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Incretin-based therapy for obesity, part 1: effects on weight loss and body composition

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Abstract

Obesity is a global public health challenge affecting more than half of the world's population. It is associated with increased morbidity, mortality, and healthcare costs. While metabolic surgery has historically provided the most effective long-term weight loss, recent advances in incretin-based pharmacotherapy have transformed non-surgical obesity management. Glucagon-like peptide-1 (GLP-1) receptor agonists and dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) receptor agonists have demonstrated good efficacy in inducing clinically significant weight loss. This review summarizes the evidence on semaglutide and tirzepatide, the two most widely used incretin-based therapies. Both drugs promote weight loss through delayed gastric emptying and central appetite regulation. Semaglutide 2.4 mg has been shown in the STEP clinical trial program to induce average weight losses of 10–18% across diverse populations. Tirzepatide, evaluated in the SURMOUNT program, demonstrated superior efficacy, achieving mean weight reductions of 20–25%. Beyond weight reduction, incretin-based therapies significantly improve body composition. Weight loss is primarily driven by reductions in fat mass, including visceral adiposity, with proportional losses of lean mass. Available evidence indicates preservation of muscle quality and physical function despite reductions in lean mass. Semaglutide and tirzepatide represent a major advancement in obesity treatment. Their efficacy, safety, and metabolic benefits support their role as long-term, disease-modifying therapies in obesity management.

Keywords: incretin-based therapies, semaglutide, tirzepatide, obesity, weight loss

Introduction

More than half of the world's population lives with weight-related problems such as overweight or obesity. This health problem also affects the pediatric population, with up to 30% of school-aged children experiencing these conditions [1]. The consequences of obesity include an increased risk of non-communicable diseases, disability and mortality. This situation underscores the urgent need for action to reduce the burden on the health-care system and economic costs, to secure a longer disease-free life expectancy and reduce the expenses associated with chronic disease management. Over recent decades, metabolic surgery has been the most effective intervention for the management of obesity, and most of the non-surgical interventions failed to achieve and maintain a normal body mass index (BMI). This unmet need has been addressed in recent years by glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and by the dual receptor agonist targeting

both GLP1 and glucose-dependent insulinotropic polypeptide (GIP) (GLP-1/GIP RA) [2].

These novel therapies, including the GLP-1 RA weekly semaglutide and GLP-1/GIP RA tirzepatide, have entered pharmacological markets in nearly 100 countries worldwide. In response, governments and health agencies have developed clinical guidelines to incorporate incretin-based therapies in the obesity management strategies [3]. Initially approved for the management of type 2 diabetes, these injectable drug classes demonstrated significant weight-loss benefits with a low risk of hypoglycemia and were therefore adopted for weight management in individuals without diabetes. Despite their growing popularity, these medications are associated with adverse effects (gastrointestinal, pancreatitis, non-arteritic anterior ischemic optic neuropathy) that may lead to treatment discontinuation. Furthermore, evidence on long-term efficacy remains limited due to their recent introduction in clinical practice [4].

To address gaps in professional knowledge and population understanding of weight management using incretin-based injectable therapy, this article summarizes the existing evidence on the two most widely used agents, semaglutide and tirzepatide. We aim to review the mechanisms of action of GLP-1 RAs and GLP-1/GIP RAs, as well as their efficacy in terms of weight reduction and body composition outcomes.

Mechanism of action

GLP-1 RA and dual GLP-1/GIP RA were initially developed for the management of type 2 diabetes due to their effect on glycemic control, cardiovascular risk reduction, and body weight benefits [2]. By binding to incretin receptors, these agents stimulate glucose-dependent insulin secretion from pancreatic β-cells and inhibit glucagon release. They also promote satiety by delaying gastric emptying and modulating appetite-related signaling pathways in key brain regions, including the hypothalamus, hindbrain, and mesolimbic system, which are central to appetite regulation [5]. These actions reduce hunger and food cravings, increase satiety and, consequently, lead to caloric intake reduction, thereby facilitating weight loss [6].

Weekly incretin-based therapy and weight loss

Semaglutide

Semaglutide is a glucagon-like peptide-1 analog, sharing 94% of the structural homology with the native GLP-1. The distinct modifications of the molecule confer resistance to DPP-IV degradation and long half-life (168 hours), that allow weekly administration of the drug [7].

The effect of semaglutide on body weight and obesity complications has been investigated in two phase-3 clinical trial programs: Semaglutide Treatment Effect in People with obesity (STEP) and Semaglutide Unabated Sustainability in Treatment of Type 2 Diabetes (SUSTAIN). The STEP program includes over 10 clinical trials and was developed to investigate the efficacy and safety of subcutaneous once-weekly semaglutide at a dose of 2.4 mg/day in patients with overweight and obesity, while SUSTAIN aimed to investigate the efficacy of semaglutide in glycemic control in patients with type 2 diabetes.

STEP clinical trial program showed that semaglutide is an effective therapeutic option for the management of obesity across various populations, including prediabetes, type 2 diabetes and different ethnic groups. The magnitude of weight loss achieved was 10-18%, outcomes previously achieved only through bariatric surgery, therefore redefining expectations with non-surgical therapies in obesity management. A significant proportion of patients achieved >10% and >15% weight loss, a percentage associated with improvement of cardiovascular and metabolic risk factors and obesity-related complications [8–18].

STEP 1 was 63 weeks randomized double blind trial comparing the efficacy of weekly 2.4 mg semaglutide *vs.* placebo in adults with obesity defined as a BMI ≥30 kg/m^2. By the end of the 68-week study period, semaglutide therapy was associated with a weight loss of 14.9% (-15.3 kg) of body weight compared to 2.4% (-2.6 kg) body weight reduction with placebo, with an absolute difference of -12.4% (-12.7 kg) between the groups ($p<0.001$). 86.4% of the semaglutide group achieved a weight reduction of ≥5%, 69.1% achieved a weight reduction of ≥10% and 50.5% achieved a weight reduction of ≥15% (*versus* 31.5%, 12.0%, and 4.9%, respectively for placebo; $p<0.001$ for all three comparisons) [8]. STEP 3 trial investigated the effect of once-weekly 2.4 mg semaglutide *versus* placebo on top of intensive behavioral therapy and low-calorie diet in adults with overweight or obesity. By the end of 68 weeks of intervention, the semaglutide group had a 16% reduction in body weight *versus* 5.7% in the placebo group (between-group difference of -10.3%). More participants treated with semaglutide obtained at least 5%, 10% or 15% weight loss *versus* placebo: 86.6% *versus* 47.6%, 75.3% *versus* 27.0%, and 55.8% *vs.* 13.2%, respectively [10].

STEP 2 trial enrolled 1210 patients with overweight or obesity and type 2 diabetes diagnosed at least 6 months before study enrollment. The patients were randomly assigned in a 1:1:1 ratio to 2.4 mg semaglutide, 1 mg semaglutide, or placebo

on top of lifestyle optimization. At the end of the study (68 weeks), the 2.4 mg semaglutide group registered a mean weight loss of 9.6% *versus* 3.4% in the placebo group. By the end of the trial, 68.8% of the patients treated with 2.4 mg semaglutide obtained a weight loss of at least 5%, compared to only 28.5% in the placebo group, with an odds ratio of achieving this clinically meaningful weight loss of 4.88 [9].

The STEP 4 and STEP 10 trials highlight obesity as a chronic disease requiring long-term treatment, as discontinuation of semaglutide led to significant weight regain, underscoring the need for sustained therapy to maintain benefits. STEP 4 study investigated the effect of continuing *versus* withdrawing semaglutide during weight loss maintenance after a period of 20 weeks of therapy. The patients who continued the treatment beyond week 20 experienced an additional 7.9% weight loss, while in patients who switched to placebo a weight gain of 6.9% of body weight was observed [11]. In the STEP 10 trial, patients with obesity and prediabetes were randomly assigned to semaglutide or placebo for 52 weeks, followed by a 28-week follow-up treatment-off period. After an initial weight loss of 13.9% in the semaglutide group and 2.7% in the placebo group during the intervention period, participants in both groups regained weight, reaching at the end of the follow-up treatment-off period an overall weight loss of 7.9% in the semaglutide group *versus* 1.3% in the placebo group [17].

STEP-6, STEP-7, and STEP-11 trials were dedicated to Asian populations (Japan, China, South Korea, Hong Kong, Thailand), with overweight (plus comorbidities) or obesity with or without type 2 diabetes [13–15]. All trials confirmed the efficacy of semaglutide in these populations, reporting at the end of the intervention, weight loss ranging between 7.5% and 16%. Also, participants receiving semaglutide were more likely to achieve a weight loss of at least 5% [13–15].

STEP-8 was a head-to-head comparison of once-weekly 2.4 mg semaglutide and once-daily 3 mg liraglutide in people with overweight or obesity. After 68 weeks, semaglutide was associated with significantly greater weight loss compared to liraglutide (15.8% *versus* 6.4% body weight). A higher proportion of patients receiving semaglutide achieved a weight loss of more than 10%, 15% or 20% (70.9%, 55.6%, and 38.5%) compared to liraglutide (25.6%, 12.0%, and 6.0%) [16].

Recently STEP UP trial investigated the efficacy and tolerability of once-weekly high-dose semaglutide (7.2 mg) compared to the standard 2.4 mg dose. After 72 weeks, mean weight loss was 18.7% of the initial body weight with 7.2 mg semaglutide compared with 15.6% of the initial body weight with 2.4 mg semaglutide, demonstrating higher efficacy with a favorable risk-benefit profile [18].

The SUSTAIN program was designed to investigate the efficacy and safety of 0.5 and 1 mg of semaglutide in people with type 2 diabetes and weight loss was assessed in most of these trials as a secondary outcome. Briefly, SUSTAIN 1 and 5 were placebo-controlled trials, while SUSTAIN 2, 3, 4 and 7 had active comparators (sitagliptin, exenatide extended release, glargine insulin, and dulaglutide). The proportions of patients achieving composite endpoints of glycemic control, weight loss, and no hypoglycemia in SUSTAIN 1-7 clinical trials are presented in Table 1 [19].

Table 1. Proportion of patients achieving composite endpoints of glycemic control, weight loss, and no hypoglycemia in SUSTAIN 1-7 clinical trials [19].

Trial	Dose of semaglutide/ comparator	HbA1c <7.0%, no weight loss and no hypoglycaemia	HbA1c <7.0%, ≥5% weight loss and no hypoglycaemia	HbA1c <7.0%, ≥10% weight loss and no hypoglycaemia
SUSTAIN-1	Semaglutide 0.5 mg	66	37	8
	Semaglutide 1 mg	65	45	13
	Placebo	19	7	2
SUSTAIN-2	Semaglutide 0.5 mg	63	46	13
	Semaglutide 1 mg	74	62	24
	Sitagliptin 100 mg	27	18	3
SUSTAIN-3	Semaglutide 1 mg	56	52	21
	Exenatide 2 mg	28	17	4
SUSTAIN-4	Semaglutide 0.5 mg	47	37	8
	Semaglutide 1 mg	64	51	16
	Glargine insulin	16	5	2

Table 1. Continued.

Trial	Dose of semaglutide/ comparator	HbA1c <7.0%, no weight loss and no hypoglycaemia	HbA1c <7.0%, ≥5% weight loss and no hypoglycaemia	HbA1c <7.0%, ≥10% weight loss and no hypoglycaemia
SUSTAIN-5 (add-on to basal insulin)	Semaglutide 0.5 mg	54	42	9
	Semaglutide 1 mg	67	66	26
	Placebo	7	11	3
SUSTAIN-7	Semaglutide 0.5 mg	64	44	14
	Dulaglutide 0.75 mg	44	23	3
	Semaglutide 1 mg	74	63	27
	Dulaglutide 1.5 mg	58	30	8

In patients with type 2 diabetes, the weight loss efficacy of once-weekly administration of 2.4 mg of semaglutide was also significantly higher *versus* placebo, but with a lower magnitude than in people without diabetes. In a recently published systematic review and meta-analysis of trials involving adult people with overweight or obesity and a treatment period of 40 to 70 weeks, the weighted mean body weight reduction was −6.34% in patients with diabetes and −11.57% in subjects without diabetes. The authors explained the results by different metabolic characteristics in people with type 2 diabetes, such as hyperinsulinemia, insulin resistance, or compensatory mechanisms linked to glycemic control [20].

Tirzepatide

The other molecule, administered subcutaneously once per week, approved for the management of obesity or overweight with another co-existing medical condition related to weight, available in clinical practice, is a dual receptor agonist GLP-1/GIP, named tirzepatide. The efficacy of this dual agonist for weight loss and improvement in glycemic control was assessed in persons with obesity in the SURMOUNT clinical trials program and in persons with type 2 diabetes in the SURPASS clinical trials program.

The SURMOUNT clinical trial program showed tirzepatide as a major advance in the pharmacological management of obesity, associated with weight reduction of 20–25%, results historically reported with metabolic surgery. Importantly, these effects were achieved in large, diverse populations, including patients with obesity-related comorbidities, reinforcing the generalizability of tirzepatide in routine clinical practice [21–28].

SURMOUNT-1 was a randomized, double blind, placebo-controlled trial evaluating once weekly 5-15 mg tirzepatide over 72 weeks in adults with obesity or overweight and at least one weight-related comorbidity, without diabetes. At study end, mean percentage weight reductions were 15.0% with 5 mg, 19.5% with 10 mg, and 20.9% with 15 mg tirzepatide, compared with 3.1% in the placebo group ($p<0.001$ for all comparisons). The proportion of participants achieving at least 5% weight loss was 85%, 89%, and 91% in the 5 mg, 10 mg, and 15 mg tirzepatide groups, respectively, *versus* 35% with placebo. Notably, 50% of participants receiving 10 mg and 57% receiving 15 mg achieved a weight reduction of ≥20%, compared with only 3% in the placebo group [21]. A post hoc analysis of SURMOUNT-1 identified early responders (82%) and late responders (18%), defined as achieving <5% weight loss at week 12. Late responders were more frequently male and had higher baseline body weight, BMI, and waist circumference. Despite delayed response, late responders achieved clinically meaningful weight loss, with a mean time to reach ≥5% weight reduction of 24.8±12.7 weeks, highlighting the importance of continued treatment before considering lack of efficacy [22].

The SURMOUNT-3 and SURMOUNT-4 trials provide evidence that obesity should be managed as a chronic, relapsing disease. In these trials, tirzepatide treatment withdrawal was associated with weight regain, whereas continued tirzepatide therapy led to further weight loss or long-term maintenance [24, 25]. SURMOUNT-3 evaluated tirzepatide for maintenance of weight loss achieved after intensive lifestyle intervention. Of 806 enrolled participants, 579 adults with obesity or overweight (excluding diabetes) who achieved ≥5% weight loss during a 12-week lifestyle intervention were randomized to once-weekly tirzepatide (maximum tolerated dose of 10 or 15 mg) or placebo for 72 weeks. Participants randomized to tirzepatide achieved a mean additional weight loss of 18.4% body weight, whereas those in the placebo group gained 2.5% body weight. The odds ratio for achieving ≥5% weight loss with tirzepatide *versus* placebo was 34.6 (95% CI 19.2–62.6;

p<0.001) [24]. SURMOUNT-4 investigated the effects of treatment continuation *versus* withdrawal. A total of 670 adults with obesity or overweight (BMI ≥27 kg/m² with at least one comorbidity, excluding diabetes) received open-label tirzepatide for 36 weeks, achieving a mean weight loss of 20.9% body weight. Participants were then randomized to continue tirzepatide or switch to placebo for an additional 52 weeks. During the double-blind phase, patients continuing tirzepatide lost an additional 5.5% body weight, whereas those switched to placebo regained 14.0% of their body weight. Overall weight reduction from baseline to week 88 was −25.3% in the tirzepatide group compared with −9.9% in the placebo group [25].

SURMOUNT-5 showed superior efficacy of tirzepatide in terms of weight loss when compared to semaglutide. It was a head-to-head trial that compared once-weekly tirzepatide with once-weekly semaglutide in adults with obesity or overweight. Participants were randomized to the maximum tolerated dose of tirzepatide (10 or 15 mg) or semaglutide (1.7 or 2.4 mg) for 72 weeks. At study completion, tirzepatide was associated with significantly higher weight loss (−20.2% of the body weight) than semaglutide (−13.7% of the body weight; p<0.001) [26]. The superiority of tirzepatide *versus* semaglutide in terms of weight loss was further confirmed in a meta-analysis of direct comparative studies with semaglutide *versus* tirzepatide. In over 27,000 patients with type 2 diabetes, tirzepatide was associated with a mean weight loss of 11.4% of body weight compared to a mean weight loss of 7.3% of body weight with semaglutide [29].

Consistent with observations from GLP-1 receptor agonist trials, the SURMOUNT program confirmed that patients with type 2 diabetes experience lower weight loss than those without diabetes. However, reductions of approximately 10–15% in this population (*versus* 21% of the body weight in persons without diabetes) remain clinically significant and exceed those previously attainable with older anti-obesity medications [30]. Sex-specific analyses across the SURMOUNT trials showed higher efficacy in terms of weight loss in women than in men, although both sexes have substantial benefits in terms of obesity-related complications and cardiometabolic risk factors [31, 32].

The efficacy and safety of once weekly 5, 10, or 15 mg of tirzepatide in patients with type 2 diabetes were investigated in multiple phase 3 randomized trials forming the SURPASS program. This program aimed to investigate the efficacy of tirzepatide in achieving optimal glycemic control in type 2 diabetes and weight loss was a secondary outcome. Briefly, SURPASS 1 and 5 were placebo-controlled randomized trials, while SURPASS 2, 3 and 4 were active-controlled trials comparing tirzepatide with 1 mg semaglutide, degludec insulin, and glargine insulin, respectively. The proportion of patients achieving composite endpoints in SURPASS 1-5 at 5 to 15 mg tirzepatide is presented in Table 2. At all doses, tirzepatide was better than placebo in achieving the composite endpoint of HbA1c ≤7%, weight loss ≥10%, and no hypoglycemia, irrespective of basal HbA1c or BMI [33, 34].

In conclusion, the new pharmacotherapy class dedicated to the management of obesity reached new performances, with significant

Table 2. Proportion of patients achieving composite endpoints of glycemic control, weight loss and no hypoglycemia in SURPASS 1-5 clinical trials [34].

Trial	Dose of tirzepatide/ comparator	HbA1c <7.0%, ≥5% weight loss and no hypoglycaemia	HbA1c <7.0%, ≥10% weight loss and no hypoglycaemia	HbA1c <7.0%, ≥15% weight loss and no hypoglycaemia
SURPASS-1	5 mg	60	26	12
	10 mg	71	38	17
	15 mg	6	44	25
	Placebo	5	0	0
SURPASS-2	5 mg	62	34	15
	10 mg	76	51	28
	15 mg	81	62	39
	Semaglutide 1 mg	51	25	8
SURPASS-3	5 mg	58	35	12
	10 mg	76	52	28
	15 mg	82	6	42
	Degludec insulin	5	3	0

Table 2. Continued.

Trial	Dose of tirzepatide/ comparator	HbA1c <7.0%, ≥5% weight loss and no hypoglycaemia	HbA1c <7.0%, ≥10% weight loss and no hypoglycaemia	HbA1c <7.0%, ≥15% weight loss and no hypoglycaemia
SURPASS-4	5 mg	50	30	11
	10 mg	67	46	21
	15 mg	73	57	25
	Glargine insulin	5	1	0
SURPASS-5	5 mg	43	17	6
	10 mg	50	35	21
	15 mg	67	40	25
	Placebo	4	1	0

weight loss versus placebo, better mean response with the dual agonism, higher weight loss in women than in man and a partial regain of the weight was observed after the stop of the treatment. The semaglutide and tirzepatide clinical trial programs and real-life evidence mark a fundamental change in the pharmacological management of obesity, establishing incretin-based therapies as first-line therapy in obesity care when substantial weight loss is targeted [35]. Additionally, clinical trial programs support the currently proposed conceptualization of obesity as a chronic, relapsing disease that requires long-term treatment [36].

Weekly incretin-based therapy and body composition

Long-term energy restriction has consequences that extend beyond simple weight loss. Clinical investigations have shown that sustained caloric restriction alters body composition and weight loss is not achieved solely from a decrease in fat mass. Approximately 60 to 85% of weight loss is attributable to fat mass, while 15% to 40% may come from lean mass reduction. Most of the lean mass loss is attributable to loss in the skeletal muscle mass; however, a small decrease has also been observed in other organs, such as the liver, kidneys, heart, connective tissue, and digestive tract [37].

Minimizing muscle mass loss during weight loss is essential, as muscle mass plays a central role in determining energy expenditure. Reduced muscle mass determines lower metabolic rates and may negatively impact weight loss and increase the risk of weight regain [38]. Additionally, loss of muscle mass increases the risk of development of sarcopenia - a condition characterized by decreased muscle mass and function - which is associated with increased morbidity and mortality in individuals with obesity [39].

Despite the effectiveness of weekly GLP-1 RA in promoting weight loss, evidence on their impact on body composition - lean mass, fat mass, and muscle function - remains limited and heterogeneous [40]. Few studies used the gold standard for body composition assessment (DXA) or evaluated changes in muscle function following GLP-1 RA therapy [41–45]. Even less is known about their long-term effects on body composition, especially with high GLP-1 RA doses [43]. Here we will summarize and critically evaluate the evidence available on this outcome with GLP-1 RA and dual GLP-1/GIP RA.

Semaglutide

The effect of weekly semaglutide, either once weekly or daily, on body composition was assessed in patients with type 2 diabetes and obesity and in patients with obesity alone. In addition to changes in body weight, therapy with semaglutide is associated with improved body composition - reduced body and visceral fat and increased proportion of lean body mass. However, long-term effects on body composition going beyond 12 months are not yet known.

SUSTAIN-8 was a phase 3 randomized double-blind trial comparing the effect of 1.0 mg weekly semaglutide *vs.* an SGLT2 inhibitor (canagliflozin) on glycemic control and body weight of patients with uncontrolled type 2 diabetes [46]. Body composition was assessed in a sub-set of participants to the SUSTATIN-8 trial by whole-body DXA scans. At the end of 52-weeks trial period, similar cumulative changes in fat mass were observed with semaglutide and canagliflozin. A higher numerical reduction in fat mass (kg) from baseline was observed in the semaglutide group but without reaching statistical significance (3.4 kg *vs.* 2.6 kg, with an estimated treatment difference of -0.79 kg [95%CI: -2.10, 0.51]). The decreases in

visceral fat mass were also similar with both treatments: 0.2 kg and 0.1 kg with semaglutide and canagliflozin, respectively. A higher reduction of the total and percentage lean mass was observed with semaglutide as compared with canagliflozin, although the treatment difference was not statistically significant. Total lean mass decreased by 2.3 kg *vs.* 1.5 kg in the semaglutide and canagliflozin treatment groups, respectively. However, lean mass as a percentage of the whole-body weight increased from baseline by 1.2 percentage points with semaglutide and 1.1 percentage points with canagliflozin [42].

The effect of semaglutide on body composition was also assessed in people with obesity without diabetes. STEP 1 was 63 weeks randomized double blind trial comparing the efficacy of weekly 2.4 mg semaglutide *vs.* placebo in adults with obesity defined as a BMI ≥30 kg/m^2. An exploratory analysis of DXA data from 140 participants from this trial showed that semaglutide significantly reduced total fat mass by 19.3% and visceral fat mass by 27.4%, respectively. Lean body mass decreased from baseline with 9.7%; however, when lean mass was expressed as a proportion of newly achieved weight, the proportion increased by 3.0%-points thus supporting an improved body composition. No changes in body composition were observed with the placebo during the follow-up period [47].

While the studies above were designed to assess the efficacy of injectable semaglutide on weight loss, and effects on body composition were secondary outcomes assessed in a subgroup of participants, the SEMALEAN study was specifically designed to investigate the weekly semaglutide 2.4 mg impact on lean mass, muscle function, and metabolic adaptations. This prospective study enrolled 115 participants with obesity and followed them for 12 months. During the study, body composition (measured by DXA), muscle function (handgrip strength), and resting energy expenditure (REE) were assessed at baseline, 7 months, and 12 months. During the study, total fat mass decreased by 18% at 12 months, while lean mass initially reduced by 3 kg in the first 7 months and stabilized thereafter. Handgrip strength improved significantly by the end of the study compared to baseline, and the prevalence of sarcopenic obesity decreased from 49% at baseline to 33% at the study end [43].

A meta-analysis recently performed, which included 7 randomized controlled trials comparing the effect of oral or injectable semaglutide *vs.* placebo or an active comparator, confirmed the effect of semaglutide on body composition observed in individual trials. Most of the weight loss with semaglutide was due to fat mass reduction despite fat-free mass loss and an improved body composition as assessed by a greater lean-to-fat mass ratio. A significant nonlinear fat mass loss with semaglutide of 0.3 kg per day was calculated, while the decrease in fat-free mass was of 0.007 kg/day, summing a total of -0.63 kg lean mass reduction at 90 days of treatment and -2.56 kg at 12 months of treatment [48]. These reductions in lean mass are well below the ones observed with bariatric surgery, for which the average loss of fat-free mass is -4.25 kg at 90 days and -8.23 kg at 12 months [49].

Real-world data from various populations are already available for daily oral or subcutaneous once-weekly semaglutide and confirm that 12 months of therapy is associated with significant fat mass reduction. Lean mass, although reduced in absolute numbers, showed improvements relative to total body mass achieved at the end of the observation period [45, 50–52].

Tirzepatide

In parallel with the greater reductions in body weight, tirzepatide induces greater changes in fat mass and percent fat mass compared to GLP-1 RA. However, these larger reductions in adiposity are accompanied by a greater absolute loss of lean mass as compared to semaglutide described above.

A dedicated body-composition subanalysis of the SOURMOUNT-1 trial, using dual-energy X-ray absorptiometry (DXA) at baseline and at 72 weeks of therapy, showed 33.9% reduction in total body fat mass and 10.9% reduction of lean mass with tirzepatide *vs.* 8.2% and 2.6%, respectively, with placebo ($p<0.001$ for all comparisons). The mean absolute reduction of fat mass was 15.9 kg with tirzepatide and 3.6 kg with placebo, while lean mass decreased by 5.6 kg and 1.2 kg, respectively. Visceral fat mass showed a marked decline, decreasing by 40.1% with tirzepatide *vs.* 7.3% with placebo. Approximately 75% of the weight loss was fat mass and 25% was lean mass proportion similar for both tirzepatide and placebo, indicating that the relative composition of weight lost was preserved despite greater absolute reductions. Changes in body composition were similar across age groups, sex, and categories of percentage weight loss [53]. Despite the greater lean mass reduction observed, tirzepatide improved patient-reported physical function compared with placebo [54].

Additional insights into muscle quality were provided by the SURPASS-3, which evaluated changes in skeletal muscle parameters using magnetic resonance imaging (MRI) in a subgroup of patients with type 2 diabetes treated with tirzepatide or insulin degludec over 52 weeks. Tirzepatide was associated with a significant reduction in muscle fat infiltration (mean change −0.36 percentage points, $p<0.0001$), muscle volume (−0.64 L, $p<0.0001$), and muscle volume Z score (−0.22, $p<0.0001$) in parallel

with a significant weight reduction. In contrast, insulin degludec was associated with a modest and significant increase in bodyweight and muscle volume, but without significant changes in the other variables [55].

Direct comparative data between tirzepatide and semaglutide regarding body-composition changes are limited. In the sub-analysis of a controlled trial enrolling 117 patients with type 2 diabetes randomly assigned to tirzepatide, semaglutide, or placebo over 28 weeks period showed greater weight loss with tirzepatide (-11 kg) compared to semaglutide (-7 kg) or placebo (0 kg). Fat mass reduction was correlated with body weight reduction and was greater in the tirzepatide group (-9.6 kg) than in the semaglutide group (-3.8 kg). Similarly, percentage fat mass decreased more in the tirzepatide group (7.1%) than in the semaglutide group (4.0%, p=0.001). Fat free mass reduction was limited, but higher in the tirzepatide group (1.5 kg) than in the semaglutide group (0.8 kg). These findings indicate that the main driver of weight loss with tirzepatide is the fat mass reduction, without excessive loss in lean mass [56].

Conclusion

Both semaglutide and tirzepatide induce clinically significant weight loss. While semaglutide 2.4 mg reduces weight in the range of 10-15%, tirzepatide shows greater efficacy, with mean weight losses over 20% of the body weight. The reduction in lean mass observed with both semaglutide and tirzepatide is a consequence of weight loss, associated with improvements in muscle quality and without deterioration of physical function. Treatment discontinuation leads to weight regain, whereas continued therapy results in further weight loss or sustained maintenance. These findings support the proposal of placing anti-obesity pharmacotherapy among long-term disease-modifying treatments, together with therapies for diabetes, hypertension, or dyslipidemia.

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Conflict of interest

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References

1. World Health Organization [Internet]. The challenge of obesity. 2024. Accessed on January 18 2026. Available from: https://www.who.int/europe/news-room/fact-sheets/item/the-challenge-of-obesity.
2. Rizvi AA, Rizzo M. The Emerging Role of Dual GLP-1 and GIP Receptor Agonists in Glycemic Management and Cardiovascular Risk Reduction. Diabetes Metab Syndr Obes. 2022 Apr 5;15:1023-1030.. doi: 10.2147/DMSO.S351982. PMID: 35411165
3. Yoo SGK, Teufel F, Theilmann M, Si Y, Toure EA, Aryal K, et al. GLP-1 receptor agonists for obesity: eligibility across 99 countries. Lancet Diabetes Endocrinol. 2026 Feb;14(2):105-108. doi: 10.1016/S2213-8587(25)00356-0.
4. Campos C, Unger J. Primary care management of type 2 diabetes: a comparison of the efficacy and safety of glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors. Postgrad Med. 2021 Nov;133(8):843-853. doi: 10.1080/00325481.2021.1971461. PMID: 34416133
5. Lupianez-Merly C, Dilmaghani S, Vosoughi K, Camilleri M. Pharmacologic management of obesity - updates on approved medications, indications and risks. Aliment Pharmacol Ther. 2024 Feb;59(4):475-491. doi: 10.1111/apt.17856. PMID: 38169126.
6. Caruso I, Cignarelli A, Sorice GP, Perrini S, Giorgino F. Incretin-based therapies for the treatment of obesity-related diseases. NPJ Metab. Health Dis. Nov 6;2(1):31. https://doi.org/10.1038/s44324-024-00030-5
7. Knudsen LB, Lau J. The Discovery and Development of Liraglutide and Semaglutide. Front Endocrinol (Lausanne). 2019 Apr 12;10:155. doi: 10.3389/fendo.2019.00155. PMID: 31031702
8. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med. 2021 Mar 18;384(11):989-1002. doi: 10.1056/NEJMoa2032183. PMID: 33567185.
9. Davies M, Færch L, Jeppesen OK, Pakseresht A, Pedersen SD, Perreault L, et al. Semaglutide 2·4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. Lancet. 2021 Mar 13;397(10278):971-984. doi: 10.1056/NEJMoa2032183. PMID: 33567185.
10. Wadden TA, Bailey TS, Billings LK, Davies M, Frias JP, Koroleva A, et al. Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults With Overweight or Obesity: The STEP 3 Randomized Clinical Trial. JAMA. 2021 Apr 13;325(14):1403-1413. doi: 10.1001/jama.2021.1831. PMID: 33625476.
11. Rubino D, Abrahamsson N, Davies M, Hesse D, Greenway FL, Jensen C, et al. Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity: The STEP 4 Randomized Clinical Trial. JAMA. 2021 Apr 13;325(14):1414-1425. doi: 10.1001/jama.2021.3224. PMID: 33755728.
12. Garvey WT, Batterham RL, Bhatta M, Buscemi S, Christensen LN, Frias JP, et al. Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. Nat Med. 2022 Oct;28(10):2083-2091. doi: 10.1038/s41591-022-02026-4. PMID: 36216945.
13. Kadowaki T, Isendahl J, Khalid U, Lee SY, Nishida T, Ogawa W, et al. Semaglutide once a week in adults with

overweight or obesity, with or without type 2 diabetes in an east Asian population (STEP 6): a randomised, double-blind, double-dummy, placebo-controlled, phase 3a trial. Lancet Diabetes Endocrinol. 2022 Mar;10(3):193-206. doi: 10.1016/S2213-8587(22)00008-0. PMID: 35131037.

14. Mu Y, Bao X, Eliaschewitz FG, Hansen MR, Kim BT, Koroleva A, et al. Efficacy and safety of once weekly semaglutide 2·4 mg for weight management in a predominantly east Asian population with overweight or obesity (STEP 7): a double-blind, multicentre, randomised controlled trial. Lancet Diabetes Endocrinol. 2024 Mar;12(3):184-195. doi: 10.1016/S2213-8587(23)00388-1. PMID: 38330988.
15. Lim S, Buranapin S, Bao X, Quiroga M, Park KH, Kang JH, et al. Once-weekly semaglutide 2·4 mg in an Asian population with obesity, defined as BMI ≥25 kg/m2, in South Korea and Thailand (STEP 11): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Diabetes Endocrinol. 2025 Oct;13(10):838-847. doi: 10.1016/S2213-8587(25)00164-0. PMID: 40825340.
16. Rubino DM, Greenway FL, Khalid U, O'Neil PM, Rosenstock J, Sørrig R, et al. Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes: The STEP 8 Randomized Clinical Trial. JAMA. 2022 Jan 11;327(2):138-150. doi: 10.1001/jama.2021.23619. PMID: 35015037
17. McGowan BM, Bruun JM, Capehorn M, Pedersen SD, Pietiläinen KH, Muniraju HAK, et al. Efficacy and safety of once-weekly semaglutide 2·4 mg versus placebo in people with obesity and prediabetes (STEP 10): a randomised, double-blind, placebo-controlled, multicentre phase 3 trial. Lancet Diabetes Endocrinol. 2024 Sep;12(9):631-642. doi: 10.1016/S2213-8587(24)00182-7. PMID: 39089293.
18. Wharton S, Freitas P, Hjelmesæth J, Kabisch M, Kandler K, Lingvay I, et al. Once-weekly semaglutide 7·2 mg in adults with obesity (STEP UP): a randomised, controlled, phase 3b trial. Lancet Diabetes Endocrinol. 2025 Nov;13(11):949-963. doi: 10.1016/S2213-8587(25)00226-8. PMID: 40961952.
19. Aroda VR, Ahmann A, Cariou B, Chow F, Davies MJ, Jódar E, et al. Comparative efficacy, safety, and cardiovascular outcomes with once-weekly subcutaneous semaglutide in the treatment of type 2 diabetes: Insights from the SUSTAIN 1-7 trials. Diabetes Metab. 2019 Oct;45(5):409-418. doi: 10.1016/j.diabet.2018.12.001. PMID: 30615985.
20. Hong B, Kim H, Lee D, Kim K. Weight Loss Effects of Once-Weekly Semaglutide 2.4 mg in Adults with and Without Type 2 Diabetes: A Systematic Review and Meta-Analysis. Pharmaceuticals (Basel). 2025 Jul 18;18(7):1058. doi: 10.3390/ph18071058. PMID: 40732345
21. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022 Jul 21;387(3):205-216. doi: 10.1056/NEJMoa2206038. PMID: 35658024.
22. Ard J, Lee CJ, Gudzune K, Addison B, Lingvay I, Cao D, et al. Weight reduction over time in tirzepatide-treated participants by early weight loss response: Post hoc analysis in SURMOUNT-1. Diabetes Obes Metab. 2025 Sep;27(9):5064-5071. doi: 10.1111/dom.16554. PMID: 40677091
23. Garvey WT, Frias JP, Jastreboff AM, le Roux CW, Sattar N, Aizenberg D, et al. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet. 2023 Aug 19;402(10402):613-626. doi: 10.1016/S0140-6736(23)01200-X. PMID: 37385275.
24. Wadden TA, Chao AM, Machineni S, Kushner R, Ard J, Srivastava G, et al. Tirzepatide after intensive lifestyle intervention in adults with overweight or obesity: the SURMOUNT-3 phase 3 trial. Nat Med. 2023 Nov;29(11):2909-2918. doi: 10.1038/s41591-024-02883-1. PMID: 38409593
25. Aronne LJ, Sattar N, Horn DB, Bays HE, Wharton S, Lin WY, et al. Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial. JAMA. 2024 Jan 2;331(1):38-48. doi: 10.1001/jama.2023.24945 PMID: 38078870
26. Aronne LJ, Horn DB, le Roux CW, Ho W, Falcon BL, Gomez Valderas E, et al. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity. N Engl J Med. 2025 Jul 3;393(1):26-36. doi: 10.1056/NEJMoa2416394. PMID: 40353578.
27. Zhao L, Cheng Z, Lu Y, Liu M, Chen H, Zhang M, et al. Tirzepatide for Weight Reduction in Chinese Adults With Obesity: The SURMOUNT-CN Randomized Clinical Trial. JAMA. 2024 Aug 20;332(7):551-560. doi: 10.1001/jama.2024.12249. PMID: 38819983.
28. Malhotra A, Grunstein RR, Fietze I, Weaver TE, Redline S, Azarbarzin A, et al. Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity. N Engl J Med. 2024 Oct 3;391(13):1193-1205. doi: 10.1056/NEJMoa2404881. PMID: 38912654
29. Wen J, Syed B, Nadora D, How-Volkman C, Bernstein E, Truong A, et al. Tirzepatide Versus Semaglutide on Weight Loss in Type 2 Diabetes Patients: A Systematic Review and Meta-Analysis of Direct Comparative Studies. Endocrinol Diabetes Metab. 2025 May;8(3):e70045. doi: 10.1002/edm2.70045. PMID: 40184508.
30. Jensen TL, Brønden A, Karstoft K, Sonne DP, Christensen MB. The Body weight Reducing Effects of Tirzepatide in People with and without Type 2 Diabetes: A Review on Efficacy and Adverse Effects. Patient Prefer Adherence. 2024 Feb 8;18:373-382. doi: 10.2147/PPA.S419304. PMID: 38352159.
31. Yang Y, He L, Han S, Yang N, Liu Y, Wang X, et al. Sex Differences in the Efficacy of Glucagon-Like Peptide-1 Receptor Agonists for Weight Reduction: A Systematic Review and Meta-Analysis. J Diabetes. 2025 Mar;17(3):e70063. doi: 10.1111/1753-0407.70063. PMID: 40040445.
32. García-Pérez LA, Chao A, Taylor R, Mojdami D, Forrester T, Chigutsa F, at al. 756 - Body weight reduction with tirzepatide by sex: a subgroup analysis of the SURMOUNT clinical trials. 60th EASD Annual Meeting of the European Association for the Study of Diabetes. Diabetologia, 2024; 67:361-2
33. De Block C, Peleshok J, Wilding JPH, Kwan AYM, Rasouli N, Maldonado JM, et al. Post Hoc Analysis of SURPASS-1 to -5: Efficacy and Safety of Tirzepatide in Adults with Type 2 Diabetes are Independent of Baseline Characteristics. Diabetes Ther. 2025 Jan;16(1):43-71.
34. Lingvay I, Cheng AY, Levine JA, Gomez-Valderas E, Allen SE, Ranta K, et al. Achievement of glycaemic targets with weight loss and without hypoglycaemia in type 2 diabetes with the once-weekly glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist tirzepatide: A post hoc analysis of the SURPASS-1 to -5 studies. Diabetes Obes Metab. 2023 Apr;25(4):965-974. doi: 10.1111/dom.14943. PMID: 36514843.
35. McGowan B, Ciudin A, Baker JL, Busetto L, Dicker D, Frühbeck G, et al. Framework for the pharmacological treatment of obesity and its complications from the European Association for the Study of Obesity (EASO). Nat Med. 2025 Oct;31(10):3229-3232. doi: 10.1038/s41591-025-03765-w. PMID: 41039115.
36. Busetto L, Dicker D, Frühbeck G, Halford JCG, Sbraccia P, Yumuk V, et al. A new framework for the diagnosis, staging and management of obesity in adults. Nat Med. 2024 Sep;30(9):2395-2399. doi: 10.1038/s41591-024-03095-3. PMID: 38969880.
37. Ludvik B, Giorgino F, Jódar E, Frias JP, Fernández Landó L, Brown K, et al. Once-weekly tirzepatide versus once-daily insulin degludec as add-on to metformin with or without SGLT2 inhibitors in patients with type 2 diabetes (SURPASS-3): a randomised, open-label, parallel-group, phase 3 trial. Lancet. 2021 Aug 14;398(10300):583-598. doi: 10.1016/S0140-6736(21)01443-4. PMID: 34370970.
38. Christoffersen BØ, Sanchez-Delgado G, John LM, Ryan DH, Raun K, Ravussin E. Beyond appetite regulation: Targeting

energy expenditure, fat oxidation, and lean mass preservation for sustainable weight loss. Obesity (Silver Spring). 2022 Apr;30(4):841-857. doi: 10.1002/oby.23374. PMID: 35333444.

39. Axelrod CL, Dantas WS, Kirwan JP. Sarcopenic obesity: emerging mechanisms and therapeutic potential. Metabolism. 2023 Sep:146:155639. doi: 10.1016/j.metabol.2023.155639. PMID: 37380015
40. Argyrakopoulou G, Gitsi E, Konstantinidou SK, Kokkinos A. The effect of obesity pharmacotherapy on body composition, including muscle mass. Int J Obes. 2025 Mar;49(3):381-387. doi: 10.1038/s41366-024-01533-3. PMID: 38745020.
41. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al. Once-weekly Semaglutide in adults with overweight or obesity. N Engl J Med. 2021 Mar 18;384(11):989-1002. doi: 10.1056/NEJMoa2032183. PMID: 33567185.
42. McCrimmon RJ, Catarig AM, Frias JP, Lausvig NL, le Roux CW, Thielke D, et al. Effects of once-weekly semaglutide vs once-daily canagliflozin on body composition in type 2 diabetes: a substudy of the SUSTAIN 8 randomised controlled clinical trial. Diabetologia. 2020 Mar;63(3):473-485. doi: 10.1007/s00125-019-05065-8. PMID: 31897524.
43. Alissou M, Demangeat T, Folope V, Van Elslande H, Lelandais H, Blanchemaison J, et al. Impact of Semaglutide on fat mass, lean mass and muscle function in patients with obesity: The SEMALEAN study. Diabetes Obes Metab. 2026 Jan;28(1):112-121. doi: 10.1111/dom.70141. PMID: 41068996
44. Xiang J, Ding XY, Zhang W, Zhang J, Zhang YS, Li ZM, et al. Clinical effectiveness of semaglutide on weight loss, body composition, and muscle strength in Chinese adults. Eur Rev Med Pharmacol Sci. 2023 Oct;27(20):9908-9915. doi: 10.26355/eurrev_202310_34169. PMID: 37916360.
45. Volpe S, Lisco G, Fanelli M, Racaniello D, Colaianni V, Triggiani D, et al. Once-Weekly Subcutaneous Semaglutide Improves Fatty Liver Disease in Patients with Type 2 Diabetes: A 52-Week Prospective Real-Life Study. Nutrients. 2022 Nov 4;14(21):4673. doi: 10.3390/nu14214673. PMID: 36364937
46. Lingvay I, Catarig AM, Frias JP, Kumar H, Lausvig NL, le Roux CW, et al. Efficacy and safety of once-weekly semaglutide versus daily canagliflozin as add-on to metformin in patients with type 2 diabetes (SUSTAIN 8): a double-blind, phase 3b, randomised controlled trial. Lancet Diabetes Endocrinol. 2019 Nov;7(11):834-844. doi: 10.1016/S2213-8587(19)30311-0. PMID: 31540867.
47. Wilding JPH, Batterham RL, Calanna S, Van Gaal LF, McGowan BM, Rosenstock J, et al. Impact of Semaglutide on Body Composition in Adults With Overweight or Obesity: Exploratory Analysis of the STEP 1 Study. J Endocr Soc. 2021 May 3;5(Suppl 1):A16–7. doi: 10.1210/jendso/bvab048.030.
48. Giorelli G, Mizumoto M, Sartoretto S, Giorelli S, Giorelli P, Bedin-Pochini A, et al. Body Composition Changes with Semaglutide: A Systematic Review and Meta-Analysis. medRxiv 2025 Sep 29.25336760. doi: https://doi.org/10.1101/2025.09.29.25336760
49. Nuijten MAH, Eijsvogels TMH, Monpellier VM, Janssen IMC, Hazebroek EJ, Hopman MTE. The magnitude and progress of lean body mass, fat-free mass, and skeletal muscle mass loss following bariatric surgery: A systematic review and meta-analysis. Obesity Rev. 2022 Jan;23(1):e13370. doi: 10.1111/obr.13370. PMID: 34664391
50. Caballero-Mateos I, Morales-Portillo C, González Aguilera B. Once-Weekly Semaglutide Improves Body Composition in Spanish Obese Adults with Type 2 Diabetes: A 48-Week Prospective Real-Life Study. J Clin Med. 2025 Aug 1;14(15):5434. doi: 10.3390/jcm14155434. PMID: 40807054;
51. Rodríguez Jiménez B, Rodríguez de Vera Gómez P, Belmonte Lomas S, Mesa Díaz ÁM, Caballero Mateos I, Galán I, et al. Transforming body composition with semaglutide in adults with obesity and type 2 diabetes mellitus. Front Endocrinol (Lausanne). 2024 Jun 4;15:1386542. doi: 10.3389/fendo.2024.1386542. PMID: 38894744
52. Chun E, Siojo A, Rivera D, Reyna K, Legere H, Joseph R, et al. Weight loss and body composition after compounded semaglutide treatment in a real world setting. Diabetes Obes Metab. 2025 Mar;27(3):1536-1543. doi: 10.1111/dom.16162. PMID: 39776038.
53. Look M, Dunn JP, Kushner RF, Cao D, Harris C, Gibble TH, et al. Body composition changes during weight reduction with tirzepatide in the SURMOUNT-1 study of adults with obesity or overweight. Diabetes Obes Metab. 2025 May;27(5):2720-2729. doi: 10.1111/dom.16275.
54. Gudzune KA, Stefanski A, Cao D, Mojdami D, Wang F, Ahmad N, et al. Association between weight reduction achieved with tirzepatide and quality of life in adults with obesity: results from the SURMOUNT-1 study. Diabetes Obes Metab. 2025 Feb;27(2):539-550. doi: 10.1111/dom.16046. PMID: 39497468
55. Sattar N, Neeland IJ, Dahlqvist Leinhard O, Fernández Landó L, Bray R, Linge J, Rodriguez A. Tirzepatide and muscle composition changes in people with type 2 diabetes (SURPASS-3 MRI): a post-hoc analysis of a randomised, open-label, parallel-group, phase 3 trial. Lancet Diabetes Endocrinol. 2025 Jun;13(6):482-493. doi: 10.1016/S2213-8587(25)00027-0. PMID: 40318682.
56. Heise T, DeVries JH, Urva S, Li J, Pratt EJ, Thomas MK, et al. Tirzepatide Reduces Appetite, Energy Intake, and Fat Mass in People With Type 2 Diabetes. Diabetes Care. 2023 May 1;46(5):998-1004. doi: 10.2337/dc22-1710. PMID: 36857477