
Weight Management In the Era of GLP-1 Pharmacotherapy

JENNIFER JUNGEN, MPAS, PA-C

IOWA HEALTH CARE

DEPARTMENT OF INTERNAL MEDICINE

DIVISION OF ENDOCRINOLOGY

WEIGHT MANAGEMENT CLINIC

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Disclosures and Definitions:

- Disclosures: None
- Glucagon-like Peptide 1 (GLP-1) receptor agonist and Glucose-Dependent Insulinotropic Polypeptide (GIP) receptor agonist pharmacotherapy will be referred to collectively as GLP-1 therapy during this presentation.
- This presentation pertains to GLP-1 therapy for weight management, not diabetes mellitus type 2

Objectives

- Review pathophysiology of obesity as a chronic disease
- Describe classification systems of obesity
- Recognize the appropriate history to obtain and physical exam to perform when evaluating a patient who wants to discuss weight management
- Identify patients who may benefit from treatment with GLP-1 therapy
- Discuss alternative therapy when GLP-1 therapy may not be appropriate, tolerated, accepted or is contraindicated
- Discuss the benefits, risks and common side effects of GLP-1 therapy
- Understand lifestyle and behavioral recommendations that are necessary in the treatment plan when prescribing GLP-1 therapy

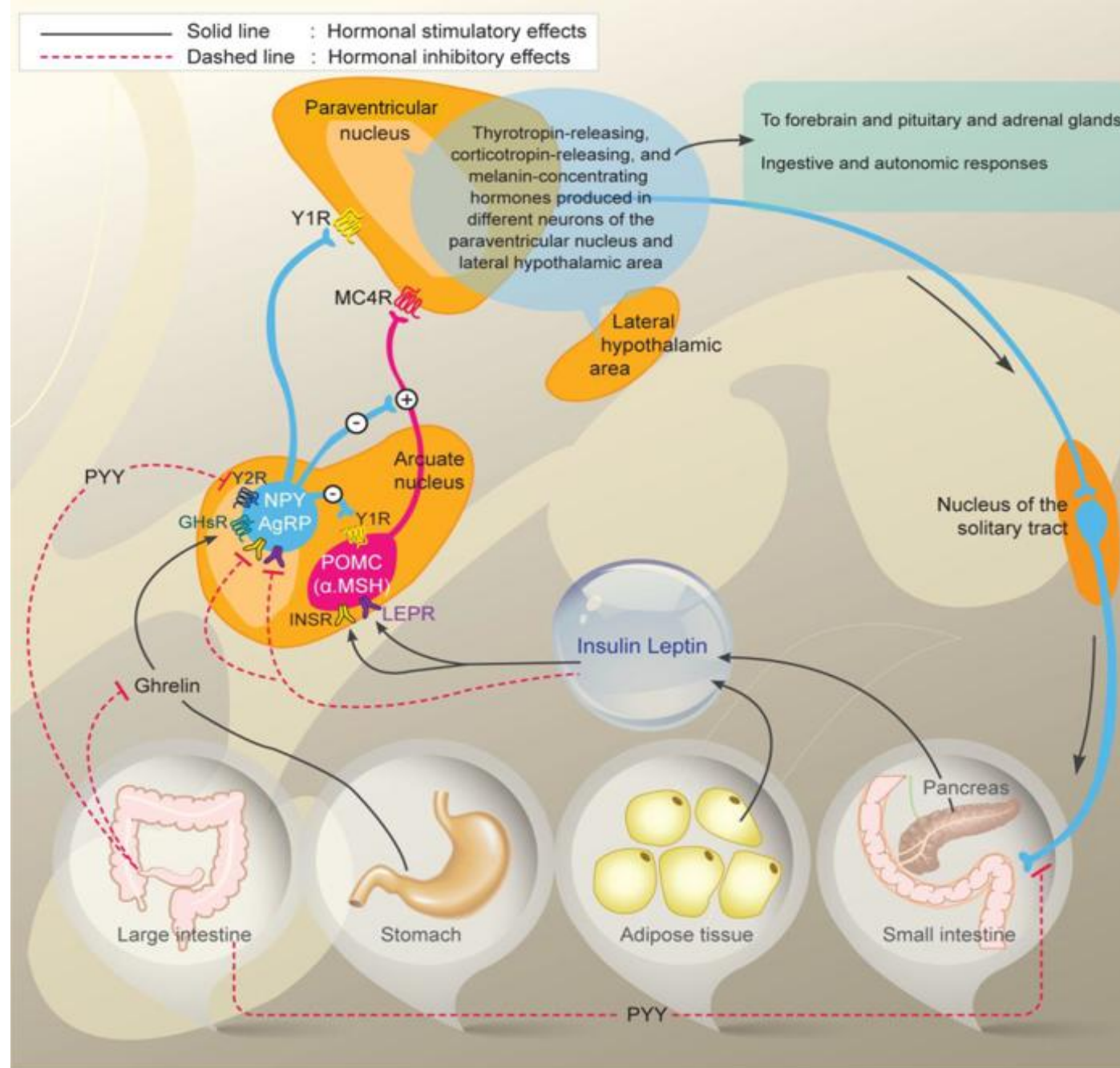
Foundation for This Presentation

- “Nutritional priorities to support GLP-1 therapy, glucagon-like peptide receptor agonists and combination”

Dariush Mozaffarian, et al. Nutritional priorities to support GLP-1 therapy for obesity: A joint Advisory from the American College of Lifestyle Medicine, the American Society for Nutrition, the Obesity Medicine Association, and The Obesity Society, Obesity (Silver Spring). 2025;33:1475–1503.

- Other references
 - Obesity Medicine Association
 - The Obesity Society
 - ConscienHealth newsletter
 - Obesity and Energetics Offerings

Obesity is Complex



Apovian, J Clin Endocrinol Metab, February 2015, 100(2):342–362

Weight Regulation

Factors affecting weight

Genetics determines 80-90% of our weight

Syndromic obesity- Bardet-Biedl, Prader Willi

Social and cultural norms

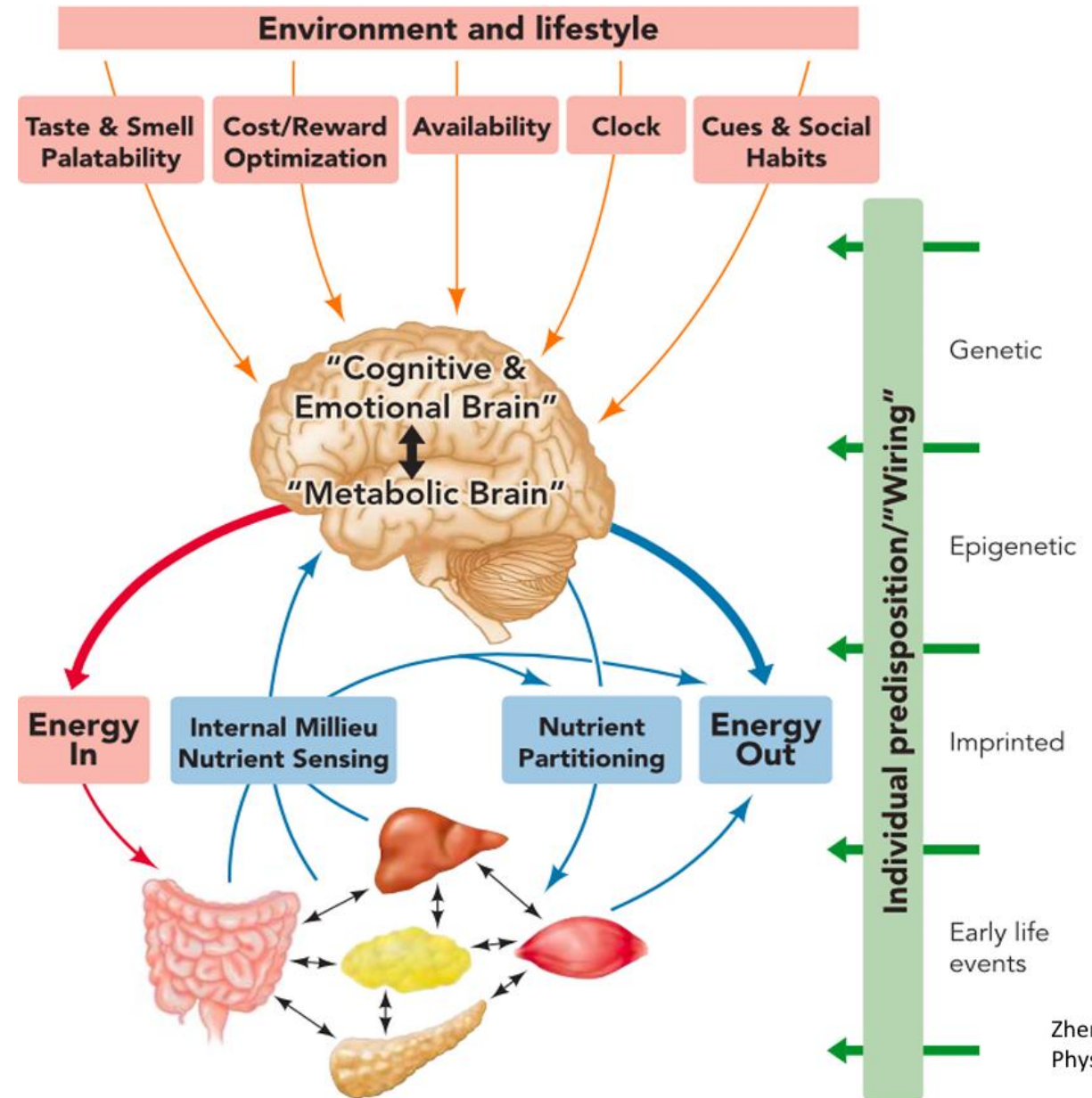
Social determinants of health

- Finances
- History of or current food insecurity
- Food deserts

Health conditions

Obesogenic Medications

- Steroids
- Anti-psychotics
- Anti-hypertensives
- Contraception
- Anti-histamines
- Anti-epileptic
- Insulin



Causes of Obesity

Clinical Signs and symptoms	Young age of onset Hyperphagia Red hair Hypopigmentation Extreme weight difference between family members	Young age of onset Dysmorphic features Developmental delay Autism or ADD Short stature (Poly-) syndactyly Retinal abnormalities Severe myopia Congenital deafness Nephropathy	Cranial radiotherapy/ Head trauma/ Surgery Neurological abnormalities Hyperphagia Decreased vision	Acne Hirsutism Irregular menses Acanthosis nigricans Erectile dysfunction Post- pregnancy Menopause	Bradycardia Muscle weakness Cushingoid features History of radiotherapy or severe head trauma	Weight increase related to initiation or dose increase of a drug with weight gain as a potential adverse effect	Severe repeated binge-eating with or without inadequate compensation behavior Depressive complaints	Unhealthy food intake Lack of exercise Average sleep < 7hrs Disturbed sleep Snoring/apnea Shift work Alcohol use Stress Smoking cessation Sociocultural background Meal timing Sedentary lifestyle
	(Mono-)genetic or syndromic		Hypothalamic	Endocrine		Medication	Mental disorders	Lifestyle
	Examples	Defect or deficiency: MC4R Leptine (R) POMC Prohormone convertase-1	Prader Willi Bardet Biedl Allbright 16p11.2deletion	Post-radiation therapy Post-surgery Hypothalamic tumor Malformation	PCOS Hypogonadism Post pregnancy weight retention Menopause	(Cyclic) Cushing's syndrome Hypothyroidism Growth Hormone Deficiency	Antidepressants Antipsychotics Anti-epileptics (local)corticosteroids (some) β-blockers Insulin	Binge-eating disorder Bulimia Nervosa Depression Other specified feeding and eating disorders

van der Valk. Diagnostic approach obesity. Obes Rev. 2019.

Obesity Prevalence

- The chronic disease of obesity affects 40.3% of Americans
- 9.4% with severe obesity- Class III Obesity or BMI >40.0
 - Linked to multiple other diseases including
 - Diabetes mellitus type 2 (50%)
 - MI
 - CKD
 - Stroke
 - OSA (70%)
 - HTN (65-78%)
 - 13 types of obesity related cancers (liver, endometrial, gallbladder, esophageal in men, stomach, colorectal, pancreatic, renal, breast, ovarian, thyroid, ect.)
 - Reduces life expectancy by up to 10 years in severe obesity
- Obesity costs the US healthcare system \$173 billion per year
- (www.cdc.gov)

Defining Obesity

BMI

Normal BMI 18.5 to less than 25 kilograms per square meter

Overweight: 25-30

Class I Obesity: 30 - <35

Class II Obesity: 35 - <40

Class III Obesity: BMI >40

Poor surrogate marker of actual adiposity or relative body fat

Asian decent obese BMI is >25 and a BMI >23 may indicate increased health risks

Waist to Height Ratio

Calculated by dividing waist circumference (in meters) by height (in meters)

WHtR >0.5 in general is associated with increased risk
<0.4 is considered underweight

Better at capturing normal BMI but with central adiposity distribution (17% of men, 6% of women)

More closely associated with CVD risk

Bioimpedence analysis

Scales send low-level electrical current through body to measure the resistance (impedance) of different body tissues

Accuracy can vary

Estimates % fat, muscle, other tissues

Overweight body fat% (varies by age)

>25% men

>36% women

Obesity body fat% (varies by age)

>30% men

>42% women

Most practical and accessible technology for routine body composition including body fat measurement. Lower cost.

Potter, et al. J Clin Endocriol Metab. 2025

Defining Obesity

- Other methods:
 - Dual x-ray absorptiometry (DXA):
Gold standard- the most accurate and reliable methods for assessing body composition, including body fat %
 - Air displacement plethysmography (bod pod)
 - Picture courtesy of uaa.alaska.edu
 - CT
 - MRI
 - U/S



Defining Obesity

- Lancet Diabetes and Endocrinology Global Commission
- Took 2.5 years to develop, consisted of 58 commissioners
- Definition requires, in addition to BMI, a measurement of body fat, such as waist circumference, waist-hip ratio, waist-height ratio
- Preclinical obesity
 - Excess body fat with no current organ dysfunction or limitations of ADLs but increased risk of future health problems
- Clinical obesity
 - BMI >40
 - In addition to BMI (>30) and fat distribution, clinical obesity requires at least 1 of 18 “obesity-related diseases” for adults or at least 1 of 13 organ, tissue or body systems for children and adolescents.

- The Lancet Diabetes Endocrinology. Redefining obesity: advancing care for better lives. Lancet Diabetes Endocrinol. 2025 Feb;13(2):75. doi: 10.1016/S2213-8587(25)00004-X. Epub 2025 Jan 15. PMID: 39826562

Initial Evaluation- this is not a 15 min visit

- Ask about patient's concerns
- Why is weight management important to the patient and goals?
- Weight history
 - Weight in childhood, adolescence, early adulthood, mid-life, current, ect.
 - History of **hyperphagia**, sneaking or hiding food and why (genetic syndrome?)
 - Women- pregnancy, starting weight, weight at delivery, did wt decrease after birth?
 - Any life events that dramatically impacted weight (increase or decrease) including marriage, divorce, children (men and women), occupations, shift work, stress, surgery, injury, change in activity level, ect.
 - Previous attempts at weight management and response including commercial programs, prescription/non-prescription medications, bariatric surgery
- Family history: Obesity, medullary thyroid cancer, MEN2 (multiple endocrine neoplasia)

Dietary History

- 24 hr dietary recall (everything patient ate in last 24 hours). Many other dietary questionnaires available (Mini-EAT) but 24 hr dietary recall is well validated and easy to implement.
 - Breakfast, lunch, dinner, snacks and timing of snacks
 - If it was an unusual meal/day, ask what is typical
 - Hydration
 - Rate of eating and what causes patient to stop eating (“clean plate club”, just satisfied, stuffed)
 - Eating out- how many meals per week and what type of establishment.
 - Cravings- does food call out to you and if so, what type?
 - Food preferences (cultural, “food fussiness”) and intolerances (celiac disease, lactose intolerance)
 - History of food insecurity now or in the past
 - Availability of energy dense low-cost food was the primary driver of obesity with food insecurity
- Carvajal-Aldaz D, Cucalon G, Ordonez C. Food insecurity as a risk factor for obesity: A review. Front Nutr. 2022 Sep 26;9:1012734. doi:10.3389/fnut.2022.1012734. PMID: 36225872; PMCID: PMC9549066.

Activity and Mental Health

- Current activity level- what type, how many days/week, how many minutes
Several screening tools available
 - Mental health screening- stress, depression, anxiety
 - May promote obesity development through the sympathetic nervous system and hypothalamic–pituitary–adrenal axis activation
 - Elevates cortisol levels
 - Interferes with insulin sensitivity
 - Promotes energy storage
 - Creates food cravings for ultra-processed “comfort foods”
- Scott KA, Melhorn SJ, Sakai RR. Effects of chronic social stress on obesity. *Curr Obes Rep*. 2012; 1(1): 16-25.
- Substance abuse, past or present
 - Social connections- who lives with the patient?

Mental Health

- Disordered eating- past or present
 - Binge eating disorder
 - Early indications that GLP-1 therapy may be beneficial as a treatment for binge eating disorder
 - Anorexia nervosa
 - Bulimia
 - Night eating syndrome
- Restrictive eating pattern
- Emotional eating
- **If you are concerned patient has an eating disorder, consider referral to an ED behavioral therapist and/or a weight management specialist prior to initiating GLP-1 therapy**

Other Screening Questions

- Sleep
 - OSA- increases hunger hormones, decrease satiety hormones, decreases patient's willingness to be active
 - "Night owl"- disrupts circadian rhythm
 - Sleep disorders
 - Shift work sleep disorder
- Current occupation and hours- sedentary? shift work?
- ROS- Cushing syndrome, PCOS, osteoporosis, osteopenia, nephrolithiasis, sarcopenia, pancreatitis, thyroid dysfunction
- Ask patient what they think their barrier is to weight management
- Thoughts about bariatric surgery
- Tondt J, Freshwater M, Benson-Davies S, et al. *2024 Obesity Algorithm® E-book*. Obesity Medicine Association; 2024

Baseline Physical Exam Screening

- Usual exam of cardiorespiratory system
- Abdominal exam- RUQ for hepatomegaly, tenderness with palpation of gallbladder (if applicable); eval for hernia, abdominal distension, abdominal striae (Cushing syndrome)
- Skin- acanthosis nigricans, striae, acne, hirsutism
- HEENT: Pupils/vision (pituitary exam), thyroid exam, buffalo hump, moon facie
- Strength- grip strength, sit to stand time, walk speed
- Extremities- edema, venous stasis
- Lipedema of arms and/or legs, cuff sign and Stemmer's sign

Lipedema

- www.lipedema.org
- Congenital disorder of connective tissue
- Primarily affects women- up to 10-11% of women globally
- Worsens at times of hormonal flux- puberty, pregnancy, menopause
- Affects legs and sometimes the arms and lower trunk
- Can cause pain, tenderness, swelling and easy bruising
- The pain may range from none to severe
- May be accompanied by unusual nodular and/or fibrotic texture within the adipose tissue
- Resistant to weight loss attempts
- Not associated with metabolic dysfunction

Lipedema



Additional Screening

- Labs: CBC, CMP, HbA1c, TSH/reflex T4, fasting lipid panel, vitamin D, others as appropriate
 - Hypertriglyceridemia (>500) is a relative contra-indication of GLP-1 use due to risk of pancreatitis. Treat this first and then initiate GLP-1
Weight loss can temporarily increase triglyceride levels as the body mobilizes fat stores for energy
- Guidelines do not recommend routine screening (beyond history and exam) of thyroid or gallbladder prior to initiation of GLP-1 therapy unless there is another reason to do so

FDA approved medications, with lifestyle and behavioral changes, for patients with obesity (BMI >30) or overweight (>27) with 1 or more weight-related conditions

Phentermine

Adipex 37.5 mg, Lomaira 8mg

Appetite suppressant

Previously short term, 12 weeks

Newer medical guidelines added it to long term treatment

5% body weight loss

SE include headache, anxiety, hypertension, insomnia, tachycardia, vision changes, dry mouth

Phentermine/topiramate

Qsymia

In addition to appetite suppression, helps with cravings

Good for patients with headaches too

5-10% body weight loss

Side effects of phentermine above. Topiramate additional SE paresthesia, dizziness, somnolence, "brain fog", vision changes, nephrolithiasis,

Bupropion/Naltrexone

Contrave

Good for pleasure/reward of food to decrease cravings and appetite

5-10% body weight loss

Side effects include nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea

Orlistat

Xenical and Alli

Lipase inhibitor, blocks fat absorption

Significant GI side effects

Setmelanotide

Imcivree

Melanocortin-4 receptor agonist

For rare genetic disorders

Studied for hypothalamic obesity

FDA approved GLP-1 Medications (in addition to lifestyle and behavioral modifications)

- FDA approval of 3 GLP-1 medications for weight management in persons with obesity (BMI >30) or overweight (>27) with 1 or more weight-related conditions
- Liraglutide (Saxenda) Dec, 2014
 - Generic liraglutide for weight management approved Aug 2025
 - Generic liraglutide for diabetes mellitus type 2 (Victoza) approved Dec 2024
- Semaglutide (Wegovy) June, 2021
- Tirzepatide (Zepbound) Nov, 2023; GLP-1 and GIP dual agonist

FDA Approved GLP-1 Medications (in addition to lifestyle and behavioral modifications)

- **Liraglutide** (Saxenda) daily injection, starting at 0.6 mg and increasing by 0.6 mg every week until reach 3 mg, SCALE trials
 - *Average weight reduction 11%.*
- **Semaglutide** (Wegovy) 0.25, 0.5, 1.0, 1.7, 2.4 mg weekly, STEP trials
 - *Average weight reduction of 14.9% at the higher doses.*
 - 2.4 mg approved to reduce the risk of **major adverse cardiovascular** events in patients with established cardiovascular disease and either obesity or overweight.
 - 2.4 mg approved to treat adults with **metabolic dysfunction-associated steatohepatitis (MASH)** with moderate to advanced liver scarring (fibrosis), but not with cirrhosis of the liver in conjunction with reduced calorie diet and increased physical activity.
 - 2.4 mg approved to prevent worsening of **kidney disease and kidney failure** in patients with chronic kidney disease and type 2 DM
- **Tirzepatide** (Zepbound) 2.5, 5, 7.5, 10, 12.5, 15 mg weekly, SURMOUNT trials
 - *Average weight reduction 20-22% at the higher doses.*
 - 15.0 mg is approved to treat **moderate to severe OSA** with AHI >15.0/hr

GLP-1 Therapy Contraindications

- Personal or family history of medullary thyroid cancer or MEN2 (multiple endocrine neoplasia)
- Allergic reaction to previous GLP-1 therapy
- Pregnancy, breastfeeding
- May be a contraindication if patient has a history of pancreatitis unless the reason for pancreatitis is resolved
 - Gallstone pancreatitis and underwent cholecystectomy
- Maybe contraindicated if the patient has a history of gastroparesis
- Avoid or use caution in patients taking sulfonylureas, (other insulin secretagogue), DPP-4 inhibitors due to concern of hypoglycemia

What is GLP-1 Hormone?

- Native hormone released in response to eating by intestinal enteroendocrine L-cells
- Present throughout the intestines and especially the distal colon.
- After eating, GLP-1 blood concentrations rise by 2- to 4-fold
- Circulating endogenous GLP-1 has a half-life of 1–2 min, being rapidly inactivated by dipeptidyl-peptidase IV (DPP4).
- GLP-1 exerts powerful metabolic effects
 - In the brain- central homeostatic (energy-intake-focused) and non-homeostatic (reward-focused) regulation of food consumption in the hypothalamus and nucleus of the solitary tract
 - A small amount of GLP-1 crosses the blood–brain barrier and, more notably, GLP-1 modulation of vagal afferent neurons
 - Certain diet patterns rich in protein, fiber, fruits and vegetables may potentiate release of endogenous GLP-1

- Bodnaruc AM, Prud'homme D, Blanchet R, Giroux I. Nutritional modulation of endogenous glucagon-like peptide-1 secretion: a review. *Nutr Metab (Lond)*. 2016; **13**: 92.

What is GLP Hormone?

- Endogenous hormone produced by enteroendocrine K-cells in the proximal small intestine
- Released in response to nutrient ingestion, esp glucose and fat
- GLP receptors are widely distributed in the pancreas, adipose tissue and other organs
- Also inactivated by DPP-4, but slower. Half life 5-7 min.
- Stimulates glucose-dependent insulin secretion from pancreatic beta cells and increases insulin sensitivity
- Influences lipid metabolism- promotes fat deposition, can increase insulin sensitivity and lipogenesis but also affects lipolysis
- Reduces food consumption via signaling in the brain
- May increase energy expenditure?

How Do GLP-1 Receptor Agonists Work?

- Resistant to the enzyme DPP-4, lasts several days
- GLP-1 reduces energy intake by 16%–39% compared with placebo, related to changes in cravings, hunger, and fullness
- Slow gastric emptying
 - Prolonged and fast satiety
 - Reduces food intake
- Enhanced release of insulin from pancreas and increase sensitivity to insulin
- Induces change in the brain
 - Affects brain regions related to appetite and reward
 - Reduction in food cravings or “**food noise**” which is the persistent, unwanted, and unpleasant thoughts about food
 - Potentially less pleasure or aversion to eating certain foods- nutrient poor processed foods, high fat or sugar foods, alcohol

- Bettadapura S, Dowling K, Jablon K, Al-Humadi AW, le Roux CW. Changes in food preferences and ingestive behaviors after glucagon-like peptide-1 analog treatment: techniques and opportunities. *Int J Obes (Lond)*. 2024
- Christensen S, Robinson K, Thomas S, Williams DR. Dietary intake by patients taking GLP-1 and dual GIP/GLP-1 receptor agonists: a narrative review and discussion of research needs. *Obes Pillars*. 2024; 11:100121
- Silver HJ, Olson D, Mayfield D, et al. Effect of the glucagon-like peptide-1 receptor agonist liraglutide, compared to caloric restriction, on appetite, dietary intake, body fat distribution and cardiometabolic biomarkers: a randomized trial in adults with obesity and prediabetes. *Diabetes Obes Metab*. 2023; 25(8): 2340-2350

GLP-1/GIP Therapy Misc. Information

- Weight loss is rapid first 6 months then slows, plateaus at 18 mo
- If stop the medication, gain 2/3 of weight back in 1 year, even with nutritional guidance- **designed for long term use**
- Responder- if lose >5% of body weight in 12 weeks
- Might take up to 20 weeks to reach maximum dose so it is reasonable to continue beyond 12 wk
- Most effective in female, lower starting HbA1c, <55 y/o, higher BMI (>40)
- Trials show adherence is 83-88% at 66-68 weeks
 - Real world around 50% adherence at 1 year, 15% at 2 years
 - Several reasons including cost, mental health, preference, stigma, switch to compounded
- **This is not unique to GLP-1 medications. 30% of all medications go unfilled and 50% of medications are not taken correctly.**

- Discontinuation and reinitiation of dual-labeled GLP-1 receptor agonists among US adults with overweight or obesity. *JAMA Netw Open.* 2025; **8**(1):e2457349
- Anderson LJ, Nuckols TK, Coles C, et al. A systematic overview of systematic reviews evaluating medication adherence interventions. *Am J Health-Syst Pharm.* 2020; **77**: 138-147.

GLP-1 Therapy Pros and Cons

Benefits

- Decreased cardiovascular events
- Improves OSA
- Improves CKD (chronic kidney disease)
- Improves MASLD (metabolically associated steatotic liver disease)
- Decreased mortality
- Decreases substance abuse disorder
- Reduces HbA1c and incidence of pre-diabetes
- Improves knee osteoarthritis
- Possible decrease in obesity related cancers

Most common side effects

- Nausea, 25-44%
- Diarrhea, 19-30%
- Vomiting, 8-24%
- Constipation, 17-24%
- Abdominal pain, 9-20%
- In trials, 10% discontinued d/t SE
- Why- GLP-1s delay gastric emptying which causes bloating, fullness, nausea
- GLP-1s activate several brain regions responsible for weight regulation, appetite and these are also responsible for nausea
- Can affect intestinal motility or secretion so can cause diarrhea

Other GLP-1 Side Effects

Less common side effects

- Dyspepsia
- Fatigue
- Headache
- Flatulence
- Eructation (belching)
- Hair loss
- GERD
- Dizziness
- Gastritis
- Tachycardia- GLP-1 receptors on SA node
- Nutritional deficiencies

Rare side effects

- Gallbladder disease
- Pancreatitis
- AKI- due to hypovolemia
- Hypersensitivity reactions
- Gastroparesis
- Ophthalmic complications
 - Felt to be due to rapid improvement in blood glucose in patients who have baseline vasculopathy
- Suicide and SI
 - No confirmed definitive risk

GLP-1 Therapy GI Side Effects and Management

- Nausea is the most common side effect
 - Morning or after prolonged period of not taking in food
 - Alcohol can worsen nausea and GERD so minimize this
 - Helpful to have smaller, more frequent meals
 - “Bland diet” especially at times of dose initiation and escalation
 - Avoid high fat, high carb, high fiber, spicy food at these times
 - Important to have adequate fluid intake- limit carbonated beverages and alcohol
 - Peppermint, ginger, acupuncture bands
 - Compazine (prochlorperazine)
 - Zofran (ondansetron)- careful due to possible worsening of constipation
- Dehydration from nausea, vomiting and diarrhea
 - Can cause acute kidney injury



GLP-1 Therapy GI Side Effects and Management

- Constipation
 - Extended constipation can cause reactive diarrhea
 - Adequate fluids and fiber from foods
 - Foods with lower calories, lower glycemic index and higher water content are helpful
 - Gradually increase intake of foods high in soluble and insoluble fiber like prunes and dried fruit
 - High protein food can WORSEN constipation
 - High fat diet can cause constipation
 - Mag citrate, fiber supplements, stool softeners, polyethylene glycol (MiraLAX).
- Diarrhea
 - Avoid high fat or large meals
 - Can occur because of increased secretions from intestine
 - Fiber capsules or powders to bulk stools; high fiber foods
 - Anti-diarrhea medications can help in acute situations in the short term

Managing GI SE & Other Lessons Learned

- Gradual dose escalation
 - Manufacturer's recommendation is dose escalation every 4 wk but this might not be the best if having significant side effects
 - It is fine to keep patients on a lower dose and to titrate slowly
 - Insurance can be a barrier as trials studied the escalation doses for no more than 8 weeks
- **Clinical pearl-** figure out what days are most challenging for the patient from a food consumption stand-point. It is usually the weekends. Take the injection on Thursday or Friday since it is most effective the first few days after the injection
- Make sure to inform patient they may not feel well for 1-2 days after the injection so plan accordingly
- Side effects most likely to occur at initiation of GLP-1 and dose escalation- bland diet and smaller portions tend to help
- Don't forget that side effects may also be associated with patient's dietary patterns- important to obtain diet recall at every visit
- If they stop GLP-1 for any reason, have them call you before starting again- titrate up

Nutritional Deficiencies

- Patient may already be deficient in nutrients due to low intake of fruits, vegetables, lean protein and high intake of highly processed food or restrictive eating patterns (“food fussiness”)
- Calories reduce by 16-39%
- GI symptoms can exacerbate this
- Can be insufficient in calories- goal >1,200 kcal for women, >1,500-1,800 for men
- Can be insufficient in vitamins/minerals including include iron, calcium, magnesium, zinc, vitamins A, D, E, K, B1, B12, and C
- Signs include:
 - Fatigue beyond expected
 - Excess hair loss
 - Skin flaking, itching
 - Poor wound healing
 - Unusual bruising



GLP-1 Therapy and Lean Mass- Muscle

- Up to 38% weight loss was lean mass (muscle, bone, non-fat tissue), half of that is muscle; SURMONT-1
- Similar to other forms of rapid weight loss like VLCD (very low-calorie diet) and bariatric surgery
- Lean mass affected by
 - Degree of caloric restriction and rapidity of weight loss (in general recommend 0.5-2.0 lb/wk)
 - Presence or absence of strength/resistance training
 - Low protein intake
- Sarcopenia risk is greatest for:
 - Older
 - Peri or post menopausal women, men with low testosterone
 - Poor protein intake
 - Sedentary behavior
 - Lack of resistance training
- Sarcopenic obesity
 - Weight cycling
 - Important to avoid using GLP-1 therapy intermittently

- 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.
- Heymsfield SB, Yang S, McCarthy C, et al. Proportion of caloric restriction-induced weight loss as skeletal muscle. *Obesity (Silver Spring)*. 2024; **32**(1)



GLP-1 Therapy and Lean Mass- Bone

- Decreased bone density

- Occurs as the result of rapid weight loss
- >14% weight loss over 3-4 months is rapid
 - Slower progression may preserve bone mass
- Influenced by:
 - Initial body weight
 - Baseline physical activity
 - Extent of energy restriction and protein intake
 - Rate of weight reduction
 - Older adults
 - Females

- Important to get adequate protein intake and strength training
- Important to avoid weight cycling as this will exacerbate bone and muscle loss- gain fat mass back, not lean mass = sarcopenic obesity

- Shapses SA, Riedt CS. Bone, body weight, and weight reduction: what are the concerns? *J Nutr.* 2006; **136**(6): 1453-1456. doi:[10.1093/jn/136.6.1453](https://doi.org/10.1093/jn/136.6.1453)



Supporting Nutrition

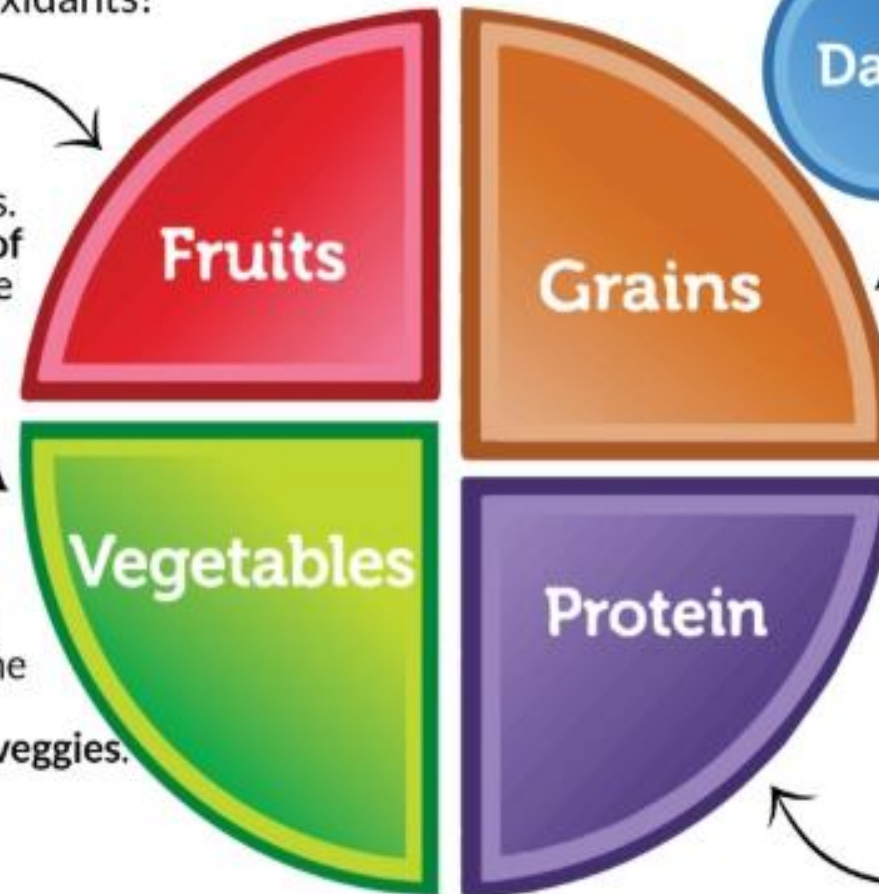
- Monitoring with phone app, journal, ect. Lose It, My Fitness Pal, My Net Diary, ect.
 - CAUTION IF HISTORY OF BULIMIA OR ANOREXIA- only focus on protein
 - Ensures patient is getting enough calories and protein
- Eating 3 meals per day (and snacks if needed)
 - Can utilize “My Plate” guideline
 - Can be smaller meals- patient can think of it as a snack
 - Always include a plant and/or animal-based protein
 - Eat protein first
 - Meals based around healthy fruits, vegetables, nuts, beans, whole grains, yogurt, lean proteins
 - Protein shakes- around 30 g protein and 5 g carbs. Fairlife, Premiere Protein are examples
 - Eat until 85% or “almost” full
- Avoid or limit refined grains, flour, starches, sugars
- Restrict sugar sweetened beverages, processed meat, most “fast foods”, ultra-processed sweets and ultra-processed savory snacks
- May consider adding in a multi-vitamin

MyPlate: A Guide

Make half your plate fruits and veggies. They're packed with fiber & antioxidants!

Fruit:
Eat fruits of all colors. Go for **fruit instead of juice**, which has more fiber and fewer calories.

Vegetables:
The more colors and types that you eat, the better! Aim to get mostly **non-starchy** veggies.



Dairy:
3 servings per day gets you the calcium you need. Choose low-fat for fewer calories.

Grains:
Eat mostly **whole** grains. Refined grains, like white bread and white rice, have less nutrition. Whole grains have more **fiber**, iron, and B vitamins.

Protein:
A palm-sized amount at lunch and dinner is all you need. Beans, nuts, fish, and chicken are good, lean choices.

Dietary Practices

Factors to encourage

Food groups

Fruits (e.g., berries, apples, citrus fruits, banana, grapes, avocado)

Vegetables (e.g., broccoli, leafy greens, tomatoes, carrots, peas, squashes)

Whole grains (e.g., oats, quinoa, brown rice, and whole-grain breads, cereals, and pastas)

Dairy (e.g., yogurt, milk, cheese)

Lean proteins (e.g., poultry, fish/seafood) and eggs

Nuts and seeds (e.g., almonds, peanuts, chia seeds, sesame seeds, hemp seeds)

Plant fats/oils (e.g., olive, canola, avocado oils)

Ginger or peppermint tea

Eating habits^b

Regular, small meals at consistent times

Flexibility with food choices

Enjoy portion-controlled treats

Ensure adequate fluids

Minimal alcohol intake

Factors to minimize/avoid

Refined carbohydrates (processed grains, flours, added sugars)

Sugar-sweetened beverages

Red and processed meats

Most fast foods

Sweets and savory snacks

Emotional, mindless, or nighttime eating

Long periods without meals (i.e., becoming overly hungry)

Consumption of large meals

- Mozaffarian D, Agarwal M, Aggarwal M, et al. Nutritional priorities to support GLP-1 therapy for obesity: A joint Advisory from the American College of Lifestyle Medicine, the American Society for Nutrition, the Obesity Medicine Association, and The Obesity Society. *Obesity* (Silver Spring). 2025;33(8):1475-1503.

Protein Recommendations

- General population is 0.8 g/kg/d
- Higher target during weight reduction of 1.2-1.6 g/kg/d
- Actual weight can significantly overestimate protein requirement so possibly factor target/goal weight
- Do not go below threshold of 0.4-0.5 g/kg/d for concern of atrophy
- Over 2 g/kg/d is not advised- converted to fat by the liver and increases visceral adiposity
- Alternative of 80-120 g per day is fine
- Alternative of 16-24% of daily energy on a 2,000 kcal diet is OK
- Patients with chronic kidney disease will require lower protein goal-dietician helpful
- Recommending one protein shake per day as a meal replacement is helpful

- Grosicki GJ, Dhurandhar NV, Unick JL, et al. Sculpting success: the importance of diet and physical activity to support skeletal muscle health during weight loss with new generation anti-obesity medications. *Curr Dev Nutr.* 2024; 8(11):104486.
- Charidemou E, Ashmore T, Li X, et al. A randomized 3-way crossover study indicates that high-protein feeding induces de novo lipogenesis in healthy humans. *JCI Insight.* 2019; 4(12)

Physical Activity- Aerobic and Strengthening

- **Aerobic activity** alone has a smaller effect on preserving lean mass during rapid weight reduction
 - 5 days of 30 min of mod-intensity, 75 min of vigorous-intensity or 7,000 steps
 - Daily steps and health outcomes in adults: a systematic review and dose-response meta-analysis Ding, Ding et al. The Lancet Public Health, Volume 10, Issue 8, e668 - e681
- **Strength training** 2-3 days per week for 20-30 min each session for a total of 60 min for the week or more. Important to include core, arms and legs
- Customize for the patient
 - Any exercise is better than no exercise- set goals and set patient up for success
 - Walking is fine
 - Swimming is excellent for patients with orthopedic conditions and/or chronic pain
 - Fitness trainers, exercise classes, local gyms, Silver Sneakers online/in person, PT if deconditioned, frail
 - Health coaching can be helpful. Seek out your resources
- Skeletal muscle is important for glucose regulation and regulates metabolism
- Skeletal muscle naturally decreases with age after 40 y/o

Follow-up

- Inform patients of how to contact you/clinic
- Return to clinic every 1-2 months, for the first few months and can extend the time frame from there
- What is going well
- How is the medicine helpful
- Discuss side effects and challenges
- 24-hr dietary recall
- Exercise routine
- Vitals- blood pressure and weight
- Physical exam- heart, lungs, palpate gallbladder (if applicable), thyroid, strength
- At 10-15% weight loss, several weight related health conditions improve considerably

Other Considerations

- Due to delayed gastric emptying, absorption of medications can be altered- oral contraception (plus fertility improves)
- Weight loss impacts overall health, and other meds may need to be adjusted
 - Anti-hypertensive medications
 - Cholesterol medications
 - Thyroid medications
 - Anti-diabetic medications
 - Oral medications that have a narrow therapeutic window- warfarin



Why is Weight Loss and Maintenance so Difficult?

- Body's metabolic adaptations to weight loss- survival mechanism
 - Body protects highest weight
 - Increased hunger hormones (ghrelin) and decreased satiety hormones (eg leptin, GLP-1)
 - Autonomic nervous system and thyroid changes. Thyroid hormones, esp T3, decrease and this leads to reduced metabolic rate and reduced thermogenesis
 - Reduced resting metabolic rate (RMR) is persistent for years
 - RMR is the largest driver of energy expenditure
 - Muscle becomes more efficient and uses less energy for same amount of work
 - Non-essential activity decreases- "wiggles"
- **Obesity of NOT a moral failure!**
 - Patients blame themselves
 - Has nothing to do with self control or will power (see above)
 - "Overeating does not cause obesity. Obesity causes overeating". David Ludwig and Kalplan

How To Support Patient Once They are at Goal

- “Goal weight”- mutually agreed upon weight that patient feels they can maintain and that has allowed them to achieve their health goals
- Behaviors that patients demonstrate when they are successful at maintaining weight loss
 - Self-monitoring of body weight, food intake and activity
 - Eat at regular times daily, including breakfast
 - Regular physical activity (>60 min per day)
 - Portion control- permitting flexibility with food choices and occasional portion-controlled treats rather than severe restrictions
- Other behaviors that are helpful
 - Avoiding sugary drinks, highly processed foods and snack foods
 - Consuming more minimally processed foods that are higher in nutrients, fiber, protein
 - Limiting screen time to <10 hours per week
 - Using coping strategies including social support, advance planning and problem-solving skills

• The National Weight Control Registry. The National Weight Control Registry- Research Findings 2025.

Some Take-Aways

- Obesity is complex and not a moral failure
- Requires more than a 15 min visit
- Screen for other causes of obesity and obtain a comprehensive weight history
- Patient centered approach is critical
- GLP-1 therapy requires appropriate guidance on dietary and activity modifications with routine follow-up
- GLP-1 therapy is designed for long term use
- Celebrate “non-scale victories” with your patients

Thank you!



Jennifer Jungen, MPAS-PAC
Iowa Health Care
Weight Management In the Era of
GLP-1 Pharmacotherapy
Department of Internal Medicine
Division of Endocrinology
Weight Management Clinic

jennifer-jungen@uiowa.edu