

### 1-Effect of glucagon-like peptide-1 receptor agonists and co-agonists on body composition: Systematic review and network meta-analysis

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#### Abstract

Background and aims: While glucagon-like peptide-1 receptor agonists (GLP-1RAs) effectively reduce body weight, their impact on lean mass remains uncertain. This meta-analysis evaluated the effects of GLP-1RAs and GLP-1/GIP receptor dual agonists (GLP-1/GIP-RAs) on body composition, focusing on total weight, fat mass, and lean mass in adults with diabetes and/or overweight/obesity. Methods: A systematic search of Medline, Embase, and the Cochrane Library was conducted through November 12, 2024. Data were analyzed using random-effects pairwise and network meta-analyses to compare interventions with placebo or active comparators. Results: Twenty-two randomized controlled trials (2258 participants) were included. GLP-1RAs significantly reduced total body weight (MD-3.55 kg, 95 %-CI [-4.81,-2.29]), fat mass (MD-2.95 kg, 95 %-CI [-4.11,-1.79]), and lean mass (MD-0.86 kg, 95 %-CI [-1.30,-0.42]), with lean mass loss comprising approximately 25 % of the total weight loss. However, the relative lean mass, defined as percentage change from baseline, was unaffected. Liraglutide, at 3.0 mg weekly or 1.8 mg daily, was the only GLP-1RA to achieve significant weight reduction without significantly reducing lean mass. Tirzepatide (15 mg weekly) and semaglutide (2.4 mg weekly) were the most effective for weight and fat mass reduction but were among the least effective in preserving lean mass. Conclusions: Potent GLP-1 RAs, such as tirzepatide and semaglutide, demonstrate greater overall weight loss but are associated with a significant reduction in lean mass.

#### Keywords

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[GLP-1 receptor agonist](#)[Obesity](#)[Diabetes](#)[Cardio-renal-metabolic health](#)[Body weight](#)[Fat mass](#)[Lean mass](#)[Body composition](#)[Sarcopenia](#)[Fat free mass](#)

#### Keywords Plus

[CARDIOVASCULAR RISK](#)[GLYCEMIC CONTROL](#)[MUSCLE MASS](#)[WEIGHT-LOSS](#)[LIRAGLUTIDE](#)[OBESITY](#)[FAT](#)[ADULTS](#)