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Efficacy and Safety of Glucagon-like Peptide-1 Receptor Agonists and Co-agonists for Weight Loss Among Adults Without Diabetes: An Updated Systematic Review

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Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly used for weight management.

We conducted an update to our prior systematic review of the safety and efficacy of GLP-1 RAs for weight loss among adults with overweight or obesity without diabetes to account for the introduction of novel agents and the expanding evidence base of these therapies.

We analyzed the findings from 38 randomized controlled trials (14 of which were newly identified) comprising 25,816 adults and measured outcomes including change in body weight, BMI, waist circumference, and blood pressure. Across the studies, participants taking GLP-1 RAs lost significantly more weight than those receiving placebo, with some emerging treatments associated with weight loss exceeding 20% of body weight. In particular, among currently available treatments, tirzepatide produced the greatest weight loss, while newer experimental drugs showed even larger effects.

Consistent with the prior review, the findings showed that GLP-1 RAs demonstrate substantial weight loss in adults without diabetes, and gastrointestinal adverse effects remained the most common across all therapies. While these were frequently reported, serious adverse events and deaths were rare, and no new safety concerns were identified.

In conclusion, GLP-1-based therapies offer effective weight-loss options for people without diabetes, with a growing range of injectable and oral treatments becoming available.

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