MELT THE POUNDS FEEL PROFOUND!

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Disclosure and Conflicts of Interest

Vicky Shah declares no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings and honoraria.

Learning Objectives

Discuss the importance of lifestyle modifications, including diet, exercise, and behavioral therapy, along with integrating pharmacotherapy

Describe each drug class's mechanisms of action, indications, contraindications and potential side effects

Review a patient-centered approach, which involves considering individual needs, preferences, and overall health goals in weight management

Pre-Test Question 1

True or False: Obesity in the adult population in the United States has doubled in the past 40 years.

Pre-Test Question 2

Which of the following are FDA approved indications for tirzepatide? SELCT ALL THAT APPLY

A. Weight Loss
B. MASH (Metabolic Dysfunction-Associated Steatohepatitis)
C. Slow CKD Progression
D. Type 2 Diabetes
E. Obstructive Sleep Apnea in Obese Patients

Pre-Test Question 3

Which medication had the highest weight loss percentage in clinical trials when using the maximum dose?

A. Liraglutide
B. Semaglutide
C. Metformin
D. Tirzepatide
E. Phentermine

Obesity

One may think obesity is a product of gluttony and laziness in industrialized regions, but it is common around the world in all demographic groups

World Health Organization. Obesity and overweight. June 9, 2021. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

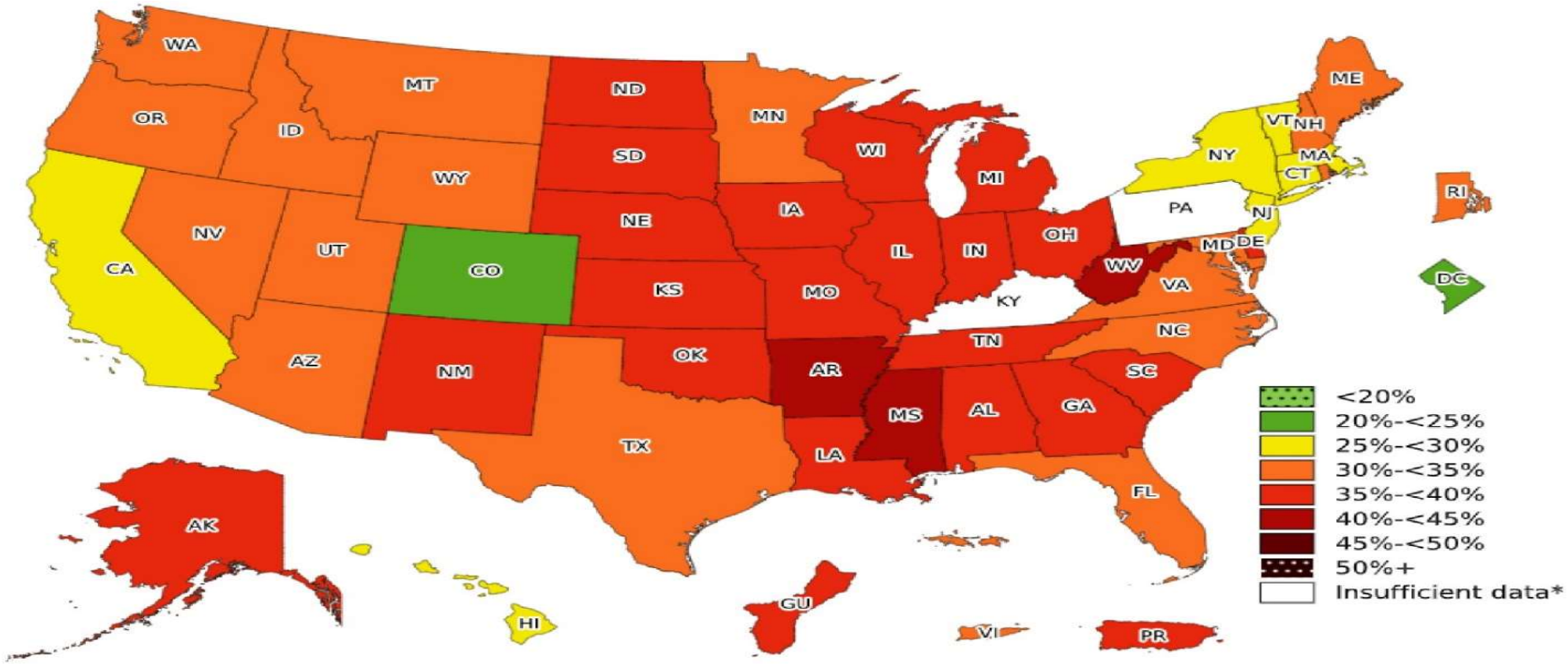
Obesity

Obesity in the adult population has tripled in the past 40 years

In 2016, 39% of adults around the world (1.9 billion people) were overweight and 13% (650 million people) were obese

World Health Organization. Obesity and overweight. June 9, 2021. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

Obesity



CDC (2023). Map used unmodified. Does not imply endorsement by CDC, HHS, or the U.S. Government.

Body Mass Index

Calculated Body Mass Index (kg/m^2)	Weight Classification
<18.5	Underweight
18.5–24.9	Normal weight
25.0–29.9	Overweight
30.0–34.9	Obese: Class I
35.0–39.9	Obese: Class II
>40.0	Obese: Class III ("severe obesity")

World Health Organization. Obesity and overweight. June 9, 2021. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
Schwartz MW, Seeley RJ, Zeltser LM, et al. Obesity pathogenesis: an Endocrine Society scientific statement. *Endocr Rev.* 2017;38(4):267–296.
Centers for Disease Control and Prevention. Adult obesity facts. June 7, 2021. https://www.cdc.gov/obesity/data/adult.html
Fang J, Hefeng Z, Ayala C, et al. Cardiovascular health among non-Hispanic Asian Americans: NHANES, 2011–2016. *J Am Heart Assoc.* 2019;8:e011324.

Waist Circumference

Country/Ethnicity	Waist Circumferences in cm (in)	
	Males	Females
United States (for those of European descent)	≥102 (40)	≥88 (35)
European	≥94 (37)	≥80 (31.5)
South Asian, Chinese, Japanese	≥90 (35.5)	≥80 (31.5)
South and Central Americans	Use South Asian recommendations until more data are available	
Sub-Saharan African	Use European recommendations until more data are available	
Mediterranean and Middle Eastern	Use European recommendations until more data are available	

Zhang C, Rexrode KM, van Dam RM, et al. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: sixteen years of follow-up in US women. *Circulation.* 2008;117(13):1658–1667.
Harvard T.H. Chan School of Public Health. Abdominal obesity measurement guidelines for different ethnic groups: the International Diabetes Federation's definition of the metabolic syndrome uses ethnic-specific criteria to define abdominal obesity. 2021. https://www.hsph.harvard.edu/obesity-prevention-source/waist-circumference-guidelines-for-different-ethnic-groups/

American Heart Association Cardiovascular-Kidney-Metabolic Staging

Stage		Clinical Characteristics (Definition)
0	No CKM risk factors	•Normal BMI and waist circumference, Normoglycemia, Normotension, Normal lipid profile, No evidence of CKD or subclinical or clinical CVD
1	Excess or dysfunctional adiposity	•Overweight/obesity, abdominal obesity, or dysfunctional adipose tissue present •No other metabolic risk factors or CKD present
2	Metabolic risk factors and CKD	•Metabolic risk factors (e.g., hypertriglyceridemia [≥ 135 mg/dL], hypertension, metabolic syndrome, T2D) or CKD present
3	Subclinical CVD in CKM	•Subclinical ASCVD or subclinical HF in individuals with excess/dysfunctional adiposity, other metabolic risk factors, or CKD
4	Stage 4a: Clinical CVD in CKM (no kidney failure)	•Clinical CVD (e.g., coronary heart disease, HF, stroke, peripheral artery disease, atrial fibrillation) in individuals with excess or dysfunctional adiposity, other CKM risk factors, or CKD
	Stage 4b: Clinical CVD in CKM (kidney failure present)	

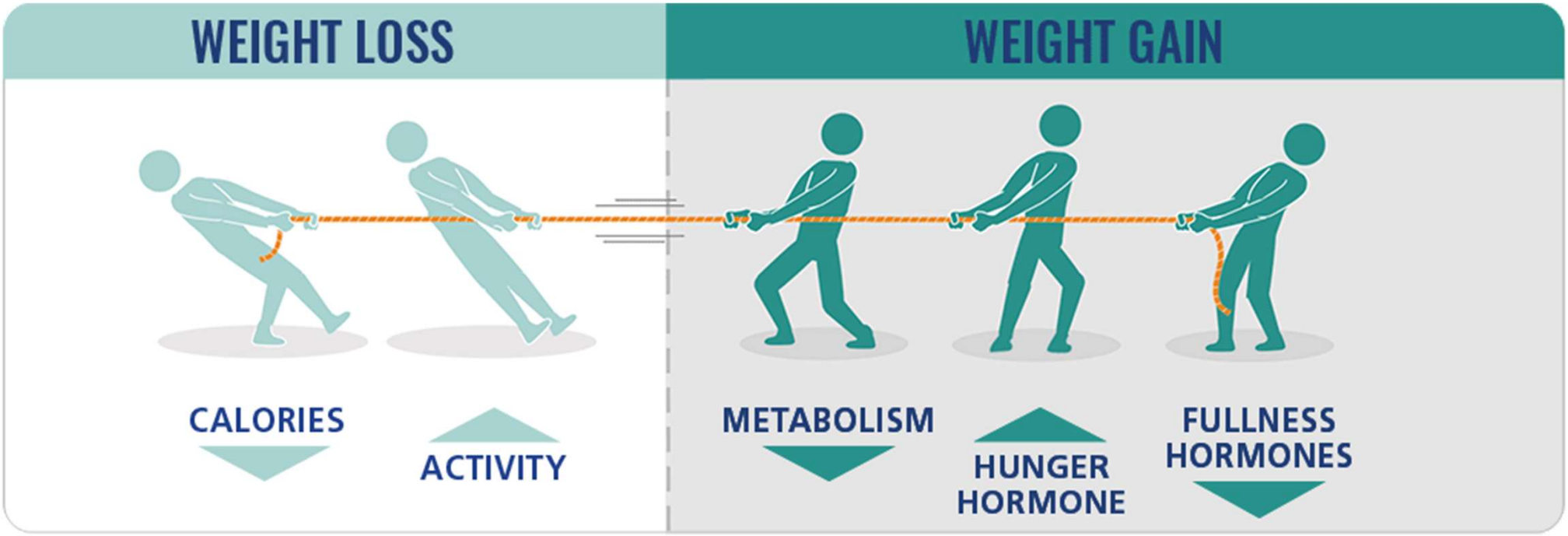
Ndumele CE, Rangaswami J, Chow SL, et al. Cardiovascular-kidney-metabolic health: A Presidential advisory from the American Heart Association. *Circulation*. 2023;148(20):1606-1635.
Ndumele CE, Neeland IJ, Tuttle KR, et al. A synopsis of the evidence for the science and clinical management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A scientific statement from the American Heart Association. *Circulation*. 2023;148(20):1636-1664.

Risk Factors/Causes of Obesity

Eating/Physical Activity Patterns	Insufficient Sleep	Social Determinants of Health (SDOH)
Genetics	Illnesses	Medications

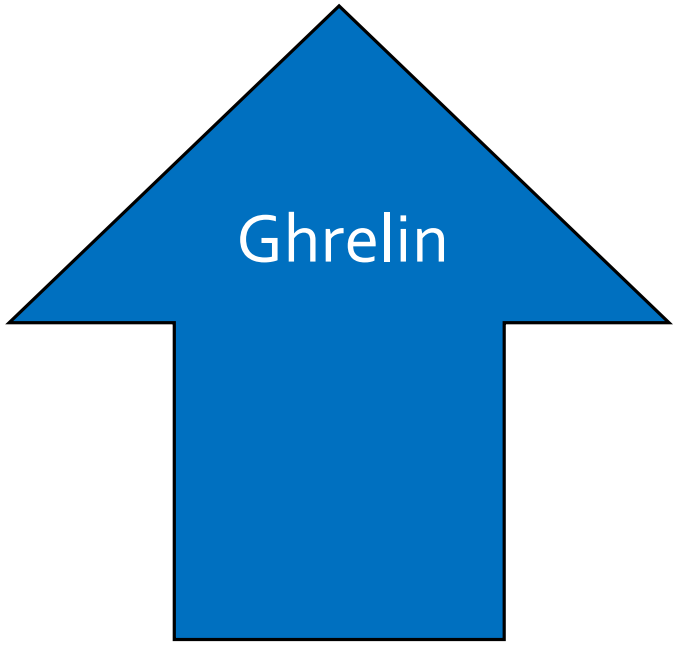
Schwartz MW, Seeley RJ, Zeltser LM, et al. Obesity pathogenesis: an Endocrine Society scientific statement. *Endocr Rev.* 2017;38(4):267–296.
Dickson SL, Chowen JA. Neuroscience of obesity. *Neuroscience.* 2020;447:1–2.

Physiology of Weight Management



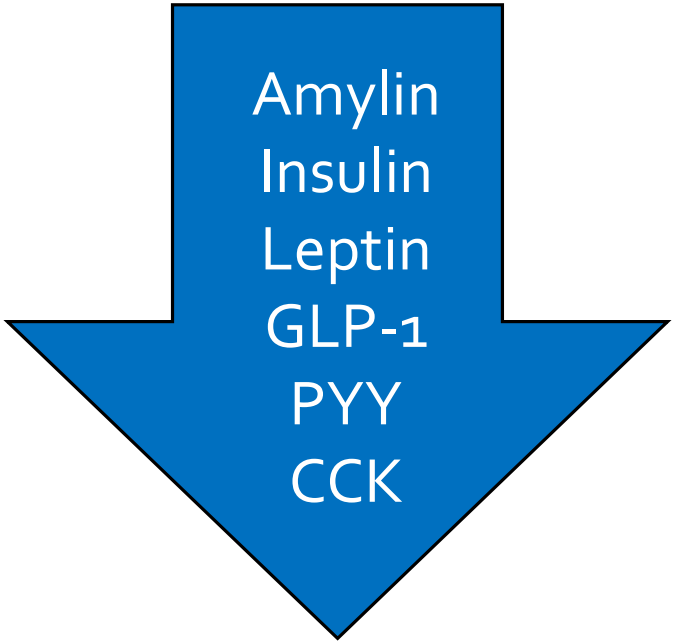
Schwartz MW, Seeley RJ, Zeltser LM, et al. Obesity pathogenesis: an Endocrine Society scientific statement. *Endocr Rev.* 2017;38(4):267–296.
Dickson SL, Chowen JA. Neuroscience of obesity. *Neuroscience.* 2020;447:1–2.

Hunger Hormones



Hunger hormones increase

Satiety hormones decrease



Schwartz MW, Seeley RJ, Zeltser LM, et al. Obesity pathogenesis: an Endocrine Society scientific statement. *Endocr Rev.* 2017;38(4):267–296.
Dickson SL, Chowen JA. Neuroscience of obesity. *Neuroscience.* 2020;447:1–2.

Influences on Obesity

- Leptin
- Glucagon-Like Peptide-1
- Medications

Madsbad S. The role of glucagon-like peptide-1 impairment in obesity and potential therapeutic implications. *Diabetes Obes Metab.* 2014;,16(1):9–21.
Bischoff SC, Schweinlin A. Obesity therapy. *Clin Nutr ESPEN.* 2020;38:9–18.
Kumar RB, Aronne LJ. Iatrogenic obesity. *Endocrinol Metab Clin North Am*. 2020;49(2):265–273.

MEDICATIONS

WEIGHT GAIN VS. WEIGHT LOSS

WHAT ANTIDEPRESSANTS CAN CAUSE WEIGHT GAIN?

WHAT ANTISEIZURE AGENTS CAN CAUSE WEIGHT LOSS?

Medications – Body Weight

Medication Classes	Agents That Increase Weight Gain	Agents That Are Weight Neutral	Agents That Increase Weight Loss
Antidepressants	Lithium, mirtazapine, monoamine oxidase inhibitors, paroxetine, tricyclic antidepressants	Bupropion, citalopram, escitalopram, fluoxetine,* sertraline*	
Antihistamines	Cetirizine, chlorpheniramine, diphenhydramine, fexofenadine, hydroxyzine, levocetirizine	Loratadine	
Antipsychotic agents	Clozapine, olanzapine, quetiapine, risperidone	Aripiprazole, lurasidone, ziprasidone	
Antiseizure agents	Carbamazepine, gabapentin, pregabalin, valproic acid	Lamotrigine, levetiracetam, phenytoin	Topiramate, zonisamide

Bischoff SC, Schweinlin A. Obesity therapy. *Clin Nutr ESPEN*. 2020;38:9–18.
Kumar RB, Aronne LJ. Iatrogenic obesity. *Endocrinol Metab Clin North Am*. 2020;49(2):265–273.

WHAT ANTIDIABETIC MEDICATIONS CAN CAUSE WEIGHT GAIN?

WHAT HIV TREATMENT CLASS CAN CAUSE WEIGHT GAIN?

Medications – Body Weight

Medication Classes	Agents That Increase Weight Gain	Agents That Are Weight Neutral	Agents That Increase Weight Loss
Cardiovascular agents	Alpha-blockers, beta-blockers (except nebivolol, carvedilol)		
Antidiabetics agents	Insulin, meglitinides, sulfonylureas, thiazolidinediones	Alpha-glucosidase inhibitors, bromocriptine colesevelam, dipeptidyl peptidase inhibitors	Glucagon-like peptide-1 receptor agonists, metformin, pramlintide, sodium glucose cotransporter-2 inhibitors
Contraceptives	Some estrogen-based oral contraceptives, progesterone-based subcutaneous implants		
Corticosteroids	Systemic corticosteroids		
Antiretroviral agents	Protease inhibitors		

Bischoff SC, Schweinlin A. Obesity therapy. *Clin Nutr ESPEN*. 2020;38:9–18.
Kumar RB, Aronne LJ. Iatrogenic obesity. *Endocrinol Metab Clin North Am*. 2020;49(2):265–273.

Obesity Related Comorbidities

Type 2 Diabetes	Cancers	Hypertension	Coronary Artery Disease	Congestive Heart Failure	Pulmonary Embolism
Stroke	Asthma	Gallbladder Disease	Osteoarthritis	Chronic Back Pain	Myocardial Infarction
	Nonalcoholic Fatty Livery Disease	Gout	Sleep Apnea	Depression	

Bischoff SC, Schweinlin A. Obesity therapy. *Clin Nutr ESPEN.* 2020;38:9–18.

Guh DP, Zhang W, Bansback N, et al. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC Public Health.* 2009;9:88.

Bray GA, Heisel WE, Afshin A, et al. The science of obesity management: an Endocrine Society scientific statement. *Endocr Rev.* 2018;39(2):79–132.

DiAngelantonio E, Bhupathiraju S, Wormser D, et al; for the Global Mortality Collaboration. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet.* 2016;388(10046):776–786.

General Guidance

Obesity is a disease and not a choice

Management is complex, multimodal and long term

Modest weight loss improves health, comorbidities, glycemic control and cardiometabolic risk factors

Overweight and Class I Obesity

- Weight loss of 5-10% reduced obesity related morbidity and mortality

Class II and III Obesity

- Requires 10-20% reduction in body weight to reduce morbidity and mortality risk

Morbid Obesity

- Requires >30% reduction in body weight to reduce morbidity and mortality risk

Substantial weight loss may only be possible with bariatric surgery in some patients

Bischoff SC, Schweinlin A. Obesity therapy. *Clin Nutr ESPEN*. 2020;38:9–18.
Garvey WT, Mechanick JI, Brett EM, et al. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract*. 2016;3:1–203.
Davies M, Bergenstal R, Bode B, et al; for the NN8022–1922 Study Group. Efficacy of liraglutide for weight loss among patients with type 2 diabetes: the SCALE diabetes randomized clinical trial. *JAMA*. 2015;314(7):687–699.

Eligibility

The American Gastroenterological Association 2022 panel strongly recommended the use of pharmacotherapy in addition to lifestyle intervention (diet and exercise) in adults with:

1) BMI ≥30 kg/m^2 OR
2) BMI ≥27 kg/m^2 and ≥1 weight-associated comorbidity

1) Lifestyle modifications

2) Medication

3) Follow-up

- If patient loses ≥ 5% body weight after 3 months, continue the medication
- If not, discontinue and try alternative medication/approach

Patient specific factors

- Comorbidities
- Patient preference
- Associated adverse effects
- Cost

Bischoff SC, Schweinlin A. Obesity therapy. *Clin Nutr ESPEN*. 2020;38:9–18.
Garvey WT, Mechanick JI, Brett EM, et al. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract*. 2016;3:1–203.
Davies M, Bergenstal R, Bode B, et al; for the NN8022–1922 Study Group. Efficacy of liraglutide for weight loss among patients with type 2 diabetes: the SCALE diabetes randomized clinical trial. *JAMA*. 2015;314(7):687–699.

Lifestyle Modifications

Meal Plan

- Calorie deficit
- Eating patterns:
  - Mediterranean
  - DASH
  - low-carb
  - low-fat
  - intermittent fasting
  - keto
  - Whole 30
  - intuitive eating
  - volumetric
  - high protein
  - vegetarian

Physical Activity

- Aerobic activity:
  - Goal > 150 mins/week
- Resistance exercise
- Decrease sedentary behavior

Behavior

- Goal setting
- Education
- Stress reduction
- Motivational interviewing
- Self-monitoring
- Stimulus control
- Cognitive restructuring
- Psych evaluation, counseling, treatment if needed

Bischoff SC, Schweinlin A. Obesity therapy. *Clin Nutr ESPEN*. 2020;38:9–18.
Garvey WT, Mechanick JI, Brett EM, et al. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract*. 2016;3:1–203.
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Do-it-Yourself	• Overeaters Anonymous • Take off Pounds Sensibly (TOPS)
Nonclinical	• Diet Center • Jenny Craig • Nutri/System • Weight Watchers • Noom • MyFitnessPal
Clinical	• Health Management Resources (HMR) • Medifast, Optifast • New Direction • Medical-based Programs

TIME-RESTRICTED EATING

14:10

16:8

1.Lowe DA, Wu N, Rohdin-Bibby L, et al. Effects of time-restricted eating on weight loss and other metabolic parameters in women and men with overweight and obesity: the TREAT randomized clinical trial. *JAMA*. 2020;180(11):1491–1499.

Bariatric Surgery

Bariatric Surgery Eligibility
BMI 30-34.9 AND diabetes or metabolic syndrome
BMI ≥ 35 AND at least one obesity-related complication (i.e. T2DM, HTN, OSA, GERD, etc)
BMI ≥ 40 without coexisting medical problems

Type	Mechanism
Biliopancreatic diversion +/- duodenal switch	Malabsorptive/Restrictive
Gastric banding	Restrictive
Sleeve gastrectomy	Restrictive (Most common)
Roux-en-Y gastric bypass	Restrictive/Malabsorptive
Vertical banded gastroplasty	Restrictive (Rarely performed)

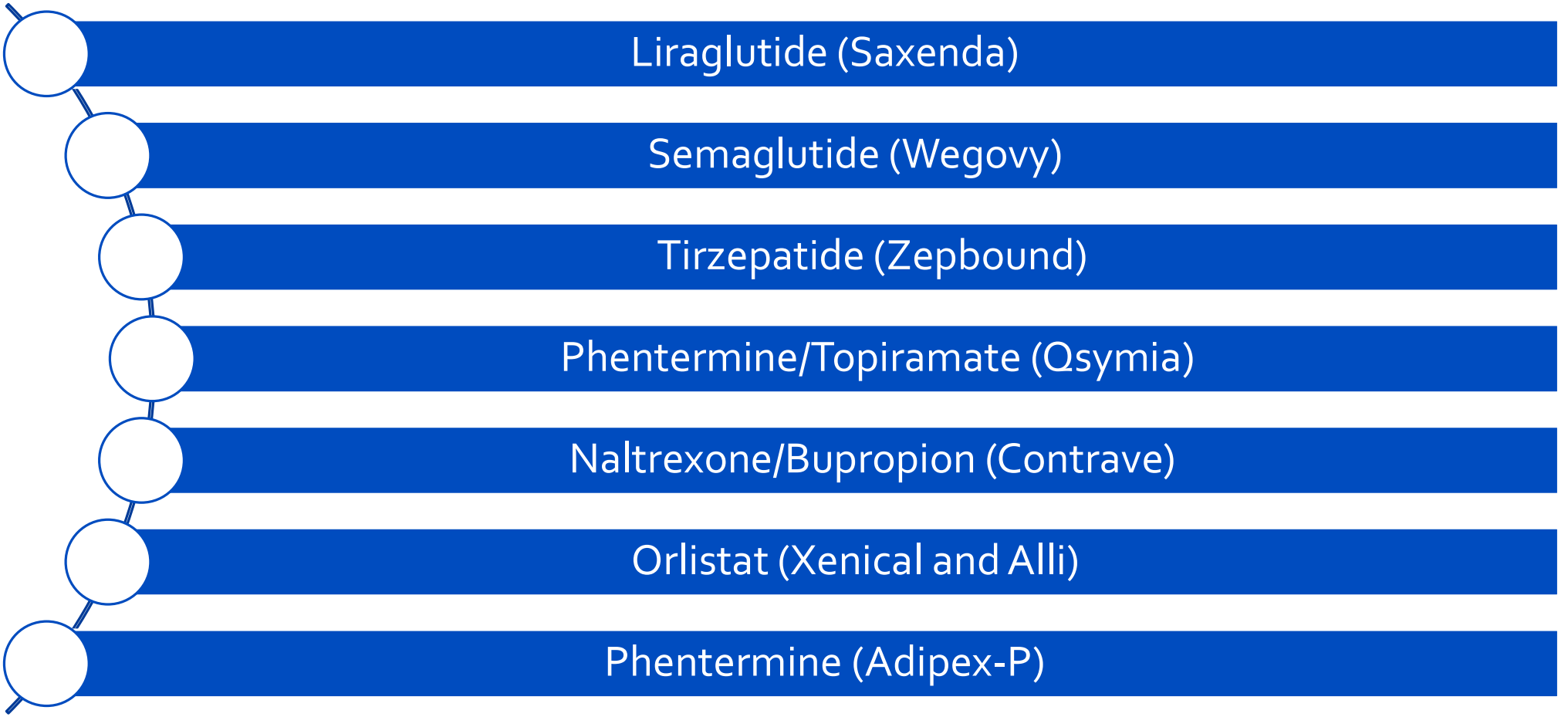
Garvey WT, et al. Endocr Pract. 2016;22(3):1-203. Bariatric Surgery and Medication Use (therapeuticresearch.com).

Special Populations

- Patient Specific Treatments
- BMI < 27 kg/m^2 with Asian descent
- Adolescents
- Pregnant Women

Bray GA, Heisel WE, Afshin A, et al. The science of obesity management: an Endocrine Society scientific statement. *Endocr Rev.* 2018;39(2):79–132.
Garvey WT, Mechanick JI, Brett EM, et al. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract.* 2016;3:1–203.
Apovian CM, ARrone LI, Bessesen DH, et al; for the Endocrine Society. Pharmacological management of obesity: an Endocrine Society clinical practice guidelines. *J Clin Endocrinol Metab.* 2015;100(2):342–362.

Medication Options



FDA Approved Indications

Indication	Dulaglutide	Exenatide	Liraglutide	Semaglutide		Tirzepatide
				SC	Oral	
Glycemic Control in T2D	X	X	X	X	X	X
MACE Reduction in Adults with T2D	X		X	X		
MACE Reduction in Adults with CVD and Overweight/ Obesity				X		
Treatment of Overweight/ Obesity			X	X		X
T2D and CKD to Slow Kidney Disease Progression				X		
Treatment of MASH				X		
Moderate to Severe OSA in Adults with Obesity						X

Saxenda [prescribing information]. Novo Nordisk, Inc.;2025. Accessed August 25, 2025.https://www.novo-pi.com/saxenda.pdf
Wegovy [prescribing information]. Novo Nordisk, Inc.;2025. Accessed August 25, 2025.https://www.novo-pi.com/wegovy.pdf
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Trulicity [prescribing information]. Eli Lilly and Company;2025. Accessed August 25, 2025.https://uspl.lilly.com/trulicity/trulicity.html#pi
Ozempic [prescribing information]. Novo Nordisk, Inc.;2025. Accessed August 25, 2025.https://www.novo-pi.com/ozempic.pdf
Rybelsus [prescribing information]. Novo Nordisk, Inc.;2024. Accessed August 25, 2025.https://www.novo-pi.com/rybelsus.pdf
Mounjaro [prescribing information]. Lilly USA, LLC.;2025. Accessed August 25, 2025.https://uspl.lilly.com/mounjaro/mounjaro.html#pi

GLP-1R

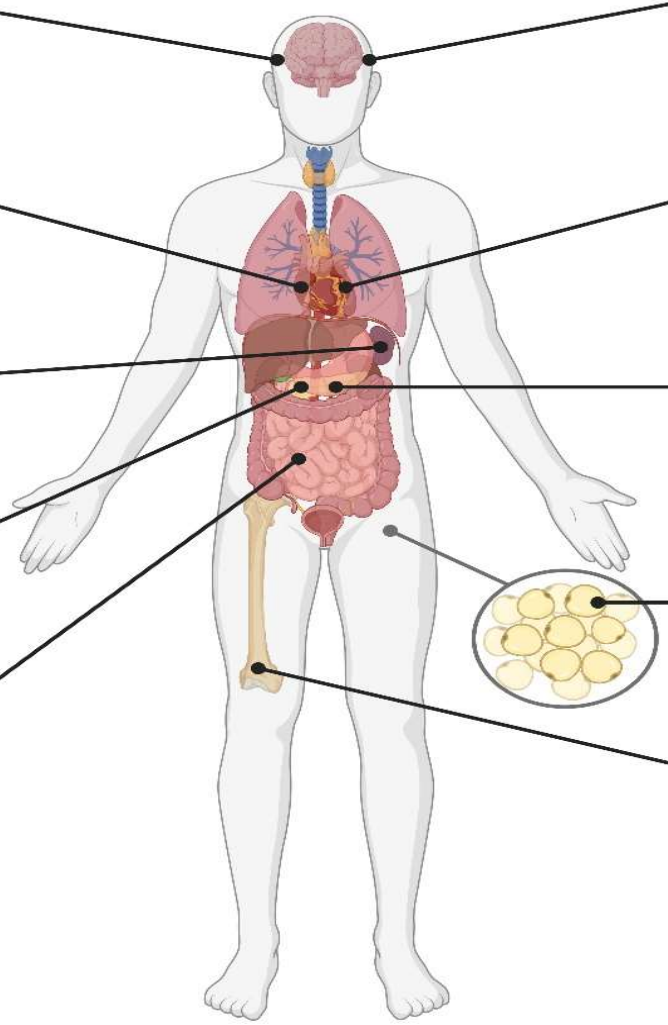
Central Nervous System
Expressed in:
Neurons, astrocytes, oligodendrocytes
Biological Effects:
↓ Caloric intake

Cardiovascular System
Expressed in:
Cardiomyocytes, endothelial cells
Biological Effects:
↑ Heart rate, ↑ cardiac contractility, ↑ vasodilation, ↓ inflammation, ↓ foam cell formation

Kidney
Expressed in:
Vascular smooth muscle cells, macrophages, T lymphocytes, proximal tubule (?)
Biological Effects:
↑ Sodium excretion & diuresis, ↓ inflammation

Pancreas
Expressed in:
β-cells, α-cells, δ-cells
Biological Effects:
↑ ↑ insulin, ↓ ↓ glucagon

Stomach & Intestine
Expressed in:
Enteric neurons, intraepithelial lymphocytes
Biological Effects:
↓ ↓ gastric emptying



GIPR

Central Nervous System
Expressed in:
Neurons, pericytes, oligodendrocytes
Biological Effects:
↓ Appetite and caloric intake (?)

Cardiovascular System
Expressed in:
Cardiomyocytes, pericytes, endothelial cells
Biological Effects:
↑ Heart rate, ↓ inflammation, ↓ foam cell formation, ↓ arterial remodeling, ↓ VSMC proliferation

Pancreas
Expressed in:
β-cells, α-cells, δ-cells, pancreatic polypeptide cells
Biological Effects:
↑ ↑ insulin, ↑ glucagon

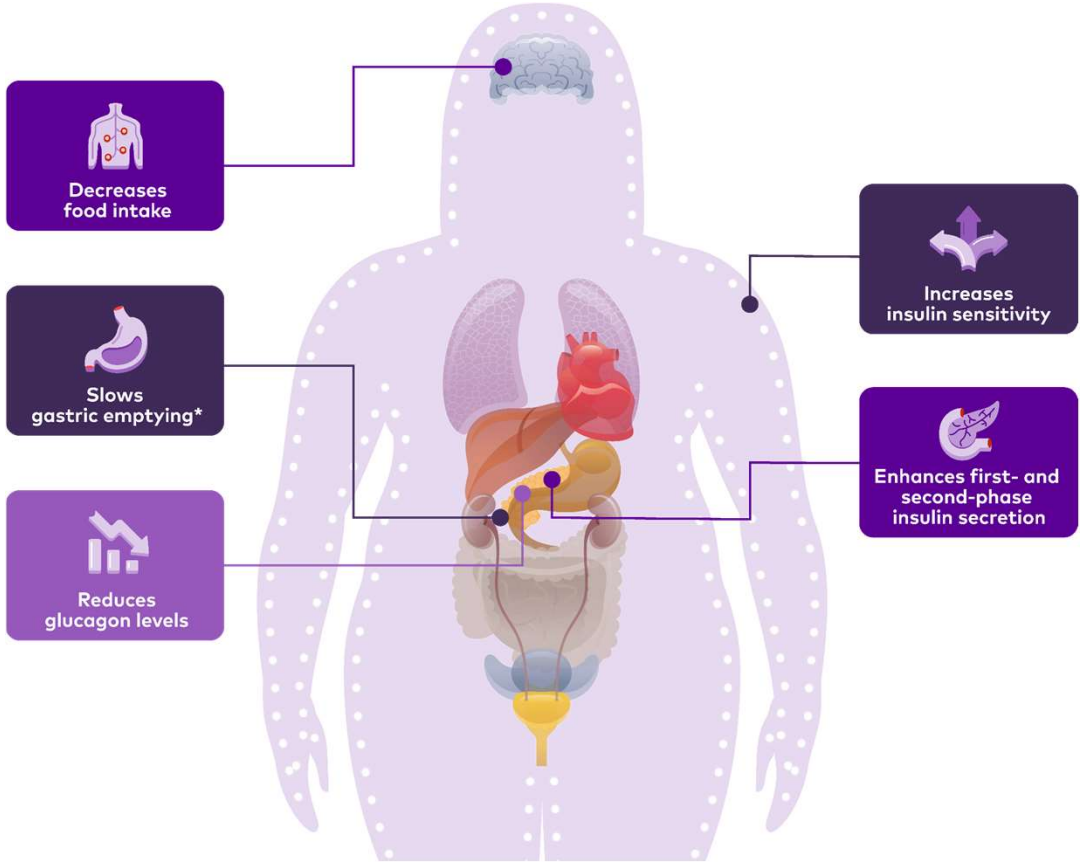
Adipose Tissue
Expressed in:
Pericytes, mesothelial cells
Biological Effects:
↑ ↑ Glucose and triglyceride uptake ↑ insulin sensitivity, ↑ lipoprotein lipase activity

Bone
Expressed in:
Osteocytes, osteoblasts, osteoclasts, myeloid cells, T cells
Biological Effects:
↑ ↑ Meal-associated bone remodeling

Glucagon-Like-Peptide-1 Receptor Agonists

Liraglutide (Saxenda)

Semaglutide (Wegovy)



Madsbad S. The role of glucagon-like peptide-1 impairment in obesity and potential therapeutic implications. *Diabetes Obes Metab.* 2014;16(1):9–21.
Wegovy [product labeling]. Plainsboro, NJ: Novo Nordisk, Inc.; 2021.

GLP1 Receptor Agonists

Contraindications

- Thyroid C-Cell Carcinomas
- Medullary Thyroid Carcinoma (MTC)
- Multiple Endocrine Neoplasia Syndrome Type 2 (MEN 2)

Warnings

- Pancreatitis
- Hypoglycemia
- Acute Gallbladder Disease
- Gastroparesis

Side Effects

- Nausea/Vomiting
- Diarrhea

Saxenda (liraglutide) [prescribing information]. Plainsboro, NJ: Novo Nordisk Inc; April 2023.
Wegovy (semaglutide) [prescribing information]. Plainsboro, NJ: Novo Nordisk Inc; July 2023.

GLP1 Receptor Agonists

Liraglutide (Saxenda)

Ages 12 years and up

- Week 1: 0.6 mg daily
- Week 2: 1.2 mg daily
- Week 3: 1.8 mg daily
- Week 4: 2.4 mg daily
- Week 5+: 3 mg daily
- Subcutaneous Injections

Semaglutide (Wegovy)

Ages 12 years and up

- Week 1-4: 0.25 mg/week
- Week 5-8: 0.5 mg/week
- Week 9-12: 1 mg/week
- Week 13-16: 1.7 mg/week
- Week 17+: 2.4 mg/week
- Subcutaneous Injections

Saxenda (liraglutide) [prescribing information]. Plainsboro, NJ: Novo Nordisk Inc; April 2023.
Wegovy (semaglutide) [prescribing information]. Plainsboro, NJ: Novo Nordisk Inc; July 2023.

XENSOR Study and SCALE Trial

- **Objective:** Compare Orlistat and liraglutide for weight loss management
- **Methods:** Retrospective, observational cohort study comparing clinical outcomes of orlistat 120 mg three times a day and liraglutide (up to 3 mg daily) in adult patients with BMI ≥30 kg/m² or ≥27 kg/m² with at least a weight-related comorbidity who had failed to lose at least 5% of their weight after 6 months of lifestyle modification. The co-primary end-points, assessed at 3-6 months and at the end of the follow-up, were weight change from baseline, proportion of patients who lost at least 5% of their baseline weight and adjusted differences in weight loss between both drugs.
- **Results:** Treatment with both drugs significantly reduced weight, fasting plasma glucose, systolic BP, low-density lipoprotein-cholesterol and alanine transaminase over a median follow-up period of 7 months. Weight loss with liraglutide (-7.7 kg) was significantly greater than that observed with orlistat (-3.3 kg), and more individuals lost at least 5% of their baseline weight with liraglutide (64.7%) than with orlistat (27.4%). Rates of prediabetes significantly decreased with liraglutide in comparison to orlistat.
- **Conclusions:** In this real-world study, liraglutide showed a greater effectiveness in weight loss compared with orlistat and improved several obesity-associated metabolic and cardiovascular risk factors.

Gorgojo-Martínez JJ, Basagoiti-Carreño B, Sanz-Velasco A, Serrano-Moreno C, Almodóvar-Ruiz F. Effectiveness and tolerability of orlistat and liraglutide in patients with obesity in a real-world setting: The XENSOR Study. Int J Clin Pract. 2019 Nov;73(11):e13399. doi: 10.1111/ijcp.13399. Epub 2019 Aug 19. PMID: 31397946.

Davies M, Bergenstal R, Bode B, et al; for the NN8022–1922 Study Group. Efficacy of liraglutide for weight loss among patients with type 2 diabetes: the SCALE diabetes randomized clinical trial. *JAMA*. 2015;314(7):687–699.

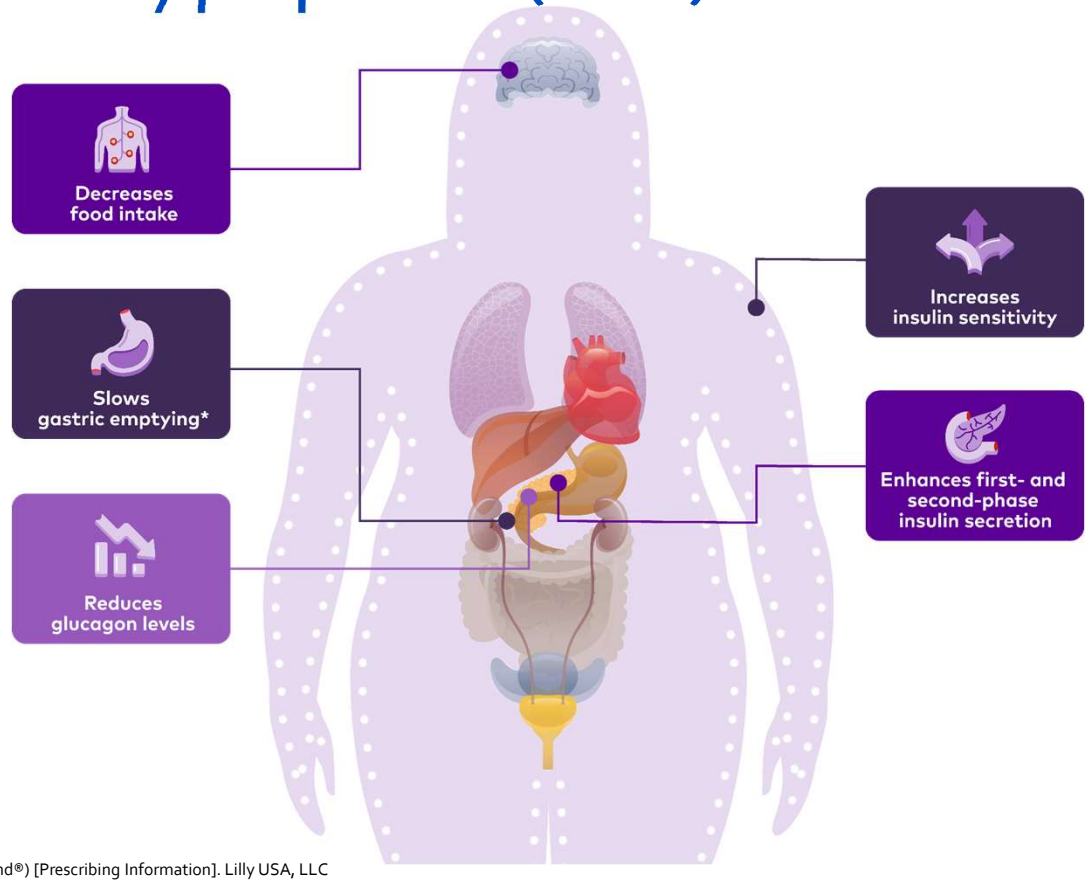
STEP 1 Trial

- **Objective:** Addition of semaglutide to lifestyle modifications versus placebo alone
- **Methods:** Double-blind trial, we enrolled 1961 adults with a body-mass index of 30 or greater (≥27 in persons with ≥1 weight-related coexisting condition), who did not have diabetes, and randomly assigned them, in a 2:1 ratio, to 68 weeks of treatment with once-weekly subcutaneous semaglutide (at a dose of 2.4 mg) or placebo, plus lifestyle intervention. The coprimary end points were the percentage change in body weight and weight reduction of at least 5%.
- **Results:** The mean change in body weight from baseline to week 68 was −14.9% in the semaglutide group as compared with −2.4% with placebo, for an estimated treatment difference of −12.4 percentage points. More participants in the semaglutide group than in the placebo group achieved weight reductions of 5% or more, 105 or more and 15% or more. The change in body weight from baseline to week 68 was −15.3 kg in the semaglutide group as compared with −2.6 kg in the placebo group. Participants who received semaglutide had a greater improvement with respect to cardiometabolic risk factors and a greater increase in participant-reported physical functioning from baseline than those who received placebo. Nausea and diarrhea were the most common adverse events with semaglutide; they were typically transient and mild-to-moderate in severity and subsided with time. More participants in the semaglutide group than in the placebo group discontinued treatment owing to gastrointestinal events.
- **Conclusions:** In participants with overweight or obesity, 2.4 mg of semaglutide once weekly plus lifestyle intervention was associated with sustained, clinically relevant reduction in body weight.

Wilding, John PH, et al. "Once-weekly semaglutide in adults with overweight or obesity." *New England Journal of Medicine* 384.11 (2021): 989-1002.

GLP-1 Agonist and Glucose-Dependent Insulinotropic Polypeptide (GIP)

Tirzepatide (Zepbound)



Tirzepatide (Zepbound®) [Prescribing Information]. Lilly USA, LLC

GLP1 Receptor Agonist/GIP

Contraindications

- Thyroid C-Cell Carcinomas
- Medullary Thyroid Carcinoma (MTC)
- Multiple Endocrine Neoplasia Syndrome Type 2 (MEN 2)

Warnings

- Pancreatitis
- Hypoglycemia
- Acute Gallbladder Disease
- Gastroparesis
- Acute Kidney Injury
- Diabetic Retinopathy
- Decreased effectiveness of OC

Side Effects

- Nausea/Vomiting
- Diarrhea

Tirzepatide (Zepbound®) [Prescribing Information]. Lilly USA, LLC

GLP1 Receptor Agonist/GIP

Tirzepatide (Zepbound)

Ages 18 years and up

- Week 1-4: 2.5 mg/week
- Week 5-8: 5 mg/week
- Week 9-12: 7.5 mg/week
- Week 13-16: 10 mg/week
- Week 17-20: 12.5 mg/week
- Weeks 21+: 15 mg/week
- Subcutaneous Injections

Tirzepatide (Zepbound®) [Prescribing Information]. Lilly USA, LLC

Surmount

- **Objective:** Comparison of tirzepatide weekly compared to placebo
- **Methods:** Double-blind, randomized, controlled trial, adults with a body-mass index (BMI) of 30 or more, or 27 or more and at least one weight-related complication, excluding diabetes, in a 1:1:1:1 ratio to receive once-weekly, subcutaneous tirzepatide (5 mg, 10 mg, or 15 mg) or placebo for 72 weeks, including a 20-week dose-escalation period. Coprimary end points were the percentage change in weight from baseline and a weight reduction of 5% or more.
- **Results:** The mean percentage change in weight at week 72 was −15.0% with 5-mg weekly doses of tirzepatide, −19.5% with 10-mg doses, and −20.9% with 15-mg doses and −3.1% with placebo ($P<0.001$ for all comparisons with placebo). Improvements in all prespecified cardiometabolic measures were observed with tirzepatide. The most common adverse events with tirzepatide were gastrointestinal, and most were mild to moderate in severity, occurring primarily during dose escalation.
- **Conclusions:** In this 72-week trial in participants with obesity, 5 mg, 10 mg, or 15 mg of tirzepatide once weekly provided substantial and sustained reductions in body weight.

Jastreboff, Ania M., et al. "Tirzepatide once weekly for the treatment of obesity." *New England Journal of Medicine* 387.3 (2022): 205-216.

Weight Loss Outcomes

	Liraglutide	SC Semaglutide	Tirzepatide
Dose(s)	3 mg daily	2.4 mg weekly	5 mg, 10 mg, 15 mg weekly
% Weight loss, PBO-subtracted (trial length)	5.4% (56 weeks)	12.5% (68 weeks)	5 mg: 11.9% (72 weeks) 10 mg: 16.4% (72 weeks) 15 mg: 17.8% (72 weeks)
Long-term % weight loss, PBO-subtracted (trial length)	4.2% (3 years)	12.6% (104 weeks)	5 mg: 11.0% (176 weeks) 10 mg: 17.4% (176 weeks) 15 mg: 18.4% (176 weeks)
% Achieving ≥ 5% weight loss (trial length)	LIRA: 63.2% (56 weeks) PBO: 27.1% (56 weeks)	SEMA: 86.4% (68 weeks) PBO: 31.5% (68 weeks)	5 mg: 85.1% (72 weeks) 10 mg: 88.9% (72 weeks) 15 mg: 90.9% (72 weeks) PBO: 34.5% (72 weeks)
% Achieving ≥ 10% weight loss (trial length)	LIRA: 33.1% (56 weeks) PBO: 10.6% (56 weeks)	SEMA: 69.1% (68 weeks) PBO: 12.0% (68 weeks)	5 mg: 68.5% (72 weeks) 10 mg: 78.1% (72 weeks) 15 mg: 83.5% (72 weeks) PBO: 18.8% (72 weeks)

Pi-Sunyer X, Astrup A, Fujioka K, et al. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. *N Engl J Med*. 2015;373(1):11-22.
le Roux CW, Astrup A, Fujioka K, et al. 3 years of liraglutide versus placebo for type 2 diabetes risk reduction and weight management in individuals with prediabetes: a randomised, double-blind trial. *Lancet*. 2017;289(10077):1399-1409.
Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384(11):989-1002.
Garvey WT, Batterham RL, Bhatta M, et al. Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. *Nat Med*. 2022;28(10):2083-2091.
Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide once weekly for the treatment of obesity. *N Engl J Med*. 2022;387(3):205-216.
Jastreboff AM, le Roux CW, Stefanski A, et al. Tirzepatide for obesity treatment and diabetes prevention. *N Engl J Med*. 2025;392(10):958-971.

Phentermine/Topiramate (Qsymia)

Mechanism of Action

- Suppresses appetite and increases satiety
- Phentermine – Andrenergic activation
- Topiramate – Unknown but may involve carbonic anhydrase inhibition-induced taste disorder and decreased appetite

REMS Program

- Teratogenic

Contraindications

- Pregnancy
- Hypertension
- Hyperthyroidism
- Glaucoma

Side Effects

- Tachycardia
- Insomnia
- Increased Serum Creatinine
- Hypokalemia
- Numbness/Tingling
- Taste disturbances

Ages 18 years and up

Week 1-2: 3.75mg/23mg capsule every morning

Week 3-12: 7.5mg/46mg capsule every morning

Week 13-14: 11.25mg/69mg capsule every morning

Week 15+: 15mg/92mg capsule every morning

Discontinue gradually if stopping

Qsymia (phentermine/topiramate) [prescribing information]. Campbell, CA: VIVUS LLC; June 2023.

Naltrexone/Bupropion (Contrave)

Mechanism of Action

- Opioid antagonist/dopamine and norepinephrine reuptake inhibitor
- Mechanism unclear, works on hypothalamus/mesolimbic dopamine circuit to reduce food cravings and appetite

Black Box Warning

- Can increase risk of suicidal thinking and behavior in children

Contraindications

- Opioid Use
- Uncontrolled Hypertension
- Seizure disorder
- Pregnancy
- Avoid with high fat meal

Side Effects

- Nausea/Vomiting
- Headache
- Constipation
- Dry Mouth

Ages 18 years and up

Dose – 8mg/90mg tablets

Week 1: 1 tablet every morning

Week 2: 1 tablet in the morning and 1 tablet in the evening

Week 3: 2 tablets in the morning and 1 tablet in the evening

Week 4+: 2 tablets in the morning and 2 tablets in the evening

Contrave (naltrexone and bupropion) [prescribing information]. Brentwood, TN: Currax Pharmaceuticals LLC; December 2022.

Orlistat (Xenical, Alli)

Mechanism of Action

- Lipase Inhibitor
- Decreases absorption of dietary fats by 30%

Contraindications

- Chronic Malabsorption Syndrome

Warnings

- Liver damage (rare)
- Cholelithiasis
- Kidney stones

Side Effects

- Gastrointestinal (flatus with discharge, fatty stool, fecal urgency)
- Decreased absorption of vitamins ADEK, recommended to add MVI taken at time other than orlistat

Ages 12 years and up

Xenical – 120mg TID with meals

Alli – 60mg TID with meals

Alli (orlistat) [prescribing information]. Warren, NJ: GSK Consumer Healthcare; received June 2017.
Xenical (orlistat) [prescribing information]. Montgomery, AL: H2-Pharma LLC; November 2022.

		Liraglutide, Semaglutide	Tirzepatide	Orlistat	Qsymia	Contrave
CVD		Monitor HR	Monitor HR	Safe	Avoid	Avoid
Hypertension		Safe	Safe	Safe	Caution	Caution
Depression		Safe	Safe	Safe	Safe	Avoid
Type 2 DM		Safe	Safe	Safe	Safe	Safe
Hx of Seizures		Safe	Safe	Safe	Caution	Avoid
Opioids		Safe	Safe	Safe	Safe	Avoid
Pregnancy		Avoid	Avoid	Avoid	Avoid	Avoid
CKD	30-49 ml/min	Avoid dehydration	Avoid dehydration	Safe	Max 7.5/46 mg QD	Max 8/90 mg BID
	<30 ml/min	Avoid dehydration	Avoid dehydration	Safe	Avoid	Avoid

Gastroenterology. 2022; 163: 1198-1225.

Withdrawn From Market

Lorcaserin (Belviq)

"Belviq, Belviq XR (lorcaserin) by Eisai: Drug Safety Communication - FDA Requests Withdrawal of Weight-Loss Drug". *U.S. Food and Drug Administration (FDA)*. 13 February 2020. Retrieved 18 February 2020.

In the Pipeline!

- Retatrutide
- Oral Semaglutide

Appropriate Language

Avoid using pejorative language, such as: "You really need to do something about your weight." Instead, use proactive language, such as: "How do you feel about your weight?"

Avoid terms like "obese," "fat," or "chubby." Instead, refer to people as "a person with obesity."

Avoid using superlatives, such as "morbid" or "extreme" to describe the severity of obesity. Instead, use terms like "severe obesity" or communicate the objective obesity class or stage.

Bannuru RR; Professional Practice Committee. Weight stigma and bias: standards of care in overweight and obesity – 2025. *BMJ Open Diabetes Res Care*. 2025;13(Suppl. 1):e004962.

Combat Weight Stigma and Bias

Implement protocols to minimize risk of stigmatization during provision of healthcare services, including anthropometric measurements and communication practices for person-centered care.

Ensure availability of clinical equipment and furniture that accommodates all individuals (e.g., waiting room chairs, examination tables, gowns, blood pressure cuffs, high-capacity scales).

Make accommodations to provide privacy during anthropometric measurements, including locating the scale in a private area.

Engage individuals in shared decision-making to individualize diagnostic and treatment approaches, including collaborative goal setting beyond weight reduction. Support and collaborate with individuals on long-term obesity care.

Ask permission to discuss an individual's weight, and respect autonomy if they decline by refraining from forcing the conversation. If individuals accept, inquire about their preferred terms/words to discuss weight.

Bannuru RR; Professional Practice Committee. Weight stigma and bias: standards of care in overweight and obesity – 2025. *BMJ Open Diabetes Res Care*. 2025;13(Suppl. 1):e004962.

MELT THE POUNDS FEEL PROFOUND!

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