
Tirzepatide vs Semaglutide for Treatment of Obesity



A new head-to-head clinical trial comparing tirzepatide and semaglutide for weight loss in people with obesity but without diabetes demonstrates that tirzepatide led to significantly greater weight reduction. Over a 72-week period, participants receiving tirzepatide achieved an average weight loss of 20.2%, compared to 13.7% with semaglutide—a difference of 47%. The results were presented at the 2025 European Congress on Obesity this week and published in *The New England Journal of Medicine*.

While both medications are effective for obesity management, this is the first direct comparison of [tirzepatide](#) and semaglutide in adults with obesity and no diagnosis of type 2 diabetes.

The study enrolled 751 adults with obesity and no type 2 diabetes. Participants were randomised to receive either tirzepatide (10 mg or 15 mg) or semaglutide (1.7 mg or 2.4 mg) via weekly subcutaneous injection for 72 weeks. The average participant age was 44.7 years; 64.7% were female and 76.1% were White. Mean body weight was 113.0 kg, BMI 39.4 kg/m², and waist circumference 118.3 cm. On average, participants had lived with obesity for 16 years, and 50% had two or more obesity-related complications.

The primary endpoint—percentage change in body weight at week 72—was met with a mean weight loss of –20.2% in the tirzepatide group compared to –13.7% in the semaglutide group. Tirzepatide also led to a greater reduction in waist circumference (–18.4 cm vs. –13.0 cm), a 42% greater improvement.

Participants on tirzepatide were 1.3 times more likely to achieve a 10% weight reduction, 1.6 times more likely to achieve a 15% reduction, 1.8 times more likely to achieve a 20% reduction and 2.0 times more likely to achieve a 25% reduction. 19.7% of those receiving tirzepatide lost at least 30% of their body weight, compared to 6.9% in the semaglutide group—a 2.8-fold difference.

The most common adverse events in both groups were gastrointestinal and primarily occurred during dose escalation. These were generally mild to moderate in severity.

Weight loss was approximately 6% lower in male participants compared to females for both treatments, which may partially explain the slightly reduced average weight loss compared to earlier trials. This study had a higher proportion of male participants (35%) than earlier STEP trials (19–26%).

The findings align with outcomes from the SURMOUNT and STEP programmes and reinforce real-world evidence suggesting greater efficacy with tirzepatide over semaglutide.

Greater weight loss was associated with improved cardiometabolic risk factors, including blood pressure and lipid and glucose profiles, for both treatments. 65% of tirzepatide users achieved at least 15% weight loss (vs. 40% for semaglutide), and 32% achieved at least 25% weight loss (vs. 16%).

The additional 5.4 cm greater waist reduction with tirzepatide is also clinically meaningful. Previous research suggests that each 5-cm increase in waist circumference is associated with a 7% and 9% increase in mortality risk for men and women, respectively. Guidelines recommend aiming for at least a 4-cm reduction in waist circumference.

Overall, this study shows that treatment with tirzepatide was superior to semaglutide with respect to reduction in body weight and waist circumference. These findings underscore tirzepatide's potential as a leading pharmacologic option for treating obesity in adults without type 2 diabetes.

Source: [NEJM](#)

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Published on : Tue, 13 May 2025