Semaglutide vs. dulaglutide for glycemic and weight control in patients with type 2 diabetes mellitus: A systematic review and meta-analysis

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Abstract. The present systematic review and meta-analysis aimed to evaluate the effectiveness of semaglutide and dulaglutide for glycemic control and weight loss in patients with type 2 diabetes mellitus (T2DM). A thorough literature search was conducted using several databases from inception until the end of July 2024. The primary outcome was the difference in glycated hemoglobin levels from the initial measurement between the groups. By contrast, the secondary outcome was the effect of the medications on body weight loss (change in body weight from baseline) during the treatment period. Appropriate statistical tests were employed to reach study endpoints. The results showed no statistically significant difference in glycemic control achievement between the two medications in patients with T2DM. Semaglutide demonstrated higher efficacy in inducing weight loss; however, sensitivity analysis indicated that the weight loss efficacy results should be interpreted cautiously. The study acknowledges the high heterogeneity and low quality among the studies included in the meta-analysis and the potential impact of individual studies on the outcome. Despite these limitations, the findings suggested that semaglutide may be a more favorable treatment option for patients with T2DM requiring weight management and glycemic control. Further research is needed to investigate the long-term benefits of glucagon-like peptide-1 receptor agonists and individual factors that may influence treatment response and outcomes.

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Introduction

Type 2 diabetes mellitus (T2DM) is a serious metabolic disorder affecting millions of individuals worldwide. It is caused by insulin resistance or dysfunction, leading to hyperglycemia and an increased risk of cardiovascular complications, neuropath, and retinopathy, among other serious risks (1). Management of T2DM typically involves lifestyle modification, pharmacologic intervention and insulin therapy to maintain stable blood glucose levels and minimize diabetes-related complications (2).

One promising class of medications for T2DM management is glucagon-like peptide-1 receptor agonists (GLP-1 RAs). The GLP-1 receptors found in the pancreas, intestines and central nervous system are the main targets of these medications. By doing so, they prevent hepatic gluconeogenesis, boost insulin secretion, reduce appetite, slow stomach emptying and cause early satiety (3). Studies have demonstrated that these medications decrease glycated hemoglobin (HbA1c) levels, body weight, blood pressure and lipids. GLP-1 RAs are associated with a minimal risk of hypoglycemia, and the most frequent adverse outcomes are related to the digestive system (4). Semaglutide and dulaglutide are two relatively new GLP-1 RAs that have garnered significant interest for their favorable efficacy and safety profiles compared with other medications used for T2DM management (5). Several clinical trials have demonstrated the efficacy of semaglutide and dulaglutide in reducing HbA1c levels, with a favorable safety profile.

There is a lack of comparative evidence on the efficacy and safety of these two drugs in T2DM management. Evidence emerging from several studies indicates that individuals who received a weekly dose of semaglutide experienced a significantly larger reduction in HbA1c compared with those receiving a weekly dose of dulaglutide. On the other hand, another study showed no statistically significant difference in glycemic control achievement between these two medications in patients with T2DM (6).

The present systematic review and meta-analysis aimed to comprehensively evaluate studies comparing the effectiveness of semaglutide and dulaglutide for T2DM management. The review aimed to critically evaluate the studies, analyze intervention durations and doses, and compare the clinical outcomes of the drugs, including glycemic control, weight management and adverse effects. This information can help

clinicians and patients make informed decisions regarding drug selection and the personalization of T2DM management.

Materials and methods

The available data were thoroughly examined and analyzed, and the findings were presented in compliance with the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (7).

Search strategy. To identify all relevant studies on the effectiveness and safety of semaglutide and dulaglutide for glycemic control and weight loss in adult patients with T2DM, a thorough literature search was conducted using the Embase (https://www.embase.com), Google Scholar (https://scholar.google.com/), MEDLINE (https://www.nlm.nih.gov/medline) and SCOPUS (https://www.scopus.com/) databases from their inception until July 2024. Specific search terms were used, including semaglutide, dulaglutide and T2DM. The search included studies in all languages but was limited to human subjects.

Inclusion and exclusion criteria. Studies that met the following criteria were only considered: i) Comparing the effectiveness and safety of various doses of semaglutide with dulaglutide in achieving glycemic control and weight loss in patients with T2DM; ii) were conducted in patients who were at least 18 years old; iii) diagnosed T2DM according to specific criteria from either the World Health Organization (8) or the American Diabetes Association (9); and iv) were published in a peer-reviewed journal. Meta-analyses, reviews, case reports, editorials, letters, commentaries, expert opinions and experimental studies were excluded.

Data extraction. Two authors reviewed the titles and abstracts of the included publications to determine whether they met specific requirements for inclusion or exclusion. If a study met the criteria, the full text was examined. In cases of disagreement between the two researchers, a third researcher was consulted to make a conclusive decision. For all included studies, the following information was extracted: Authorship, year of publication, study design, study duration, randomization process, intervention method, sample size, study location, population studied, therapy duration and follow-up period, patients' body weight or body mass index (BMI) and adverse events.

Outcome measures for efficacy. The primary outcome of effectiveness was the difference in HbA1c levels from the initial measurement between the groups. The secondary outcome was the effect of the medications on body weight loss (change in body weight from baseline) during the treatment period.

Quality and risk of bias assessment. The quality of citations included in the study was evaluated using the Cochrane Collaboration's Risk of Bias Tool (10) and Review Manager. The evaluation considered several factors: Allocation concealment, blinding of participants and personnel, random sequence generation, blinding of outcome assessors, selective outcome reporting, incomplete outcome data and other biases. The studies were categorized into three levels of risk: high, unclear and low. Two authors conducted the quality appraisal and consulted a third reviewer in case of any discrepancies.

Statistical analysis. Comprehensive Meta-Analysis (CMA) 2 was utilized for all the analyses. Data were expressed as the mean ± standard deviation (SD). The effect size statistic for continuous measurement data was the standardized mean difference (SMD). In cases where SD was not provided, the following formula was used to convert standard error to SD, where N represents the sample size (11):

$$SD = \sqrt{N} \times SE$$

In studies where confidence intervals (CIs) were provided, the following formula was used to convert CIs to SDs. As before, N represents the sample size (11):

$$SD = \sqrt{N} \times \frac{(Upper\ limit - Lower\ limit)}{3.92}$$

In the present meta-analysis, a random-effects model was employed to consider the differences in effect size estimates. This enables us to make inferences at the population level and is more rigorous than a fixed-effects model (12). The authors did not rely on the I^2 statistic to indicate the level of heterogeneity in effect size because it is not designed for that purpose. Unless the I^2 value is zero, it cannot provide information on the extent of heterogeneity. While the I^2 statistic measures the proportion of variability due to heterogeneity, it does not provide insight into the absolute variation or its practical significance. By contrast, prediction intervals indicate the range within which future study results are likely to fall, making them directly interpretable in real-world contexts. This allows for an improved understanding of how markedly study results might vary and whether that variation is meaningful for clinical or practical decisions. Additionally, prediction intervals are not as sensitive to the number and size of included studies, addressing some of the limitations of the I^2 statistic. Therefore, prediction intervals were used to report heterogeneity in the data. Prediction intervals were calculated using a random-effects model, which considers both within-study and between-study variability. The interval was derived from the overall effect size estimate, accounting for the standard error and variability between studies (13).

A funnel plot was used to determine if there was any bias in the published material. A balanced funnel plot indicated no bias, while an unbalanced one suggested that there was bias. Egger's and Begg's tests were also used to confirm the presence of bias in the publications because the interpretation of the funnel plot can be subjective.

Moderator analysis, performed through meta-regression, explores how study-level characteristics influence the effect sizes across different studies. In this approach, potential moderators, such as treatment duration, were identified and data were collected for each included study. The meta-regression model was then set up using CMA, with the effect size as the dependent variable and the moderator as the independent variable. The analysis estimated a regression line to describe the relationship, and a significant P-value (typically <0.05) indicated that the

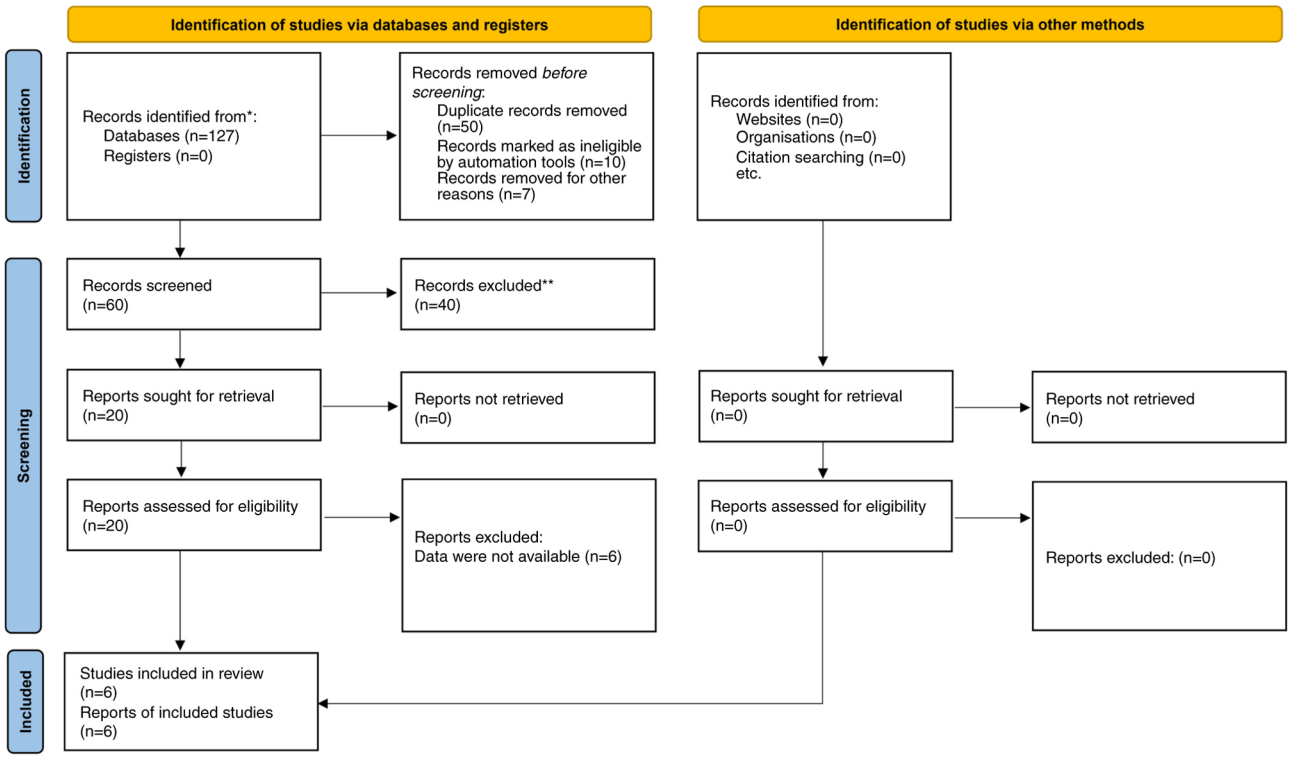

Figure 1. PRISMA flow diagram showing how studies were chose for the present systematic review and meta-analysis. A thorough search across numerous databases yielded the articles, and preliminary screening eliminated duplicates and irrelevant research. Following the first screening of titles and abstracts for possibly pertinent studies, a full-text screening was conducted to determine the studies' ultimate inclusion. At each step of the selection process, the causes of elimination were noted.

moderator significantly impacts the effect size (14). If the P-value of either test was less than 0.05, it indicated bias. P<0.05 was deemed to indicate a statistically significant difference.

Results

Search results and study characteristics. The search for relevant literature yielded 127 publications. After eliminating duplicates and examining the titles and abstracts of the sources, 20 were selected for a thorough review. Out of these 20, only six met the criteria for inclusion (6,15-19). A total of 3 of these studies had several subgroups and comparisons, resulting in 10 comparisons in the present meta-analysis. A total of 2 studies were non-randomized (6,18), while 4 were randomized clinical trials. A flowchart in Fig 1 shows the steps involved in including and excluding the studies. The duration of the studies ranged between 12-52 weeks. There were 1,038 patients in the semaglutide group and 847 patients in the dulaglutide group. In the included trials, semaglutide and dulaglutide doses varied between 0.5-14 mg and between 0.75-1.5 mg, respectively. The study characteristics are included in Table I.

Efficacy of semaglutide vs. dulaglutide in the achievement of glycemic control and weight loss. The analysis included 10 different comparisons. The initial global examination of all glycemic control measures using a CMA required the inclusion of each study only once in a nested analysis. The results demonstrated no difference between semaglutide and dulaglutide in achieving glycemic control in patients with T2DM, with an SMD of 0.613 (95% CI, -0.164-1.391; P=0.122) (Fig. 2A).

Similar to the previous analysis, this examination included 10 different comparisons. It was found that semaglutide was more effective than dulaglutide in inducing weight loss in patients with T2DM, with an SMD of 2.45 (95% CI, 0.467-4.434; P=0.015) (Fig. 2B).

Sensitivity analysis. The analysis was conducted 10 times, with each iteration excluding one study to demonstrate the impact of that particular study on the outcome. It was found that the exclusion of no single study affects the outcome of glycemic control efficacy data (Fig. 3A). However, the exclusion of one of the comparisons conducted by Pratley *et al* (15) caused a change in the initial assumption that semaglutide had higher efficacy than dulaglutide in inducing weight loss in patients with T2DM. This means that these results should be interpreted with caution (Fig. 3B).

Data heterogeneity. The prediction interval analysis for glycemic control data found that the mean effect size was 0.61, with a 95% CI of -0.164 -1.39. In 95% of similar populations, the true effect size falls between -2.37-3.60 (Fig. 4A). This indicates a large amount of heterogeneity among the studies analyzed, as the prediction interval is wider than the CI and suggests a broader range of potential treatment effects. The presence of a statistically significant effect is not confirmed here, as all values in the CI and prediction interval do not fall

Table I. Characteristics of the included studies. Clinical studies comparing semaglutide and dulaglutide in patients with type 2 diabetes are summarized, focusing on study design, sample size, location, patient characteristics and outcomes. Key findings on glycemic control, weight changes and adverse events are highlighted, showing that semaglutide often provided improved glycemic control and weight loss compared with dulaglutide, with similar safety profiles, primarily involving gastrointestinal issues.

First author, year	Study design	Duration	Randomization	Intervention	Sample size	Location	Population	Duration of therapy/ follow up	BMI/ Weight	Adverse events	(Refs.)
Takahashi *et al*, 2023	Multicentre, prospective, randomized, open-label	24 weeks	Third-party, 1:1 randomization	Semaglutide vs. liraglutide/ dulaglutide	110 (100 completed)	Japan	Patients with T2DM on GLP-1 therapy	24 weeks	BMI ≥22 kg/m^2	Hypoglycemia, gastrointestinal issues	(19)
Iacobellis and Villasante Fricke, 2019	Controlled, parallel study	12 weeks	Based on preference/ insurance coverage	Semaglutide 1 mg vs. Dulaglutide 1.5 mg vs. Metformin	80	USA	Overweight/ obese type 2 diabetics	12 weeks	BMI ≥27 kg/m^2, weight loss noted	No significant difference between groups in HbA1c improvement, gastrointestinal issues	(18)
Iijima *et al*, 2023	Open-label, randomized, parallel-group	26 weeks	1:1 randomization	Semaglutide 0.5 mg vs. Dulaglutide 0.75 mg	32 (30 completed)	Japan	Patients with T2DM on liraglutide	26 weeks	Weight loss in semaglutide group (-2.6 kg)	Higher adverse events in semaglutide group, severe vomiting	(17)
Pratley *et al*, 2018	Randomized, open-label, phase 3b	40 weeks	Interactive web-response system	Semaglutide (0.5 mg, 1.0 mg) vs. Dulaglutide (0.75 mg, 1.5 mg)	1201	16 countries (Global)	Patients with T2DM on metformin	40 weeks	Body weight reduction: semaglutide > dulaglutide	Gastrointestinal disorders, similar safety profiles	(15)
Seijas-Amigo *et al*, 2023	Non-randomized, multicenter study	3 months	Not randomized	GLP-1 RAs: Semaglutide (oral/subcutaneous), Dulaglutide	94	Spain	Patients with T2DM with BMI >30 kg/m^2	3 months	Mean body weight: 99.3 kg; BMI, 36.7 kg/m^2	Gastrointestinal disorders, more frequent in dulaglutide group	(6)
Yabe *et al*, 2020	Randomized, open-label, phase 3a	52 weeks	2:2:2:1 randomization	Oral Semaglutide vs. Dulaglutide 0.75 mg	458	Japan	Patients with T2DM with uncontrolled glucose	52 weeks	Body weight change: varied by dose	Gastrointestinal events, mostly constipation	(16)

T2DM, type 2 diabetes mellitus; BMI, body mass index.

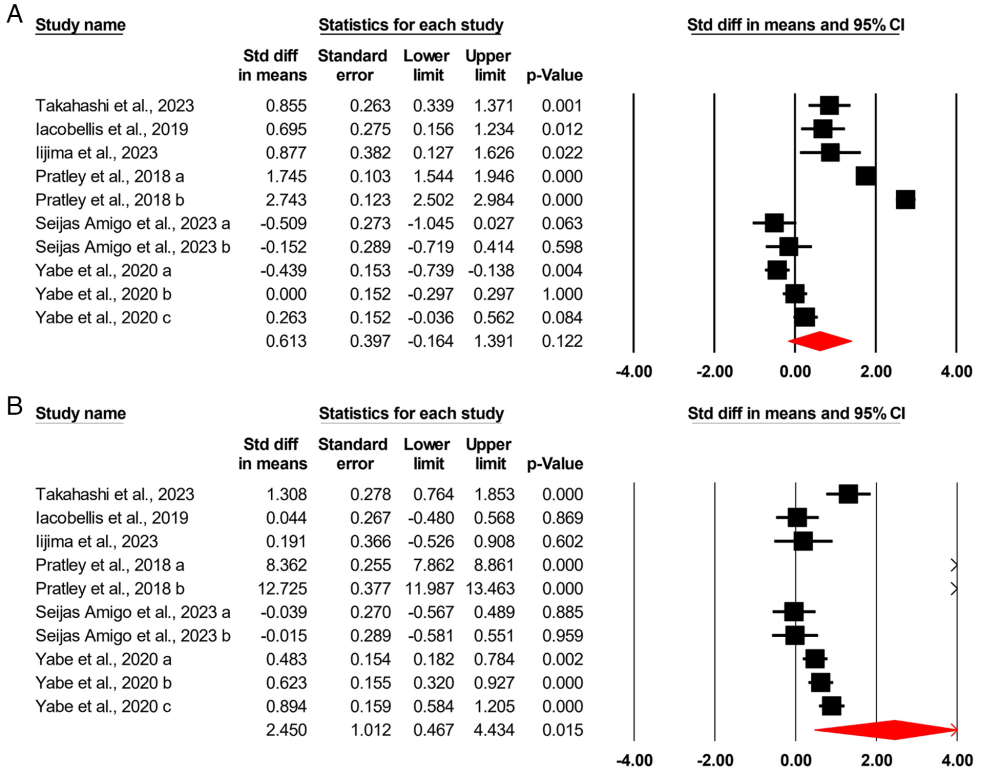

Figure 2. Forest plot that summarizes the SMD for each study comparison that was considered for the meta-analysis regarding (A) glycemic control and (B) weight loss. The SMD is shown on the plot as a representation of the effect size for each research and is denoted by a square. The effect size estimate's 95% CI is shown as a horizontal line emanating from each square. The estimate of the total effect size and its 95% CI are shown in the red diamond at the bottom of the plot. SMD, standardized mean difference; CI, confidence interval.

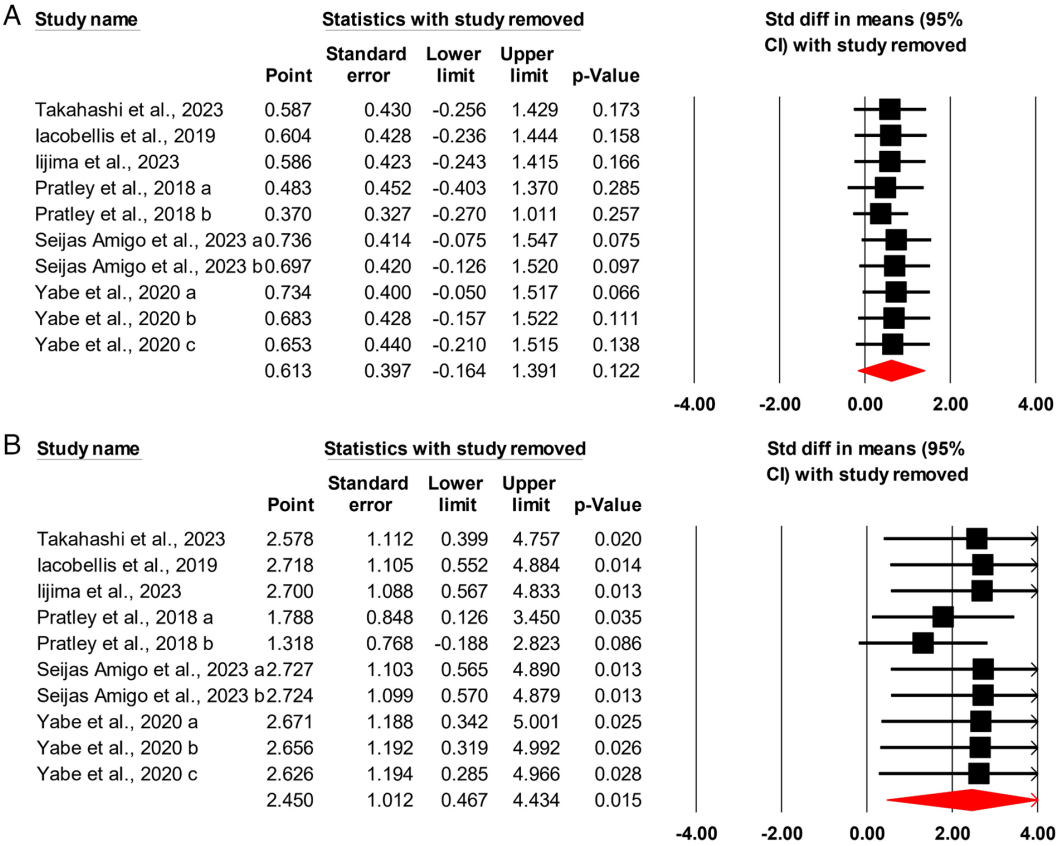

Figure 3. Forest plot showing the outcomes of the leave-one-out analysis for the studies included in the meta-analysis based on the SMD regarding (A) glycemic control and (B) weight loss. For each study, the SMD and its 95% CI are displayed as a square and a horizontal line, respectively. A red diamond at the plot's bottom represents the estimated total effect size and its 95% CI. SMD, standardized mean difference; CI, confidence interval.

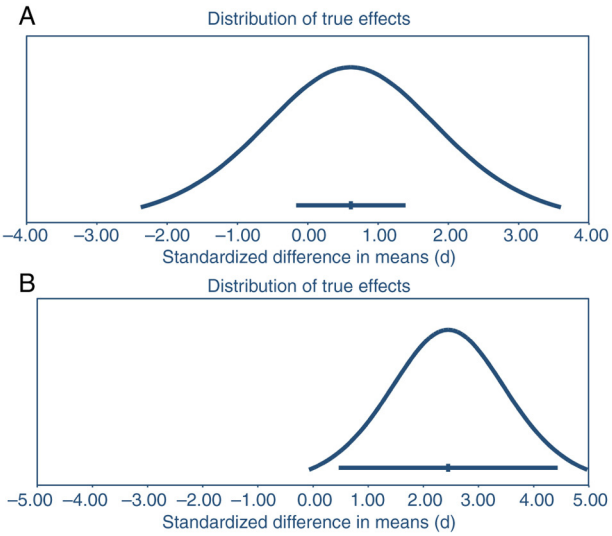

Figure 4. Prediction interval analysis. Prediction interval is used to evaluate how heterogeneous the data are regarding (A) glycemic control and (B) weight loss.

on one side of the null. The mean effect size for the weight loss data was found to be 2.45, with a 95% CI of 0.47-4.43. The true effect size in 95% of all comparable populations fell from -0.07-4.97. Again, the data heterogeneity was considered high because the prediction interval was wider than the CI. All CI values on one side of the null confirm the presence of a statistically significant effect. At the same time, the prediction interval suggests the possibility of values on both sides of the null (Fig. 4B).

Risk of bias. For the first set of comparisons, the funnel plot was reasonably symmetric. However, one study was found to be missing to the right of the mean, while no study was missing to the left of the mean (Fig. 5A). The Begg's and Mazumdar rank correlation showed no publication bias (2-tailed P=0.05 in Kendall's tau with continuity correction). Similarly, Egger's regression revealed no sign of publication bias (two-tailed P=0.22).

For the second set of comparisons, the shape of the funnel plot was also symmetric. Nevertheless, two studies were missing to the right of the mean in the trim-and-fill analysis. No study was found missing to the left of the mean (Fig. 5B). The Begg's and Mazumdar rank correlation showed no publication bias (2-tailed P=0.05 in Kendall's tau with continuity correction). Similarly, Egger's regression revealed no sign of publication bias (two-tailed P=0.22).

Meta-regression or moderator analysis. No correlation was found between treatment duration or semaglutide/dulaglutide doses and glycemic control (slope P>0.05 for all comparisons; data not shown). However, a correlation was found between treatment duration and weight loss, indicating that a longer treatment duration was associated with higher weight loss (slope P=0.02; Fig. 6).

Quality of the studies. Based on the Cochrane risk of bias assessment tool, the general quality of the included studies was low. Only one of the studies was blinded (18), and randomization was performed in four of the studies. None of the studies implemented allocation concealment (Fig. 7).

Safety and adverse events. No serious adverse events were reported in the study of Takahashi *et al* (19). During the study period, three patients experienced hypoglycemia (one with dulaglutide and two with semaglutide). However, none of these incidents required the patients to stop their treatment (19). In line with that Iacobellis and Villasante Fricke (18) demonstrated no adverse events or need for hospitalization. Iijima *et al* (17) reported treatment discontinuation in one patient due to intractable vomiting and weight loss. In the course of the study by Pratley *et al* (15), six participants lost their lives: One and two individuals succumbed while using semaglutide and dulaglutide, respectively. The incidence of serious adverse effects was similar across all treatment groups. Gastrointestinal problems were the most common adverse effects (6,16), with similar rates in all groups except for those receiving dulaglutide 0.75 mg, where fewer patients experienced gastrointestinal issues (15). Seijas-Amigo *et al* (6) reported one cardiovascular-related death during dulaglutide treatment.

Discussion

One of the most important T2DM therapy options is using GLP-1 RAs. The present meta-analysis aimed to compare the efficacy of semaglutide and dulaglutide in achieving glycemic control and weight loss in patients with T2DM. This analysis revealed no significant difference in glycemic control between semaglutide and dulaglutide, while semaglutide was more effective in inducing weight loss than dulaglutide.

Glycemic control efficacy. Previous studies have shown mixed results regarding the efficacy of these medications in achieving glycemic control in patients with T2DM, with some indicating that there is no significant difference between the two medications (6), while others show that semaglutide has improved efficacy in reducing HbA1c levels compared with dulaglutide (15,16). When semaglutide was compared with other GLP-1 RAs in a meta-analysis, it was identified that it lowers HbA1c and fasting plasma glucose levels more effectively and increases the likelihood of achieving both targeted and intense HbA1c level reductions by >2 times. Although the likelihood of significant HbA1c reductions with semaglutide was comparable to that of liraglutide, the absolute reduction in HbA1c and fasting plasma glucose levels obtained with semaglutide was not larger than that attained with dulaglutide (20). In another meta-analysis, despite substantial variation in the length of the trials and the therapy regimens employed, semaglutide was shown to be more efficient than dulaglutide in terms of glycemic control, with a significant decrease in HbA1c by 0.47% (21). Another meta-analysis revealed that semaglutide 1 mg significantly outperformed other GLP-1 RAs, such as dulaglutide, in decreasing HbA1c, with a similar drop of 0.38% (22). In a similar vein, a network meta-analysis showed that semaglutide 1 mg was more substantially associated with a decrease in HbA1c among individuals with T2DM than dulaglutide (23).

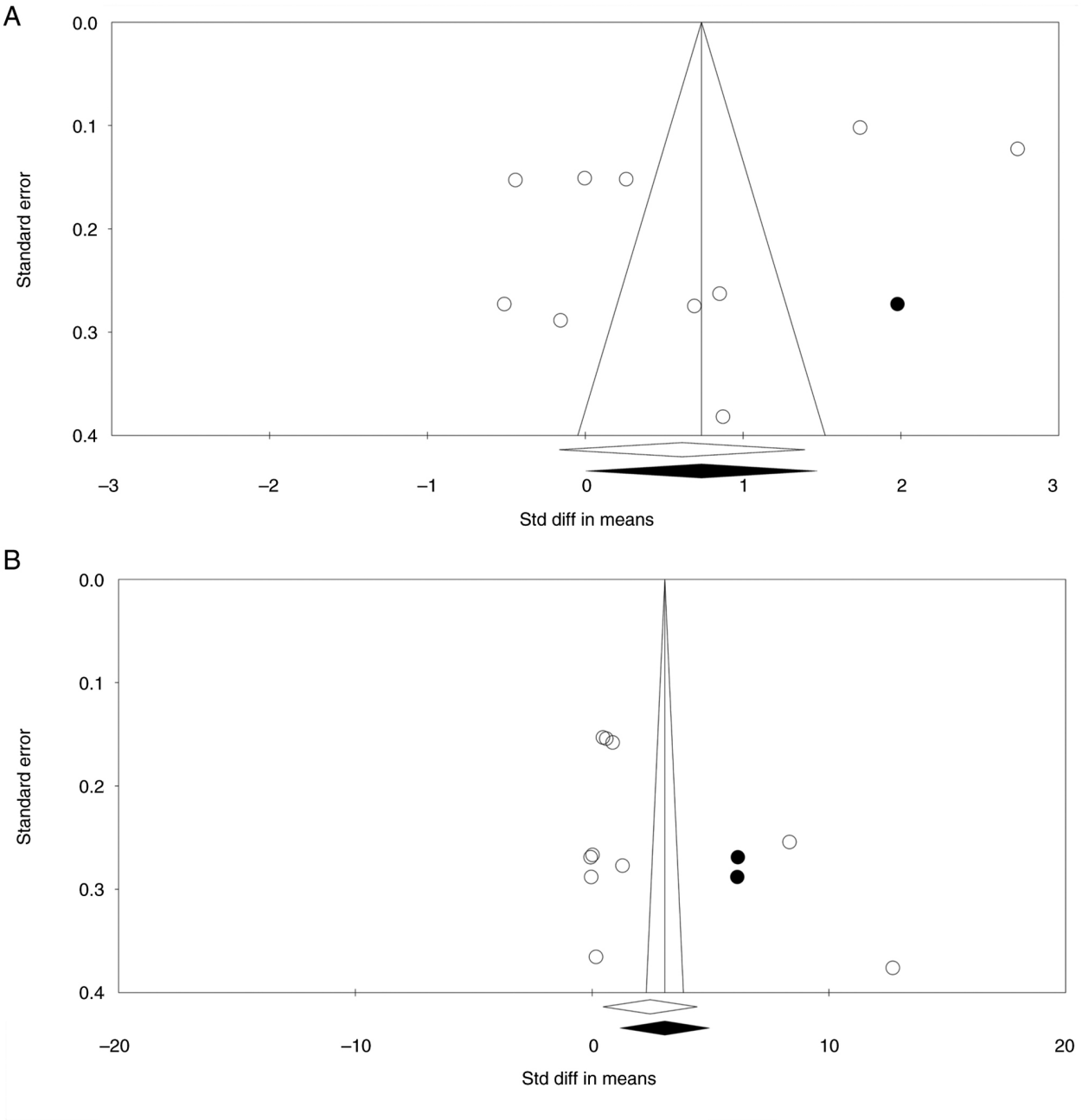

Figure 5. A funnel plot showing how the standard error and standardized mean difference for the studies included in the meta-analysis relate to one another. The asymmetry and publication bias of the meta-analysis are visually inspected using the funnel plot regarding (A) glycemic control and (B) weight loss.

Several factors could cause the variations in the results provided. These could include differences in study design, sample sizes and patient populations. Additionally, variations could be caused by differences in dosage, administration route (oral vs. subcutaneous) and formulation. Other factors, such as patient adherence, treatment duration and lifestyle modifications, could also contribute to the differences observed in the results. It is thus important to carefully consider these factors when interpreting and comparing the results of different studies.

Weight loss efficacy. Moderate weight reduction can improve blood glucose control, decrease the need for hypoglycemic medications, and is linked to a substantial decrease in the risk of various obesity-connected complications in overweight or obese patients with T2DM. Therefore, the impact on weight should be considered when glucose-lowering medications are prescribed for overweight or obese patients with T2DM. GLP-1 RAs exhibit both the effectiveness of weight reduction and a favorable hypoglycemic impact (24). The results concerning the efficacy of semaglutide vs. dulaglutide in inducing weight loss are more consistent. According to the findings of Patoulias *et al* (20), semaglutide was found to be more effective than dulaglutide when looking at absolute weight loss, probabilities for attaining weight loss between 5-10%, and BMI decrease. Similarly, in two other aforementioned meta-analyses, semaglutide was substantially more effective than dulaglutide in reducing

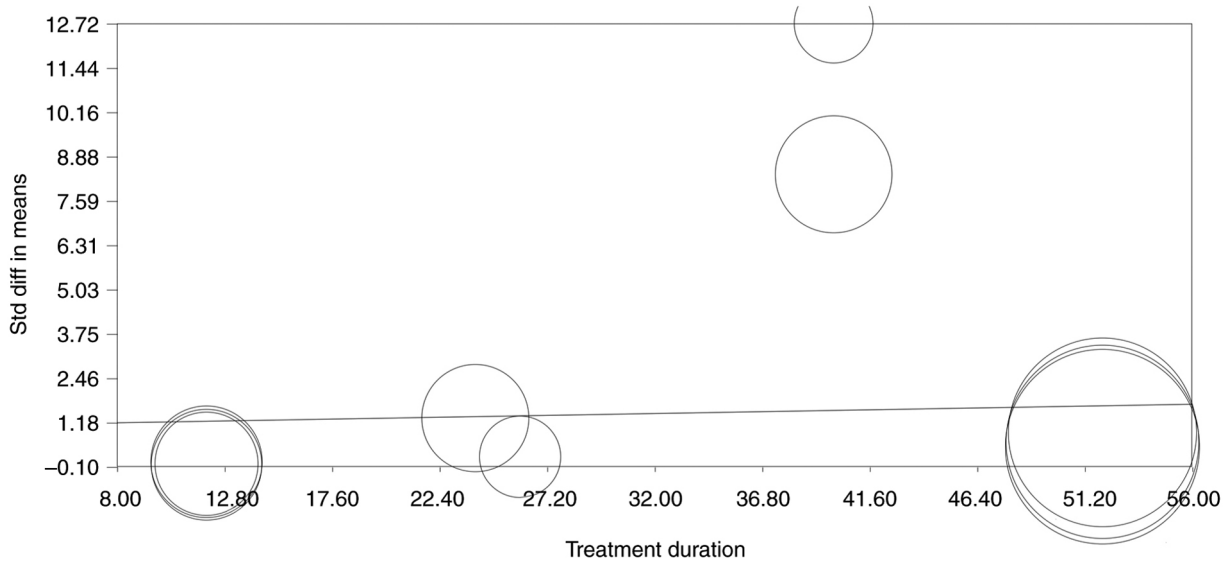

Figure 6. Meta-regression evaluating the relationship between the treatment duration and its effect size magnitude. With its effect size estimate plotted against the appropriate treatment period, each trial is shown as a circle. The circle's size represents the study's sample size. The association between the duration of therapy and the effect size is depicted by a regression line that is drawn between the points.

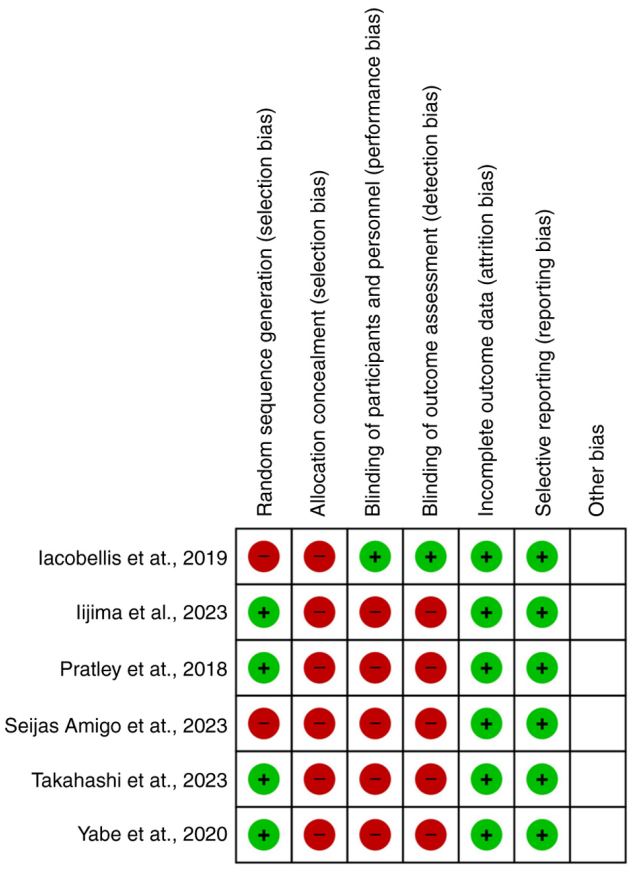

Figure 7. The Cochrane risk of bias assessment approach. It is used for quality evaluation of the studies included in the meta-analysis. Low and high risks, respectively, are indicated by the green and red dots.

body weight. In direct connection with these findings, Andreadis *et al* (25) found that compared with dulaglutide, semaglutide 1 mg was more effective at lowering body weight.

Safety. Due to a lack of data, a safety analysis could not be performed in the present study. It was found that the most common side effect of treatment in these therapies was gastrointestinal complications such as nausea and vomiting. However, a direct comparison between medications was not possible. Mishriky *et al* (22) showed that, compared with other GLP-1 RAs, semaglutide was considerably more likely to cause nausea and vomiting. On the other hand, Shi *et al*'s (21) meta-analysis of semaglutide and other GLP-1 RAs (for example, dulaglutide) failed to detect a higher incidence of gastrointestinal side effects in the former as opposed to the latter (21). In addition, a meta-analysis by Mishriky *et al* (22) found no statistically significant difference between semaglutide and other GLP-1 RAs in the incidence of any serious adverse events.

Data heterogeneity and sensitivity analysis. Heterogeneity is a common issue in meta-analyses, arising from differences in study design, patient characteristics, interventions and outcome measures among included studies. In the present study, high heterogeneity was found among the studies included in the meta-analysis, as evidenced by prediction interval analysis, which suggested significant between-study variability. This heterogeneity is important to acknowledge, as it can affect the precision, validity and generalizability of the meta-analysis results.

The I^2 statistic is commonly used in meta-analyses to quantify the percentage of total variation across studies due to heterogeneity rather than chance. It measures the inconsistency or diversity among studies and can range from 0-100%, with higher values indicating greater heterogeneity (26). However, it has been recently argued that the I^2 statistic does not adequately reveal the degree of variation in effect size in a meta-analysis (27). In that light, prediction interval analysis was used instead. Prediction interval analysis is a statistical method used to calculate CIs for the true effect size based on the distribution of the data and the sampling error. Given

the observed data and sampling variability, it provides a range of values within which the true effect size is likely to fall. Prediction interval analysis is particularly useful when estimating small or large effect sizes, as CIs are narrower for larger samples and effect sizes and wider for smaller samples and effect sizes.

To assess the potential impact of individual studies on the meta-analysis results, a sensitivity analysis was conducted by sequentially removing one study at a time and recalculating the effect size and pooled estimate. The sensitivity analysis results showed that removing one study (15) had a substantial effect on the overall effect size of the weight loss data and the statistical significance of the meta-analysis. This underscores the importance of cautious interpretation of meta-analysis results and the potential impact of individual studies on the outcome.

Limitations. The present study has several limitations that must be acknowledged. Despite the comprehensive search strategy used, it is still possible that some eligible studies may have been missed, which may influence the precision of the meta-analysis results. Besides, the number of studies available for this meta-analysis was limited which might be attributed to several factors. Firstly, semaglutide and dulaglutide are relatively new therapeutic options for the management of T2DM, and head-to-head comparisons between these two drugs have only recently become the focus of clinical research. This has resulted in a smaller pool of studies that directly compare their efficacy and safety. Additionally, our strict inclusion criteria, which required randomized controlled trials with specific outcome measures such as glycemic control and weight loss, further narrowed the range of eligible studies. As a result, some potentially relevant studies may have been excluded due to differences in study design, populations, or intervention protocols that did not align with the objectives of the current analysis.

Additionally, the quality of the included studies was variable, with some studies being of lower quality. This variability could have contributed to the observed heterogeneity and the sensitivity analysis results. The heterogeneity of the included data was also high. Although random-effects model was used to account for heterogeneity, it is important to acknowledge that some residual heterogeneity may remain, affecting the precision of the estimates. The high degree of heterogeneity observed in the present meta-analysis is likely influenced by differences in study design, patient populations, treatment regimens and dosage levels among the included studies. Specifically, variations in baseline HbA1c levels, treatment duration and dosing strategies (for example, semaglutide doses ranging from 0.5-14 mg vs. dulaglutide doses between 0.75-1.5 mg) may have contributed to the observed variability in outcomes. While subgroup analyses could provide further insights into the impact of these factors, the limited number of studies and variability in study characteristics made such analyses impractical. Instead, using moderator analysis allowed us to identify a significant relationship between longer treatment duration and greater weight loss, suggesting that duration may be an important factor to consider when choosing between these treatments. The broad prediction intervals indicate that, while semaglutide generally shows an advantage in weight loss, results may vary across different clinical settings and patient populations, highlighting the need for individualized treatment decisions. Future studies should aim for more consistent study designs and larger sample sizes to better delineate the comparative effectiveness of these therapies. The current sensitivity analysis identified that the exclusion of one study could significantly impact the overall results of weight loss data. This suggests that the present conclusions depend on including all studies and that one or more studies may have an undue influence on the overall estimate. Finally, meta-analyses are inherently limited by the quality and availability of the primary studies and the limitations of the meta-analytic methods used. While it was aimed to minimize potential biases and increase transparency in our review process, the present results may be subject to publication bias, incomplete reporting of results and other methodological limitations.

Conclusion. The present meta-analysis compared the efficacy of two important GLP-1 RAs, semaglutide and dulaglutide, in achieving glycemic control and weight loss in patients with T2DM. The results revealed that while there was no significant difference in glycemic control between the two drugs, semaglutide was more effective in inducing weight loss than dulaglutide. It is important to note that although random-effects model was used to account for heterogeneity, some residual heterogeneity may have remained, which could affect the precision of the estimates. Despite this, the present findings suggested that semaglutide may be a more favorable treatment option for patients with T2DM requiring weight management and glycemic control. Further research is needed to investigate the long-term anti-diabetic and cardiovascular benefits of GLP-1 RAs, the optimal dosages and regimens, and individual factors that may influence treatment response and outcomes. Nevertheless, the present meta-analysis provides valuable insights for clinicians and patients when making treatment decisions for T2DM.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

LX, LS and HA drafted and wrote the manuscript, collected and analyzed data. LS revised the manuscript for intellectual content, provided general supervision and gave final approval for publication. SH performed data analysis, language editing and obtained materials. LX and HA developed the study protocol and confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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