Review Article

Comparative efficacy and safety of Dual GIP/GLP1 agonists versus GLP1 receptor agonists for weight loss: A Scoping Review

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Abstract

Background: The management of obesity is complex and has evolved considerably in recent years owing to the addition of incretin homologues like semaglutide, liraglutide and tirzepatide. Despite studies suggesting their potential use for weight loss, there is a dearth of accessible knowledge regarding their comparative benefits and effectiveness, limiting their use in the management of obesity.

Objective: The present study aims to provide a scoping review of available literature on the effectiveness, adverse events, cost efficiency and future prospects of glucagon-like peptide 1(GLP-1) receptor agonists and dual GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) agonists in promoting weight loss among obese individuals.

Methods: This review was conducted according to the PRISMA-ScR guidelines. A thorough database search was conducted in PubMed and Google Scholar to identify relevant articles assessing the use of dual GIP/GLP-1 agonists versus GLP-1 agonists in obese patients.

Results: Dual agonists were found to be more effective, producing a greater decrease in body weight and improving the metabolic profile and general health of patients. GLP-1 agonists were more frequently associated with gastrointestinal side effects, while the dual agonists reported greater psychiatric adverse effects, including depression and self-harm. Poor adherence and discontinuation of therapy were problems faced during treatment with both groups, owing to their high cost and supply shortage.

Conclusion: Current research provides sufficient evidence suggesting superior efficacy of dual agonists for weight loss, although future studies focusing on alternative dosing schedules and cost-friendly options for incretin mimetics are needed.

Introduction

Obesity is an adiposity-based chronic disease (ABCD) resulting from complex genetic, neurobiological, and environmental interactions, leading to excessive fat deposition in the body.[1-3] As of 2022, about 43% adults worldwide were classified as overweight or obese, and over 890 million individuals were living with obesity; a number that has more than doubled since 1990 and is currently on the rise.[3] Obesity has wide-ranging health implications, being associated with an increased risk of non-communicable diseases like type 2 diabetes mellitus, cardiovascular diseases, and cancer, which in turn takes a toll on the economic and healthcare system of society.[3,4] If current trends continue, the global economic cost of the condition is projected to reach approximately $4.32 million by 2035.[4]

As with other chronic metabolic diseases, the initial line of management of obesity is lifestyle and dietary interventions, an approach that often tends to fail in the long-term, necessitating the use of pharmacotherapy.[5] The US Food and Drug Administration (FDA) recommends medications as part of a comprehensive strategy for obesity management in individuals with a Body Mass Index(BMI) of 27-29.9 kg/m2 and ≥ 1 obesity-related complication or a BMI ≥ 30 kg/m2.[6] Anti-obesity medications have been in use since the 1940s but were often riddled with several complications and safety concerns, including cancer, cardiotoxicity and neuropsychiatric disorders, along with limited efficacy.[5]

Recent advances in understanding the biochemical and metabolic pathways underlying obesity have led to the development of superior anti-obesity medications, namely glucagon-like peptide 1(GLP-1) receptor agonists, most notably semaglutide and liraglutide, glucose-dependent insulinotropic polypeptide (GIP) agonists and dual agonists like tirzepatide.

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GLP-1 and GIP receptor agonists work by enhancing insulin secretion, delaying gastric emptying, and improving satiety.[7,8] These newer drugs, especially dual GLP-1 and GIP agonists, have generated newfound interest among researchers due to their ability to not only achieve substantial weight reduction but also alleviate obesity related complications.[2,9] Clinical trials on semaglutide, which was approved for weight control in June 2021, have shown significant positive effects, including greater weight loss, ease of administration, improvements in quality of life, as well as substantial cardiometabolic improvements.[10] Tirzepatide, a dual agonist, has also shown improved metabolic outcomes, blood pressure control, and lipid levels, sometimes surpassing the effect of GLP-1 agonists.[11]

Although incretin mimetics are known to have a superior therapeutic effect in obesity, physicians were found to be less willing to prescribe them due to a lack of knowledge on the drug, despite believing in its pharmacological effect.[12] As these are relatively newer drugs, studies exploring their pros and cons are limited. Clarity on the variety of incretin mimetics available, their comparative efficacies, adverse effects, future implications, and costs is lacking. This highlights the need for more accessible knowledge on this subject, justifying the need for this review.

This scoping review aims to provide a comprehensive overview of the comparative effects of GLP-1 agonists and dual GIP/GLP-1 receptor agonists on weight loss management in obese individuals without comorbidities, highlighting their effectiveness, adherence, and cost benefit analysis.

Methodology

This review was drafted using the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) guideline.[13]

Study selection

Systematic reviews, meta-analysis and randomised controlled trials (RCTs) published between 2021 to 15 April 2026 were screened, and those evaluating the use of dual GIP/GLP-1 Receptor Agonists versus GLP-1 Agonists for weight loss in obese individuals were included. Articles involving populations with comorbid conditions such as type 2 diabetes mellitus, metabolic syndrome, cardiovascular diseases, non-alcoholic steatohepatitis, hypertension, and obstructive sleep apnoea syndrome, among others, were rejected. Cohort studies, narrative reviews, cross-sectional studies and editorials were not included as part of this review. Further details of the PICO framework are provided in Table 1.

Table 1: PICO Framework

Features	Inclusion criteria	Exclusion criteria
Population	Obese patients	Patients with comorbidities, notably type 2 diabetes mellitus
Intervention	Dual GIP/ GLP-1 Receptor Agonists	Absence of dual GIP/GLP-1 agonists
Control	GLP-1 Receptor Agonists	Placebo, dipeptidyl peptidase, bariatric surgery
Outcome	Weight Loss	Other outcomes, such as glycemic and lipid control

Information sources and search strategy

An extensive literature search was conducted on PubMed and Google Scholar using the following search strategy: ("Tirzepatide"[MeSH]) OR ("DA-JC4" [Supplementary Concept] OR "DA5-CH peptide" [Supplementary Concept]) OR "Sitagliptin Phosphate"[MeSH] OR (Dual GIP/GLP-1 Receptor Agonists)) AND (("Weight Loss"[Mesh]) OR (weight loss) OR ("Weight Loss"[Title]) OR ("Weight Loss"[Abstract])) AND (("Glucagon-Like Peptide-1 Receptor Agonists"[Mesh]) OR (Semaglutide) OR (Ozempic) OR (Wegovy). The relevant articles were retrieved and reviewed by all authors for eligibility. Table 2 depicts the search strategy and various MeSH terms (Medical Subject Headings) and Boolean operators used.

Table 2: Search strategy

Database	Search strategy	Results
PubMed	((("Tirzepatide"[Mesh]) OR ("DA-JC4" [Supplementary Concept] OR "DA5-CH peptide" [Supplementary Concept])) OR "Sitagliptin Phosphate"[Mesh] OR (Dual GIP/GLP-1 Receptor Agonists)) AND (("Weight Loss"[Mesh]) OR (weight loss) OR ("Weight Loss"[Title]) OR ("Weight Loss"[Abstract])) AND (("Glucagon-Like Peptide-1 Receptor Agonists"[Mesh]) OR (Semaglutide) OR (Ozempic) OR (Wegovy)))	176
Google Scholar 10/04/2026	Dual GIP and Glp 1 receptor agonists AND Glp 1 receptor agonists AND weight loss	22,700
		n=22,876

Data charting and synthesis

Data from the selected studies were charted by 2 reviewers independently on Google Sheets. The data items extracted included the country and year of study, intervention and control drug characteristics, outcomes analysed, and adverse effects reported. The articles were grouped according to the study design, effectiveness in promoting weight loss and the cost benefit ratio, and the results were presented in tables 3,4 and 5.

Results

Selection of sources of evidence

Database search yielded a total of 22,876 articles, which were screened for duplicates and relevance to the research question. Articles were excluded if they did not meet the predefined selection criteria for population, intervention, and control, or if the full text could not be retrieved. A total of 13 studies were included in this scoping review, of which 6 were meta-analyses, 3 were systematic reviews, 2 were RCTs, and the rest were cost effective analysis.

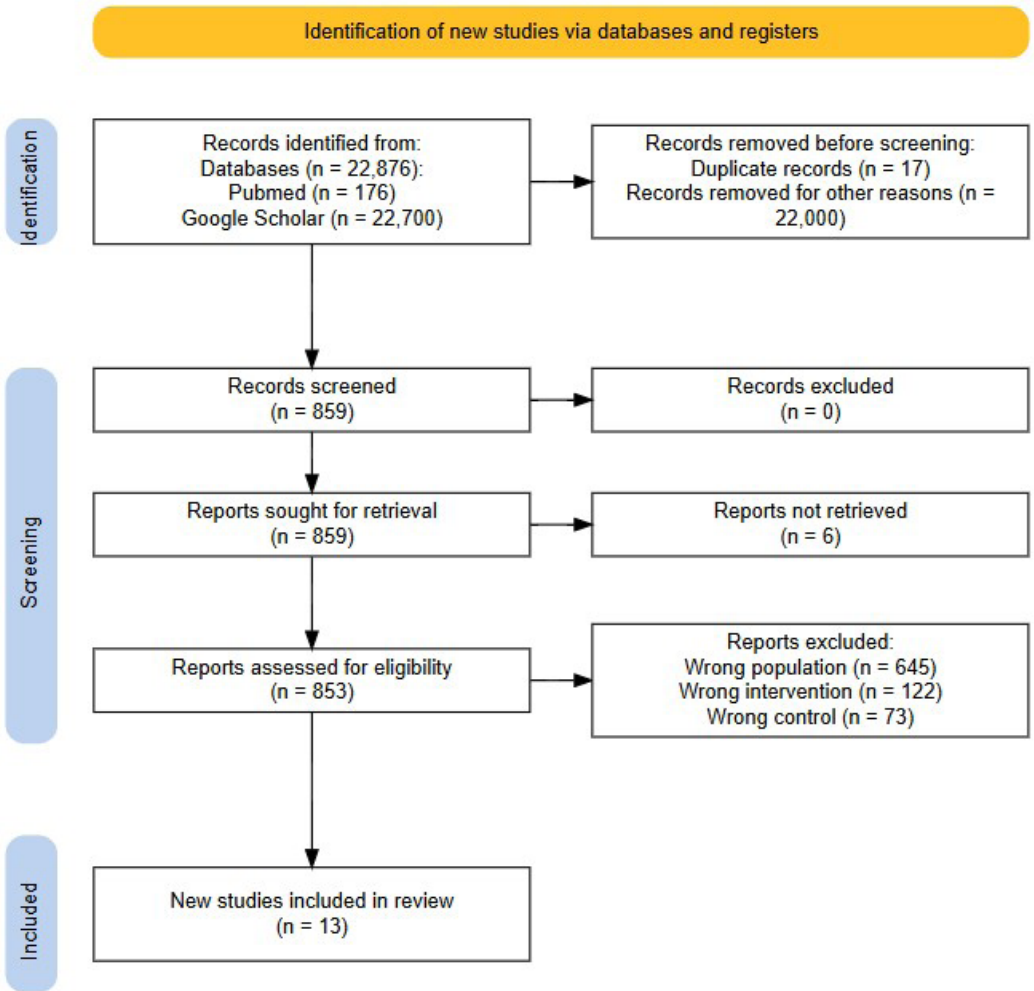

Figure 1: PRISMA flow diagram[14]

Characteristics of the included systematic reviews and meta-analyses, such as author, year of publication as well as intervention and control drugs used, are presented in (Table 3).[15-23]

The number of RCTs analysed by each study and the ability of our database search to detect them are also mentioned.

Table 3: Study characteristics of the included systematic reviews and meta-analyses

Author, Year	Study Type	Number of RCTs assessed by study	RCT that fits the eligibility criteria of the scoping review	Missed eligible RCTs	Dual gip/glp1 assessed	Glp1 assessed
Baba AH et al,2026[15]	Meta-analysis	3	2	0	Tirzepatide	Semaglutide
Benardi JC et al,2026[16]	Meta-analysis	28	1	0	Tirzepatide	Semglutide
Sinha B et al,2025[17]	Meta-analysis	19	0	0	Tirzepatide	Semaglutide
Kasagga A et al,2025[18]	Meta-analysis	8	1	0	Tirzepatide	Semaglutide
Khawaji et al,2025[19]	Meta-analysis	6	0	0	Tirzepatide	Semaglutide
Xie Z et al,2025[20]	Systematic Review	19	0	0	Tirzepatide	Semaglutide
Munawar N et al,2025[21]	Meta-analysis	2	1	0	Tirzepatide	Semaglutide
Singh A et al,2025[22]	Systematic review	4	0	0	Tirzepatide	Semaglutide
Müllertz ALO et al,2024[23]	Systematic review	7	0	0	Tirzepatide	Semaglutide

A total of 6 meta-analyses and 3 systematic reviews were assessed. All RCTs that matched the eligibility criteria of this review were obtained on literature review and assessed individually through the study. Most commonly assessed dual gip/glp1 was Tirzepatide, and most commonly assessed glp-1ra was Semaglutide.

Table 3 depicts the study characteristics of the RCTs and cost-effectiveness analysis included in this review, including the author, year, place of study, population and drugs assessed.[24-27]

Table 4: Study characteristics of RCTs and cost-effective analysis

Author, Year	Study Type	Place of Study	Population	Dual GIP/GLP-1 assessed	GLP-1 assessed
Shukla AP et al.,2025[24]	RCT	United States	Obese patient	Tirzepatide at 10 mg or 15 mg	Semaglutide at 1.7mg or 2.4 mg
Liu L et al.,2025[25]	Cost effective anaylsis	United States	Obese patient	Oral and Subcutaneous Tirzepatide	Oral and Subcutaneous Semaglutide
Aronne LJ et al,2025[26]	RCT	United States and Puerto Rico	Obese patient	Tirzepatide at 10 mg or 15 mg	Semaglutide at 1.7mg or 2.4mg
Hwang JH et al.,2025[27]	Cost-effective analysis	United States	Obese patient	Tirzepatide	Semaglutide

Of the 4 articles assessed in the table, 2 were RCTs, and 2 were cost-effectiveness analyses. The overall population was obese patients, and drugs assessed were Tirzepatide and Semaglutide

Characteristics of the individual studies, including the effectiveness of weight loss, additional benefits, adverse effects and discontinuation rates, are reported in Table 4.Tirzepatide demonstrated a greater percentage of weight loss in all studies, while GLP-1 agonists were associated with more serious side effects, particularly pertaining to the gastrointestinal tract.

Table 5: Results of individual studies including weight loss effectiveness, discontinuation, additional benefits, adverse effects and cost effectiveness

Author, Year	Study Type	Weight loss	Discontinuation	Additional benefits	Adverse effects	Cost effectiveness
Baba AH et al,2026[15]	Meta-analysis	Tirzepatide results in significantly greater weight loss than semaglutide	No significant difference was observed	nil	Tirzepatide users reported more serious side effects than Semaglutide	nil
Benardi JC et al,2026[16]	Meta-analysis	Greater weight loss was observed with Tirzepatide	nil	Tirzepatide was better at regulating glycemic parameters	nil	nil
Shukla AP et al,2025[24]	RCT	Greater weight loss was observed with Tirzepatide when compared to Semaglutide	Only inadvertent discontinuation reported	Tirzepatide demonstrated a greater increase in the general health of patients, but overall quality of health and physical function was increased for both dual gip/glp1 and glp1-ra	nil	nil
Sinha B et al,2025[17]	Meta-analysis	Greater weight loss with dual gip/glp1 when compared with glp1	nil	nil	Glp1 were more commonly associated with treatment adverse effect and serious adverse effect while dual gip/glp1 were more associated with diarrhea and hypoglycemia	nil

Kasagga A et al,2025[18]	Meta-analysis	Tirzepatide at MTD demonstrated the greatest amount of weight loss	More commonly was due to adverse effects with MTD and more common for semaglutide followed by Tirzepatide at MTD	nil	Both were associated with adverse effects. Semaglutide was mostly associated with vomiting while tirzepatide was mostly associated with nausea and diarrhoea	nil
Khawaji et al,2025[19]	Meta-analysis	Tirzepatide was more effective than glp1 for weight loss	nil	nil	Gastrointestinal side effects appeared similar for both dual gip/glp1 and glp1-ra	nil
Xie Z et al,2025[20]	Systematic Review	More weight loss was observed for Tirzepatide	nil	Better glycemic regulation was observed with Tirzepatide	Tirzepatide users experienced less gastrointestinal side effects than Semaglutide users	nil
Munawar N et al,2025[21]	Meta-analysis	Tirzepatide demonstrated higher weight losing potential than Semaglutide	Similar low discontinuation due to gastrointestinal side effects	nil	Similar gastrointestinal side effects observed for both drugs	nil
Liu L et al,2025[25]	Cost effective analysis	Most weight loss were observed for Tirzepatide	Discontinuations were mostly associated with development of serious adverse effects and high cost. BMI appeared to be maintained through short follow-up	nil	Serious adverse effects were more commonly associated with Liraglutide	Subcutaneous Tirzepatide and Oral Semaglutide were both ruled as the most cost effective options
Aronne LJ et al,2025[26]	RCT	Tirzepatide users were more likely to experience weight loss than Semglutide users	nil	nil	Most common adverse effects across groups was gastrointestinal adverse effects	nil
Hwang JH et al,2025[27]	Cost effective analysis	Tirzepatide registered higher weight loss than Semaglutide	Quality of life decreased observed with discontinuation rates increase	nil	Gastrointestinal adverse events were the most commonly reported	Tirzepatide was considered the most cost effective when compared with Semaglutide

Singh A et al,2025[22]	Systematic review	Tirzepatide had the greatest weight loss inducing potential than glp1-ra assessed	nil	nil	Liraglutide had the most serious adverse effects followed by Semaglutide while Tirzepatide was most commonly affected by hypoglycemic events	nil
Müllertz ALO et al,2024[23]	Systematic review	Significant weight loss for both Tirzepatide and Semaglutide	nil	nil	Similar gastrointestinal side effects were observed for both drugs, with more serious adverse events reported for Semaglutide	nil

Tirzepatide was reported as the most efficient drug for weight loss in obese patients by all 13 of the articles assessed. It was also reported as the most cost-effective option and the one with the least associated side effects.

Discussion

Summary of evidence

A total of 13 articles were reviewed during the study, of which 6 were meta-analyses, 3 systematic reviews, 2 RCTs and 2 cost-effective analyses. All eligible RCTs assessed by 8 review articles were also reviewed individually. The most commonly assessed dual GIP/GLP-1 agonist was Tirzepatide, while the most commonly assessed GLP-1 agonist was Semaglutide, followed by Liraglutide.[15-27]

The most effective incretin mimetics to manage weight loss were ruled to be Tirzepatide by all 13 articles, as it was noted to have the greatest percentage weight loss, decrease in subcutaneous fat, and the greatest associated percentage certainty to weight loss.[15-27] This has predominantly been due to its superior metabolic effects, which, on top of making it the most efficient weight loss treatment, make it the most efficient at regulating glycaemic index reported by Benardi JC et al, 2026 and Xie Z et al, 2025.[16,20, 28-30] These superior metabolic effects have also been associated with improved cardiovascular health, whose comparison with glp1-ra has not been reported by any of the assessed studies.[31,32] Other additional benefits missing from the study that have been associated with Tirzepatide are improved lipid profile, reduced liver fat, and improved kidney protection.[33-35]

Being the most effective drug is not the only driving factor for the success of a drug in the real world; its cost and associated adverse effects are all factors contributing to the endpoint adherence rate and discontinuation rates of the drug.[35,36]

Tirzepatide has once again been ruled as the most cost-effective of the 2 options when assessed.[25-27] More specifically, subcutaneous Tirzepatide and oral Semaglutide have been ruled out as the most cost-effective option by Liu L et al, 2025[25] Despite both being cited here, Tirzepatide is for the most part considered a worthier option due to higher efficacy rates as observed by Hwang JH et al, 2025.[27]

Despite Tirzepatide trumping Semaglutide in cost effectiveness, the discontinuation rates of both drugs remain mostly similar, with the most common cause being serious adverse effects and the high cost of the drug.[38-42] Low adherence rate has also been associated with the same causes, noting how important finding a solution to the high cost of the drug, apart from decreasing the vial size.[38-42]

In the case of adverse effects (ades), most of the ades reported have been gastrointestinal complaints ranging from nausea to diarrhoea[15,17-23, 43-46] The more serious adverse effects were associated with use of the maximum therapeutic dose of the drug and generally related to semaglutide.[18,23] Liraglutide, when assessed, was reported as the one with the most side effects of the glp1-ra.[22] Dual gip/glp1 was mostly similarly matched to glp1-ra and its most commonly reported side effect was the occurrence of hypoglycemic events.[15,17-23,47-48] Side effects mentioned that required further investigation were psychiatric symptoms, most commonly associated with Semaglutide.[49-51]

Conclusion

Tirzepatide (dual GIP/GLP-1) can be concluded to trump Semaglutide/Liraglutide (GLP-1 agonist), being a more efficacious and cost-effective drug with fewer reported serious side effects. However, more RCTs and studies directly comparing the 2 groups of drugs need to be done to cement its place as the superior obesity management option. And even more pressing, more research in developing more cost-effective variables has to be done to further increase adherence and accessibility to the drugs.

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