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Efficacy and Safety of Mazdutide in Adults with Obesity or Overweight, With or Without Diabetes: A Bayesian Network Meta-Analysis

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Abstract

Background: Mazdutide, a dual glucagon-like peptide-1 receptor (GLP-1R) and glucagon receptor (GCGR) agonist, has emerged as a promising therapy for obesity and overweight. However, its comparative dose-dependent efficacy and safety across multiple cardiometabolic outcomes remain to be comprehensively evaluated. Therefore, a Bayesian network meta-analysis was conducted to assess the effects of different Mazdutide doses in adults with obesity or overweight, with or without type 2 diabetes.

Methods: A systematic literature search was performed in PubMed, Embase, Web of Science, the Cochrane Library, and ClinicalTrials.gov from inception to January 15, 2026. Randomized controlled trials (RCTs) evaluating Mazdutide at any dose against placebo or active comparators in adults with obesity or overweight were included. Efficacy outcomes included changes in body weight, waist circumference, body mass index (BMI), glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), blood pressure, lipid profiles, and alanine aminotransferase (ALT). Safety outcomes included adverse events (AE), serious adverse events (SAE), gastrointestinal disorders, decreased appetite, and hypoglycemia.

Results: Nine RCTs with 2,292 participants were included. Compared with placebo, multiple Mazdutide doses significantly improved anthropometric and metabolic outcomes. Mazdutide 16 mg induced the largest reductions in waist circumference (mean difference [MD] −14.46 cm, 95% credible interval [CrI]: −20.83 to −8.14) and LDL cholesterol (−0.80 mmol/L, −1.27 to −0.33). Mazdutide 9 mg showed the greatest effect on body weight (−7.65 kg, −13.90 to −1.40) and BMI (−2.96, −5.35 to −0.59). For glycemic control, Mazdutide 4.5 mg and 6 mg reduced HbA1c by −0.85% (−1.43 to −0.31) and −0.82% (−1.29 to −0.38) in patients with type 2 diabetes. Subgroup analyses revealed that weight loss was significantly greater in non-diabetic individuals (e.g., Mazdutide 6 mg: −9.6 kg vs −4.5 kg in diabetic patients), whereas HbA1c reduction was more pronounced in those with type 2 diabetes (−1.6% vs −0.31%). Gastrointestinal adverse events were increased with Mazdutide (odds ratios 3.5 to 6.3 for effective doses), but serious adverse events were not significantly elevated.

Conclusions: Mazdutide demonstrates dose-dependent, clinically meaningful improvements in weight, central adiposity, glycemic control, blood pressure, lipids, and liver enzymes in adults with obesity or overweight. Treatment effects are appropriately modified by diabetes status, with enhanced weight loss in non-diabetic individuals and greater glycemic benefits in patients with type 2 diabetes. These findings support Mazdutide as an effective therapeutic option for obesity management.

Introduction

Obesity has emerged as a complex, chronic, and pervasive global health crisis, with its prevalence rising dramatically over recent decades[1, 2]. Current estimates indicate that approximately 810 million adults were living with obesity in 2020, a figure projected to reach 1.25 billion by 2030[3]. The repercussions extend far beyond individual health. Obesity is a well-established, independent risk factor for numerous comorbidities, most notably type 2 diabetes mellitus, but also cardiovascular diseases, nonalcoholic fatty liver disease, certain cancers, and psychological disorders[4, 5]. Consequently, it imposes a substantial economic burden on healthcare systems globally, encompassing both direct medical costs and indirect losses from reduced productivity[6].

Current therapeutic strategies for managing obesity follow a stepwise approach: lifestyle modifications, pharmacotherapy, and bariatric surgery for severe cases[7-9]. However, lifestyle interventions alone often yield only modest and frequently unsustainable weight loss[10]. Bariatric surgery, though highly effective, carries inherent operative risks and necessitates lifelong medical follow-up[9]. This therapeutic landscape has created a critical demand for pharmacological interventions that are not only safe and effective but can also address the complex metabolic dysregulation associated with excess adiposity[11].

In recent years, incretin-based therapies have revolutionised obesity pharmacotherapy. The success of glucagon-like peptide-1 receptor agonists (GLP-1RAs), such as semaglutide and liraglutide, confirmed that targeting appetite suppression and gastric emptying could induce clinically meaningful weight loss[12]. This success spurred the development of unimolecular dual and triple polyagonists that simultaneously target multiple receptors, potentially replicating the profound weight loss effects of metabolic surgery through non-surgical means[13].

Mazdutide (also known as IBI362 or LY3305677) is a promising dual agonist for both the glucagon-like peptide-1 receptor (GLP-1R) and the glucagon receptor (GCGR)[14]. Its mechanism leverages synergistic effects: GLP-1R agonism promotes satiety and reduces caloric intake, while GCGR activation directly increases energy expenditure[14]. Importantly, this dual action balances the GCGR's potential hyperglycaemic effect with the glucose-lowering properties of GLP-1R agonism, thereby preserving both glycaemic control and weight loss benefits[15]. Early-phase randomised controlled trials (RCTs) have demonstrated Mazdutide's potential to induce weight loss and improve metabolic parameters in individuals with obesity or overweight, both with and without type 2 diabetes[16-19].

Given the expanding landscape of GLP-1-based therapies, the efficacy, safety, and dosing requirements of each agent need rigorous evaluation to inform clinical decision-making. A preliminary meta-analysis confirmed Mazdutide's superiority over placebo but was limited to pairwise comparisons and did not explore dose-specific efficacy[20]. Concurrently, broader network meta-analyses (NMAs) have evaluated various GLP-1 receptor agonists and polyagonists for weight management[21, 22]. However, their necessarily broad scope offers limited granularity on Mazdutide itself, lacking dose-specific comparisons against active comparators like dulaglutide and not fully leveraging recent phase III trial data. Furthermore, another recent meta-analysis grouped incretin-based polyagonists together, obscuring the unique efficacy and safety profiles of individual drugs like Mazdutide[23].

The absence of a dedicated, high-resolution synthesis of Mazdutide's effects represents a collective evidence gap, creating uncertainty for clinicians facing a novel, potent therapeutic option without a comprehensive comparative framework. Therefore, we performed a Bayesian network meta-analysis to evaluate

and compare the efficacy and safety of all investigated doses of Mazdutide in adults with obesity or overweight, with or without type 2 diabetes. By synthesising both direct and indirect evidence, and including placebo and an active comparator (dulaglutide), this NMA delineates the dose-dependent effects of Mazdutide, quantifies its comparative advantages, and provides clinicians, researchers, and policymakers with the robust, granular evidence synthesis necessary for informed treatment selection in the rapidly evolving landscape of obesity pharmacotherapy.

Methods

Registration

This systematic review is reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines[24] and was conducted according to a registered protocol (PROSPERO identifier: CRD420261335722). PRISMA checklists are provided in electronic supplementary Appendix 1.

Search Strategy

We searched PubMed, EMBASE, Web of Science, the Cochrane Library, and ClinicalTrials.gov for randomised controlled trials of Mazdutide, from database inception to 15 January 2026. Two reviewers independently screened the retrieved citations, and any discrepancies were resolved by consulting a third reviewer. All identified records were imported into EndNote X9 for duplicate removal. The complete search strategies, including specific keywords and syntax tailored to each database, are provided in eTable 1 in the supplementary materials.

Inclusion and Exclusion Criteria

Eligible RCTs enrolled adults with a confirmed diagnosis of obesity or overweight. The intervention was Mazdutide administered at any investigated dosage, compared with either placebo or active comparator agents. For efficacy outcomes, we assessed changes from baseline in body weight, waist circumference, body mass index (BMI), glycated haemoglobin (HbA1c), fasting plasma glucose (FPG), systolic and diastolic blood pressure (SBP and DBP), lipid profiles (total cholesterol [TC], triglycerides [TG], low-density lipoprotein cholesterol [LDL], high-density lipoprotein cholesterol [HDL]), and alanine aminotransferase (ALT). Safety outcomes included incidence of adverse events (AE), serious adverse events (SAE), gastrointestinal disorders, decreased appetite, and hypoglycaemia.

Only RCTs published in English were considered. And we excluded republished articles, conference proceedings, animal studies, retrospective studies, and studies from which data could not be extracted.

Quality assessment and data extraction

The risk of bias of the incorporated RCTs was evaluated utilizing the Cochrane Risk of Bias 2 (ROB2) instrument[25], the most recent methodological guideline updated by the Cochrane Collaboration in 2019. This appraisal encompassed five critical domains: the randomization procedure, adherence to intended interventions, management of missing outcome data, techniques of outcome measurement, and selectivity in reporting results. Each category was appraised and categorized as exhibiting low, high, or some concerns regarding risk of bias.

To characterize the enrolled trials, the following data were systematically extracted: foundational details (including lead author, publication year, and trial design), demographic and clinical attributes of participants (such as disease duration, age, and BMI), intervention specifics (treatment regimens and group sample sizes), baseline values for all relevant outcomes, and the total duration of treatment and follow-up.

Data analysis

A Bayesian network meta-analysis was conducted using R software (version 4.3.3; R Foundation for Statistical Computing) with the gemtc and rjags packages. Treatment effects for continuous outcomes (e.g., FPG, HbA1c) were expressed as mean differences (MD) with 95% credible intervals (CrI), after harmonizing all units to standardized scales (mmol/L or %) to ensure comparability. For binary outcomes (e.g., AE), odds ratios (OR) with 95% CrI were calculated. The relative ranking of interventions was estimated using the surface under the cumulative ranking curve (SUCRA), where higher SUCRA values indicate a greater likelihood of being the most effective intervention (Table 2).

All Markov chain Monte Carlo (MCMC) simulations were performed using four parallel chains with 20,000 adaptation iterations and 50,000 inference iterations per chain (thin=1). Convergence of the MCMC algorithm was assessed using two complementary approaches: (i) visual inspection of trace plots and posterior density plots (eFigure 3), and (ii) the Gelman–Rubin diagnostic, where a potential scale reduction factor (PSRF) < 1.05 was considered indicative of satisfactory convergence (eFigure 4).

Model fit was evaluated by examining residual deviance and leverage plots, which identify influential studies and assess the overall adequacy of the consistency model. The leverage-versus-deviance scatter plots for all outcomes are provided in eFigure 5.

Heterogeneity was quantified using the I^2 statistic, with values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively. Inconsistency between direct and indirect evidence was examined using two approaches: (i) a node-splitting analysis, which assesses local inconsistencies for each closed loop in the network, and (ii) comparison of model fit between consistency and inconsistency models via the deviance information criterion (DIC), where a ΔDIC < 5 favored the consistency model. The detailed numerical results of the node-splitting and DIC comparisons are presented in eTable 3 and eTable 4.

Potential publication bias was assessed for each outcome using comparison-adjusted funnel plot, which were visually inspected for asymmetry. In addition, Egger's linear regression test and Begg's rank correlation test were performed to statistically evaluate small-study effects[26]. All analyses were conducted using Stata (version 16.0; StataCorp LLC, College Station, TX, USA). A P-value less than 0.05 from either test was considered indicative of statistically significant publication bias.

Meta-regression and Subgroup Analyses

To investigate potential effect modifiers, we performed a meta-regression and subgroup analysis within our network meta-analysis framework, restricted to placebo-controlled trials. T2DM status was incorporated as a study-level covariate to assess its influence on treatment effects. Studies were categorized as enrolling either an exclusive population with diagnosed type 2 diabetes or a population without type 2 diabetes (i.e., with obesity or overweight but without diabetes). The results of the meta-regression and subgroup analysis are presented in eTable 6 and eTable 5.

Patient and public involvement

No patient representatives or members of the public were directly involved in the planning, design, conduct, or reporting of this study, and no primary data were collected.

Results

Study selection and characteristics

The screening process and basic patient characteristics are presented in Figure 1 and Table 1, respectively. A total of 129 articles were initially retrieved, with 100 remaining after removing duplicates. Subsequent preliminary screening excluded non-randomized controlled trials and studies with inconsistent content, resulting in 66 articles. Following a detailed examination of the full texts, 9 RCTs involving 2292 patients were ultimately included.

Quality assessment of included study

All 9 RCTs included in this network meta-analysis were assessed as having low risk of bias across all domains (eFigure 1). Each study demonstrated adequate random sequence generation, allocation concealment, and blinding of participants, personnel, and outcome assessors. Incomplete outcome data were appropriately addressed, and all prespecified outcomes were reported.

Publication Bias

The assessment of publication bias for all outcomes is summarized in eFigure 2 (comparison-adjusted funnel plots) and eTable 2 (Egger's and Begg's tests). Collectively, the included trials exhibited a low risk of bias, strengthening confidence in the pooled estimates.

Assessment of Inconsistency and Heterogeneity

The consistency model provided a good fit for most outcomes, as indicated by favourable Deviance Information Criterion (DIC) values (eTable 4). Leverage-versus-deviance scatter plots (eFigure 5) further supported this finding; no study exhibited both high leverage and poor fit (upper-right quadrant), suggesting that network estimates were robust and not disproportionately influenced by any single trial.

Heterogeneity was assessed using the I^2 statistic derived from both pairwise and consistency models (eTable 3). For most comparisons, I^2 values indicated low to moderate heterogeneity, with the majority falling below 50%. However, some comparisons showed higher heterogeneity, reflecting clinical or methodological differences across included studies

To assess local inconsistency, we performed node-splitting analysis, which evaluates the alignment between direct and indirect evidence for each comparison in the network. This analysis revealed evidence of inconsistency in several comparisons across multiple outcomes, with Bayesian p-values < 0.05 indicating significant disagreement between evidence sources (eTable 3). The detailed results of the node-splitting analysis for all outcomes are presented in eTable 7.

However, model fit was not uniform across all endpoints. For eight outcomes—low-density lipoprotein cholesterol, systolic blood pressure, triglycerides, total cholesterol, alanine aminotransferase, gastrointestinal disorders, hypoglycaemia, and adverse events—the difference in DIC values between the consistency and inconsistency models exceeded the prespecified threshold of 5, indicating potential global inconsistency within these networks. Given these findings, treatment effect estimates for these eight outcomes should be interpreted with caution. Further exploration of potential effect modifiers or sensitivity analyses may be warranted to investigate sources of inconsistency.

Efficacy outcomes

Waist circumference

For waist circumference reduction, the network meta-analysis comprised 9 trials involving 2292 participants. Compared with placebo, several Mazdutide doses significantly reduce waist circumference (Figures 2-4). Mazdutide 16 mg induced the most substantial reduction (MD −14.46 cm, 95% CrI −20.83 to −8.14; SUCRA 43.1%), followed by Mazdutide 6 mg (−5.84 cm, −7.51 to −4.10; SUCRA 58.6%), Mazdutide 4 mg (−5.01 cm, −7.22 to −2.76; SUCRA 80.7%), and Mazdutide 4.5 mg (−4.45 cm, −6.51 to −2.38; SUCRA 27.2%). Mazdutide 3 mg also showed significant efficacy compared with placebo (−2.55 cm, −4.65 to

−0.40; SUCRA 10.9%). Dulaglutide 1.5 mg ranked highest according to SUCRA (87.5%) but did not achieve statistical significance versus placebo (−2.18 cm, −4.44 to 0.13).

Body Weight

For body weight reduction, the network meta-analysis comprised 9 trials involving 2292 participants. Compared with placebo, multiple Mazdutide doses significantly reduced body weight (Figures 2-4). Mazdutide 9 mg induced the largest reduction (−7.65 kg, −13.90 to −1.40; SUCRA 46.8%), followed by Mazdutide 6 mg (−7.04 kg, −9.25 to −4.83; SUCRA 54.9%), Mazdutide 4.5 mg (−6.16 kg, −8.84 to −3.49; SUCRA 44.5%), Mazdutide 4 mg (−5.57 kg, −8.61 to −2.53; SUCRA 86.5%), and Mazdutide 3 mg (−3.93 kg, −6.58 to −1.23; SUCRA 49.0%). Dulaglutide 1.5 mg showed no significant reduction versus placebo (−2.54 kg, −5.62 to 0.57; SUCRA 58.6%). The highest ranked treatment according to SUCRA was Mazdutide 4 mg (86.5%).

BMI

For BMI reduction, the network meta-analysis comprised 8 trials involving 2218 participants. Compared with placebo, multiple Mazdutide doses significantly reduce body mass index (Figures 2-4). Mazdutide 9 mg induced the largest reduction (−2.96, 95% −5.35 to −0.59; SUCRA 81.4%), followed by Mazdutide 6 mg (−2.49, −3.30 to −1.67; SUCRA 78.3%), Mazdutide 4.5 mg (−2.14, −3.13 to −1.14; SUCRA 62.9%), Mazdutide 4 mg (−1.99, −3.12 to −0.86; SUCRA 56.6%), and Mazdutide 3 mg (−1.43, −2.41 to −0.46; SUCRA 34.5%). Dulaglutide 1.5 mg showed no significant reduction versus placebo (−0.93, −2.05 to 0.20; SUCRA 0.9%). Mazdutide 10 mg also did not achieve statistical significance (−2.41, −4.87 to 0.04; SUCRA 19.0%).

SBP

For SBP reduction, the network meta-analysis comprised 7 trials involving 2194 participants. Compared with placebo, all Mazdutide doses investigated significantly reduced SBP (Figures 2-4). Mazdutide 6 mg induced the largest reduction (−6.08 mm Hg, 95% −8.65 to −3.35; SUCRA 79.9%), followed by Mazdutide 4.5 mg (−5.89 mm Hg, −9.44 to −2.54; SUCRA 76.2%), Mazdutide 3 mg (−5.30 mm Hg, −9.00 to −2.01; SUCRA 64.2%), and Mazdutide 4 mg (−5.10 mm Hg, −8.28 to −1.68; SUCRA 59.0%). Dulaglutide 1.5 mg showed no significant reduction versus placebo (−1.11 mm Hg, −4.41 to 3.01; SUCRA 15.5%).

DBP

For DBP reduction, the network meta-analysis comprised 7 trials involving 2184 participants. Compared with placebo, several Mazdutide doses significantly reduce DBP (Figures 2-4). Mazdutide 4.5 mg induced the largest reduction (−4.04 mm Hg, −6.80 to −1.52; SUCRA 87.2%), followed by Mazdutide 3 mg (−3.64 mm Hg, −6.48 to −1.13; SUCRA 79.9%) and Mazdutide 6 mg (−2.78 mm Hg, −4.72 to −0.56; SUCRA 61.5%). Mazdutide 4 mg showed no significant reduction versus placebo (−2.17 mm Hg, −4.67 to 0.59; SUCRA 45.8%), as did Dulaglutide 1.5 mg (−0.87 mm Hg, −3.46 to 2.29; SUCRA 20.2%).

HbA1c

For HbA1c reduction, the network meta-analysis comprised 8 trials involving 2178 participants with type 2 diabetes. Compared with placebo, multiple Mazdutide doses significantly reduced HbA1c concentrateions (Figures 2-4). Mazdutide 4.5 mg induced the largest reduction (−0.85%, −1.43% to −0.31%; SUCRA 73.7%), followed by Mazdutide 6 mg (−0.82%, −1.29% to −0.38%; SUCRA 70.5%), Mazdutide 4 mg (−0.74%, −1.37% to −0.13%; SUCRA 58.1%), and Mazdutide 3 mg (−0.70%, −1.26% to −0.15%; SUCRA 55.9%). Dulaglutide 1.5 mg also showed significant efficacy compared with placebo (−0.72%, −1.41% to −0.07%; SUCRA 54.5%). Mazdutide 16 mg did not achieve statistical significance (−0.38%, −1.47% to 0.70%; SUCRA 33.3%).

FPG

For FPG reduction, the network meta-analysis comprised 8 trials involving 2152 participants with type 2 diabetes. Compared with placebo, several Mazdutide doses and dulaglutide significantly reduced FPG concentrations (Figures 2-4). Mazdutide 6 mg induced the largest reduction (−1.28 mmol/L, −2.00 to −0.62; SUCRA 74.0%), followed by Mazdutide 4 mg (−1.19 mmol/L, −2.15 to −0.27; SUCRA 65.0%), dulaglutide 1.5 mg (−1.13 mmol/L, −2.15 to −0.16; SUCRA 61.1%), and Mazdutide 4.5 mg (−1.10 mmol/L, −1.96 to −0.27; SUCRA 59.1%). Mazdutide 3 mg (−0.78 mmol/L, −1.62 to 0.04; SUCRA 35.2%) and Mazdutide 16 mg (−1.00 mmol/L, −2.65 to 0.66; SUCRA 53.8%) did not achieve statistical significance.

LDL

For LDL reduction, the network meta-analysis comprised 8 trials involving 2214 participants. Compared with placebo, all Mazdutide doses investigated and dulaglutide significantly reduced LDL concentrations (Figures 2-4). Mazdutide 16 mg induced the largest reduction (−0.80 mmol/L, −1.27 to −0.33; SUCRA 98.3%), followed by Mazdutide 4.5 mg (−0.42 mmol/L, −0.59 to −0.27; SUCRA 77.2%), Mazdutide 6 mg (−0.40 mmol/L, −0.52 to −0.29; SUCRA 72.4%), Mazdutide 4 mg (−0.29 mmol/L, −0.42 to −0.16; SUCRA 44.5%), Mazdutide 3 mg (−0.20 mmol/L, −0.37 to −0.04; SUCRA 27.5%), and dulaglutide 1.5 mg (−0.20 mmol/L, −0.35 to −0.01; SUCRA 30.0%).

HDL

For HDL cholesterol, the network meta-analysis comprised 6 trials involving 2136 participants. Compared with placebo, most Mazdutide doses did not significantly alter HDL cholesterol concentrations, although the direction of effect suggested modest reductions (Figure 2-4). Mazdutide 6 mg showed a small but statistically significant reduction (−0.05 mmol/L, −0.10 to −0.01; SUCRA 37.6%). No significant differences were observed for other doses: Mazdutide 16 mg (−0.14 mmol/L, −0.39 to 0.11; SUCRA 73.1%), Mazdutide 4.5 mg (−0.05 mmol/L, −0.12 to 0.01; SUCRA 54.2%), Mazdutide 4 mg (−0.04 mmol/L, −0.09 to 0.01; SUCRA 32.8%), and Mazdutide 3 mg (−0.06 mmol/L, −0.13 to 0.00; SUCRA 22.4%). Dulaglutide 1.5 mg ranked highest according to SUCRA (93.4%) but did not significantly alter HDL compared with placebo (−0.02 mmol/L, −0.09 to 0.04). These findings indicate that Mazdutide has minimal clinically meaningful impact on HDL cholesterol across the dose range studied.

TC

For TC reduction, the network meta-analysis comprised 8 trials involving 2214 participants. Compared with placebo, all investigated Mazdutide doses and dulaglutide significantly reduced TC concentrations (Figures 2-4). Mazdutide 16 mg induced the largest reduction (−1.55 mmol/L, −2.04 to −1.05; SUCRA 100.0%), followed by Mazdutide 4.5 mg (−0.67 mmol/L, −0.90 to −0.48; SUCRA 77.4%), Mazdutide 6 mg (−0.62 mmol/L, −0.80 to −0.50; SUCRA 71.3%), Mazdutide 4 mg (−0.45 mmol/L, −0.64 to −0.29; SUCRA 40.2%), Mazdutide 3 mg (−0.45 mmol/L, −0.68 to −0.24; SUCRA 38.9%), and dulaglutide 1.5 mg (−0.34 mmol/L, −0.55 to −0.12; SUCRA 22.2%).

TG

For TG reduction, the network meta-analysis comprised 8 trials involving 2214 participants. Compared with placebo, several Mazdutide doses and dulaglutide significantly reduced TG concentrations (Figures 2-4). Mazdutide 6 mg induced the largest reduction (−0.70 mmol/L, −0.86 to −0.57; SUCRA 8.8%), followed by Mazdutide 4.5 mg (−0.54 mmol/L, −0.72 to −0.36; SUCRA 67.0%), Mazdutide 4 mg (−0.49 mmol/L, −0.67 to −0.32; SUCRA 26.1%), Mazdutide 3 mg (−0.46 mmol/L, −0.66 to −0.26; SUCRA 63.1%), and dulaglutide 1.5 mg (−0.23 mmol/L, −0.48 to −0.03; SUCRA 62.8%). Mazdutide 16 mg did not achieve statistical significance (−0.40 mmol/L, −0.89 to 0.08; SUCRA 85.7%).

ALT

For ALT reduction, the network meta-analysis comprised 5 trials involving 1888 participants. Compared with placebo, several Mazdutide doses significantly reduce alanine ALT concentrations (Figures 2-4). Mazdutide 4 mg induced the largest reduction (−7.73 U/L, −10.94 to −4.42; SUCRA 87.8%), followed by Mazdutide 6 mg (−7.60 U/L, −10.39 to −4.59; SUCRA 87.7%) and Mazdutide 4.5 mg (−5.52 U/L, −9.97 to −1.30; SUCRA 63.1%). Mazdutide 3 mg (−2.37 U/L, −6.41 to 1.65; SUCRA 36.7%) and dulaglutide 1.5 mg (−0.39 U/L, −3.88 to 2.93; SUCRA 14.8%) did not achieve statistical significance.

Safety outcomes

AE

For any AE, the network meta-analysis comprised 9 trials involving 2292 participants. Compared with placebo, several Mazdutide doses were associated with significantly higher odds of AEs (Figures 2-4). When ranking the interventions (where higher SUCRA values indicate a safer profile), Dulaglutide 1.5 mg emerged as a well-tolerated option, showing no significant increase in AE compared with placebo (OR 1.67, 95% CrI 0.85 to 3.46; SUCRA 76.2%). In contrast, multiple doses of Mazdutide exhibited significantly increased odds of AEs. The risk was most pronounced with Mazdutide 4.5 mg (3.47, 1.68 to 8.42; SUCRA 43.8%) and Mazdutide 6 mg (3.27, 1.95 to 5.91; SUCRA 34.0%), followed by Mazdutide 3 mg (2.55, 1.20 to 5.50; SUCRA 50.4%) and Mazdutide 4 mg (2.51, 1.34 to 4.76; SUCRA 51.1%). Notably, for several higher doses (Mazdutide 9 mg, 10 mg, and 16 mg), the effect estimates were highly uncertain with extremely wide CrIs, primarily reflecting sparse data and network connectivity limitations for these specific nodes.

SAE

For SAE, the network meta-analysis comprised 9 trials involving 2292 participants. Compared with placebo, no Mazdutide dose or dulaglutide showed a statistically significant increase in the odds of SAE (Figures 2-4). Point estimates varied across doses: Mazdutide 3 mg (0.26, 0.02 to 2.48; SUCRA 81.4%), Mazdutide 4.5 mg (0.79, 0.12 to 6.59; SUCRA 70.0%), Mazdutide 6 mg (1.48, 0.48 to 7.90; SUCRA 53.2%), Mazdutide 4 mg (1.97, 0.54 to 13.30; SUCRA 33.4%), and dulaglutide 1.5 mg (2.40, 0.49 to 21.11; SUCRA 22.2%). For several doses (Mazdutide 10 mg, 16 mg, and 9 mg), the estimates were highly uncertain with extremely wide CrI, reflecting sparse data or network connectivity issues for these nodes.

gastrointestinal disorders

For gastrointestinal disorders, the network meta-analysis comprised 9 trials involving 2292 participants. Compared with placebo, several Mazdutide doses and dulaglutide were associated with significantly higher odds of gastrointestinal adverse events (Figures 2-4). Mazdutide 6 mg showed the highest odds (6.32, 3.47 to 11.06; SUCRA 21.4%), followed by Mazdutide 4.5 mg (6.11, 2.88 to 13.08; SUCRA 26.4%), Mazdutide 4 mg (4.79, 2.36 to 9.32; SUCRA 36.9%), Mazdutide 3 mg (3.58, 1.60 to 7.59; SUCRA 50.2%), and dulaglutide 1.5 mg (2.56, 1.10 to 5.55; SUCRA 63.3%). Mazdutide 16 mg showed an extremely high point estimate with wide CrI (174.83, 8.13 to 14784.73; SUCRA 2.5%), reflecting sparse data for this dose. Mazdutide 10 mg (0.17, 0.01 to 2.97; SUCRA 94.9%) and Mazdutide 9 mg (0.95, 0.02 to 41.92; SUCRA 71.4%) did not show a statistically significant association with gastrointestinal disorders compared with placebo.

Hypoglycemia

For hypoglycaemia, the network meta-analysis comprised 8 trials involving 2016 participants. Compared with placebo, no Mazdutide dose or dulaglutide showed a statistically significant increase in the odds of hypoglycaemic events (Figures 2-4). Point estimates varied across doses: Mazdutide 9 mg (0.00, 0.00 to 0.56; SUCRA 73.3%), Mazdutide 6 mg (0.58, 0.12 to 2.45; SUCRA 76.8%), dulaglutide 1.5 mg (0.98, 0.18 to 5.48; SUCRA 65.3%), Mazdutide 10 mg (1.13, 0.02 to 86.53; SUCRA 46.6%), Mazdutide 4 mg (1.67, 0.39 to 8.01; SUCRA 32.6%), Mazdutide 3 mg (1.71, 0.25 to 10.15; SUCRA 44.6%), and Mazdutide 4.5 mg (3.68, 0.69 to 21.54; SUCRA 13.4%). For several doses, the CrI were wide, reflecting imprecision in estimates.

Decreased Appetite

For decreased appetite, the network meta-analysis comprised 9 trials involving 2292 participants. Compared with placebo, several Mazdutide doses and dulaglutide were associated with significantly higher odds of decreased appetite (Figures 2-4). Mazdutide 6 mg showed the highest odds (7.44, 3.38 to 15.65; SUCRA 19.1%), followed by Mazdutide 4 mg (7.18, 2.82 to 17.61; SUCRA 22.4%), Mazdutide 4.5 mg (6.83, 2.78 to 20.26; SUCRA 32.4%), dulaglutide 1.5

mg (3.42, 1.15 to 9.51; SUCRA 59.1%), and Mazdutide 3 mg (3.11, 1.00 to 8.10; SUCRA 59.4%). For Mazdutide 10 mg (0.33, 0.01 to 7.43; SUCRA 91.8%), 9 mg (6.25, 0.49 to 108.00; SUCRA 38.3%), and 16 mg (6.90, 0.46 to 313.20; SUCRA 39.0%), the estimates were highly uncertain with wide CrI, reflecting sparse data or network connectivity issues for these doses.

Subgroup Analysis

We performed subgroup analyses to explore the potential influence of diabetes status on the efficacy and safety outcomes (eTable 5). Overall, the direction of treatment effects was generally consistent between patients with and without type 2 diabetes, although the magnitude of effects differed notably across several outcomes.

For anthropometric measures, the weight-lowering effects of Mazdutide were more pronounced in patients without type 2 diabetes compared with those with type 2 diabetes. In non-diabetic individuals, Mazdutide 6 mg reduced body weight by −9.6 kg (95% CrI −12.0 to −7.6), BMI by −3.4 (−4.2 to −2.7), and waist circumference by −8.5 cm (−9.6 to −7.2), whereas corresponding reductions in patients with type 2 diabetes were −4.5 kg (−6.4 to −2.6), −1.5 (−2.3 to −0.84), and −4.1 cm (−5.1 to −3.0), respectively. A similar pattern was observed across other Mazdutide doses.

For glycaemic control, the glucose-lowering effects were, as expected, more pronounced in patients with type 2 diabetes. Mazdutide 6 mg reduced HbA1c by −1.6% (−1.8 to −1.3) and FPG by −2.4 mmol/L (−2.8 to −1.9) in diabetic patients, whereas corresponding reductions in non-diabetic individuals were −0.31% (−0.46 to −0.15) and −0.44 mmol/L (−0.78 to −0.14), respectively.

For blood pressure outcomes, reductions in SBP were observed in both subgroups, with Mazdutide 6 mg showing numerically greater reduction in non-diabetic patients (−8.2 mm Hg, −11.0 to −5.1) compared with diabetic patients (−4.0 mm Hg, −7.0 to −1.0). For DBP, significant reductions were observed predominantly in non-diabetic patients, with Mazdutide 3 mg, 4.5 mg, and 6 mg showing significant effects only in this subgroup.

For lipid profiles, both subgroups showed improvements across multiple parameters. In patients with type 2 diabetes, Mazdutide 6 mg reduced TC by −0.71 mmol/L (−0.97 to −0.51), TG by −0.80 mmol/L (−1.0 to −0.58), and LDL by −0.44 mmol/L (−0.64 to −0.28). Corresponding reductions in non-diabetic patients were −0.57 mmol/L (−0.79 to −0.38), −0.65 mmol/L (−0.85 to −0.47), and −0.38 mmol/L (−0.54 to −0.21), respectively. For alanine aminotransferase, significant reductions were observed with Mazdutide 4 mg, 4.5 mg, and 6 mg in the overall analysis; these effects were primarily driven by non-diabetic patients, with no significant reductions in diabetic patients.

For safety outcomes, the pattern of AE was generally consistent across subgroups, although CrI were wider in subgroup analyses owing to smaller sample sizes. The increased odds of gastrointestinal disorders and decreased appetite with Mazdutide doses were observed in both diabetic and non-diabetic patients, with point estimates suggesting potentially higher odds in non-diabetic patients for some doses. For SAE and hypoglycaemia, no significant increases were observed in either subgroup, with estimates remaining imprecise for several doses.

Meta Regression

We performed Bayesian meta-regression to explore the influence of type 2 diabetes status on treatment effects (eTable 6). Diabetes status significantly modified treatment effects for anthropometric and glycaemic outcomes.

Specifically, positive regression coefficients with 95% CrI excluding zero were observed for body weight (β range 5.05 to 5.25), BMI (β range 1.85 to 1.93), and waist circumference (β range 4.21 to 4.57), indicating attenuated weight loss effects in patients with type 2 diabetes compared with non-diabetic individuals. Conversely, negative coefficients excluding zero were observed for HbA1c (β range −1.28 to −1.15) and fasting plasma glucose (β range −1.94 to −1.23), substantiating the greater glucose-lowering effects in the diabetic subpopulation.

For blood pressure, lipid parameters, alanine aminotransferase, and all safety outcomes (AE, SAE, gastrointestinal disorders, decreased appetite, and hypoglycaemia), regression coefficients had 95% CrI crossing zero, indicating no significant modification by diabetes status. These analyses confirm that diabetes status differentially influences efficacy outcomes—enhancing glycaemic effects while attenuating weight loss—but does not substantially affect safety profiles.

Discussion

Key findings

Our network meta-analysis provides a comprehensive, dose-resolved summary of Mazdutide's cardiometabolic effects. Across outcomes, higher doses tended to produce larger benefits: intermediate/high doses (4.5–16 mg) yielded large, consistent weight loss and meaningful improvements in waist circumference, while even higher doses produced still larger percent weight reductions and marked reductions in central adiposity and LDL cholesterol[20-23]. These trial-level observations are concordant with the phase-2 clinical development programme for Mazdutide and with the evolving pipeline of entero-pancreatic polyagonists in obesity management[18, 27].

Clinical Efficacy and Subgroup Differences

A consistent and clinically important interaction with diabetes status emerged: weight-lowering effects were larger in participants without type 2 diabetes, whereas glucose-lowering effects were greater among participants with type 2 diabetes. For example, the network and subgroup analyses indicate substantially greater absolute weight loss in non-diabetic participants (Mazdutide 6 mg: −9.6 kg non-diabetic vs −4.5 kg in diabetic participants), while glycaemic responses in people with type 2 diabetes were larger (HbA1c reductions reported up to 1.6% in some trial subgroups; network averages for

commonly effective doses were 0.8–0.9% for 4.5–6 mg). These results mirror patterns reported for other dual/triple agonists—patients with type 2 diabetes often derive proportionally greater glycaemic benefit but smaller absolute weight loss than non-diabetic individuals[21, 28, 29]. The finding that glycaemic reductions are strongly modified by baseline glycaemia is concordant with general GLP-1 literature showing larger HbA1c reductions at higher baseline HbA1c values[30-32].

Beyond anthropometric and glycaemic changes, Mazdutide produced clinically relevant SBP reductions (5–6 mmHg) and consistent improvements in lipid parameters, with larger LDL and TC reductions at the highest network-ranked dose (16 mg). These findings align with class effects reported for GLP-1–based therapies, which likely reflect both weight-mediated and weight-independent mechanisms[33, 34].

Mechanistic considerations

Mazdutide's dual GLP-1/glucagon receptor agonism provides complementary mechanisms that plausibly explain the clinical profile observed above. Mechanistically, this differential response between type 2 diabetes and non-type 2 diabetes cohorts likely reflects a combination of factors: insulin resistance, concurrent weight-promoting medications, loss of urinary glucose excretion when glycaemia improves, and other biological differences that blunt weight loss in diabetes [30, 31]. Furthermore, GLP-1 receptor agonism reduces appetite, delays gastric emptying, and augments glucose-dependent insulin secretion. Conversely, glucagon receptor agonism can increase energy expenditure and hepatic fatty acid oxidation, which may potentiate visceral fat loss and improve lipid parameters when appropriately balanced with GLP-1 activity[21, 35]. Net glycaemic benefit is preserved because GLP-1–mediated insulin secretion and glucagon suppression offset the potential hyperglycaemic tendencies of isolated glucagon receptor activation[35]. These mechanistic rationales are supported by trial observations of disproportionate reductions in visceral fat, ALT and liver fat proxies with dual agonists and co-agonists in some studies[21].

Safety, tolerability and practical mitigation

In our network the odds ratios for gastrointestinal disorders across effective doses ranged roughly from 3.6 to 6.3 compared with placebo. As expected for GLP-1–based and polyagonist molecules, gastrointestinal adverse events (nausea, diarrhoea, vomiting) and decreased appetite were the dominant tolerability signals for Mazdutide and were dose-related. Most gastrointestinal events were mild–moderate and clustered around dose escalation periods, consistent with prior GLP-1 literature[36-38]. SAE were not significantly increased in pooled comparisons and clinically significant hypoglycaemia was uncommon when Mazdutide was used as monotherapy; however, combined use with insulin or insulin secretagogues requires anticipatory dose adjustment and close glucose monitoring. Practical strategies to mitigate gastrointestinal events include slower or individualized up-titration schedules, patient counselling about transient nature of symptoms, and antiemetic support when appropriate[36]. Antibody formation to Mazdutide has been observed in development trials (treatment-induced antibodies reported in a subset of participants), and the clinical significance for long-term efficacy requires further monitoring[38].

Strengths and Limitations

This study has several strengths. To our knowledge, it is the first Bayesian network meta-analysis to explicitly model multiple Mazdutide doses across a broad range of cardiometabolic and safety outcomes in adults with and without type 2 diabetes. The Bayesian framework enabled probabilistic dose ranking and coherent interval estimation, and pre-specified subgroup and meta-regression analyses clarified effect modification by diabetes status.

However, several limitations should be considered. First, for some outcomes and doses—particularly the highest doses (10 mg, 16 mg)—the number of direct RCTs was limited, resulting in wide CrI and imprecise estimates. Second, the network synthesises study-level data and therefore cannot fully adjust for individual-level modifiers such as baseline BMI distribution, obesity duration, and race. Third, heterogeneity in trial design (inclusion criteria, background therapy, follow-up duration) may influence pooled estimates despite acceptable global consistency diagnostics for many endpoints. Fourth, much of the randomised evidence to date is relatively short-term (12–32 weeks) and does not inform long-term maintenance, durability of weight loss, or major clinical outcomes such as cardiovascular events—questions that require dedicated outcome trials and longer follow-up. Finally, the current evidence base is overwhelmingly derived from Chinese populations. Given potential ethnic differences in body composition, beta-cell function, and incretin sensitivity, the global generalisability of these dose-response patterns must be confirmed in larger, multinational phase 3 programmes.

Clinical Implications and Future Perspectives

For clinicians, these data suggest that Mazdutide is a potent pharmacologic option for adults with overweight or obesity, with expected benefits diverging by diabetes status. When prescribing, larger absolute weight loss should be anticipated in non-diabetic patients, while robust glycaemic improvement is the primary driver in patients with type 2 diabetes.

The evidence base for Mazdutide is growing rapidly. For researchers and regulators, priority areas include the completion of ongoing phase 3 trials and head-to-head studies against established GLP-1 agents (e.g., the GLORY-2, DREAMS-3, and GLORY-3 trials) to clarify comparative effectiveness. Furthermore, long-term cardiovascular outcome trials and real-world safety surveillance are essential to assess durability, characterise rare immunogenicity consequences, and evaluate organ-specific outcomes, including MASLD and obstructive sleep apnoea. Dedicated mechanistic studies quantifying lean versus fat mass changes will also be critical to clarify implications for sarcopenia risk during rapid weight loss.

Conclusion

In summary, this Bayesian network meta-analysis indicates that Mazdutide produces dose-dependent, clinically meaningful improvements in weight, central adiposity, glycaemia (in type 2 diabetes), blood pressure, and lipids, with a safety profile dominated by dose-related gastrointestinal effects. The magnitude and pattern of benefits vary appropriately by dose and diabetes status. Ongoing phase 3 and head-to-head trials will be critical to confirm its comparative positioning, evaluate long-term cardiovascular safety, and guide optimal clinical use in the rapidly evolving landscape of obesity pharmacotherapy.

Abbreviations

AE, adverse events; ALT, alanine aminotransferase; BMI, body mass index; CrI, credible intervals; DBP, diastolic blood pressure; DIC, Deviance Information Criterion; FPG, fasting plasma glucose; GCGR, glucagon receptor; GLP-1, glucagon-like peptide-1; GLP-1R, glucagon-like peptide-1 receptor; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; MD, mean differences; Metabolic dysfunction-associated steatotic liver disease, MASLD; NMA, network meta-analysis; OR, odds ratio; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCTs, randomized controlled trials; SAE, serious adverse events; SBP, systolic blood pressure; SUCRA, surface under the cumulative ranking curve; T2DM, type 2 diabetes mellitus; TC, total cholesterol; TG, triglycerides.

Declarations

Author Contributions: Adili Tuersun and Guo Ma had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Adili Tuersun, Guo Ma, Zhoufang Mei.

Acquisition, analysis, or interpretation of data: Adili Tuersun, Xinyi Hu, Shan Wang, Liyuan Pang, Qiuxia Yu, Yu Zhong.

Drafting of the manuscript: Adili Tuersun, Xinyi Hu, Shan Wang.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Adili Tuersun, Xinyi Hu, Haiyang Liu, Yulin Wu.

Administrative, technical, or material support: Guo Ma, Zhoufang Mei.

Obtained funding: Guo Ma.

Supervision: Guo Ma, Zhoufang Mei.

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Data Availability Statement

All data generated or analyzed during this study are included in this published article. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Tables

Table 1. Baseline Characteristics of Included Studies

Author (year)	Trial registration	Treatments	Number	BMI (Kg/m^2)	HbA1c(%)	Mean Age	Diabetic status	RCT Phase	Outcom
Ji 2021[16]	NCT04440345	Mazdutide3.0mg	8	31.1±2.4	5.3±0.6	34.4±15.2	Non-DM	Phase 1b	ABCDEI
		Mazdutide4.5mg	8	29.4±3.9	5.2±0.2	28.6±6.0			
		Mazdutide6.0mg	8	30.5±2.0	5.3±0.3	39.5±18.0			
		Placebo	12	29.5±4.0	5.2±0.3	35.5±7.1			
Jiang 2022[39]	NCT04466904	Mazdutide3.0mg	8	24.1±1.4	8.9±0.7	58.6±5.3	T2DM	Phase 1b	ABCDEI
		Mazdutide4.5mg	8	25.7±3.4	8.8±1.0	47.9±8.9			
		Mazdutide6.0mg	8	26.0±2.2	8.5±1.1	54.6±10.6			
		Dulaglutide1.5mg	6	26.6±3.0	8.3±1.4	50.7±4.8			
		Placebo	12	26.5±2.7	8.3±0.7	50.2±8.5			
Ji 2022[17]	NCT04440345	Mazdutide9.0mg	8	30.1±3.8	NA	37.9±9.7	Non-DM	Phase 1b	ABDMN
		Mazdutide10mg	8	31.8±5.1	NA	36.0±9.1			
		Placebo	8	29.6±3.3	NA	39.9±11.7			
Ji 2023[18]	NCT04904913	Mazdutide3.0mg	62	31.8±3.9	5.41±0.27	37.2±10.7	Non-DM	Phase 2	ABCDEI
		Mazdutide4.5mg	63	31.8±4.7	5.40±0.32	33.6±10.0			
		Mazdutide6.0mg	61	31.7±4.0	5.34±0.35	35.8±9.2			
		Placebo	62	32.0±4.2	5.45±0.35	35.5±7.1			
Zhang 2024[19]	NCT04965506	Mazdutide3.0mg	51	28.0±4.8	8.11±0.84	52.5±13.4	T2DM	Phase 2	ABCDEI
		Mazdutide4.5mg	49	27.3±3.8	8.11±0.91	55.1±10.7			
		Mazdutide6.0mg	49	27.2±3.4	7.94±0.93	54.4±9.8			
		Dulaglutide1.5mg	50	26.7±3.2	7.94±0.92	52.8±12.7			
		Placebo	51	27.5±3.5	8.16±0.91	52.6±11.1			
Zhu 2025[40]	NCT05628311	Mazdutide4.0mg	106	28.2±4.0	8.19±0.76	50.8±11.7	T2DM	Phase 3	ABCDEI
		Mazdutide6.0mg	106	27.8±3.8	8.21±0.83	50.3±11.4			
		Placebo	107	28.6±4.0	8.33±0.78	50.1±9.8			
Ji 2025[14]	NCT05607680	Mazdutide4.0mg	203	31.0±3.5	5.5±0.35	34.8±7.9	Non-DM	Phase 3	ABCDEI
		Mazdutide6.0mg	202	31.3±3.8	5.5±0.34	33.2±8.2			
		Placebo	205	31.1±3.3	5.5±0.33	34.5±7.9			
Guo 2025[41]	NCT05606913	Mazdutide4.0mg	242	27.6±3.6	8.21±0.83	51.7±11.5	T2DM	Phase 3	ABCDEI
		Mazdutide6.0mg	244	28.1±4.1	8.21±0.86	52.1±11.6			
		Dulaglutide1.5mg	245	28.0±4.1	8.23±0.86	51.7±10.5			
Bhattachar 2025[42]	NCT05623839	Mazdutide16mg	24	32.5±3.81	5.3±0.35	37.3±10.22	Non-DM	Phase 1	BDEFGI
		Placebo	8	32.6±5.09	5.5±0.28	33.5±13.39			

Note: NA, Not Applicable; Type 2 Diabetes (T2DM); A, Body Mass Index (BMI); B, Body Weight; C, Diastolic Blood Pressure (DBP); D, Decreased Appetite; E, Fasting Plasma glucose (FPG); F, Glycated hemoglobin (HbA1c); G, High-density lipoprotein cholesterol (HDL); H, Low-density lipoprotein cholesterol (LDL); I, Systolic Blood Pressure (SBP); J, Triglyceride (TG); K, Total Cholesterol (TC); L, Alanine Aminotransferase (ALT); M, Waist circumference; N, Gastrointestinal Disorders; O, Hypoglycemia; P, Adverse Event (AE); Q, Serious Adverse Event (SAE).

Table 2. SUCRA (%) Ranking Data for Different Intervention

Treatment	Placebo	Dulaglutide1.5mg	Mazdutide4.0mg	Mazdutide3.0mg	Mazdutide10mg	Mazdutide9.0mg	Mazdutide4.5mg	M
Waist Circumference	16.6	87.5	80.7	10.9	82.9	42.3	27.2	58
Body Weight	10.0	58.6	86.5	49.0	86.4	46.8	44.5	54
BMI	NA	0.9	56.6	34.5	19.0	81.4	62.9	78
SBP	5.2	15.5	59.0	64.2	NA	NA	76.2	79
DBP	5.3	20.2	45.8	79.9	NA	NA	87.2	61
HbA1c	3.9	54.5	58.1	55.9	NA	NA	73.7	70
FPG	1.8	61.1	65.0	35.2	NA	NA	59.1	74
LDL	0.1	30.0	44.5	27.5	NA	NA	77.2	72
HDL	36.5	93.4	32.8	22.4	NA	NA	54.2	37
TC	0.0	22.2	40.2	38.9	NA	NA	77.4	71
TG	36.4	62.8	26.1	63.1	NA	NA	67.0	8.
ALT	9.9	14.8	87.8	36.7	NA	NA	63.1	87
AE	93.3	76.2	51.1	50.4	45.5	45.2	43.8	34
SAE	44.0	22.2	33.4	81.4	47.3	45.2	70.0	53
Hypoglycemia	47.3	65.3	32.6	44.6	46.6	73.3	13.4	76
Gastrointestinal Disorders	82.9	63.3	36.9	50.2	94.9	71.4	26.4	21
Decreased Appetite	88.6	59.1	22.4	59.4	91.8	38.3	32.4	19

Note: NA, Not Applicable; Body Mass Index (BMI); Systolic Blood Pressure (SBP); Diastolic Blood Pressure (DBP); Triglyceride (TG); Total Cholesterol (TC); Alanine Aminotransferase (ALT); Fasting Plasma glucose (FPG); High-density lipoprotein cholesterol (HDL); Glycated hemoglobin (HbA1c); Low-density lipoprotein cholesterol (LDL); Adverse Event (AE); Serious Adverse Event (SAE).

Figures

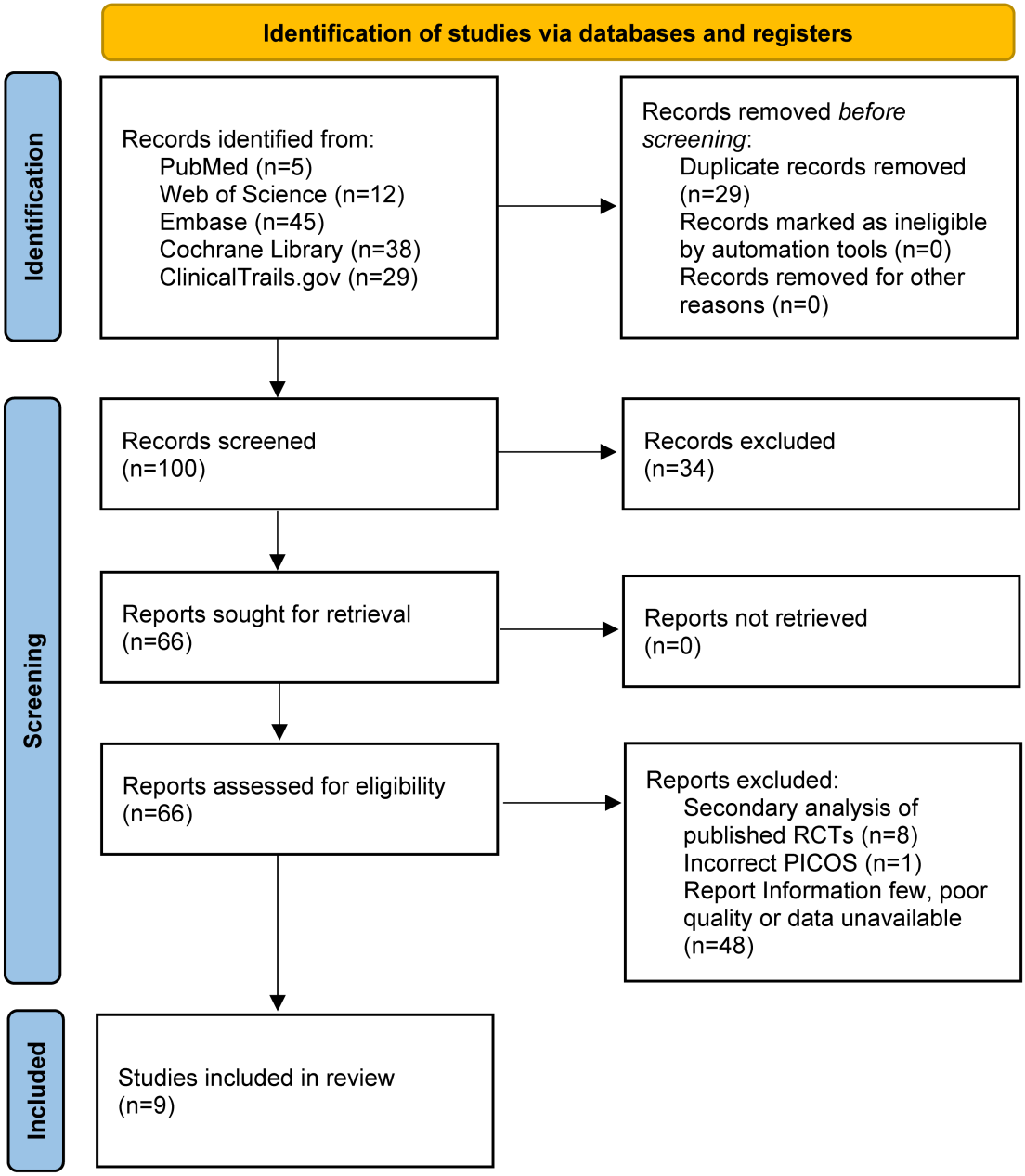


Figure 1

Study Flow Diagram of Study Selection Process.

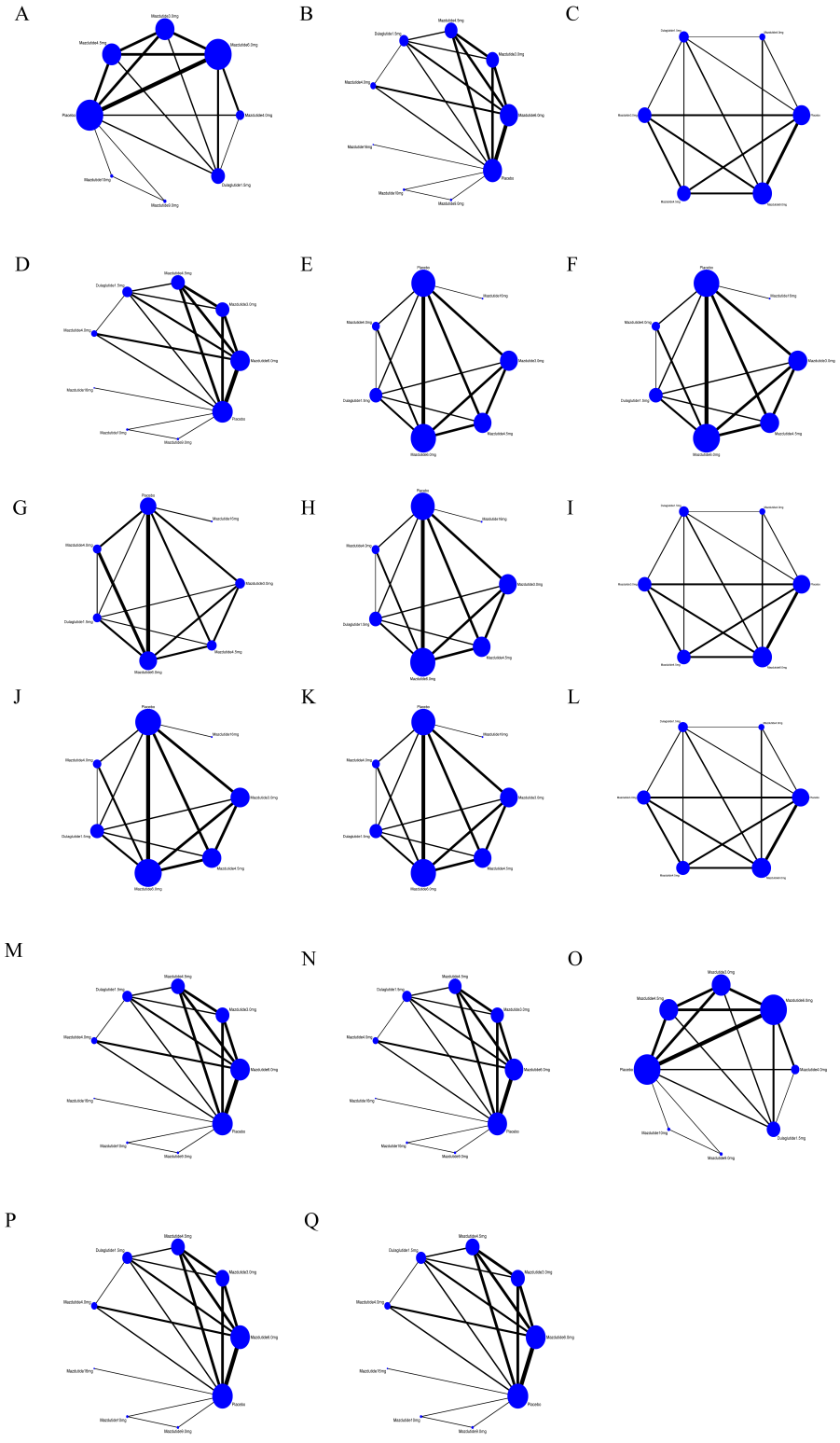


Figure 2

Network Diagram of Different Interventions. A, Body Mass Index (BMI); B, Body Weight; C, Diastolic Blood Pressure (DBP); D, Decreased Appetite; E, Fasting Plasma glucose (FPG); F, Glycated hemoglobin (HbA1c); G, High-density lipoprotein cholesterol (HDL); H, Low-density lipoprotein cholesterol (LDL); I, Systolic Blood Pressure (SBP); J, Triglyceride (TG); K, Total Cholesterol (TC); L, Alanine Aminotransferase (ALT); M, Waist circumference; N, Gastrointestinal Disorders; O, Hypoglycemia; P, Adverse Event (AE); Q, Serious Adverse Event (SAE). The size of the nodes is proportional to the number of trial participants, and the thickness of the line connecting the nodes is proportional to the randomised number of trial participants directly comparing the two treatments.

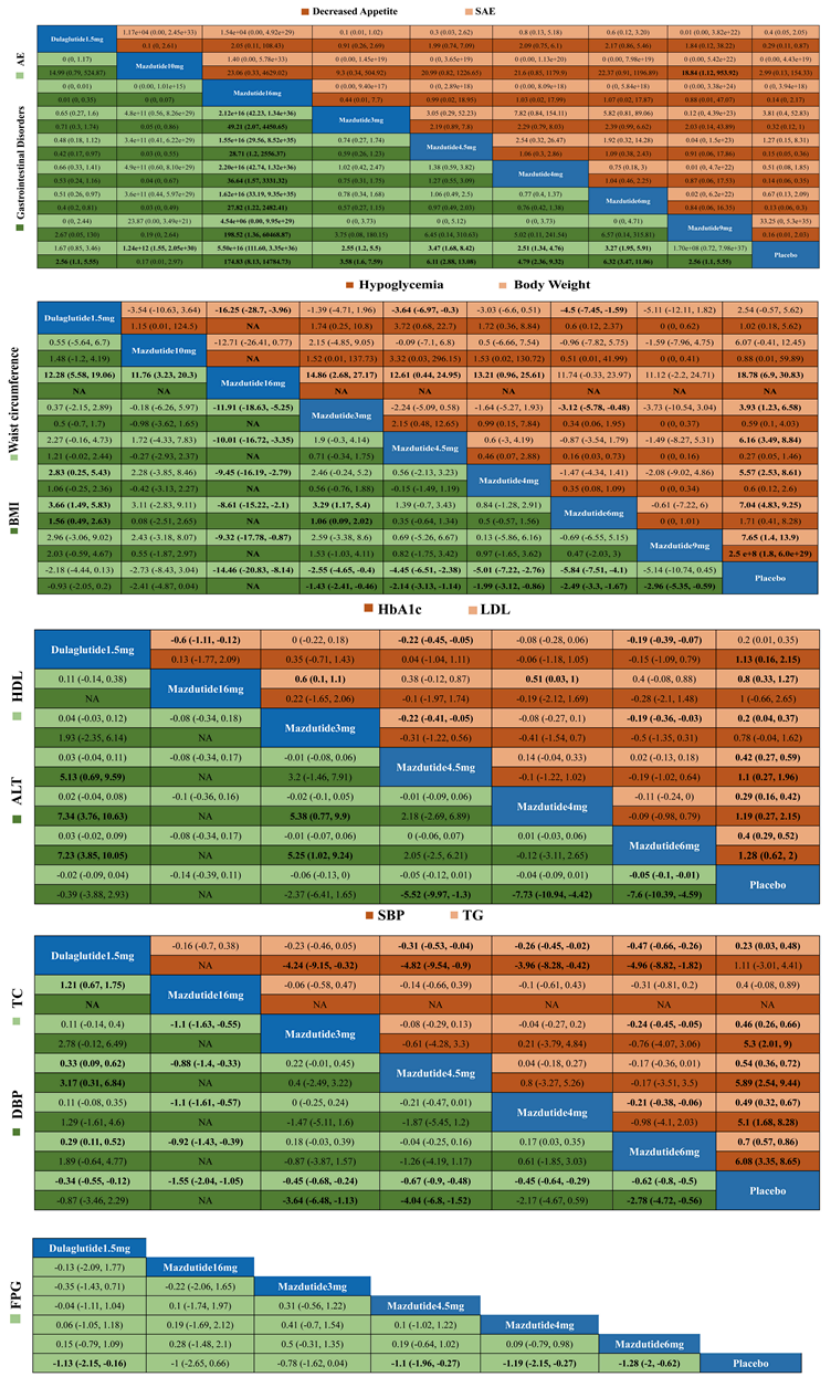


Figure 3

League tables of outcome analyses. Bold font indicates that the comparison is statistically significant. Adverse events; Serious adverse events (SAE); Diastolic Blood Pressure (DBP); Systolic Blood Pressure (SBP); Fasting Plasma glucose (FPG); Glycated hemoglobin (HbA1c); Body Mass Index (BMI); High-density lipoprotein cholesterol (HDL); Alanine Aminotransferase (ALT); Low-density lipoprotein cholesterol (LDL); Total Cholesterol (TC); Triglyceride (TG). The relative effects are measured as a mean difference for ALT, BMI, body weight, DBP, FPG, HbA1c, HDL, LDL, SBP, TG, TC and Waist circumference, odds ratios for AE, SAE, Gastrointestinal Disorders, Decreased Appetite ,and Hypoglycemia, along with 95% CrI.

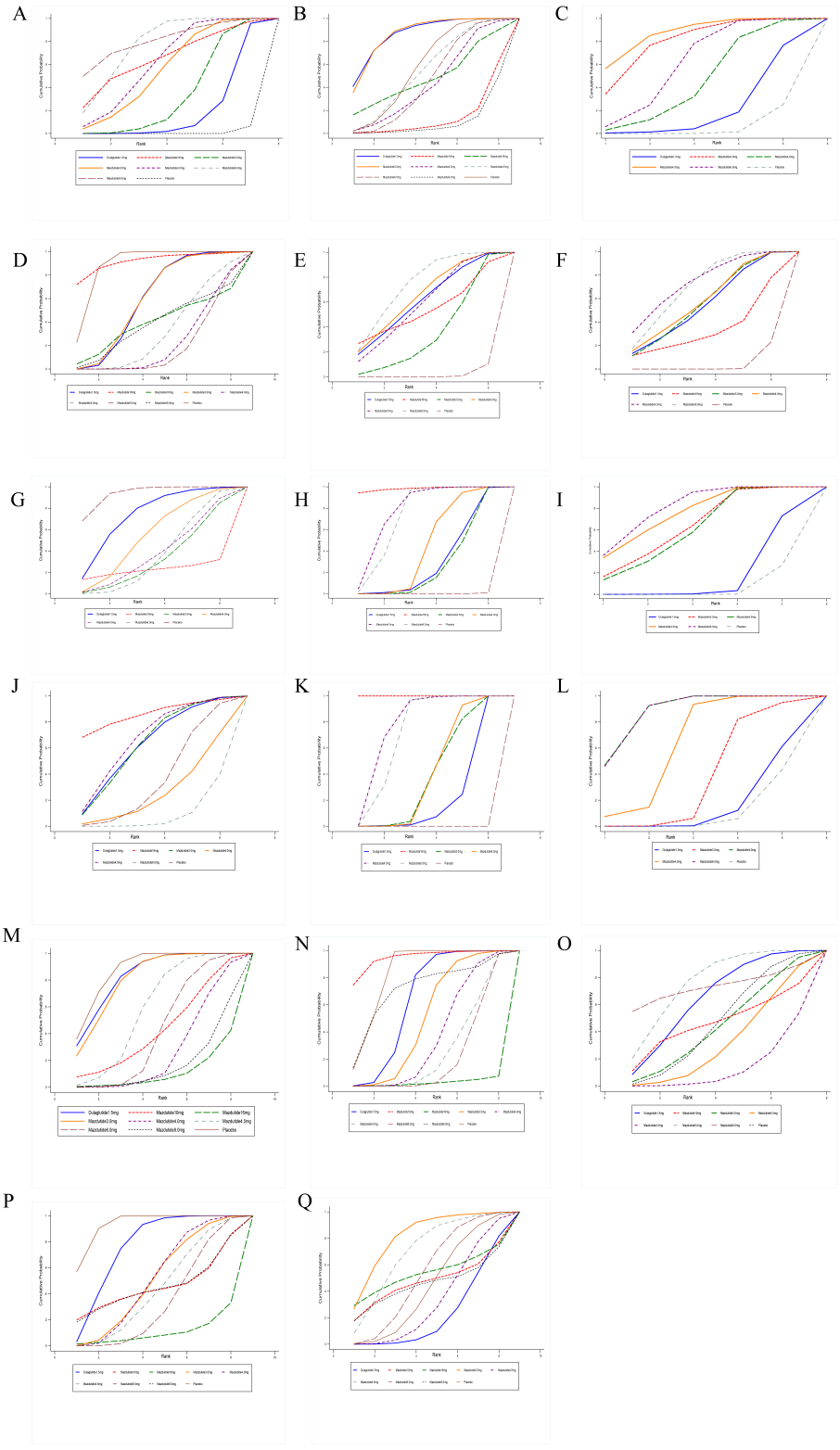


Figure 4

SUCRA Values for Different Interventions. A, Body Mass Index (BMI); B, Body Weight; C, Diastolic Blood Pressure (DBP); D, Decreased Appetite; E, Fasting Plasma glucose (FPG); F, Glycated hemoglobin (HbA1c); G, High-density lipoprotein cholesterol (HDL); H, Low-density lipoprotein cholesterol (LDL); I, Systolic Blood Pressure (SBP); J, Triglyceride (TG); K, Total Cholesterol (TC); L, Alanine Aminotransferase (ALT); M, Waist circumference; N, Gastrointestinal Disorders; O, Hypoglycemia; P, Adverse Event (AE); Q, Serious Adverse Event (SAE).

Supplementary Files

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