

# OVERCOMING OBESITY

A PCP'S GUIDE TO COMPREHENSIVE OBESITY CARE



This activity is supported by an educational grant from Eli Lilly and Company.





# Activity Overview

## TARGET AUDIENCE

US primary care physicians, NPs, and PAs including those who are community-based, practice in large ACOs; in rural communities; and who serve patients in underserved areas

## EDUCATIONAL OBJECTIVES

After completing this activity, the participant should be better able to:

- Integrate evidence-based approaches to diagnose, manage, and treat obesity, such as BMI, waist circumference, body fat percentage, and routine visits, especially in patients with concurrent comorbidities.
- Determine appropriate treatment with consideration of the latest clinical evidence, mechanism of action, side effects, drug administration frequency, and patient-specific factors when developing individualized treatment plans for patients with obesity.
- Employ shared decision-making and multidisciplinary approaches when discussing weight management strategies, including treatment and lifestyle modifications, to support optimal adherence and outcomes for patients with overweight/obesity.

# Part 2: No One-Size-Fits-All Approach: Individualizing Obesity Treatment



# Faculty



**Robert Kushner, MD, MS**

Professor, Departments of  
Medicine and Medical Education  
Northwestern University Feinberg School of Medicine  
Chicago, IL, USA



**Jay H. Shubrook, DO, FACOFP, FAAFP**

Professor and Diabeteologist, Department of  
Clinical Sciences and Community Health  
Touro University California  
College of Osteopathic Medicine  
Vallejo, CA, USA

# Barriers to treatment initiation and adherence





# Treatment Considerations for Patients with Overweight/Obesity

## Successful Treatment Requires:

### An Experienced Team

- Endocrinologists
- Primary Care/Family Practice
- Obesity Medicine Specialist
- Registered Dietitians
- Gastroenterologist
- Bariatric Surgeon
- Psychologists
- Support Staff

### Treatments That Work

- Lifestyle
- Medication
- Devices
- Surgery

*Often lacking or behind barriers*

### Insurance Coverage for Treatment

*Often lacking or behind barriers*

*Importance of documentation and coding*



# Weight Discrimination

- The prevalence of weight discrimination in the US is increasing and **is comparable to that of race and gender discrimination**
- There are few other medical diseases in our society that are as stigmatized and shunned as obesity
- The societal stigma often associated with excess **weight is perpetuated with focus on personal responsibility for obesity**



## Case Study

Andrea is a 42-year-old female patient who presents to your clinic for a routine checkup. She has experienced weight loss and gain in the past. Andrea has been researching weight loss therapies online and mentions various options, including prescription medications, meal replacement programs, and bariatric surgery. She asks for your professional opinion on whether these are suitable options to support her long-term weight loss goals. Her current body mass index (BMI) is 34.







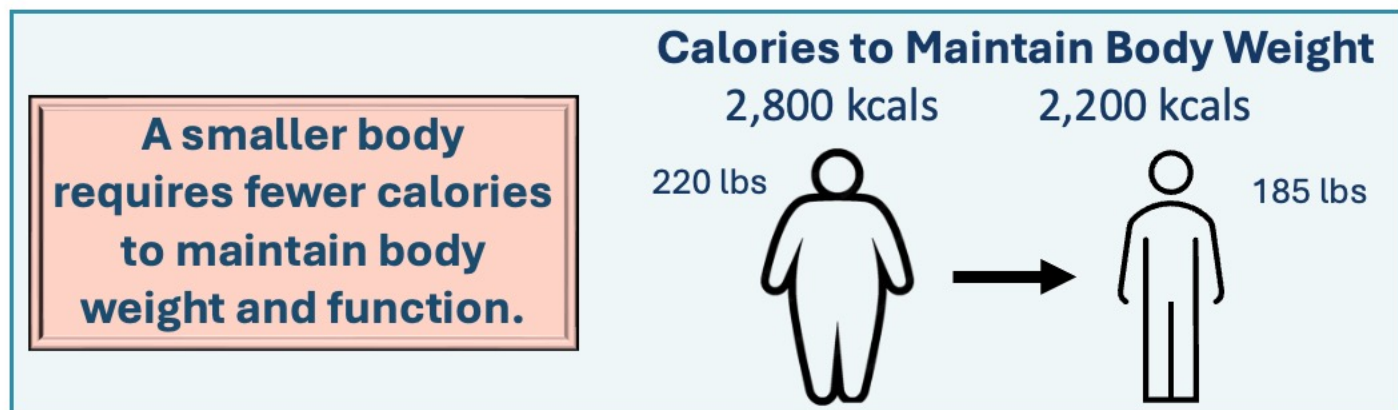
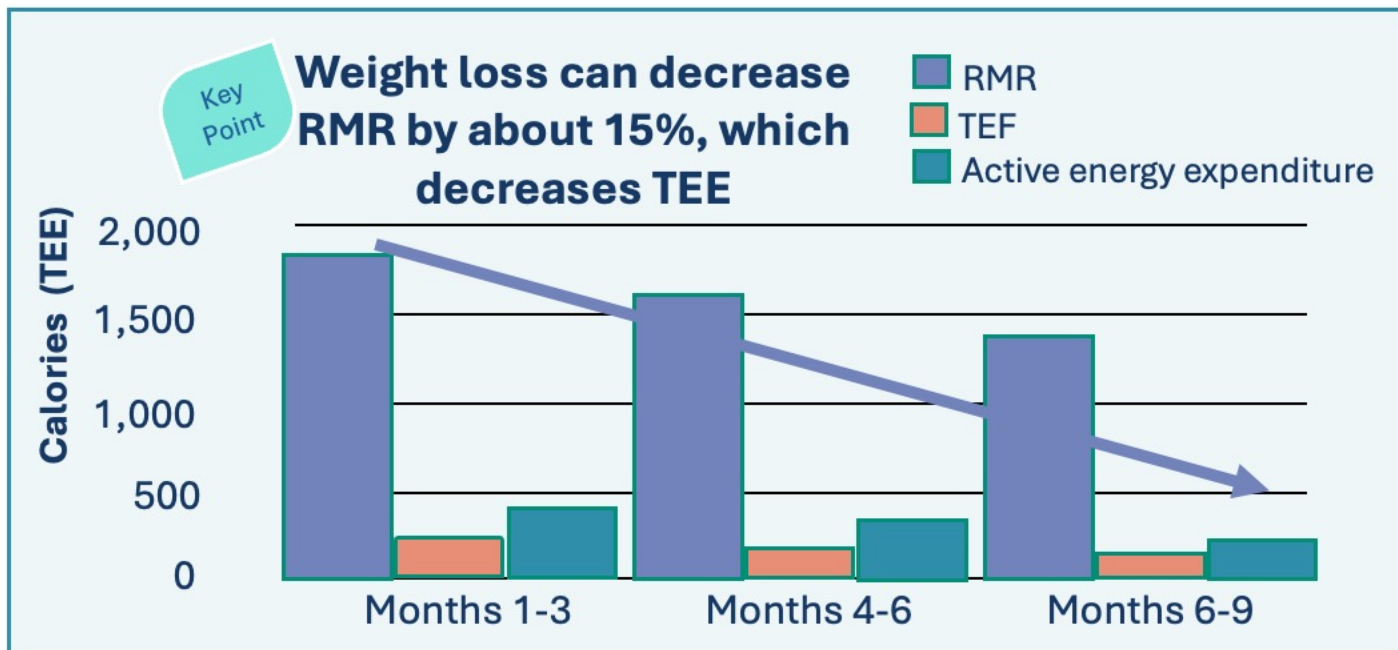
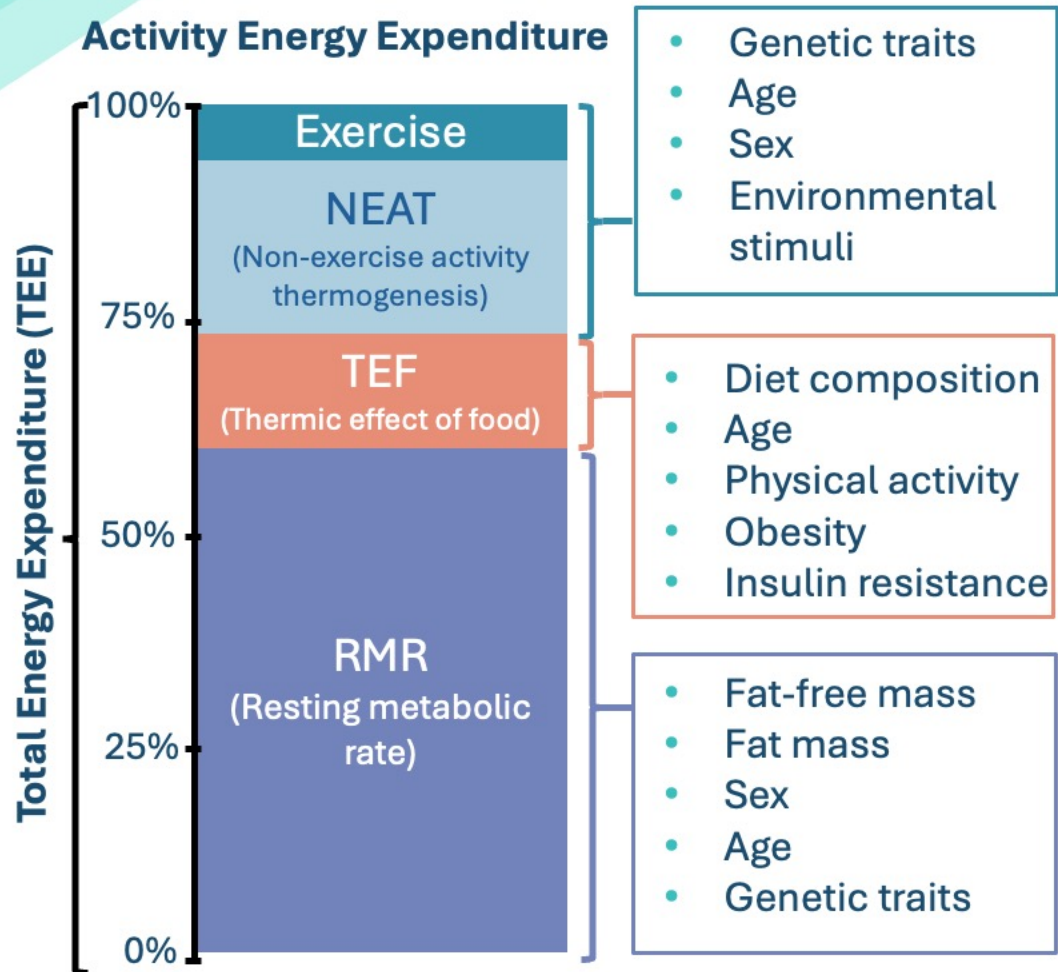
# Case Study

## What's Happening Here?





# Calories in vs Calories Out is a Moving Target



RMR, resting metabolic rate; TEE, total energy expenditure.

How Metabolic Adaptation Is Stalling Your Weight Loss Efforts. Box Nutrition. <https://www.boxnutrition.co.uk/single-post/how-metabolic-adaptation-is-stalling-your-weight-loss-efforts>.

Copyright © 2024 | Medical Learning Institute Inc.

# Clinical evidence of the evolving treatment landscape of obesity





# Obesity Management Goals

## Patient-Centered Language

Improve  
Patient  
Health

Improve  
Body Weight  
and  
Composition

Improve  
Quality of  
Life

*Shared Decision Making*



# Obesity Treatment Guidelines

Multimodal

Multidisciplinary

BMI Category (kg/m <sup>2</sup> )	Staging	Suggested therapy	Care Setting
<b>18.5-24.9</b> <23 in patients of certain ethnicities	Normal weight (no obesity)	Healthy lifestyle	<ul style="list-style-type: none"> <li>Primary care</li> </ul>
<b>25-29.9</b> 23-24.9 in patients of certain ethnicities	Overweight	Lifestyle therapy	<ul style="list-style-type: none"> <li>Primary care</li> <li>Consider referral to obesity medicine specialist if treatment is not effective</li> </ul>
<b>≥ 30</b> ≥ 25 in patients of certain ethnicities	Obesity stage 1 (no complications)	Lifestyle therapy Anti-obesity medications <i>Consider if lifestyle therapy fails to prevent progressive weight gain (BMI ≥27)</i>	<ul style="list-style-type: none"> <li>Primary care</li> <li>Consider referral to obesity medicine specialist</li> </ul>
	Obesity stage 2 (≥ 1 mild to moderate complications)	Lifestyle therapy Anti-obesity medications <i>Consider if lifestyle therapy fails to achieve therapeutic target or initiate with lifestyle therapy (BMI ≥27)</i>	<ul style="list-style-type: none"> <li>Primary care</li> <li>Consider referral to obesity medicine specialist</li> </ul>
	Obesity stage 3 (≥ 1 severe complication)	Lifestyle therapy Anti-obesity medications <i>Initiate with lifestyle therapy (BMI ≥27)</i> <i>Consider bariatric surgery (BMI ≥35)</i>	<ul style="list-style-type: none"> <li>Primary care</li> <li>Consider referral to obesity medicine specialist</li> </ul>



# Obesity Treatment Options: Nutrition

## Limit

- Unhealthy **ultra-processed foods** of minimum nutritional value
- **Energy-dense foods** high in calories
- **Energy-dense beverages:** sugar-sweetened beverages, juice, cream
- Avoid **trans fats** and **excessive sodium**

## Encourage

- Consumption of healthful proteins and fats, vegetables, leafy greens, fruits, berries, nuts, legumes, whole grains
- **Complex carbohydrates** over simple sugars: Low glycemic index over high glycemic index foods
- **High-fiber foods** over low-fiber foods
- Many dairy products (while being mindful of caloric content)
- Reading labels rather than marketing claims

## Encourage foods that result in a negative caloric balance to achieve and maintain a healthy weight

### Consider:

- Eating behaviors, and meal patterns
- Cultural background, traditions, and food availability
- Time constraints and financial issues
- Nutritional knowledge and cooking skills
- Medical conditions potentially affected by the nutrition plan
- Mediterranean diet
- Therapeutic lifestyle diet
- DASH (Dietary Approaches to Stop Hypertension)
- Ketogenic (modified Atkins) diet
- Ornish diet
- Paleo diet
- Vegetarian or vegan diet
- Intermittent fasting / time restricted eating
- Commercial diet programs



# Obesity Treatment Options: Physical Activity

## Routine Physical Activity May Improve:

- Body composition
- Adiposopathic endocrine and immune body processes
- Metabolic, musculoskeletal, cardiovascular, pulmonary, mental, sexual, and cognitive health

## Goal: Increase Energy Expenditure

- Dynamic (aerobic) training
- Resistive (anaerobic) strength training

## Goal: Decrease Physical Inactivity

- Leisure time physical activity
- Transportational/occupational non-exercise activity thermogenesis (NEAT)

Medical evaluation to ensure safety before beginning new exercise program

Tracking Progress



# Synthesis of Exercise: Recommendations and Evidence

Evidence Statement	Strength of Evidence
Aerobic training reduces body weight ~2-3 kg without dietary intervention and by 1 kg compared to resistance training alone	High
Aerobic training alone or combined with resistance training performed during a weight loss diet leads to an additional 1.5 kg weight loss	High
Resistance training but not aerobic training performed during a weight loss diet decreases the loss of lean body mass (LBM)	Moderate
Aerobic training and high intensity interval training (HIIT) but not resistance training reduce abdominal visceral fat	High
Resistance training alone or in combination with aerobic training improve muscle strength	High





# Obesity Treatment Options: Behavioral Therapy

## Challenges around eating behaviors

- Physiologic
- Mental stress
- Timing and emotions
- Environment
- Information gap
- Reward
- Eating disorders

## Elements for success in behavioral therapy

- Doable
- Efficacious
- Measurable/Accountable
- Self-ownership

## Why do people plateau with weight reduction or regain body weight?

- Physiologic priority imbalance
- Neurobiology
- Dynamic energy balance
- Behavior

## Barriers to routine physical activity

- Physiologic
- Lack of time
- Disinterest
- Environment

## SMART goals

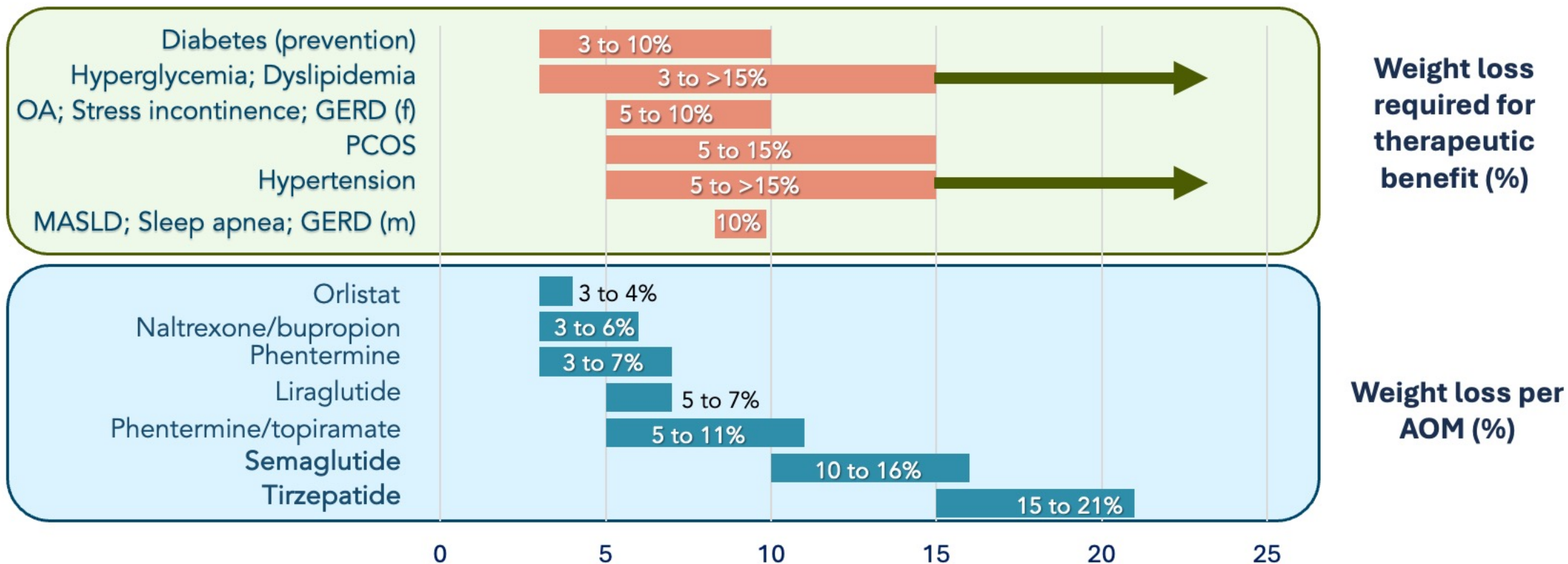
- **S**pecific
- **M**easurable
- **A**ssignable
- **R**ealistic
- **T**ime-related



# Obesity Treatment Options: Pharmacotherapy

Adjunct to Nutritional, Physical Activity, and Behavioral Therapies

5 to 10% weight reduction may improve metabolic and fat mass disease



A1C, glycated hemoglobin; BP, blood pressure; GERD, gastroesophageal reflux disease; MASLD, metabolic dysfunction-associated steatotic liver disease; OA, osteoarthritis; PCOS, polycystic ovary syndrome; TG, triglycerides; AOM, anti-obesity medication.

Cefalu WT, et al. *Diabetes Care*. 2015;38(8):1567-1582; Garvey WT, et al. *Endocr Pract*. 2016;22 Suppl 3:1-203; Tondt J, et al. *Obesity Algorithm eBook*. Obesity Medicine Association; 2023. <https://obesitymedicine.org/obesity-algorithm-powerpoint/>. Accessed July 9, 2024.

Copyright © 2024 | Medical Learning Institute Inc.



## Case Study

In addition to presenting with a BMI of 34, your evaluation leads you to suspect Andrea may suffer from OSA and PCOS.





# Obesity Pharmacotherapy Treatment: A Timeline





# Pharmacologic Management of Obesity

## 1st and 2nd Generation AOMs

	Generic (Brand)	Indication	MOA	Effect	How taken	Weight loss
1st generation	Phentermine (Adipex)	Chronic Obesity Management	Sympathomimetic amine	↓ appetite	PO, up to TID	~3-7%
	Orlistat (Alli, Xenical)	Chronic Obesity Management	Gastrointestinal lipase inhibitor	↓ fat absorption	PO, up to TID	~3-4%
	Phentermine/Topiramate-ER (Qsymia)	Chronic Obesity Management	Sympathomimetic amine + anticonvulsant, carbonic anhydrase inhibitor, gabaminergic	↓ appetite	PO, once daily	~5-11%
	Naltrexone-ER/Bupropion-ER (Contrave)	Chronic Obesity Management	Opioid receptor antagonist + dopamine-norepinephrine reuptake inhibitor	↓ appetite	PO, twice daily	~3-6%
	Liraglutide (Saxenda)	Chronic Obesity Management	GLP-1 RA	↓ appetite	SQ, once daily	~5-7%
2nd generation	Semaglutide (Wegovy)	Chronic Obesity Management; Mitigate CV risk	GLP-1 RA	↓ appetite	SQ, once weekly	~10-16%
	Tirzepatide (Zepbound)	Chronic Obesity Management	Dual GIP/GLP-1 RA	↓ appetite	SQ, once weekly	~15-21%

Key Point

GLP-1, glucagon-like peptide-1; PO, oral; SQ, subcutaneous injection; TID, three times a day.

## GLP-1 receptor agonism

### CNS

↑ Satiety ↑ Nausea ↓ Food intake ↓ Body weight

### Pancreas

↑ Insulin ↓ Glucagon

### Stomach

↓ Gastric emptying

### Systemic

↓ Hyperglycemia

### Liver

↑ Insulin sensitivity ↓ Hepatic glucose production  
↓ Ectopic lipid accumulation

## GIP receptor agonism

### CNS

↓ Food intake  
↓ Nausea  
↓ Body weight

### Pancreas

↑ Insulin ↓ Glucagon

### Subcutaneous white adipose tissue

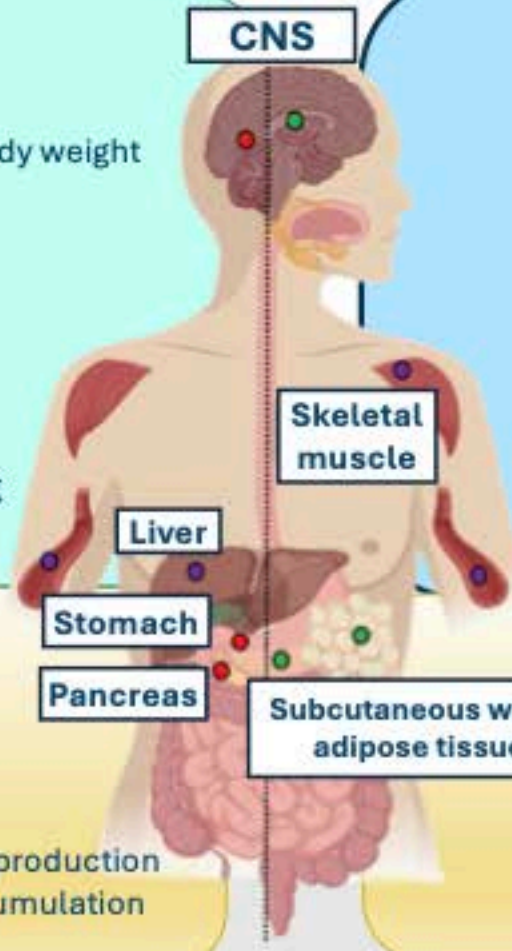
↑ Insulin sensitivity ↓ Proinflammatory immune-cell infiltration  
↑ Lipid buffering capacity  
↑ Blood flow  
↑ Storage capacity

### Systemic

↓ Hyperglycemia  
↓ Dietary TG

### Skeletal muscle

↑ Insulin sensitivity ↓ Ectopic lipid accumulation  
↑ Metabolic flexibility



GLP-1 receptor agonism



GIP receptor agonism



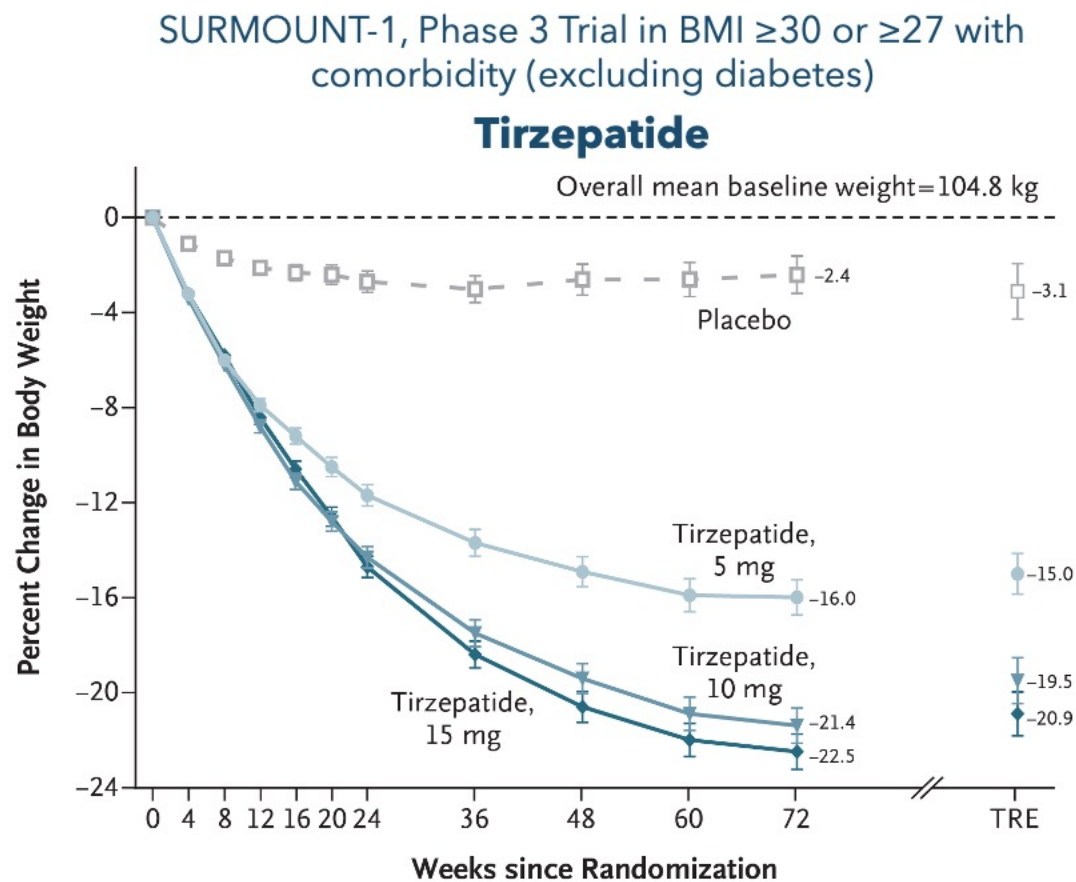
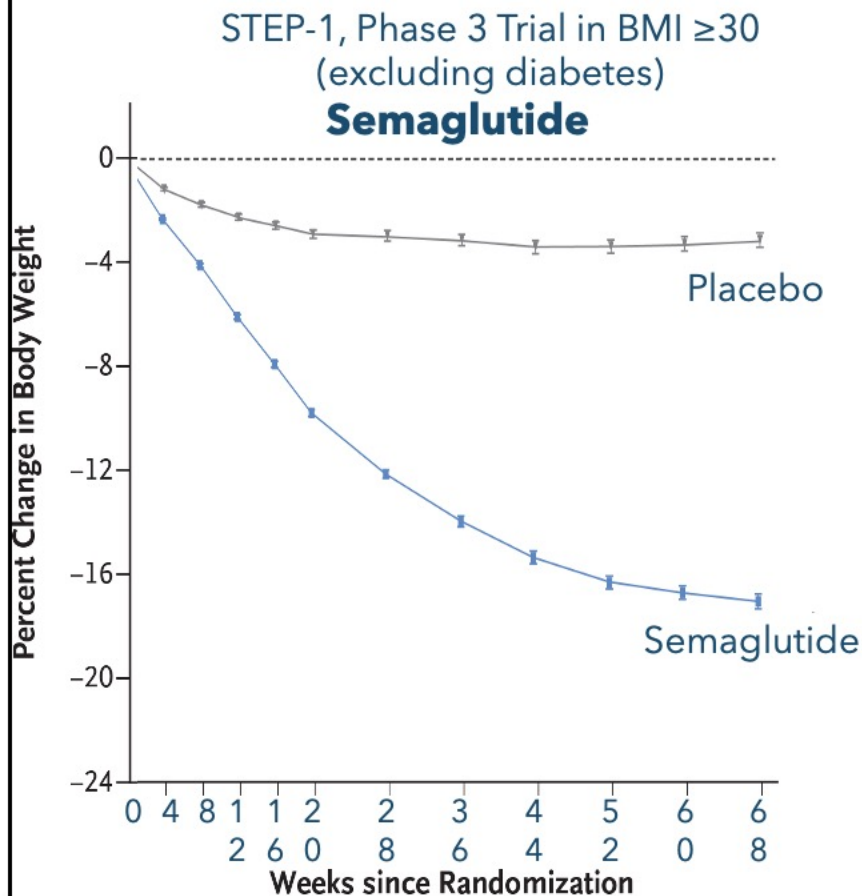
Indirect action





# Treatment of Obesity: Weight Loss with Semaglutide and Tirzepatide vs Placebo

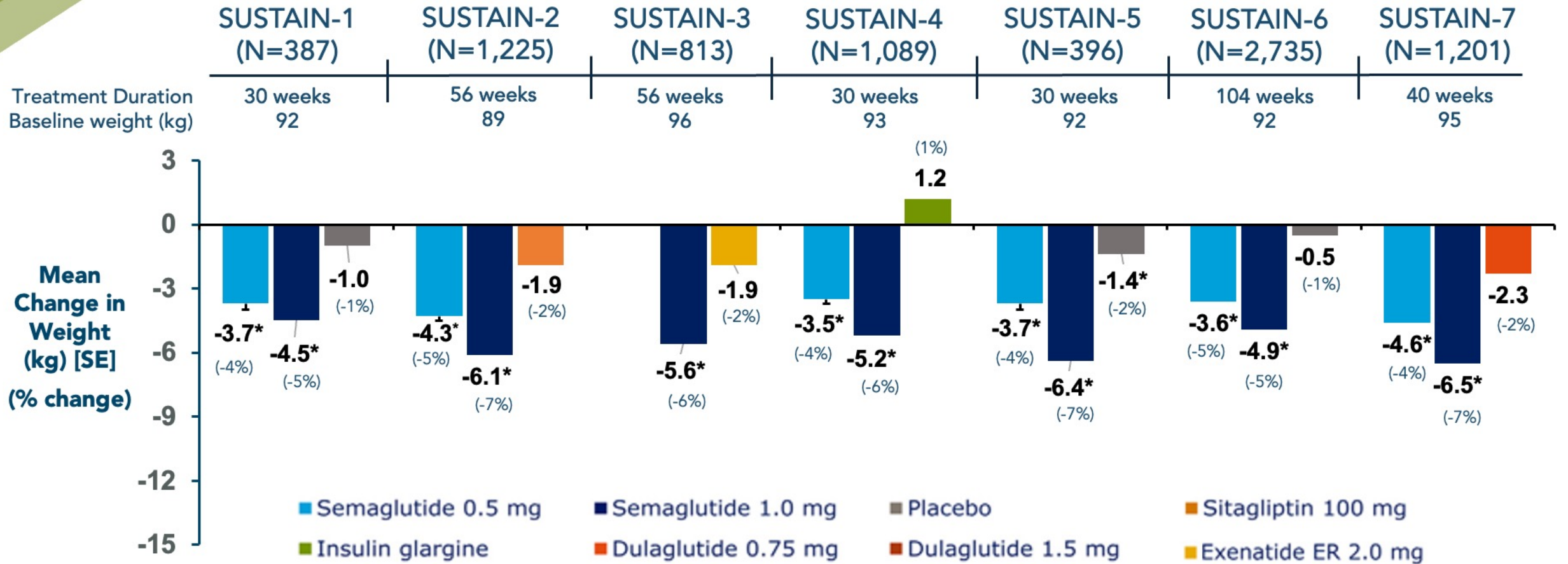
## Patients without T2D



\*Please note: these are not head-to-head trials.



# Weight Loss with Semaglutide vs Comparators in SUSTAIN Trials Patients with T2D



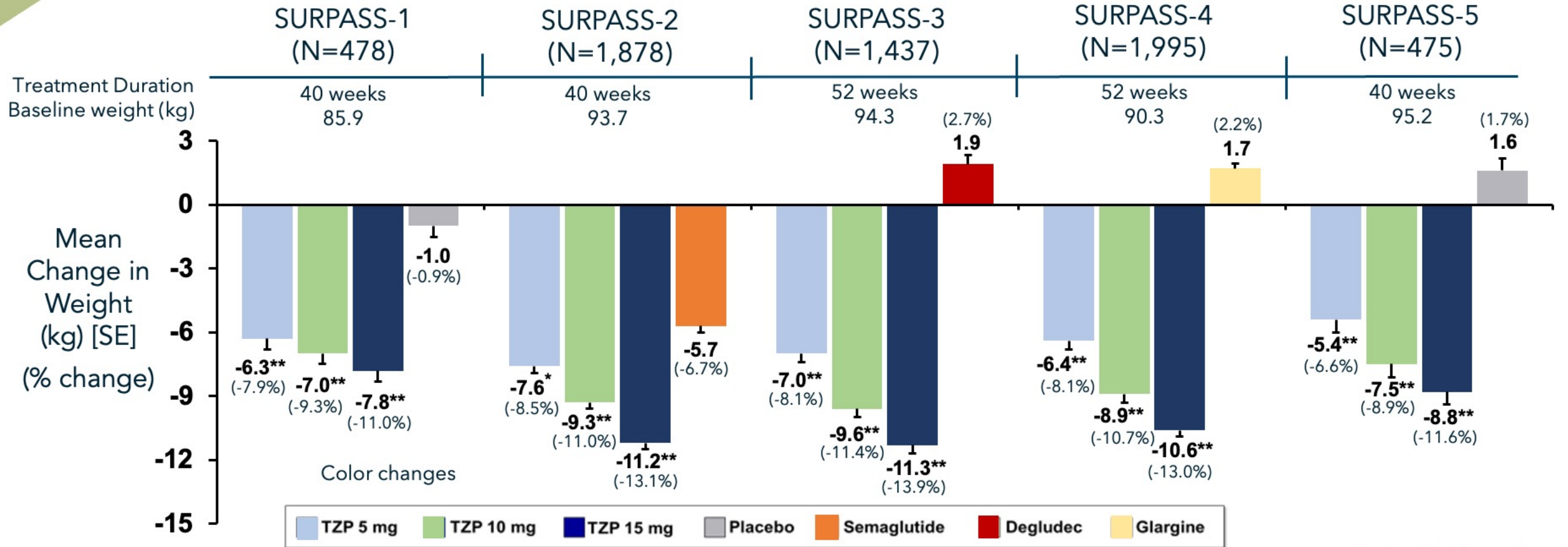
Treatment-regimen estimate  
Superiority vs placebo or active comparator: \*P<0.01.





# Weight Loss with Tirzepatide vs Comparators in SURPASS Trials

## Patients with T2D



Treatment-regimen estimand  
Superiority vs placebo or active comparator: \*P<0.05; \*\*P<0.001



# Obesity Treatment Options: Bariatric Surgery

## 2022 American Society for Metabolic and Bariatric Surgery

- BMI  $\geq 30$  with T2D  
or
- BMI  $\geq 30$  without substantial or durable weight loss or comorbidity improvement using nonsurgical methods
- BMI  $\geq 25$  in people of Asian ethnicity
- BMI  $\geq 40$
- BMI  $\geq 27.5$  in people of Asian ethnicity

## Two Most Common Bariatric Procedures

The two most common bariatric surgical procedures are Roux-en-Y gastric bypass and vertical sleeve gastrectomy (often performed laparoscopically), which provide clinically meaningful improvement in metabolic diseases such as T2D

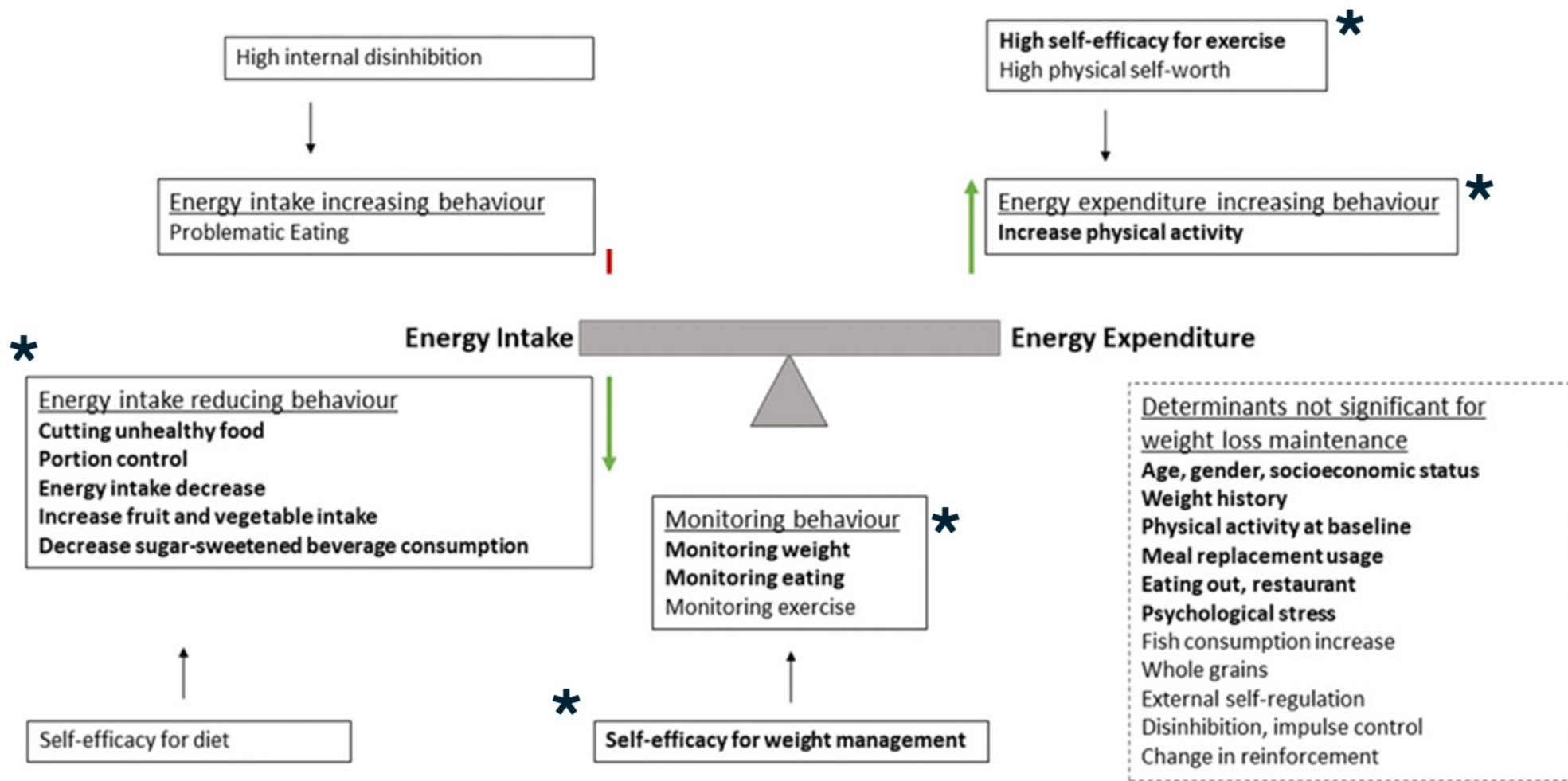
## Poor Candidates

- Not seeking to lose weight
- Medical condition contraindicating surgery
- IBS, untreated gastric ulcer, GI motility disorders
- Pregnancy or planned pregnancy
- Dependence on drugs or alcohol
- Uncontrolled depression, psychosis, or EDs
- Inability to commit to life-long lifestyle changes



# Determinants of Weight Loss Maintenance

## A Systematic Review



## Case Study

Andrea wants to know what medications can help her lose weight and says she wants an “easy fix.” When asked, you learn that Andrea unsuccessfully tried to lose weight in the past with popular diet programs, such as the keto diet and paleo diet. She also says she dislikes aerobic exercise.



# Integration of new and emerging anti-obesity medicines into clinical practice

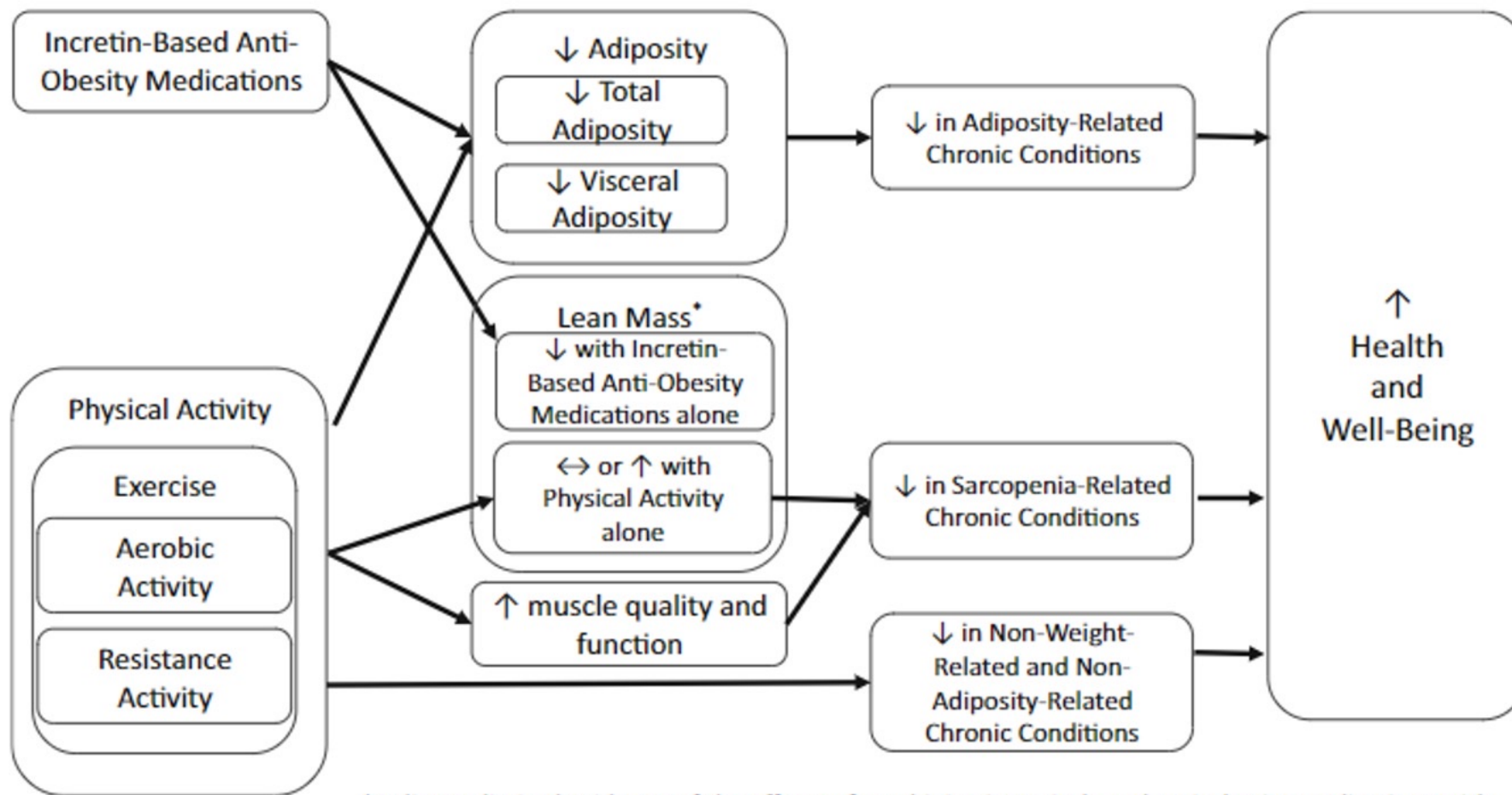


# Professional Society Recommendations of Anti-Obesity Medications for Appropriate Patients





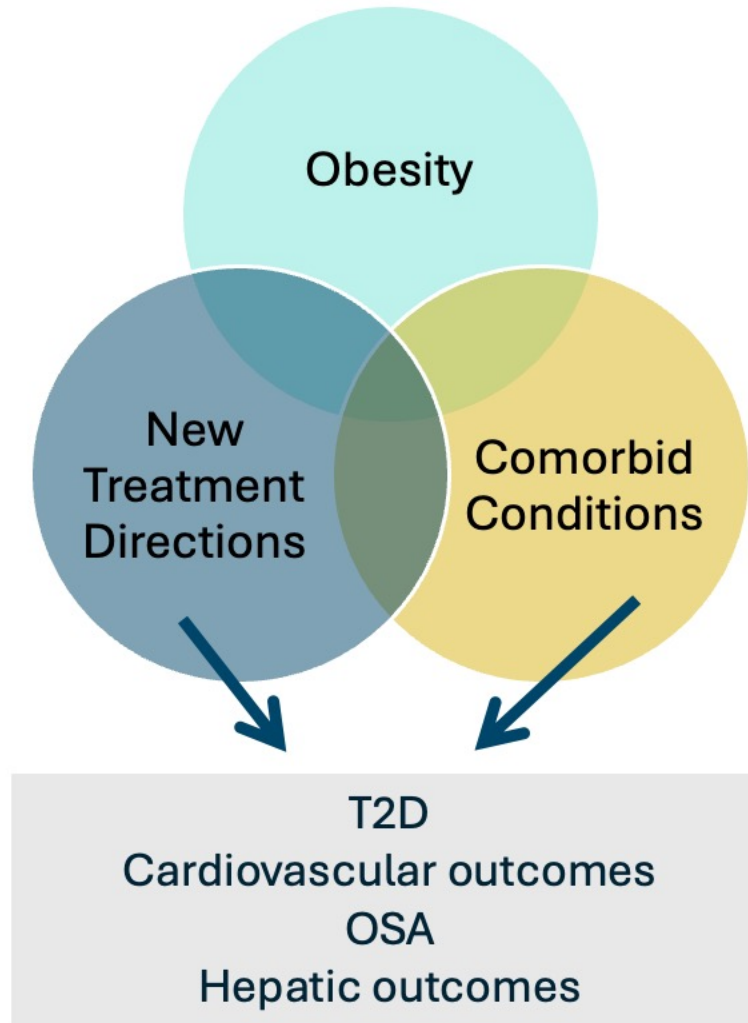
# Benefits of Combined Use of AOM with Exercise



\*Indicates limited evidence of the effects of combining incretin-based anti-obesity medications with physical activity on the change in lean mass.



# New Treatment Directions: Comorbidities of Obesity







# Approaches to Glucose-Lowering Therapies in T2D Treatment

Weight Loss	Weight Neutral	Weight Gain
GLP-1 RA	DPP-4 inhibitors	Insulin secretagogues
Dual GIP and GLP-1 RA	Centrally acting dopamine agonist	Thiazolidinediones
SGLT2 inhibitors	A-glucosidase inhibitors	Insulin
Metformin	Bile acid sequestrants	
Amylin mimetics		

DPP, dipeptidyl peptidase-4; SGLT2, Sodium-glucose cotransporter-2

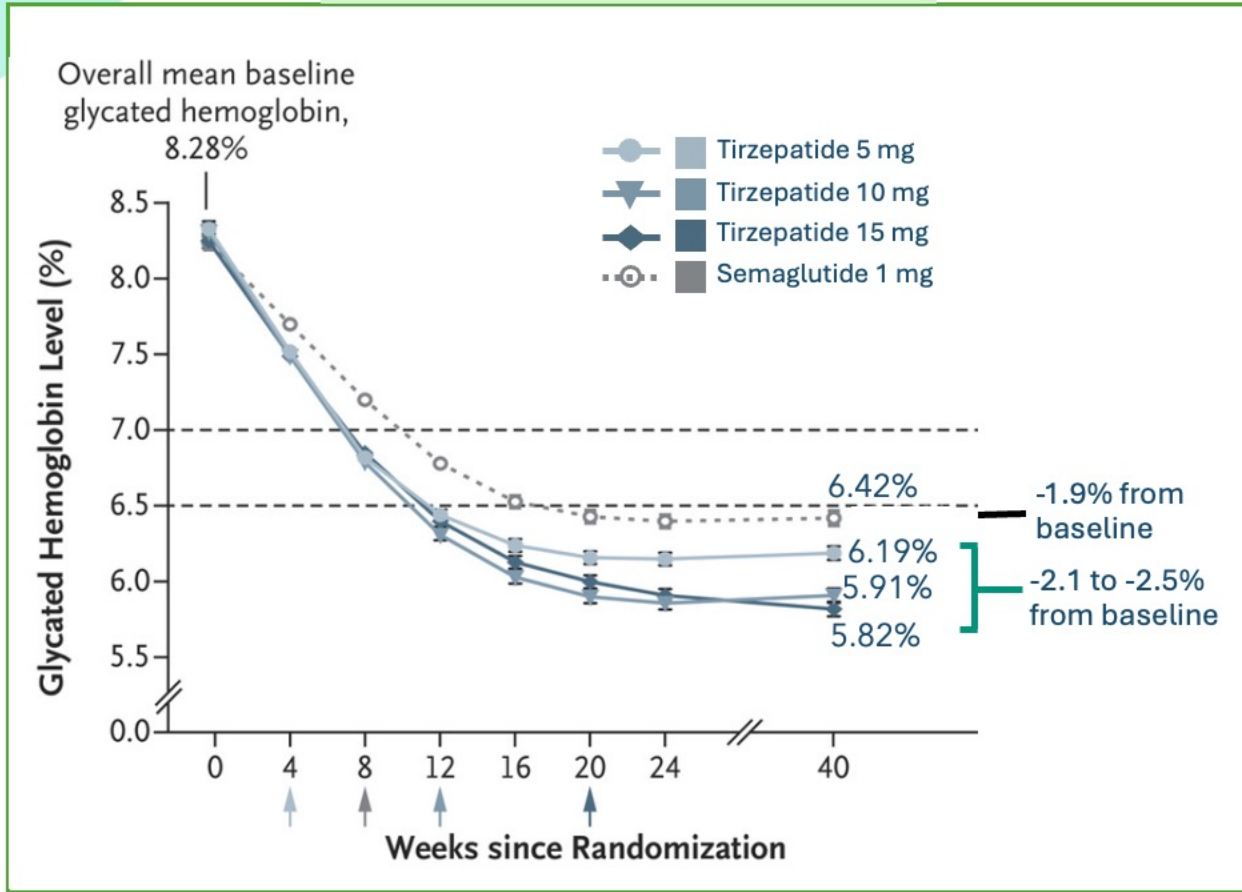
American Diabetes Association. *Diabetes Care*. 2024; Nauck MA, et al. *J Clin Endocrinol Metab*. 1993;76(4):912-917.

Copyright © 2024 | Medical Learning Institute Inc.

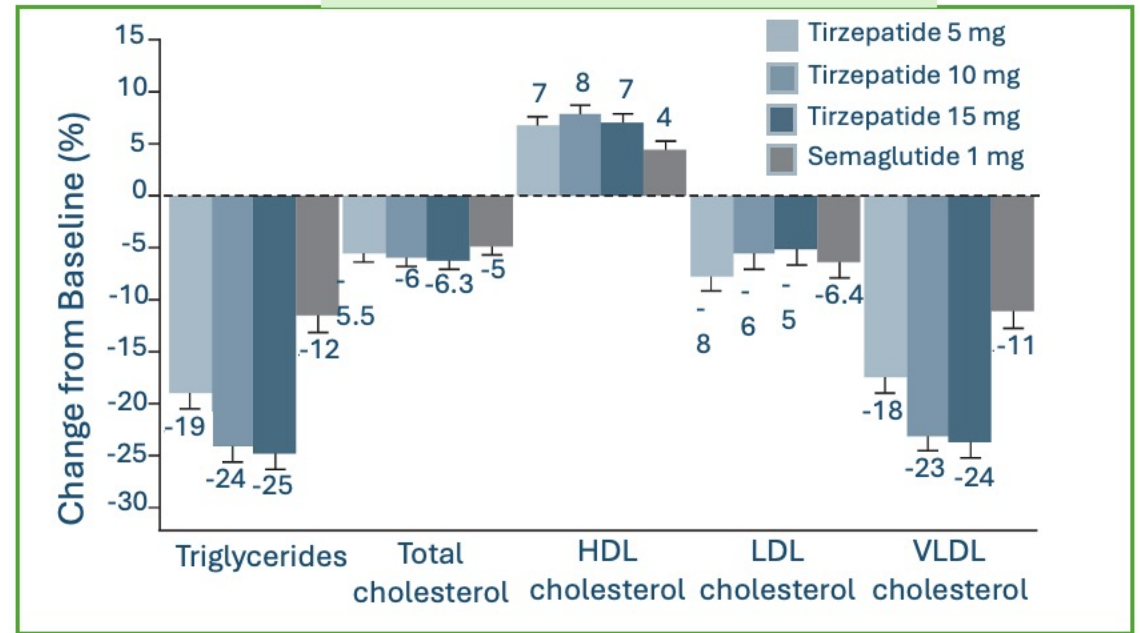


# Benefits Beyond Weight Loss with Tirzepatide and Semaglutide

## Glycemic Control in T2D



## Lipid Levels in T2D



Lipid Levels in Obesity % baseline change	Semaglutide	Tirzepatide
<b>TC</b>	-3.3 to 7.1	-4.9 to -7.4
<b>LDL-C</b>	-6.5 to 1	-5.3 to -8.6
<b>TG</b>	-6 to -22.5	-24 to -31
<b>HDL-C</b>	-0.3 to 18	7 to 8.6



# Cardiovascular Outcomes in Obesity without Diabetes with Semaglutide

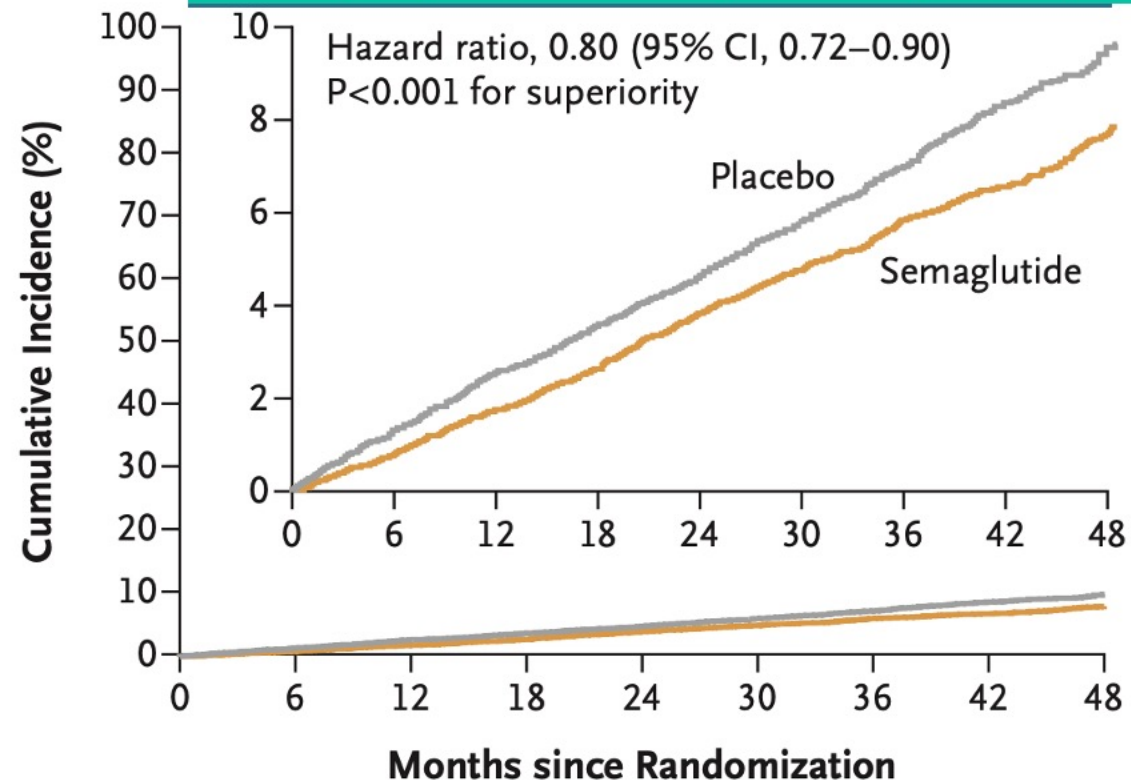
March 2024

New FDA Indication for Semaglutide 2.4 mg:

To reduce the risk of major adverse **cardiovascular events** (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight

*Pivotal trial results of SELECT found weekly subcutaneous semaglutide at a dose of 2.4 mg was superior to placebo in reducing the incidence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke at a mean follow-up of 39.8 months in a cohort with CVD and overweight or obesity (no diabetes)*

SELECT – BMI >27 with **CVD disease (no diabetes)**  
Patients with Primary Outcome Event  
(composite of CV death, nonfatal MI, or stroke)

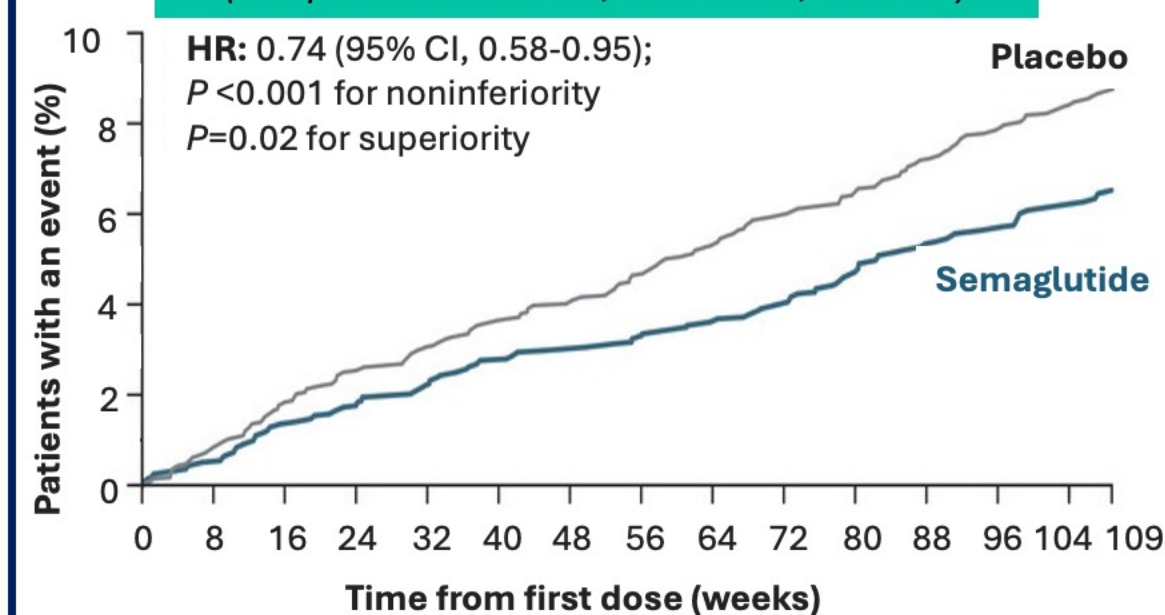


The insets show the same data on an enlarged y axis. The x axis is truncated at 48 months because of the limited number of patients in the trial after 48 months



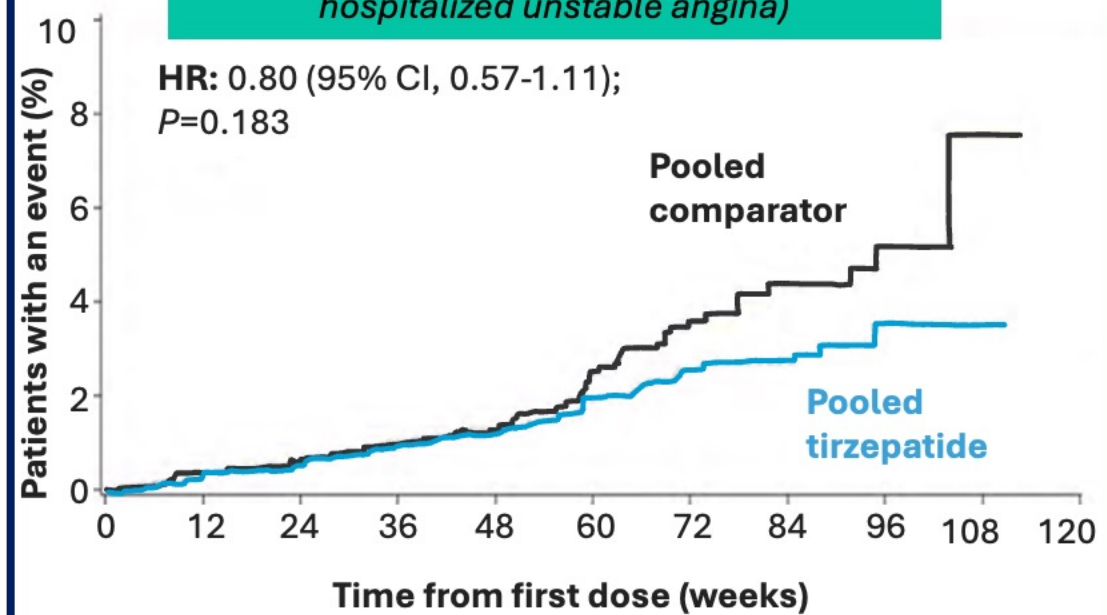
# Cardiovascular Risk with Tirzepatide & Semaglutide Among Patients with T2D

**SUSTAIN 6 – T2D with CVD Risk**  
Patients with Primary Outcome Event  
(composite of CV death, nonfatal MI, or stroke)



Important to note the differences in outcomes being measured between studies, as well as comparator vs placebo

**SURPASS T2D Trials Meta-Analysis**  
Patients with Primary Outcome Event  
(MACE-4; CV death, MI, stroke, and  
hospitalized unstable angina)

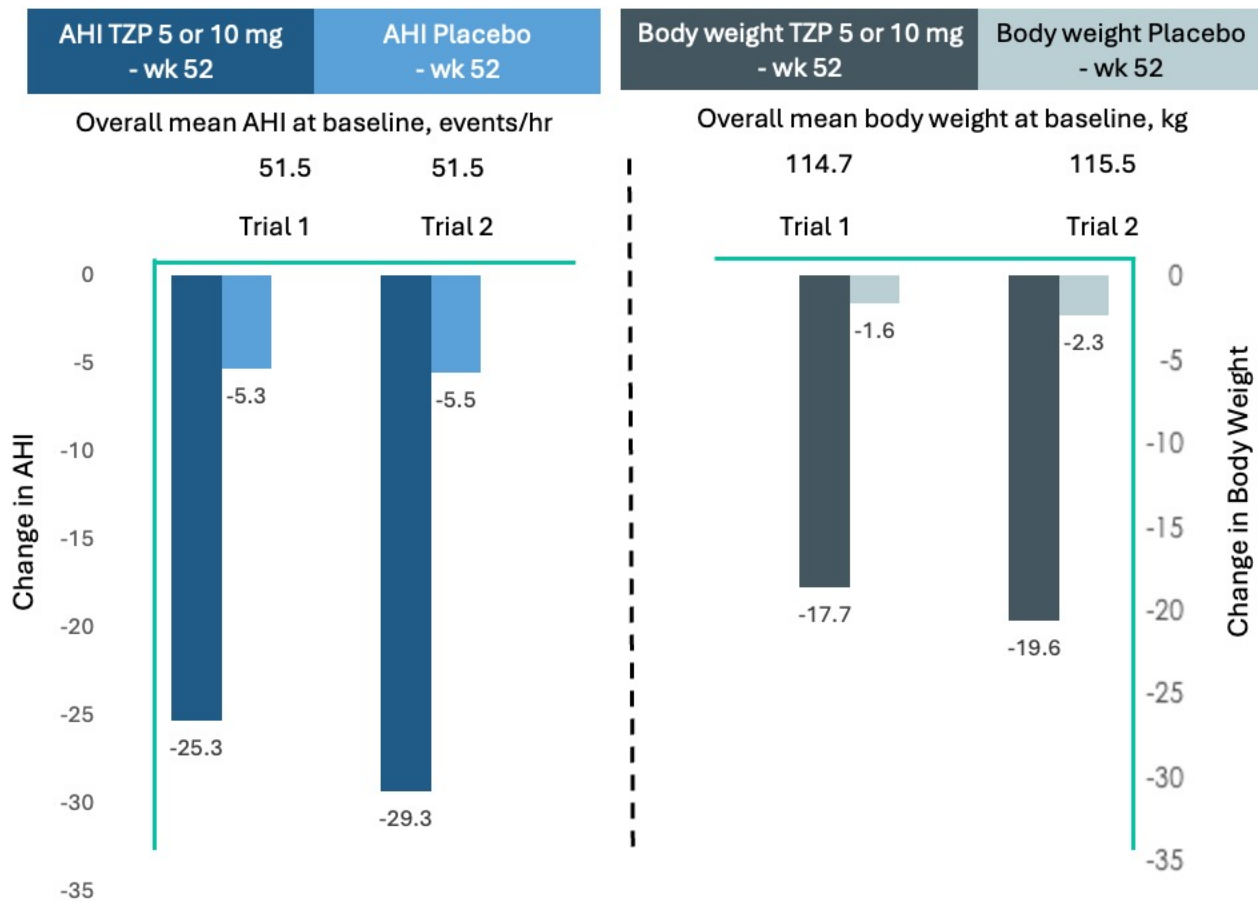


Meta-analysis included over 7,000 patients, comparing tirzepatide to comparator. Tirzepatide had a statistically significant lower risk of MACE-4 (CV death, MI, stroke, hospitalized unstable angina) compared to comparators. CVOT data with tirzepatide will be available later in 2024.



# AHI and Weight Change With Tirzepatide vs Placebo in SURMOUNT-OSA

## OSA AND OBESITY



Two phase 3, double-blind, randomized, controlled trials involving adults with moderate-to-severe OSA and obesity

**Trial 1:** Participants who were not receiving treatment with PAP at baseline

**Trial 2:** Participants who were receiving PAP therapy at baseline

### Primary Endpoint

- Change in AHI

### Secondary Endpoints

- Percent change in AHI and body weight and changes in hypoxic burden, patient-reported sleep impairment and disturbance, hsCRP concentration, and systolic blood pressure

### Results

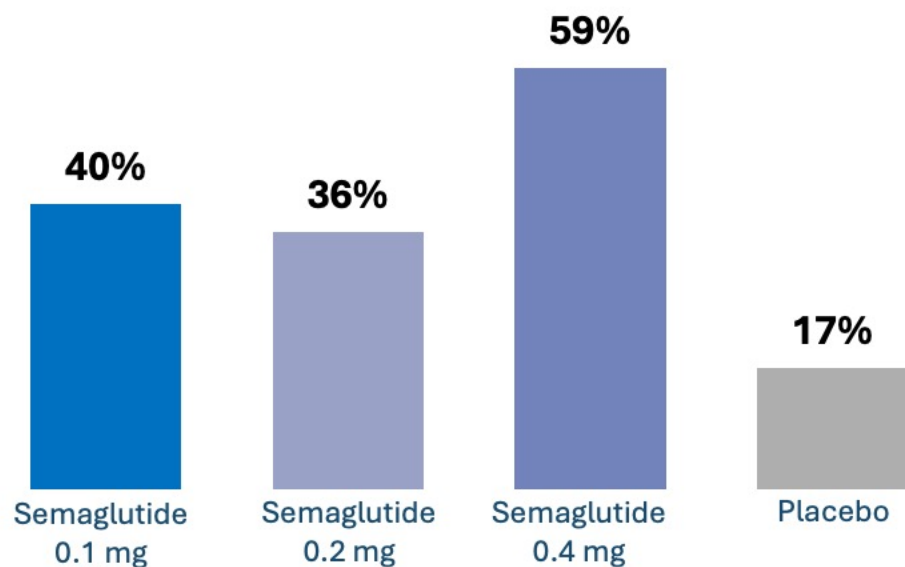
- Significant improvements in the measurements for all prespecified key secondary end points were observed with tirzepatide as compared with placebo
- Most frequently reported AEs with tirzepatide were GI in nature and mostly mild to moderate in severity



# Hepatic Outcomes with Tirzepatide and Semaglutide

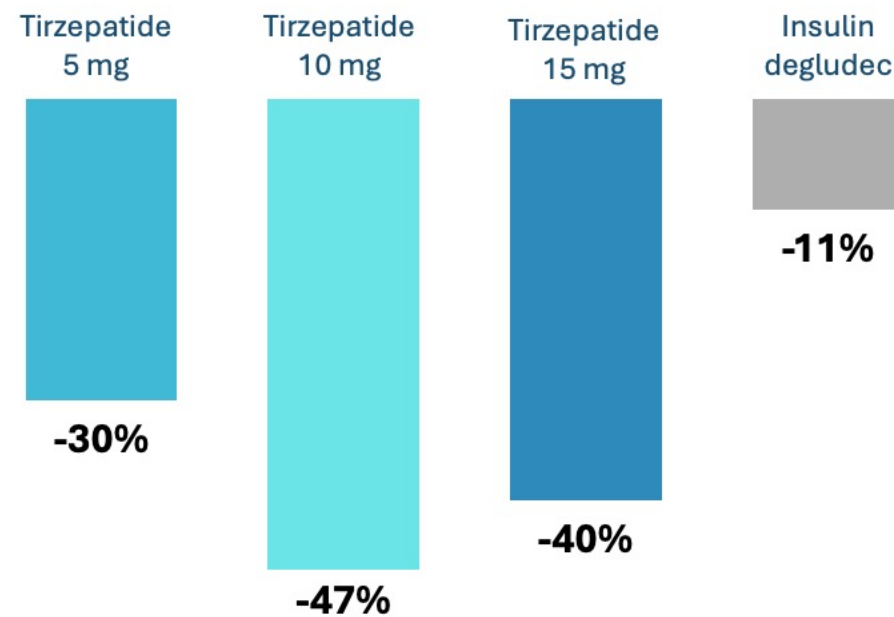
## Semaglutide Phase 2 Trial for Biopsy-Confirmed MASH (no diabetes)

Resolution of MASH with no worsening of liver fibrosis



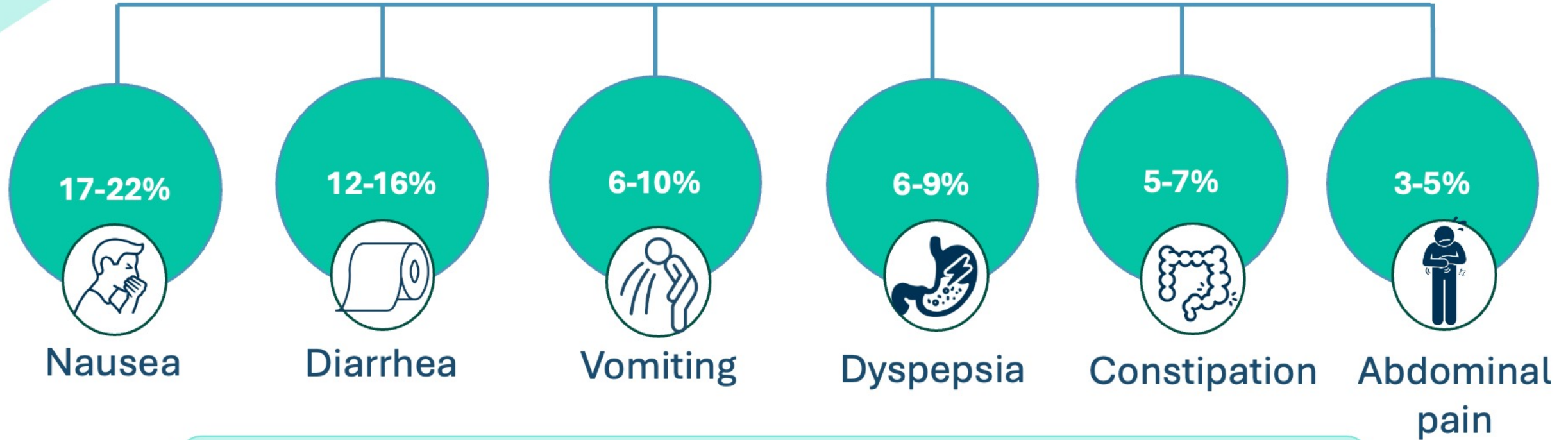
## SURPASS-3 MRI: Sub study with Tirzepatide (with diabetes)

Relative Change (%) of Liver Fat Content (LFC)





# Most Common Side Effects of Semaglutide and Tirzepatide



It is important to communicate with your patient about strategies to manage side effects to encourage adherence to therapy



# Contraindications and Limitations of Use

## *Semaglutide and Tirzepatide*

### Contraindications

- Personal or family history of medullary thyroid cancer or patients with multiple endocrine neoplasia syndrome type 2
- Known serious hypersensitivity to tirzepatide/semaglutide or any of the excipients

### Limitations of Use

- Has not been studied in patients with a history of pancreatitis
- Is not indicated for use in patients with type 1 diabetes





# Patient Consulting and Counseling

GI side effects are typically mild to moderate and temporary in nature  
HCPs should titrate doses up to help mitigate adverse events.

✓ **Eat slowly**

✓ **Smaller portions**

✓ **Do not skip meals**

✓ **Eat when hungry**

✓ **Increase meal frequency**

✓ **Limit overactivity after meal**

✓ **Incorporate a low-fat diet**

✓ **Refrain from lying down after a meal**

## Other Considerations

**Muscle mass change**

**Role of combination therapies**

**Duration of pharmacotherapy  
treatment**

Up Next Part 3  
**Best Practices in Shared  
Decision-Making to  
Enhance Patient  
Outcomes**



**THANK  
YOU**