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Poster 51

Efficacy and safety of semaglutide for obesity: A systematic review of phase 3 clinical trials

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Abstract

Background: Obesity is a chronic disease with significant metabolic and cardiovascular complications, yet effective long-term pharmacological treatments remain limited. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have emerged as a promising therapeutic class for weight management due to their effects on appetite regulation and energy balance. Semaglutide (SMG), a potent GLP-1 RA originally developed for type 2 diabetes, has demonstrated substantial weight-loss benefits, leading to its investigation as an obesity treatment. **Objective:** This review evaluates phase 3 clinical trials assessing the efficacy and safety of both subcutaneous and oral SMG in individuals with obesity or overweight, with and without type 2 diabetes. **Methods:** A search was conducted using PubMed, Web of Science, and ClinicalTrials.gov databases from inception through to December 31, 2024. Inclusion and exclusion criteria were designed to identify clinical trials evaluating the efficacy and safety of SMG for weight management. **Results:** The STEP (Semaglutide Treatment Effect in People with Obesity) program, targeting individuals with obesity or overweight with comorbidities, evaluated subcutaneous SMG 2.4 mg, demonstrating superior weight loss compared to placebo and liraglutide. Key strengths include well-designed randomized controlled trials demonstrating significant weight loss and metabolic benefits. The OASIS (Oral Semaglutide Treatment Effect in People with Obesity) studies explored higher-dose oral SMG (up to 50 mg) in obesity, achieving weight loss comparable to subcutaneous SMG 2.4 mg. Results showed that SMG achieved a significantly higher reduction in mean body weight (–15.5 kg and –15.1%) compared with placebo (−2.5 kg and –2.4%). Gastrointestinal adverse events, primarily nausea and vomiting, were common but typically mild to moderate and transient. **Conclusions:** SMG, in subcutaneous and oral formulations, has proven to be highly effective in significantly reducing body weight. Clinical studies confirm the superiority of SMG over most GLP-1 RAs, promoting safe and effective weight loss. Collectively, these studies underscore SMG's efficacy and acceptable safety profile, positioning it as a transformative option in obesity pharmacotherapy.

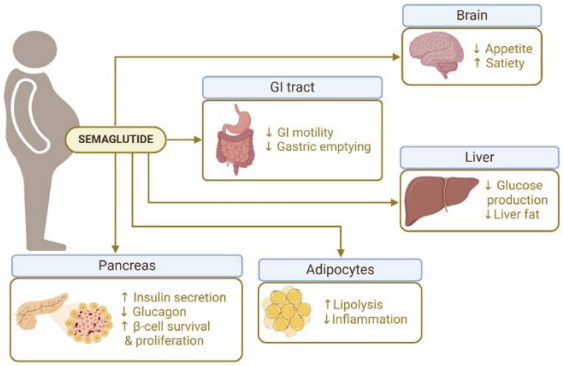

Figure 1. Mechanism of semaglutide for the management of obesity (Created in BioRender. Carvalho, M. (2025) https://BioRender.com/l84z782).

Keywords: semaglutide; GLP-1 receptor agonist; obesity; weight loss therapy

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