

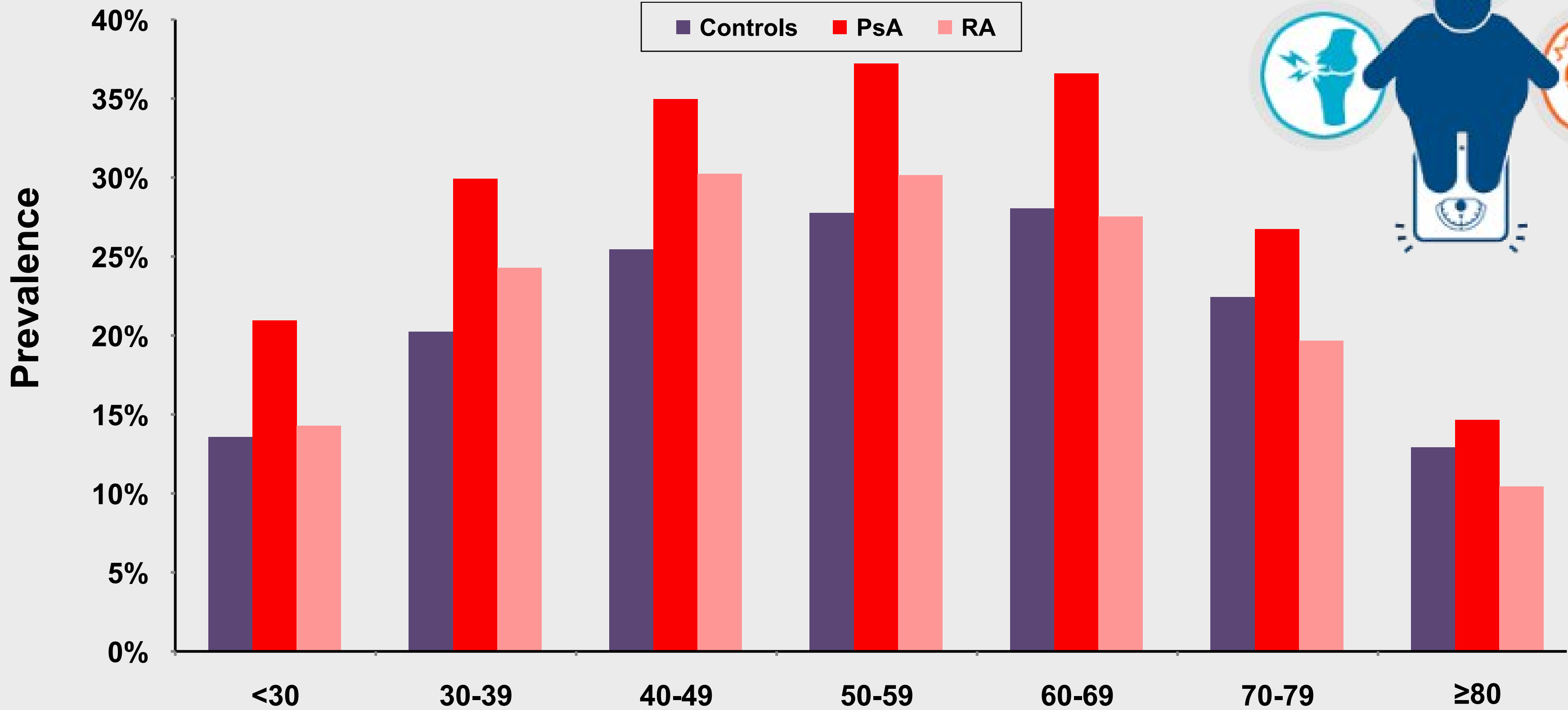
# Why Are We Here?

- Obesity (BMI  $\geq 30$ ) is extremely common, affecting >40% of adults in the United States
  - 9.2% of adults have severe obesity (BMI  $\geq 40$ )
  - ~20% of children ages 2 to 19 years have obesity
- The risk for inflammatory rheumatologic conditions (eg, PsA, RA) is highly associated with obesity, and response to treatment is also associated with BMI
- Now more than ever, obesity is a **modifiable** risk factor
- If we want to care for our patients with any IMIDs, addressing modifiable comorbid conditions, including obesity, is a necessary role
  - And 1 we may not need to do alone!

BMI = body mass index; PsA = psoriatic arthritis; RA = rheumatoid arthritis

Emmerich SD, et al. *NCHS Data Brief*. 2024;508:10.15620/cdc/159281. National Institutes of Health (NIH). Overweight and obesity statistics, 2021 (<https://www.niddk.nih.gov/health-information/health-statistics/overweight-obesity>). Accessed 12/11/2025.

# Prevalence of Obesity in PsA



RA = rheumatoid arthritis.  
Jafri K, et al. *Arthritis Care Res (Hoboken)*. 2017;69(1):51-57 and supplemental materials.

**Age (years)**

# Pathophysiology: Direction of Causation?

## Possible interpretations

- Obesity is a driver in the development of PsA
- PsA and psoriasis contribute to obesity risk
- Shared mechanism—metabolic syndrome as driver of obesity and PsO/PsA

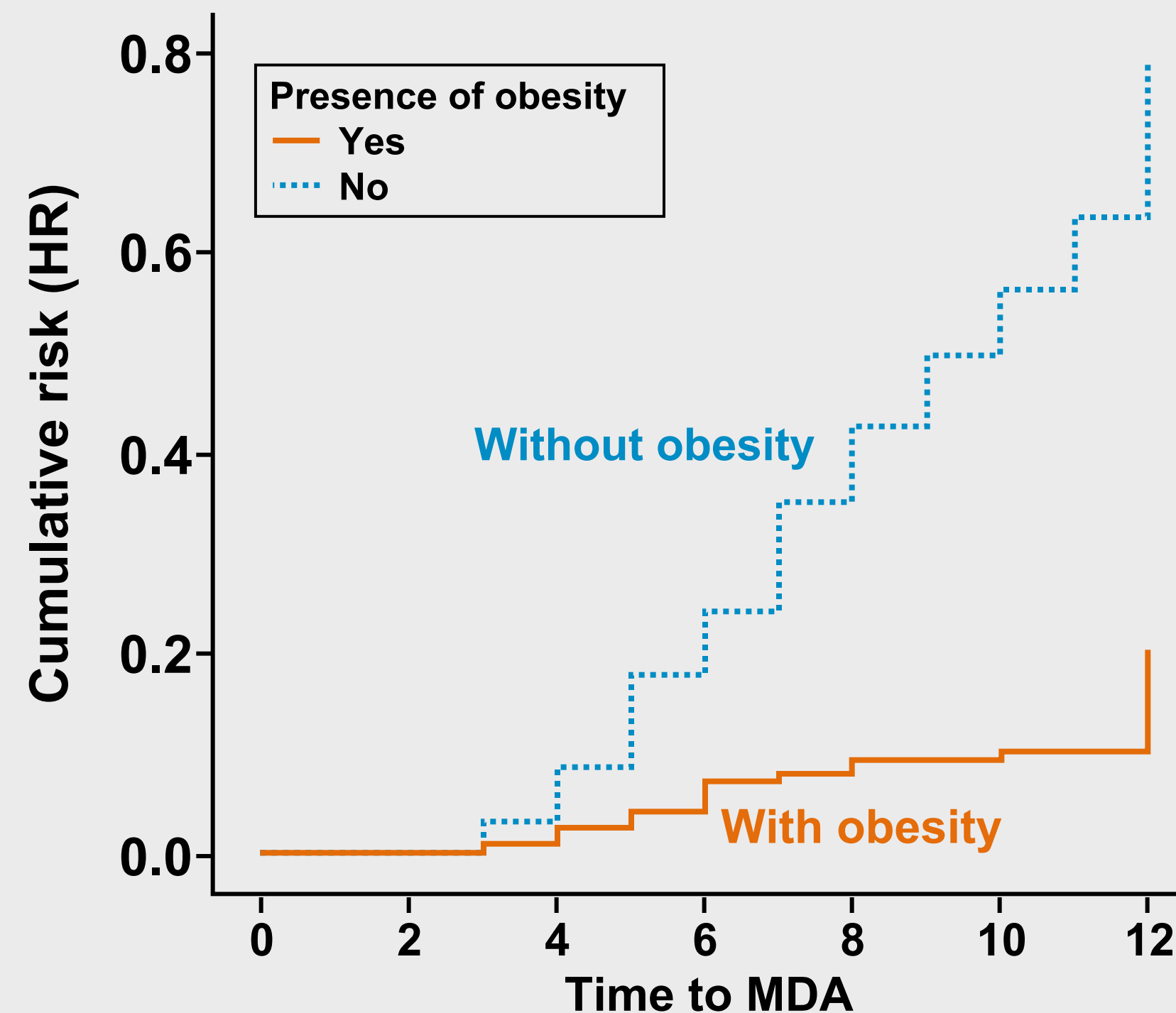
# Obesity Influences Response to Therapy

## Odds of achieving MDA

Body weight	OR
Normal	Ref
Overweight	0.66 (0.50–0.87)
Obese	0.53 (0.41–0.69)

\*Adjusted for age, sex, duration, DMARD use, NSAIDs.

## Achieving MDA



DMARD = disease-modifying antirheumatic drug; MDA = minimal disease activity; NSAIDs = nonsteroidal anti-inflammatory drugs; OR = odds ratio.

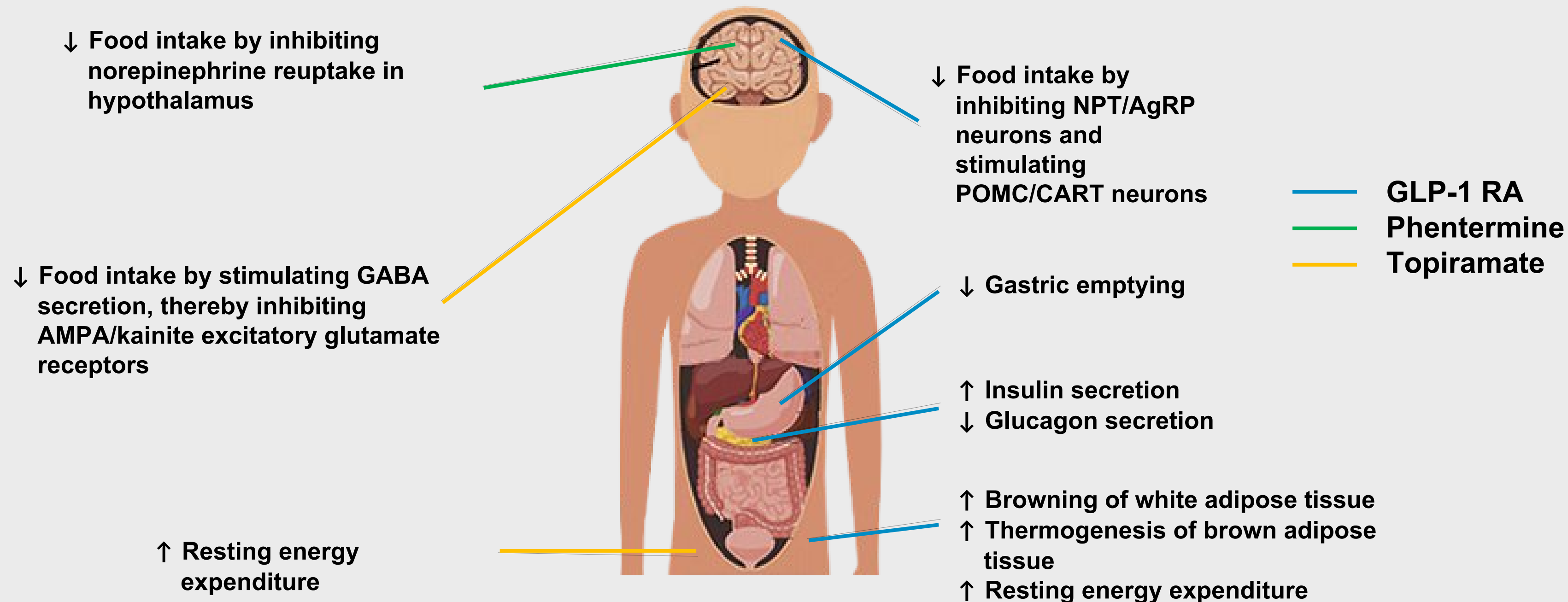
Eder L, et al. *Ann Rheum Dis*. 2015;74(5):813-817. Di Minno MN, et al. *Arthritis Care Res (Hoboken)*. 2013;65(1):141-147.

# Tools to Facilitate a Collaborative Approach in Obesity

## 5As of obesity management and behavior change

<b>Ask</b>	<b>Assess</b>	<b>Advise</b>	<b>Agree</b>	<b>Assist</b>
<ul style="list-style-type: none"><li>▪ Permission to discuss weight</li><li>▪ Explore readiness to change/address</li></ul>	<ul style="list-style-type: none"><li>▪ Obesity stage and/or BMI for comorbidities</li><li>▪ Drivers, complications, and barriers</li></ul>	<ul style="list-style-type: none"><li>▪ Discuss benefits of modest weight loss in context</li><li>▪ Discuss treatment options</li></ul>	<ul style="list-style-type: none"><li>▪ Agree on realistic weight loss expectations</li><li>▪ Agree on SMART behavior and change goals</li><li>▪ Agree on a treatment plan</li></ul>	<ul style="list-style-type: none"><li>▪ Assist in addressing drivers and barriers</li><li>▪ Assist in accessing resources</li><li>▪ Refer as needed/ arrange follow-up</li></ul>

# Drug-Induced Weight Loss Mechanism



AMPA =  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; GABA = gamma-aminobutyric acid; GLP-1RA = GLP-1 receptor agonist; NPT/AgRP = neuropeptide Y/agouti-related peptide; POMC/CART = proopiomelanocortin/cocaine- and amphetamine-regulated transcript.

# FDA-Approved Antiobesity Pharmacotherapy Agents

<b>Drug</b>	<b>Main mechanism of action</b>
<b>Phentermine with topiramate*</b>	Noradrenaline releaser and anticonvulsant
<b>Diethylpropion*</b>	Secondary to CNS effects, including stimulation of hypothalamus to release norepinephrine
<b>Phendimetrazine*</b>	Stimulates release of norepinephrine
<b>Benzphetamine*</b>	Stimulates release of norepinephrine
<b>Bupropion with naltrexone</b>	Noradrenaline/dopamine reuptake inhibitor and opioid receptor antagonist
<b>Orlistat</b>	Gastric and pancreatic lipase inhibitor
<b>Liraglutide</b>	GLP-1 receptor agonist
<b>Semaglutide</b>	GLP-1 receptor agonist
<b>Tirzepatide</b>	GLP-1/GIP dual agonist

\* Controlled substance.

CNS = central nervous system; GLP-1 = glucagon-like peptide 1.

Adan RAH. *Trends Neurosci.* 2013;36:133-140. FDA. News release 6/4/2021 ([www.fda.gov/news-events/press-announcements/fda-approves-new-drug-treatment-chronic-weight-management-first-2014](http://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-treatment-chronic-weight-management-first-2014)). Accessed 12/11/2025.

# Guidelines for Selecting Obesity Treatment



Treatment	BMI category (kg/m <sup>2</sup> )				
	25–26.9	27–29.9	30–34.9	35–39.9	≥40
Diet, physical activity, and behavioral therapy	With comorbidities	With comorbidities	+	+	+
Antiobesity pharmacotherapy		With comorbidities	+	+	+
Metabolic and bariatric surgery			With comorbidities		

+ = Use of indicated treatment regardless of comorbidities.

# Polling Question

Which of the following organizations most recently released guidelines on the use of GLP-1 therapies for obesity treatment?

1. World Health Organization and American Diabetes Association
2. Centers for Disease Control and Prevention
3. American College of Rheumatology

# WHO and ADA/TOS Guidelines on GLP-1/GIP Therapies for Obesity Treatment

December

**2025** WHO Guidelines

“In adults living with obesity, GLP-1 therapies may be used as a long-term treatment for obesity.”

***Conditional recommendation; moderate certainty evidence***

“In adults living with obesity who are prescribed GLP-1 therapies, intensive behavioral therapy may be provided as part of a comprehensive multimodal clinical algorithm.”

***Conditional recommendation; low certainty evidence***

January 2026

ADA/Obesity Association Guidelines

“Obesity medications should be offered as part of initial treatment for obesity to adults with or at high risk of obesity-related diseases or complications.”

***A recommendation***

“In adults with overweight or obesity and T2DM, the preferred obesity medication should be a GLP-1 RA or dual GLP-1/GIP RA given their weight reduction and glucose-lowering efficacy.”

***A recommendation***

*Note: this guideline includes many other recommendations surrounding lifestyle intervention, treatment goals, medications, dosing, comorbidities, special populations, and counseling.*

Please see guidelines for full recommendations and context.

ADA = American Diabetes Association; GIP = glucose-dependent insulinotropic polypeptide; TOS = The Obesity Society

Celletti F, et al. *JAMA*. 2025 (<https://doi.org/10.1001/jama.2025.24288>). ADA Professional Practice Committee for Obesity. 2026. <https://diabetesjournals.org/docm-care/article/doi/10.2337/doci25-0008/164233/Pharmacologic-Treatment-of-Obesity-in-Adults>. Accessed 1/14/26.

# American Diabetes Association/Obesity Association: 2026 Guidelines on Obesity Pharmacotherapy

**Goal: achievement and maintenance of weight reduction and prevention of obesity-related diseases and complications**

**Without related diseases or complications**

**Weight-reducing effect of obesity medication beyond 3% weight loss with lifestyle change alone\***

**High (>10%)**  
Tirzepatide (A)  
Semaglutide (A)

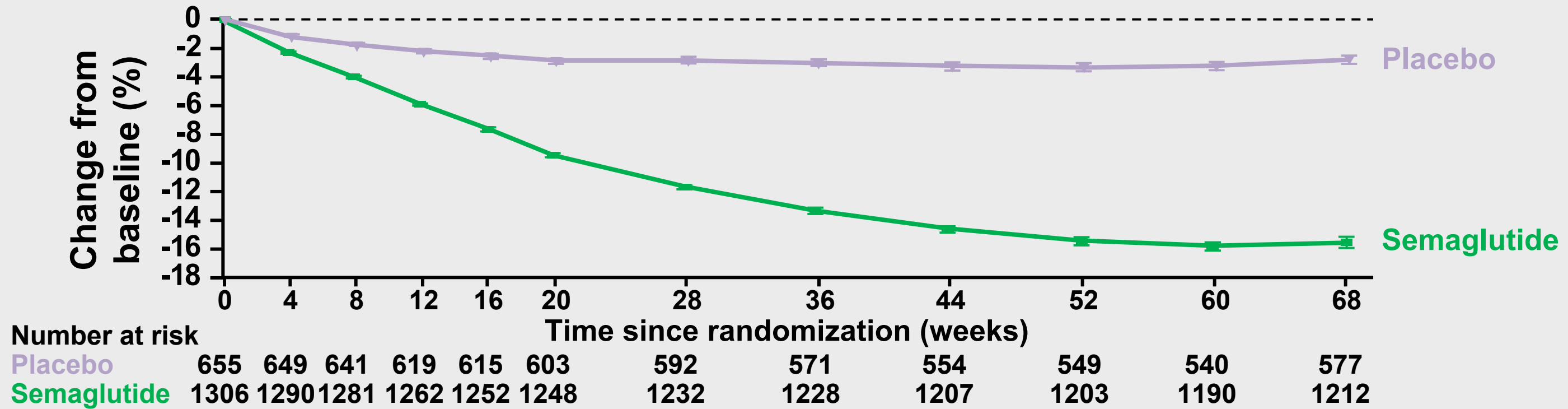
**Moderate (5–10%)**  
Phentermine-topiramate (A)

**Modest (<5%)**  
Naltrexone-bupropion (A)  
Liraglutide (A)  
Phentermine (C)  
Orlistat (A)

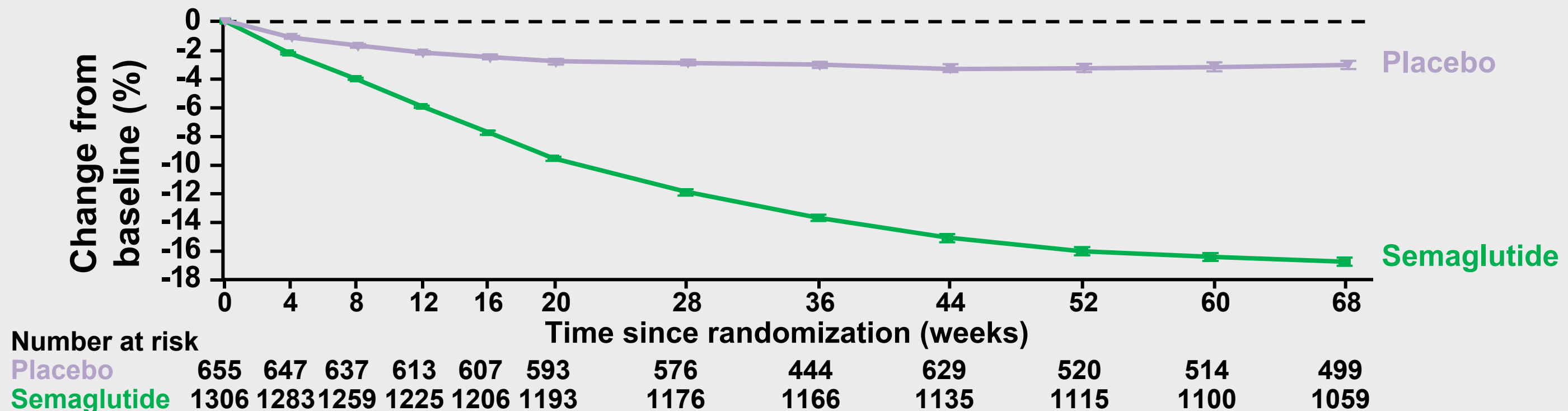
**Select obesity medication that aligns with individual goals and does not present barriers to its long-term use**

# Effect of Once-Weekly Semaglutide vs Placebo on Body Weight (STEP-1)

Body weight change from baseline by week, observed in-trial data



Body weight change from baseline by week, on-treatment data



# Oral Semaglutide: Significant Weight Loss in OASIS 4

## Approved by the FDA December 2025

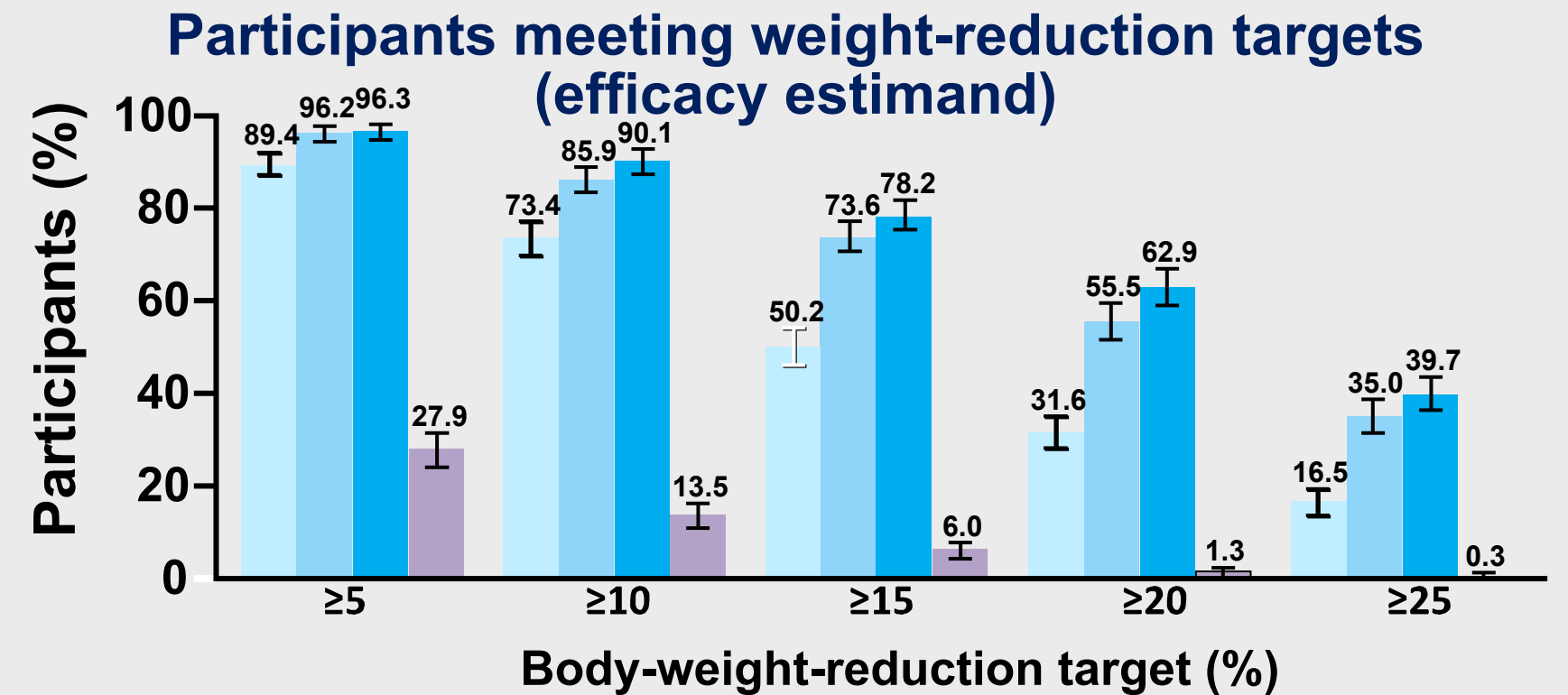
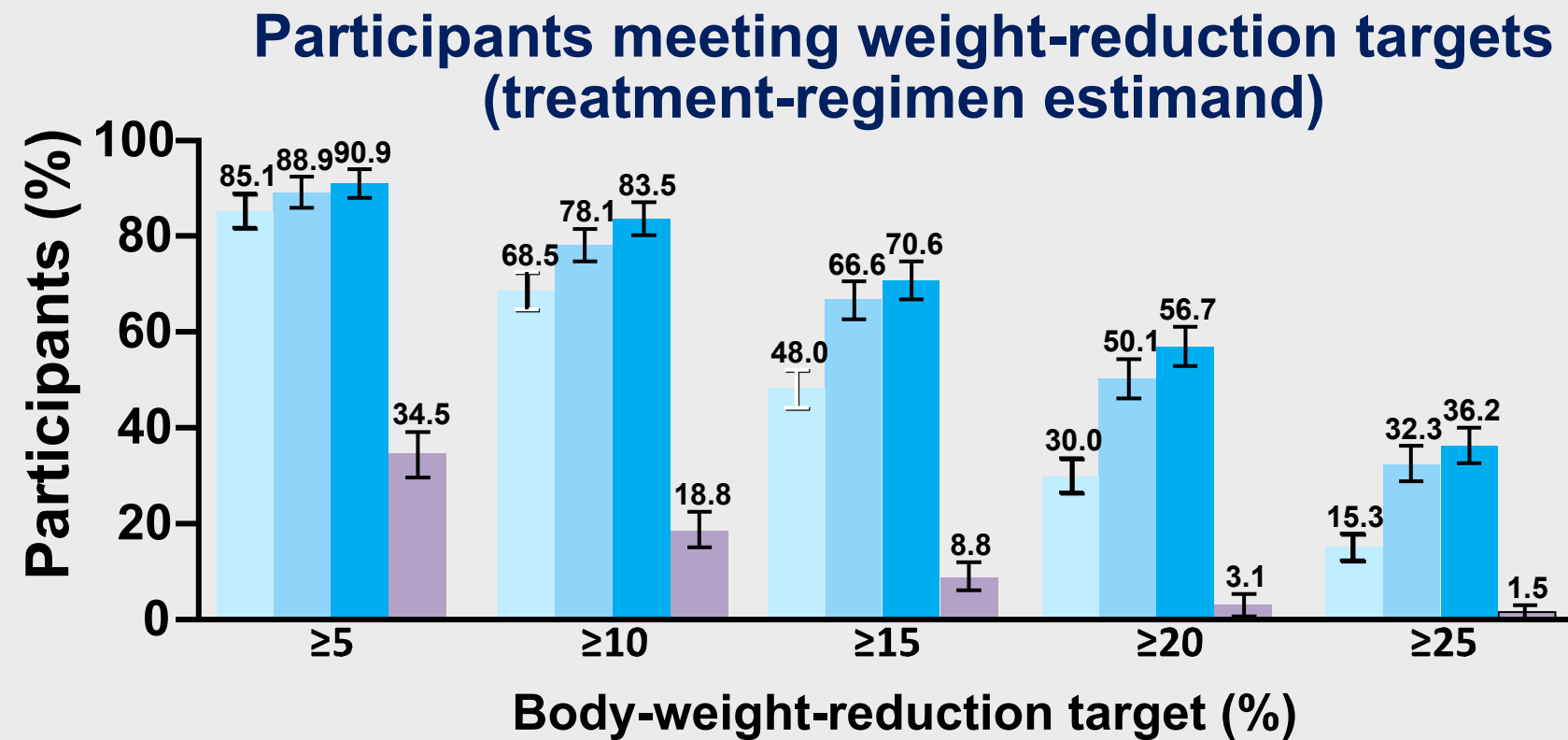
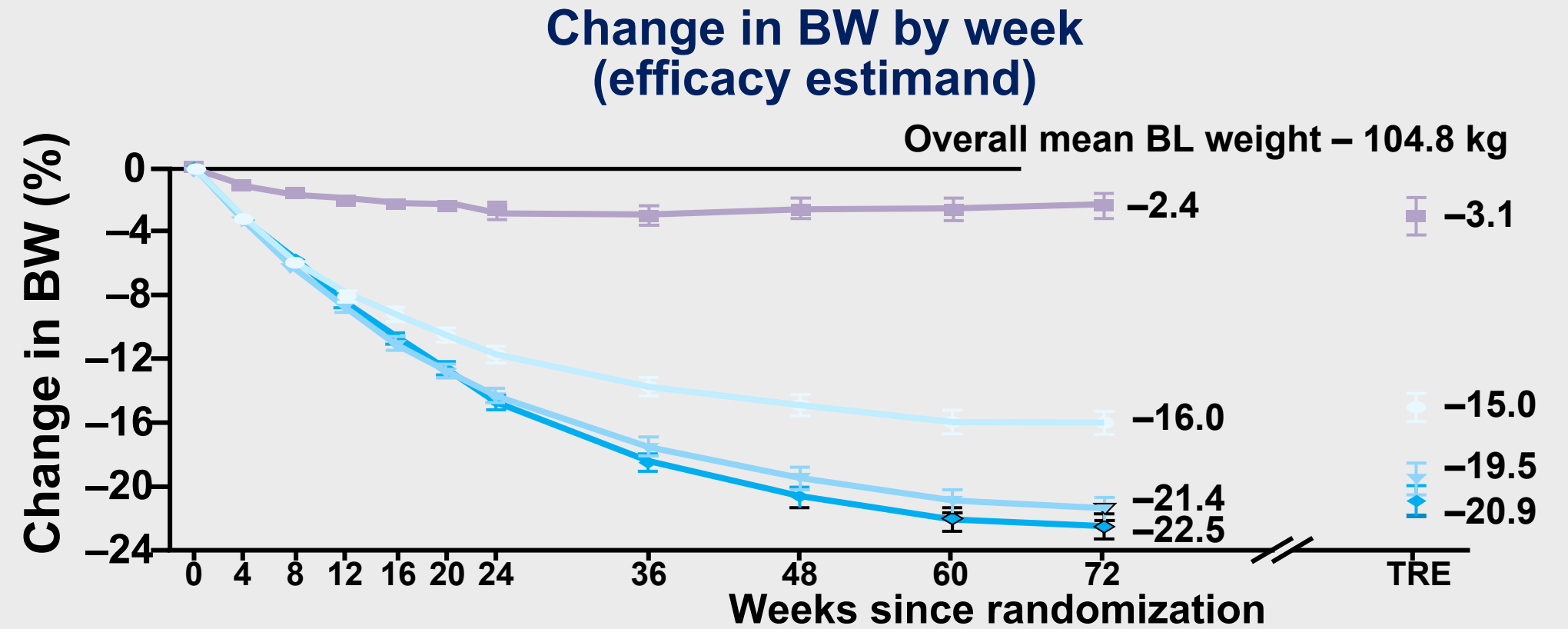
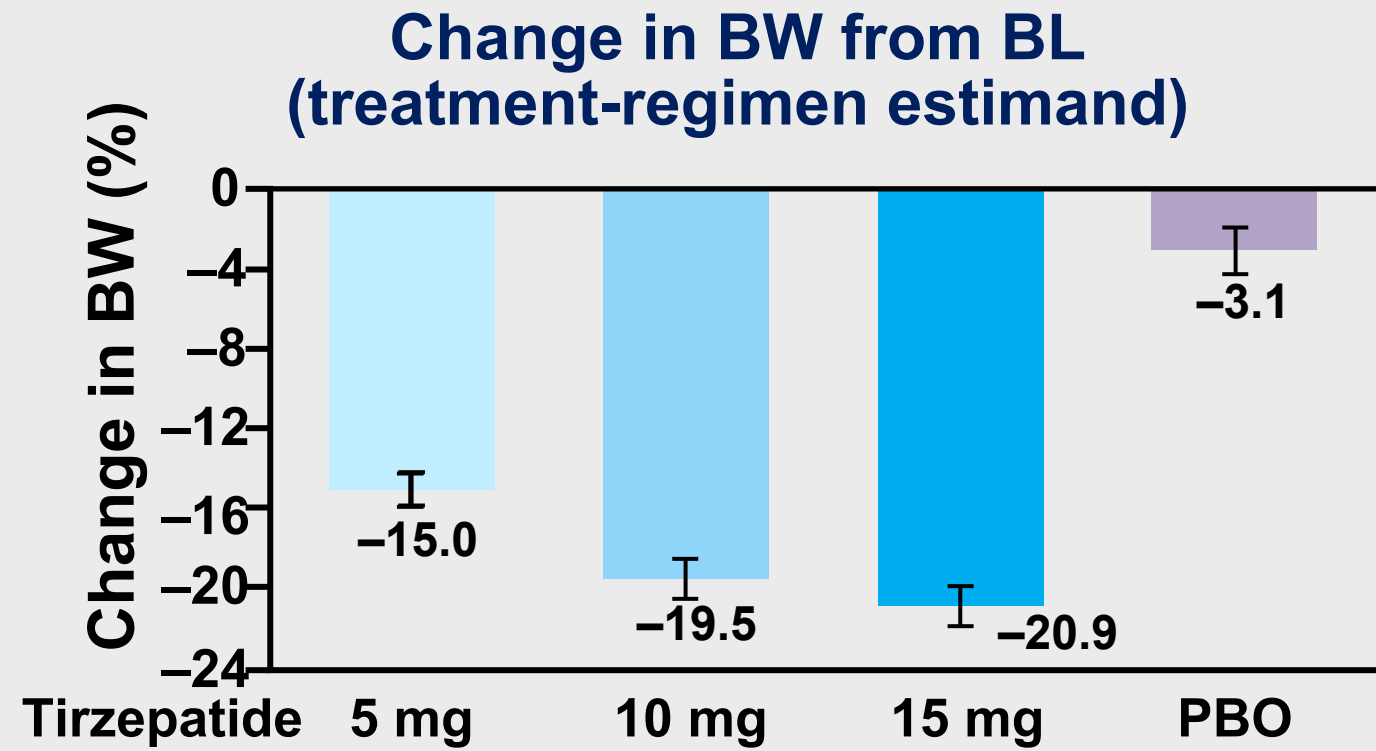
- 71-week randomized controlled trial (RCT) (N = 205 patients with obesity, without diabetes)

Semaglutide 25 mg	Placebo	95% CI	P-value
-13.6%	-2.2%	-13.9 to -9.0	< .001

- Semaglutide group
  - Significantly more likely to achieve 5%, 10%, 15%, and 20% weight reduction
  - Significantly higher improvement in physical function
  - Gastrointestinal (GI) events more common (74% vs 42% placebo)

# Effect of Once-Weekly Tirzepatide vs Placebo on Body Weight (SURMOUNT-1)

Tirzepatide 5 mg Tirzepatide 10 mg Tirzepatide 15 mg PBO



# TOGETHER-PsO/PsA: Ixekizumab + Tirzepatide Combination Therapy

- Phase 3b trials; n = 274 (PsO) or 271 (PsA)
- Mean BMI of 37.6 – 39.0 kg/m<sup>2</sup>
- Primary endpoint at 36 weeks: PASI 100/ACR50 AND ≥10% weight loss

	TOGETHER-PsO		TOGETHER-PsA	
	PASI 100 + ≥10% weight loss	PASI 100 alone (secondary EP)	ACR50 + ≥10% weight loss	ACR50 alone (secondary EP)
Ixekizumab + tirzepatide	27.1%	40.6%	31.7%	33.5%
Ixekizumab alone	5.8%	29.0%	0.8%	20.4%
<i>P</i> -value	< .001	< .05	< .001	< .05

ACR50 = a 50% improvement in American College of Rheumatology joint criteria; PASI 100 = 100% improvement in Psoriasis Area and Severity Index; EP = endpoint  
Eli Lilly. News release 1/8/26 (<https://lilly.gcs-web.com/news-releases/news-release-details/lillys-taltz-ixekizumab-and-zepbound-tirzepatide-used-together>). Accessed 2/24/26.  
Eli Lilly. News release 2/18/26 (<https://investor.lilly.com/news-releases/news-release-details/lillys-taltz-ixekizumab-and-zepbound-tirzepatide-used-together-0>). Accessed 2/24/26.

# Weight Loss Outcomes of Injectable GLP-1/GIP Receptor Agonists in Randomized Clinical Trials (maximum doses)

- Not a head-to-head study; data are derived from SCALE (liraglutide), STEP (semaglutide), and SURMOUNT-1 (tirzepatide)

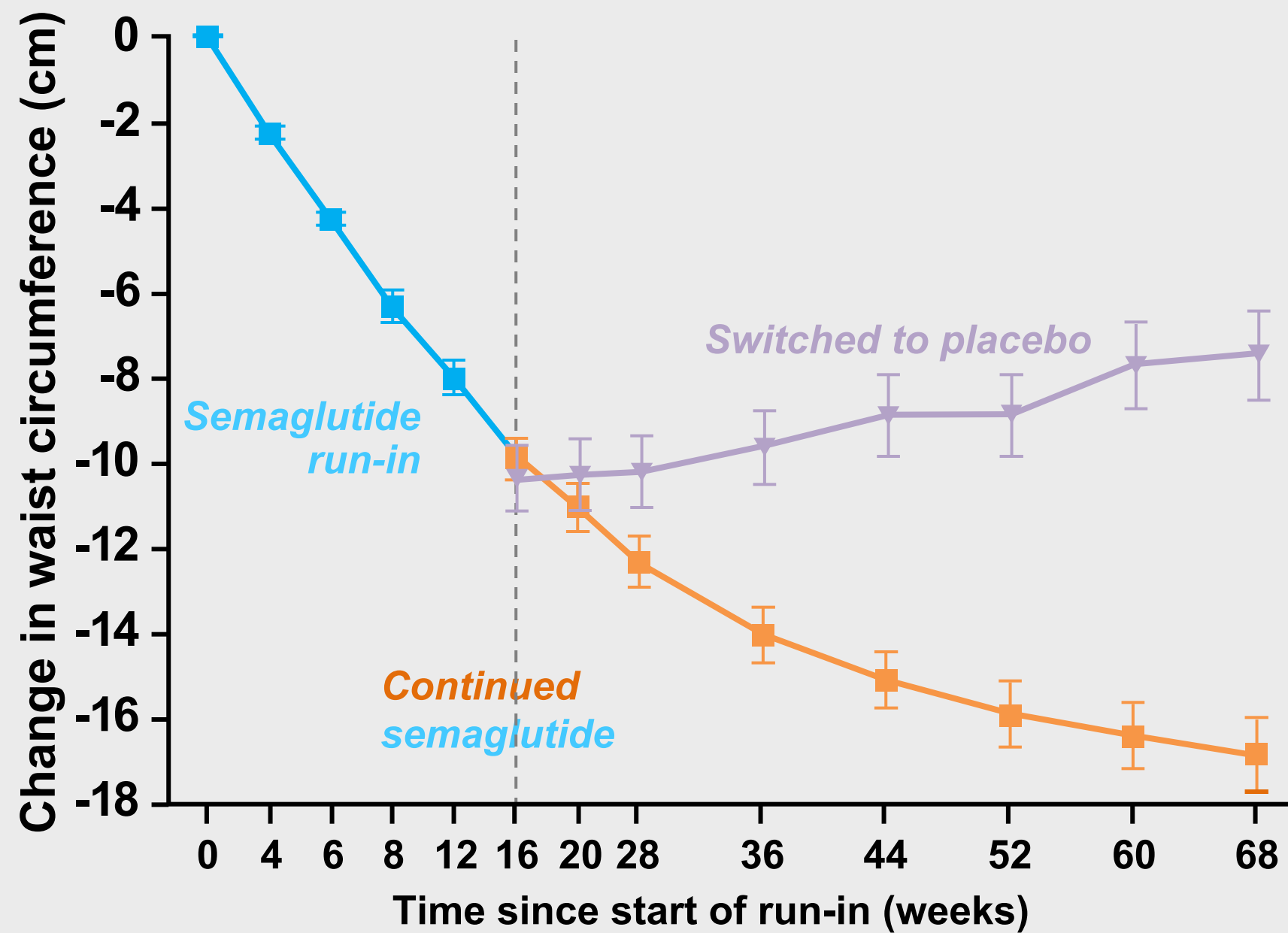
Treatment (max dosage)	3 months	6 months	9 months	12 months
Liraglutide 3.0 mg	6%	8%	9%	9%
Semaglutide 2.4 mg	6%	10%	14%	15%
Tirzepatide 15 mg	8%	15%	18%	20%

- Consider loss of *lean* mass with more potent agents (semaglutide and tirzepatide)
- Monitor safety, tolerability, and patient desires with individual agents

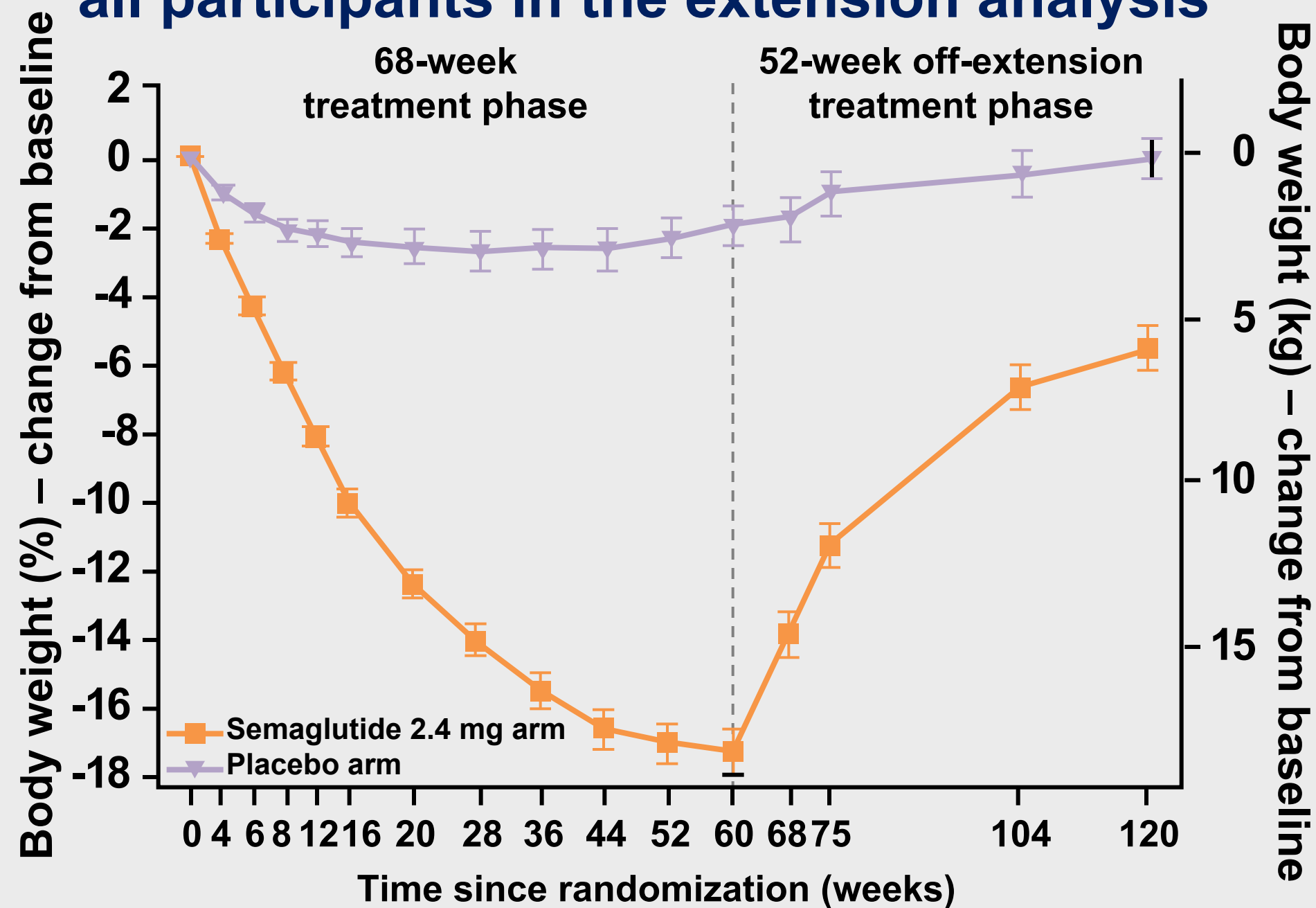
# Weight Regain After Drug Withdrawal?



## Mean change in waist circumference Weeks 0 to 68, observed in-trial data



## Change from baseline in body weight for all participants in the extension analysis



# Investigational Weight Loss Medications: Future Directions

## Oral orforglipron

- Once daily oral GLP-1 RA (small molecule nonpeptide for absorption in stomach)
- **Anticipated FDA approval Q2 2026**

## Retatrutide

- Triple inhibitor (GLP-1, GIP, glucagon receptors)
- Phase 2: 8.7% to 24.2% weight loss for once-1weekly injection
- **Anticipated FDA approval late 2026 or 2027**

## Efpeglenatide

- As T2DM monotherapy: Significant improvement in glycemic control and body weight; safety and tolerability similar to other GLP-1 RAs; potential for once-monthly injection
- **Anticipated FDA approval late 2026 or 2027**

## Maridebart cafraglutide

- Phase 2: 8.4% to 16.2% weight loss for once-monthly injection

# ATTAIN-1: Significant Weight Loss With Oral Orforglipron

- 72-week RCT (N = 3127 patients with obesity, without diabetes)

Orforglipron (95% CI)		Placebo	P-value
6 mg	-7.5% (-8.2 to -6.8)	-2.1% (-2.8 to -1.4)	< .001
12 mg	-8.4% (-9.1 to -7.7)		< .001
36 mg	-11.2% (-12.0 to -10.4)		< .001

- Orforglipron group
  - Significantly more likely to achieve 10%, 15%, and 20% weight reduction
  - Significantly higher improvement in waist circumference, systolic blood pressure (SBP), triglycerides, and non-high-density lipoprotein (HDL)
  - GI effects were most common, mostly mild/moderate

Not FDA approved for obesity.

# The Many Varieties of Weight Loss Surgery

**Laparoscopic adjustable gastric banding**

**Biliopancreatic diversion with duodenal switch**

**Sleeve gastrectomy**

**Single anastomosis duodeno-ileal bypass with sleeve gastrectomy**

**Intragastric balloon**

**One-anastomosis gastric bypass**

**Roux-en-Y gastric bypass**

**Vagal nerve blocking therapy**

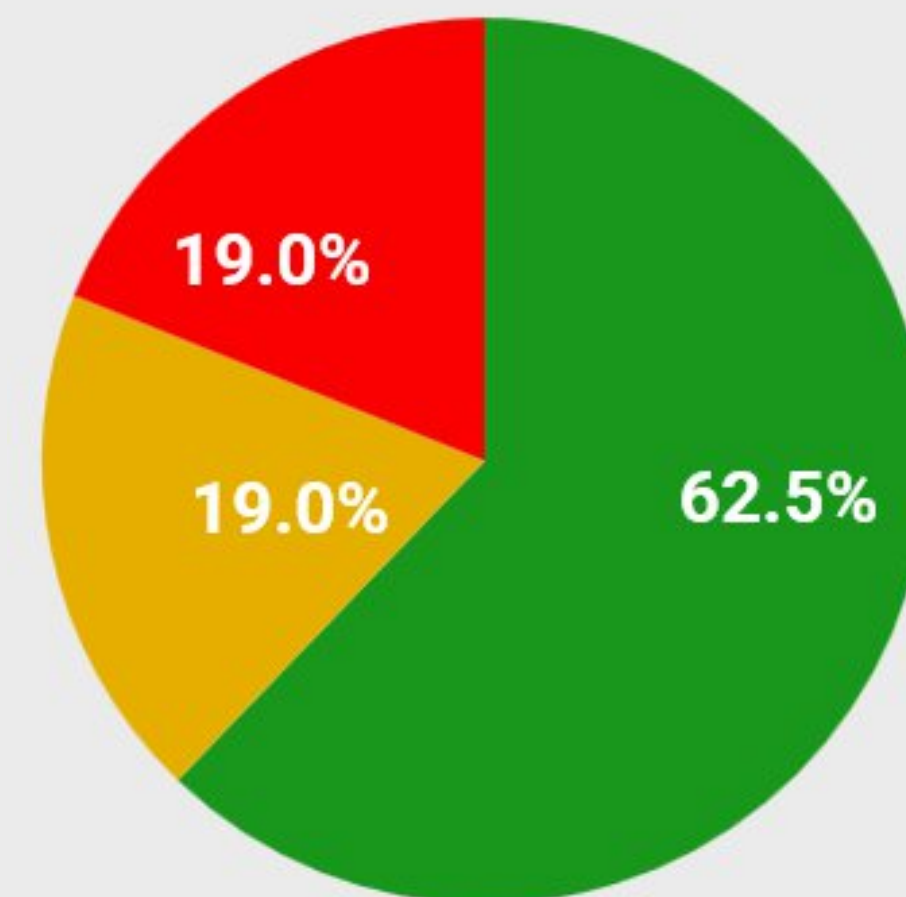
**Transpyloric bulb**

# Bariatric Surgery Improves PsA/PsO Outcomes

## Hazard ratios for PsO and PsA in patients undergoing bariatric surgery

Crude and Adjusted Hazard Ratios of Psoriasis, Severe Psoriasis, and Psoriatic Arthritis in Patients Undergoing Bariatric Surgery						
Characteristic	Crude		Age Adjusted and Sex Adjusted		Fully Adjusted*	
	Hazard Ratio (95% CI)	P-value	Hazard Ratio (95% CI)	P-value	Hazard Ratio (95% CI)	P-value
<b>Gastric bypass</b>						
Any psoriasis	0.54 (0.34–0.84)	.006	0.52 (0.32–0.81)	.004	0.52 (0.33–0.81)	.004
Severe psoriasis	0.45 (0.23–0.88)	.02	0.44 (0.22–0.73)	.02	0.44 (0.23–0.86)	.02
Psoriatic arthritis	0.31 (0.13–0.76)	.01	0.30 (0.12–0.73)	.01	0.29 (0.12–0.71)	.01
<b>Gastric banding</b>						
Any psoriasis	1.42 (0.47–4.30)	.54	1.23 (0.41–3.74)	.71	1.23 (0.40–3.75)	.72
Severe psoriasis	1.32 (0.14–12.11)	.81	1.28 (0.14–11.85)	.83	1.18 (0.12–11.48)	.89
Psoriatic arthritis	0.62 (0.10–3.89)	.61	0.58 (0.09–3.68)	.57	0.53 (0.08–3.56)	.52

## PsA Self-reported Outcomes



- Improvement after surgery
- No change after surgery
- Worsened after surgery



# Call to Action: 12-Point Framework to Support Multidisciplinary Care of Psoriatic Arthritis

- Collaborative care should be standard
- Optimal management of PsA requires regular multidisciplinary care
- Patients require support from multiple healthcare providers including psychologists/dieticians
- Nurse-led approaches can ease pressure on resources and consultation time
- Patient satisfaction is linked to continuity of care across multiple domains



# Conclusions

- Several immune messengers are common to both obesity and IMiDs
- Obesity guidelines and supporting data should be taken into account when managing obesity in patients with rheumatologic conditions
- Weight loss treatment modalities include lifestyle modification, pharmacotherapy, and bariatric surgery
- GLP-1/GIP RAs are becoming more mainstream with good efficacy, manageable safety/toxicity, and several emerging approaches (orals, long-acting, etc)
- A collaborative approach among specialists, primary care, and others should be standard