Semaglutide in obesity and type 2 diabetes: A review of clinical trial evidence from 1 to 5 semaglutide treatment effect in people with obesity program

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Abstract:

Obesity and type 2 diabetes mellitus (T2DM) are widespread health concerns that often coexist, contributing to increased cardiometabolic risks and premature death. Despite advancements in both lifestyle interventions and medical treatments, achieving lasting weight reduction and stable glycemic control remains a major clinical challenge. This review examines findings from the semaglutide treatment effect in people with obesity 1 (STEP) 1–5 trials, which assessed the effectiveness, safety, and long-term outcomes of once-weekly semaglutide 2.4 mg for weight management in adults. These trials included individuals with and without T2DM, enabling comparison across different populations and interventions. In nondiabetic participants (STEP 1, 3, and 4), semaglutide led to average weight reductions between 10% and 17%, while in patients with T2DM (STEP 2), the reduction was around 10%. The inclusion of intensive behavioral therapy in STEP 3 further enhanced weight loss outcomes. Results from STEP 4 highlighted notable weight regain following treatment withdrawal, reflecting the relapsing nature of obesity. STEP 5 confirmed semaglutide's ability to maintain significant weight loss (~15%) and improve metabolic health over a 2-year period. The most common side effects were gastrointestinal in nature but were generally manageable and nonsevere. Collectively, these trials support semaglutide 2.4 mg as an effective and sustainable option for managing obesity and overweight, including in people with T2DM. The data also emphasize the importance of combining pharmacological therapy with lifestyle modifications and recognize obesity as a long-term condition that necessitates continuous treatment.

Keywords:

Glucagon-like peptide-1 antagonist, obesity, semaglutide, semaglutide treatment effect in people with obesity trials, type 2 diabetes