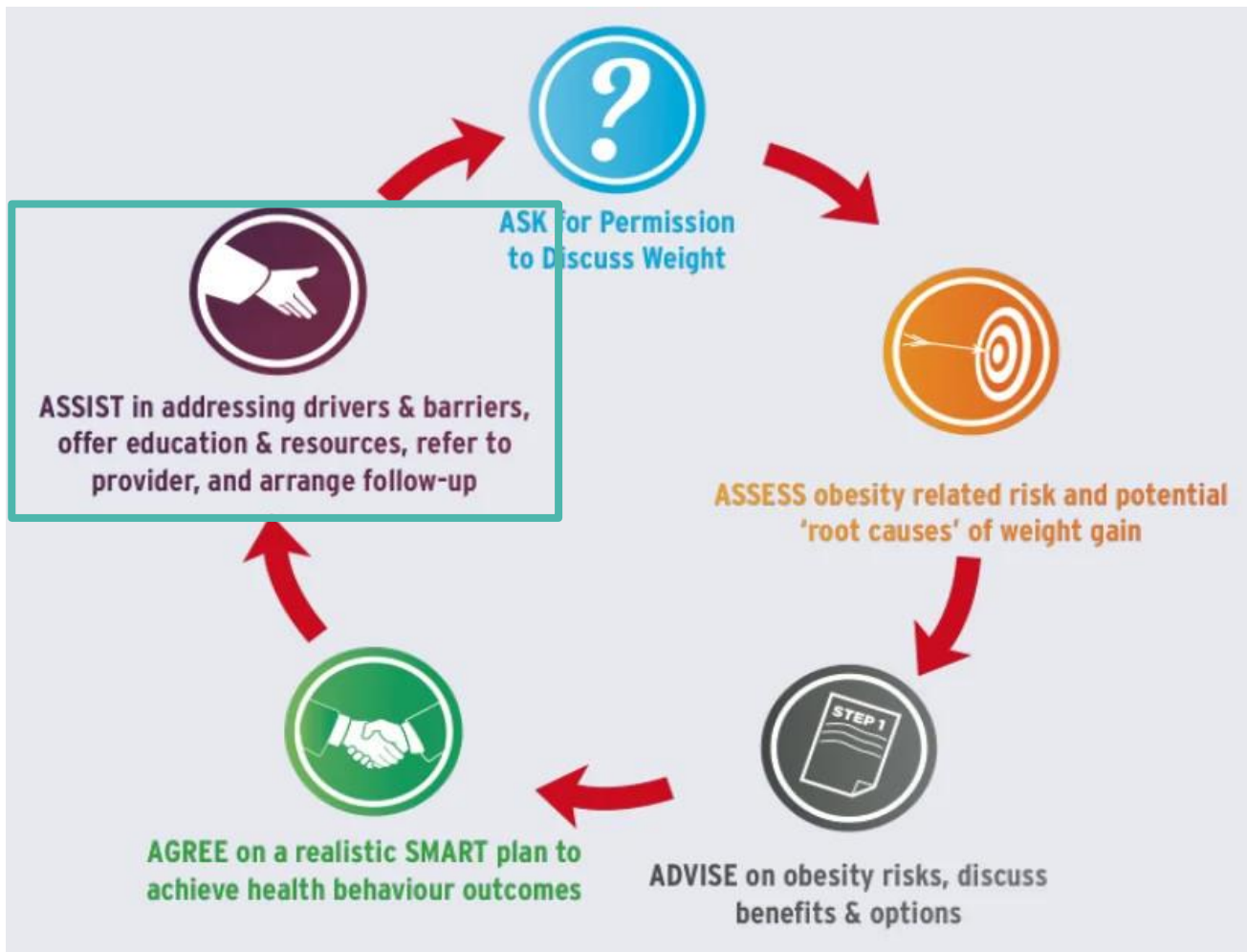
Medication/ How it works	Dosing	Mean Body Weight Loss	Side-Effects- Precautions	Limitations of Use	Cost with GoodRx per month
Xenical, Alli (Orlistat) Decreases fat absorption in the intestines	120 mg three times per day with fat-containing meals up or up to 1 hour after meal	5%	Cramps, flatulence, fecal incontinence, bowel urgency, oily stools,, frequent bowel movements. Decreased absorption of Vitamins A, D, E and K- must separate by 2 hours	Omit dose if meal is missed or contains no fat.	OTC: \$68. Rx: \$556
Phentermine Works on hunger and fullness regions in the brain. Stimulant medication.	Immediate release 15, 30 or 37.5mg Daily or Twice Daily Lomaira: 8 mg Three times daily 30 min before meals	5%	Increase in heart rate, blood pressure, insomnia, dry mouth, constipation, nervousness, anxiety. Contraindicated in patients with cardiovascular disease, poorly controlled hypertension, glaucoma, hyperthyroidism.	Only FDA approved for short term use (12 weeks) after that use is off-label. Stimulant medication that may have potential for abuse.	\$12.35
Qsymia (Phentermine/ Topiramate) Works on hunger and fullness regions in the brain. Decreasing appetite and increasing feeling of fullness. Contains stimulant medication.	3.75/23 mg daily for 14 days then increase dose to 7.5 /46 mg daily for 12 weeks then evaluate possible increase	10%	Dry mouth, taste disturbance, constipation, paresthesias, depression, anxiety, elevated heart rate, cognitive disturbances. Caution in patients with history of kidney stones, Contraindicated in patients with glaucoma, hyperthyroidism, and pregnancy.	Administer in the morning due to potential for insomnia After 12 weeks if <3% weight loss can discontinue or increase to 11.25/69 mg for 14 days then 15/92 mg daily. Then after 12 weeks at the highest dose if <5% weight loss then D C therapy.	\$170 Can get through Medvantx for \$99
Contrave (Naltrexone ER/Bupropion ER) Works on hunger and fullness regions of the brain to decrease appetite as well as decreasing cravings.	Week 1: 1 tab in the AM Week 2: 1 tab Am and Pm Week 3: 2 tabs Am and 1 tab PM Week 4: 2 tabs twice daily	5-8%	Headache, nausea, vomiting, constipation, hypertension, dizziness, insomnia, dry mouth. Contraindicated in patients with a history of seizures, uncontrolled hypertension, eating disorders, chronic opioid use, or on other bupropion medications.	Avoid taking with high fat meals	\$515.50 Can get through manufacturer for \$99

<p>Saxenda (liraglutide)</p> <p>Works on hunger and fullness by slowing stomach emptying and increasing feeling of fullness. Also suppresses hunger centers in the brain. Decreases insulin resistance</p>	<p>0.6 mg SubQ injection daily for 1 week and then increase by 0.6 mg weekly to target dose of 3 mg Daily.</p>	<p>5-10%</p>	<p>Nausea, vomiting, diarrhea, constipation, hypoglycemia in patients with Type 2 Diabetes, injection site reactions Rarely reported: Pancreatitis, gallbladder disease, renal impairment. Contraindicated in patients with a personal history or family history of medullary thyroid cancer or MEN2.</p>	<p>After 12 weeks at maximum tolerated dose OR 16 weeks after initiation discontinue if <4-5% baseline body weight not attained</p>	<p>\$1382</p>
<p>Wegovy (semaglutide)</p> <p>Works on hunger and fullness by slowing stomach emptying and increasing feeling of fullness. Also suppresses hunger centers in the brain. Decreases insulin resistance.</p>	<p>0.25 mg subQ injection weekly, increase dose at 4 week intervals until target dose of 2.4 mg weekly.</p>	<p>10-16%</p>	<p>Nausea, vomiting, diarrhea, constipation, hypoglycemia in patients with Type 2 Diabetes, injection site reactions Rarely reported: Pancreatitis, gallbladder disease, renal impairment. Contraindicated in patients with a personal history or family history of medullary thyroid cancer or MEN2.</p>	<p>After 12 weeks at 2.4 mg weekly OR maximum tolerated dose: D/c if at least 5% of baseline body weight is not attained. Monitor patients with diabetic retinopathy for eye complications</p>	<p>\$1382</p>
<p>Mounjaro** (tizaparatide)</p>	<p>Titration starting at 2.5mg weekly and increasing at 4 week intervals to maximum tolerated dose</p>	<p>Currently being studied for weight loss in absence of diabetes.</p>			<p>\$1057</p>
<p>Plenity</p>	<p>3 capsules with 16 oz of water 20-30 min before lunch and dinner</p>	<p>5-10%</p>	<p>Fullness, bloating, flatulence, abdominal pain</p> <p>Should not be taken at the same time as other medications.</p>	<p>If pre-meal dose is missed take with 20 oz of water during or immediately after meals</p> <p>Nor for those with BMI >40</p>	<p>\$98. Not covered by insurance.</p>

Set SMART Goals for the Next Month

- Weight goal- usually no more than 5 pounds
- Eating habits
- Water intake
- Physical activity
- Sleep
- Self care
- Medication- including expectations about insurance coverage and timeline of prior authorization process
- Follow up appointment





Patient Case

49 y.o. Female- NPV, Weight loss and labs

- Presented to establish care and wanting to lose weight
- History of HTN, anxiety, depression, sleep apnea, and prediabetes
- Previously tried: metformin and phentermine
- Current weight 104 kg (224 lbs) , BMI 39.63
- BP 120/78, P 101, T 36.7
- Wanting to start medical weight loss program

- Current medications
 - Duloxetine 60 mg Daily
 - Lisinopril-hctz 20 mg- 12.5 mg daily
 - Trazodone 100 mg at bedtime
 - Hydroxyzine 25 mg daily
- Labs obtained at NPV
 - TC 244 Trig 148, LDL 143, HDL 71
 - A1c 5.1%
 - TSH wnl
 - AST 297, ALT 432, Alk phos 236
 - CBC, Creatinine, electrolytes normal
- No FHx of Thyroid cancer, no personal hx of glaucoma, seizures, or palpitations

49 y.o F continued

Obtained sono of the RUQ: Hepatic steatosis; cholelithiasis; no acute abnormality is seen

Patient also had mammogram ordered at initial visit which showed no areas of concern

Patients comorbidities:

- History of prediabetes
- Dyslipidemia
- Obstructive sleep apnea
- Hepatic steatosis

Patient had started working with personal trainer and was also referred to meet with dietician

With BMI of 39 + comorbidities patient would have been a candidate for referral for bariatric surgery. However patient was interested in starting medication options first

Coverage/Cost

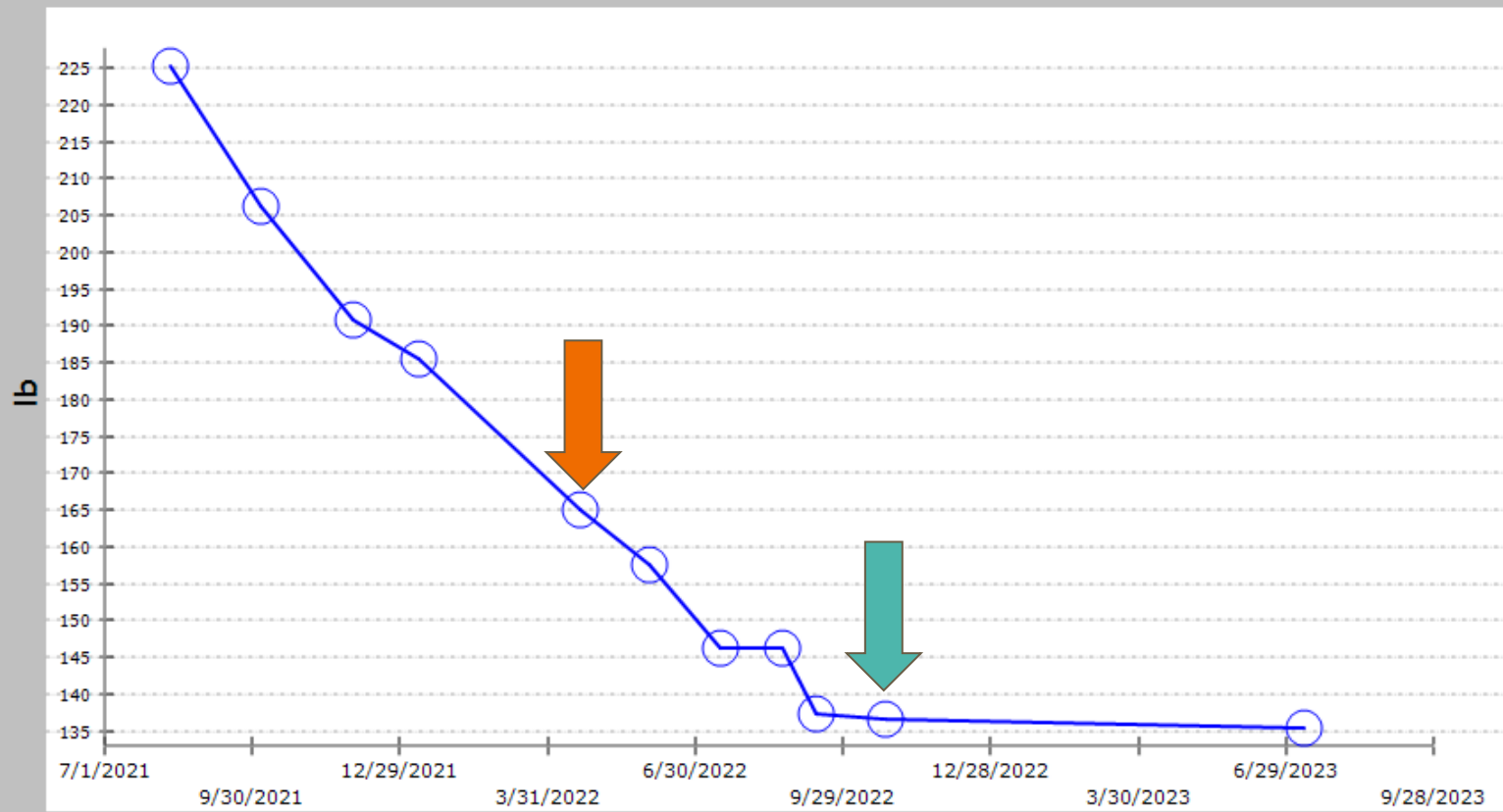
Contraindications/ Cautions

Comorbidities/Co- Indications

Cues

Combinations

Weight - lbs



Questions?

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