

# Once-Weekly Semaglutide in Adults with Overweight or Obesity

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## CLINICAL PROBLEM

Clinical guidelines suggest pharmacologic intervention in addition to diet and exercise to promote weight loss among adults with BMI  $\geq 30$  (or  $\geq 27$  in those with coexisting conditions). Barriers to medication use include limited efficacy, adverse effects, and cost. Subcutaneous semaglutide, a glucagon-like peptide-1 analogue FDA-approved to treat type 2 diabetes in adults, has been accompanied by weight loss in previous clinical trials.

## CLINICAL TRIAL

A phase 3, double-blind, randomized, controlled trial comparing semaglutide with placebo, plus lifestyle changes, in overweight or obese adults without diabetes.

1961 participants were assigned to receive 2.4 mg of subcutaneous semaglutide (with gradual increase to the 2.4 mg dose) or placebo weekly for 68 weeks; both groups received a counseling intervention involving diet and exercise. Coprimary end points were percentage change in body weight and weight reduction  $\geq 5\%$ .

## RESULTS

### Efficacy:

By week 68, mean weight declined more with semaglutide than with placebo (14.9% vs. 2.4%; estimated difference,  $-12.4$  percentage points; 95% CI,  $-13.4$  to  $-11.5$ ). In addition, more participants in the semaglutide group than in the placebo group had weight loss of  $\geq 5\%$  (86.4% vs. 31.5%).

### Safety:

Adverse events, mainly gastrointestinal, were most often mild to moderate but led to treatment discontinuation in 7.0% of the semaglutide group and 3.1% of the placebo group. Serious adverse events, primarily gastrointestinal and hepatobiliary events, were reported more often with semaglutide.

## LIMITATIONS AND REMAINING QUESTIONS

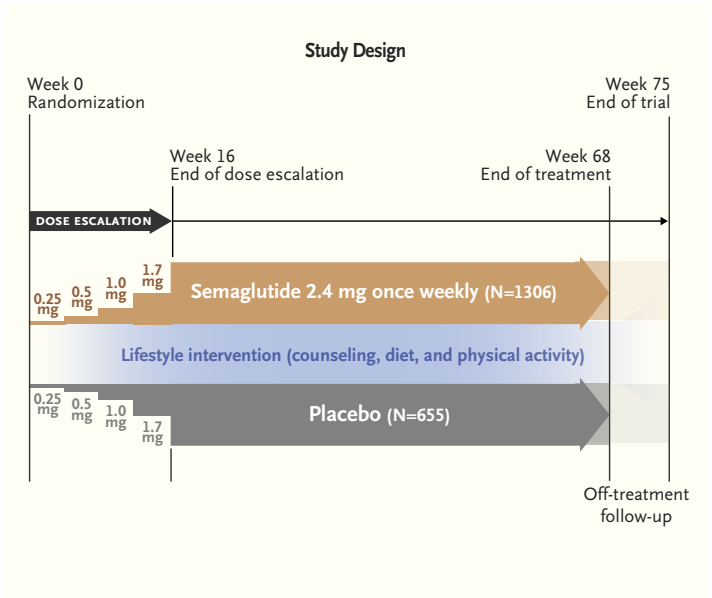
### Limitations:

- 43.7% of participants had prediabetes and might have responded differentially to the effects of semaglutide on weight gain.

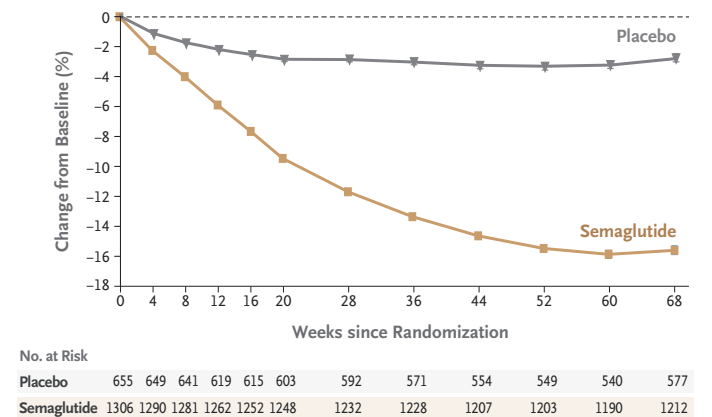
### Further study is required to understand the following:

- Whether results would be similar in persons who differ from the study participants, who were mainly female, White, and potentially highly motivated to lose weight
- Longer-term outcomes
- The mechanism by which semaglutide affects weight-related measures of health (e.g., body composition and glycated hemoglobin) in patients without diabetes

Links: [Full article](#) | [NEJM Quick Take](#) | [Editorial](#)



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



## CONCLUSIONS

Adults without diabetes who were overweight or obese had clinically relevant weight loss with weekly injections of semaglutide (2.4 mg) added to lifestyle changes.