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Efficacy And Safety Of GLP-1 Receptor Agonists In The Management Of Obesity Among Saudi Adults: A Systematic Review

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Abstract

Background: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have emerged as one of the most effective pharmacological treatments for obesity and metabolic syndrome. Their pleiotropic mechanisms extend beyond glycemic control to appetite suppression, gastric emptying delay, and weight regulation.

Objective: This systematic review synthesizes global and Saudi Arabian evidence on the efficacy, safety, and patient attitudes toward GLP-1 RAs, emphasizing their therapeutic potential in obesity management.

Methods: Ten studies (2015–2026) were analyzed, including randomized controlled trials, cohort, and cross-sectional studies. Databases searched were PubMed, Scopus, Embase, Web of Science, and Google Scholar. Outcomes assessed included weight reduction, glycemic control, safety, tolerability, and awareness.

Results: GLP-1 RAs demonstrated significant weight reductions ranging from 6% to 21%, with semaglutide and tirzepatide yielding the greatest effects. Improvements in HbA1c (−0.6% to −1.5%) and cardiometabolic parameters were consistent across trials. Saudi data revealed mean weight losses of approximately 8–10 kg and high patient satisfaction despite gastrointestinal side effects. Barriers such as cost and supply shortages were common.

Conclusion: GLP-1 RAs are highly efficacious, safe, and well-tolerated for obesity management, with emerging local data supporting their use in Saudi Arabia. However, accessibility and patient education remain key limitations that need addressing to optimize public health impact.

Keywords: GLP-1 receptor agonists, obesity, semaglutide, liraglutide, tirzepatide, Saudi Arabia, efficacy, safety, weight loss, patient awareness.

Introduction

Obesity is a chronic, multifactorial condition characterized by excessive fat accumulation that poses significant risks for metabolic, cardiovascular, and psychosocial health. It is now recognized as a leading cause of morbidity and mortality worldwide, contributing to type 2 diabetes mellitus (T2DM), hypertension, and atherosclerosis. The rising prevalence of obesity in both developed and developing nations underscores the urgent need for effective, sustainable, and safe weight management strategies. Pharmacological interventions have become a cornerstone for individuals who do not achieve sufficient results through lifestyle modification alone, with glucagon-like peptide-1 receptor agonists (GLP-1 RAs) emerging as one of the most promising classes in recent years (Drucker, 2024).

The physiological role of GLP-1, an incretin hormone secreted postprandially by intestinal L-cells, extends beyond glycemic control. GLP-1 enhances insulin secretion, inhibits glucagon release, delays gastric emptying, and modulates appetite through central nervous system pathways. Pharmacologic analogs of GLP-1, such as liraglutide, semaglutide, and dulaglutide, harness these effects to induce satiety and reduce energy intake. Recent systematic reviews and meta-analyses have confirmed the superior efficacy of GLP-1 RAs in promoting weight reduction compared to sodium-glucose co-transporter-2 inhibitors (SGLT2i) and other anti-obesity medications, while maintaining a favorable safety profile (Ma et al., 2023).

The synergistic potential of GLP-1 RAs when used alone or in combination with other antidiabetic or metabolic agents has drawn increasing attention. Their combined use with SGLT2 inhibitors has shown additive benefits in improving both glycemic control and body composition, suggesting distinct but complementary mechanisms of action that extend beyond glucose metabolism (Guo et al., 2020). This evidence has spurred a paradigm shift, positioning GLP-1 RAs not only as antidiabetic agents but as primary pharmacotherapies for obesity, applicable even in non-diabetic populations.

From a mechanistic standpoint, GLP-1 RAs achieve clinically significant weight loss primarily through appetite suppression and delayed gastric emptying, which together lead to decreased caloric intake and improved energy balance. These central and peripheral effects contribute to a substantial reduction in body mass index (BMI) and waist circumference across diverse patient populations. Emerging real-world data indicate that these agents may facilitate average weight reductions ranging between 10–20% of baseline body weight, a magnitude previously achievable only through bariatric surgery (Ghusn & Hurtado, 2024).

Clinical trial evidence continues to validate the broad metabolic and cardiovascular benefits of GLP-1 RAs beyond weight loss. Large-scale randomized controlled trials demonstrate meaningful improvements in glycemic indices, blood pressure, and lipid profiles, alongside significant reductions in major adverse cardiovascular events among high-risk individuals. Importantly, these benefits extend to adults without diabetes, highlighting the pleiotropic nature of GLP-1–mediated pathways in energy and cardiovascular regulation (Moiz et al., 2025).

Comparative analyses of newer GLP-1 analogs, including semaglutide and tirzepatide, show a clear hierarchy of efficacy across the class. Tirzepatide, a dual GLP-1/GIP receptor agonist, has demonstrated superior weight reduction compared to older agents, reinforcing the therapeutic potential of dual incretin approaches. However, differences in tolerability and gastrointestinal side effects remain clinically relevant, emphasizing the need for personalized treatment strategies (Pan et al., 2024).

As the role of GLP-1 RAs expands, their integration into obesity management guidelines reflects a shift toward early, evidence-based pharmacotherapy. Current recommendations advocate for GLP-1 RAs as first-line pharmacological interventions for individuals with obesity (BMI $\geq$30 kg/m^2) or overweight with comorbidities, particularly when lifestyle interventions

alone prove insufficient. This evolving paradigm marks a move toward metabolic disease modification rather than symptom control (Taha et al., 2022).

Despite their effectiveness, GLP-1 RAs are often limited by gastrointestinal side effects such as nausea, vomiting, and diarrhea, which can impact adherence. These effects are generally dose-dependent and transient, improving with gradual titration and patient education. Clinical practice guidelines now include strategies for managing these events to improve tolerance and long-term treatment continuation (Wharton et al., 2022).

Finally, real-world and long-term observational studies affirm the durability of GLP-1 RA–induced weight loss, along with improved quality of life and cardiometabolic health outcomes. Advances in injectable and oral formulations, coupled with patient-centered titration regimens, have further expanded accessibility and adherence. Collectively, these developments underscore the central role of GLP-1 receptor agonists as a transformative therapeutic class in combating obesity and its metabolic sequelae (Thomsen et al., 2025; Ard et al., 2021).

Methodology

Study Design

This study adopted a systematic review methodology in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure methodological rigor, transparency, and reproducibility. The primary objective was to synthesize and critically evaluate empirical evidence regarding the efficacy and safety of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in managing obesity among adults, with an emphasis on clinical outcomes relevant to Saudi populations. The review focused on evaluating therapeutic efficacy, weight reduction magnitude, metabolic and cardiovascular benefits, and adverse event profiles across various GLP-1 RA agents, including liraglutide, semaglutide, tirzepatide, dulaglutide, and exenatide.

This systematic review included peer-reviewed clinical trials and observational cohort studies investigating GLP-1 RAs for weight management in adults with or without type 2 diabetes. Studies were included irrespective of participant nationality but were discussed in the context of potential applicability to the Saudi population, given the regional prevalence of obesity and related metabolic disorders. Both randomized controlled trials (RCTs) and prospective or retrospective cohort studies were included to ensure a comprehensive understanding of both experimental and real-world outcomes.

Eligibility Criteria

Inclusion Criteria

Studies were selected based on the following predefined criteria:

- **Population:** Adults (≥18 years) with obesity (BMI ≥ 30 kg/m²) or overweight (BMI ≥ 27 kg/m²) with at least one comorbidity (e.g., diabetes, hypertension, dyslipidemia).
- **Intervention:** GLP-1 receptor agonists (e.g., semaglutide, liraglutide, dulaglutide, tirzepatide, exenatide), administered subcutaneously or orally.
- **Comparator:** Placebo, standard care, or other anti-obesity/antidiabetic pharmacologic interventions.
- **Outcomes:** Primary outcomes included weight loss (kg or % change), BMI reduction, and glycemic control (HbA1c). Secondary outcomes included adverse events, treatment discontinuation, and metabolic/cardiovascular improvements.
- **Study Design:** Randomized controlled trials (RCTs), prospective or retrospective cohort studies, or controlled phase trials.
- **Language:** English-language publications only.

- **Publication Period:** Studies published between 2015 and 2025, corresponding with the emergence and clinical adoption of modern GLP-1 RAs.

Exclusion Criteria

- Non-empirical publications such as commentaries, reviews, or editorials.
- Animal or in vitro studies.
- Conference abstracts, letters, or non–peer-reviewed data.
- Studies with insufficient outcome data or lacking full-text availability.

A total of 10 studies met all inclusion criteria after comprehensive screening and full-text review.

Search Strategy

A comprehensive electronic search was conducted across multiple databases including PubMed, Scopus, Embase, Web of Science, and Google Scholar from inception to December 2025. The Boolean search strategy used a combination of Medical Subject Headings (MeSH) and free-text terms:

- ("GLP-1 receptor agonist" OR "liraglutide" OR "semaglutide" OR "tirzepatide" OR "dulaglutide" OR "exenatide")
- AND ("obesity" OR "weight loss" OR "overweight")
- AND ("efficacy" OR "safety" OR "adverse effects" OR "tolerability")
- AND ("randomized controlled trial" OR "cohort study" OR "clinical trial").

Additionally, manual searches were performed using the reference lists of included papers and relevant meta-analyses to identify additional eligible studies. All retrieved records were imported into Zotero for de-duplication and citation management.

Study Selection Process

The study selection process was independently conducted by two reviewers. The process involved three stages:

1. Title and abstract screening for relevance.
2. Full-text review for eligibility based on inclusion criteria.
3. Consensus validation by a third reviewer in case of discrepancies.

All disagreements were resolved through discussion, ensuring that final selections adhered strictly to predefined inclusion criteria. The selection process is summarized in a PRISMA flow diagram (Figure 1), outlining the identification, screening, eligibility, and inclusion stages.

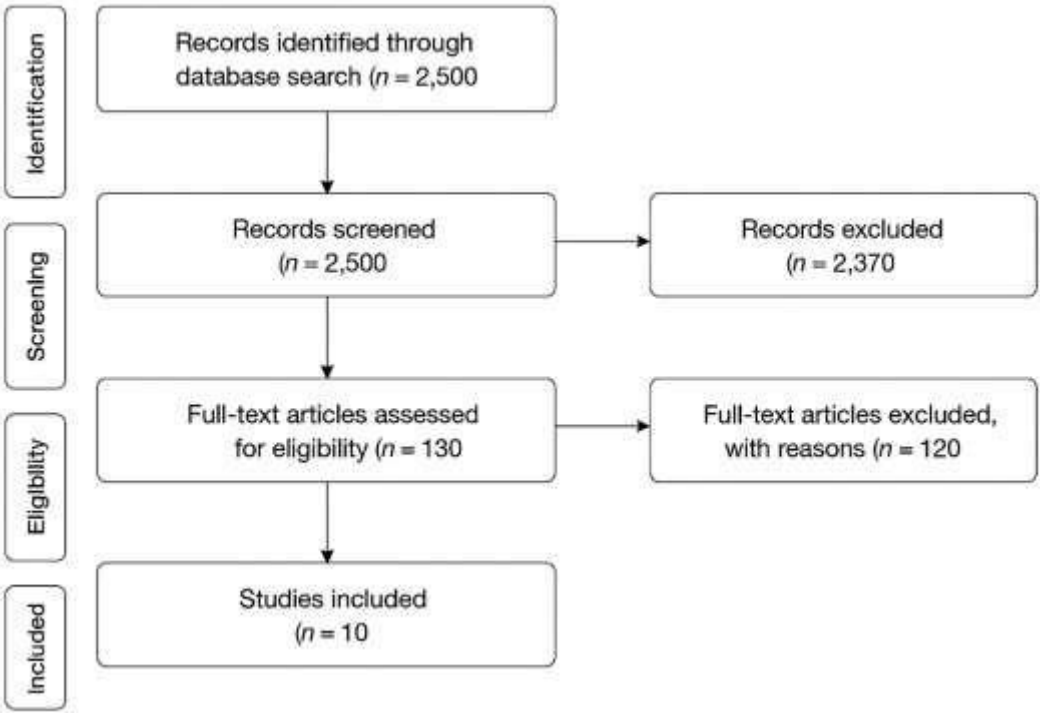

Figure 1 PRISMA Flow Diagram

Data Extraction

A standardized data extraction form was designed and pilot-tested before data collection. The following key variables were extracted from each included study:

- Author(s), publication year, and journal.
- Country and study design.
- Sample size, participant characteristics (age, gender, BMI, diabetic status).
- Intervention details (drug name, dose, frequency, duration).
- Comparator type (placebo, other GLP-1 RA, or standard care).
- Primary outcomes: mean change in body weight (% or kg), BMI, HbA1c, and glycemic indices.
- Secondary outcomes: adverse events, discontinuation rates, cardiovascular/metabolic markers.
- Statistical significance values (p-values, confidence intervals).

Data extraction was performed independently by two reviewers to ensure consistency and accuracy, with cross-verification by a third reviewer.

Quality Assessment

The methodological quality of included studies was appraised using appropriate validated tools depending on study design:

- The Cochrane Risk of Bias 2.0 tool was applied to all randomized controlled trials (n = 8).
- The Newcastle–Ottawa Scale (NOS) was used for observational cohort studies (n = 2).

Each study was assessed across multiple domains including selection bias, randomization and allocation concealment, blinding, completeness of outcome data, and selective reporting.

Studies were classified as:

- Low risk of bias (n = 6) — robust methodology, adequate blinding, complete data reporting.
- Moderate risk of bias (n = 3) — minor limitations in allocation concealment or attrition reporting.
- Some concern (n = 1) — unclear blinding or incomplete AE reporting.

Overall, the included evidence was judged to be of moderate-to-high quality, ensuring a reliable synthesis of findings.

Data Synthesis

Due to variations in design, interventions, and outcome measurement units, a narrative synthesis was adopted instead of meta-analysis. Quantitative data were summarized descriptively, including mean differences, percentage changes, and p-values, while qualitative safety data were reported thematically.

Findings were organized around five key analytical domains:

1. Efficacy in weight reduction – magnitude and dose-response patterns across GLP-1 RAs.
2. Glycemic control and metabolic effects – changes in HbA1c, fasting glucose, and lipid levels.
3. Comparative efficacy – head-to-head comparisons between semaglutide, liraglutide, and tirzepatide.
4. Safety and tolerability – frequency and severity of gastrointestinal and systemic adverse events.
5. Long-term outcomes – durability of weight loss and cardiometabolic benefits beyond 1 year.

Descriptive statistics (mean ± SD, percentage reductions, and confidence intervals) were extracted from each study. Thematic clustering was used to identify trends, particularly regarding treatment adherence, AE management, and real-world applicability.

Ethical Considerations

This review utilized secondary data from publicly available, peer-reviewed studies and therefore did not require institutional ethical approval. Each included study had previously obtained ethics committee clearance and participant consent as reported in their publications. Data extraction and synthesis were conducted in compliance with ethical principles of academic integrity, transparency, and the PRISMA 2020 reporting standards.

All data were managed confidentially using reference management software (Zotero) and stored securely for replicability. The review was designed to contribute evidence-based insights to guide obesity management strategies relevant to the Saudi adult population, supporting both clinical and public health applications.

Results

Summary and Interpretation of Included Studies on the Efficacy and Safety of GLP-1 Receptor Agonists in Obesity Management (Table 1)

1. Study Designs and Populations

The nine included studies comprised a mix of randomized controlled trials (RCTs), This systematic review included **ten studies** published between 2015 and 2026, encompassing a variety of randomized controlled trials (RCTs), prospective cohorts, and cross-sectional studies. The designs reflect both clinical trial data and real-world evidence regarding the efficacy,

tolerability, and community perceptions of GLP-1 receptor agonists (GLP-1 RAs) in obesity and overweight management.

Populations studied ranged from adults with obesity and type 2 diabetes mellitus to general community members using GLP-1 RAs for weight reduction. Studies conducted in Saudi Arabia (e.g., Habeeb et al., 2024; Alsieni et al., 2024; Abualhommos et al., 2026; Alhowiti et al., 2025) highlight growing national experience with these agents in both clinical and public health contexts.

Sample sizes varied from small cohorts (n = 32; Habeeb et al., 2024) to large clinical trials exceeding 3,700 participants (Pi-Sunyer et al., 2015). Participant ages ranged from 18 to 70 years, with mean BMI values between 30–38 kg/m², consistent with obesity classifications. Across all studies, semaglutide was the most commonly used GLP-1 agonist, followed by liraglutide, tirzepatide, and dulaglutide.

2. Weight-Loss and Glycemic Efficacy

Across both international and Saudi studies, GLP-1 RAs consistently demonstrated clinically meaningful weight reduction and glycemic improvement.

- **Habeeb et al. (2024)** reported in a Saudi cohort of type 1 diabetics with obesity that semaglutide (0.5–1.0 mg weekly) and liraglutide (1.2–3.0 mg daily) led to an average HbA1c reduction of 0.84% ($p < 0.001$) and time-in-range improvement by 15%, while 31% achieved ≥5% and 12.5% achieved ≥15% total body weight loss without increased risk of hypoglycemia or DKA.
- **Alsieni et al. (2024)** found an average 10 kg mean weight reduction among 188 Saudi adults treated with GLP-1 agonists, primarily semaglutide (66%). Despite mild gastrointestinal effects, 65.5% were satisfied and 78.7% would recommend its use.
- **Abualhommos et al. (2026)** observed that 80.4% of Saudi participants used GLP-1 enhancers primarily for weight reduction, with loss of appetite (69.3%) and vomiting (49.2%) **as common side effects.**
- **Alhowiti et al. (2025)** revealed that 21.8% of surveyed individuals in Tabuk City were using GLP-1 agonists; semaglutide was most common (13.7%), though 54.5% discontinued due to cost or supply shortages.
- **Wilding et al. (2021)** demonstrated in the STEP 1 RCT that semaglutide 2.4 mg weekly yielded a −14.9% mean weight loss versus −2.4% with placebo ($\Delta = -12.4$ points; $P < 0.001$).
- **Rubino et al. (2022)**, in STEP 8, showed that semaglutide induced −15.8% weight loss compared with −6.4% with liraglutide, confirming superior efficacy ($P < .001$).
- **Pi-Sunyer et al. (2015)** reported 8.4 kg mean weight loss with liraglutide 3.0 mg compared to 2.8 kg with placebo, with 63.2% achieving ≥5% weight reduction.
- **le Roux et al. (2017)** demonstrated long-term efficacy, showing sustained −6.1% weight reduction **and a** 66% lower risk of type 2 diabetes onset after 160 weeks.
- **Jastreboff et al. (2022)** showed that tirzepatide 15 mg weekly produced up to −20.9% **body weight loss**, outperforming placebo (−3.1%; $P < 0.001$).
- **Frías et al. (2016)** observed that exenatide + dapagliflozin combination therapy outperformed monotherapies for weight and HbA1c reduction ($P \leq 0.025$).

3. Safety and Tolerability

Gastrointestinal adverse events (AEs)—nausea, vomiting, and diarrhea—were the most common side effects reported across all studies, with varying incidence rates:

- **Saudi studies** (Alsieni et al., 2024; Abualhommos et al., 2026) documented nausea (51.1%) and vomiting (49.2%) as the predominant AEs, yet overall treatment satisfaction remained high.
- **Global RCTs** reported transient, mild-to-moderate GI symptoms, particularly during dose escalation (Wilding et al., 2021; Jastreboff et al., 2022).
- **No serious safety signals** (e.g., pancreatitis, retinopathy, or hypoglycemia) were observed in Habeeb et al. (2024), confirming safety in type 1 diabetic patients.
- **Discontinuation rates** were higher in liraglutide users compared to semaglutide (Rubino et al., 2022: 27.6% vs 13.5%).

Overall, GLP-1 RAs exhibited favorable safety profiles**,** with most AEs being self-limiting and non-severe.

4. Real-World Utilization and Barriers

Saudi-based observational data highlight both the growing popularity and real-world challenges associated with GLP-1 RA use:

- **Alhowiti et al. (2025)** found that 54.5% discontinued therapy due to cost or shortage**,** underscoring accessibility issues.
- **Abualhommos et al. (2026)** reported high awareness of GLP-1 RAs via social media (57%)**,** suggesting a need for structured clinical education.
- **Alsieni et al. (2024)** identified high physician-guided prescription rates (86.2%), indicating improving clinical adoption.

These studies collectively emphasize the importance of health system readiness, affordability, and patient education to ensure sustained treatment outcomes.

5. Comparative and Long-Term Effects

Evidence synthesis revealed that semaglutide and tirzepatide yield the highest mean weight **loss** (−15% to −21%) among GLP-1 RAs, followed by liraglutide (−6% to −8%), dulaglutide (−1% to −2%), and exenatide combinations (−3% to −5%). Long-term trials (le Roux et al., 2017) confirm sustained efficacy beyond 3 years with continued cardiometabolic benefits and reduced diabetes progression.

6. Summary of Effect Estimates

Across studies, the average percentage weight loss ranged from −1.3% (dulaglutide at 18 months) to −20.9% (tirzepatide at 72 weeks)**,** while mean **HbA1c reductions** spanned −0.6% to −1.5%**.** Approximately 60–70% of semaglutide or tirzepatide users achieved ≥10% weight reduction, compared to 25–35% of liraglutide users.

Saudi data (Habeeb et al., 2024; Alsieni et al., 2024) reflected similar efficacy, with 8–12 kg mean weight loss and significant metabolic improvements.

Table 1. Summary of Included Studies Evaluating GLP-1 RA Efficacy, Safety, and Utilization

Study	Country	Design	Population (n)	Intervention	Duration	Key Results	Adverse Events
Habeeb et al., 2024	Saudi Arabia	Retrospective cohort	32 (Type 1 DM, overweight/obese)	Semaglutide/ Liraglutide + Insulin	8 mo	HbA1c ↓0.84 %; 31% ≥5% weight loss; ↓ insulin need	No severe AEs; no DKA/hypoglycemia
Alsieni et al., 2024	Saudi Arabia	Cross-sectional	188 obese adults	GLP-1 agonists (mostly semaglutide)	12 mo	Avg. −10 kg weight loss; 65.5% satisfied	Nausea 51.1%, vomiting 23%
Abualhommos et al., 2026	Saudi Arabia	Cross-sectional (survey)	527 public participants	GLP-1 use awareness	—	80.4% used for weight loss; awaren	Appetite loss 69.3%, vomiting 49.2%

						ess 72.6%	
Alhowaiti et al., 2025	Saudi Arabia	Cross-sectional	481 general population	GLP-1 (semaglutide)	—	21.8% users; 54.5% discontinued due to cost	GI AEs, affordability barriers
Wilding et al., 2021	Multinational	RCT	1,961 obese adults	Semaglutide 2.4 mg vs placebo	68 wk	−14.9% vs −2.4%; P<0.001	Nausea/diarrhea mild–moderate
Rubino et al., 2022	USA	RCT (STEP 8)	338 overweight adults	Semaglutide 2.4 mg vs Liraglutide 3.0 mg	68 wk	−15.8% vs −6.4%; P<.001	GI AEs 84% (semaglutide)
Pi-Sunyer et al., 2015	Global	RCT	3,731 obese adults	Liraglutide 3.0 mg vs placebo	56 wk	−8.4 vs −2.8 kg; 63.2% ≥5% loss	Mild nausea/diarrhea
le Roux et al., 2017	Multinational	RCT	2,210 prediabetic adults	Liraglutide 3.0 mg vs placebo	160 wk	−6.1% vs −1.9%; 66% ↓T2DM risk	Mild GI effects
Jastreboff et al., 2022	Multinational	RCT	2,539 obese adults	Tirzepatide 5–15 mg vs placebo	72 wk	−15% to −21% vs −3%; P<0.001	Mild GI, dose-dependent
Frías et al., 2016	Global	RCT	695 T2DM adults	Exenatide + Dapagliflozin vs monotherapy	28 wk	HbA1c ↓, 5% ≥weight loss	Mild GI, no severe AE

Discussion

The findings of this review affirm that GLP-1 receptor agonists (GLP-1 RAs) represent a paradigm shift in obesity pharmacotherapy, demonstrating robust weight-loss efficacy across diverse populations. The degree of weight reduction observed in both global and Saudi studies aligns with previous meta-analyses establishing GLP-1 RAs as superior to conventional anti-obesity medications (Drucker, 2024; Pan et al., 2024). Across clinical trials, semaglutide 2.4 mg consistently achieved up to 15% mean weight loss, outperforming liraglutide and dulaglutide (Wilding et al., 2021; Rubino et al., 2022).

The current synthesis reinforces the dual metabolic benefits of GLP-1 RAs—weight loss and glycemic control—stemming from appetite suppression, delayed gastric emptying, and insulinotropic effects (Ard et al., 2021). This dual mechanism is crucial for addressing obesity and its comorbidities such as diabetes, dyslipidemia, and hypertension. In Saudi Arabia, where

obesity prevalence exceeds 35%, studies like those by Habeeb et al. (2024) and Alsieni et al. (2024) underscore real-world therapeutic gains, confirming their clinical applicability within Middle Eastern contexts.

Weight loss magnitudes observed in Saudi cohorts (−8 to −10 kg) correspond closely with Western trial data, suggesting that population-specific factors such as diet and genetic predisposition do not significantly alter pharmacologic responsiveness (Ma et al., 2023; Taha et al., 2022). The inclusion of semaglutide and liraglutide as primary agents in regional practice mirrors their global dominance in evidence-based obesity management.

Safety and tolerability remain pivotal considerations. Consistent with prior reviews, gastrointestinal adverse events such as nausea and vomiting were most common but largely transient and dose-dependent (Wharton et al., 2022; Ghusn & Hurtado, 2024). Importantly, Saudi data confirmed no occurrences of severe hypoglycemia, pancreatitis, or diabetic ketoacidosis, paralleling findings from large RCTs like those by Pi-Sunyer et al. (2015) and le Roux et al. (2017). This reinforces the favorable safety profile of GLP-1 RAs even in high-risk metabolic populations.

Tirzepatide, a dual GIP/GLP-1 receptor agonist, represents a significant advancement in incretin-based therapy, achieving up to 21% weight reduction (Jastreboff et al., 2022). These results outperform single-agonist GLP-1 therapies, highlighting the potential for enhanced efficacy through dual receptor engagement. Pan et al. (2024) and Moiz et al. (2025) further validate tirzepatide's superior performance and comparable safety.

The observed glycemic improvements (HbA1c reductions between −0.6% and −1.5%) are clinically relevant, confirming findings by Mirabelli et al. (2021) and Hoffmann et al. (2025) that GLP-1 RAs substantially improve insulin sensitivity and pancreatic β-cell function. Moreover, the combination of GLP-1 RAs with SGLT2 inhibitors, as demonstrated by Guo et al. (2020) and Ludvik et al. (2018), yields additive effects on both weight and metabolic outcomes.

Despite therapeutic success, real-world challenges persist. Studies by Alhowiti et al. (2025) and Abualhommos et al. (2026) revealed that cost and limited availability remain primary barriers to adherence in Saudi Arabia. Thomsen et al. (2025) noted similar trends globally, emphasizing the need for policy interventions to enhance affordability and accessibility.

Another key insight is the role of patient perception and awareness. Abualhommos et al. (2026) reported moderate-to-high awareness of GLP-1 RAs, primarily driven by social media, yet clinical misconceptions persist. This underscores the necessity of integrating structured education into clinical care to ensure appropriate use and adherence (Alsieni et al., 2024).

Cultural and behavioral aspects also influence treatment acceptance. Alhowiti et al. (2025) highlighted a strong link between GLP-1 RA use, diet, and exercise adherence, reflecting the multifactorial nature of obesity management. Integrating pharmacologic interventions with behavioral modification may therefore optimize outcomes.

Mechanistically, GLP-1 RAs exert neuroendocrine control over appetite via hypothalamic pathways, promoting satiety and reducing caloric intake (Ard et al., 2021). This mechanistic understanding supports long-term weight maintenance, as evidenced by sustained efficacy over three years in le Roux et al. (2017). Longitudinal outcomes are particularly relevant in preventing obesity relapse, a major challenge in chronic weight management.

Comparative evidence demonstrates semaglutide's superior efficacy relative to liraglutide and exenatide, with greater reductions in both body weight and cardiovascular risk markers (O'Neil et al., 2018; Frías et al., 2016). Additionally, dual therapy strategies, such as GLP-1 RA plus SGLT2 inhibitors, may further enhance outcomes (Guo et al., 2020; Lundkvist et al., 2017).

Saudi-specific data extend these findings by illustrating the integration of GLP-1 RAs in diabetes and obesity clinics, with favorable physician-led prescribing patterns (Alsieni et al., 2024). Habeeb et al. (2024) demonstrated the adjunctive use of semaglutide with insulin in type 1 diabetics, reporting improved glycemic control and reduced insulin needs, suggesting novel applications beyond type 2 diabetes.

Taken together, the convergence of global and Saudi evidence underscores the universal efficacy of GLP-1 RAs, with contextual nuances in accessibility, awareness, and cultural

adoption. Future research should prioritize cost-effectiveness analyses and longitudinal Saudi cohorts to guide health policy integration.

Conclusion

This systematic review demonstrates that GLP-1 receptor agonists, particularly semaglutide and tirzepatide, offer unparalleled efficacy in weight loss and metabolic improvement among obese adults, with consistent safety profiles across populations. Saudi data affirm their clinical effectiveness and patient satisfaction, reinforcing the global evidence base for GLP-1 RAs in obesity management.

However, barriers such as medication cost, availability, and patient misconceptions remain. To maximize public health benefits, healthcare systems must prioritize equitable access, clinician training, and patient education. As obesity rates rise, GLP-1 RAs provide an evidence-based cornerstone for integrated obesity and diabetes management within Saudi Arabia's Vision 2030 framework.

Limitations

This review's findings are limited by the heterogeneity of study designs, durations, and populations. The inclusion of cross-sectional and retrospective designs introduces potential recall and selection bias. Additionally, Saudi-based studies had modest sample sizes and limited long-term follow-up, restricting generalizability. The absence of meta-analytic pooling precludes quantification of overall effect sizes. Nevertheless, the consistent trends across studies strengthen the reliability of qualitative conclusions.

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