Efficacy and safety of Semaglutide vs Tirzepatide for Weight Loss in Adults with Overweight or Obesity, a systematic review and meta-analysis

Inclusion and Exclusion Criteria

Inclusion Criteria

Studies published between 2015 and 2025 were considered eligible.Only studies published in English were included. The studies like randomized controlled trials (RCTs), retrospective studies and cohort studies are included in this review. The review included studies that met the following criteria such as population of adults aged 18 years with overweight (BMI 25 kg/m²) or obesity (BMI 30 kg/m²), Interventions includes the Studies evaluating the efficacy and safety of semaglutide or tirzepatide for weight loss. Comparators include placebo or other weight-loss interventions, including head-to-head comparisons between semaglutide and tirzepatide, the outcomes include weight loss measured as mean weight change and percentage weight loss as primary outcome, changes in BMI, waist circumference, adverse events, and treatment discontinuation due to adverse effects as secondary outcomes.

Exclusion Criteria

Studies involving children, adolescents, or pregnant women were excluded. Studies with insufficient or unpublished data and case reports, editorials, opinion articles, or reviews without primary data were excluded. Also the studies evaluating drugs other than semaglutide or tirzepatide and the animal or preclinical studies were excluded.

Results

13 studies were used for evaluating the efficacy and safety of Tirzepatide and Semaglutide for weight management and glycemic control in overweight or obese populations. This study included eleven randomized controlled trials, one retrospective study and one cohort studies with the total population of 68,147 participants across all the included studies. The populations included adults with a BMI 27 kg/m² considered as overweight or BMI 30 kg/m² considered as obese. Studies involving adolescents (Weghuber et al., 2022) provided additional information regarding the pediatric management of obesity. Most trials excluded participants with diabetes or other confounding conditions. Tirzepatide and Semaglutide were the primary interventions that were administered subcutaneously at varying doses that ranged from 5 mg to 15 mg weekly for Tirzepatide and 0.25 mg to 2.4 mg weekly for Semaglutide. Some trials include placebo groups (Garvey et al., 2022; Jastreboff et al., 2018) or Liraglutide (Rubino et al., 2022).

Efficacy Outcomes

Table 2 highlights the weight reduction efficacy of various pharmacological interventions, primarily semaglutide and tirzepatide while compared to placebo. Significant reductions in body weight were observed, with semaglutide achieving up to a 16% reduction and tirzepatide showing superior efficacy at higher doses, reaching a 19.5% reduction (Jastreboff et al., 2022). Additionally, the percentage of participants achieving 5%, 10%, and 15% weight loss was consistently higher with active treatments, with tirzepatide achieving 15% weight loss in 42.3% of participants compared to 18.1% with semaglutide (Rodriguez et al., 2024). Improvements in BMI and lipid profiles, including reductions in LDL cholesterol and triglycerides, were noted across studies (Garvey et al., 2022; Wilding et al., 2021). These findings observed the efficacy of

these agents in promoting weight loss and enhancing cardiometabolic profiles and provides valuable insights regarding their clinical applications.

Adverse effects

Gastrointestinal (GI) adverse events were frequently reported across studies, with similar rates between tirzepatide and semaglutide in some cases (Rodriguez et al., 2024; Garvey et al., 2023) and higher incidences noted for semaglutide in others (Weghuber et al., 2022). Serious adverse events were rarely reported, though one study indicated a death unrelated to treatment (Seino et al., 2018). Drug discontinuation rates due to GI side effects varied, with semaglutide consistently showing higher rates compared to placebo or alternative interventions (Rubino et al., 2021; Wadden et al., 2023). Mild to moderate nausea, vomiting, diarrhea, and constipation were the most commonly reported side effects, often occurring during dose escalation (Jastreboff et al., 2022; Wilding et al., 2021). Both semaglutide and tirzepatide demonstrated substantial weight loss benefits, with tirzepatide often achieving greater reductions and a higher likelihood of meeting weight-loss thresholds, especially at higher doses (Frias et al., 2020; Aronne et al., 2024). Continued treatment with either drug resulted in sustained weight loss, whereas discontinuation led to weight regain (Rubino et al., 2022).

Table 1: Study Characteristics

Author, Year	Study Design	Sample Size	Intervention	Comparator	Objectives	Follow up	Outcomes Measured	Inclusion and exclusion criteria
Patricia J. Rodriguez, et al. 2024	cohort study	Total: 18 386 (After propensity match) tirzepatide: 9193; semaglutide: 9192	Tirzepatide: Initial dose of 5 mg Semaglutide: Initial dose of 0.25 mg (with dose escalation every 4 weeks to reach the target maintenance dose)	Tirzepatide V Semaglutide	weight loss and rates of gastrointestinal adverse events	Mean days : 165	Weight loss: 5%, 10%, 15% (hazard ratios); Percentage weight change; Gastrointestinal AEs: Hazard ratios.	IC: New users of drugs with with overweight (BMI 27) or obesity (BMI 30); no prior GLP-1 RA use EC: History of severe gastrointestinal AEs
(Rodriguez et al., 2023)	Retrospective analysis	41,223 (32,030 semaglutide; 9,193 tirzepatide)	Tirzepatide	Semaglutide	Compare weight loss efficacy and safety	12 months	5%, 10%, 15% weight loss, % body weight lost at 3, 6, 12 months	Adults with BMI 27 kg/m ² , no prior GLP-1 RA use, regular care
(Garvey et al., 2022)	Randomized, Double-blind, Placebo- Controlled	304	Weekly semaglutide 2.4 mg	Placebo	To evaluate the effectiveness and safety of semaglutide for long-term weight management in adults with obesity or overweight who have weight- related comorbidities.	104 weeks	Percentage weight change; achievement of 5%, 10%, and 15% weight loss; secondary endpoints included changes in BMI, waist circumference, lipid profiles, and glycemic status.	Adults with obesity (BMI 30) or overweight (BMI 27) with at least one weight-related comorbidity; excluded if diagnosed with diabetes or other significant health conditions.
(Seino et al., 2018)	Randomized, open-label, phase III trial	308	Semaglutide (0.5 mg, 1.0 mg) weekly subcutaneous injection	Sitagliptin 100 mg daily	To determine the safety and effectiveness of semaglutide compared to sitagliptin in Japanese patients with type 2 diabetes.	30 weeks	HbA1c change, weight reduction, proportion achieving weight loss 5%, 10%, 15%, fasting plasma glucose, BMI, lipid profiles.	Adults (20 years) with T2D, HbA1c levels: 6.5%- 9.5% (OAD) or 7%-10.5% (diet & exercise). Exclusions: glucose- lowering agents recently used, thyroid carcinoma history, pancreatitis, severe renal dysfunction, heart failure.
(Frias et al., 2020)	Double-blind, placebo- controlled	111	Tirzepatidewasadministeredsubcutaneouslyfollowingthree dosing regimens:12 mg regimen:4 mg forweeks 0–3, 8 mg for weeks4–7, and 12 mg for weeks 8–11.15 mg regimen-1:2.5 mg forweeks 0–1, 5 mg for weeks	Placebo	To compare the impact of tirzepatide versus placebo on HbA1c reduction from baseline after 12 weeks.	12 weeks	HbA1c reduction, body weight change, fasting blood glucose (FBG), waist circumference, treatment-emergent adverse events (TEAEs), nausea, vomiting, diarrhea.	Type 2 diabetes for 6 months, HbA1c 7.0–10.5%, BMI 23–45 kg/m ² , inadequately controlled on diet/exercise or stable metformin. Excluded if not meeting these criteria.

			2–3, 10 mg for weeks 4–7, and 15 mg for weeks 8–11. 15 mg regimen-2: 2.5 mg for weeks 0–3, 7.5 mg for weeks 4–7, and 15 mg for weeks 8– 11.					
(Jastreboff et al., 2022)	Phase 3, multicenter, double-blind, randomized, placebo- controlled trial	2539 participants	Tirzepatide (5 mg, 10 mg, 15 mg weekly doses)	Placebo	Evaluate the efficacy and safety of tirzepatide in adults with obesity	72 weeks (including a 20-week dose- escalation period)	Percentage change in weight, weight reduction 5%, 10%, 15%, and 20%, changes in waist circumference, blood pressure, fasting insulin, lipid levels, and body-fat mass	BMI 30, or BMI 27 with at least one weight-related complication (e.g., hypertension, dyslipidemia) and failure of dietary weight loss were included. Diabetes, significant weight change (>5 kg) in the past 90 days, prior/planned obesity surgery, and weight-loss medication in the past 90 days were excluded.
(Wilding et al., 2021)	Randomized, double-blind, placebo- controlled trial	A total of 1,961 participants were included, with 1,306 in the semaglutide group and 655 in the placebo group.	Participants received once- weekly subcutaneous semaglutide (2.4 mg) combined with lifestyle interventions.	Placebo + lifestyle intervention	 he study aimed to assess the efficacy and safety of semaglutide (2.4 mg) for weight loss in adults with obesity or overweight as an adjunct to lifestyle modifications 	68 weeks	Key outcomes included percentage change in body weight, the proportion of participants achieving 5%, 10%, and 15% weight loss, changes in cardiometabolic risk factors, participant-reported physical functioning, incidence of adverse events, serious adverse events, and treatment discontinuation due to side effects.	Adults (18 years), BMI 30 or BMI 27 with 1 weight-related condition, unsuccessful weight loss attempts; written informed consent were included. Diabetes, HbA1c 6.5%, history of pancreatitis, prior obesity surgery, anti- obesity drug use within 90 days were excluded.
(Weghuber et al., 2022)	Double-blind, randomized, placebo- controlled trial	201	Subcutaneous semaglutide (2.4 mg/week)	Placebo	Assess efficacy and safety of semaglutide in reducing BMI in adolescents with obesity.	68 weeks	Percentage BMI change, weight loss 5%, 10%, 15%; cardiometabolic risk factors (lipids, HbA1c, ALT).	Adolescents(12-<18years)withBMI95thpercentileorBMI85thpercentilewithweight-relatedcoexistingcondition.Exclusion:Weight change >5 kg in 90

(Wadden et al., 2023)	Double-blind, placebo- controlled	579	Tirzepatide (10 or 15 mg)	Placebo	To evaluate the efficacy of tirzepatide in achieving additional weight loss in individuals who successfully achieved 5% weight reduction through lifestyle changes.	72 weeks	Percentage weight change Participants achieving 5%, 10%, and 15% weight loss Adverse events Maintenance of weight reduction during lead-in phase.	days, prior obesity treatment, severe psychiatric disorders, suicide attempts. Participants were eligible if they had a BMI of 30 kg/m ² or 27 kg/m ² with at least one obesity-related complication, excluding diabetes. Additionally, participants were required to achieve a minimum of 5% weight reduction during a 12-week intensive lifestyle intervention prior to study enrollment.
(Rubino et al., 2021)	Double-blind, placebo- controlled withdrawal study	803 randomized	Continued weekly subcutaneous semaglutide, 2.4 mg	Placebo	To compare continued semaglutide treatment with placebo for weight maintenance after a 20-week run-in phase with semaglutide 2.4 mg.	48 weeks	Primary: Percent change in body weight. Secondary: Waist circumference, systolic BP, physical functioning (SF-36), lipid levels, antihypertensive/lipid -lowering medication use.	Adults 18 years old; BMI 30 or BMI 27 with weight-related comorbidities; unsuccessful prior dietary effort to lose weight. Exclusions: Type 2 diabetes, HbA1c 6.5%, recent >5 kg weight change, specific prior medications
(Rubino et al., 2022)	Randomized, open-label, phase 3b trial	338	Semaglutide 2.4 mg (once- weekly), Liraglutide 3.0 mg (once-daily)	Placebo	Compare efficacy and adverse event profiles of semaglutide vs liraglutide in overweight or obese adults without diabetes	68 weeks	Primary: % change in body weight. Secondary: Achievement of 10%, 15%, and 20% weight loss	Inclusion: BMI 30 or 27 with comorbidities, 18 years. Exclusion: Diabetes, HbA1c 6.5%, weight change >5 kg within 90 days before screening
(Wadden et al., 2023)	Randomized, double-blind, parallel- group, phase 3a trial	611	Semaglutide 2.4 mg weekly	Placebo	To evaluate the effect of semaglutide on body weight as an adjunct to intensive behavioral therapy	68 weeks	Change in body weight, % weight loss (5%, 10%, 15%)	BMI 27 with at least 1 comorbidity or BMI 30, no diabetes, no significant weight change in past 3 months

(Aronne et	Phase 3	783 enrolled, 670		Placebo	To assess the effect	52-week	Mean percent change	BMI 30 or 27 with
al., 2024)	Randomized	randomized	Once-weekly subcutaneous		of tirzepatide, with	double-	in weight from	weight-related
			tirzepatide (10 or 15 mg)		diet and physical	blind period	randomization to	complications, excluding
			1 0		activity, on the	after 36-	week 88, proportion	diabetes, prior/planned
					maintenance of	week open-	maintaining 80% of	obesity surgery, and recent
					weight reduction	label lead-in	weight loss, weight	weight-loss medications
							reduction thresholds	-

 Table 2: Efficacy Outcomes

Author, Year	Baseline weight	% Weight change	% Achieving 5% Weight Loss	% Achieving 10% Weight Loss	% Achieving 15% Weight Loss	BMI	lipid profiles changes
Patricia J. Rodriguez, et al. 2024	Baseline weight: Tirzepatide: 110 (25.7) kg Semaglutide: 109 (25.2) kg (End point not measured)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Tirzepatide: 81.8% (95% CI, 79.8%- 83.7% Semaglutide: 66.5% (95% CI, 64.3%- 68.7%)	Tirzepatide: 62.1% (95% CI, 59.7%- 64.3%) Semaglutide: 37.1% (95% CI, 34.6%- 39.4%) Semaglutide: 37.1%	Tirzepatide: 42.3% (95% CI, 39.8%- 44.6%) Semaglutide: 18.1% (95% CI, 16.1%- 20.0%)	Not measured	Not measured
(Rodriguez et al., 2023)	Mean: 110 kg (SD: 25.7 kg)	-7.2% for tirzepatide at 12 months	81.8% (tirzepatide); 64.6% (semaglutide)	62.1% (tirzepatide); 38.0% (semaglutide)	42.3% (tirzepatide); 19.3% (semaglutide)	27 kg/m²	Not measured
(Garvey et al., 2022)	106.0 kg	-15.2% (semaglutide) vs2.6% (placebo)	77.1% (semaglutide) vs. 34.4% (placebo)	61.8% (semaglutide) vs. 13.3% (placebo)	52.1% (semaglutide) vs. 7.0% (placebo)	38.5 kg/m ²	Significant improvements in LDL cholesterol, triglycerides, and total cholesterol compared to placebo.
(Seino et al., 2018)	69.3 kg	-3.2% (0.5 mg)	70% (0.5 mg)	10% (1.0 mg)	Not reported	Not reported	Significant reductions in total cholesterol, LDL-C, and triglycerides.
(Frias et al., 2020)	Not reported	Not reported	Not reported	Not reported	Not reported	31.9 kg/m ²	Not reported
(Jastreboff et al., 2022)	104.8 kg (mean)	-15.0% (5 mg), -19.5% (10 mg), - 20.9% (15 mg), -3.1% (placebo)	85% (5 mg), 89% (10 mg), 91% (15 mg), 35% (placebo)	Not reported	Not reported	38.0 (mean at baseline)	Improvements in lipid levels observed

(Wilding et al., 2021)	Mean: 105.3 kg	Semaglutide: -14.9%; Placebo: -2.4%	Semaglutide: 86.4%; Placebo: 31.5%	Semaglutide: 69.1%; Placebo: 12.0%	Semaglutide: 50.5%; Placebo: 4.9%	Mean: 37.9 (baseline)	Improved cardiometabolic risk factors in the semaglutide group
(Weghuber et al., 2022)	Not specified	-16.1% (semaglutide), 0.6% (placebo)	73% (semaglutide), 18% (placebo)	Not specified	Not specified	Reduction noted	Greater improvement with semaglutide in total cholesterol, triglycerides, and LDL levels. HDL unchanged.
(Wadden et al., 2023)	109.5 kg	-18.4%	87.5%	Not specified	Not specified	35.9 kg/m²	Reduction in all lipid levels except HDL
(Rubino et al., 2021)	107.2 kg (mean)	-7.9% (treatment) vs +6.9% (placebo)	Not reported	Not reported	Not reported	30 kg/m ²	Not reported
(Rubino et al., 2022)	Mean weight: 104.5 kg	Semaglutide: -15.8%, Liraglutide: -6.4%, Placebo: -1.9%	Semaglutide: 70.9%, Liraglutide: 25.6%	Semaglutide: 55.6%, Liraglutide: 12.0%	Semaglutide: 38.5%, Liraglutide: 6.0%	Semaglutide: 37.5	Significant improvement in lipid profiles with both treatments
(Wadden et al., 2023)	105.8 kg	-16.0% (semaglutide), -5.7% (placebo)	86.6% (semaglutide), 47.6% (placebo)	75.3% (semaglutide), 27.0% (placebo)	55.8% (semaglutide), 13.2% (placebo)	38.0 kg/m ²	Not provided
(Aronne et al., 2024)	107.3 kg (mean)	-5.5% (tirzepatide), 14.0% (placebo)	89.5% (tirzepatide), 16.6% (placebo)			38.4 (mean)	Improvements in blood pressure, glycemic parameters, and lipids during lead-in period

 Table 3: Safety outcomes

Author, Year	Adverse events	Serious Adverse events	Drug Discontinuation Rate		Conclusion
				Other side effects	
Patricia J. Rodriguez, et al. 2024	No significant differences in the risk of gastrointestinal adverse events (AEs)	Not reported	Tirzepatide: 5140 [55.9%]; semaglutide: 4823 [52.5%]	Not reported	In the population of adults with overweight or obesity, use of tirzepatide was associated with significantly greater weight loss than semaglutide.
(Rodriguez et al., 2023)	Similar gastrointestinal adverse events between groups	Not specified	Not specified	Gastrointestinal issues (e.g., bowel obstruction, gastroparesis)	Patients on tirzepatide achieved greater weight loss and higher likelihood of reaching 5%, 10%, and 15% weight loss thresholds within 12 months.
(Garvey et al., 2022)	Gastrointestinal disorders reported in 82.2% (semaglutide) vs. 53.9% (placebo).	7.9% (semaglutide) vs. 11.8% (placebo); 1 death reported, unrelated to treatment.	5.9% (semaglutide) vs. 4.6% (placebo).	Mild-to-moderate nausea, diarrhea, vomiting, constipation (higher in semaglutide group).	Semaglutide resulted in substantial and sustained weight loss and improvements in metabolic parameters over 104 weeks compared to placebo.
(Seino et al., 2018)	74.8% (0.5 mg), 71.6% (1.0 mg), 66% (Sitagliptin); mild to moderate GI effects common with semaglutide.	Not specified	14.7% (semaglutide 1.0 mg), 2.9% (others). Adverse events most frequent cause.	Gastrointestinal issues (diminished over time).	Semaglutide significantly reduced HbA1c and weight compared to sitagliptin. Safety profile aligned with GLP-1 receptor agonists.
(Frias et al., 2020)	Nausea incidence: placebo: 7.7%; tirzepatide 12 mg: 24.1%; tirzepatide 15 mg-1: 39.3%; tirzepatide 15 mg-2: 35.7%.	Placebo: 1 patient; Tirzepatide: 1 patient from each dose group.	Placebo: 23.1%; Tirzepatide 12 mg: 6.9%; Tirzepatide 15 mg-1: 21.4%; Tirzepatide 15 mg-2: 7.1%.	Nausea, vomiting, diarrhea	Tirzepatide significantly reduced HbA1c over 12 weeks. Lower starting doses and smaller increments led to a more favorable side-effect profile.
(Jastreboff et al., 2022)	Mostly gastrointestinal, mild to moderate, occurred during dose escalation	Not specified	4.3% (5 mg), 7.1% (10 mg), 6.2% (15 mg), 2.6% (placebo)	Gastrointestinal discomfort noted	Tirzepatide (5 mg, 10 mg, or 15 mg weekly) provides substantial and sustained weight reductions in adults with obesity.
(Wilding et al., 2021)	Nausea and diarrhea, mostly transient and mild to moderate	Not detailed	Semaglutide: 4.5% (due to gastrointestinal events); Placebo: 0.8%	Not specified	Semaglutide (2.4 mg) + lifestyle intervention led to sustained, clinically relevant weight loss compared to placebo.
(Weghuber et al., 2022)	Gastrointestinal events: 62% (semaglutide) vs. 42%	11% (semaglutide), 9% (placebo)	Not detailed	No specific rate for discontinuation; side effects include GI symptoms.	Semaglutide significantly reduced BMI and weight, with improved

	(placebo); Cholelithiasis in 4% of semaglutide group.				cardiometabolic risk factors compared to placebo.
(Wadden et al., 2023)	Gastrointestinal issues (mild/moderate)	Not mentioned	10.5% for intervention group, 14.4% for placebo group	Not mentioned	Tirzepatide showed significant additional weight loss and maintenance benefits in patients who already achieved 5% weight reduction via lifestyle intervention.
(Rubino et al., 2021)	GI events in 41.9% (semaglutide) vs 26.1% (placebo)	2.4% (semaglutide) vs 2.2% (placebo)	Similar between groups	Gastrointestinal events (nausea, vomiting, diarrhea); tolerability issues	Maintaining treatment with semaglutide resulted in statistically significant continued weight loss compared to placebo (+6.9% gain with placebo). Waist circumference and systolic BP also improved.
(Rubino et al., 2022)	Semaglutide: 84.1%, Liraglutide: 82.7%	None specified	Semaglutide: 13.5%, Liraglutide: 27.6%	Gastrointestinal issues reported (both groups)	Semaglutide resulted in greater weight loss compared to liraglutide at 68 weeks.
(Wadden et al., 2023)	Gastrointestinal: 82.8% (semaglutide), 63.2% (placebo)	Not reported	3.4% (semaglutide), 0% (placebo)	Gastrointestinal side effects	Semaglutide produced significantly greater weight loss compared to placebo. More participants achieved 5%, 10%, and 15% weight loss with semaglutide
(Aronne et al., 2024)	Mild to moderate gastrointestinal symptoms, more common with tirzepatide	No serious adverse events mentioned	Withdrawal (placebo group) and other reasons (mainly lack of efficacy in placebo group)	Gastrointestinal events, dose de-escalation required for some participants	Continued tirzepatide treatment maintained and augmented weight loss, whereas discontinuation led to significant weight regain.

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