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SYSTEMATIC REVIEW OPEN

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GLP-1 agonists and changes in body mass and composition in adults with overweight or obesity with or without type 2 diabetes mellitus: a systematic review and meta-analysis

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BACKGROUND: The systematic review aimed to assess the effects of GLP-1 receptor agonists (GLP-1 RA) and dual GLP-1/GIP agonists on weight loss and body composition in individuals with overweight or obesity, with or without type 2 diabetes mellitus.
METHODS: The study protocol was registered in PROSPERO (CRD420251002447). A systematic search of PubMed, Scopus, and Web of Science was conducted up to December 2024 according to PRISMA guidelines. Following the predefined inclusion and exclusion criteria, 36 studies were included in this systematic review and underwent qualitative analysis. In addition, 24 studies met the criteria for quantitative synthesis (meta-analysis). Data were pooled using random-effects models with subgroup analyses by drug type and treatment duration (3, 6, and 12 months).
RESULTS: GLP-1 RA treatment consistently reduced body weight, BMI, and waist circumference across all time points. At 3 months, mean body weight decreased by approximately 9%, accompanied by marked reductions in fat mass and visceral adipose tissue. At 6 months, weight reduction averaged 5%, with semaglutide, liraglutide, and exenatide showing comparable effects, while lean mass remained largely preserved. At 12 months, weight loss persisted at around 4%, with variability between agents, most notably liraglutide. Across studies, fat mass decline predominated, whereas reductions in lean body mass were modest.
CONCLUSION: GLP-1 RAs provide clinically meaningful weight loss primarily through selective fat mass reduction, with relative preservation of lean tissue, supporting their role in achieving "quality" weight loss. Differences between agents highlight the importance of individualized treatment strategies, complemented by nutritional and exercise interventions to optimize long-term outcomes.

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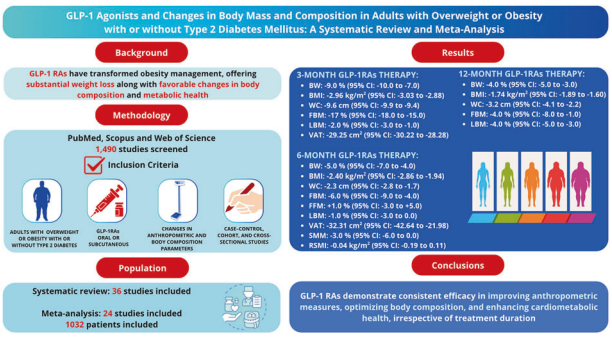
Graphical Abstract



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INTRODUCTION

Obesity is a complex, multifactorial chronic disease characterized by excess adiposity, with or without abnormal distribution or function of adipose tissue, leading to adverse effects on health. Over the past several decades, its prevalence has risen at an alarming rate worldwide, reaching pandemic proportions and showing no signs of stabilization [1, 2]. The pathogenesis of obesity involves a dynamic interplay of genetic, environmental, behavioral, and metabolic factors [2, 3]. Obesity is associated with numerous cardiometabolic complications and contributes to increased overall mortality [4, 5]. These comorbidities contribute to a marked reduction in both life expectancy and quality of life. Beyond physical health, obesity often carries substantial psychological and social burdens, such as depression, stigma, and reduced self-esteem [6]. Given its complexity, effective obesity management necessitates a multidisciplinary, individualized approach that combines nutritional and behavioral interventions, physical activity, pharmacological therapies, and metabolic-bariatric surgery when indicated. The primary goal of treatment should extend beyond weight loss to encompass the preservation of lean mass, improvement in metabolic health, and long-term prevention of obesity-related complications [7].

Glucagon-like peptide-1 (GLP-1) is an incretin hormone released from enteroendocrine L-cells in the gastrointestinal tract in response to nutrient intake. It plays a pivotal role in energy balance and postprandial metabolism by enhancing glucose-dependent insulin secretion, suppressing glucagon release, delaying gastric emptying, and promoting satiety through central mechanisms [8, 9]. Due to its rapid enzymatic degradation, the physiological half-life of GLP-1 is short; however, GLP-1 receptor agonists (GLP-1RAs) have been developed to prolong its activity and maximize its metabolic benefits. GLP-1RAs exert pleiotropic effects that extend well beyond their initial use in glycemic management [8]. In individuals with obesity, these agents contribute to significant and sustained weight reduction by enhancing satiety, reducing appetite, and lowering overall caloric intake [9]. Weight loss achieved through GLP-1 RAs therapy is accompanied by meaningful improvements in multiple obesity-related comorbidities. Additionally, GLP-1 RAs have demonstrated cardioprotective properties, including favorable effects on cardiac function, vascular integrity, and endothelial performance [10]. Their metabolic actions include enhanced peripheral glucose uptake, reduced hepatic glucose output, and improved lipid metabolism [11]. The development of next-generation GLP-1 RAs and dual agonists further expands the therapeutic potential of this drug class in addressing the complex, multisystem consequences of obesity [8].

The weight-lowering effects of GLP-1 RAs are mediated through multiple, interrelated mechanisms. Primarily, they act on the hypothalamus to enhance satiety, delay gastric emptying, and reduce caloric intake, leading to a preferential reduction in fat body mass (FBM). GLP-1 RAs also improve insulin sensitivity, reduce ectopic fat deposition, and modulate adipose tissue metabolism by stimulating lipolysis and inhibiting lipogenesis [12, 13]. Importantly, their influence extends to skeletal muscle, where GLP-1 RAs promote glucose uptake via the AMP-activated protein kinase pathway, increase vascular blood flow, and mitigate glucotoxicity, thereby supporting muscle protein synthesis and inhibiting catabolic pathways [14, 15]. Preclinical data further indicate that liraglutide activates the SIRT1 signaling cascade, suppresses atrophy-related genes, and upregulates myogenic differentiation factors, thereby protecting against obesity-induced muscle atrophy and contributing to structural muscle integrity [14, 16]. Collectively, these findings highlight the dual capacity of GLP-1 RAs to reduce FBM while supporting skeletal muscle health, a distinction of clinical importance in the long-term management of obesity.

Despite these favorable mechanisms, concerns remain regarding the impact of GLP-1 RAs on lean body mass (LBM) and the potential risk of sarcopenia. Clinical and meta-analytic data indicate that, although FBM reduction predominates, modest decreases in LBM can occur, particularly during substantial weight loss [17, 18]. This raises questions about whether GLP-1 RAs may contribute to muscle loss in vulnerable populations, such as older adults or those with pre-existing frailty. Sporadic reports of skeletal muscle decline highlight the need for careful monitoring, as sarcopenia, characterized by reduced muscle mass and impaired physical function, may worsen metabolic outcomes and increase morbidity [19, 20]. Importantly, the observed LBM reduction has not consistently translated into functional impairment, and emerging evidence suggests that GLP-1 RAs may counterbalance this effect by improving muscle quality and metabolism [21]. Nonetheless, in patients at high risk of sarcopenia, tailored management including nutritional optimization and concurrent resistance training should be considered to mitigate potential adverse consequences during pharmacologically induced weight loss [20].

Given the heterogeneity among GLP-1RAs in terms of pharmacokinetic profiles, therapeutic efficacy, adverse event rates, and dosing regimens, each agent should be assessed individually. Moreover, a thorough understanding of the specific benefits and limitations of each GLP-1 RA is essential for informed clinical decision-making. To address this need, we conducted a systematic review and meta-analysis to evaluate and compare the efficacy of GLP-1 RAs in promoting weight loss and modulating body composition in individuals with overweight or obesity with or without T2DM.

METHODS

Data sources and search strategy

This systematic review was conducted up to 01 December 2024 in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines. A comprehensive literature search was performed across three databases: PubMed, Scopus, and Web of Science. The search strategy was developed to identify clinical studies investigating the effects of GLP-1RAs on body composition and anthropometric indices for individuals with overweight or obesity, with or without T2DM. The following search algorithm was applied: ((“GLP-1 receptor agonist” OR “glucagon-like peptide-1 receptor agonist” OR “GIP receptor agonist” OR “glucose-dependent insulinotropic polypeptide” OR liraglutide OR semaglutide OR dulaglutide OR tirzepatide) AND (“body composition” OR “fat mass” OR “muscle mass” OR “lean mass” OR “adiposity” OR “body fat” OR “sarcopenia”)) AND (“clinical trial” OR “study” OR “randomized controlled trial” OR “RCT” OR “intervention study”).

The literature search was independently performed by three investigators. After the removal of duplicates, titles and abstracts were screened for eligibility. Full-text articles were assessed against prespecified inclusion and exclusion criteria. Discrepancies during the screening process were resolved by consulting the clinical experts and methodologists. The specific criteria for inclusion and exclusion of relevant studies in terms of PI(E)COS (“Population”, “Intervention”/”Exposure”, “Comparison”, “Outcomes”, and “Study design”) are provided in Table 1. A detailed search flowchart is shown in Supplementary Fig. S1.

The study protocol was registered in the International Prospective Register of systematic reviews PROSPERO (CRD420251002447).

Quality assessment and critical appraisal for the systematic review of the included studies

The methodological quality of the included studies was evaluated independently by two reviewers using the Study

Table 1. Inclusion and exclusion criteria according to the PICOS.

Parameter	Inclusion Criteria	Exclusion Criteria
Population	Adult patients with overweight or obesity, with or without T2DM	• Patients aged <18 years • Patients with a history of T1DM, genetic obesity syndromes or who undergo bariatric surgery • In vitro, in vivo, or animal studies
Intervention/ Exposure	Pharmacologic treatment with GLP1RAs or dual GIP/GLP1RAs in different dosages and any route of administration	
Comparison	• Placebo, active comparator, or standard of care • Studies without control groups (single-arm studies)	
Outcomes	Primary outcomes: • Changes in body composition parameters: fat mass (kg and %), lean body mass (kg and %), fat-free mass (kg and %), visceral adipose tissue area, total skeletal muscle mass, relative skeletal muscle index, and bone mineral content measured by validated methods, such as BIA, DXA, MRI, or CT scan • Changes in anthropometric parameters: body weight, BMI, waist and hip circumference, waist-to-hip ratio Secondary outcomes: • Changes in cardiometabolic parameters: fasting plasma glucose, fasting insulin, HbA1c, HOMA-IR, total cholesterol, LDL-C, HDL-C, triglycerides, systolic and diastolic blood pressure, and heart rate	• Studies with unclear methods of measurement of body composition and anthropometric indices • Studies not providing data to calculate the effect estimates of the outcome of interest • Studies with a follow-up period other than 3, 6, 12 months
Study design	• Case–control, cohort, and cross-sectional studies • Published from the inception date of each database until 01 December 2024	• Literature reviews, case reports, expert opinion, letters to the editor, conference reports • Not published in English

Quality Assessment Tools developed by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH), tailored to the design of each included study. Each study was assessed across key domains, including clarity of objectives, eligibility criteria, sample size justification, outcome measurement, blinding (if applicable), and adequacy of statistical analyses. Studies were then categorized as having low, moderate, or high risk of bias based on cumulative scoring. A summary of the risk of bias assessment is presented in Supplementary Fig. S2.

Data synthesis and analysis

All included studies were discussed as part of the quantitative analysis. The quantitative analysis comprised 24 studies involving a total of 1,032 patients who presented numerical data on changes in selected anthropometric and body composition parameters resulting from GLP-1 RA therapy. A subgroup meta-analysis was conducted based on the type of GLP-1 RA used, separately for three treatment durations: 3 months, 6 months, and 12 months. For each parameter, the mean difference or ratio of means was calculated. Selected relationships of particular clinical significance were additionally presented graphically using forest plots. The results of the meta-analysis for the associated biochemical parameters are presented in Supplementary Tables S1–S3. Due to study heterogeneity, random-effects models were applied. Egger's test was used to assess publication bias. A significance level of alpha = 0.05 was adopted for all analyses. All analyses were conducted using Statistica 13.3 software (StatSoft, Kraków, Poland).

RESULTS

Descriptive data are summarized in Table 2. The included studies showed notable geographical diversity, with the majority originating from Europe and Asia. Studies were categorized according to the duration of therapy, with the majority reporting outcomes after a 6-month follow-up period. Both patients with T2DM (24 studies) and those without T2DM were included. The most frequently investigated GLP-1 RAs were liraglutide and semaglutide, predominantly administered via the subcutaneous route. Body composition (BC) was assessed using various methods, most commonly bioelectrical impedance analysis (BIA), followed by dual-energy X-ray absorptiometry (DXA).

3-month GLP-1 RA therapy

Following 3 months of GLP-1 RA therapy, significant improvements were observed across anthropometric and body composition parameters (Table 3).

Meta-analysis revealed a substantial 9% reduction in body mass (RoM 0.91; 95% CI: 0.90 to 0.93; $p < 0.001$), BMI (MD $-2.96\ kg/m^2$; 95% CI: -3.03 to -2.88; $p < 0.001$), and waist circumference (MD -9.6 cm; 95% CI: -9.9 to -9.4; $p < 0.001$). These effects were consistently notable across individual studies, with the greatest reductions observed in those receiving beinaglutide.

Regarding body composition, GLP-1 RA therapy led to a significant 17% decline in fat mass (RoM 0.83; 95% CI: 0.82–0.85; $p < 0.001$) and visceral adipose tissue area (MD $-29.25\ cm^2$; 95% CI: -30.22 to -28.28; $p < 0.001$). A modest but statistically significant 2% reduction in lean body mass was also observed (RoM 0.98; 95% CI: 0.97–0.99; $p = 0.004$).

Intergroup comparisons revealed statistically significant differences between GLP-1 RAs across most parameters ($p < 0.001$), except from lean body mass. Egger's test indicated potential publication bias for some outcomes.

6-month GLP-1 RA therapy

Following six months of GLP-1 RA therapy, a meta-analysis revealed statistically significant improvements in multiple anthropometric and body composition parameters (Table 4).

Body mass was significantly reduced by 5% (RoM 0.95; 95% CI: 0.93–.96; $p < 0.001$). Consistent reductions were observed across studies utilizing exenatide, liraglutide, and semaglutide, without significant intergroup differences ($p = 0.310$). Similarly, BMI decreased significantly (MD $-2.40\ kg/m^2$; 95% CI: -2.86 to -1.94; $p < 0.001$), again without significant differences between GLP-1 RA types ($p = 0.513$). Waist circumference also improved modestly but significantly (MD -2.3 cm; 95% CI: -2.8 to -1.7; $p < 0.001$), with significant intergroup heterogeneity ($p = 0.012$).

Regarding body composition, fat body mass decreased significantly by 6% (RoM 0.94; 95% CI: 0.91–0.96; $p < 0.001$), with differences between GLP-1 RAs ($p < 0.001$). Fat-free mass did not significantly change (RoM 1.01; 95% CI: 0.97–1.05; $p = 0.657$), nor

Table 2. The characteristics of included studies.

Author	Setting	Study design	GLP-1 RA	Target dose	Frequency of administration	Route of administration	Study Group (F/M; Age)	Diabetes status	Outcomes	Body composition assessment
3-month GLP-1 RA therapy										
Anyiam et al. [30]	United Kingdom	Single-centre open-label, randomized, parallel group pilot	Semaglutide	1.0 mg	Weekly	SC	10 (5/5; 61.1 ± 3.0)	T2DM	BW, BMI, FBM, LBM	DXA
Chen et al. [31]	China	Retrospective, cohort	Dulaglutide	1.5 mg	Weekly	SC	70 (13/57; 44.19 ± 10.57)	T2DM	BW, BMI, FBM, FBM %, LBM, LBM%, VAT, SMM, SMM %, BMC	BIA
Gao et al. [54]	China	Randomized, single-site clinical trial	Beinaglutide	0.2 mg	Three times Daily	SC	32 (16/16; 32.5 ± 1.6)	—	BW, BMI, WC, FBM, FBM%, LBM, AF, GF, VAT	DXA
Jensterle et al. [55]	Slovenia	Clinical trial	Liraglutide	1.2 mg	Daily	SC	36 (36/0; 31.2 ± 7.8)	—	BW, BMI, WC, FBM%, VAT	DXA
Jensterle et al. [56]	Slovenia	Open-label, randomized, prospective	Liraglutide	1.2 mg	Daily	SC	14 (14/0; NR)	—	BW, BMI, WC, FBM%	DXA
Jensterle et al. [57]	Slovenia	Open-label, randomized, prospective	Liraglutide	1.2 mg	Daily	SC	14 (14/0; NR)	—	BW, BMI, WC, VAT	DXA
Li et al. [58]	China	Prospective, observational	Liraglutide	1.2 mg	Daily	SC	31 (15/16; 48.5 ± 11.4)	T2DM	BW, BMI, WC, FBM, FBM%, LBM	DXA
Muñoz et al. [24]	Mexico	Single-center, quasi-experimental, prospective	Liraglutide	3 mg	Daily	SC	37 (28/9; 44 ± 9.8)	T2DM	BW, BMI, FBM, FBM %, FFM, VAT	BIA
Ozeki et al. [41]	Japan	Retrospective, pilot	Semaglutide	NR	NR	NR	13 (NR; 52.0 ± 6.9)	T2DM	BW, BMI, FBM, FBM %, SMM, SMM%, BMC	BIA
Seko et al. [32]	Japan	Retrospective, case-series	Dulaglutide	0.75 mg	Weekly	SC	15 (12/3; 66.8 ± 2.7)	T2DM	BMI, FBM, LBM, SMM, RSMI,BMC	BIA
Yu et al. [23]	China	Prospective, randomized, controlled	Liraglutide	1.8 mg	Daily	SC	47 (24/23; 51.53 ± 9.11)	T2DM	BW, BMI, WC, HC, WHR, FBM, FBM%, VAT	CT, BIA

Table 2. continued

Author	Setting	Study design	GLP-1 RA	Target dose	Frequency of administration	Route of administration	Study Group (F/M; Age)	Diabetes status	Outcomes	Body composition assessment
Zakaria et al. [22]	United Arab Emirates	Observational, retrospective	Semaglutide	1.0 mg	Weekly	SC	115 (69/46; 43.09 ± 9.90)	—	BW, BMI, FBM, SMM	BIA
			Tirzepatide	10 mg	Weekly	SC				
			Liraglutide	3 mg	Daily	SC				
6-month GLP-1 RA therapy										
Agcakaya et al. [34]	Turkey	Retrospective	Exenatide	10 μg	Daily	SC	50 (46/4; 56.28 ± 9.72)	T2DM	BW, BMI, FBM%, FFM %	BIA
Akyay et al. [59]	Turkey	Prospective, randomized, active-controlled	Exenatide	10 μg	Daily	SC	17 (15/2; 49.88 ± 7.76)	T2DM	BMI, FBM	BIA
Cuthbertson et al. [35]	United Kingdom	Prospective	Exenatide (19)	10 μg	Twice daily	SC	25 (13/12; 50 ± 10)	T2DM	BW, BMI, WC, VAT	MRI
			Liraglutide (6)	1.2 mg	Daily	SC				
Elkind-Hirsch et al. [60]	USA	Randomized, single-blind, parallel, prospective study trial	Exenatide	2 mg	Weekly	SC	20 (20/0; 30 ± 1.1)	—	BW, BMI, WC, WHR, WHtR, FBM, FBM%, LBM, AGR	DXA
Feng et al. [61]	China	Single-center, open-label, prospective, randomized trial	Liraglutide	1.8 mg	Daily	SC	29 (8/21; 46.8 ± 1.8)	T2DM	BW, BMI, WC, FBM, LBM, AF, GF	DXA
Freitas et al. [53]	Brazil	Prospective, non-randomized	Liraglutide	3 mg	Daily	SC	57 (24/33; F: 46 ± 9, M: 42 ± 11)	—	BW, BMI, HC, WHR, FBM, FBM %, SMM	BMI
Mittag-Roussou et al. [36]	Germany	Prospective, real-world data	Exenatide	10 μg	Twice daily	SC	17 (9/8; 66 [49, 62])	T2DM	BW, BMI, WC, FBM, FFM, VAT	BIA
			Liraglutide	1.8 mg	Daily	SC				
			Dulaglutide	1.5 mg	Weekly	SC				
Nakaguchi et al. [63]	Japan	Open-label, parallel-group, randomized controlled trial	Liraglutide	0.9 mg	Daily	SC	30 (9/21; 67.2 ± 9.0)	T2DM	BW, BMI, WC, FBM, FBM%, LBM	DXA
Pantanetti et al. [28]	Italy	Double-center, single-arm, observational, prospective	Semaglutide	14 mg	Daily	PO	61 (13/48; 61 ± 9.90)	T2DM	BW, BMI, FBM%, SMM%	BIA
Perna et al. [40]	Italy	Perspective, case-series	Liraglutide	3.0 mg	Daily	SC	9 (3/6; 68.22 ± 3.86)	T2DM	BW, BMI, WC, FBM, FBM%, FFM, FFM%, AF %, GF%, AGR, RSMI	DXA

Table 2. continued

Author	Setting	Study design	GLP-1 RA	Target dose	Frequency of administration	Route of administration	Study Group (F/M; Age)	Diabetes status	Outcomes	Body composition assessment
Rodríguez Jiménez et al. [26]	Italy	Quasi-experimental, retrospective	Semaglutide	1.0 mg	Weekly	SC	55 (26/29; 55.3 ± 10.4)	T2DM	BW, BMI, FBM, FBM %, FFM, FFM%, LBM, VAT, SMM, RSMI, BMC	BIA
			Semaglutide	14 mg	Daily	PO	33 (11/22; 61.8 ± 7)			
Rondanelli et al. [64]	Italy	Cohort study	Liraglutide	3.0 mg	Daily	SC	28 (12/16; 58.75 ± 9.33)	T2DM	BW, BMI, WC, FBM, FBM%, FFM, AF%, GF%, AGR, RSMI	DXA
Uchiyama et al. [65]	Japan	Retrospective, longitudinal	Semaglutide	14 mg	Daily	PO	25 (11/14; 54.1 ± 2.7)	T2DM	BMI, FBM, LBM, RSMI	BIA
Volpe et al. [29]	Italy	Open-label, real-life prospective	Semaglutide	7 mg	Daily	PO	32 (18/14; 66.3 ± 8.5)	T2DM	BW, BMI, WC, FBM, FBM%, FFM, FFM%, VAT, SMM, RSMI	BIA
Volpe et al. [66]	Italy	Prospective, single-arm, open-label, real-life	Semaglutide	1.0 mg	Weekly	SC	40 (19/21; NR)	T2DM	BW, BMI, WC, VAT, SMM, RSMI	BIA
Xiang et al. [27]	China	Retrospective, cohort	Semaglutide	1.0 mg	Weekly	SC	43 (33/10; 30.4 ± 8.1)	—	BW, BMI, WC, HC, FBM, FBM %, VAT, SMM, RSMI	BIA
Zhang et al. [33]	China	Randomized, controlled, open-label	Dulaglutide	1.5 mg	Weekly	SC	35 (35/0; 30.31[28.58, 32.05])	NR	BMI, BMI, WC, FBM, FBM%, LBM, LBM %, VAT	DXA
12-month GLP-1 RA therapy										
Capristo et al. [25]	Italy	Three-arm non-randomized, controlled, pilot	Liraglutide	3.0 mg	Daily	SC	25 (20/5; 46.2 ± 17.35)	—	BW, BMI, FBM, LBM	DXA
McCrimmon et al. [67]	USA, Canada, UK, Ireland, Sweden, Lebanon, Malaysia, Argentina, Mexico, Brazil, India	Randomized, double-blind, double-dummy, parallel-group trial	Semaglutide	1.0 mg	Weekly	SC	88 (NR, 57.8 ± 9.9)	T2DM	BW, BMI, WC, FBM, FBM%, LBM, LBM%	DXA
Pantanetti et al. [68]	Italy	Single-center, observational, prospective	Semaglutide	1.0 mg	Weekly	SC	90 (37/53; 63.0 ± 10.0)	T2DM	BW, BMI, WC, FBM, FBM%, LBM, LBM%	BIA

Table 2. continued

Author	Setting	Study design	GLP-1 RA	Target dose	Frequency of administration	Route of administration	Study Group (F/M; Age)	Diabetes status	Outcomes	Body composition assessment
Sandsdal et al. [69]	Denmark	Randomized, double-blind, placebo-controlled trial	Liraglutide	3.0 mg	Daily	SC	36 (NR)	—	BW, BMI, WC, FBM%, AF%, GF%, AGR	DXA
Vedtofte et al. [70]	Denmark	Longitudinal, randomized, placebo-controlled trial	Liraglutide	1.8 mg	Daily	SC	37 (37/0; 38.8 [34.3, 40.7])	—	BW, BMI, WC, WHR, FBM%, AGR	DXA
Volpe et al. [62]	Italy	Prospective, single-arm, real-life	Semaglutide	1.0 mg	Weekly	SC	48 (22/26; 57.7 ± 8.4)	T2DM	BW, BMI, WC, VAT, RSMI	BIA, US
Yabe et al. [71]	Japan	Multi-center, randomized, double-blind, parallel, active-controlled	Dulaglutide	0.75 mg	Weekly	SC	19 (3/16; 59.3 ± 8.6)	T2DM	BW, BMI, LBM, FBM	BIA

F female, *M* male, *NR* not reported, *T2DM* type 2 diabetes mellitus, *SC* subcutaneous, *PO* per os, *BW* body weight, *BMI* Body Mass Index, *WC* waist circumference, *HC* hip circumference, *WHR* waist-to-hip ratio, *WHtR* waist-to-height ratio, *FBM* fat-body mass, *FBM%* fat-body mass percentage, *FFM* fat-free mass, *FFM%* fat-free mass percentage, *LBM* lean body mass, *LBM%* lean body mass percentage, *AF* android fat, *GF* gynoid fa, *AGR* android-to-gynoid fat ratio, *RSMI* Relative Skeletal Muscle Index, *BMC* bone mineral content, *BIA* bioelectrical impedance analysis, *DXA* dual-energy x-ray absorptiometry, *CT* computed tomography, *MRI* magnetic resonance imaging, *US* ultrasound.

did the relative skeletal muscle index (MD −0.04 kg/m^2; 95% CI: −0.19 to 0.11; $p = 0.563$). Lean body mass was significantly reduced by 1% (RoM 0.99; 95% CI: 0.97–1.00; $p = 0.021$), and skeletal muscle mass significantly declined by 3% (RoM 0.97; 95% CI: 0.94–1.00; $p = 0.034$); both without intergroup heterogeneity ($p = 0.516$ and $p = 0.716$, respectively). Also, visceral adipose tissue area significantly decreased (MD −32.31 cm^2; 95% CI: −42.64 to −21.98; $p < 0.001$).

For the majority of outcomes, no significant evidence of publication bias was detected.

12-month GLP-1 RA therapy

After 12 months of GLP-1 RA therapy, significant improvements were observed across several anthropometric and body composition parameters (Table 5).

Body mass was significantly reduced by 4% (RoM 0.96; 95% CI: 0.95–0.97; $p < 0.001$). The effect was most pronounced with liraglutide in Capristo et al. – 24% (RoM 0.76), while smaller reductions were noted with semaglutide—6% (RoM 0.94) and dulaglutide – 1% (RoM 0.99). Intergroup differences were statistically significant ($p < 0.001$). Similarly, BMI was significantly reduced by −1.74 kg/m^2 (95% CI: −1.89 to −1.60; $p < 0.001$), with larger reductions again seen in the liraglutide group (−9.72 kg/m^2). However, no significant intergroup differences were detected ($p = 0.323$). Waist circumference decreased significantly by −3.2 cm (95% CI: −4.1 to −2.2; $p < 0.001$), with consistent reductions across semaglutide and liraglutide studies—no intergroup differences were observed ($p = 0.575$).

Regarding body composition, fat mass was significantly reduced by 4% (RoM 0.96; 95% CI: 0.92–0.99; $p < 0.001$), although with substantial intergroup differences ($p < 0.001$). A significant 4% reduction was also observed in lean body mass (RoM 0.96; 95% CI: 0.95–0.97; $p < 0.001$), again with notable intergroup heterogeneity.

Egger's test indicated no evidence of significant publication bias across most outcomes, with the exception of waist circumference, where bias could not be excluded ($p = 0.019$).

DISCUSSION

Anthropometric and body composition changes during GLP-1 RA treatment

The results of this meta-analysis consistently highlight the substantial effectiveness of GLP-1RAs therapy in reducing key anthropometric indicators associated with obesity. BW, BMI, and WC all decreased significantly after 3, 6, and 12 months of treatment, suggesting both short- and long-term benefits (Fig. 1). The most rapid and substantial changes occurred during the initial three months of therapy, with beinaglutide emerging as the most potent agent in this early phase, particularly in terms of weight and BMI reduction. Specifically, after 3 months of therapy, BW decreased by approximately 9%. By 6 months, the effects remained pronounced, with BW reduced by 5%, largely comparable across agents, though semaglutide and liraglutide demonstrated a more sustained impact. At 12 months, BW reduction ranged around 4%, with liraglutide appearing to produce the most significant individual reduction in BW in one outlying study, although interstudy variability must be considered when interpreting this finding. In addition, the attenuation of BW loss observed at longer treatment durations may plausibly reflect more challenging long-term adherence to therapy and lifestyle recommendations, as well as potential adaptive physiological responses over time. Reductions in WC, a key marker of visceral adiposity, paralleled weight loss at all time points and were especially notable in early treatment phases. While intergroup differences were present, particularly in the short term, they became less distinct over time, reflecting convergence in therapeutic efficacy among agents with prolonged use. Although longer-term interventions sustained the anthropometric benefits, the rate of

Table 3. Meta-analysis results for ratios of means and mean differences in anthropometric and body composition parameters after 3 months of GLP-1 RA therapy.

Study	GLP-1 RA		SE	−95%CI	+95%CI	*p*-value	weight [%]
RoM of Body mass							
Chen et al. [31]	Dulaglutide	0.96	0.02	0.92	1.00	0.054	100.00
Gao et al. [54]	Beinaglutide	0.90	0.01	0.89	0.91	< 0.001*	100.00
Jensterle et al. [55]	Liraglutide	0.96	0.04	0.89	1.04	0.364	23.05
Li et al. [58]		0.94	0.03	0.88	1.01	0.107	28.65
Munoz et al. [24]		0.94	0.04	0.86	1.03	0.222	16.87
Yu et al. [23]		0.96	0.03	0.90	1.03	0.293	31.43
		0.96	0.02	0.92	0.99	0.017*	100.00
Volpe et al. [29]	Semaglutide	0.96	0.01	0.95	0.97	<0.001*	49.35
Volpe et al. [66]		0.92	0.00	0.92	0.93	<0.001*	50.65
		0.94	0.02	0.91	0.98	<0.001*	100.00
Summary (random effects)		0.91	0.01	0.90	0.93	<0.001*	
Intergroup comparison						0.001*	
Egger's test						0.504	
MD of Body mass index [kg/m^2]							
Chen et al. [31]	Dulaglutide	−1.20	0.16	−1.51	−0.89	<0.001*	100.00
Gao et al. [54]	Beinaglutide	−3.10	0.04	−3.18	−3.02	<0.001*	100.00
Jensterle et al. [55]	Liraglutide	−1.40	0.38	−2.15	−0.65	<0.001*	24.33
Li et al. [58]		−1.80	0.30	−2.39	−1.21	<0.001*	27.98
Munoz et al. [24]		−2.99	0.55	−4.06	−1.92	<0.001*	17.90
Yu et al. [23]		−1.15	0.26	−1.66	−0.64	<0.001*	29.80
		−1.72	0.32	−2.36	−1.09	<0.001*	100.00
Uchiyama et al. [65]	Semaglutide	−0.80	0.06	−0.92	−0.68	<0.001*	33.66
Volpe et al. [29]		−1.10	0.05	−1.19	−1.01	<0.001*	33.77
Volpe et al. [66]		−3.05	0.15	−3.33	−2.77	<0.001*	32.57
		−1.63	0.42	−2.45	−0.82	<0.001*	100.00
Summary (random effects)		−2.96	0.04	−3.03	−2.88	<0.001*	
Intergroup comparison						<0.001*	
Egger's test						0.703	
MD of Waist circumference [cm]							
Gao et al. [54]	Beinaglutide	−10.2	0.1	−10.5	−9.9	<0.001*	100.00
Jensterle et al. [55]	Liraglutide	−3.4	1.0	−5.4	−1.4	<0.001*	20.41
Li et al. [58]		−3.0	0.7	−4.4	−1.6	<0.001*	38.57
Yu et al. [23]		−3.4	0.7	−4.8	−2.1	<0.001*	41.02
		−3.3	0.5	−4.2	−2.4	<0.001*	100.00
Volpe et al. [29]	Semaglutide	−3.1	0.1	−3.3	−2.9	<0.001*	50.16
Volpe et al. [66]		−6.3	0.2	−6.7	−5.9	<0.001*	49.84
		−4.7	1.6	−7.9	−1.6	0.004*	100.00
Summary (random effects)		−9.6	0.1	−9.9	−9.4	<0.001*	
Intergroup comparison						<0.001*	
Egger's test						0.949	
RoM of Fat body mass							
Chen et al. [31]	Dulaglutide	0.87	0.04	0.79	0.96	0.006*	100.00
Gao et al. [54]	Beinaglutide	0.83	0.01	0.81	0.84	<0.001*	100.00
Li et al. [58]	Liraglutide	0.89	0.08	0.75	1.05	0.159	17.08
Munoz et al. [24]		0.94	0.05	0.85	1.03	0.202	51.64
Yu et al. [23]		0.94	0.06	0.84	1.07	0.356	31.28
		0.93	0.03	0.87	1.00	0.044*	100.00
Uchiyama et al. [65]	Semaglutide	0.95	0.02	0.92	0.98	<0.001*	49.50
Volpe et al. [29]		0.84	0.01	0.83	0.86	<0.001*	50.50
		0.89	0.05	0.80	1.00	0.050	100.00

Table 3. continued

Study	GLP-1 RA		SE	−95%CI	+95%CI	*p*-value	weight [%]
Summary (random effects)		0.83	0.01	0.82	0.85	<0.001*	
Intergroup comparison						0.004*	
Egger's test						0.237	
RoM of Lean body mass							
Chen et al. [31]	Dulaglutide	0.99	0.03	0.94	1.04	0.651	100.00
Gao et al. [54]	Beinaglutide	0.97	0.01	0.95	0.99	0.003*	100.00
Li et al. [58]	Liraglutide	0.97	0.04	0.90	1.05	0.475	100.00
Uchiyama et al. [65]	Semaglutide	0.99	0.01	0.97	1.01	0.463	100.00
Summary (random effects)		0.98	0.01	0.97	0.99	0.004*	
Intergroup comparison						0.587	
Egger's test						0.841	
MD of Visceral adipose tissue [cm^2]							
Chen et al. [31]	Dulaglutide	−28.30	2.06	−32.34	−24.26	<0.001*	100.00
Gao et al. [54]	Beinaglutide	−29.60	0.51	−30.60	−28.60	<0.001*	100.00
Jensterle et al. [55]	Liraglutide	−10.30	4.19	−18.52	−2.08	0.014*	29.81
Munoz et al. [24]		6.00	2.87	0.37	11.63	0.037*	33.85
Yu et al. [23]		−7.10	1.87	−10.77	−3.43	<0.001*	36.34
		−3.62	4.83	−13.09	5.85	0.454	100.00
Summary (random effects)		−29.25	0.49	−30.22	−28.28	<0.001*	
Intergroup comparison						<0.001*	
Egger's test						0.104	

*statistical significance.

improvement appeared to attenuate over time, possibly reflecting adaptive metabolic responses or changes in treatment adherence.

Beyond improvements in total BW, GLP-1 RAs induced favorable alterations in BC, underscoring their impact on both quantity and quality of weight loss (Fig. 2). Treatment led to significant reductions in total fat body mass (FBM) and visceral adipose tissue (VAT), with the most pronounced effects observed within the first 6 months, aligning with earlier reductions in WC. Notably, beinaglutide was particularly effective in early reduction of FBM, while semaglutide achieved the most substantial decreases in visceral fat area at 6 and 12 months. Liraglutide also consistently demonstrated efficacy in reducing fat depots over longer durations. While a concurrent decline in LBM was detected, especially at the 3- and 12-month time points, these changes were proportionally modest relative to the overall BW loss. Among the agents, no single drug consistently preserved lean tissue better than others. However, liraglutide was associated with a more pronounced reduction in LBM in one long-term study, which may warrant closer monitoring in specific populations. These findings highlight the importance of integrating resistance training and nutritional support into pharmacological weight loss strategies.

Consistent with these meta-analytic findings, additional insights are provided by real-world observational studies. In a retrospective observational study applying a hybrid care model, patients with obesity with or without pre-diabetes were treated with semaglutide titrated to 1 mg weekly, tirzepatide escalated to 10 mg weekly, or liraglutide administered at 3 mg daily, alongside structured lifestyle support. After 3 months, the overall mean BW reduction reached 8.5% from baseline. Patients receiving semaglutide and tirzepatide achieved similar outcomes, with reductions of 8.3% and 8.8% respectively, while liraglutide was associated with a somewhat smaller decrease of 7.0%. BW loss was driven predominantly by reductions in FBM: 15.5% in the tirzepatide group, 13.9% with liraglutide, and 12.5% with semaglutide. Clinically meaningful thresholds were achieved in the majority of participants, with most patients surpassing a 10% reduction in BW within the first three months, and over one-third of those treated with tirzepatide exceeding a 15% reduction [22].

Multiple clinical studies have demonstrated that GLP-1 RAs are effective in inducing clinically meaningful BW loss across diverse patient populations, depending on the specific agent, dose, and treatment regimen. Yu et al. [23] examined the impact of liraglutide compared with lifestyle interventions on BC and abdominal fat distribution in patients with obesity and T2DM. Over the 12-week intervention, liraglutide in a dose up to 1.8 mg produced consistent improvements across key anthropometric parameters, with reductions in BW, BMI, and WC that exceeded those achieved with lifestyle modification alone. However, the overall degree of BW loss was modest and did not reach the clinically meaningful threshold of 5%. Importantly, BC analyses revealed not only a decrease in total FBM but also a preferential reduction in visceral and subcutaneous abdominal fat, accompanied by a decline in liver fat content. This is especially important, as ectopic fat distribution may be a critical determinant of cardiometabolic risk, in addition to overall obesity. Furthermore, Muñoz et al. [24] evaluated the use of liraglutide as an adjuvant therapy for preoperative BW loss in a high-risk cohort of patients with severe obesity undergoing preparation for bariatric-metabolic surgery. After 12 weeks of treatment with liraglutide 3.0 mg combined with lifestyle management, 94.6% of patients experienced BW reduction, with a mean total weight loss of 5.5%. In turn, Capristo et al. [25] went further and evaluated liraglutide 3.0 mg in combination with a highly structured lifestyle intervention that included a very low-calorie diet (VLCD) followed by a high-protein, low-carbohydrate regimen and intensive physical activity. This integrated approach resulted in an impressive 24% reduction in baseline BW, nearly twice the loss achieved by lifestyle modification alone and approaching the outcomes seen

Table 4. Meta-analysis results for ratios of means and mean differences in anthropometric and body composition parameters after 6 months of GLP-1 RA therapy.

Study	GLP-1 RA		SE	−95%CI	+95%CI	*p*-value	weight [%]
RoM of Body mass							
Agcakaya et al. [34]	Exenatide	0.93	0.03	0.89	0.99	0.012*	15.96
Elkind-Hirsch et al. [60]		0.96	0.01	0.94	0.98	<0.001*	84.04
		0.96	0.01	0.94	0.98	<0.001*	100.00
Feng et al. [61]	Liraglutide	0.93	0.01	0.92	0.94	<0.001*	29.66
Freitas et al. [53]		0.88	0.03	0.81	0.94	<0.001*	15.61
Freitas et al. [53]		0.88	0.03	0.82	0.95	0.002*	15.13
Nakaguchi et al. [63]		0.98	0.01	0.96	1.00	0.074	28.89
Rondanelli et al. [64]		0.97	0.05	0.88	1.08	0.617	10.71
		0.93	0.02	0.90	0.97	0.001*	100.00
Pantanetti et al. [28]	Semaglutide	0.97	0.01	0.94	0.99	0.004*	18.27
Pantanetti et al. [68]		0.95	0.01	0.94	0.96	<0.001*	20.09
Rodríguez Jiménez et al. [26]		0.90	0.04	0.83	0.98	0.016*	6.97
Rodríguez Jiménez et al. [26]		0.91	0.04	0.83	0.99	0.029*	6.77
Volpe et al. [29]		0.95	0.01	0.94	0.96	<0.001*	20.32
Volpe et al. [66]		0.90	0.00	0.90	0.91	<0.001*	20.67
Xiang et al. [27]		0.89	0.04	0.82	0.97	0.007*	6.91
		0.93	0.01	0.91	0.96	<0.001*	100.00
Summary (random effects)		0.95	0.01	0.93	0.96	<0.001*	
Intergroup comparison						0.310	
Egger's test						0.847	
MD of Body mass index [kg/m^2]							
Agcakaya et al. [34]	Exenatide	−2.77	0.32	−3.40	−2.14	<0.001*	33.60
Akyay et al. [59]		−1.58	0.50	−2.56	−0.60	0.002*	28.36
Elkind-Hirsch et al. [60]		−1.30	0.11	−1.52	−1.08	<0.001*	38.04
		−1.87	0.52	−2.89	−0.86	<0.001*	100.00
Feng et al. [61]	Liraglutide	−1.90	0.05	−2.00	−1.80	<0.001*	21.48
Freitas et al. [53]		−4.90	0.35	−5.58	−4.22	<0.001*	19.73
Freitas et al. [53]		−4.50	0.44	−5.37	−3.63	<0.001*	18.77
Nakaguchi et al. [63]		−0.50	0.07	−0.63	−0.37	<0.001*	21.45
Rondanelli et al. [64]		−0.86	0.46	−1.76	0.04	0.062	18.57
		−2.49	0.54	−3.54	−1.43	<0.001*	100.00
Pantanetti et al. [28]	Semaglutide	−1.19	0.11	−1.41	−0.97	<0.001*	13.47
Pantanetti et al. [68]		−3.18	0.16	−3.50	−2.86	<0.001*	13.21
Rodríguez Jiménez et al. [26]		−4.00	0.65	−5.28	−2.72	<0.001*	8.48
Rodríguez Jiménez et al. [26]		−3.20	0.32	−3.83	−2.57	<0.001*	11.95
Uchiyama et al. [65]		−1.30	0.06	−1.42	−1.18	<0.001*	13.64
Volpe et al. [29]		−1.40	0.05	−1.49	−1.31	<0.001*	13.68
Volpe et al. [66]		−3.36	0.13	−3.61	−3.11	<0.001*	13.39
Xiang et al. [27]		−3.60	0.29	−4.18	−3.02	<0.001*	12.18
		−2.56	0.31	−3.16	−1.96	<0.001*	100.00
Summary (random effects)		−2.40	0.24	−2.86	−1.94	<0.001*	
Intergroup comparison						0.513	
Egger's test						0.051	
MD of Waist circumference [cm]							
Elkind-Hirsch et al. [60]	Exenatide	−2.0	0.3	−2.6	−1.4	<0.001*	100.00
Nakaguchi et al. [63]	Liraglutide	−2.3	0.2	−2.7	−1.9	<0.001*	51.77
Rondanelli et al. [64]		−6.9	0.9	−8.6	−5.1	<0.001*	48.23
		−4.5	2.3	−9.0	0.0	0.048*	100.00

Table 4. continued

Study	GLP-1 RA		SE	−95%CI	+95%CI	*p*-value	weight [%]
Pantanetti et al. [68]	Semaglutide	−2.6	0.2	−2.9	−2.3	<0.001*	26.00
Volpe et al. [29]		−3.6	0.1	−3.8	−3.4	<0.001*	26.06
Volpe et al. [66]		−7.3	0.2	−7.7	−6.9	<0.001*	25.88
Xiang et al. [27]		−6.9	0.9	−8.6	−5.2	<0.001*	22.06
		−5.0	1.0	−7.1	−3.0	<0.001*	100.00
Summary (random effects)		−2.3	0.3	−2.8	−1.7	<0.001*	
Intergroup comparison						0.012*	
Egger's test						0.597	
RoM of Fat body mass							
Akyay et al. [59]	Exenatide	0.99	0.09	0.83	1.19	0.926	3.25
Elkind-Hirsch et al. [60]		0.96	0.02	0.93	0.99	0.021*	96.75
		0.96	0.02	0.93	0.99	0.023*	100.00
Feng et al. [61]	Liraglutide	0.86	0.06	0.75	0.98	0.019*	20.20
Freitas et al. [53]		0.75	0.06	0.63	0.89	<0.001*	17.29
Freitas et al. [53]		0.76	0.06	0.65	0.88	<0.001*	18.92
Nakaguchi et al. [63]		0.97	0.02	0.94	1.01	0.097	26.01
Rondanelli et al. [64]		0.94	0.08	0.80	1.11	0.490	17.58
		0.86	0.05	0.76	0.97	0.012*	100.00
Pantanetti et al. [68]	Semaglutide	0.94	0.01	0.92	0.95	<0.001*	21.33
Rodríguez Jiménez et al. [26]		0.82	0.06	0.71	0.94	0.004*	11.33
Rodríguez Jiménez et al. [26]		0.80	0.05	0.71	0.90	<0.001*	13.10
Uchiyama et al. [65]		0.90	0.01	0.87	0.93	<0.001*	20.63
Volpe et al. [29]		0.82	0.01	0.81	0.84	<0.001*	21.17
Xiang et al. [27]		0.85	0.05	0.75	0.96	0.009*	12.44
		0.86	0.03	0.81	0.92	<0.001*	100.00
Summary (random effects)		0.94	0.01	0.91	0.96	<0.001*	
Intergroup comparison						0.004*	
Egger's test						0.530	
RoM of Fat free mass							
Rodríguez Jiménez et al. [26]	Semaglutide	0.96	0.04	0.89	1.05	0.379	19.36
Rodríguez Jiménez et al. [26]		0.99	0.05	0.90	1.09	0.822	15.93
Volpe et al. [29]		1.03	0.01	1.02	1.05	<0.001*	64.71
		1.01	0.02	0.97	1.06	0.590	100.00
Rondanelli et al. [64]	Liraglutide	0.99	0.05	0.90	1.10	0.893	100.00
Summary (random effects)		1.01	0.02	0.97	1.05	0.657	
Intergroup comparison						0.427	
Egger's test						0.068	
RoM of Lean body mass							
Elkind-Hirsch et al. [60]	Exenatide	0.99	0.01	0.97	1.01	0.180	100.00
Feng et al. [61]	Liraglutide	1.00	0.04	0.91	1.09	0.931	3.54
Nakaguchi et al. [63]		0.99	0.01	0.97	1.01	0.212	96.46
		0.99	0.01	0.97	1.01	0.214	100.00
Pantanetti et al. [68]	Semaglutide	0.94	0.01	0.93	0.96	<0.001*	39.93
Rodríguez Jiménez et al. [26]		0.96	0.04	0.88	1.05	0.351	12.37
Rodríguez Jiménez et al. [26]		0.99	0.05	0.90	1.09	0.782	10.80
Uchiyama et al. [65]		0.99	0.01	0.97	1.01	0.354	36.90
		0.97	0.02	0.93	1.00	0.069	100.00
Summary (random effects)		0.99	0.01	0.97	1.00	0.021*	
Intergroup comparison						0.516	
Egger's test						0.624	
MD of Visceral adipose tissue [cm^2]							

Table 4. continued

Study	GLP-1 RA		SE	−95%CI	+95%CI	*p*-value	weight [%]
Rodríguez Jiménez et al. [26]	Semaglutide	−30.60	3.66	−37.78	−23.42	<0.001*	32.92
Rodríguez Jiménez et al. [26]		−42.30	3.71	−49.58	−35.02	<0.001*	32.78
Xiang et al. [27]		−24.40	3.16	−30.60	−18.20	<0.001*	34.30
Summary (random effects)		−32.31	5.27	−42.64	−21.98	<0.001*	100.00
Intergroup comparison						n/a	
Egger's test						0.368	
RoM of Total skeletal muscle mass							
Freitas et al. [53]	Liraglutide	0.96	0.03	0.89	1.02	0.207	36.71
Freitas et al. [53]		0.96	0.03	0.92	1.02	0.174	63.29
		0.96	0.02	0.92	1.00	0.066	100.00
Rodríguez Jiménez et al. [26]	Semaglutide	0.96	0.05	0.87	1.05	0.366	14.30
Rodríguez Jiménez et al. [26]		0.99	0.05	0.89	1.09	0.801	12.78
Volpe et al. [29]		1.02	0.01	0.99	1.04	0.159	29.30
Volpe et al. [66]		0.95	0.01	0.93	0.96	<0.001*	30.40
Xiang et al. [27]		0.95	0.05	0.86	1.05	0.307	13.22
		0.97	0.02	0.93	1.02	0.265	100.00
Summary (random effects)		0.97	0.02	0.94	1.00	0.034*	
Intergroup comparison						0.716	
Egger's test						0.656	
MD of Relative skeletal muscle index [kg/m^2]							
Rodríguez Jiménez et al. [26]	Semaglutide	−0.30	0.08	−0.46	−0.14	<0.001*	15.97
Rodríguez Jiménez et al. [26]		−0.20	0.09	−0.38	−0.02	0.032*	15.60
Uchiyama et al. [65]		0.00	0.02	−0.04	0.04	>0.999	17.36
Volpe et al. [29]		0.10	0.02	0.07	0.13	<0.001*	17.38
Volpe et al. [66]		−0.51	0.02	−0.56	−0.46	<0.001*	17.29
Xiang et al. [27]		−0.20	0.07	−0.33	−0.07	0.003*	16.40
		−0.18	0.11	−0.41	0.04	0.108	100.00
Rondanelli et al. [64]	Liraglutide	0.07	0.10	−0.13	0.27	0.497	100.00
Summary (random effects)		−0.04	0.08	−0.19	0.11	0.563	
Intergroup comparison						0.099	
Egger's test						0.496	

*statistical significance.

with sleeve gastrectomy. Total FBM decreased substantially, while LBM was better preserved than in patients undergoing surgery, likely due to the combination of high-protein intake and resistance-based exercise. Although patients lost over 8 kg of LBM, the proportional loss was smaller than in the surgical group, highlighting the protective effect of combining pharmacotherapy with diet and resistance training.

In turn, Rodríguez Jiménez et al. [26] demonstrated that 24 weeks of treatment with semaglutide, administered either orally at a maintenance dose of 14 mg daily or subcutaneously at 1 mg weekly, resulted in an average BW loss close to 10% of baseline BW. Patients treated with the oral formulation lost on average 8.6 kg, corresponding to 9.4% of initial BW, while those receiving the subcutaneous formulation lost 10.0 kg, or 9.5% of baseline BW. Importantly, the BW reduction was primarily attributable to loss of FBM, which declined by 8.0 kg in the oral group and 8.5 kg in the subcutaneous group, whereas LBM decreased only modestly by 0.7 kg and 1.7 kg, respectively. Additionally, in a retrospective analysis of Chinese patients with obesity, weekly subcutaneous semaglutide at a maintenance dose of 1.0 mg combined with lifestyle intervention over 24 weeks resulted in an average BW reduction of approximately 11%, with more than half of participants achieving at least a 10% decrease from baseline. BC analysis revealed that the majority of BW loss was attributable to reductions in FBM, which declined more than threefold compared with LBM. Notably, SMM percentage increased despite small absolute losses, and muscle strength, as assessed by grip testing, remained stable [27].

Compared with injectable formulations, oral semaglutide is associated with a more modest reduction in BW. For example, in a study by Pantanetti et al. [28], patients with obesity and T2DM treated with oral semaglutide titrated to a maintenance dose of 14 mg daily over 6 months experienced modest but significant improvements in anthropometric parameters. Average BW decreased by just over 3 kg, corresponding to a reduction of roughly 3–4% from baseline, and this was accompanied by a parallel decline in BMI. It is worth noting that the observed decrease in FBM percentage was minimal, as were the changes observed for other parameters, such as muscle mass and water content. Additionally, in a real-world study by Volpe et al. [29], patients with obesity and T2DM who received oral semaglutide at a maintenance dose of 7 mg daily for six months experienced an average BW reduction of approximately 4 kg, corresponding to a roughly 5% decrease from baseline, accompanied by significant

Table 5. Meta-analysis results for ratios of means and mean differences in anthropometric and body composition parameters after 12 months of GLP-1 RA therapy.

Study	GLP-1 RA		SE	−95%CI	+95%CI	*p*-value	weight [%]
RoM of Body mass							
Capristo et al. [25]	Liraglutide	0.76	0.04	0.69	0.84	<0.001*	49.45
Vedtofte et al. [70]		0.95	0.04	0.87	1.04	0.238	50.55
		0.85	0.09	0.69	1.05	0.138	100.00
Pantanetti et al. [68]	Semaglutide	0.94	0.01	0.93	0.96	<0.001*	100.00
Yabe et al. [71]	Dulaglutide	0.99	0.01	0.97	1.01	0.375	100.00
Summary (random effects)		0.96	0.01	0.95	0.97	<0.001*	
Intergroup comparison						<0.001*	
Egger's test						0.587	
MD of Body mass index [kg/m^2]							
Capristo et al. [25]	Liraglutide	−9.72	0.46	−10.62	−8.82	<0.001*	49.94
Vedtofte et al. [70]		−1.70	0.37	−2.42	−0.98	<0.001*	50.06
		−5.71	4.01	−13.56	2.15	0.155	100.00
Pantanetti et al. [68]	Semaglutide	−1.74	0.07	−1.89	−1.59	<0.001*	100.00
Summary (random effects)		−1.74	0.07	−1.89	−1.60	<0.001*	
Intergroup comparison						0.323	
Egger's test						0.495	
MD of Waist circumference [cm]							
McCrimmon et al. [67]	Semaglutide	−3.9	0.9	−5.7	−2.1	<0.001*	31.54
Pantanetti et al. [68]		−2.4	0.2	−2.7	−2.1	<0.001*	68.46
		−2.9	0.7	−4.2	−1.5	<0.001*	100.00
Vedtofte et al. [70]	Liraglutide	−3.4	0.7	−4.7	−2.1	<0.001*	100.00
Summary (random effects)		−3.2	0.5	−4.1	−2.2	<0.001*	
Intergroup comparison						0.575	
Egger's test						0.019*	
RoM of Fat body mass							
Capristo et al. [25]	Liraglutide	0.71	0.04	0.63	0.80	<0.001*	100.00
McCrimmon et al. [67]	Semaglutide	0.90	0.04	0.83	0.97	0.007*	37.51
Pantanetti et al. [68]		0.97	0.01	0.95	0.99	0.016*	62.49
		0.94	0.03	0.88	1.01	0.103	100.00
Yabe et al. [71]	Dulaglutide	0.99	0.02	0.95	1.03	0.639	100.00
Summary (random effects)		0.96	0.02	0.92	0.99	0.007*	
Intergroup comparison						< 0.001*	
Egger's test						0.160	
RoM of Lean body mass							
Capristo et al. [25]	Liraglutide	0.85	0.05	0.75	0.96	0.010*	100.00
McCrimmon et al. [67]	Semaglutide	0.96	0.02	0.92	1.00	0.036*	10.40
Pantanetti et al. [68]		0.94	0.01	0.93	0.95	<0.001*	89.60
		0.94	0.01	0.93	0.95	<0.001*	100.00
Yabe et al. [71]	Dulaglutide	0.99	0.01	0.98	1.01	0.526	100.00
Summary (random effects)		0.96	0.01	0.95	0.97	<0.001*	
Intergroup comparison						<0.001*	
Egger's test						0.801	

*statistical significance.

parallel reductions in BMI and WC. Importantly, BC analysis revealed a selective reduction in total FBM and fat mass index, while FFM and SMM were preserved. Indeed, indices of SMM showed a tendency to increase, leading to a more favorable SMM/VAT ratio, despite the absence of specific exercise recommendations. The favorable evolution of the SMM/VAT ratio suggests that semaglutide not only promotes adiposity loss but also helps to counteract the development of sarcopenic visceral obesity, a condition strongly linked to insulin resistance and cardiometabolic risk. The preservation of lean tissue may reflect the pleiotropic effects of GLP-1 RAs on skeletal muscle, including improved vascular perfusion, stimulation of glucose uptake via AMP-

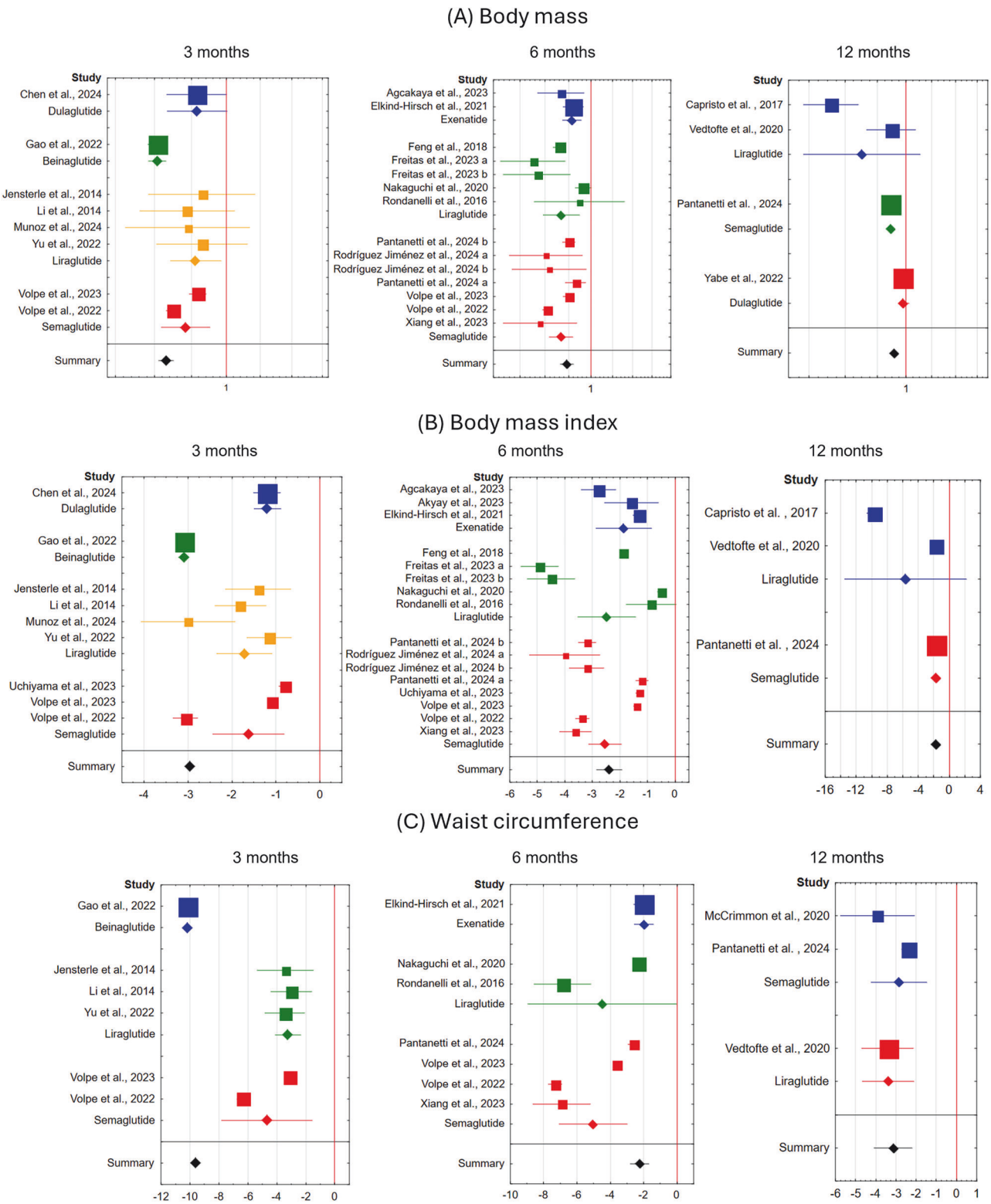

Fig. 1 The forest plots for anthropometric parameters after GLP-1 RA therapy. A The ratios of means in body weight. **B** The mean differences in body mass index. **C** The mean differences in waist circumference [23–29, 31, 34, 53–56, 58, 60, 61, 63–68, 70, 71].

activated protein kinase, and enhanced microvascular recruitment, all of which can favor protein synthesis and limit muscle breakdown. These physiological actions contribute to maintaining muscle integrity while promoting preferential fat loss, ultimately leading to a more metabolically favorable BC profile in patients with T2DM.

In the pilot trial by Anyiam et al. [30], individuals with obesity and T2DM were randomized to receive once-weekly subcutaneous semaglutide titrated to a target dose of 1 mg, VLCD, or a combination of both for 12 weeks. Individuals treated with semaglutide alone achieved an average BW reduction of 6 kg, corresponding to nearly 6% of baseline BW. In contrast,

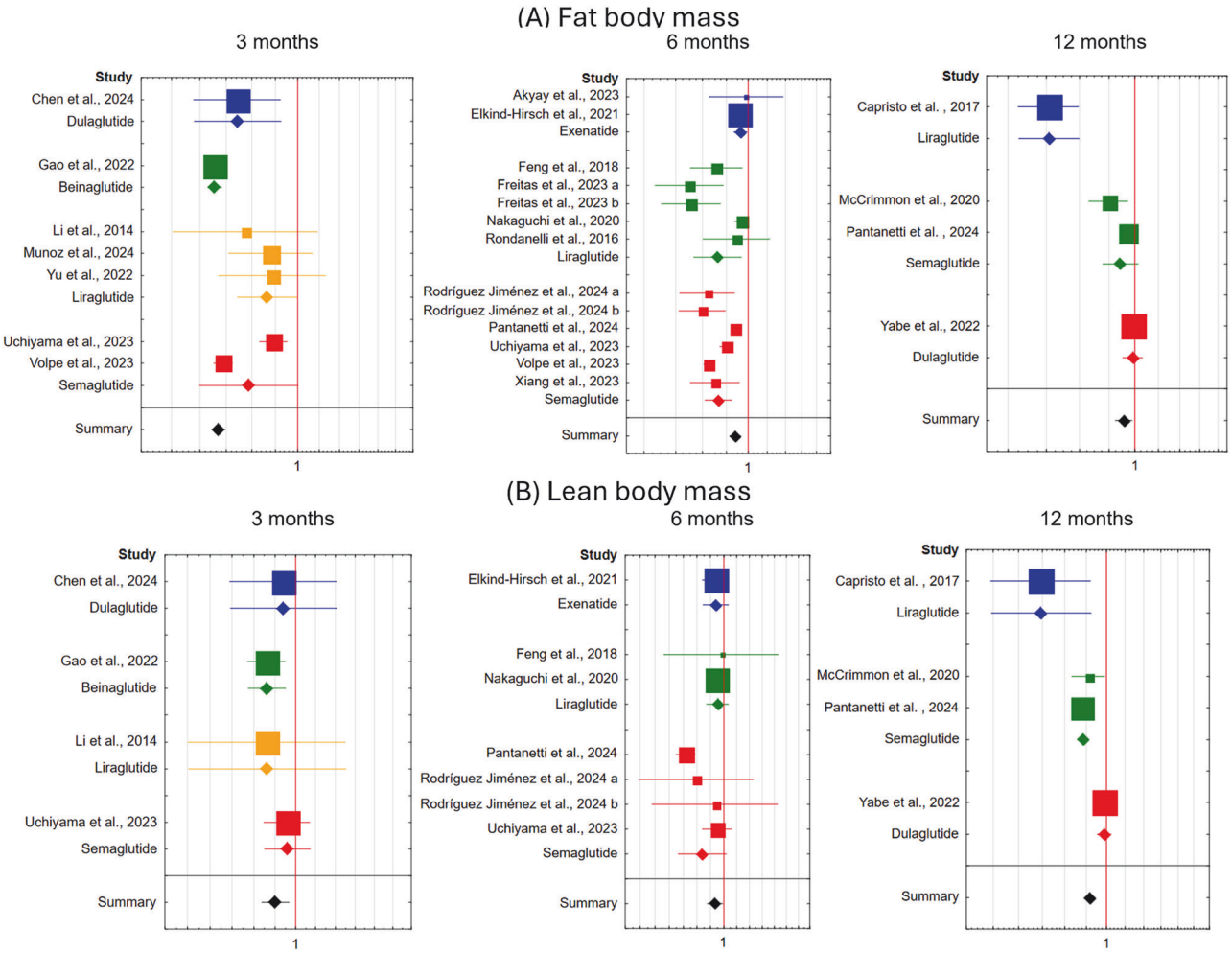

Fig. 2 The forest plots for body composition parameters after GLP-1 RA therapy. A The ratios of means in fat body mass. **B** The ratios of means in lean body mass [23–27, 29, 31, 53, 54, 58–61, 63–65, 67, 68, 71].

participants following a VLCD or the combination regimen experienced greater BW loss of approximately 13 kg, representing reductions of 11–13%. BC analysis confirmed that FBM loss was the dominant driver of these changes, with semaglutide alone reducing FBM by about 4 kg, compared with 9 kg reductions observed in both the VLCD and combined groups. Importantly, LBM decreased modestly across all interventions, without significant between-group differences, suggesting that the preferential reduction in adipose tissue was preserved irrespective of treatment allocation.

In contrast, dulaglutide treatment appears to exert a more modest effect on BW reduction, and its use has largely been restricted to Asian populations. In the study by Chen et al. [31], treatment with dulaglutide 1.5 mg once weekly for 3 months in patients with overweight or obesity and T2DM resulted in a meaningful reduction in BW of approximately 4%, accompanied by significant decreases in visceral fat area and total FBM. Importantly, although LBM and SMM showed slight absolute declines, their relative proportions within total BC increased. A similar efficacy in BW reduction was observed in the study by Seko et al. [32], where patients with NAFLD and T2DM received 12 weeks of treatment with dulaglutide 0.75 mg once weekly. Notably, BC analysis demonstrated a significant reduction in total FBM, while SMM and muscle distribution were preserved throughout the intervention. In turn, in the study by Zhang et al. [33], women with overweight and obesity with PCOS experienced a mean BW reduction of about 7% from baseline after intervention with either a calorie-restricted diet alone or in combination with dulaglutide 1.5 mg once weekly. While the overall magnitude of BW loss and accompanying decreases in VAT, total FBM, and LBM were comparable across groups, the addition of dulaglutide allowed participants to reach the BW loss target in a shorter time.

Exenatide treatment was also consistently associated with significant reductions in BW, BMI, and total FBM, often accompanied by favorable changes in fat distribution. In the study by Agcakaya et al. [34], a six-month exenatide regimen in metformin-treated patients with T2DM resulted in a mean BW reduction of >7 kg and a BMI decrease of 2.8 kg/m^2. These changes were paralleled by marked decreases in total, abdominal, leg, and arm fat percentage, along with increases in FFM and total body muscle percentage. Improvements in visceral adiposity exceeded those observed in the comparator group receiving a sodium-glucose cotransporter 2 (SGLT2) inhibitor. Evidence also supports a beneficial effect of exenatide on ectopic fat depots, with potential mechanisms that may not be entirely weight dependent. In patients with T2DM and hepatic steatosis, Cuthbertson et al. [35] reported that a 6-month exenatide-based therapy produced a 42% relative reduction in intrahepatic lipid content, accompanied by a mean BW loss of 5 kg and significant decreases in both abdominal subcutaneous and visceral fat volumes. In contrast, Mittag-Roussou et al. [36], in a real-world cohort treated with GLP-1 RAs including exenatide, observed a mean BW loss of 2.5 kg and a BMI reduction of 0.9 kg/m^2 without a significant change in

intrahepatic lipid content, reflecting variability in hepatic responses across populations.

These findings collectively emphasize that while GLP-1RAs are effective in reducing FBM, strategies to preserve or enhance SMM, such as resistance training and adequate protein intake, should be integral to obesity management. Beyond quantitative preservation, maintaining skeletal muscle function, including strength and metabolic capacity, remains a critical therapeutic goal in ensuring long-term health outcomes. While LBM loss appears to be less pronounced than FBM loss in many studies, the clinical significance of even modest reductions in skeletal muscle remains uncertain, particularly in older adults or individuals at risk of sarcopenia. Importantly, lean tissue has a higher metabolic rate than adipose tissue, and its preservation is critical for sustaining metabolic health, physical function, and long-term weight maintenance. The distinction between adaptive and maladaptive muscle loss is central to understanding the quality, not just the quantity, of BW loss achieved with GLP-1 RA-based therapies [37, 38]. Given the emerging concern around potential muscle loss, strategies to mitigate reductions in FFM during pharmacologically induced BW loss should be prioritized. Nutritional interventions, especially increased protein intake, may offer protective effects against muscle loss, though GLP-1 RAs therapies may inadvertently suppress protein-rich food consumption. Likewise, resistance exercise remains one of the most effective tools for preserving muscle mass and strength during caloric restriction [37].

Cardiometabolic parameters during GLP-1 RA treatment

GLP-1 RAs have also demonstrated important cardioprotective benefits that extend beyond their impact on BW loss. Emerging evidence indicates their potential role in the management of diverse obesity-related comorbidities, including metabolic dysfunction-associated steatotic liver disease, obstructive sleep apnea, polycystic ovary syndrome, neurodegenerative disorders, and even substance use disorders. While BW reduction likely contributes to improvements in conditions, such as hepatic steatosis or sleep apnea, GLP-1 RAs may also exert direct disease-specific effects, particularly through central mechanisms implicated in neurodegeneration and addiction [39]. Consistent with these observations, patients included in the studies analyzed in this systematic review frequently reported significant cardiometabolic benefits in addition to BW loss. These were reflected in improvements in lipid profiles and glycemic control, with notable reductions in HbA1c and insulin requirements, although the magnitude of benefit varied by specific GLP-1 RA, dosage, and duration of follow-up.

Factors associated with response to GLP-1 RA treatment

Older adults and GLP-1 RA treatment response. In elderly patients with overweight or obesity with T2DM, Perna et al. [40] reported that liraglutide 3.0 mg over 24 weeks achieved modest BW loss of about 2.5% but substantial reduction in FBM, particularly in the android region. Importantly, LBM remained largely stable, with slight gains in leg and arm FFM in some patients, resulting in minimal changes in skeletal muscle index and no cases of sarcopenia. Also, in elderly diabetic patients with obesity, semaglutide therapy led to a moderate but clinically relevant reduction in BW and BMI after 3 months. BC analysis revealed that these changes were primarily driven by significant reductions in FBM and FBM percentage, while BMC and extracellular fluid balance remained unaffected. Importantly, SMM declined slightly in absolute terms, yet its proportion relative to total BW was preserved. Detailed segmental analysis further confirmed the stability of both upper and lower limb muscle mass as well as the ratio of lower-to-upper extremity musculature, indicating that semaglutide facilitated selective adiposity reduction while maintaining muscular distribution [41].

Type 2 diabetes and GLP-1 RA treatment response

It is also important to note that therapeutic responses may differ between patients with and without T2DM, a difference likely driven by several interrelated mechanisms [42]. Physiologically, insulin resistance and compensatory hyperinsulinemia in T2DM may attenuate the incretin effect of GLP-1 RAs through impaired insulin signaling or reduced GLP-1 receptor responsiveness. Also, as an anabolic hormone, insulin promotes fat storage, and chronic hyperinsulinemia, commonly observed in T2DM, further stimulates lipogenesis while suppressing lipolysis, thereby counteracting BW reduction. Additionally, improved glycemic control with GLP-1 RAs in T2DM patients may reduce glycosuria, a process known as "glycemic buffering", which reduces caloric loss through urine and offsets part of the energy deficit induced by treatment [43–45]. Concomitant use of weight-promoting medications, such as insulin or sulfonylureas, may further blunt the weight loss effects of GLP-1 RAs [45]. Additional contributors may include a longer duration of obesity, older age, lower adherence to exercise, and possible behavioral factors in the T2DM population [46]. Finally, individual differences in baseline metabolic rate and prior exposure to dietary or behavioral weight loss strategies may influence the magnitude of BW reduction achieved with GLP-1 RAs, highlighting the complexity of therapeutic response in patients with T2DM [45].

Sex differences in GLP-1 RA treatment response

Beyond diabetes status, growing evidence also highlights the importance of sex differences in obesity, particularly regarding their impact on the effectiveness and tolerability of GLP-1 RA treatment. Female sex is widely recognized as an independent factor associated with greater BW loss achievement following treatment with GLP-1 RAs, a superiority observed in the majority of studies [47, 48]. This phenomenon may be partly explained by biological differences such as variations in sex hormone levels, pancreatic β-cell composition, and gene expression patterns related to insulin secretion and glucose metabolism [49]. For example, estrogen signaling has been shown to enhance the anorexigenic effects of GLP-1 RAs by modulating central pathways involved in food reward, which could account for the more pronounced weight loss observed in premenopausal women [49, 50]. Additionally, epigenetic differences, such as increased methylation of protective genes, such as DUSP9, in females, may influence insulin sensitivity and drug response [49, 51]. However, clinical outcomes are complicated by behavioral factors, including lower adherence rates reported among women, which may obscure the true extent of sex-related efficacy differences [52]. Given the heterogeneity in study populations and the predominance of post hoc analyses, further prospective research is essential to clarify these mechanisms and to evaluate whether personalized, sex-specific approaches to GLP-1 RA therapy could improve obesity treatment outcomes. All but one of the studies included in the systematic review did not provide sex-disaggregated data, limiting the interpretation of the impact of GLP-1 RAs on the measured outcomes. A prospective study assessed the impact of six months of liraglutide treatment on BC and cardiometabolic parameters in patients with metabolic syndrome, with analyses stratified by sex and compared to a control group treated with sibutramine. Both men and women receiving liraglutide showed significant improvements in BW loss, AC, and FBM, particularly trunk fat mass, a key parameter measured by BIA. Importantly, women exhibited a more pronounced reduction in AC and FMT, whereas men demonstrated significant decreases in overall BW and total FBM, as well as in regional fat, particularly in the arms. These results reflect sex-specific patterns of fat distribution and differential response to liraglutide, with reductions in visceral adiposity strongly correlated with decreases in AC across both sexes. In turn, the overall BW loss, defined as achieving 5% and 10% reduction, was similar

between men and women. Nonetheless, the distinct regional and quantitative differences in fat loss between the sexes highlight the need to consider sex-specific effects in obesity treatment [53].

Study limitations

This meta-analysis has several limitations that should be considered when interpreting the findings. Most notably, the number of included studies providing detailed data on both BC and cardiometabolic parameters was relatively limited. While strict inclusion criteria ensured methodological quality, they may have reduced the breadth of eligible evidence, limiting the scope of subgroup analyses and the generalizability of certain findings. A second important limitation relates to the substantial heterogeneity observed across studies. This variability likely reflects differences in study populations, such as the presence or absence of T2DM, degree of obesity, sex distribution, and comorbid conditions, as well as differences in intervention characteristics, including the type, dose, and duration of GLP-1 RA therapy. Although random-effects models were employed to account for between-study variance, some unmeasured confounders may have influenced the results. Also, LBM reduction was often assessed using BIA or DXA, both of which have limitations in distinguishing between muscle, organ mass, and extracellular fluid. As a result, interpretations regarding skeletal muscle preservation or loss must be made with caution, particularly in the absence of direct assessments of muscle strength or function. Moreover, differences in outcome reporting, such as the use of absolute versus relative changes, or inconsistent definitions of endpoints like visceral adiposity or insulin resistance, further limited the ability to standardize data extraction and synthesis. Also, several studies lacked full disclosure of variance measures or raw data, preventing the inclusion of potentially relevant findings. Finally, publication bias cannot be excluded, especially given the increasing clinical interest in GLP-1RAs and the greater likelihood of publishing studies with favorable outcomes. Despite attempts to minimize bias through a systematic and comprehensive search strategy, unpublished or negative studies may have been overlooked.

CONCLUSIONS

This meta-analysis highlights the substantial and multidimensional clinical benefits of GLP-1 RAs therapy in individuals with overweight or obesity, with or without T2DM. Across all treatment durations, GLP-1 RAs consistently produced significant improvements in anthropometric parameters, including BW, BMI, and WC, while also inducing favorable alterations in BC through pronounced reductions in FBM and VAT. Importantly, the reduction in LBM was modest relative to the overall BW loss, suggesting that GLP-1 RAs favor selective adipose tissue reduction over loss of lean tissue. The most pronounced improvements in BC were observed after 3 and 6 months of treatment, whereas after 12 months these beneficial effects tended to diminish. Notably, the observed variability in efficacy between agents, particularly in the early phases of treatment, emphasizes the importance of individualized therapeutic strategies, tailored to specific clinical goals, baseline metabolic profiles, and patient preferences. Looking ahead, further research should aim to define the most effective combinations of pharmacotherapy and lifestyle interventions, with a focus on preserving lean mass and sustaining long-term metabolic health.

DATA AVAILABILITY

No datasets were generated or analyzed during the current study.

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