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EFFICACY AND RISKS PROFILES OF "GLP-1 RECEPTOR AGONISTS" IN TYPE 2 DIABETES AND OBESITY: A SYSTEMATIC REVIEW OF BENEFITS AND RISKS

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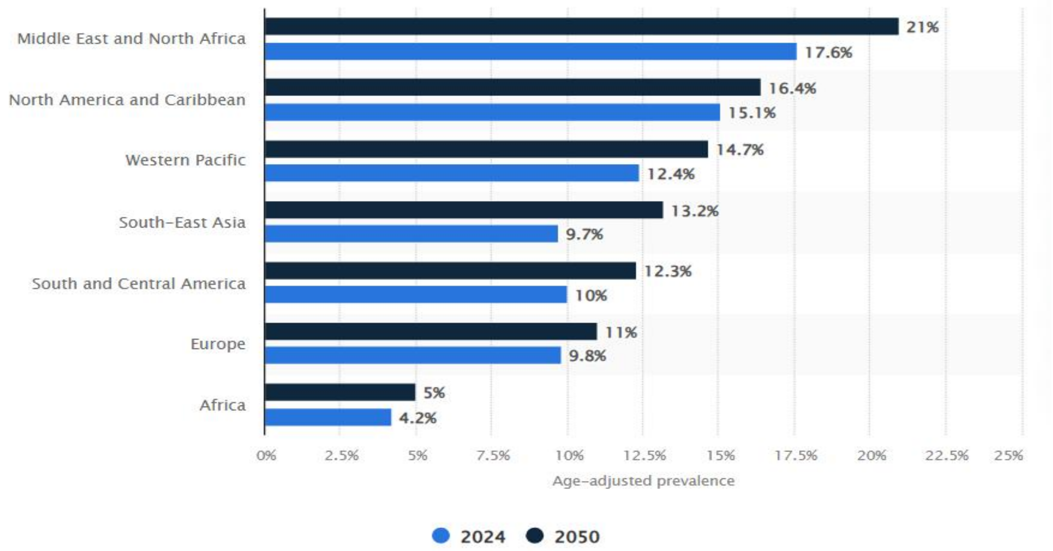
ABSTRACT
Type 2 diabetes (T2D) and obesity are among the most pressing global health challenges, with rising prevalence and severe associated complications, including cardiovascular disease, kidney failure, and premature mortality. "Glucagon-like peptide-1 receptor agonists (GLP-1RAs)" have emerged as promising therapeutic agents that address both conditions by improving glycemic control, reducing body weight, and offering cardiometabolic benefits. However, their clinical application is tempered by safety concerns and adherence challenges. This systematic literature review (SLR), conducted in accordance with PRISMA 2020 guidelines, critically examines both the efficacy as well as risk profiles of "GLP-1RAs" in the management of obesity and T2D. A search strategy was designed to identify 20 eligible articles from PubMed, Scopus, Cochrane, ScienceDirect, and Google Scholar. These articles mainly included randomized controlled trials, meta-analyses, cohort studies, and systematic reviews published between 2016 and 2025. Thematic analysis revealed consistent evidence supporting "GLP-1RAs"' benefits, including "significant reductions in HbA1c, fasting plasma glucose, body mass index, and waist circumference, alongside cardioprotective and renoprotective outcomes." Agents such as "semaglutide" and "tirzepatide" demonstrated the most pronounced effects, particularly when used in combination therapies. At the same time, gastrointestinal adverse events (e.g., nausea, vomiting, diarrhea) were the most common risks, often leading to high discontinuation rates. Rare but serious events such as pancreatitis, gallbladder disease, and potential cancer associations were also reported, though evidence remains inconclusive. Subgroup vulnerabilities and socioeconomic disparities further complicate treatment access and adherence. This review highlights the need for personalized prescribing strategies, better management of gastrointestinal side effects, and long-term pharmacovigilance. Future research should explore cost-effectiveness, patient adherence, and comparative safety against alternative therapies to guide clinical and policy decisions.
Keywords: Type 2 Diabetes, GLP-1RA, Obesity, Risks, Benefits, Weight Reduction

INTRODUCTION

"Type 2 diabetes (T2D) and obesity" have become the major global health concerns. They are high-prevalent "non-communicable diseases" (NCDs) worldwide (Ruze et al., 2023). Obesity is considered to increase the risk of T2D. Different factors contribute to T2D and obesity. These factors include sedentary lifestyle, increased age, intake of sugary drinks and processed food, sleep deprivation, and chronic stress (Zhang et al., 2023). According to WHO (2024), the number of individuals, suffering from T2D has increased from 200 million to 830 million from 1990 to 2022. This disease is highly prevalent in low as well as middle-income nations due to limited resources. Figure 1 shows that the prevalence of T2D is expected to increase worldwide, especially in the Middle East, North Africa, North America, and Caribbean regions. T2D is likely to cause kidney failure, amputation of lower limb, stroke, blindness and different heart issues (Statista, 2025). Similarly, in 2022, every 1 out of 8 individuals was found to be obese. In 2022, the prevalence of obese individuals increased by 890 million. About 160 million of these individuals aged between 5 to 19 years (WHO, 2025).

Figure 1

Prevalence of T2D worldwide (2024-2050)

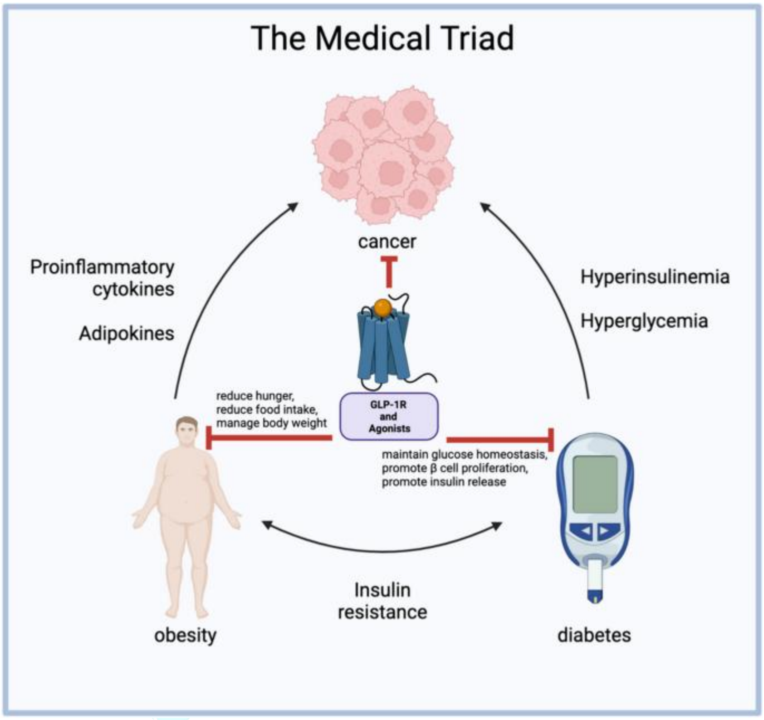


Source: (Statista, 2025)

A meta-analysis and SLR conducted by Cioana et al. (2022) showed that obesity is prevalent in 75.27% of the pediatric patients with T2D. The male participants were found to have higher rates of obesity as compared to female participants. At the same time, the Asian participants were found to have a lower prevalence of obesity than White participants. These findings show that obesity cannot be stated as a universal phenotype in T2D patients. According to Chong et al. (2023), "obesity-related disability-adjusted life years" (DALYs) increased by 0.48% from 2000-2019. However, an increase of 39.8% is also expected in obesity-related DALYs from 2020-2030. Different therapeutic agents have been formulated to manage T2D and obesity. One of these therapeutic agents include "GLP-1 Receptor Agonists (GLP-1RA)" integration. Alfaris et al. (2024) also demonstrated the significance of "GLP-1RAs" in T2D and obesity management. These agents are also found to be beneficial in impacting insulin sensitivity, glucose metabolism, insulin secretion and gastric emptying. Moreover, "GLP-1RAs" are also used for decreasing the levels of HbA1c, which is vital for T2D patients. They also prevent cardiovascular effects and facilitate weight loss. Therefore, "GLP-1RAs" are also being used for "obesity and T2D management." Another systematic review focused on the safety as well as efficacy of different "GLP-1RAs" such as danuglipron and orforglipron (Karakasis et al., 2023). Both danuglipron and orforglipron were found to have beneficial effects in reducing weight and controlling glycemic levels in T2D and obese patients. Moreover, "GLP1-Ras" are also used for treating "T2D, obesity, and cancer" (figure 2) (Ibrahim et al., 2024). This results in the formation of a medical triad.

Figure 2

Impact of GLP-1RA on "obesity, cancer, and T2D"



Source: (Ibrahim et al., 2024)

"GLP-1RAs" also possess potential risks which can impact their performance in managing obesity and T2D. For instance, "GLP-1RAs" have different gastrointestinal (GI) side effects. These side effects have decreased their usage. Some of the common GI adverse effects of GLP-IRAs include constipation, diarrhea, nausea, and vomiting, at higher doses (Lu et al., 2023). Other related GI effects include pancreatitis, gastroparesis, gallstones, and abdominal pain. These GI side effects are uncertain and involve various factors that vary between the patients and the "GLP-1RAs". The main contributors integrate GLP-RAs' duration of action. These agents, in combination with short-acting agents, are likely to induce vomiting and nausea as compared to long-acting agents for T2D treatment (Wharton et al., 2022). Another cohort study by Eberly et al. (2021) showed a decrease usage of GLP-1RA among patients with subgroup vulnerabilities. For instance, the "Hispanic, Black, and Asian T2D patients" in the US are unable to use "GLP-1RAs" due to lower income. The combination of "GLP-1RAs" and "tirzepatide" for T2D treatment is considered to cause different mental health issues among patients. However, a review by Di Stefano et al. (2025) reassured no association between this combination and suicidal thoughts among the patients. According to Rodriguez et al. (2025), different factors such as weight changes, socio-demographic factors, GI adverse events, and weight changes also contribute to discontinuation of "GLP-1RAs" among patients with T2D and obesity.

Although the previous SLRs and meta-analyses have focused on the efficacy and negative impacts of "GLP-1RAs", no current systematic review has focused on these factors simultaneously. This has encouraged the current systematic literature review (SLR) to overcome this limitation by focusing on both benefits (weight reduction, prevention of cardiovascular effects, and glycemic control) and risks (discontinuation of GLP-1RA, adverse events, and subgroup vulnerabilities) of "GLP-1RAs" within the context of obesity and T2D patients.

To fulfil the identified research gap, the present SLR has addressed the following research questions: (a) What are the potential benefits of "GLP-1RAs" in obesity and T2D? and (b) what are the potential risks of "GLP-1RAs" in obesity and T2D?

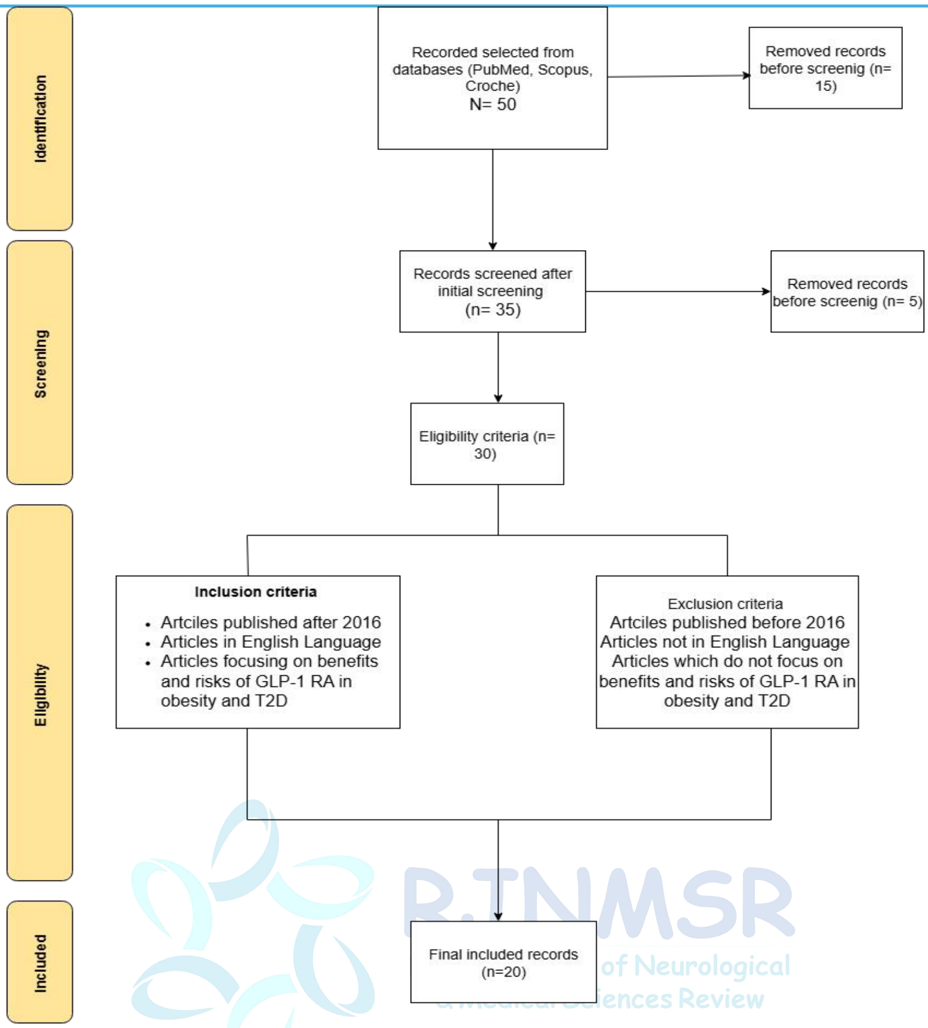
This SLR will be effective in highlighting "the benefits and risks of GLP-RAs in the treatment of T2D and obesity." This detailed SLR will be efficient in providing important information for endocrinologists and patients regarding the safe usage of "GLP-1RAs" for treating T2D and obesity. This evidence-based research will also present the beneficial and harmful effects of "GLP-1RAs" based on their dosage, duration of action, prescription, guidelines, monitoring, and target populations. The discussion on these factors will provide important safety clues and comparative effectiveness within the context of "GLP-1RAs" for future research. Additionally, this SLR can also encourage different policymakers to formulate and implement important guidelines considering the "benefits and potential risks of "GLP-1RAs" in T2D and obesity management."

Figure 3

PRISMA flow diagram

METHODOLOGY

The "Preferred Reporting Items for Systematic reviews and Meta-Analyses" (PRISMA) 2020 guidelines (Parums, 2021) were used for reporting this SLR. It is used for reporting different systematic reviews. It emphasizes consistency, completeness, and transparency. These guidelines are applicable in health sciences and other related fields. This makes it a suitable approach for current research. A PRISMA flow diagram (Figure 3) was also prepared to ensure an effective research process.



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2.1 SEARCH STRATEGY

As this SLR focuses on "the benefits and risks of "GLP-1RAs" in T2D and obesity treatment," the literature was searched from PubMed, Cochrane, ScienceDirect, and Scopus databases. The required literature was searched from a period of 2016 to 2025 with important language restrictions. The main keywords which were used for the search string included "GLP-1 receptor agonists; "Type 2 diabetes," "Obesity," "Risk," "Benefits," "Doses," "Weight Reduction," "Glycemic Control," and "Adverse Events." Manual searches were also performed by using Google Scholar. The selected studies/articles were then transported to EndNote, and all repeated citations were removed.

2.2 ELIGIBILITY CRITERIA

Effective eligibility criteria were formulated for the selection of required studies. Table 1 presents the "inclusion and exclusion criteria" that were developed for this SLR.

Table 1

Eligibility criteria

Inclusion	Exclusion
• Articles published after 2016.	• Articles published before 2016.
• Articles in the English language.	• Articles published in other languages.
• Articles discuss the "benefits/risks of GLP-1-Based Therapies in obesity."	• Articles do not discuss the "benefits and risks of GLP-1-Based Therapies in obesity."
• The article discusses the "benefits/risks of GLP-1-Based Therapies in Type 2 diabetes."	• The article which do not discuss the "benefits and risks of GLP-1-Based Therapies in Type 2 diabetes."

2.3 OUTCOMES

The studies/ reviews/ meta-analyses that presented "the benefits and potential risks of "GLP-1RAs" in the treatment of T2D and obesity" were selected. The selected studies mainly included RCTs, systematic reviews, meta-analyses, cohort studies, and other related research.

The benefits of the "GLP-1RAs" mainly included their role in "weight reduction, glycemic control, prevention of heart diseases, and other related benefits." However, the potential risks of "GLP-1RAs" mainly included their GI side effects, subgroup vulnerabilities, and other related issues.

2.4 SELECTION OF STUDIES

Under this step, the records obtained on the basis of the search strategy were screened. For this initial screening, the title and abstract of the studies were considered by the researcher. No study was excluded on the basis of any disagreement in this process to increase the selection process' sensitivity. Therefore, a total of 55 articles were selected initially for the current SLR.

2.5 DATA EXTRACTION

The preliminary data extracted was evaluated on the basis of "Article type, Author, Publication Years, Title, Journal, Abstract, Keywords, Country, What are the potential benefits of GLP-1 receptor agonists in obesity and type 2 diabetes? and what are the potential risks of GLP-1 receptor agonists in obesity and type 2 diabetes?"

This process was carried out independently, and any identified discrepancy was addressed. The extracted data was presented in the form of an Excel sheet based on the aforementioned characteristics. Any duplication of the study was removed, and the eligibility criteria were considered. Based on these factors, a final sample of 20 articles was selected for further analysis.

2.6 RISK OF BIAS (ROB) ASSESSMENT

Within the context of the current SLR, the ROB within the integrated studies was determined independently by the researcher. In this regard, the guidelines of the PRISMA statement 2020 were considered. Any disagreements during this process were dealt with the help of an external researcher.

2.7 DATA ANALYSIS

This SLR was exploratory in nature. It supported the implementation of inductive analysis. For this purpose, thematic analysis was conducted on the extracted data. Six phases of thematic analysis by Braun and Clarke (2006) were performed. No predefined conceptual framework was integrated due to the analytic approach of the SLR. The following steps were performed for this analysis: (1) the researcher familiarized himself with the extracted data by re-reading them, leading to the formulation of initial notes, (2) after this step of familiarization, coding of the data was done by identifying and labelling of repeated patterns regarding the benefits/ risks of "GLP-1RAs" in obesity and T2D treatment, (3) after the initial coding, the formulated codes were then organized in the form of themes, (4) these themes were then reviewed by the researcher and their consistency was ensured, (5) each theme's specifics were clarified and they were named properly and (6) a final report of the main findings was presented to address the proposed research questions.

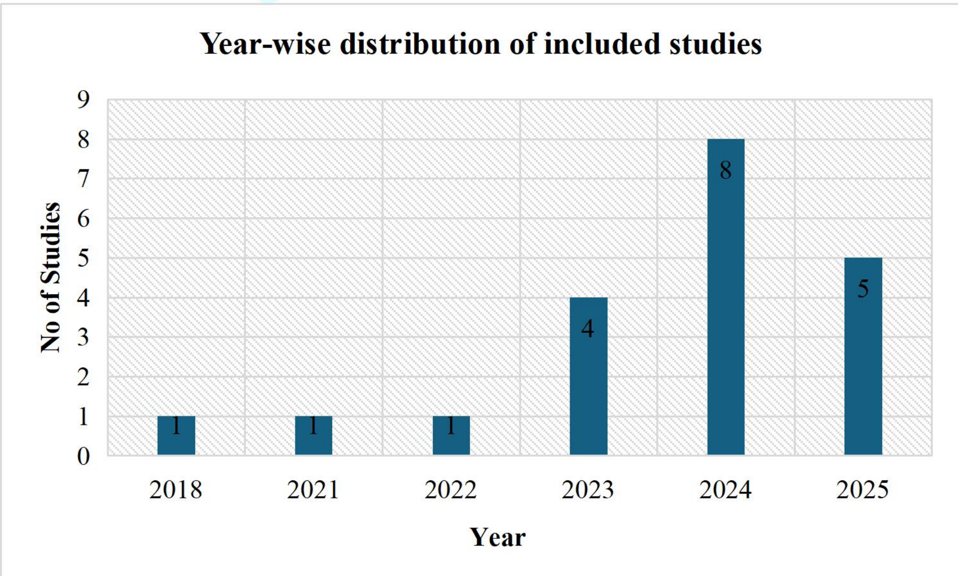
RESULTS

3.1 DESCRIPTION OF INCLUDED STUDIES

20 peer-reviewed journal articles were analyzed in this SLR. They were published between 2018 and 2025. They mainly reflected on the growing research interest in the efficacy and safety of "GLP-1RAs" in "type 2 diabetes" and "obesity" management. The earliest study (Dalsgaard et al., 2018) offered a narrative review of cardiovascular risk factor outcomes, while more recent contributions (de Oliveira Almeida et al., 2024; Do et al., 2024; Ghusn & Hurtado, 2024; Guo et al., 2024; Kim & Yoo, 2025; Li et al., 2024; Moiz et al., 2025) highlight the surge in systematic reviews, meta-analyses, and narrative syntheses in this field.

Figure 4

Distribution of included studies by year



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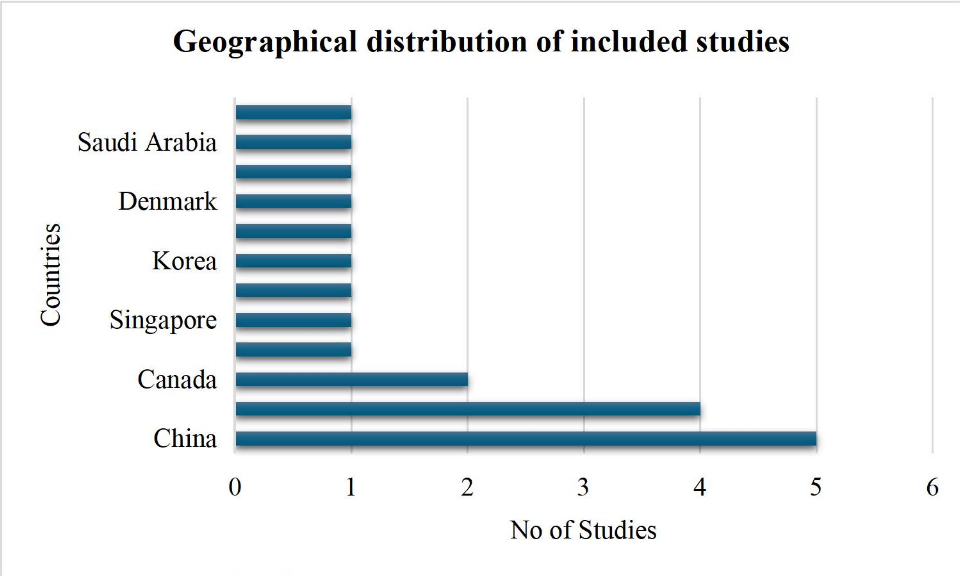
Geographic distribution was broad, with studies originating from Asia (China, Korea, Singapore, Taiwan, Saudi Arabia) (Kim & Yoo, 2025; Li et al., 2024; Liu et al., 2023; Ma et al., 2023; Wong et al., 2025), Europe (Italy, Denmark, Greece, UK) (Dalsgaard et al., 2018; Giugliano et al., 2021; Patoulias et al., 2023), and the Americas (United States, Brazil, Canada) (de Oliveira Almeida et al., 2024; Ghusn & Hurtado, 2024; Sabina & Alsamman, 2024; Sodhi et al., 2023). This diversity provides insights into both global trial data and region-specific safety concerns.

Figure 5

Distribution of included studies by geography



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The clinical focus varied: some studies concentrated on cardiovascular outcomes (de Oliveira Almeida et al., 2024; Giugliano et al., 2021; Patoulias et al., 2023; Sabina & Alsamman, 2024), while others examined weight loss and obesity management (Abdullah bin Ahmed, 2024; Li et al., 2024; Liu et al., 2023; Wong et al., 2025). Several articles assessed safety signals, including gastrointestinal events (Sodhi et al., 2023), pancreatitis (Guo et al., 2024), gallbladder disease (He et al., 2022), and cancer risk (Zhong et al., 2025). Discontinuation patterns were also highlighted (Do et al., 2024), underscoring tolerability challenges.

3.2 THEMATIC FINDINGS ON BENEFITS (RQ1)

3.2.1 Glycemic Control

The included studies have also highlighted the significant role of GLP-1 in glycemic regulation. Different meta-analyses and RCTs have also reported significant impacts of "GLP-1RAs" in decreasing hemoglobin (HbA1c) and fasting plasma glucose (FPG). This demonstrates different benefits of "GLP-1RAs" in managing T2D and obesity. Wong et al. (2025) also documented that "GLP-1RAs" enhance glucose-stimulated insulin release and decrease the postprandial glucose variants to mediate challenges in clinical substantial differences in HbA1c. A study by Patoulias et al. (2023) also showed a decrease in FPG (MD = -0.53 mmol/L) and an increase in lipid profiles. This confirms the double metabolic advantage of "GLP-1RAs". In mega-comparative surveys, "GLP-1RAs" are found to be more effective than anti-diabetic agents within the context of glycemic control. Ma et al. (2023) demonstrated that the effects of "GLP-1RAs" have better HbA1c decreases over "SGLT-2" inhibitors (mean difference -0.39%), especially in overweight or obese patients with T2DM.

Giugliano et al. (2021) have also emphasized the significance of "GLP-1RAs" in decreasing HbA1c levels in different cardiovascular outcome trials (CVOTs). Within this context, "tirzepatide" has produced the most significant effect (-2.10) among 15 "GLP-1RAs" studied. The evidence is further supported by subgroup findings. It was proven that continuous-acting "GLP-1RAs" CAs have greater glycemic benefits compared to short-acting formulations (Dalsgaard et al., 2018). It was beneficial to patients who had co-morbidities like chronic kidney disease (CKD). According to Chen et al. (2025) GLP-1RA is not used for decreasing glycemic levels, it is also used for reducing risks of eGFR deterioration and mortality. Altogether, the results obtained support the ability of "GLP-1RAs" to provide a stable glycemic control in diverse patient populations and comorbid groups.

3.2.2 Weight Loss and Obesity Outcomes

One of the most common benefits of "GLP-1RAs" include weight reduction. These agents are found to be clinically beneficial in obesity-focused populations, as compared with placebo. Wong et al. (2025) have also reported significance of "GLP-1RAs" in reducing mean body weight (−4.57 kg), BMI (−2.07 kg/m²), and waist circumference (−4.55 cm). Similarly, Liu et al. (2023) confirmed conclusive evidence of weight-loss efficacy through trial-sequential analysis. This study reported a weight decrease of −5.32 kg and BMI reduction of −2.37 kg/m², with "semaglutide".

Meta-analyses reinforced these findings and emphasized clinically relevant thresholds of ≥5% body-weight reduction. Ma et al. (2023) demonstrated that both "GLP-1RAs" and "SGLT-2" inhibitors produced significant weight-loss effects, although "GLP-1RAs" were superior in lowering HbA1c. Other studies highlighted the magnitude of placebo-corrected reductions, with Ghusn and Hurtado (2024) reporting liraglutide achieving approximately 5% weight loss, "semaglutide" 12%, and "tirzepatide" 18%.

Surgery and chemotherapy were also better. Li et al. (2024) discovered that cagrelintide "semaglutide" (CagriSema) showed more weight loss than "semaglutide" alone, with a weight loss of 14.13 kg/kg. Dose-response analysis reported that the higher the dose, the more significantly he was deemed to be effective. The potential mechanism that received explanations in the increased satiety, arrested appetite, slower gastric emptying, and control of energy expenditure pathways was referred to as the mechanism used to explain these outcomes (Moiz et al., 2025; Wong et al., 2025). The combined findings show great evidence of the ability of "GLP-1RAs" in long-term obesity treatment with high probabilities of their reliability and reproducibility.

3.2.3 Cardiovascular Outcomes

Another dominant theme was the cardioprotective benefit of "GLP-1RAs". de Oliveira Almeida et al. (2024) reported improvements in blood pressure (systolic −4.76 mmHg, diastolic −1.41 mmHg) and reductions in myocardial infarction risk (RR 0.72). Giugliano et al. (2021) further demonstrated a 14% reduction in major adverse cardiovascular events (MACE) compared with placebo, alongside significant reductions in cardiovascular death (−13%), stroke (−16%), and all-cause mortality (−12%).

Large outcome trials such as SUSTAIN-6 and SELECT also provided compelling evidence.

Sabina and Alsamman (2024) highlighted a 20% reduction in composite cardiovascular endpoints among overweight or obese patients without diabetes, while "semaglutide" 2.4 mg was associated with fewer nephropathy events. Improvements in lipid parameters were also consistent. Patoulias et al. (2023) found reductions in total cholesterol and LDL-C and modest increases in HDL-C, while de Oliveira Almeida et al. (2024) observed improvements in overall lipid profiles in obese and diabetic populations.

Evidence from subgroup analyses supports the durability of these effects. Dalsgaard et al. (2018) found modest but reproducible reductions in blood pressure and cholesterol across head-to-head comparisons, and Chen et al. (2025) reported protective renal outcomes (OR 0.85 for composite kidney decline) that likely contribute to reduced long-term CV risk. Taken together, the evidence establishes "GLP-1RAs" as not only anti-diabetic and anti-obesity agents but also effective cardiometabolic therapies.

3.2.4 Psychosocial and Quality of Life Benefits

Although less frequently reported, psychosocial and quality of life improvements were noted across several studies. Wong et al. (2025) described increased satiety and appetite suppression, outcomes that can enhance lifestyle adherence and improve dietary self-control. Other mechanistic analyses Moiz et al. (2025) suggested potential neuropsychological pathways, including modulation of hypothalamic appetite circuits and effects on gut microbiota, that could support improved well-being beyond weight loss.

Sabina and Alsamman (2024) also highlighted improved adherence to treatment in long-term trials, noting that cardiometabolic benefits likely motivated patients to continue therapy. Furthermore, narrative reviews such as Moiz et al. (2025) suggested broader mental health implications, including reductions in depressive symptoms or lifestyle-related stigma associated with obesity, though these findings remain preliminary. Overall, the psychosocial benefits, while not as extensively studied as glycemic or cardiovascular outcomes, reflect an important and emerging dimension of GLP-1RA therapy.

Table 2

Potential Benefits of GLP-1 Receptor Agonists in Obesity and Type 2 Diabetes

Study	Population Focus	Weight Loss Outcomes	Glycemic Control	Cardiovascular Outcomes	Renal/Other Benefits	Psychosocial / Other	Overall Stated Benefit
(de Oliveira Almeida et al., 2024)	Overweight/obesity ± T2DM	Effective weight loss reported	Improved glycemic control, lipid profile	↓ SBP (−4.76 mmHg), ↓ DBP (−1.41 mmHg), ↓ MI (RR 0.72)	-	-	Demonstrated combined benefit for weight, glycaemia, CV risk
(Wong et al., 2025)	Obesity/overweight	−4.57 kg weight, −2.07 BMI, −4.55 cm waist	↑ insulin secretion, ↓ postprandial glucose	-	-	↑ satiety, appetite suppression	Significant weight reduction and metabolic regulation
(Patoulias et al., 2023)	Obesity with antipsychotic drug use	−3.80 kg weight, −1.04 BMI	↓ FPG (−0.53 mmol/L)	↓ TC (−0.46 mmol/L), ↓ LDL-C (−0.31), ↑ HDL-C (0.09)	-	-	"GLP-1RAs" improve body weight, glucose, and lipid profile
(Kim & Yoo, 2025)	Obesity + T2DM	Supports weight management	Improved glycemic regulation	CV outcome improvements reported from major trials	-	Clinical approvals for weight loss and diabetes	Established clinical benefit across obesity and T2DM
(Ma et al., 2023)	Obesity ± T2DM	≥5% weight loss achieved	↓ HbA1c, ↓ FPG; superior to "SGLT-2"i for HbA1c (MD −0.39%)	-	-	-	"GLP-1RAs" effective for glycaemia and weight; superior to "SGLT-2"i in HbA1c
(Liu et al.,	Non-diabetic	−5.32 kg weight, −2.37	-	-	-	-	Conclusive weight-loss effect; "semaglutide"

2023)	obesity	BMI, −4.30 cm waist					most effective
(Li et al., 2024)	Obesity	CagriSema: −14.13 kg weight	↓ HbA1c (−0.33%)	-	-	-	High-dose and combination therapy achieved greatest weight loss
(Ghusn & Hurtado, 2024)	Obesity	Liraglutide ~5%, "semaglutide" ~12%, "tirzepatide" ~18% placebo-corrected weight loss	-	-	-	-	Strong agent-specific weight-loss efficacy
(Sabina & Alsamman, 2024)	Obesity ± T2DM	Effective for weight loss	Glycemic benefits reported	SUSTAIN-6: ↓ MACE (6.6% vs 8.9%); SELECT: ↓ CV events by 20%	↓ nephropathy rates	-	"tirzepatide" and "semaglutide" highlighted as leading agents
(Sodhi et al., 2023)	T2DM	-	↓ HbA1c, ↓ FPG	↓ CV risk, improved lipids	-	-	"GLP-1RAs" beneficial for glycaemia and cardiovascular health
(Yao et al., 2024)	T2DM	-	HbA1c lowering	↓ MACE by 14%, ↓ CV death (−13%), ↓ stroke (−16%), ↓ HF hospitalizations (−10%), ↓ mortality (−12%)	↓ renal composite outcome (−17%)	-	Strong cardiorenal protection
(Giugliano et al., 2021)	T2DM	↓ body weight	↓ HbA1c, ↓ FPG	Modest ↓ SBP and ↓ total cholesterol	-	-	Continuous-acting agents showed stronger glycemic effects

(Dalsgaard et al., 2018)	CKD patients	-	-	↓ CV outcomes	↓ risk of eGFR decline ≥30% (OR 0.78), ≥40% (OR 0.76), ≥50% (OR 0.72)	↓ all-cause mortality	Significant kidney and CV protective effects
(Chen et al., 2025)	T2DM	-	Improved glycaemia without hypoglycemia risk	↓ MACE in large CVOTs	-	-	Safe glucose regulation + cardiometabolic benefit
(Guo et al., 2024)	Obesity + T2DM	Substantial weight loss highlighted	-	CV benefit potential emphasized	Broader indications: liver, neurodegenerative disease, substance use	-	Expanded therapeutic scope beyond diabetes/obesity
(Moiz et al., 2025)	T2DM	-	Glycemic control	↓ CVD risk reported in prior studies	-	-	Effective for diabetes + weight reduction per cited trials
(He et al., 2022)	Obesity	-	-	-	-	-	Discussed therapeutic role: "GLP-1RAs" reduce weight during use (focus on post-discontinuation weight gain)
(Abdullah bin Ahmed,	Obesity/T2DM	-	-	-	-	-	Highlighted clinical benefits before discontinuation

2024)							
(Do et al., 2024)	T2DM (colorectal cancer risk focus)	-	Glycemic management	CV support noted in the background.	-	-	"GLP-1RAs" maintain weight and cardiovascular health alongside glucose control
(Zhong et al., 2025)	Mixed	Appetite suppression, caloric intake reduction, ↑ energy expenditure	Improved insulin secretion, ↓ glucagon	↓ CV risk	Other metabolic benefits (gut microbiota, brown fat activation)	-	Mechanistic support for weight and glucose regulation

3.3 THEMATIC FINDINGS ON RISKS (RQ2)

3.3.1 Gastrointestinal Adverse Events

Gastrointestinal adverse events (GI AEs) were the most frequently reported and well-documented risks of "GLP-1RAs". Across trials and observational studies, nausea, vomiting, diarrhea, and constipation were consistently identified as the most common side effects. Kim and Yoo (2025) noted that up to 50–60% of patients experienced GI AEs during early treatment. Patoulias et al. (2023) and Ghusn and Hurtado (2024) confirmed that these effects were typically mild to moderate and transient, though they frequently led to discontinuation.

Discontinuation due to GI events was especially high with "semaglutide". de Oliveira Almeida et al. (2024) and Sabina and Alsamman (2024) reported higher dropout rates among "semaglutide" users compared with placebo, particularly at higher doses. Yao et al. (2024) reinforced this finding in a network meta-analysis, identifying gastrointestinal events as the main safety signal across the class.

Several studies also raised procedural concerns. Ghusn and Hurtado (2024) highlighted delayed gastric emptying as a risk factor for aspiration during anesthesia and difficulties with bowel preparation for colonoscopy. Collectively, these findings suggest that while GI AEs are manageable with titration and dose adjustments, they remain the leading cause of intolerance and discontinuation.

3.3.2 Rare but Notable Adverse Events

Beyond gastrointestinal issues, rare but serious adverse events were identified. Gallbladder and biliary disorders emerged repeatedly. Kim and Yoo (2025) and Moiz et al. (2025) reported increased risks of cholelithiasis and cholecystitis, with pooled relative risks ranging from 1.27 to 1.55. Risk was found to be higher in weight-loss trials and at higher doses (Moiz et al., 2025).

Pancreatitis was another major concern. Sodhi et al. (2023) found markedly increased risks of acute pancreatitis (HR 9.09), bowel obstruction, and gastroparesis among patients on "GLP-1RAs" compared with bupropion–naltrexone. Chen et al. (2025) corroborated these findings in pharmacovigilance analyses, identifying 6,751 reports of acute pancreatitis in FAERS data, with liraglutide showing the strongest disproportionality signal.

Cancer risk signals were mixed. Zhong et al. (2025) reported a possible increased risk of colorectal cancer (RR 2.31) across retrospective cohort studies, though results were heterogeneous and confounded. Guo et al. (2024) noted that earlier concerns about thyroid cancer have largely been refuted, but gallbladder and psychiatric risks require continued surveillance.

Other unique findings included a consistent increase in resting heart rate with liraglutide across head-to-head trials (Giugliano et al., 2021) and potential sarcopenia or lean mass loss during weight reduction (Kim & Yoo, 2025). These data illustrate that while rare events are not universally observed, they remain clinically significant and warrant ongoing monitoring.

3.3.3 Discontinuation and Adherence Issues

High discontinuation rates were a recurrent theme. Do et al. (2024) reported that 26% of patients discontinued GLP-1RA therapy at 3 months, increasing to 30.8% at 6 months and 36.5% at 12 months. Among patients with obesity only, discontinuation rates were as high as 50% at one year. Abdullah bin Ahmed (2024) similarly reported that discontinuation often led to weight regain and a reversal of cardiometabolic benefits, highlighting the challenge of long-term adherence.

de Oliveira Almeida et al. (2024) and Sabina and Alsamman (2024) further demonstrated that discontinuation was frequently linked to intolerable GI side effects. Ma et al. (2023) also reported higher discontinuation rates compared with "SGLT-2" inhibitors, underscoring the comparative tolerability disadvantage. Collectively, these findings reveal that adherence is a critical barrier to maximizing the long-term benefits of GLP-1RA therapy.

3.3.4 Subgroup Vulnerabilities

Subgroup-specific vulnerabilities were less consistently reported but remain noteworthy. Chen et al. (2025) highlighted greater renal benefits in patients with impaired kidney function, but safety risks, particularly pancreatitis, may be higher in such populations. Kim and Yoo (2025) flagged psychiatric vulnerabilities, such as depression and suicidal ideation, which require close monitoring.

Geographic variability was also apparent. Some pharmacovigilance signals (e.g., pancreatitis in FAERS data) were stronger in regions with higher reporting standards, suggesting that underreporting may bias results in other contexts. Moiz et al. (2025) indicated that risk profiles may differ by drug and dose, suggesting population-level differences in tolerability. Overall, while most patients tolerate "GLP-1RAs" well, certain vulnerable subgroups warrant tailored monitoring.

Table 3

Potential Risks of GLP-1 Receptor Agonists in Obesity and Type 2 Diabetes

Study	Population Focus	Gastrointestinal Risks	Gallbladder / Biliary Risks	Pancreatitis / Cancer Risks	Cardiovascular / Other Risks	Discontinuation / Adherence	Overall Stated Risk
(de Oliveira Almeida et al., 2024)	Obesity, T2DM	Common GI AEs, higher with high-dose; nausea/vomiting/diarrhea	Gallbladder disorders noted	Pancreatitis risk cited	-	↑ discontinuation with "semaglutide"	Safety concerns at higher doses; GI events main driver
(Patoulias et al., 2023)	Obesity + antipsychotic use	Mostly mild, transient nausea, vomiting, diarrhea	-	-	-	-	Generally well tolerated, GI side effects only
(Kim & Yoo, 2025)	General	GI AEs common (50-60% early); constipation, nausea, diarrhea, vomiting	↑ gallbladder/biliary disease	Pancreatitis risk debated; flagged ocular risks (retinopathy, NAION), psychiatric signals (suicidal ideation)	Sarcopenia risk (lean mass loss ~40% of WL)	-	Broad safety concerns, highlight the need for monitoring
(Ma et al., 2023)	Obesity, T2DM	↑ adverse events vs placebo/"SGLT-2"i	-	-	-	↑ discontinuation vs "SGLT-2"i	Safety profile is less favorable than "SGLT-2"i
(Liu et al., 2023)	Obesity (non-diabetic)	Overall AE risk "low to moderate" ("semaglutide")	-	-	-	-	Low-moderate AE risk in trials
(Ghusn & Hurtado,	Obesity	Common GI AEs: nausea, diarrhea,	Rare gallbladder	Rare acute pancreatitis reported;	-	-	AE profile dominated by GI +

2024)		constipation, vomiting	events	aspiration risk flagged peri-procedure			rare serious
(Sabina & Alsamman, 2024)	Mixed	GI events are common; higher with "semaglutide" vs placebo	↑ gallbladder-related disorders with "semaglutide" in trials	Pancreatitis risk is inconsistent across large trials	-	↑ discontinuation due to GI AEs	Heterogeneous signals, dose/drug dependent
(Sodhi et al., 2023)	Obesity (weight-loss trials)	-	-	↑ pancreatitis (HR 9.09), bowel obstruction (HR 4.22), gastroparesis (HR 3.67)	-	-	Rare but serious events highlighted
(Yao et al., 2024)	T2DM	↑ GI AE risk vs placebo; dose-related	-	-	-	↑ discontinuation risk	GI safety main class-wide signal
(Giugliano et al., 2021)	T2DM	n/a	n/a	n/a	↑ resting heart rate with liraglutide in trials	-	HR increase flagged in head-to-head studies
(Chen et al., 2025)	CKD patients	-	-	Robust pancreatitis signal (6,751 FAERS reports; highest for liraglutide/exenatide)	-	-	Strong pharmacovigilance signal for acute pancreatitis
(Guo et al., 2024)	T2DM	GI AEs noted	Gallbladder disorders ongoing concern	Pancreatic/thyroid cancer early signals mostly refuted;	Lean mass loss, weight regain after	-	Long

		psychiatric & aspiration risks noted	discontinuation	

DISCUSSION

The utilization of “GLP-1RAs” is rapidly increasing in patients with “T2D and obesity.” These therapeutic agents are considered to possess different benefits and potential risks. In recent literature, many systematic reviews and meta-analyses have focused on determining the benefits and risks of “GLP-1RAs” separately. This provides an opportunity for the present SLR to evaluate “the risks and benefits of “GLP-1RAs”” simultaneously.

The findings of this SLR have highlighted different benefits of “GLP-1RAs” in T2D and obesity patients. The main benefits of “GLP-1RAs” include glycemic control, weight reduction, improved quality of life (QoL) and prevention of cardiovascular issues. This study has also highlighted the significance of “GLP-1RAs” in decreasing HbA1c and FPG for managing T2D. Past research has also supported the anti-diabetic impact of “GLP-1RAs” (Wong et al., 2025). It has also been observed that continuous-acting “GLP-1RAs” are more effective as compared to the short-acting “GLP-1RAs” (Dalsgaard et al., 2018). They help in decreasing glycemic levels which is vital to manage insulin secretion. The role of “GLP-1RAs” is also inevitable within the context of weight reduction. For instance, different “GLP-1RAs”, such as ““semaglutide” and “tirzepatide”” are being used in weight reduction (Ghusn & Hurtado, 2024). Another study by Ma et al. (2023) has also highlighted the role of “GLP-1RAs” in weight reduction.

Moreover, T2D and obesity are also found to be associated with different cardiovascular diseases. Therefore, “GLP-1RAs” are also being used for preventing cardiovascular issue in T2D and obesity patients. According to Giugliano et al. (2021) “GLP-1RAs” are found to be effective in reducing MACE. Thus, “GLP-1RAs” also help in improving the overall QoL. “GLP-1RAs” also possess different risks. The main risks of “GLP-1RAs” include GI side effects, other adverse events, and subgroup vulnerabilities. Different GI AEs of “GLP-1RAs” include “nausea, vomiting, diarrhea, and constipation” (Kim & Yoo, 2025). Other AEs of these agents include pancreatitis, gastroparesis, gallstones, and abdominal pain. Moreover, different socio-economic factors also contribute to the discontinuation of “GLP-1RAs”. Therefore, the identification of potential risks of “GLP-1RAs” can help healthcare professionals to make important dose adjustments.

4.1 RESEARCH IMPLICATIONS

This study has highlighted the risks/ benefits of “GLP-1RAs” in obesity and T2D patients. This has helped in increasing the novelty of the current research. Previous systematic reviews and meta-analyses (Karakasis et al., 2023; Rodriguez et al., 2025) have mainly focused on the risks or benefits of “GLP-1RAs”. This has encouraged the current SLR to focus on both risks and benefits of “GLP-1RAs” simultaneously. This can also encourage future researchers to explore other potential risks of “GLP-1RAs” in association with different anti-diabetic drugs. Additionally, this research has also provided a detailed understanding of different adverse events of “GLP-1RAs” in patients with T2D and obesity.

The findings of this evidence-based research can also provide important GLP-1RA-related information for endocrinologists, patients, and other healthcare professionals. This can help them manage the dose of the “GLP-1RAs” according to the requirements of the patients. This approach will be beneficial in reducing the risks of these therapeutic agents. In addition, the findings of this research can also motivate policymakers to develop and implement effective guidelines for the usage and administration of "GLP-1RAs" among patients with T2D and obesity.

4.2 STRENGTHS AND LIMITATIONS

Although this study largely contributed to the evaluation of different benefits and risks of "GLP-1RAs" in obesity and T2D treatment simultaneously, it also includes a few limitations. This review was limited to meta-analyses and systematic reviews conducted within the context of the benefits/ risks of "GLP-1RAs" in treating T2D and obesity. This was due to the limited number of current primary studies conducted in this regard. The data extraction and analysis techniques were also limited to the benefits and risks of "GLP-1RAs" in T2D and obesity. This decreases the value of this SLR, preventing an in-depth interpretation of associated findings. Another limitation observed in this SLR is the lack of transparency around the findings and conflicts of interest. The inclusion criteria are also limited to the studies that focus on the benefits/ risks of "GLP-1RAs". However, no particular population or research study design has been defined. Similarly, cost-effectiveness, patient adherence, and comparative safety are also essential topics within the context of "GLP-1RAs" (Yang et al., 2021), which are not studied in the current SLR.

4.3 FUTURE RESEARCH

Although this study plays a vital role in improving literature regarding "GLP-1RAs", it also incorporates the aforementioned limitations. These limitations can be overcome in future research. First, the future research can focus on integrating different cohort studies and RCTs to explore different benefits/ risks of the "GLP-1RAs". Second, the data extraction and analysis techniques can be improved by developing a detailed eligibility criteria. For this purpose, specific population and study settings can be defined. Finally, other factors related to "GLP-1RAs" such as safety, cost-effectiveness and patient adherence, can also be discussed in future studies.

CONCLUSION

Along with different benefits, "GLP-1RAs" also possess potential risks. This SLR has been effective in highlighting different benefits/ risks of "GLP-1RAs". Different benefits of "GLP-1RAs" include their role in glycemic control, insulin secretion, weight reduction, and insulin sensitivity. Additionally, this SLR has also reported the significance of "GLP-1RAs" in reducing the cardiovascular impacts of obesity and T2D. In this study, the potential risks of "GLP-1RAs" have also been presented. A few of these risks include GI AEs, subgroup vulnerabilities, and discontinuation of "GLP-1RAs". Common GI AEs of "GLP-1RAs" include diarrhea, vomiting and nausea. Other potential risks of "GLP-1RAs" include pancreatitis, gastroparesis, gallstones, and abdominal pain. Moreover, socio-economic disparities and other related factors also contribute to the discontinuation of "GLP-1RAs". Therefore, the findings of this SLR have emphasized the integration of personalized prescribing strategies for "GLP-1RAs". This approach is crucial to improve the management of T2D and obese patients. Thus, the current research can also be beneficial for improving the clinical practice of different endocrinologists and other healthcare professionals. It can guide them regarding the effective uses of "GLP-1RAs".

REFERENCES

Abdullah bin Ahmed, I. (2024). A Comprehensive Review on Weight Gain following Discontinuation of Glucagon-Like Peptide-1 Receptor Agonists for Obesity. *Journal of Obesity*, *2024*(1), 8056440. https://doi.org/https://doi.org/10.1155/2024/8056440

Alfaris, N., Waldrop, S., Johnson, V., Boaventura, B., Kendrick, K., & Stanford, F. C. (2024). GLP-1 single, dual, and triple receptor agonists for treating type 2 diabetes and obesity: a narrative review. *EClinicalMedicine*, 75. https://doi.org/10.1016/j.eclinm.2024.102782

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative research in psychology*, 3(2), 77-101. https://doi.org/10.1191/1478088706qp063oa

Chen, J.-Y., Hsu, T.-W., Liu, J.-H., Pan, H.-C., Lai, C.-F., Yang, S.-Y., & Wu, V.-C. (2025). Kidney and Cardiovascular Outcomes Among Patients With CKD Receiving GLP-1 Receptor Agonists: A Systematic Review and Meta-Analysis of Randomized Trials. *American Journal of Kidney Diseases*, *85*(5), 555-569.e551. https://doi.org/10.1053/j.ajkd.2024.11.013

Chong, B., Jayabaskaran, J., Kong, G., Chan, Y. H., Chin, Y. H., Goh, R., Kannan, S., Ng, C. H., Loong, S., & Kueh, M. T. W. (2023). Trends and predictions of malnutrition and obesity in 204 countries and territories: an analysis of the Global Burden of Disease Study 2019. *EClinicalMedicine*, *57*. https://doi.org/10.1016/j.eclinm.2023.101850

Cioana, M., Deng, J., Nadarajah, A., Hou, M., Qiu, Y., Chen, S. S. J., Rivas, A., Banfield, L., Toor, P. P., & Zhou, F. (2022). The prevalence of obesity among children with type 2 diabetes: a systematic review and meta-analysis. *JAMA Network Open*, *5*(12), e2247186-e2247186. https://doi.org/10.1001/jamanetworkopen.2022.47186

Dalsgaard, N. B., Vilsbøll, T., & Knop, F. K. (2018). Effects of glucagon-like peptide-1 receptor agonists on cardiovascular risk factors: A narrative review of head-to-head comparisons. *Diabetes, Obesity and Metabolism*, *20*(3), 508-519. https://doi.org/https://doi.org/10.1111/dom.13128

de Oliveira Almeida, G., Nienkötter, T. F., Balieiro, C. C. A., Pasqualotto, E., Cintra, J. B., Carvalho, H. C. P., Silva, A. L. S., Kabariti, J. C., Minucci, B. S., Bertoli, E. D., & Guida, C. M. (2024). Cardiovascular Benefits of GLP-1 Receptor Agonists in Patients Living with Obesity or Overweight: A Meta-analysis of Randomized Controlled Trials. *Am J Cardiovasc Drugs*, *24*(4), 509-521. https://doi.org/10.1007/s40256-024-00647-3

Di Stefano, R., Rindi, L. V., Baldini, V., Rossi, R., Pacitti, F., Jannini, E. A., & Rossi, A. (2025). Glucagon-Like Peptide-1 Receptor Agonists, dual GIP/GLP-1 Receptor Agonist "tirzepatide" and Suicidal Ideation and Behavior: A Systematic Review of Clinical studies and Pharmacovigilance Reports. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 103238. https://doi.org/10.1016/j.dsx.2025.103238

Do, D., Lee, T., Peasah, S. K., Good, C. B., Inneh, A., & Patel, U. (2024). GLP-1 Receptor Agonist Discontinuation Among Patients With Obesity and/or Type 2 Diabetes. *JAMA Network Open*, 7(5), e2413172-e2413172. https://doi.org/10.1001/jamanetworkopen.2024.13172

Eberly, L. A., Yang, L., Essien, U. R., Eneanya, N. D., Julien, H. M., Luo, J., Nathan, A. S., Khatana, S. A. M., Dayoub, E. J., & Fanaroff, A. C. (2021). Racial, ethnic, and socioeconomic inequities in glucagon-like peptide-1 receptor agonist use among patients with diabetes in the US. JAMA Health Forum,

Ghusn, W., & Hurtado, M. D. (2024). Glucagon-like Receptor-1 agonists for obesity: Weight loss outcomes, tolerability, side effects, and risks. *Obesity Pillars*, *12*, 100127. https://doi.org/https://doi.org/10.1016/j.obpill.2024.100127

Giugliano, D., Scappaticcio, L., Longo, M., Caruso, P., Maiorino, M. I., Bellastella, G., Ceriello, A., Chiodini, P., & Esposito, K. (2021). GLP-1 receptor agonists and cardiorenal outcomes in type 2 diabetes: an updated meta-analysis of eight CVOTs. *Cardiovascular Diabetology*, 20(1), 189. https://doi.org/10.1186/s12933-021-01366-8

Guo, H., Guo, Q., Li, Z., & Wang, Z. (2024). Association between different GLP-1 receptor agonists and acute pancreatitis: case series and real-world pharmacovigilance analysis [Original Research]. *Frontiers in Pharmacology*, *Volume 15 - 2024*. https://doi.org/10.3389/fphar.2024.1461398

He, L., Wang, J., Ping, F., Yang, N., Huang, J., Li, Y., Xu, L., Li, W., & Zhang, H. (2022). Association of Glucagon-Like Peptide-1 Receptor Agonist Use With Risk of Gallbladder and Biliary Diseases: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Internal Medicine*, *182*(5), 513-519. https://doi.org/10.1001/jamainternmed.2022.0338

Ibrahim, S. S., Ibrahim, R. S., Arabi, B., Brockmueller, A., Shakibaei, M., & Büsselberg, D. (2024). The effect of GLP-1R agonists on the medical triad of obesity, diabetes, and cancer. *Cancer and Metastasis Reviews*, *43*(4), 1297-1314. https://doi.org/10.1007/s10555-024-10192-9

Karakasis, P., Patoulias, D., Pamporis, K., Stachteas, P., Bougioukas, K. I., Klisic, A., Fragakis, N., & Rizzo, M. (2023). Safety and efficacy of the new, oral, small-molecule, GLP-1 receptor agonists orforglipron and danuglipron for the treatment of type 2 diabetes and obesity: systematic review and meta-analysis of randomized controlled trials. *Metabolism*, *149*, 155710. https://doi.org/10.1016/j.metabol.2023.155710

Kim, J. A., & Yoo, H. J. (2025). Exploring the Side Effects of GLP-1 Receptor Agonist: To Ensure Its Optimal Positioning. *Diabetes Metab J*, *49*(4), 525-541. https://doi.org/10.4093/dmj.2025.0242

Li, H., Yu, G., Huang, Q., Yang, B., Nie, J., Liu, Y., & Tu, X. (2024). Efficacy and safety of "GLP-1RAs" for people with obesity: A systematic review based on RCT and Bayesian network meta-analysis. *Biomedicine & Pharmacotherapy*, *171*, 116150. https://doi.org/https://doi.org/10.1016/j.biopha.2024.116150

Liu, Y., Ruan, B., Jiang, H., Le, S., Liu, Y., Ao, X., Huang, Y., Shi, X., Xue, R., Fu, X., & Wang, S. (2023). The Weight-loss Effect of "GLP-1RAs" Glucagon-Like Peptide-1 Receptor Agonists in Non-diabetic Individuals with Overweight or Obesity: A Systematic Review with Meta-Analysis and Trial Sequential Analysis of Randomized Controlled Trials. *The American Journal of Clinical Nutrition*, *118*(3), 614-626. https://doi.org/10.1016/j.ajcnut.2023.04.017

Lu, J., Liu, H., Zhou, Q., Wang, M.-W., & Li, Z. (2023). A potentially serious adverse effect of GLP-1 receptor agonists. *Acta Pharmaceutica Sinica. B*, *13*(5), 2291. https://doi.org/10.1016/j.apsb.2023.02.020

Ma, H., Lin, Y. H., Dai, L. Z., Lin, C. S., Huang, Y., & Liu, S. Y. (2023). Efficacy and safety of GLP-1 receptor agonists versus "SGLT-2" inhibitors in overweight/obese patients with or without diabetes mellitus: a systematic review and network meta-analysis. *BMJ Open*, *13*(3), e061807.

https://doi.org/10.1136/bmjopen-2022-061807

Moiz, A., Filion, K. B., Tsoukas, M. A., Yu, O. H. Y., Peters, T. M., & Eisenberg, M. J. (2025). The expanding role of GLP-1 receptor agonists: a narrative review of current evidence and future directions. *EClinicalMedicine*, *86*, 103363. https://doi.org/10.1016/j.eclinm.2025.103363

Parums, D. V. (2021). Review articles, systematic reviews, meta-analysis, and the updated preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 guidelines. *Medical science monitor: international medical journal of experimental and clinical research*, *27*, e934475-934471. https://doi.org/10.12659/MSM.934475

Patoulias, D., Michailidis, T., Dimosiari, A., Fragakis, N., Tse, G., & Rizzo, M. (2023). Effect of Glucagon-like Peptide-1 Receptor Agonists on Cardio-Metabolic Risk Factors among Obese/Overweight Individuals Treated with Antipsychotic Drug Classes: An Updated Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Biomedicines*, *11*(3).

Rodriguez, P. J., Zhang, V., Gratzl, S., Do, D., Cartwright, B. G., Baker, C., Gluckman, T. J., Stucky, N., & Emanuel, E. J. (2025). Discontinuation and reinitiation of dual-labeled GLP-1 receptor agonists among US adults with overweight or obesity. *JAMA Network Open*, 8(1), e2457349-e2457349. https://doi.org/10.1001/jamanetworkopen.2024.57349

Ruze, R., Liu, T., Zou, X., Song, J., Chen, Y., Xu, R., Yin, X., & Xu, Q. (2023). Obesity and type 2 diabetes mellitus: connections in epidemiology, pathogenesis, and treatments. *Frontiers in endocrinology*, *14*, 1161521. https://doi.org/10.3389/fendo.2023.1161521

Sabina, M., & Alsamman, M. M. (2024). Pulse of Progress: A Systematic Review of Glucagon-Like Peptide-1 Receptor Agonists in Cardiovascular Health. *Cardiol Res*, *15*(1), 1-11. https://doi.org/10.14740/cr1600

Sodhi, M., Rezaeianzadeh, R., Kezouh, A., & Etminan, M. (2023). Risk of Gastrointestinal Adverse Events Associated With Glucagon-Like Peptide-1 Receptor Agonists for Weight Loss. *JAMA*, *330*(18), 1795-1797. https://doi.org/10.1001/jama.2023.19574

Statista. (2025). *Diabetes prevalence by world region in 2024 and 2050*. https://www.statista.com/statistics/495292/diabetes-prevalance-forecast-globally-by-region/

Wharton, S., Davies, M., Dicker, D., Lingvay, I., Mosenzon, O., Rubino, D. M., & Pedersen, S. D. (2022). Managing the gastrointestinal side effects of GLP-1 receptor agonists in obesity: recommendations for clinical practice. *Postgraduate Medicine*, *134*(1), 14-19. https://doi.org/10.1080/00325481.2021.2002616

WHO. (2024). *Diabetes*. https://www.who.int/news-room/fact-sheets/detail/diabetes

WHO. (2025). *Obesity and overweight*. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

Wong, H. J., Sim, B., Teo, Y. H., Teo, Y. N., Chan, M. Y., Yeo, L. L. L., Eng, P. C., Tan, B. Y. Q., Sattar, N., Dalakoti, M., & Sia, C.-H. (2025). Efficacy of GLP-1 Receptor Agonists on Weight Loss, BMI, and Waist Circumference for Patients With Obesity or Overweight: A Systematic Review, Meta-analysis, and Meta-regression of 47 Randomized Controlled Trials. *Diabetes Care*, *48*(2), 292-300. https://doi.org/10.2337/dc24-1678

Yang, C.-Y., Chen, Y.-R., Ou, H.-T., & Kuo, S. (2021). Cost-effectiveness of GLP-1 receptor agonists versus insulin for the treatment of type 2 diabetes: a real-world study and systematic review. *Cardiovascular Diabetology*, *20*(1), 21. https://doi.org/10.1186/s12933-020-01211-4

Yao, H., Zhang, A., Li, D., Wu, Y., Wang, C.-Z., Wan, J.-Y., & Yuan, C.-S. (2024). Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis. *BMJ*, *384*, e076410. https://doi.org/10.1136/bmj-2023-076410

Zhang, Y., Liu, C., Xu, Y., Wang, Y., Zhang, Y., Jiang, T., Zhang, Q., & Group, C. N. D. C. C. S. (2023). The relationship between sugar-sweetened beverages, sleep disorders, and diabesity. *Frontiers in endocrinology*, *13*, 1041977. https://doi.org/10.3389/fendo.2022.1041977

Zhong, Y., Wu, T., & Khan, N. U. (2025). Association between GLP-1 receptor agonists as a class and colorectal cancer risk: a meta-analysis of retrospective cohort studies. *BMC Gastroenterology*, *25*(1), 614. https://doi.org/10.1186/s12876-025-04211-4