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The efficacy of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose cotransporter-2 inhibitors (SGLT2 inhibitors) in the treatment of obesity in patients with type 2 diabetes mellitus (T2DM) - A literature review

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ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) and obesity are closely connected conditions. Therefore, the therapeutic approach should focus on treating both of them equally. In this review, we aimed to summarise the latest research on the efficacy of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose cotransporter-2 inhibitors (SGLT2 inhibitors) in the treatment of obesity in patients with type 2 diabetes. Methods: A study search was conducted from January 2020 to October 2025 across the PubMed, Scopus and Google Scholar databases using the following keywords: Type 2 diabetes mellitus, obesity, weight control, GLP-1 receptor agonists, SGLT2 inhibitors. The primary outcome of interest was whether these agents were effective in the obesity therapy in patients with type 2 diabetes. Results: Ultimately, 5 articles met the inclusion criteria in the final review of 1176 found in databases. Conclusions: This systematic review suggests that adding medications, both GLP-1 agonists and SGLT2 inhibitors, is integral to the management of overweight or obesity in patients with type 2 diabetes.

Keywords: Type 2 diabetes mellitus, obesity, weight control, GLP-1RAs, S GLT2 inhibitors

1. INTRODUCTION

Obesity has become one of the most challenging health problems worldwide. This condition constitutes a basis for the development of numerous other diseases

involving all organ systems in the human body. It also plays a particularly key role in the development of T2DM. Excess adipose tissue promotes insulin resistance, low-grade systemic inflammation, lipotoxicity, loss of functional β-cells and progressive increase in glycaemia. All these mechanisms are involved in the transition of compensated dysglycaemia to overt T2DM (Ruze et al., 2023; Rendell, 2023).

Patients with T2DM and increased body mass have to face not only worse glycaemic control but also higher cardio-renal risk (Artasensi et al., 2023; Ruze et al., 2023). However, studies have shown that intentional weight loss improves metabolic parameters and long-term clinical outcomes in this population (Ghusn et al., 2022; Allocca et al., 2025; Agarwal et al., 2025). Given the above, we should focus on treatment strategies that have a mutual effect on both conditions.

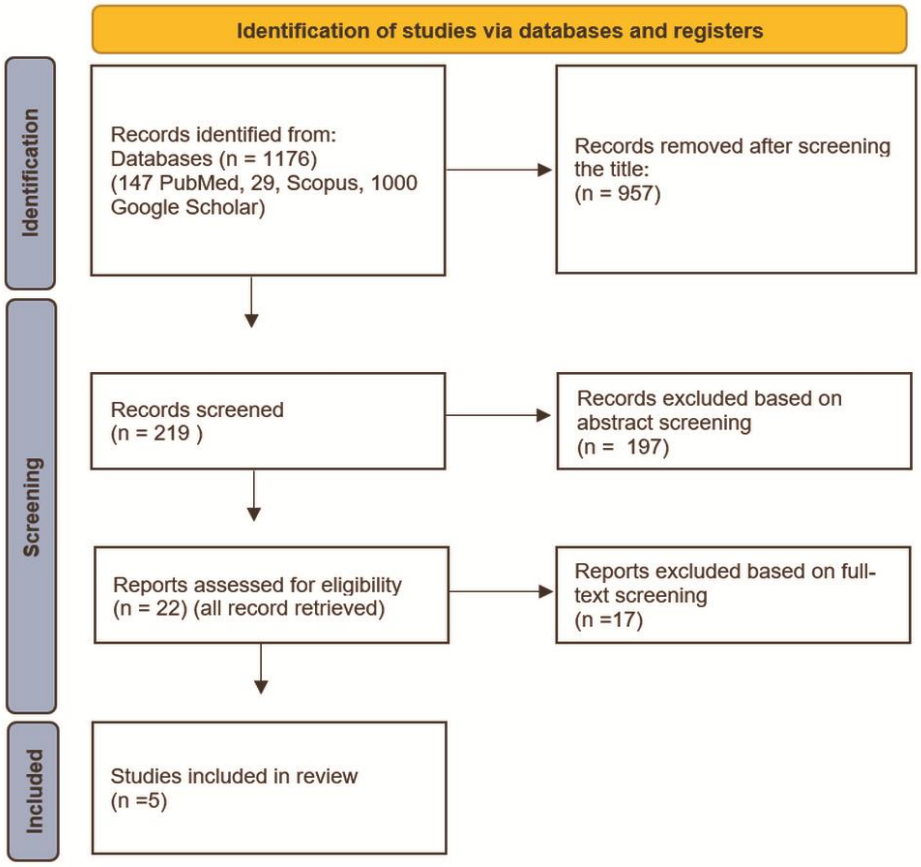

Figure 1. PRISMA flow diagram.

2. REVIEW METHODS

Inclusion and Exclusion Criteria

Inclusion criteria

Articles published between January 2020 and October 2025

Studies in the English language

Full-text, open-access articles

Randomised controlled trials or cohort studies

Patients with T2DM and obesity or overweight

Exclusion criteria

Case reports, review articles, and meta-analyses

Patients with diabetes other than type 2 and without overweight or obesity

Search strategy and study selection

The study search was carried out in the PubMed, Scopus and Google Scholar databases with the following keywords: type 2 diabetes mellitus, obesity, weight control, GLP-1 receptor agonists, and SGLT2 inhibitors. We considered only articles published in English from January 2020 to October 2025, including randomised controlled trials and prospective or retrospective observational cohort studies. Trails thought to evaluate treatment with GLP-1 RAs and/or SGLT2 inhibitors in patients with T2DM and overweight or obesity and reported changes in body weight and/or body mass index (BMI). We selected the articles according to PRISMA recommendations (Figure 1).

3. RESULTS & DISCUSSION

Our search initially resulted in 1176 records: 147 from PubMed, 29 from Scopus, and 1000 from Google Scholar. Due to the large number of records in Google Scholar (over 20000), we considered only the first 1000 ordered by relevance. We excluded 957 articles after title screening and identified 22 articles after an abstract review of the remaining studies. Finally, 5 trials met the pre-specified eligibility criteria and were included in the final analysis. We summarised the identification and selection process in Figure 1. Four randomised controlled trials and one cohort study appeared in the final set of included studies (Table 1).

Table 1. Characteristics of published studies.

Author and year of publication	Sample size	Region	GLP-1 RA treatment	SGLT2i treatment	GLP-1 RA + SGLT2i treatment	Study type
Berra et al., 2024	583	Italy	Yes (add-on)	Yes	Yes	Observational cohort study
Sargeant et al., 2022	68	UK	No	Yes	No	Randomised controlled trial
Zhu et al., 2024	145	China	Yes	No	No	Randomised controlled trial
Aroda et al., 2025	245	Greece, Hungary, Poland, USA	Yes	No	No	Randomised controlled trial
Babar et al., 2021	240	Pakistan	No	Yes	No	Randomised controlled trial

In the AWARE-2 study, Berra et al., (2024) evaluated changes in HbA1c and BMI after adding once-weekly dulaglutide to patients already receiving treatment with an SGLT2 inhibitor. The study population consisted of patients with T2DM, obesity, suboptimal metabolic control and high cardiovascular risk. Over the 6 months, added dulaglutide to ongoing SGLT2 inhibitor therapy resulted not only in a statistically significant reduction in HbA1c but also in BMI by 1.1 kg/m² (95% CI, −1.22 to −0.98 kg/m²; $p < 0.0001$) and body weight by 3.1 kilograms (95% CI, −3.44 to −2.76; p t< 0.0001) in all groups.

In the SEESAW, researchers aimed to evaluate the effects of once-daily empagliflozin, dietary energy restriction and their combination on patients with type 2 diabetes and overweight or obesity (Sargeant et al., 2022). This study showed that in the empagliflozin-plus-diet group was observed the most significant weight reduction: -5,62 kilograms (95% CI, −7,79 to −3,44; $p < 0,001$), in the empagliflozin-only group: -2,23 kilograms (95% CI, −4,45 to −0,01; $p = 0,049$) and in placebo-plus-diet group: -1,52 kilograms (95% CI, −3,79 to 0,76; $p = 0,191$).

Zhu et al., (2024) examined the impact of ecnoglutide at doses of 0.4 mg, 0.8 mg and 1.2 mg in a 20-week trial. Weight reduction was a secondary endpoint in this study. From baseline to the end of treatment in all groups, ecnoglutide showed a dose–response relationship. In comparison to placebo, patients receiving the lowest studied dose of 0.4 mg lost 2,07 kilograms (95% CI, −2,93 to −1,21;

p <0,0001), those receiving 0.8 mg lost 2.16 kilograms (−2,07 kg (95% CI, −2,93 to −1,21; p <0,0001) and those receiving 1.2 mg lost 2.77 kilograms (95% CI, −3,64 to −1,89; p <0,0001).

Aroda et al., (2025) studied a dose-dependent effect of GLP-1 RA as well. A group of 245 patients with T2DM and a BMI ≥27 kg/m² already receiving metformin were enrolled in a 40-week trial. Participants were assigned to three treatment groups receiving semaglutide at doses of 16 mg, 8 mg and 2 mg. The study showed that the highest dose of the drug resulted in a significant difference in body weight reduction compared to the lowest one (−3.4 kilograms; 95% CI, −6.0 to −0.8; p < 0,01). However, changes in HbA1c in all groups showed no significant differences (p > 0,05).

In 2021, Babar et al., investigated the effect of adding empagliflozin to standard T2DM therapy with metformin and sitagliptin on body weight, HbA1c, and blood pressure. They conducted a trial with 240 patients were randomised to two groups: metformin–sitagliptin–placebo or metformin–sitagliptin–empagliflozin. After 24 weeks, mean body weight decreased by 3.1 kilograms (95% CI −3.24 to −2.96; p < 0.001) in the placebo group and by 6.9 kilograms (95% CI, −7.33 to −6.47; p < 0.001) in the empagliflozin group with a between-group difference of −3.8 kilograms (95% CI, −4.25 to −3.35; p < 0.001).

Mechanism of action

Gourdy et al., (2023) described mechanisms of action for both classes of agents. GLP-1 RAs reduce energy intake and improve β-cell function, whereas SGLT2 inhibitors increase urinary glucose excretion and improve haemodynamics. It supports the additive effects on weight and cardiovascular risk factors seen in trials and meta-analyses of these agents.

Central nervous system mechanisms additionally play a role in the weight effects of GLP-1 RAs and SGLT2 inhibitors. Functional MRI data from van Ruiten et al., (2022) showed that dapagliflozin alone increased brain reward responses to food expectation and consumption, which may limit weight loss. However, the addition of exenatide, a GLP-1 RA, attenuated these responses and was correlated with greater weight reduction.

Clinical benefits

Treating with both GLP-1 RAs and SGLT2 inhibitor therapy improves weight, blood pressure and cardiovascular outcomes in high-risk patients (Brown et al., 2021; Gourdy et al., 2023) and reduces major cardiovascular events in obese diabetic patients (Uneda et al., 2021). Moreover, findings from many studies indicate that GLP-1 RA and SGLT2 inhibitor combination therapy leads to greater reductions in HbA1c, fasting glucose, body weight and systolic blood pressure than either class alone (Li et al., 2022; Zhou et al., 2020; Simms-Williams et al., 2024). Patel et al., (2024) showed that adding GLP-1 RA to ongoing therapy with an SGL2 inhibitor in patients with T2DM, obesity and heart failure with preserved ejection fraction (HFpEF) may further enhance therapeutic results, including exercise capacity.

Lifestyle modification

Kempf et al., (2025) sought to determine which strategy yields better weight-control outcomes in patients with diabetes. They conducted a systematic review that considered two strategies: a formula-based diet intervention and pharmacological antiglycemic therapy. In the long-term follow-up, the reduction in HbA1c was similar in both approaches. However, formula-diet-based lifestyle intervention led to greater weight loss than pharmacological therapy with GLP-1 RAs or SGLT2 inhibitors.

4. CONCLUSION

To summarise, our study suggests that therapy with both GLP-1 RAs and SGLT2 inhibitors is an effective tool for glycaemic control and body weight management. Compared with placebo or older antidiabetic drugs, both drug classes addressed in this review cause clinically relevant weight loss and HbA1c reduction. Despite the presented evidence that supports the effectiveness of these medications, for the best outcomes, patients with diabetes and overweight or obesity should integrate pharmacological treatment with healthy lifestyle practices.

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Conceptualization: JB, MK
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Writing-review and editing: MM, KF
Supervision: TW, MD, AM
Project administration: JB, MK, AM, KF, WC, ZKC, MD, TW, MM
All authors have read and agreed with the published version of the manuscript.

Informed consent

Not applicable.

Ethical approval

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

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Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on reasonable request to the corresponding author.

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