

WEIGHING THE OPTIONS: DRUGS FOR WEIGHT MANAGEMENT

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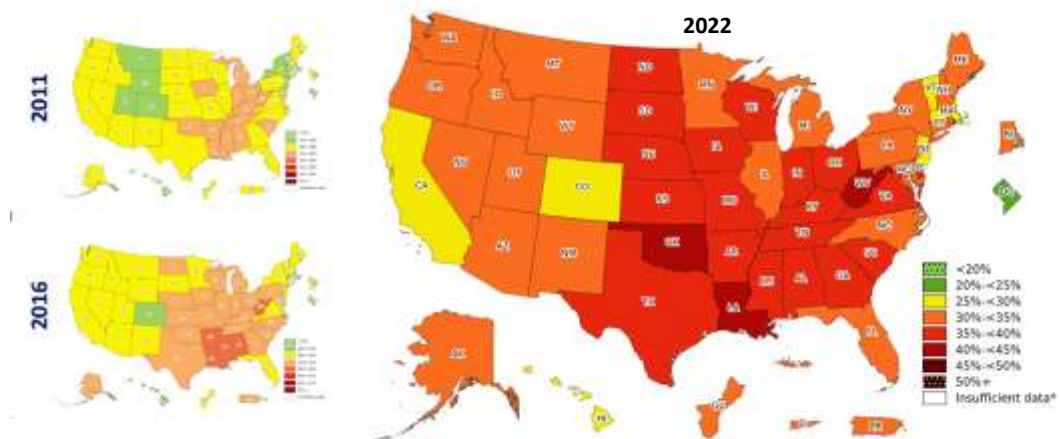
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Learning Objectives

- At the end of this presentation, participants should be able to...
 - Discuss the rationale for utilizing medications in the treatment of overweight and obesity
 - Identify medications FDA-approved for weight management
 - Discuss the pros and cons of medications used for weight management

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Prevalence of Self-Reported Obesity



<https://www.cdc.gov/obesity/data/prevalence-maps.html#overall>

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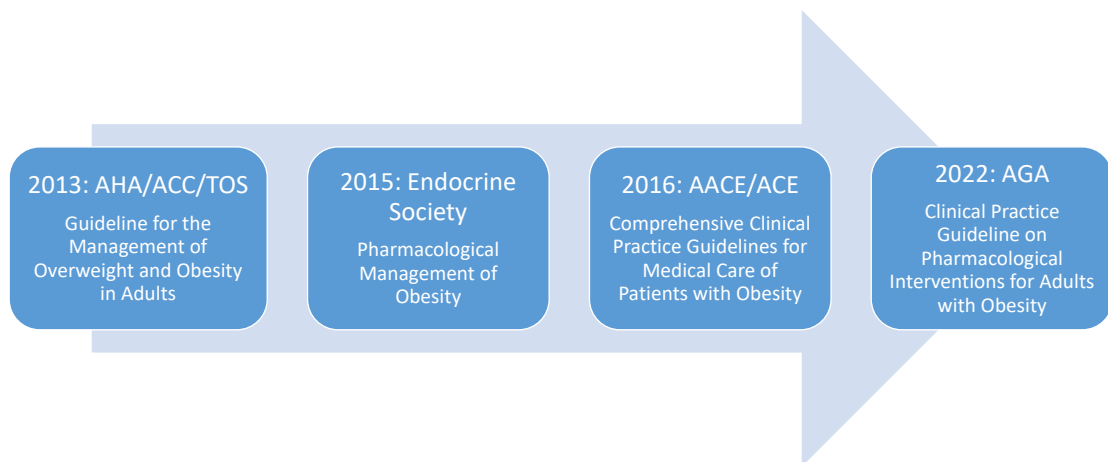
Health Effects of Adiposity-Based Chronic Disease (ABCD)

- Prediabetes/diabetes
- Dyslipidemia
- Hypertension
- NAFLD
- ASCVD
- HFrEF
- HFpEF
- Obstructive sleep apnea
- Osteoarthritis
- GERD
- Urinary incontinence
- Hypogonadism
- Polycystic ovary syndrome
- Reduced fertility

Endocrine Practice 29 (2023) 305e340

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Clinical Practice Guidelines



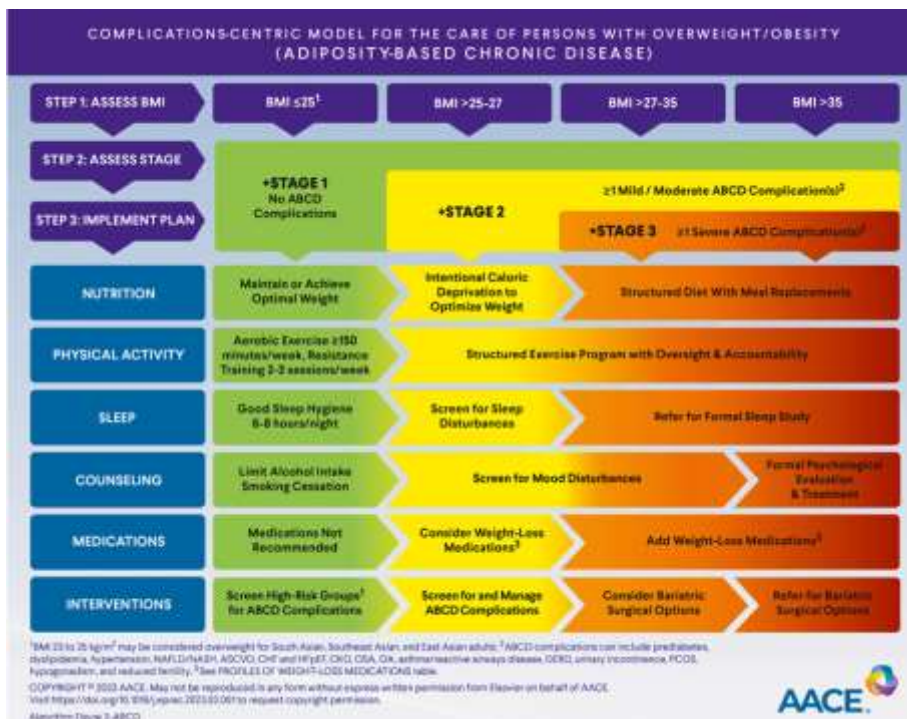
AACE: American Association of Clinical Endocrinology, ACC: American College of Cardiology, ACE: American College of Endocrinology, AGA: American Gastroenterological Association, AHA: American Heart Association, TOS: The Obesity Society

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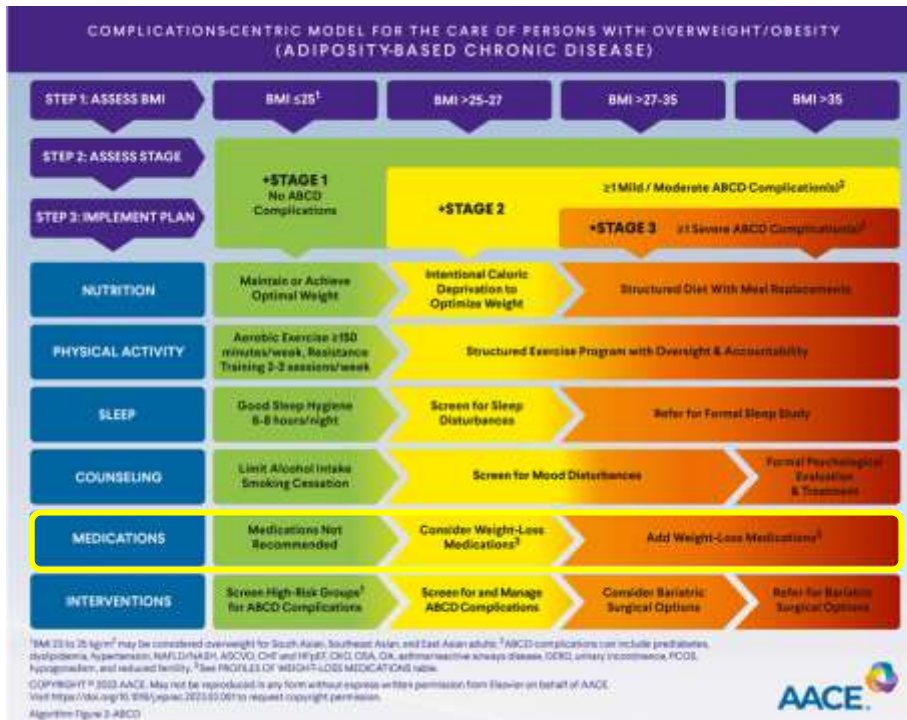
Clinical Practice Guidelines

- American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm – 2023 Update
- American Diabetes Association Standards of Care in Diabetes – 2024
 - 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes

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Medications FDA-Approved for Weight Management

1995	• Phentermine (Lomira, Adipex)
1999	• Orlistat (Xenical, Alli)
2012	• Phentermine/topiramate ER (Qsymia)
2014	• Naltrexone/bupropion ER (Contrave); liraglutide (Saxenda)
2020	• Setmelanotide (Imcivree)
2021	• Semaglutide (Wegovy)
2023	• Tirzepatide (Zepbound)

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General Indication for Weight-Loss Medications

- Adjunct to a reduced-calorie diet and increased physical activity for weight management in adults with an initial body mass index (BMI) of:
 - 30 kg/m² or greater (obesity)
 - 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes mellitus, obstructive sleep apnea, or cardiovascular disease)

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Phentermine

- **Class:** sympathomimetic amine anorectic
 - Stimulates hypothalamus causing release of norepinephrine resulting in appetite suppression
- **Side Effects**
 - Increased blood pressure/heart rate, palpitations, headache, insomnia, anxiety, dry mouth, constipation
- **Contraindications & Precautions**
 - History of cardiovascular disease
 - Hyperthyroidism
 - Glaucoma
 - History of drug abuse
 - Use of MAOIs/CNS stimulants
 - Pregnancy

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Phentermine Pearls

- Indicated for short-term use only
 - Generally defined as 12 weeks of continuous use
 - Weight loss typically greatest during first few weeks of therapy
- Chemical structure is a substituted amphetamine
- Take early in the day to decrease risk of insomnia
- Renal dose adjustment considerations

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Orlistat

- Class: lipase inhibitor
 - Inhibits gastric and pancreatic lipases, decreasing the absorption of dietary fats by about 30%
- Side Effects
 - Intestinal cramping, abdominal pain/discomfort, flatulence, oily spotting/leakage, fecal incontinence, malabsorption of fat-soluble vitamins
- Contraindications & Precautions
 - Chronic malabsorption syndrome
 - Cholestasis
 - Pregnancy

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Orlistat Pearls

- Should be taken during or up to 1 hour after each meal
- Daily multivitamin supplement recommended
 - Take 2 hours apart from orlistat
 - Should include fat-soluble vitamins
- Potential for drug interactions
 - Levothyroxine, antiseizure medications, warfarin

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Phentermine/Topiramate ER

- **Class:** sympathomimetic amine anorectic + GABA receptor modulator
 - Stimulates hypothalamus causing release of norepinephrine + modulation of GABA receptors resulting in appetite suppression
- **Side Effects**
 - Increased blood pressure/heart rate, palpitations, headache, insomnia, anxiety, dry mouth, taste disturbance, constipation + cognitive impairment, paresthesias
 - Rare: metabolic acidosis, kidney stones
- **Contraindications & Precautions**
 - History of cardiovascular disease
 - Hyperthyroidism
 - Glaucoma
 - History of drug abuse
 - Use of MAOIs/CNS stimulants
 - Pregnancy

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Phentermine/Topiramate ER Pearls

- Pearls applicable to phentermine apply
- Risk Evaluation and Mitigation Strategy (REMS)
 - Teratogenic
 - Negative pregnancy test needed prior to and monthly during use
- May help with migraine prophylaxis
- Renal dose adjustment considerations

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Naltrexone/Bupropion ER

- Class: opioid antagonist + norepinephrine/dopamine reuptake inhibitor antidepressant
 - Affects appetite regulatory center of the hypothalamus and mesolimbic dopamine circuit (reward system)
- Side Effects
 - Nausea, vomiting, constipation, headache, dizziness, insomnia, dry mouth
 - Transient increases in blood pressure and/or heart rate
- Contraindications & Precautions
 - Use of other bupropion-containing products, opioid therapy, or MAOIs
 - Seizure disorder
 - Eating disorders
 - Uncontrolled hypertension
 - Pregnancy

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Naltrexone/Bupropion ER Pearls

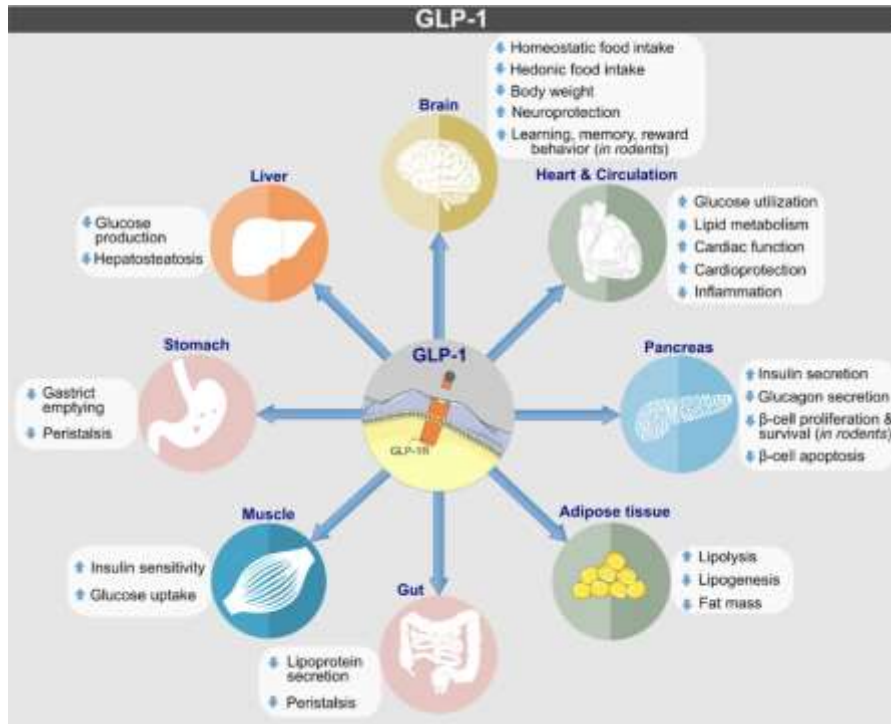
- Boxed warning: suicidal thoughts and behaviors
- May provide benefit in patients with depression or tobacco use disorder
- Take early in the day to decrease risk of insomnia
- Avoid administration with high-fat meals
- Renal dose adjustment considerations

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Liraglutide and Semaglutide

- Class: glucagon-like peptide-1 (GLP-1) receptor agonist
 - Aids in regulation of appetite and caloric intake
- Side Effects
 - Primarily GI: nausea, vomiting, diarrhea, constipation; injection site reactions
 - Rarely: pancreatitis, gallbladder disease
- Contraindications & Precautions
 - Personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2
 - Pregnancy
 - Hypoglycemia
 - Renal impairment
 - Suicidal ideation
 - Retinopathy associated with type 2 diabetes

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Liraglutide and Semaglutide Pearls

- Alternate brand names/dosing approved by the FDA for treatment of type 2 diabetes mellitus
 - Preferred injectable before insulin or as an add-on if insulin intensification needed
 - Dose adjustment of other diabetes medications may be needed to prevent hypoglycemia
 - Do not use with DPP-4 inhibitors
- Cardiovascular risk reduction
- Dose titration considerations

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Tirzepatide

- **Class:** glucose-dependent insulinotropic polypeptide (GIP) receptor and GLP-1 receptor agonist
 - Aids in regulation of appetite and caloric intake
- **Side Effects**
 - Primarily GI: nausea, vomiting, diarrhea, constipation; injection site reactions
 - Rarely: pancreatitis, gallbladder disease
- **Precautions & Contraindications**
 - Personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2
 - Pregnancy
 - Hypoglycemia
 - Renal impairment
 - Suicidal ideation
 - Retinopathy associated with type 2 diabetes

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Tirzepatide

- Potential for promoting the most weight loss among any agent to date
- Similar pearls as liraglutide/semaglutide

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A Side-by-Side Comparison of Popular Weight Loss Drugs

	DOSE	DOSE FORM	SUITABLE FOR LONG-TERM USE	EFFICACY*
Metformin**	1-2 DAILY		YES	
Contrave*** <small>PHENYLETHANAMINE/NALTREXONE</small>	2 DAILY		YES	
Phentermine <small>(ADIPEN H)</small>	1-3 DAILY		NO	
Qsymia <small>(PHENYLETHANAMINE/PRIMAMINE HCl)</small>	1 DAILY		YES	
Saxenda <small>(LIRAGLUTIDE)</small>	1 DAILY		YES	
Wegovy <small>(SEMAGLUTIDE)</small>	1 WEEKLY		YES	
Tirzepatide <small>(ZEPHYRUS)</small>	1 WEEKLY		YES	

*Efficacy isn't the whole picture when it comes to weight loss drugs. Having a choice of options allows you to find one that works best for you and your lifestyle.
 **Currently only approved for Type 2 diabetes.
 ***Dosing after initial titration.

<https://www.goodrx.com/conditions/weight-loss/best-pills>

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A Side-by-Side Comparison of Popular Weight Loss Drugs

	DOSE	DOSE FORM	SUITABLE FOR LONG-TERM USE	EFFICACY*	Comparative Cost
Metformin**	1-2 DAILY		YES		\$
Contrave*** <small>PHENYLETHANAMINE/NALTREXONE</small>	2 DAILY		YES		\$\$\$
Phentermine <small>(ADIPEN H)</small>	1-3 DAILY		NO		\$
Qsymia <small>(PHENYLETHANAMINE/PRIMAMINE HCl)</small>	1 DAILY		YES		\$\$
Saxenda <small>(LIRAGLUTIDE)</small>	1 DAILY		YES		\$\$\$\$
Wegovy <small>(SEMAGLUTIDE)</small>	1 WEEKLY		YES		\$\$\$\$
Tirzepatide <small>(ZEPHYRUS)</small>	1 WEEKLY		YES		\$\$\$\$

*Efficacy isn't the whole picture when it comes to weight loss drugs. Having a choice of options allows you to find one that works best for you and your lifestyle.
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PROFILES OF WEIGHT-LOSS MEDICATIONS						
	SEMAGLUTIDE	LIRAGLUTIDE	PHENTERMINE/ TOPIRAMATE ER	NALTREXONE-ER/ BUPROPION-ER	ORLISTAT	PHENTERMINE [†]
CLASS	GLP-1 RA	GLP-1 RA	Sympathomimetic Action/Gabapentinergic	Opioid-Receptor Antagonist/DA-Receptor Reuptake Inhibitor	5F Lipase Inhibitor	Sympathomimetic
WEIGHT LOSS [§]	15%-18%	5%-8%	8%-10%	4%-6%	4%	3% [†]
MECHANISM	Decreased Appetite Delayed Gastric Emptying	Decreased Appetite Delayed Gastric Emptying	Decreased Appetite Increased Satiety	Decreased Cravings Decreased Appetite	Decreased Fat Absorption	Decreased Appetite
DELIVERY	Weekly Subcutaneous Injection	Daily Subcutaneous Injection	Oral	Oral	Oral	Oral
STARTING DOSE	0.25 mg/week	0.6 mg/day	3.75 mg/25 mg daily	8 mg/90 mg daily	120 mg three times daily	18 mg daily
TREATMENT DOSE	2.4 mg/week	3 mg/day	7.5 mg/46 mg daily (maximum 15 mg/50 mg daily)	16 mg/180 mg twice per day	120 mg three times daily	37.5 mg daily [†]
POTENTIAL SIDE EFFECTS	Nausea/Vomiting Diarrhea Constipation Headache Fatigue	Nausea/Vomiting Diarrhea Constipation Headache Fatigue	Headaches Nausea Headache Dry Mouth Blurred Vision Tachycardia ^{§§} Exitation/Paresthesia Dizziness Mental Clouding/Wood Changes	Nausea/Vomiting Diarrhea Constipation Headache Fatigue Insomnia Dry Mouth Blurred Vision Agitation/Mood Changes	Flatulence Fecal Urgency Dry Stools Fur/Skinny Stool Drug Malabsorption	Headaches Nausea Headache Dry Mouth Tachycardia ^{§§} Exitation
CAUTIONS AND CONTRAINDICATIONS [¶]	MITOMENS Tetracycline Piperacillin Gallbladder Disease Diabetic Retinopathy	MITOMENS Tachycardia Pain/ventilator Gallbladder Disease	Glucose Hypertension Urinary Metabolic Acidosis	Seizure Risk Uncontrolled Hypertension Chronic Opioid Use	Organ Transplant Urinary Diabetes Drooling	Active CAD Uncontrolled Hypertension Hypothyroidism Agitated States
ACCESS/COST	\$\$\$	\$\$\$	\$\$	\$\$	\$\$	\$

[§] Approved for short-term (<3 months, 5 mg / 30 mg / 30.5 mg phentermine hydrochloride + 10 mg / 36 mg / 38 mg phentermine).

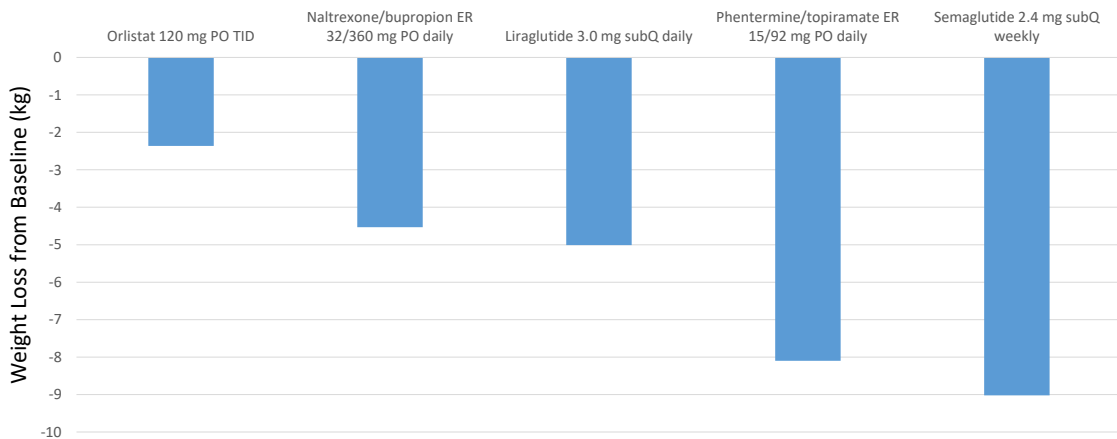
[†] Approximate placebo-subtracted with 1 year of therapy except phentermine 10 weeks. [¶] All agents are contraindicated in pregnancy/breastfeeding.

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Algorithm Figure 10 Weight Loss Medications

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Average Weight Loss at 1 Year Iannone, et al.



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Other Considerations

- “... indicated as an adjunct to a reduced-calorie diet and increased physical activity...”
- Weight rebound following discontinuation
- *Shift treatment landscape to treat obesity as a chronic disease*

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Other Considerations

- Cost can limit access
 - Coverage for weight loss medications variable
 - Ensure prescribing is for medication indicated for weight management
 - Prior authorization may be required
 - Updated labs and other documentation
 - Resources include co-pay cards, patient assistance programs, etc.

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Key Takeaways

- Lifestyle intervention is still the foundation of weight management
- Medications can help enhance weight loss in appropriate patients
 - Patient selection
 - Follow-up and monitoring
 - Maintenance strategies
- Weight management interventions can decrease risk of ABCD and improve health status

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Questions?

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