

# Regulate Your Appetite: A GLP-1 Agonist for Adult Weight Loss

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## Learning Objectives:

- Identify health problems commonly associated with overweight and obese individuals
- Identify the most common types of side effects associated with GLP-1 agonists used for weight loss
- Identify the place in therapy of GLP-1 agonists for the weight management of adults

## Background:

- Obesity prevalence in US:
  - 1999-2000: 30.5%
  - 2017-2020: 41.9%
- 2019 estimated annual medical cost of obesity: \$173 billion
- Severe obesity (BMI > 40kg/m<sup>2</sup>) increased from 5.7% in 2007 to 9.2% in 2018

## **Medical complications arising from obesity:**

- Hypertension
- Dyslipidemia
- Insulin resistance
- Type 2 diabetes
- Cardiovascular disease
- Reduced life expectancy

## **COVID-19 specific, increased:**

- Hospitalizations
- Need for mechanical ventilation
- Death

## **Trials / Data:**

Trial	Population	Primary Outcome Results
STEP-1	Semaglutide 2.4mg vs. placebo + lifestyle intervention in patients <b>without diabetes</b>	Semaglutide: Average 14.9% body weight reduction compared to 2.4% with placebo (P<0.001)

STEP-2	Semaglutide 2.4mg, 1mg, or placebo + lifestyle intervention compared in patients <b>with type 2 diabetes</b>	Percent body weight reduction (P<0.001): Semaglutide 2.4mg: 9.64% Semaglutide 1mg: 6.99% Placebo: 3.42%  Percent achieving ≥ 5% body weight reduction (P<0.001): Semaglutide 2.4mg: 68.8% Semaglutide 1mg: 57.1% Placebo: 28.5%
STEP-3	Semaglutide 2.4mg + intensive behavioral therapy with initial low-calorie diet in patients <b>without diabetes</b>	Semaglutide: Average 16% body weight reduction compared to 5.7% with placebo (P<0.001)  Percent achieving ≥5% body weight reduction (P<0.001): Semaglutide 2.4mg: 86.6% Placebo: 47.6%
STEP-4	Continuing semaglutide 2.4mg vs. placebo + lifestyle intervention after reaching treatment dose during 20-week run-in in patients <b>without diabetes</b>	Mean weight change from week 20-68: Semaglutide 2.4mg: -7.9% Placebo: +6.9%
STEP-8	Semaglutide 2.4mg versus Liraglutide 3.0mg + lifestyle intervention in patients <b>without diabetes</b>	Percent body weight reduction (P<0.001): Semaglutide 2.4mg weekly: -15.8% Liraglutide 3.0mg daily: -6.4%
SURMOUNT-1	Tirzepatide 5mg, 10mg, 15mg, or placebo + lifestyle intervention in patients <b>without diabetes</b>	Percentage body weight reduction (P<0.001): Tirzepatide 5mg: 15% Tirzepatide 10mg: 19.5% Tirzepatide 15mg: 20.9% Placebo: 3.1%

**STEP = Semaglutide Treatment Effect in People with obesity**

**Lifestyle intervention:** 500 kcal deficit in daily expenditure (which was determined at trial initiation) + 150 minutes physical activity per week

**Intensive behavioral therapy with initial low-calorie diet:** 1000-1200 kcal diet for first 8 weeks, transitioned to low-calorie 1200-1800 kcal diet for the remainder of the trial. Physical activity included 100 minutes weekly over 4-5 days, increased by 25 minutes every 4 weeks to reach a goal of 200 minutes per week.

**Assessment Questions** (Answers with explanations at the end of handout)

1. Which of the following disease states is most likely to improve from a substantial loss in body weight?

- A. Chronic Obstructive Pulmonary Disease
- B. Cardiovascular Disease
- C. Congestive Heart Failure - Stage 3
- D. Crohn's Disease

2. Which type of side effect is most common for GLP-1 agonists?

- A. Gastrointestinal upset
- B. Cardiovascular arrhythmia
- C. Hair loss
- D. Nephrotoxicity

3. Which of the following FDA approved medications is most effective for weight loss?

- A. Qsymia (Phentermine-Topiramate)
- B. Contrave (Naltrexone-Bupropion)
- C. Wegovy (Semaglutide)
- D. Xenical / Alli (Orlistat)

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1. B - Obesity is the number 1 most modifiable risk factor for cardiovascular disease. While weight loss may help some patients with complications from CHF, the damage to the heart cannot be reversed. Weight loss will not help with COPD for similar reasons, and will not help Crohn's disease.

2. A - The most common side effects are nausea, vomiting, diarrhea, and constipation. Tirzepatide can cause alopecia, but in a low percentage of patients.

3. C - Semaglutide on average produces approximately 15% total body weight loss, compared to roughly 10% for Qsymia, and 6% for orlistat or Contrave.