

# Medications for Weight Management

May 2025

**Indian Health Service**  
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Consultant



# Objectives



- 1. Utilize BMI as a screening tool for weight status.*
- 2. Identify various patient risk factors and associated complications of weight gain.*
- 3. Appraise medical management techniques utilized for weight management to determine appropriate therapies based on individual patient needs and risk factors.*

# Which medicine is obesogenic?

1. Naltrexone
2. Omeprazole
3. Metoprolol
4. Bupropion



# What are some risk factors of weight gain?



1. Sedentary lifestyle
2. Food insecurity
3. Poor Sleep Quality
4. Medications
5. All of above

# What is obesity?



Obesity is defined as a chronic progressive, relapsing, and treatable multifactorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic biomechanical, and psychosocial health consequences

- Obesity Medicine Association

Adiposity-Based Chronic Disease (ABCD), which explicitly identified the chronicity of the disease and the underlying adiposity driving the pathophysiology and complications that confer morbidity and mortality

- AACE 2016

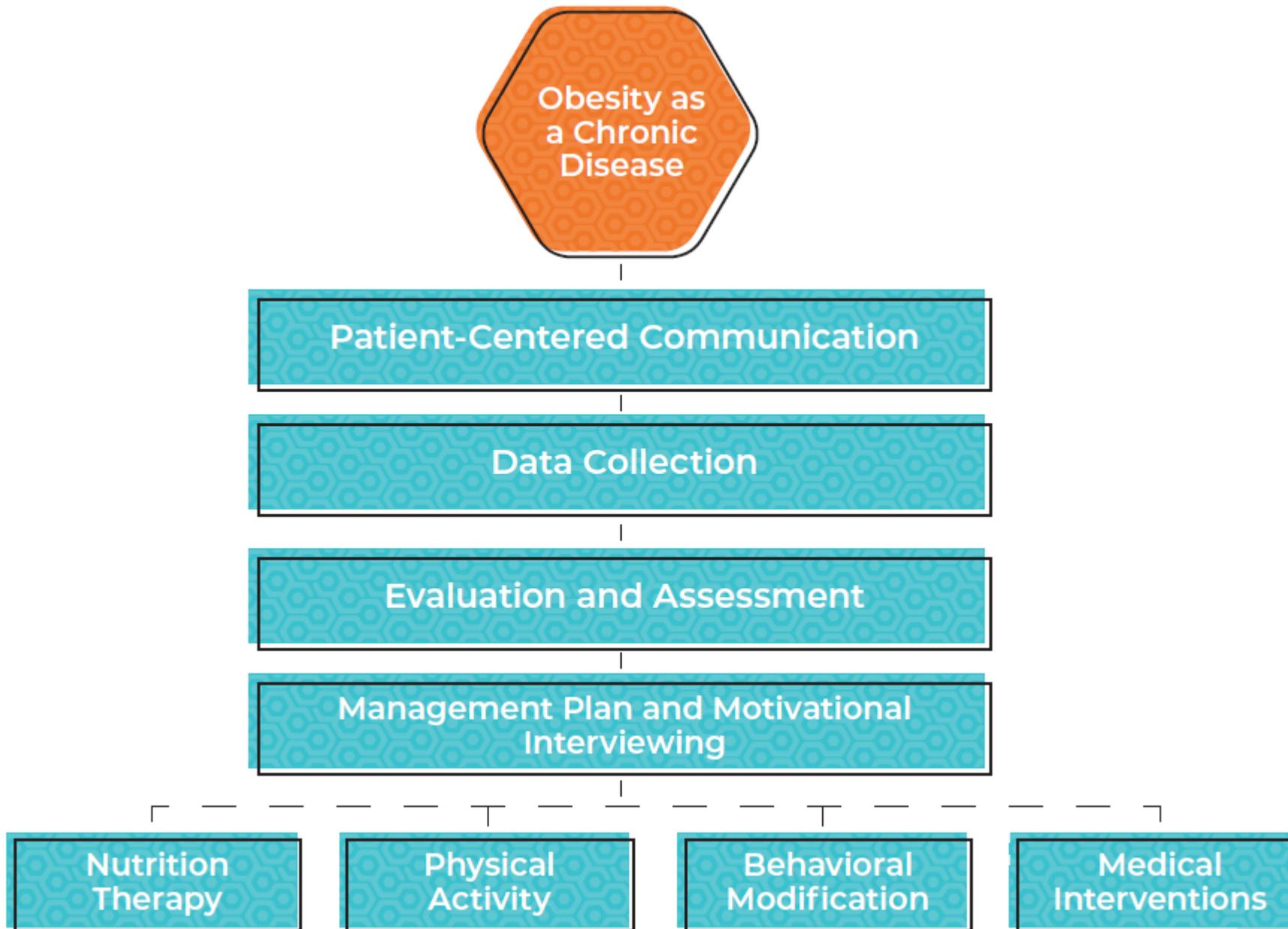


Diagnosis	Evaluation	<ul style="list-style-type: none"> <li>• Medical history</li> <li>• Physical examination</li> <li>• Clinical laboratory</li> <li>• Review of systems, emphasizing weight-related complications</li> <li>• Obesity history: graph weight vs age, lifestyle patterns/preferences, previous interventions</li> </ul>					
	Anthropometric Diagnosis	<ul style="list-style-type: none"> <li>• Confirm that elevated BMI represents excess adiposity</li> <li>• Measure waist circumference to evaluate cardiometabolic disease risk</li> </ul>					
	Clinical Diagnosis	<p><b>BMI kg/m<sup>2</sup></b></p> <p>&lt;25 NORMAL WEIGHT   25–29.9 OVERWEIGHT   ≥30 OBESITY</p> <p><b>Checklist of Obesity-Related Complications</b> (staging and risk stratification based on complication-specific criteria)</p> <table border="1"> <tr> <td>None</td> <td>Mild to Moderate</td> <td>Severe</td> </tr> </table>	None	Mild to Moderate	Severe		
None	Mild to Moderate	Severe					
Diagnostic Categories	NORMAL WEIGHT (no obesity)	<p>STAGE 0</p> <p>No complications</p> <p>OVERWEIGHT BMI 25–29.9 OBESITY BMI ≥30</p>	<p>STAGE 1</p> <p>One or more mild-to-moderate complications or may be treated effectively with moderate weight loss</p> <p>BMI ≥25</p>	<p>STAGE 2</p> <p>At least one severe complication or requires significant weight loss for effective treatment</p> <p>BMI ≥25</p>			
Phases of Chronic Disease Prevention and Treatment Goals	<p>PRIMARY</p> <p>Prevent overweight/obesity</p>	<p>SECONDARY</p> <p>Prevent progressive weight gain or achieve weight loss to prevent complications</p>	<p>TERTIARY</p> <p>Achieve weight loss sufficient to ameliorate the complications and prevent further deterioration</p>				
Treatment Based on Clinical Judgment	<ul style="list-style-type: none"> <li>• Healthy meal plan</li> <li>• Physical activity</li> <li>• Health education</li> <li>• Built environment</li> </ul>	<ul style="list-style-type: none"> <li>• Lifestyle/behavioral therapy</li> <li>• Consider pharmacotherapy if lifestyle alone not effective</li> </ul>	<ul style="list-style-type: none"> <li>• Lifestyle/behavioral therapy</li> <li>• Consider pharmacotherapy (BMI ≥27)</li> </ul>	<ul style="list-style-type: none"> <li>• Lifestyle/behavioral therapy</li> <li>• Add pharmacotherapy (BMI ≥27)</li> <li>• Consider bariatric surgery (BMI ≥35)</li> </ul>			

(1) an anthropometric component using BMI as a screening tool with subsequent clinical confirmation of excess adiposity based on examination along with waist circumference (WC) as an indicator of central adiposity reflecting cardiometabolic risk, and (2) a clinical component comprising the risk, presence, and severity of obesity complications.

*Nadolsky, Karl et al. "American Association of Clinical Endocrinology Consensus Statement: Addressing Stigma and Bias in the Diagnosis and Management of Patients with Obesity/Adiposity-Based Chronic Disease and Assessing Bias and Stigmatization as Determinants of Disease Severity." 2023. Endocrine Practice, Volume 29, Issue 6, 417 - 427*

W. Timothy Garvey et al., American Association of Clinical Endocrinologists and American College of Endocrinology Comprehensive Clinical Practice Guidelines For Medical Care of Patients with Obesity, Endocrine Practice, Volume 22, Supplement 3, 2016. Pages 1-203. ISSN 1530-891X. <https://doi.org/10.4158/EP161365.GL>.



*"Obesity Algorithm"  
2025. Obesity  
Medicine Association.  
Accessed May 2025*

# Body Mass Index: Increased Body Fat (Adiposity)



Body Mass Index (BMI) in kilograms per meters squared (kg/m<sup>2</sup>)\*



\*Different BMI cut-off points may be more appropriate based upon gender, race, ethnicity, and menopausal status. For example, the BMI cut-points for many (but not all) Asian populations are a BMI  $\geq 23$  kg/m<sup>2</sup> for pre-obesity, a BMI  $\geq 25$  kg/m<sup>2</sup> for class I obesity, a BMI  $\geq 30$  kg/m<sup>2</sup> for class II obesity, and a BMI  $\geq 35$  kg/m<sup>2</sup> for class III obesity.

“Obesity Algorithm” 2025. Obesity Medicine Association. Accessed May 2025



# Metabolic Syndrome

Parameters	NCEP ATP III 2005*	IDF 2009	EGIR 1999	WHO 1999	AACE 2003
<b>Required</b>			Insulin resistance or fasting hyperinsulinemia (ie, in top 25% of the laboratory-specific reference range)	Insulin resistance in top 25% <sup>¶</sup> ; fasting glucose $\geq 6.1$ mmol/L (110 mg/dL); 2-hour glucose $\geq 7.8$ mmol/L (140 mg/dL)	High risk of insulin resistance <sup>Δ</sup> or BMI $\geq 25$ kg/m <sup>2</sup> or waist $\geq 102$ cm (men) or $\geq 88$ cm (women)
<b>Number of abnormalities</b>	<b><math>\geq 3</math> of:</b>	<b><math>\geq 3</math> of:</b>	<b>And <math>\geq 2</math> of:</b>	<b>And <math>\geq 2</math> of:</b>	<b>And <math>\geq 2</math> of:</b>
Glucose	Fasting glucose $\geq 5.6$ mmol/L (100 mg/dL) or drug treatment for elevated blood glucose	Fasting glucose $\geq 5.6$ mmol/L (100 mg/dL) or diagnosed diabetes	Fasting glucose 6.1 to 6.9 mmol/L (110 to 125 mg/dL)		Fasting glucose $\geq 6.1$ mmol/L (110 mg/dL); $\geq 2$ -hour glucose 7.8 mmol/L (140 mg/dL)
HDL cholesterol	$< 1.0$ mmol/L (40 mg/dL; men); $< 1.3$ mmol/L (50 mg/dL; women) or drug treatment for low HDL cholesterol <sup>◇</sup>	$< 1.0$ mmol/L (40 mg/dL; men); $< 1.3$ mmol/L (50 mg/dL; women) or drug treatment for low HDL cholesterol	$< 1.0$ mmol/L (40 mg/dL)	$< 0.9$ mmol/L (35 mg/dL; men); $< 1.0$ mmol/L (40 mg/dL; women)	$< 1.0$ mmol/L (40 mg/dL; men); $< 1.3$ mmol/L (50 mg/dL; women)
Triglycerides	$\geq 1.7$ mmol/L (150 mg/dL) or drug treatment for elevated triglycerides <sup>◇</sup>	$\geq 1.7$ mmol/L (150 mg/dL) or drug treatment for high triglycerides	or $\geq 2.0$ mmol/L (180 mg/dL) or drug treatment for dyslipidemia	or $\geq 1.7$ mmol/L (150 mg/dL)	$\geq 1.7$ mmol/L (150 mg/dL)
Obesity	Waist $\geq 102$ cm (men) or $\geq 88$ cm (women) <sup>§</sup>	Waist $\geq 94$ cm (men) or $\geq 80$ cm (women) <sup>‡</sup>	Waist $\geq 94$ cm (men) or $\geq 80$ cm (women)	Waist/hip ratio $> 0.9$ (men) or $> 0.85$ (women) or BMI $\geq 30$ kg/m <sup>2</sup>	
Hypertension	$\geq 130/85$ mmHg or drug treatment for hypertension	$\geq 130/85$ mmHg or drug treatment for hypertension	$\geq 140/90$ mmHg or drug treatment for hypertension	$\geq 140/90$ mmHg	$\geq 130/85$ mmHg



Meigs, James. "Metabolic Syndrome." 2025. Uptodate.com. Accessed May 2025.

# Metabolic Syndrome



3 out of 5

Central obesity:	A waistline that measures: ≥ 35 inches (89 cm) for women or ≥ 40 inches (102 cm) for men; ≥ 80 cm for Asian women or ≥ 90 cm for Asian men
High blood pressure	>130/80 mmHg
Elevated fasting glucose	Blood glucose: >100mg/dl
Low HDL	HDL<40 mg/dl
High triglycerides	TG >150mg/dl

# 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

*“Obesity Algorithm” 2025. Obesity  
 Medicine Association.*

# Waist Circumference: Population Differences for Abdominal Obesity

Population	Men	Women
United States, Canada and Europe	≥102 cm	≥88 cm
Caucasian	≥94 cm (increased risk) ≥102 cm (still higher risk)	≥80 cm (increased risk) ≥88 cm (still higher risk)
Middle East, Mediterranean and Sub-Saharan Africa	≥94 cm	≥80 cm
Ethnic Central and South America	≥90 cm	≥80 cm
Asia (World Health Organization)	≥90 cm	≥80 cm
Japan (Japanese Obesity Society)	≥85 cm	≥90 cm
China (Cooperative Task Force)	≥85 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*

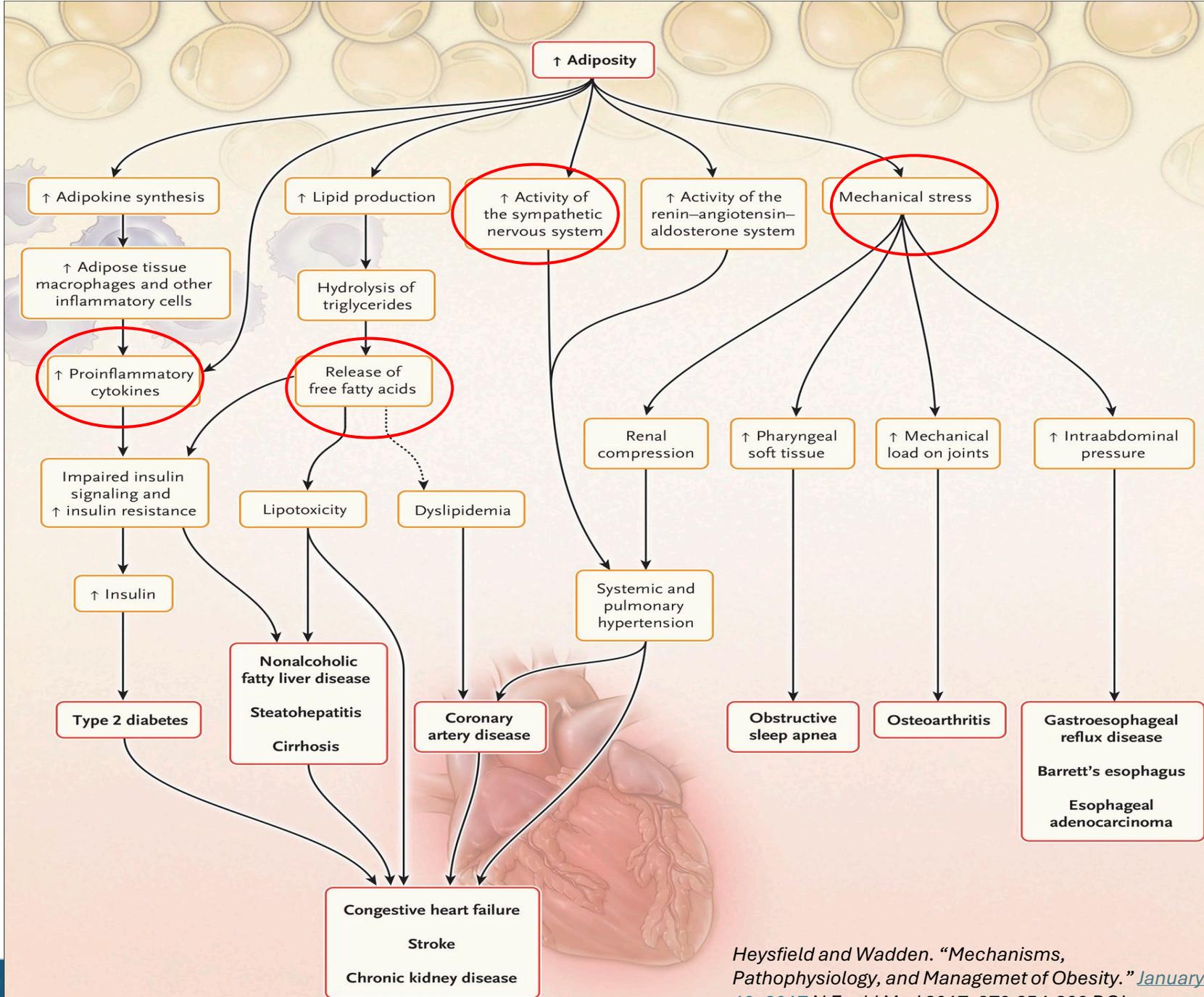


**Table 7. Waist Circumference Thresholds for Abdominal Obesity (32 [EL4; NE])**

POPULATION	ORGANIZATION	MEN	WOMEN
Europid	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Caucasian	WHO	≥94 cm (↑ risk) ≥37 inches  ≥102 cm (↑↑ risk) ≥40 inches	≥80 cm (↑ risk) ≥31 inches  ≥88 cm (↑↑ risk) ≥35 inches
United States	AHA/NHLBI (ATPIII)	≥102 cm ≥40 inches	≥88 cm ≥35 inches
Canada	Health Canada	≥102 cm ≥40 inches	≥88 cm ≥35 inches
European	European Cardiovasc. Societies	≥102 cm ≥40 inches	≥88 cm ≥35 inches
Asian (including Japanese)	IDF	≥90 cm ≥35 inches	≥80 cm ≥31 inches
Asian	WHO	≥90 cm ≥35 inches	≥80 cm ≥31 inches
Japanese	Japanese Obesity Society	≥85 cm ≥33 inches	≥90 cm ≥35 inches
China	Cooperative Task Force	≥85 cm ≥33 inches	≥80 cm ≥31 inches
Middle East, Mediterranean	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Sub-Saharan African	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Ethnic Central and South American	IDF	≥90 cm ≥35 inches	≥80 cm ≥31 inches

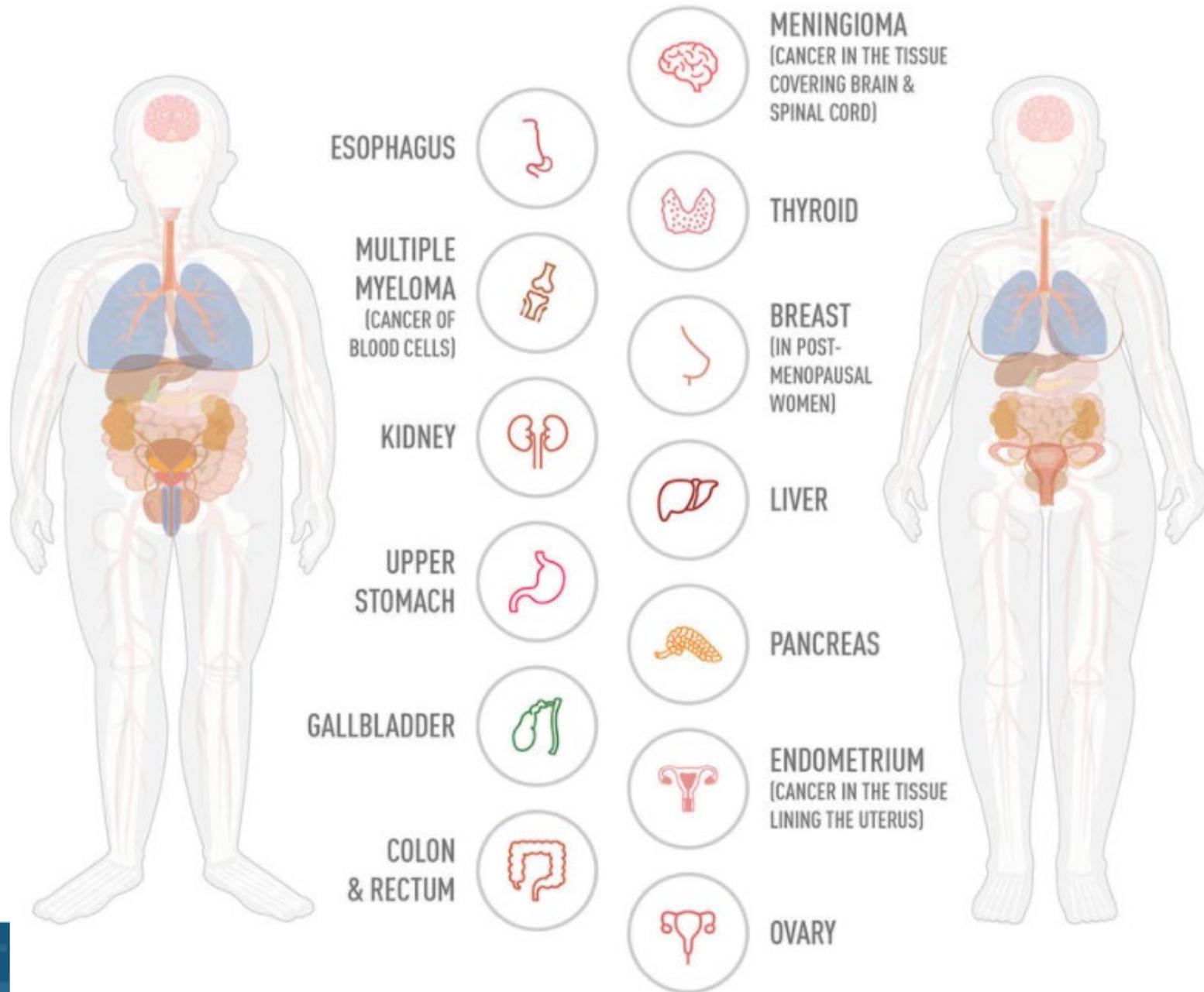
**Abbreviations:** AHA = American Heart Association; ATPIII = Adult Treatment Panel III; IDF = International Diabetes Federation; WHO = World Health Organization.

W. Timothy Garvey et al.. American Association of Clinical Endocrinologists and American College of Endocrinology Comprehensive Clinical Practice Guidelines For Medical Care of Patients with Obesity,. Endocrine Practice. Volume 22, Supplement 3,. 2016. Pages 1-203. ISSN 1530-891X. <https://doi.org/10.4158/EP161365.GL>.



Heysfield and Wadden. "Mechanisms, Pathophysiology, and Management of Obesity." *January 19, 2017 N Engl J Med* 2017; 376:254-266 DOI: 10.1056/NEJMr1514009

# OBESEITY INCREASES THE RISK OF 13 CANCER TYPES<sup>1</sup>



<https://www.cancer.gov/research/annual-plan/scientific-topics/obesity/obesity-and-cancer-infographic>

# 43F hx of DM2, BMI 57 & depression here for DM2 eval

*Pere PCP note, patient desires bariatric procedure*



BP: 121/78, HR 96

150kg, 163cm

Fib4 : 0.7 (alt and ast >30)

A1C 8.4; glucose 241

TSH 3.37

Microalb/cr 0.7

PMH:

Major depression, Bipolar d/o

Tobacco use

Hx of methamphetamine use d/o

DM2

Class III obesity

Mild OSA not on CPAP

Allergies: Bactrim

Sx: Stay-home Mom with a 5 year old.

Quit tobacco Sept 2022

PSH: at 5yo, she broke her finger and had it “reattached”

# How much ?



**Table 8.1—Treatment options for overweight and obesity in type 2 diabetes**

Treatment	BMI category (kg/m <sup>2</sup> )		
	25.0–26.9 (or 23.0–24.9*)	27.0–29.9 (or 25.0–27.4*)	≥30.0 (or ≥27.5*)
Nutrition, physical activity, and behavioral counseling	†	†	†
Pharmacotherapy		†	†
Metabolic surgery			†

\*Recommended cut points for Asian American individuals (expert opinion). †Treatment may be indicated for select motivated individuals.

Nuha A. ElSayed, Grazia Aleppo, Vanita R. Aroda, Raveendhara R. Bannuru, Florence M. Brown, Dennis Bruemmer, Billy S. Collins, Marisa E. Hilliard, Diana Isaacs, Eric L. Johnson, Scott Kahan, Kamlesh Khunti, Jose Leon, Sarah K. Lyons, Mary Lou Perry, Priya Prahalad, Richard E. Pratley, Jane Jeffrie Seley, Robert C. Stanton, Robert A. Gabbay, American Diabetes Association; 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: Standards of Care in Diabetes—2023. *Diabetes Care* 1 January 2023; 46 (Supplement\_1): S128–S139. <https://doi.org/10.2337/dc23-S008>

# Obesity and Type 2 Diabetes and MASLD



- Weight loss:
  - At least 3-5% body weight loss improve hepatosteatosis
  - if >5% weight loss showed stabilized or improved fibrosis in 94% of the cases
  - >10% weight loss associated with improvement in all features of NASH including portal inflammation and fibrosis

*Brunner KT, Henneberg CJ, Wilechansky RM, Long MT. Nonalcoholic Fatty Liver Disease and Obesity Treatment. Curr Obes Rep. 2019 Sep;8(3):220-228. doi: 10.1007/s13679-019-00345-1. PMID: 30945129; PMCID: PMC6770992.*

**8.5** Provide weight management treatment, aiming for any magnitude of weight loss. Weight loss of 3–7% of baseline weight improves glycemia and other intermediate cardiovascular risk factors. **A** Sustained loss of >10% of body weight usually confers greater benefits, including disease-modifying effects and possible remission of type 2 diabetes, and may improve long-term cardiovascular outcomes and mortality. **B**

**8.8a** Interventions including high frequency of counseling ( $\geq 16$  sessions in 6 months) with focus on nutrition changes, physical activity, and behavioral strategies to achieve a 500–750 kcal/day energy deficit should be recommended for weight loss and should be considered when available. **A**

**8.8b** If access to such interventions is limited, consider alternative structured programs delivering behavioral counseling (face-to-face or remote). **E**

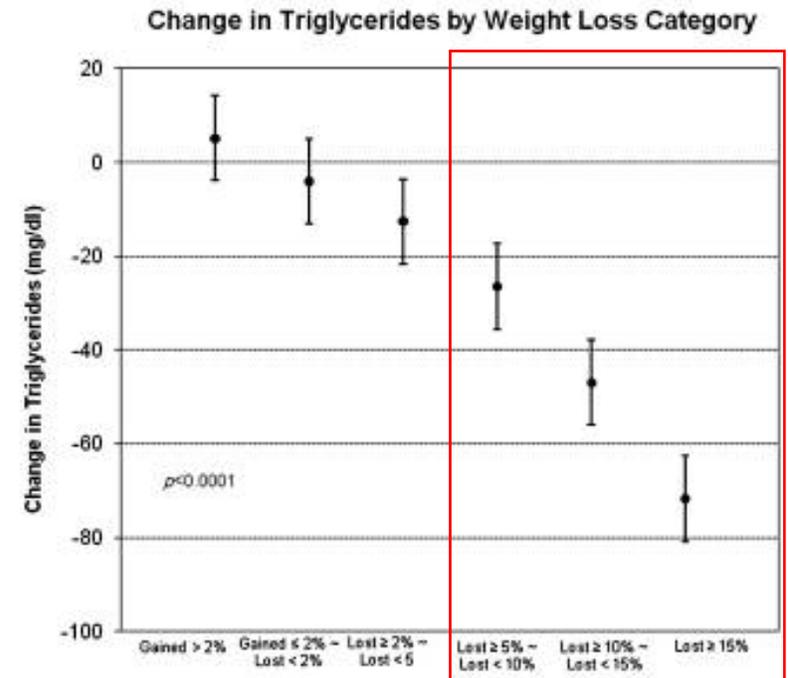
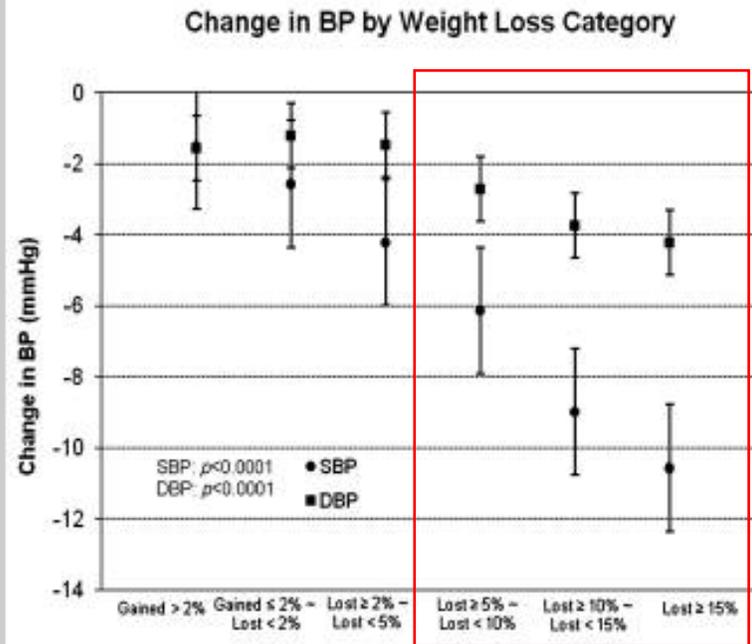
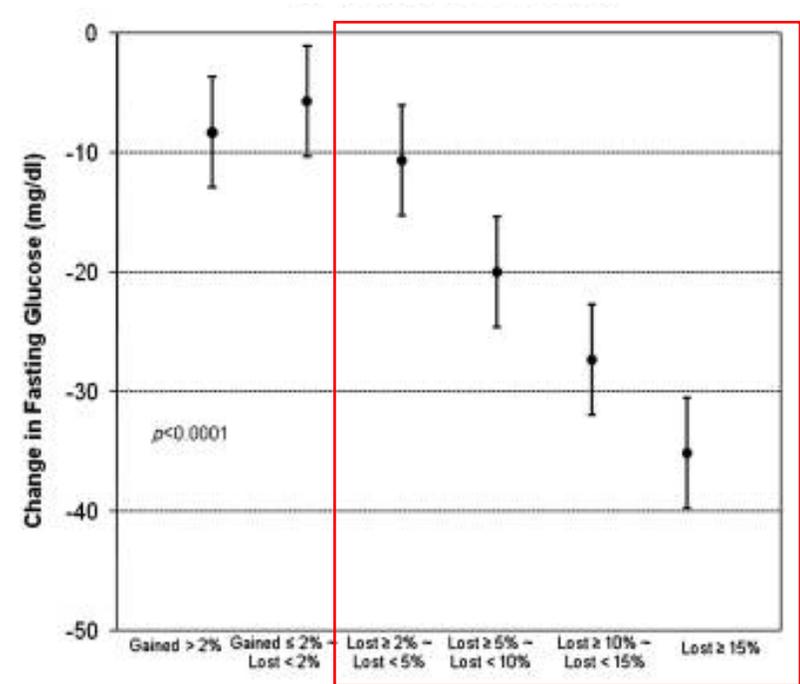
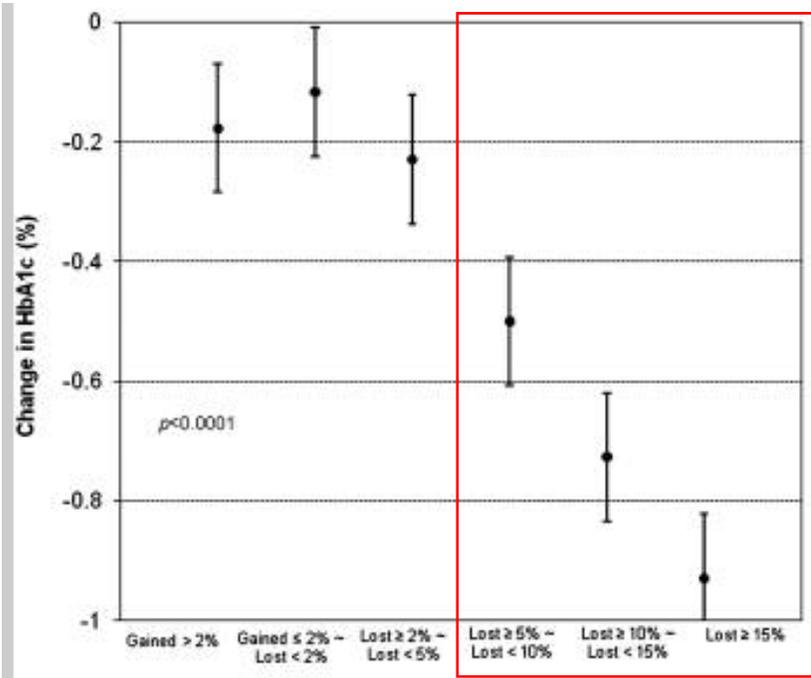


# How much weight loss is needed???

## LookAHEAD, 2011

- 2-5% weight loss
- 5-10%
- 10-15%
- >15%

Wing RR, Lang W, Wadden TA, et al. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care*. 2011;34(7):1481-1486. doi:10.2337/dc10-2415



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# 43F hx of DM2, BMI 57 & depression here for DM2 eval



Disordered eating?

Current meds?

Medication List:

Semaglutide sc 1mg weekly

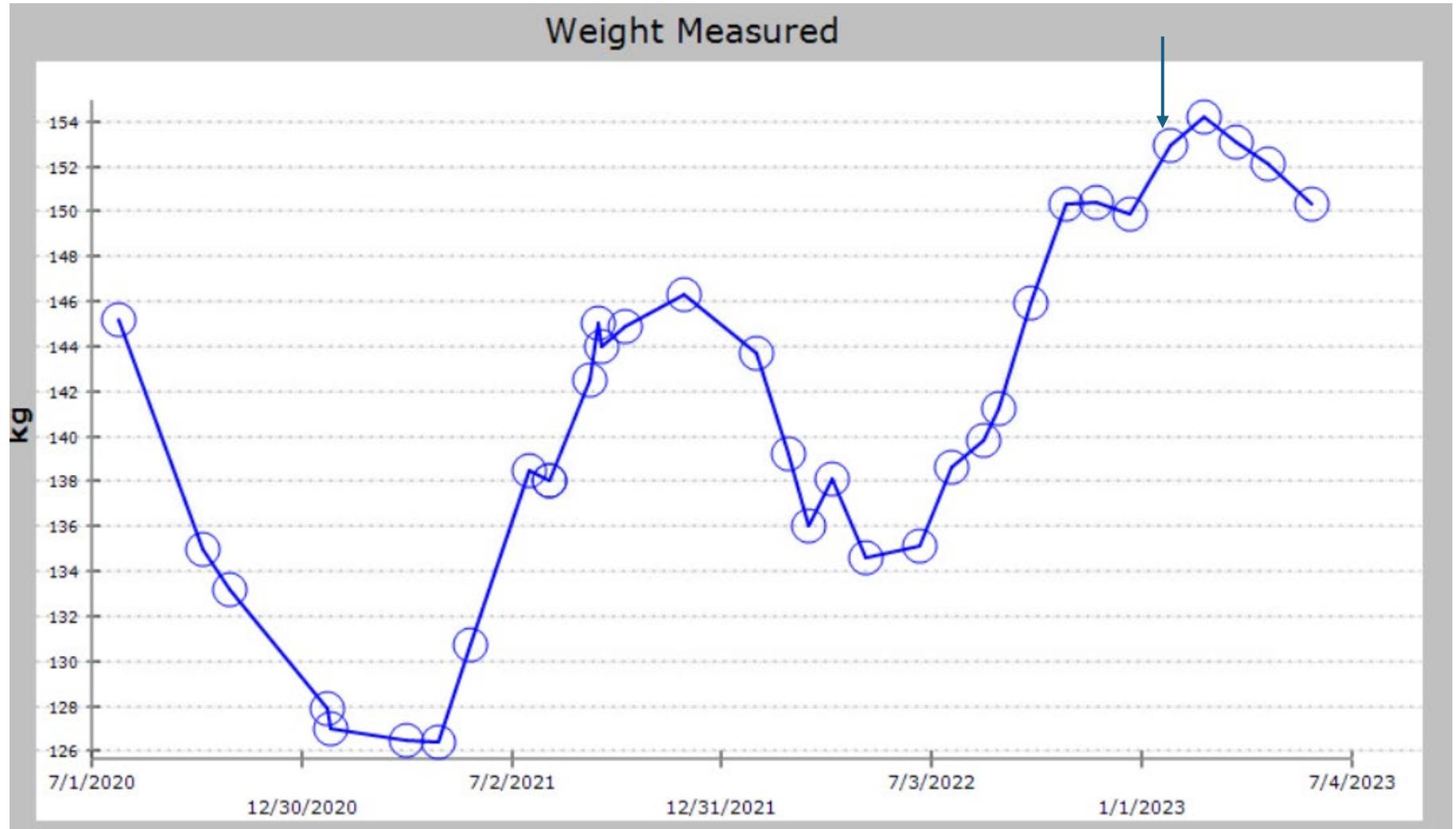
Metformin PO 1000mg bid

**Degludec 30u sc daily**

Lamotrigine PO 100mg bid

Baclofen TID prn spasm

B12, magnesium oxide, vitD



## Medications associated with weight gain and alternatives



Category	Drug class	Weight gain	Alternatives
Psychiatric agents	Antipsychotic	Clozapine, risperidone, olanzapine, quetiapine, haloperidol, perphenazine	Ziprasidone, aripiprazole
	Antidepressants/mood stabilizers: tricyclic antidepressants	Amytriptyline, doxepin, imipramine, nortriptyline, trimipramine, mirtazapine	Bupropion*, nefazodone, fluoxetine (short term), sertraline (<1 year)
	Antidepressants/mood stabilizers: SSRIs	Fluoxetine <sup>†</sup> , sertraline <sup>†</sup> , paroxetine, fluvoxamine	
	Antidepressants/mood stabilizers: MAOIs	Phenylzine, tranylcypromine	
	Lithium	-	
Neurologic agents	Anticonvulsants	Carbamazepine, gabapentin, valproate	Lamotrigine <sup>†</sup> , topiramate*, zonisamide*
Endocrinologic agents	Diabetes drugs	Insulin (weight gain differs with type and regimen used), sulfonylureas, thiazolidinediones, sitagliptin <sup>†</sup> , metiglinide	Metformin*, acarbose*, miglitol*, pramlintide*, edematide*, liraglutide*
Gynecologic agents	Oral contraceptives	Progestational steroids, hormonal contraceptives containing progestational steroids	Barrier methods, IUDs
	Endometriosis treatment	Depot leuprolide acetate	Surgical methods
Cardiologic agents	Antihypertensives	alpha-blocker <sup>†</sup> , beta-blocker <sup>†</sup>	ACE inhibitors <sup>†</sup> , calcium channel blockers <sup>†</sup> , angiotensin-2 receptor antagonists
Infectious disease agents	Antiretroviral therapy	Protease inhibitors	-
General	Steroid hormones	Corticosteroids, progestational steroids	NSAIDs
	Antihistamines/anticholinergics	Diphenhydramine <sup>†</sup> , doxepin <sup>†</sup> , cyproheptadine <sup>†</sup>	Decongestants, steroid inhalers

\* Weight-neutral or promotes weight loss.

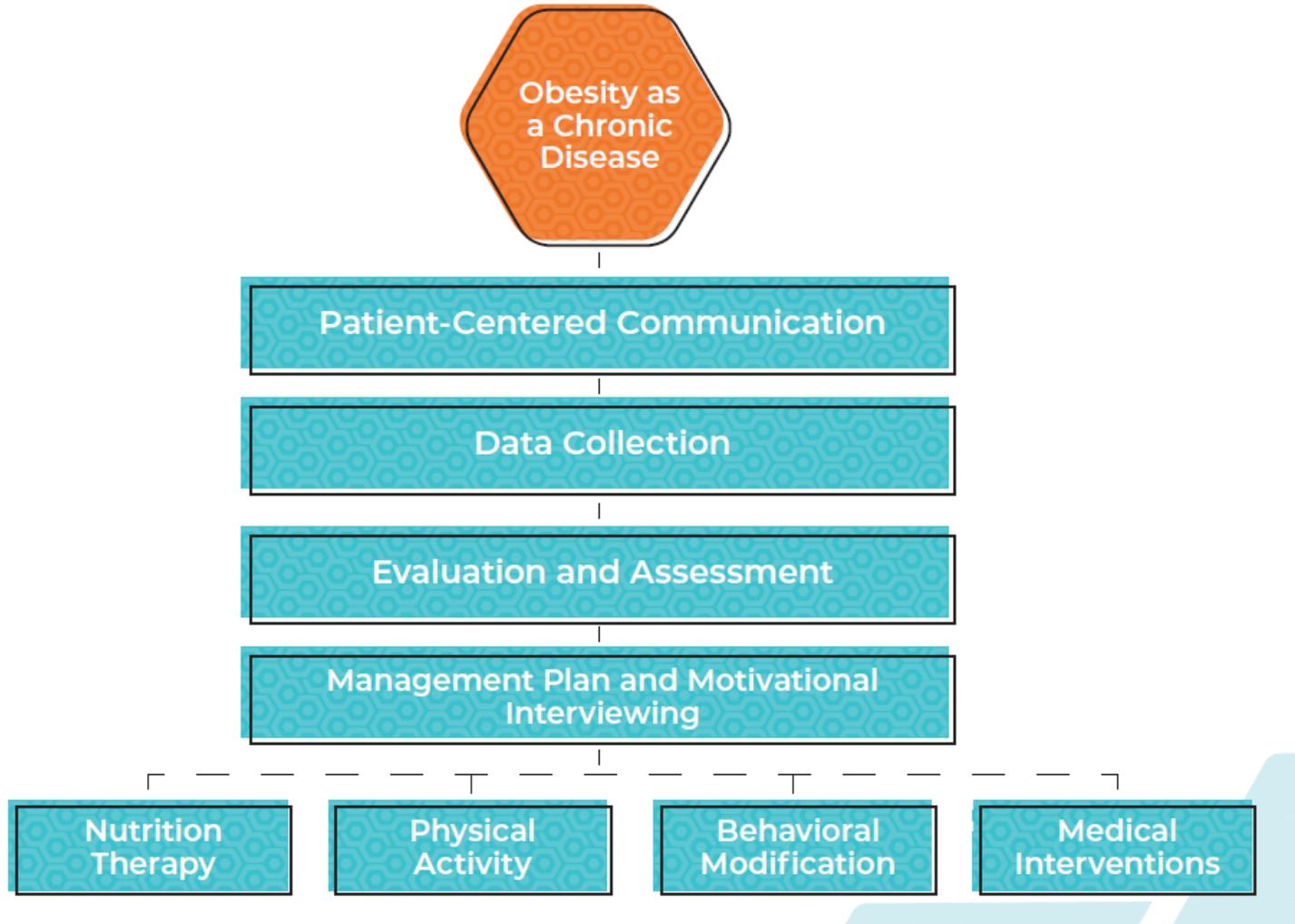
† The data supporting the effects of these medications on weight gain are low quality or conflicting.

Information from: Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2015; 100:342.

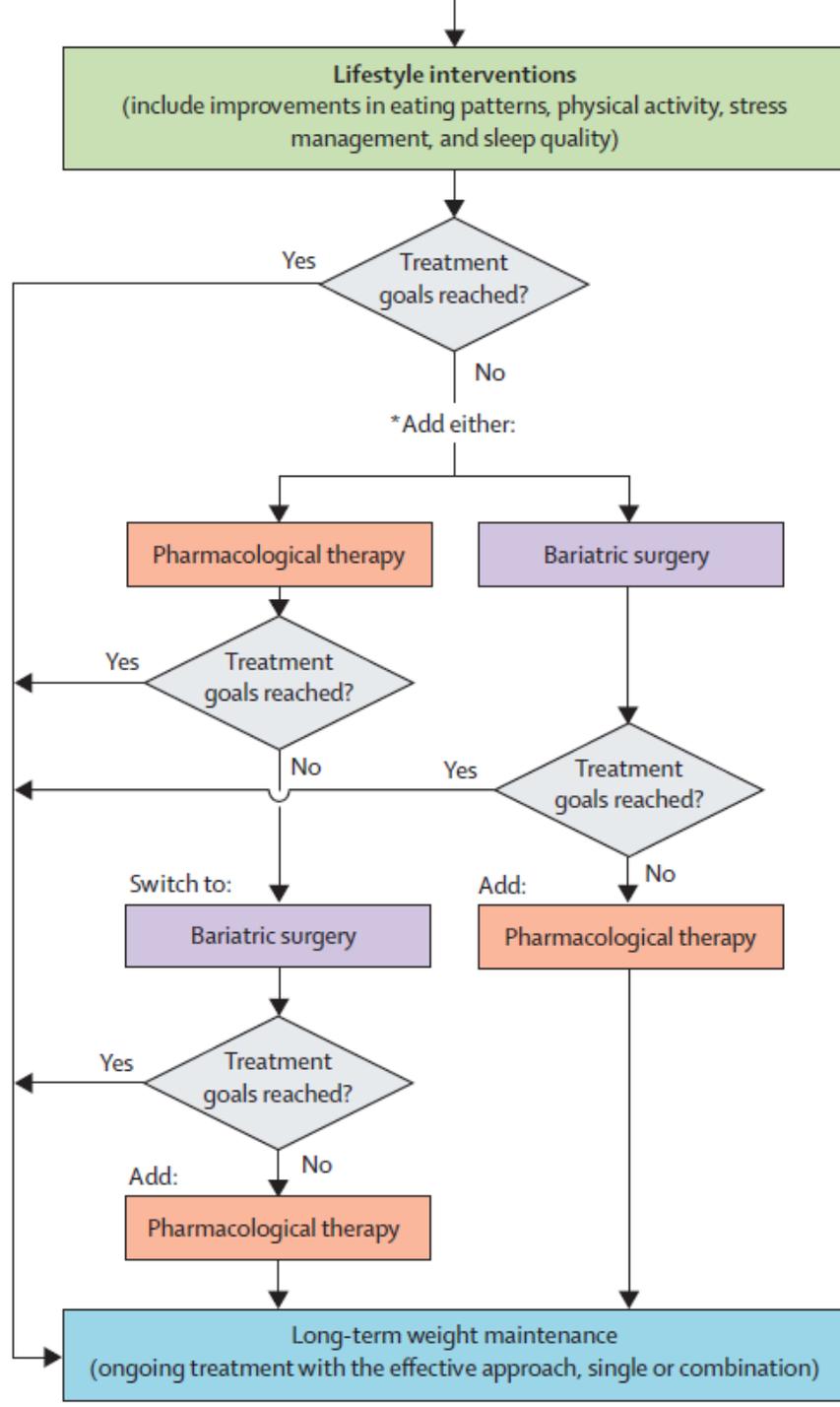
Leigh Perreault and Tirissa Reid  
 "Obesity in Adults: Drug therapy" 2025.  
 uptodate.com accessed May 2025.  
<https://www.uptodate.com/contents/obesity-in-adults-drug-therapy>

UpToDate

# Multidisciplinary Approach



*“Obesity Algorithm” 2025. Obesity Medicine Association. Page 16.*



# 5A's of Obesity Management

## Ask

- Ask for permission to discuss body weight.
- Explore readiness for change.

## Assess

- Assess BMI, waist circumference, and obesity stage.
- Explore drivers and complications of excess weight.

## Advise

- Advise the patient about the health risks of obesity, the benefits of modest weight reduction (i.e., 5-10 percent), the need for long-term strategy, and treatment options.

## Agree

- Agree on realistic weight reduction expectations, targets, behavioral changes, and specific details of the treatment plan.

## Arrange/ Assist

- Assist in identifying and addressing barriers; provide resources; assist in finding and consulting with appropriate providers; arrange regular follow up.

# 43F hx of DM2, BMI 57 & depression here for DM2 eval

Immediate Goal:

Walk around DisneyWorld with her 5 year old daughter next month

Medication changes

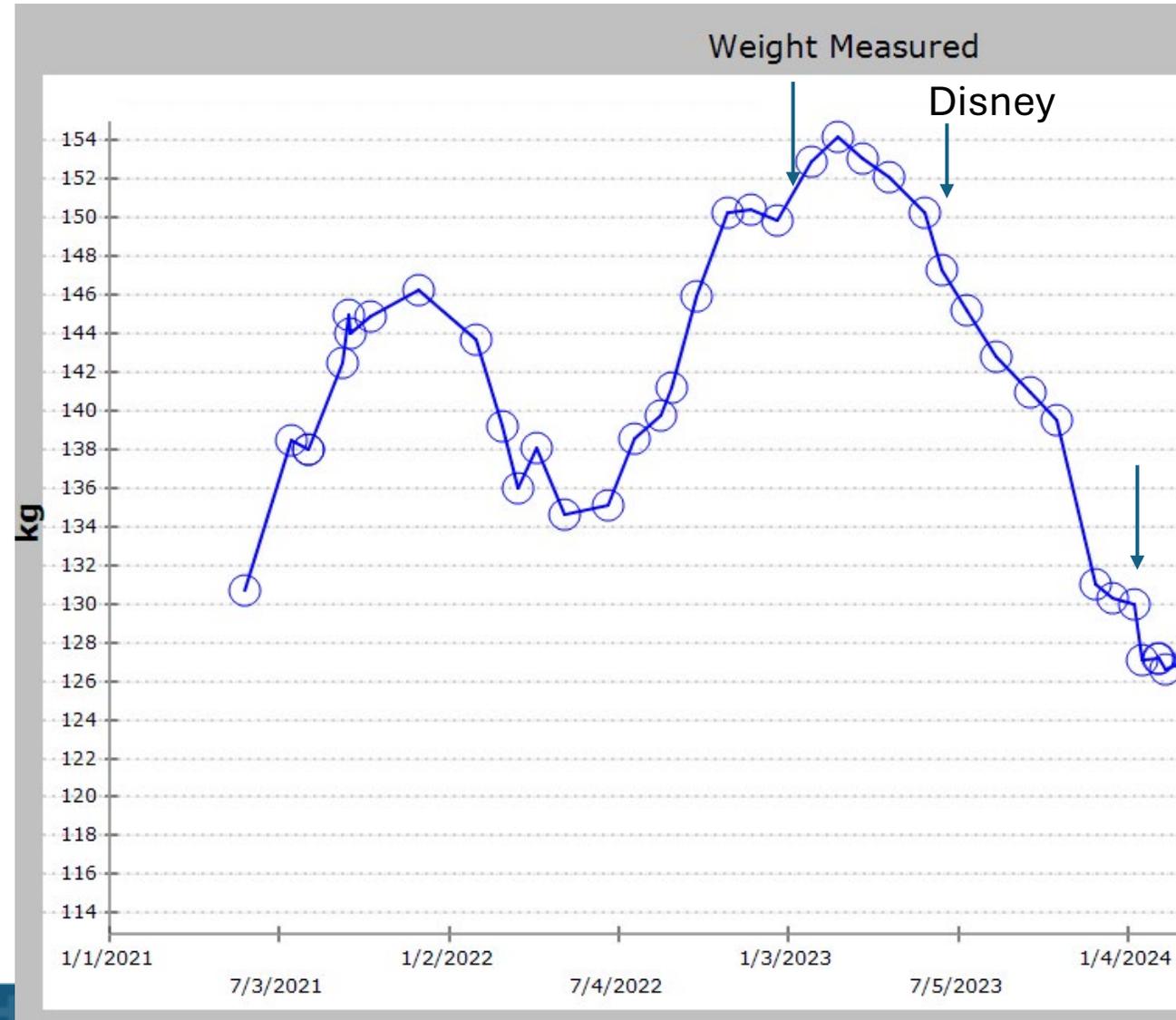
*Resistance in increasing GLP1 due to GI side effects*

1year goal:

10% weight loss in 1yr

- 15kg or 30lbs in 12 months

-- 3 lbs weight loss a month



## Approved Weight Management Pharmacotherapy

The U.S. Food and Drug Administration (FDA) has approved several medications for weight management as adjuncts to a reduced-calorie eating pattern and increased physical activity in individuals with BMI  $\geq 30$  kg/m<sup>2</sup> or  $\geq 27$  kg/m<sup>2</sup> with one or more obesity-associated comorbid conditions (e.g., type 2 diabetes, hypertension, and/or dyslipidemia). Nearly all FDA-approved weight

*American Diabetes Association Professional Practice Committee; 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: Standards of Care in Diabetes—2025. Diabetes Care 1 January 2025; 48 (Supplement\_1): S167–S180. <https://doi.org/10.2337/dc25-S008>*

# Long term use

Discontinue if not effective in 12 weeks



Lingvay, Ildiko et al. "Obesity in adults." 2024. The Lancet, Volume 404, Issue 10456, 972 - 987

	Naltrexone plus Bupropion	Phentermine plus topiramate extended release	Orlistat	Liraglutide 3 mg	Semaglutide 2.4 mg	Tirzepatide
Dosage form and dosing	8 mg naltrexone–90 mg bupropion; starting at one tablet daily; increasing by one tablet daily once per week over 4 weeks to maximum two tablets twice daily	3.75 mg phentermine–23 mg topiramate once daily, oral for 14 days; then 7.5/46 mg; after 12 weeks when <3% weight loss, can increase to 15/92 mg	60–120 mg three times a day, with meals, oral	Starting at 0.6 mg daily, subcutaneous; increasing every week: 1.2 mg, 1.8 mg, 2.4 mg, and 3.0 mg (maximum)	Starting at 0.25 mg weekly, subcutaneous; increasing every 4 weeks: 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg (maximum)	Starting at 2.5 mg weekly, subcutaneous; increasing by 2.5 mg weekly after at least 4 weeks; maintenance 5, 10, or 15 mg weekly
Mechanism of action for weight reduction	Dopamine and noradrenaline reuptake inhibitor (bupropion); opioid receptor antagonist (naltrexone)	Sympathomimetic (phentermine); GABA receptor activation, and carbonic anhydrase inhibition (topiramate)	Inhibition of gastric and pancreatic lipase	GLP-1 receptor agonism in appetite and reward centres; slowing gastrointestinal transit	GLP-1 receptor agonism in appetite and reward centres; slowing gastrointestinal transit	Dual GIP/GLP-1 receptor agonism
Contraindications	Chronic opioid use, acute opioid withdrawal, uncontrolled hypertension, seizure disorder, abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiseizure drugs, and monoamine oxidase inhibitors use	Glaucoma, hyperthyroidism, monoamine oxidase inhibitors, hypersensitivity to sympathomimetic amines, and pregnancy	Chronic malabsorption syndrome, cholestasis, and pregnancy	Personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2, pregnancy	Personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2, pregnancy	Personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2, pregnancy

# Long term use

## Side effects and % of weight loss



Lingvay, Ildiko et al. **“Obesity in adults.”** 2024.  
The Lancet, Volume 404, Issue 10456, 972 - 987

	Naltrexone plus Bupropion	Phentermine plus topiramate extended release	Orlistat	Liraglutide 3 mg	Semaglutide 2-4 mg	Tirzepatide
*Side-effects	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhoea, and sleep disorders	Elevation in heart rate, mood and sleep disorders, cognitive impairment, metabolic acidosis, paraesthesia, and dry mouth	Oily rectal leakage, abdominal distress, abdominal pain, flatulence with discharge, faecal urgency, steatorrhea, faecal incontinence, and increased defecation	Increased heart rate, constipation, diarrhoea, nausea, vomiting, and headache	Nausea, vomiting, diarrhoea, abdominal pain, constipation, and headache	Nausea, diarrhoea, vomiting, constipation, dyspepsia, and abdominal pain
Mean placebo-subtracted weight loss (%) in participants without diabetes	5% <sup>74</sup> (at 1 year)	9% <sup>75</sup> (at 1 year)	4% <sup>76</sup> (at 1 year)	6% <sup>77</sup> (at 1 year)	12.5% <sup>78</sup> (at 68 weeks)	17.8% <sup>79</sup> (72 weeks)
Mean placebo-subtracted weight loss (%) in participants with diabetes	3.2% <sup>80</sup> (at 1 year)	6.7% <sup>81</sup> (at 1 year)	2.5% <sup>82</sup> (at 1 year)	4.0% <sup>83</sup> (at 1 year)	6.2% <sup>84</sup> (at 68 weeks)	11.6% <sup>85</sup> (at 72 weeks)

# Long term use

Improvement in blood pressure and A1C

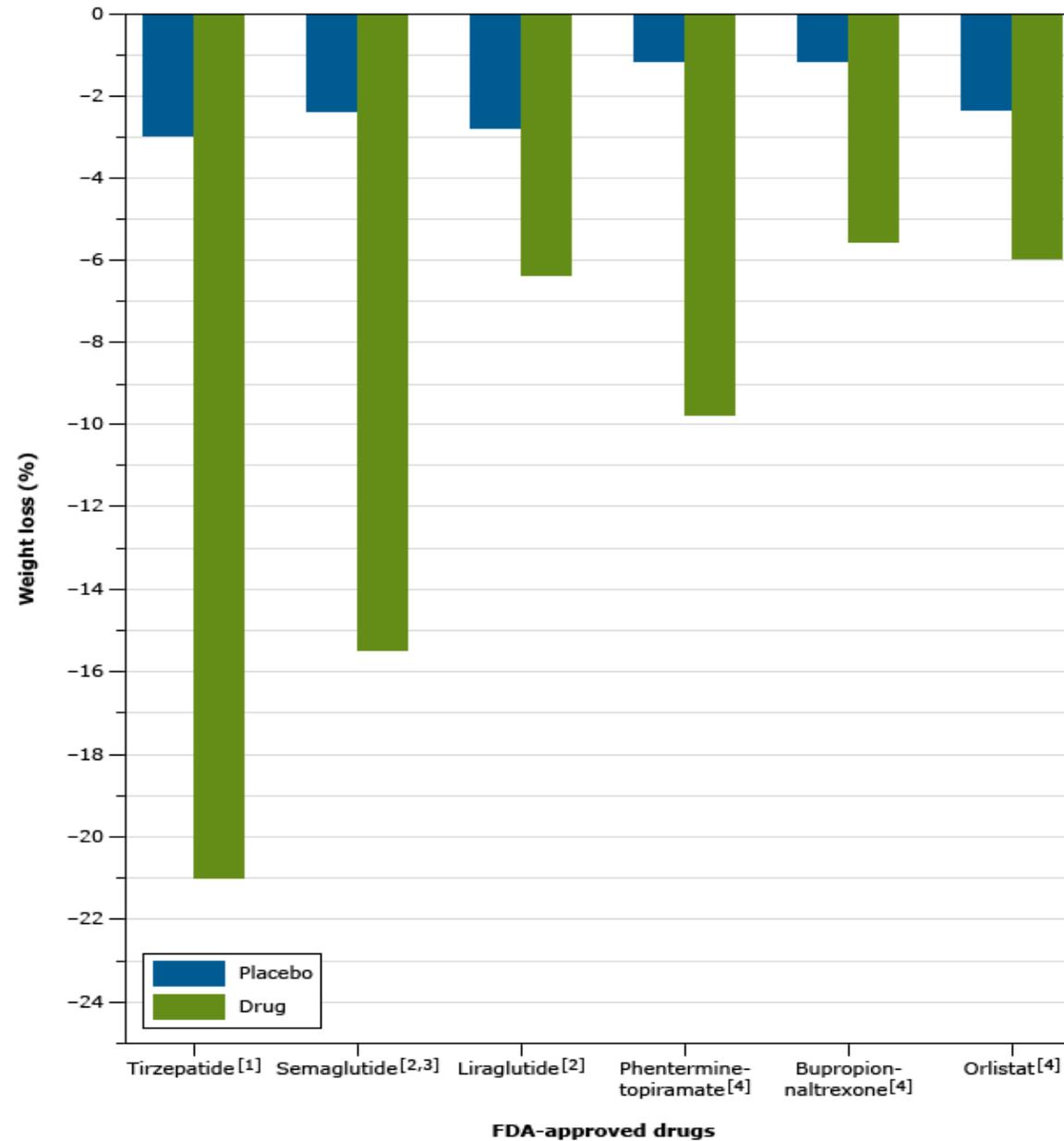


Lingvay, Ildiko et al. "Obesity in adults." 2024. The Lancet, Volume 404, Issue 10456, 972 - 987

	Naltrexone plus Bupropion	Phentermine plus topiramate extended release	Orlistat	Liraglutide 3 mg	Semaglutide 2.4 mg	Tirzepatide
Proportion of participants with 5% and 10% weight loss at 12 to 18 months (vs placebo) in participants without diabetes	48% and 25% (16 and 7% placebo)	67% and 47% (17 and 7% placebo)	73% and 41% (45 and 21% placebo)	63% and 33% (27 and 11% placebo)	86% and 69% (31 and 12% placebo)	91% and 84% (35 and 19% placebo)
Proportion of participants with 5% and 10% weight loss at 12 to 18 months (vs placebo) in participants with diabetes	45% and 19% (vs 19 and 6% placebo)	65% and 37% (vs 24 and 9% placebo)	33% and 10% (vs 13 and 4% placebo)	54% and 25% (vs 21 and 7% placebo)	69% and 46% (vs 28 and 8% placebo)	83% and 65% (vs 33 and 10% placebo)
Mean change from baseline in systolic blood pressure/diastolic blood pressure mm Hg (placebo)	-0.1/0.0 (vs -1.9/-0.9 placebo)	-2.9/-1.5 (vs 0.9/0.4 placebo)	-7.3/-3.6 (vs -5.2/-2.6 placebo)	-4.2/-2.6 (vs -1.5/-1.9 placebo)	-6.2/-1.1 (vs -0.4/-0.4 placebo)	-7.2/-4.8 (vs -1.0/-0.8 placebo)
Mean % change from baseline in HbA <sub>1c</sub> in participants with diabetes (vs placebo)	-0.6% (-0.1% in placebo)	-1.6% (-1.2% in placebo)	-0.6% (-0.3% in placebo)	-1.3% (-0.3% in placebo)	-1.6% (-0.4% in placebo)	-2.1% (-0.5% in placebo)



## Weight loss outcomes with FDA-approved medications



Leigh Perreault and Tirissa Reid  
“Obesity in Adults: Drug therapy”  
2025. uptodate.com accessed May 2025.  
<https://www.uptodate.com/contents/obesity-in-adults-drug-therapy>

# Short-term (12 weeks)

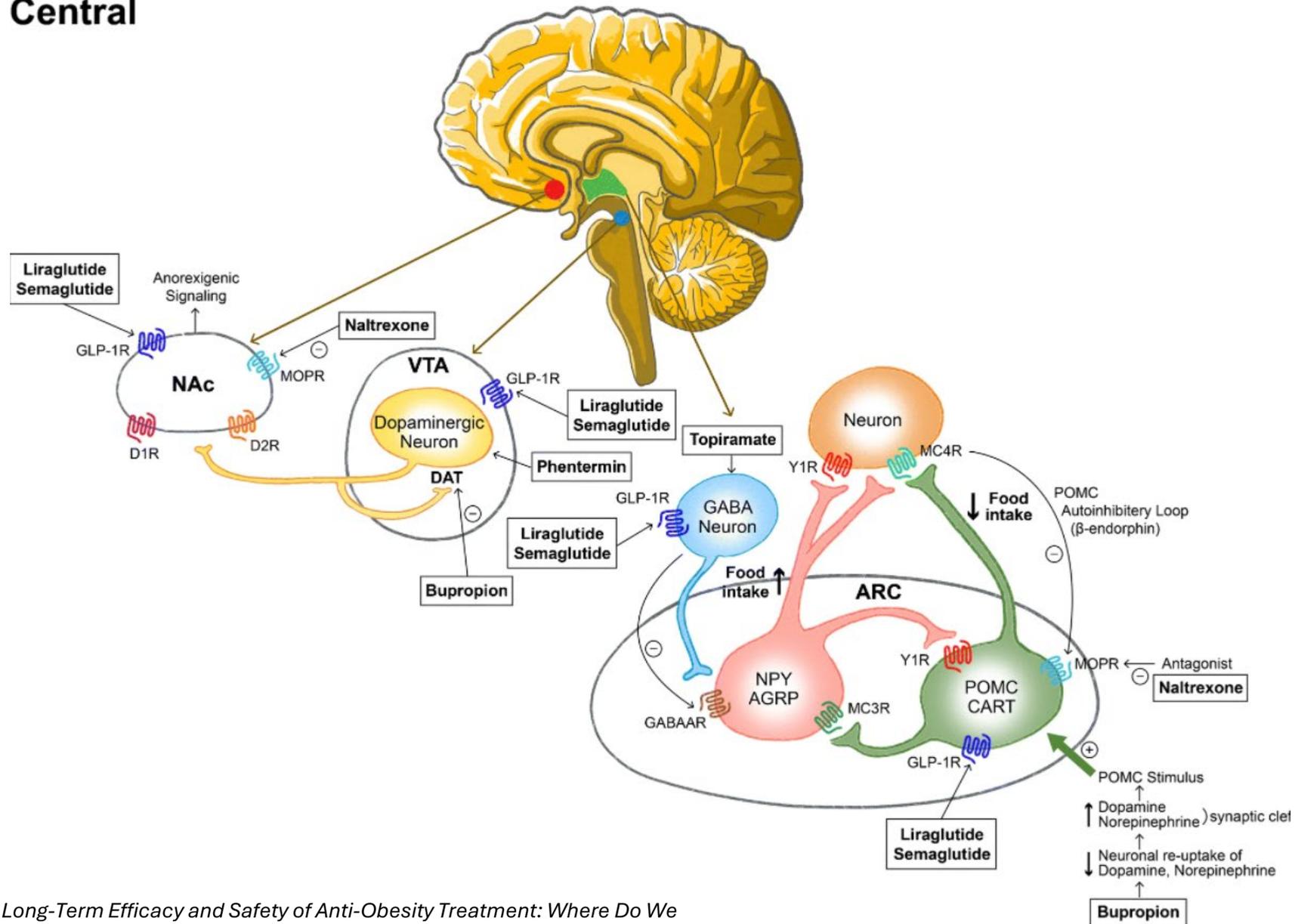
>5% weight loss



Noradrenergic sympathomimetic drugs approved for short-term use			
Benzphetamine	Initial: 25 mg once daily; may increase up to 50 mg 3 times daily if needed and tolerated. Maximum dose: 50 mg 3 times daily.	C-III	Applies to all sympathomimetic agents: <ul style="list-style-type: none"> <li>▪ If prescribed, limit to short-term (<math>\leq 12</math> weeks) use.</li> <li>▪ Adverse effects include increase in heart rate, blood pressure, insomnia, dry mouth, constipation, nervousness.</li> <li>▪ Abuse potential due to amphetamine-like effects.</li> <li>▪ May counteract effect of blood pressure medications.</li> <li>▪ Avoid in patients with heart disease, uncontrolled hypertension, pulmonary hypertension, or history of substance use disorder.</li> <li>▪ Contraindicated in patients with a history of CVD, hyperthyroidism, glaucoma, agitated states, pregnancy, breastfeeding, or within 14 days of MAO inhibitors.</li> </ul>
Diethylpropion	Immediate release: 25 mg 3 times daily, 1 hour before meals. Controlled release: 75 mg once daily in the morning.	C-IV	
Phentermine	Immediate release (Adipex-P and generics): 15 to 18.75 mg once daily or 30 to 37.5 mg in 1 or 2 divided doses. Immediate release (Lomaira): 8 mg 3 times daily before meals.	C-IV	
Phendimetrazine	Immediate release: 17.5 to 35 mg 2 or 3 times daily, 1 hour before meals; may increase to 70 mg 3 times daily if needed and tolerated. Maximum dose: 70 mg 3 times daily. Sustained release: 105 mg once daily in the morning.	C-III	

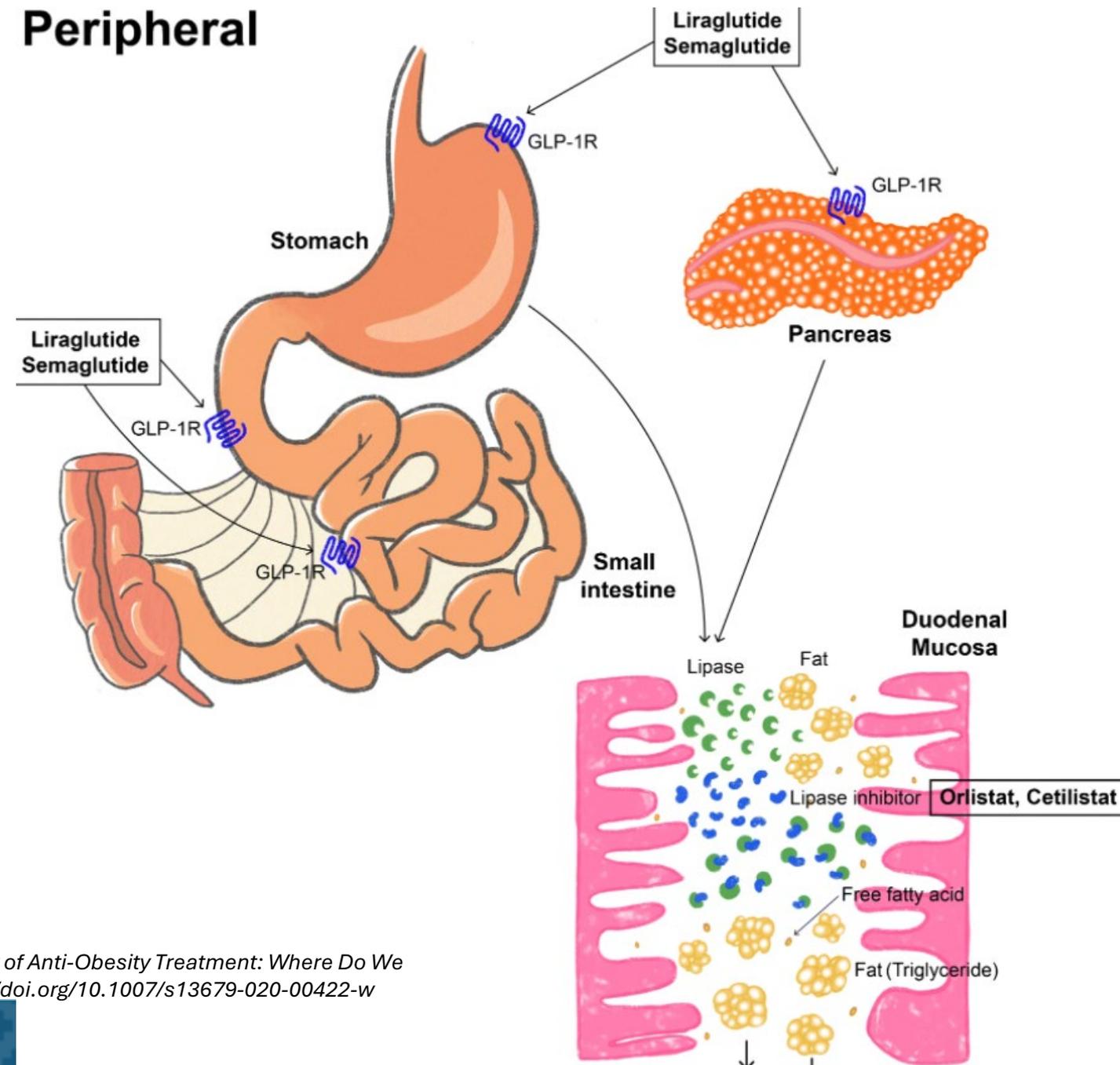
Leigh Perreault and Tirissa Reid “Obesity in Adults: Drug therapy” 2025.  
 uptodate.com accessed May 2025. <https://www.uptodate.com/contents/obesity-in-adults-drug-therapy>

# Central



Tak, Y.J., Lee, S.Y. Long-Term Efficacy and Safety of Anti-Obesity Treatment: Where Do We Stand?. *Curr Obes Rep* **10**, 14–30 (2021). <https://doi.org/10.1007/s13679-020-00422-w>

# Peripheral



Tak, Y.J., Lee, S.Y. Long-Term Efficacy and Safety of Anti-Obesity Treatment: Where Do We Stand?. *Curr Obes Rep* **10**, 14–30 (2021). <https://doi.org/10.1007/s13679-020-00422-w>

## Glucagon-like Peptide-1 Receptor Agonism

## Glucose-dependent Insulinotropic Polypeptide Receptor Agonism

### Central Nervous System

- ↑ Satiety
- ↓ Food Intake
- ↑ Nausea
- ↓ Body Weight

### Pancreas

- ↑ Insulin
- ↓ Glucagon

### Stomach

- ↓ Gastric Emptying

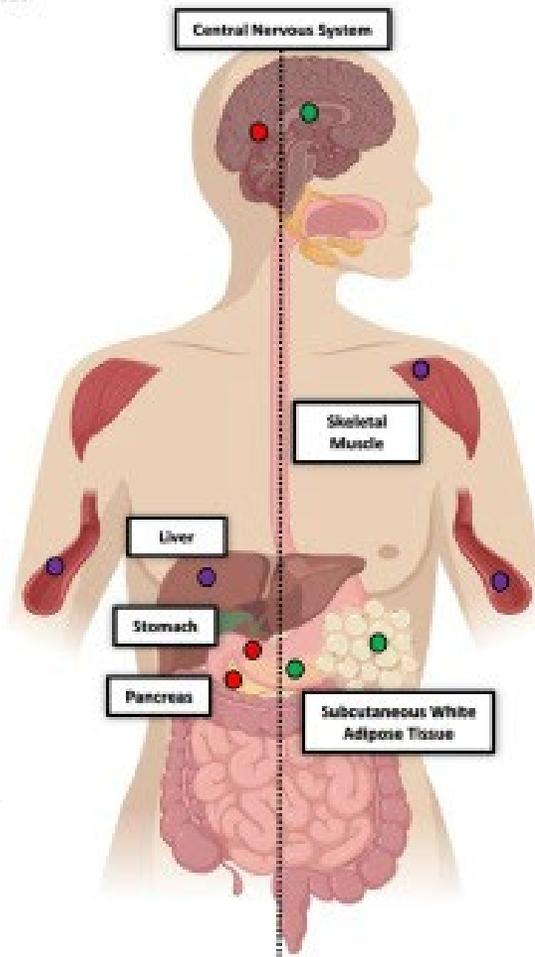
### Systemic

- ↓ Hyperglycemia

### Liver

- ↑ Insulin Sensitivity
- ↓ Hepatic Glucose Production
- ↓ Ectopic Lipid Accumulation

- Glucose-dependent Insulinotropic Polypeptide Receptor Agonism
- Glucagon-like Peptide 1 Receptor Agonism
- Indirect Action



### Central Nervous System

- ↓ Food Intake
- ↓ Nausea
- ↓ Body Weight

### Pancreas

- ↑ Insulin
- ↑ Glucagon

### Subcutaneous White Adipose Tissue

- ↑ Insulin Sensitivity
- ↑ Lipid Buffering Capacity
- ↑ Blood Flow
- ↑ Storage Capacity
- ↓ Proinflammatory Immune Cell Infiltration

### Systemic

- ↓ Hyperglycemia
- ↓ Dietary Triglyceride

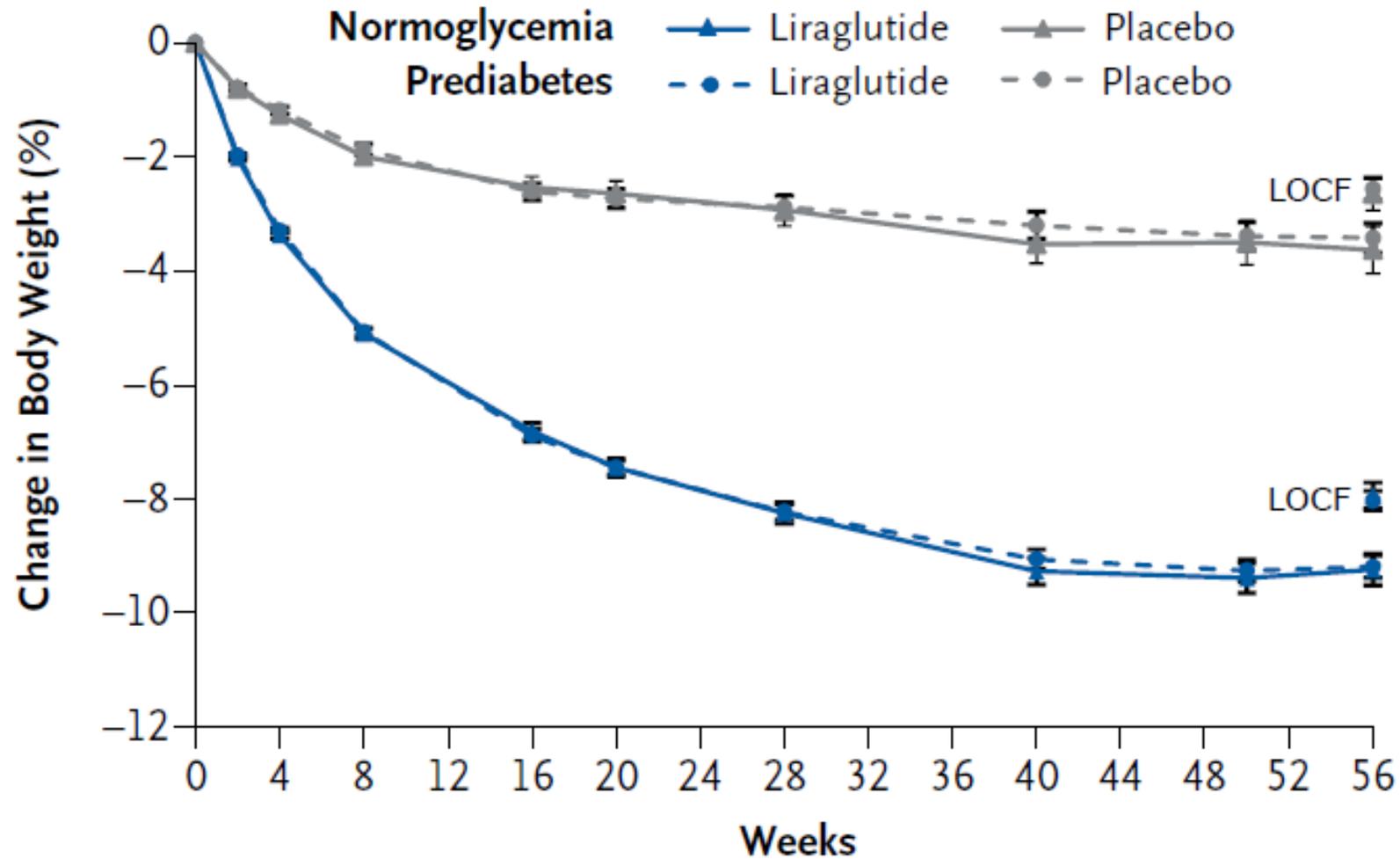
### Skeletal Muscle

- ↑ Insulin Sensitivity
- ↑ Metabolic Flexibility
- ↓ Ectopic Lipid Accumulation

# Liraglutide 3mg



A



Pi-Sunyer X, Astrup A, et al., "A randomized controlled trial of 3mg liraglutide in weight management." *July 2, 2015 N Engl J Med* 2015; 373:11-22. DOI: 10.1056/NEJMoa1411892



# Semaglutide

0.25

0.5

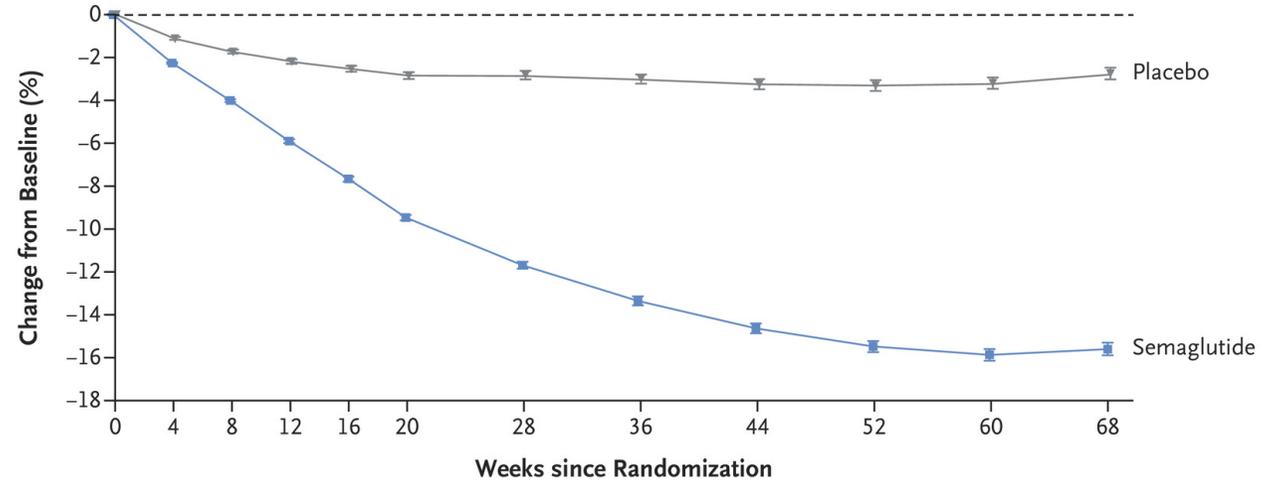
1.0

1.7

2.4

Wilding, John, et al. "Once-Weekly Semaglutide in Adults with Overweight or Obesity." March 18, 2021 N Engl J Med 2021; 384:989-1002. DOI: 10.1056/NEJMoa2032183

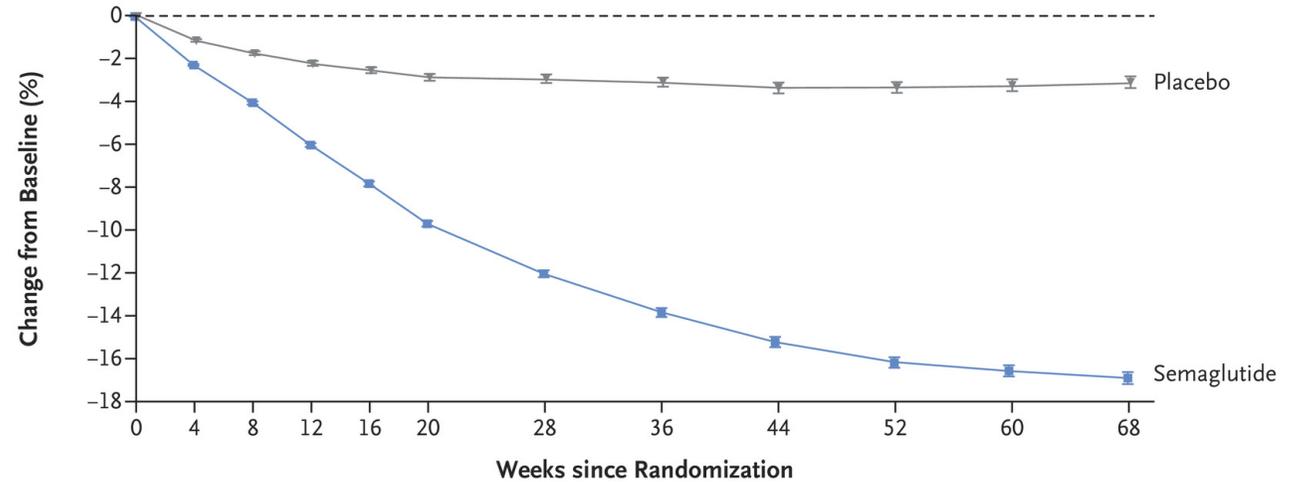
**A Body Weight Change from Baseline by Week, Observed In-Trial Data**



**No. at Risk**

Placebo	655	649	641	619	615	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212

**B Body Weight Change from Baseline by Week, Observed On-Treatment Data**



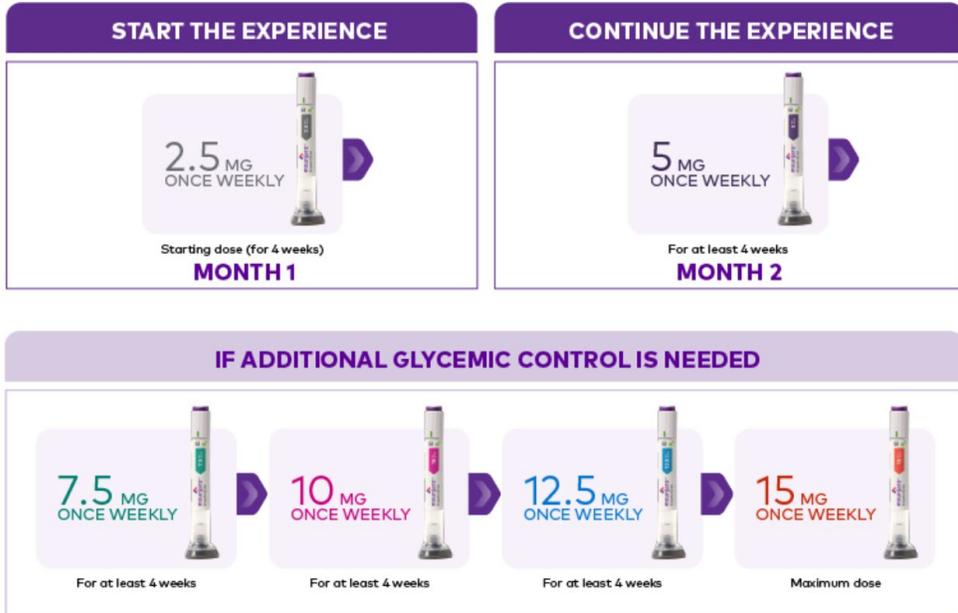
**No. at Risk**

Placebo	655	647	637	613	607	593	576	555	529	520	514	499
Semaglutide	1306	1283	1259	1225	1206	1193	1176	1166	1135	1115	1100	1059

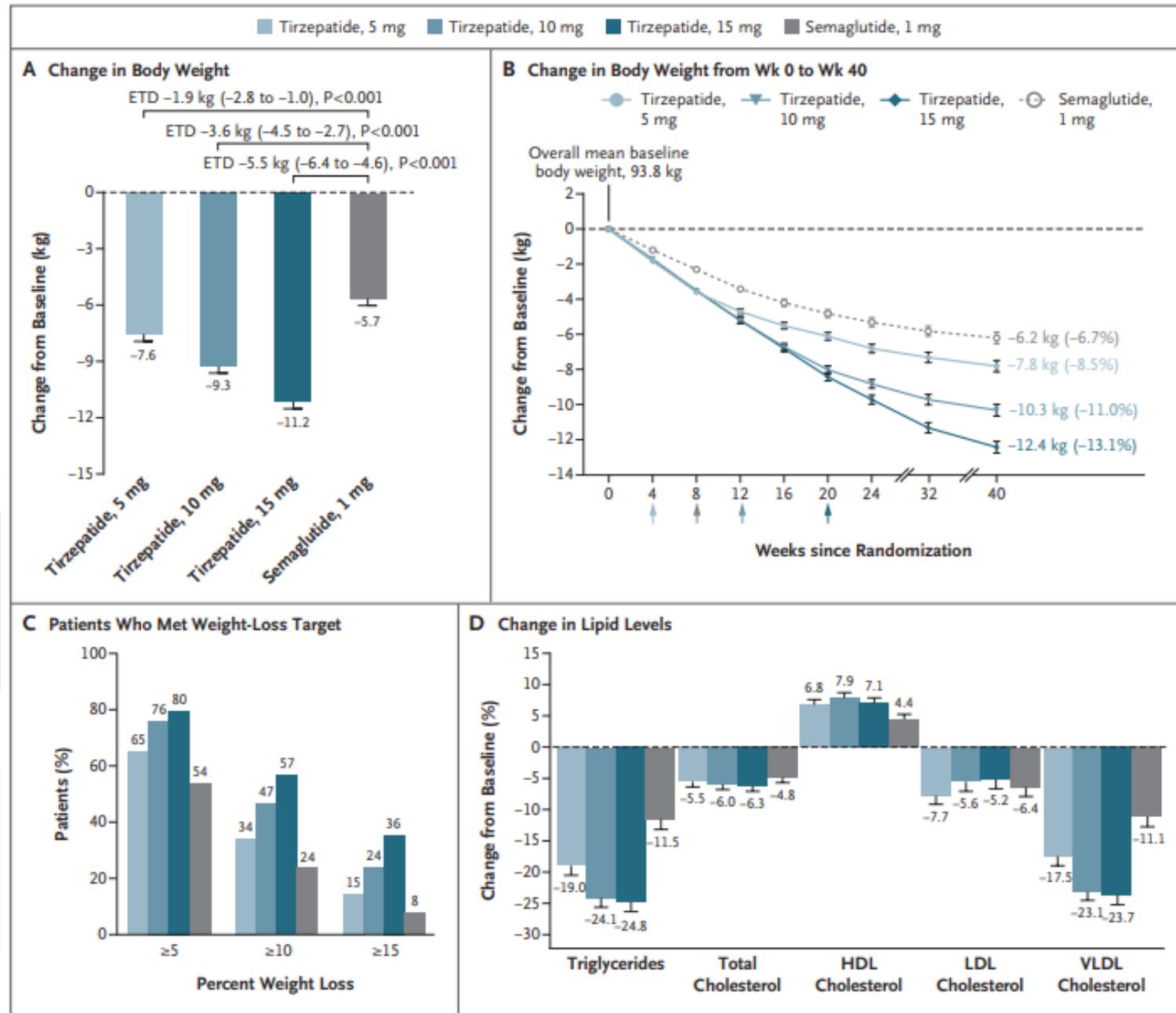
# Tirzepatide

GIP/GLP1 (incretin)

**GIP** Glucose-dependent Insulinotropic Polypeptide  
**GLP-1** Glucagon-like Peptide - 1



Frías JP, Davies MJ, Rosenstock J, Pérez Manghi FC, Fernández Landó L, Bergman BK, Liu B, Cui X, Brown K; SURPASS-2 Investigators. Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes. *N Engl J Med.* 2021 Aug 5;385(6):503-515. doi: 10.1056/NEJMoa2107519. Epub 2021 Jun 25. PMID: 34170647.



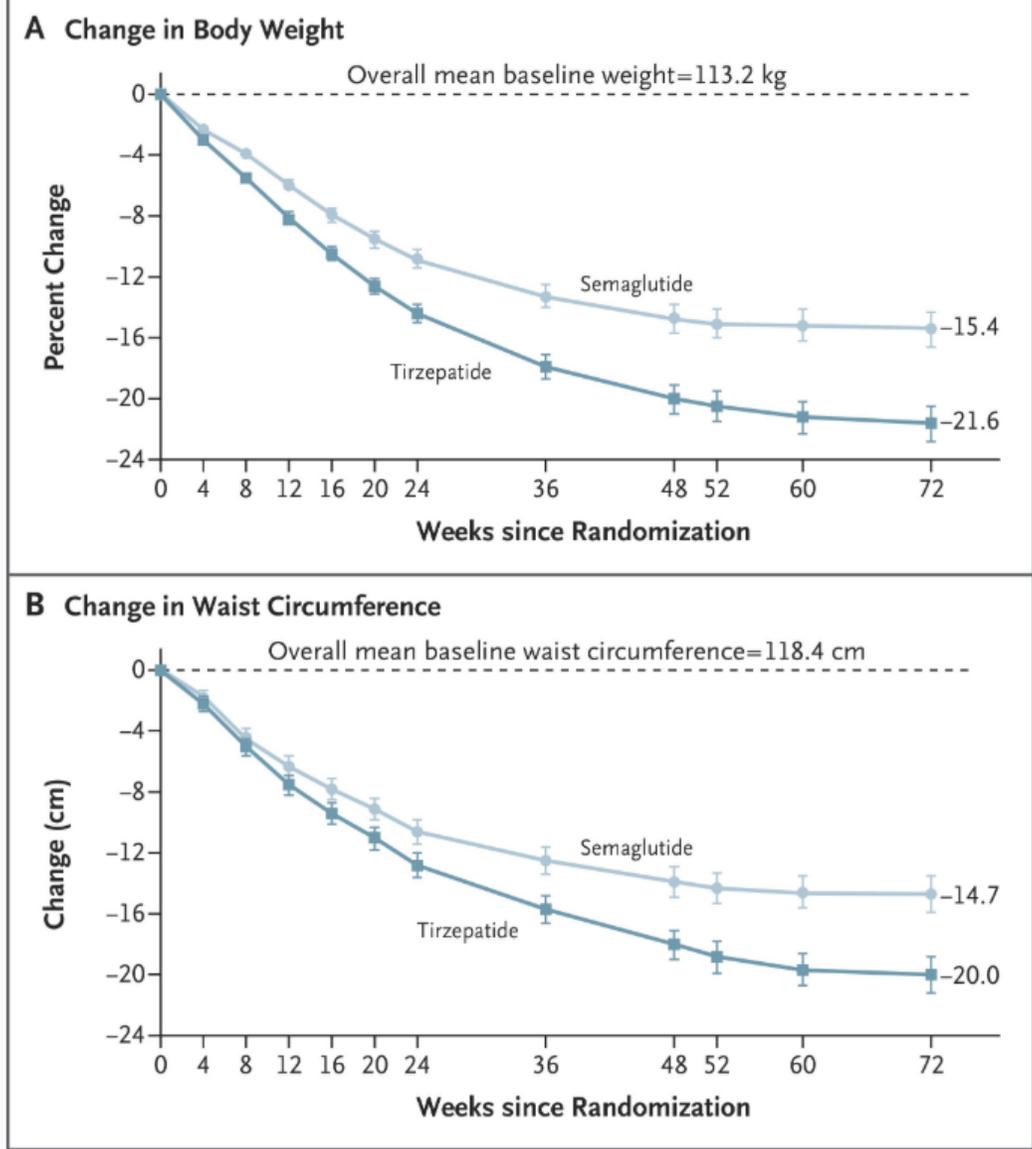
**Figure 2.** Effect of Once-Weekly Tirzepatide, as Compared with Semaglutide, on Body Weight, the Percentage of Patients Who Met Weight-Loss Goals, and the Lipid Profile.

# SURMOUNT-5

Tirzepatide vs Semaglutide

FIGURE 2

Change in Body Weight and Waist Circumference from Baseline to Week 72 (Efficacy Estimand).



A Louis J. et al. "Tirzepatide as Compared with Semaglutide for the Treatment of Obesity" *New England Journal of Medicine*.  
doi:10.1056/NEJMoa2416394 %U  
<https://www.nejm.org/doi/full/10.1056/NEJMoa2416394>

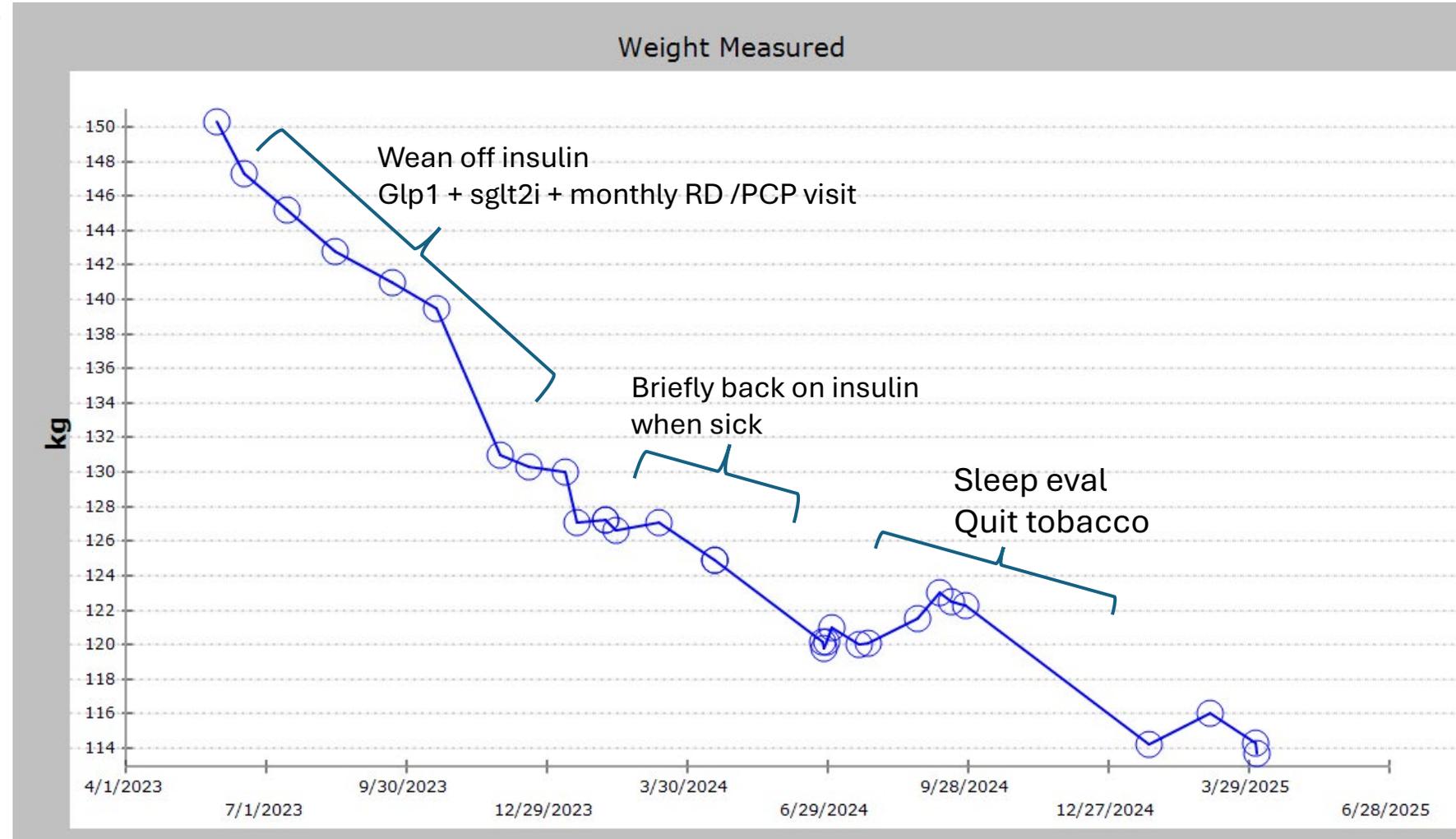
# BMI 57 → 43

Waiting for bariatric procedure

## Medication List:

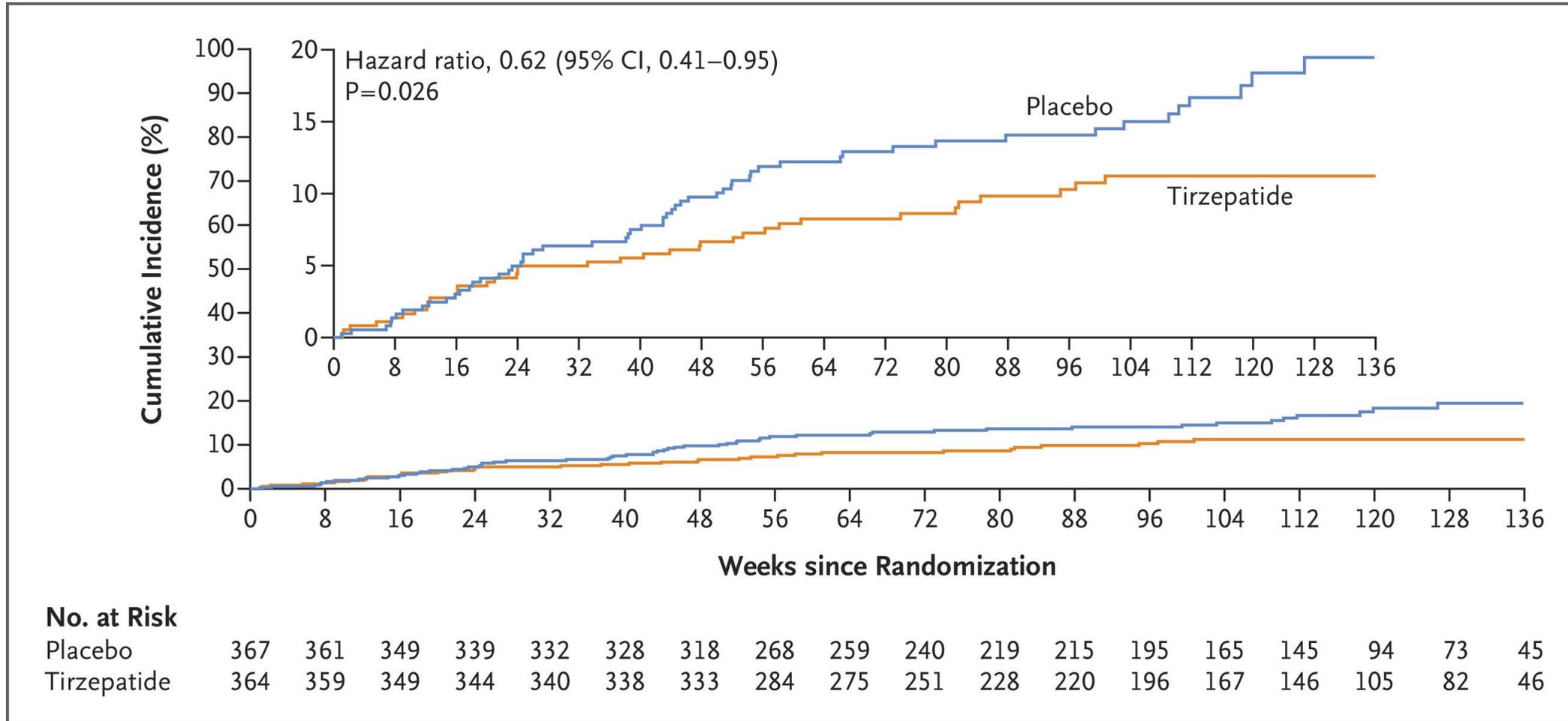
- Semaglutide sc 2mg weekly
- Metformin PO 1000mg daily
- Empagliflozin PO 10mg daily
- Lamotrigine PO 100mg bid
- B12, magnesium oxide, vitD

Now a1c 6.8



# SUMMIT Trial

Tirzepatide with HFpEF



A Milton Packer, et al.  
 “Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity” 2025  
 New England Journal of Medicine. 427-437.  
 doi:10.1056/NEJMoa2410027



# Newer Meds

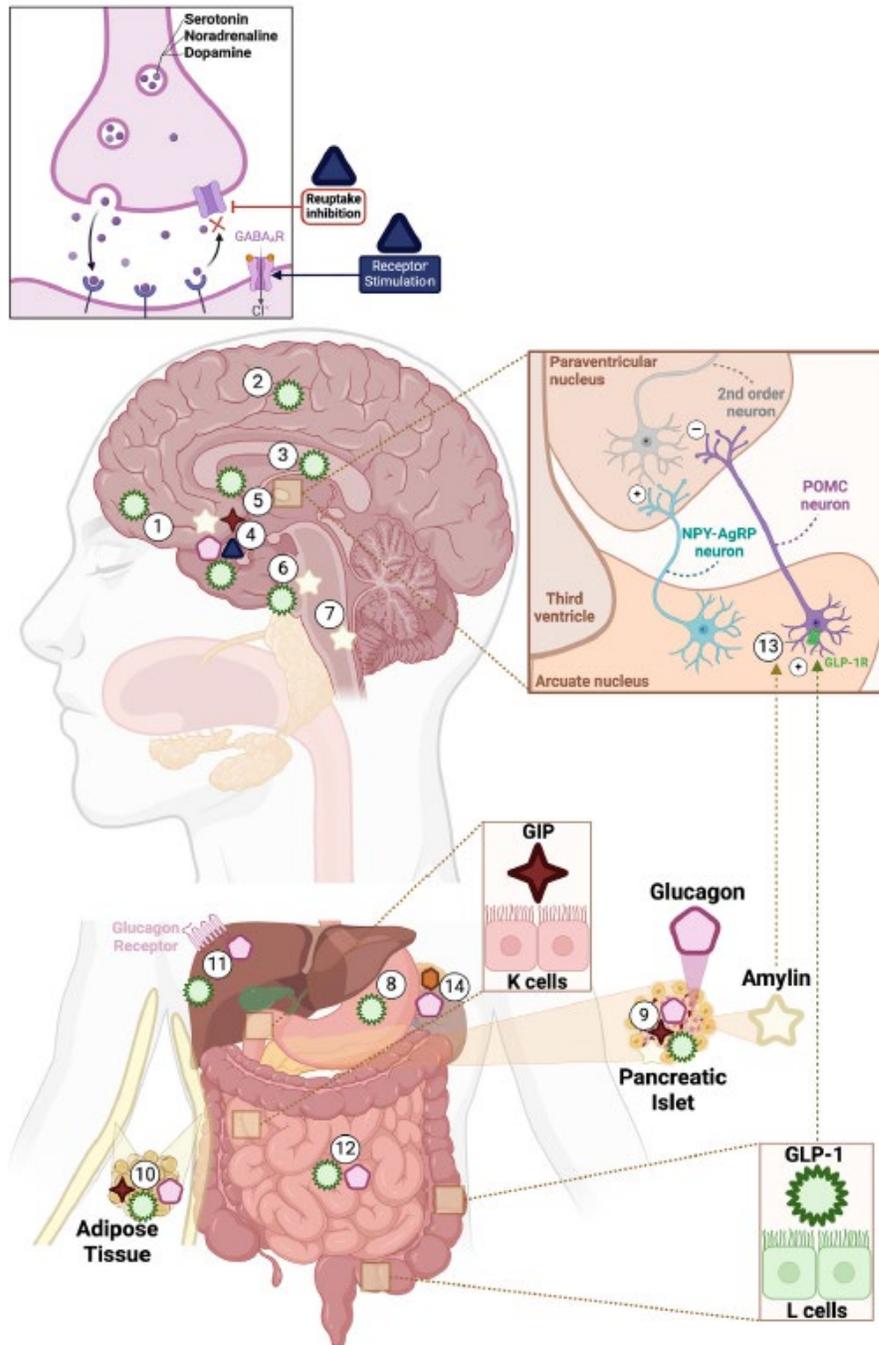
Oral semaglutide 25mg

Others GLP1...

Retatrutide

Cagrisema

etc



## Completed & Ongoing Phase 3 Drugs

**CagriSema**  
 Amylin analog & GLP-1 receptor agonist

**Dapagliflozin**  
 SGLT-2 inhibitor

**Mazdutide, Survodutide**  
 Dual GLP-1 & Glucagon receptor agonist

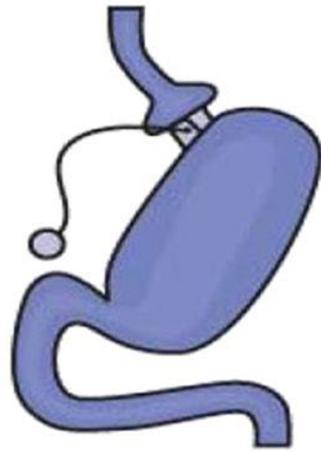
**Ecnoglutide, Orforglipron, Semaglutide<sup>1</sup>, TG103**  
 GLP-1 receptor agonist

**Retatrutide**  
 Triple GLP-1, GIP, and Glucagon receptor agonist

**Sibutramine/ Topiramate XR**  
 Norepinephrine, serotonin, and dopamine reuptake inhibition & GABA<sub>A</sub>R stimulation

Kokkorakis M, Chakhtoura M, Rhayem C, Al Rifai J, Ghezzawi M, Valenzuela-Vallejo L, Mantzoros CS. Emerging pharmacotherapies for obesity: A systematic review. *Pharmacol Rev.* 2025 Jan;77(1):100002. doi: 10.1124/pharmrev.123.001045. Epub 2024 Nov 22. PMID: 39952695.

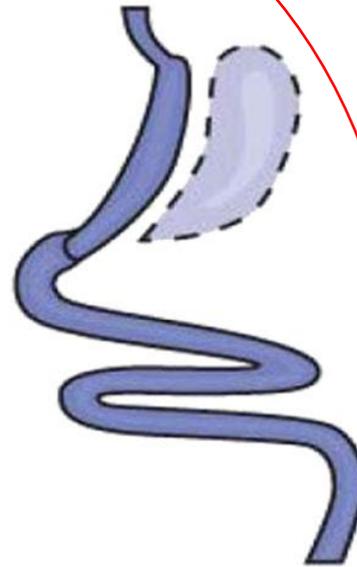
# Bariatric Surgery



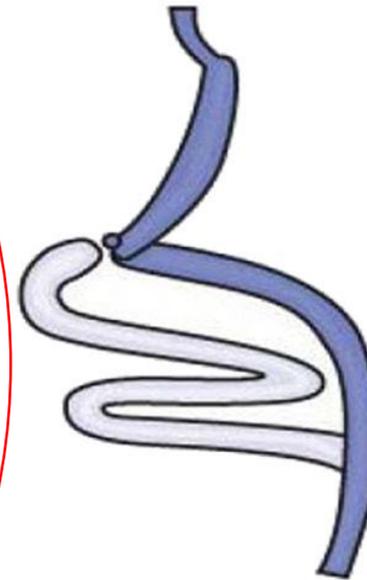
**Adjustable  
Gastric Band  
(AGB)**



**Roux-en-Y  
Gastric Bypass  
(RYGB)**



**Vertical Sleeve  
Gastrectomy  
(VSG)**



**Biliopancreatic  
Diversion With a  
Duodenal Switch  
(BPD-DS)**

# Which medicine is obesogenic?

*Can cause weight gain*

1. Naltrexone
2. Omeprazole
3. Metoprolol
4. Bupropion



# What are some risk factors of weight gain?



1. Sedentary lifestyle
2. Food insecurity
3. Poor Sleep Quality
4. Medications
5. All of above

# Any Questions?



[Contact: ai-ling.lin@ihs.gov](mailto:ai-ling.lin@ihs.gov)

