Efficacy and Safety of Tirzepatide in Overweight and Obese Individuals: A Meta-Analysis of Randomized Controlled Trials

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Abstract: *Purpose:* Aimed to comprehensively investigate the efficacy and safety of the dual GIP/GLP-1 receptor agonist Tirzepatide on overweight and obesity. *Methods:* Embase, PubMed/Medline, Web of Science, Cochrane, CNKI, Wanfang and VIP databases were searched using standard keywords to identify all controlled trials investigating the weight loss effects of Tirzepatide. RevMan 5.3 was used for analysis. *Results:* Eleven randomized controlled trials with 11,710 participants were included in this systematic review and meta-regression analysis. The pooled findings showed that Tirzepatide vs control significantly reduced body weight (mean difference (MD): -7.38, 95% confidence interval (CI): -13.66 to -1.09). The results of subgroup analysis showed that the trend of weight loss is dose-dependent (5mg: MD: -6.87, 95%CI:-10.29 to -3.45; 10 mg: MD: -9.62, 95%CI: -13.11 to -6.13; 15mg: MD: -11.00, 95%CI: -14.29 to -7.70). HbA1c (MD: -1.38, 95% CI: -1.52 to -1.23). The total incidence of adverse reactions in Tirzepatide vs control was significantly increased (Odds Ratio (OR): 1.57, 95%CI: 1.35 to 1.81), and these adverse reactions were even greater, especially with higher doses and duration of Tirzepatide. *Conclusions:* The administration of Tirzepatide medication has demonstrated noteworthy effects on weight management, resulting in reductions in both body weight and HbA1c levels. These effects may potentially be dependent on the dosage administered. Consequently, for individuals with diabetes who experience significant impacts on body weight, the utilization of Tirzepatide can be regarded as a viable therapeutic approach for obese individuals.

Keywords: Tirzepatide; The Dual GIP/GLP-1 Receptor Agonist; Efficacy; Safety; Systematic Rerview

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1 Introduction

Overweight and obesity is the result of a prolonged imbalance in energy homeostasis, specifically between caloric intake and expenditure [1]. When there is an excess of calories, they are stored in the body as fat [2]. This excessive fat content or abnormal fat distribution in the human body can lead to various health issues, including type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), obstructive sleep apnea (OSA), increased risks of

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various cancers, mortality, reduced quality of life, and increased risk of death [1, 2]. Research has indicated that 44% of T2DM cases, 23% of CVD cases and 7% to 41% of specific cancers are associated with obesity [3]. Furthermore, it has been projected that a significant proportion of the global adult population will experience obesity by the year 2030. In the specific case of China, the prevalence of childhood obesity stands at approximately 30%, while a staggering 70% of the adult population is classified as either overweight or obese. It has been approximated that the economic burden of overweight and obesity in China will amount to ¥418 billion by 2023, constituting approximately 22% of the nation's total medical costs [4]. In cases where lifestyle interventions prove ineffective, drug therapy is often considered the primary treatment option. Currently, the Food and Drug Administration (FDA) has approved several medications, including Orlistat, Phentermine, Phentermine/Topiramate, Liraglutide and Semaglutide for the management of obesity. However, there are many side effects and limited therapeutic effects with long-term use, those treatment has some limitations [5].

Tirzepatide (TZP, LY3298176) is a peptide modified with fatty acids that exhibits dual agonist activity for glucose-dependent insulinotropic polypeptide (GIP)/ Glucagon-like peptide-1 (GLP-1) receptors. It was approved by the FDA in May 2022 and by the European Medicines Agency (EMA) in November 2022 for the purpose of enhancing glycemic control in adults diagnosed with T2DM [6, 7]. TZP has been observed to stimulate insulin secretion, suppress glucagon secretion, reduce hepatic gluconeogenesis, enhance insulin sensitivity, delay gastric emptying, decrease food intake, and promote weight loss [8, 9]. Furthermore, a phase 3 clinical trial involving 2539 individuals with obesity and overweight demonstrated that weekly administration of TZP at doses of 5mg, 10mg, or 15mg yielded significantly and continuously reduce body weight for 72 weeks [6]. However, the appropriate dose and duration of Tirzepatide therapy which is effective in weight loss is an issue that needs more comprehensive studies. The present systematic review, based on clinical trials, aimed to investigate the effects of Tirzepatide on weight loss and safety.

2 Methods

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline. Our protocol was registered on PROSPERO (CRD42024506165) with the title “Management of Overweight and Obese People with the Dual GIP/GLP-1 Receptor Agonist Tirzepatide: A Systematic Rerview”.

2.1 Search Strategy

The Chinese biomedical literature database, CNKI, Wanfang Data, PubMed, Embase, Web of Science, and Cochrane Library and Clinical Trials website were searched from inception to 6 May 2024. Searches were designed using a combination of Medical Subject Heading (Medline), Emtree (Embase subject headings), and free-text terms such as SCLC, as follow (Tizepatide OR Ly3298176 OR TZP) AND (“weight” OR “Body Mass Index” OR “BMI” OR “diabetes mellitus” OR “type 2 diabetes mellitus” OR “T2DM”) AND (“Clinical Trials as Topic” OR “Cross-Over Studies” OR “Double-Blind Method” OR “Single-Blind Method” OR “Random Allocation” OR “Clinical Trial”). In order to discover potentially overlooked eligible trials, the reference lists of the papers found and associated review studies were also manually examined.

2.2 Eligibility Criteria

Studies were included if they fulfilled the following criteria: (1) Participants: Obesity (BMI ≥28kg/m2). Patients were older than 18 years old. No restrictions on gender, age, and ethnicity. (2) Intervention: Test group: Tirzepatide (5mg, 10mg, 15mg). (3) Comparison: placebo, semaglutide, dulaglutid, insulin. (4) Outcomes: Primary outcome indicators: bodyweight (kg). Secondary outcome indicators: glycated haemoglobin A1c (HbA1c), adverse reactions, serious adverse event, diarrhea, nausea. (5) Study: RCTs. We excluded meta-analyses and systematic reviews, comments, editorials, pharmacokinetic/pharmacodynamic studies, and studies not reporting the outcome of interest.

2.3 Data Extraction

Relevant data from eligible trials were independently extracted by two investigators. A third author was consulted to resolve discrepancies. Briefly, we recorded the baseline characteristics of the RCTs including the name of the first author, publication year, phase of the RCT, type of diabetes, trial duration, follow-up duration, background insulin therapy, number of participants, intervention

measures, age, sex ratio, HbA1c, FPG, body weight, and body mass index (BMI). The primary outcome of the quantitative meta-analysis was body weight. Secondary outcomes were HbA1c, any adverse event, serious adverse events, any severe adverse events probably or possibly related to nausea, diarrhea.

2.4 Quality Assessment

Two investigators evaluated the quality of each trial using the Cochrane Risk of Bias Tool 5.1.0 in seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. Items were scored as low, high, or unclear risk of bias. A third author was consulted to resolve discrepancies. Finally, publication bias was visually assessed using a funnel plot.

2.5 Statistical Analysis

Statistical analysis was performed using RevMan5.3. Assessment of heterogeneity the $\chi 2$ test was used to analyze heterogeneity, test level is $\alpha=0.1$, and the magnitude of heterogeneity was judged by combining the findings with the I^2 test. When no obvious heterogeneity exists ($P > 0.1$, $I^2 < 50\%$), we used a fixed effect model; otherwise, we used the random-effects mode. The results were presented as relative risk (RR) and 95% credible intervals (CI). If $P \leq 0.05$ was considered to indicate a statistically significant difference; in the publication bias was identified with funnel plots.

3 Results

3.1 Search Results

The initial 716 articles were searched, and the duplicate literature was first removed with Endnote software, then the literature was further read for screening, and finally, the 11 studies that conformed to inclusion criteria were included [6, 10-19]. All 11 articles were RCTs, including 11,710 patients and published in English. See Figure 1 for literature screening diagram and Table 1 for basic characteristics of the included articles.

Table 1 Basic features of the included studies

Studies	Type	Course	Interventions	Cases	Age	Body weight (kg)	BMI (kg/m^2)
NCT03131687 [14]	Phase 2	26w	placebo	51	56.6 (8.9)	91.5 (23.1)	32.4 (6.0)
Frias 2018			TZP 5mg	55	57.9 (8.2)	92.8 (19.0)	32.9 (5.7)
			TZP 10mg	51	56.5 (9.9)	92.7 (19.5)	32.6 (5.8)
			TZP 15mg	53	56.0 (7.6)	89.1 (22.7)	32.2 (6.2)
			dulaglutid 1.5mg	54	58.7 (7.8)	89.8 (16.9)	32.4 (5.4)
NCT03311724 [13]	Phase 2	12w	placebo	26	56.0 (10.13)	89.6 (23.7)	32.5 (5.7)
Frias 2020			TZP 15mg-1	28	55.5 (8.54)	88.7 (18.21)	32.0 (5.56)
			TZP 15mg-2	28	56.6 (9.21)	89.6 (16.91)	31.1 (4.21)
NCT04184622 [6]	Phase 3	72w	TZP 5mg	630	45.6 (12.7)	102.9 (20.71)	37.4 (6.63)
Jastreboff 2022			TZP 10mg	636	44.7 (12.4)	105.8 (23.32)	38.2 (7.01)
			TZP 15mg	630	44.9 (12.3)	105.6 (22.92)	38.1 (6.69)
			placebo	643	44.4 (12.5	104.8 (21.37)	38.2 (6.89)
NCT04657003 [16]	Phase 3	72w	TZP 10mg	312	54.3 (10.7)	100.9 (20.9)	36.0 (6.4)
Garvey 2023			TZP 15mg	311	53.6 (10.6)	99.6 (20.1)	35.7 (6.1)
			placebo	315	54.7 (10.5)	101.7 (22.3)	36.6 (7.3)
NCT03861052 [17]	Phase 3	52w	TZP 5mg	159	56.8 (10.1)	78.5 (16.3)	28.6 (5.4)
Nobuya 2022			TZP 10mg	158	56.2 (10.3)	78.9 (13.7)	28.0 (4.1)
			TZP 15mg	160	56.0 (10.7)	78.9 (14.3)	28.1 (4.4)
			dulaglutid 0.75mg	159	57.5 (10.2)	76.5 (13.2)	27.8 (3.7)
NCT03954834 [19]	Phase 3	40w	TZP 5mg	121	54.1 (11.9)	87.0 (21.2)	32.2 (7.0)
Rosenstock 2021			TZP 10mg	121	55.8 (10.4)	86.2 (19.5)	32.2 (7.6)

Studies	Type	Course	Interventions	Cases	Age	Body weight (kg)	BMI (kg/m^2)
			TZP 15mg	121	52.9 (12.3)	85.4 (18.5)	31.5 (5.5)
			placebo	115	53.6 (12.8)	84.8 (20.0)	31.7 (6.1)
NCTO3882970 [18]	Phase 3	52w	TZP 5mg	358	57.2 (10.1)	94.4 (18.9)	33.6 (5.9)
Bernhard 2021			TZP 10mg	360	57.4 (9.7)	93.8 (19.8)	33.4 (6.2)
			TZP 15mg	359	57.5 (10.2)	94.9 (21.0)	33.7 (6.1)
			insulin degludec	360	57.5 (10.1)	94.0 (20.6)	33.4 (6.1)
NCT03730662 [11]	Phase 3	52w	TZP 5mg	329	62.9 (8.6)	90.3 (20.32)	32.6 (6.06)
Stefano 2021			TZP 10mg	328	63.7 (8.7)	90.6 (18.21)	32.8 (5.51)
			TZP 15mg	338	63.7 (8.6)	90.0 (16.34)	32.5 (5.02)
			insulin degludec	1000	63.8 (8.5)	90.2 (19.00)	32.5 (5.55)
NCT04039503 [10]	Phase 3	40w	TZP 5mg	116	62 (10)	95.8 (19.8)	33.6 (5.9)
Dominik 2022			TZP 10mg	119	60 (10)	94.5 (22.2)	33.4 (6.2)
			TZP 15mg	120	61 (10)	96.3 (22.8)	33.4 (5.9)
			placebo	120	60 (10)	94.1 (21.8)	33.2 (6.3)
NCT04093752 [15]	Phase 3	40w	TZP 5mg	230	53.1 (11.2)	77.7 (14.2)	28.1 (3.9)
Gao 2023			TZP 10mg	228	53.5 (11.1)	76.3 (15.0)	27.7 (3.8)
			TZP 15mg	229	54.3 (11.6)	76.2 (13.6)	27.8 (3.8)
			insulin glarginea	220	55.6 (11.4)	76.0 (15.2)	28.0 (4.6)
NCT03987919 [12]	Phase 3	40w	TZP 5mg	470	56.3 (10.0)	92.5 (21.76)	33.8 (6.85)
Juan 2021			TZP 10mg	469	57.2 (10.5)	94.8 (22.71)	34.3 (6.60)
			TZP 15mg	470	55.9 (10.4)	93.8 (21.83)	34.5 (7.11)
			semaglutide 1mg	469	56.9 (10.8)	93.7 (21.12)	34.2 (7.15)

3.2 Study Characteristics

A total of 11,710 patients from 11 studies reporting outcomes of interest met the eligibility criteria. The mean body weight of the diabetic patients at baseline ranged from 76.0 to 105.8 kg, with a BMI ranging from 28 to 38.2 kg/m^2 (Table 1).

3.3 Quality Assessment

All the included studies were double-blind, randomized clinical trial. Six studies described the specific methods used for random sequence generation; Six studies described the allocation concealment in an acceptable manner. The number of patients lost to follow-up was reported in all studies. In all studies, the JADADscore was above 5, which is satisfactory for inclusion in this systematic review [6, 10-19]. The results are shown in Table 2. This is a figure. Schemes follow another format. If there are multiple panels, they should be listed as: (a) Description of what is contained in the first panel; (b) Description of what is contained in the second panel. Figures should be placed in the main text near to the first time they are cited.

Table 2 The quality assessment of included studies

Studies	Random sequence generation	Concealed versus	Blinded	Drop-out/lost to follow-up	Complete outcome data	Selective reporting	Other selection bias	JADAD score
NCT03131687 [14] Frias 2018	Unclear	Unclear	double-blind	Yes	Yes	Unclear	Unclear	5
NCT03311724 [13] Frias 2020	Unclear	Unclear	double-blind	Yes	Yes	Unclear	Unclear	5
NCT04184622 [6] Jastreboff 2022	Unclear	Unclear	double-blind	Yes	Yes	Unclear	Unclear	5
NCT04657003 [16] Garvey 2023	interactive web-response system	interactive web-response system	double-blind	Yes	Yes	Unclear	Unclear	7

Studies	Random sequence generation	Concealed versus	Blinded	Drop-out/lost to follow-up	Complete outcome data	Selective reporting	Other selection bias	JADAD score
NCT03861052 [17] Nobuya 2022	interactive web-response system	interactive web-response system	double-blind	Yes	Yes	Unclear	Unclear	7
NCT03954834 [19] Rosenstock 2021	interactive web-response system	interactive web-response system	double-blind	Yes	Yes	Unclear	Unclear	7
NCT03987919 [12] Juan 2021	Unclear	Unclear	double-blind	Yes	Yes	Unclear	Unclear	5
NCTO3882970 [18] Bernhard 2021	interactive web-response system	interactive web-response system	double-blind	Yes	Yes	Unclear	Unclear	7
NCT03730662 [11] Stefano 2021	interactive web-response system	interactive web-response system	double-blind	Yes	Yes	Unclear	Unclear	7
NCT04039503 [10] Dominik 2022	interactive web-response system	interactive web-response system	double-blind	Yes	Yes	Unclear	Unclear	7
NCT04093752 [15] Gao 2023	Unclear	Unclear	double-blind	Yes	Yes	Unclear	Unclear	5

3.4 Efficacy Outcomes

3.4.1 Body Weight

Eleven studies [6, 10-19] reported the comparison of the changes in body weight about Tirzepatide vs. control group, significant heterogeneity among studies (P<0.00001, I^2=100%), a random-effects model was used for meta-analysis. Compared to control, the difference was statistically significant (mean difference (MD): -7.38, 95% CI: -13.66 to -1.09, P=0.02). We did a subgroup analysis by the difference between the doses used for the treatments and significant differences were found among subgroups, presented a dose dependent effect (5mg: MD: -6.87, 95%CI: -10.29 to -3.45, P<0.0001; 10 mg: MD: -9.62, 95%CI: -13.11 to -6.13, P<0.00001; 15mg: MD: -11.00, 95%CI: -14.29 to -7.70, P<0.00001) (Figure 2).

3.4.2 HbA1c

Nine studies [10, 11, 13-19] reported the comparison of the changes in HbA1c about Tirzepatide vs. control group, significant heterogeneity among studies (P<0.00001, I^2=75%), a random-effects model was used for meta-analysis. Compared to control, the difference was statistically significant (MD: -1.38, 95%CI: -1.52 to -1.23, P<0.000 01). Subgroup analysis by the difference between the doses used for the treatments and significant differences were found among subgroups (5mg: MD: -1.17, 95%CI: -1.45 to -0.90, P<0.00001; 10 mg: MD: -1.40, 95%CI: -1.66 to -1.15, P<0.00001; 15mg: MD: -1.51, 95%CI: -1.72 to -1.29, P<0.000 01) (Figure 3).

3.4.3 Safety Outcomes

Eleven studies [6, 10-19] reported the comparison of the adverse reactions about Tirzepatide vs. control group, significant heterogeneity among studies (P<0.000 01, I^2=75%), a random-effects model was used for meta-analysis. Compared to control, the difference was statistically significant (odds ratio (OR): 1.57, 95% CI: 1.35 to 1.81, P<0.000 01). We did a subgroup analysis by the difference between the doses used for the treatments and significant differences were found among subgroups, presented a dose dependent effect (5mg: OR: 1.40, 95%CI: 1.14 to 1.71, P=0.001; 10 mg: OR: 1.59, 95%CI: 1.23 to 2.07, P=0.0005; 15mg: OR: 1.73, 95%CI: 1.29 to 2.31, P=0.0002) (Figure 4) . The results of the analysis of other outcomes are shown in Table A1.

3.4.4 Publication Bias Analysis

Publication bias was assessed for Tirzepatide vs. control meta-analyses. In the 11 literatures [6, 10-19] evaluated with body weight as outcome indicator, RR value was used to evaluate the publication bias of the included studies, and funnel plots were drawn. The funnel diagram showed that the points were roughly symmetrically distributed in an inverted funnel shape, and there was no publication bias (Figure A1).

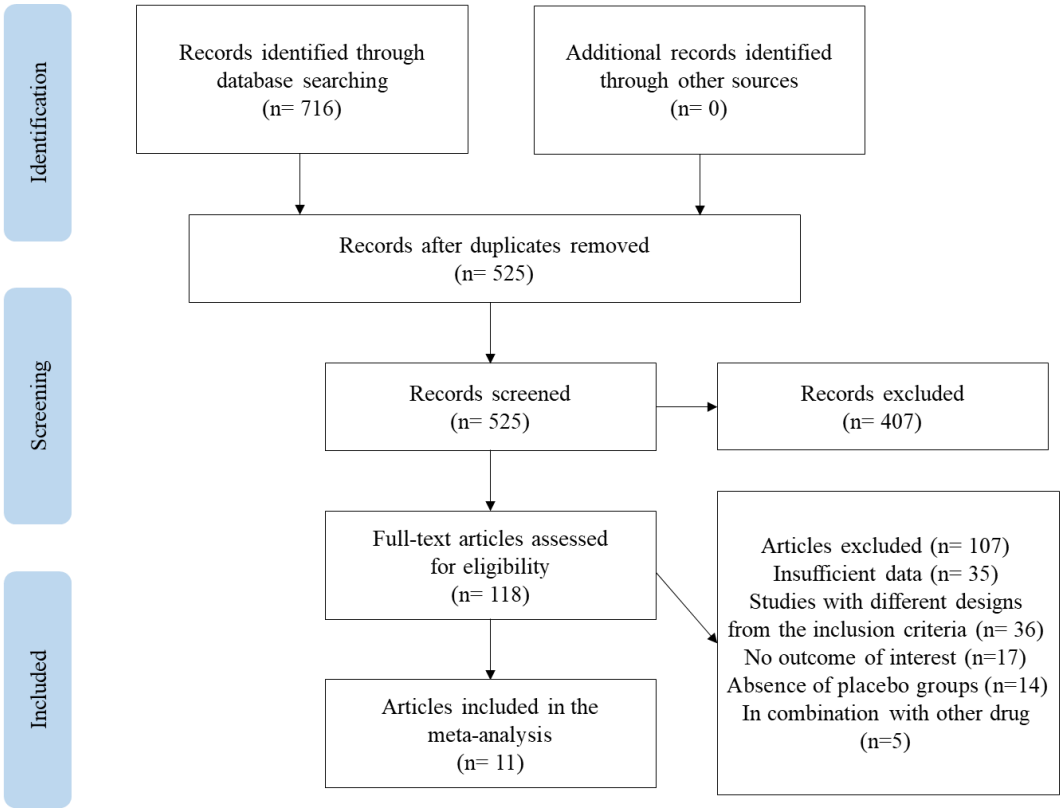

Figure 1 Literature screening process and results

Study or Subgroup	Tirzepatide Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.5.1 Tirzepatide 5mg vs Control								
Bernhard 2021	-7.5	7.82	358	2.3	5.48	360	3.3%	-9.80 [-10.79, -8.81]
Dominik 2022	-6.2	2.61	116	1.7	8.09	120	3.3%	-7.90 [-9.42, -6.38]
Frias 2018-1	-4.8	10.97	55	-0.4	15.08	51	3.3%	-4.40 [-9.45, 0.65]
Gao 2023	-5	7.82	230	1.5	4.11	220	3.3%	-6.50 [-7.65, -5.35]
Jastreboff 2022	-16	5.48	630	-2.4	5.49	643	3.3%	-13.60 [-14.20, -13.00]
Juan 2021	-7.8	4.525	470	-6.2	4.525	469	3.3%	-1.60 [-2.18, -1.02]
Nobuya 2022	-5.8	6.86	159	-5	5.48	159	3.3%	-0.80 [-2.16, 0.56]
Rosenstock 2021	-7	5.48	121	0.7	7.4	115	3.3%	-7.70 [-9.37, -6.03]
Stefano 2021	-7.1	5.48	329	1.9	4.52	1000	3.3%	-9.00 [-9.66, -8.34]
Subtotal (95% CI)			**2468**			**3137**	**30.0%**	**-6.87 [-10.29, -3.45]**
Heterogeneity: Tau² = 26.49; Chi² = 930.67, df = 8 (P < 0.00001); I² = 99%								
Test for overall effect: Z = 3.94 (P < 0.0001)								
1.5.2 Tirzepatide 10mg vs Control								
Bernhard 2021	-10.7	5.48	360	2.3	5.48	360	3.3%	-13.00 [-13.80, -12.20]
Dominik 2022	-8.2	7.95	119	1.7	8.09	120	3.3%	-9.90 [-11.93, -7.87]
Frias 2018-1	-8.7	10.56	51	-0.4	15.08	51	3.3%	-8.30 [-13.35, -3.25]
Gao 2023	-7	4.11	228	1.5	4.11	220	3.3%	-8.50 [-9.26, -7.74]
Garvey 2023	-12.9	5.35	312	-3.2	6.86	315	3.3%	-9.70 [-10.66, -8.74]
Jastreboff 2022	-21.4	5.48	636	-2.4	5.49	643	3.3%	-19.00 [-19.60, -18.40]
Juan 2021	-10.3	4.662	469	-62	4.525	469	3.3%	51.70 [51.11, 52.29]
Nobuya 2022	-8.5	5.48	158	-5	5.48	159	3.3%	-3.50 [-4.71, -2.29]
Rosenstock 2021	-7.8	7.13	121	0.7	7.4	115	3.3%	-8.50 [-10.36, -6.64]
Stefano 2021	-9.5	4.66	328	1.9	4.52	1000	3.3%	-11.40 [-11.98, -10.82]
Subtotal (95% CI)			**2782**			**3452**	**33.4%**	**-4.01 [-21.58, 13.57]**
Heterogeneity: Tau² = 802.70; Chi² = 37106.69, df = 9 (P < 0.00001); I² = 100%								
Test for overall effect: Z = 0.45 (P = 0.66)								

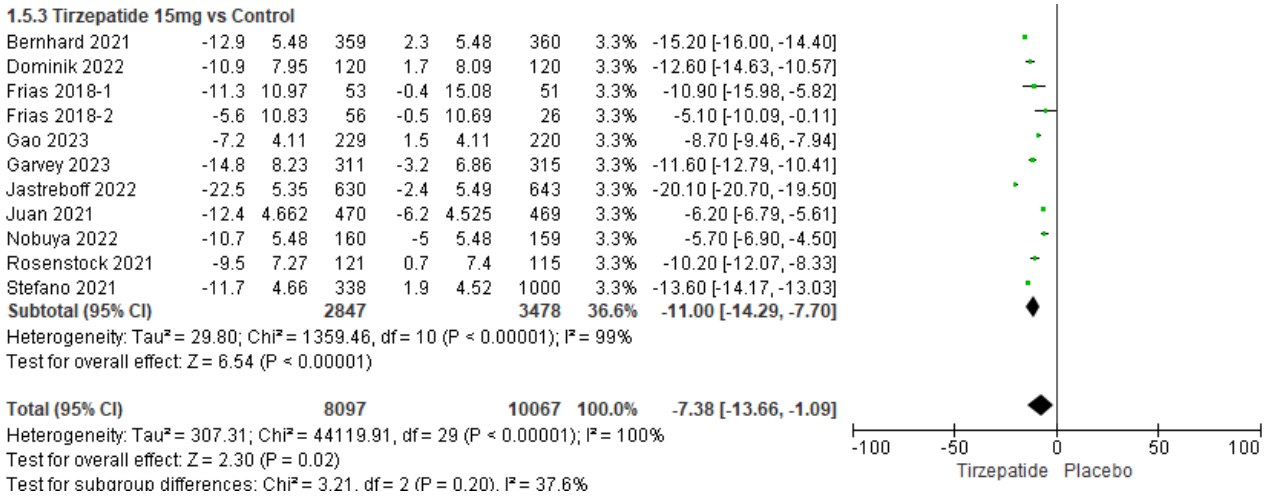

Figure 2 Forest plot of the meta-analysis for bodyweight, Tirzepatide vs Control

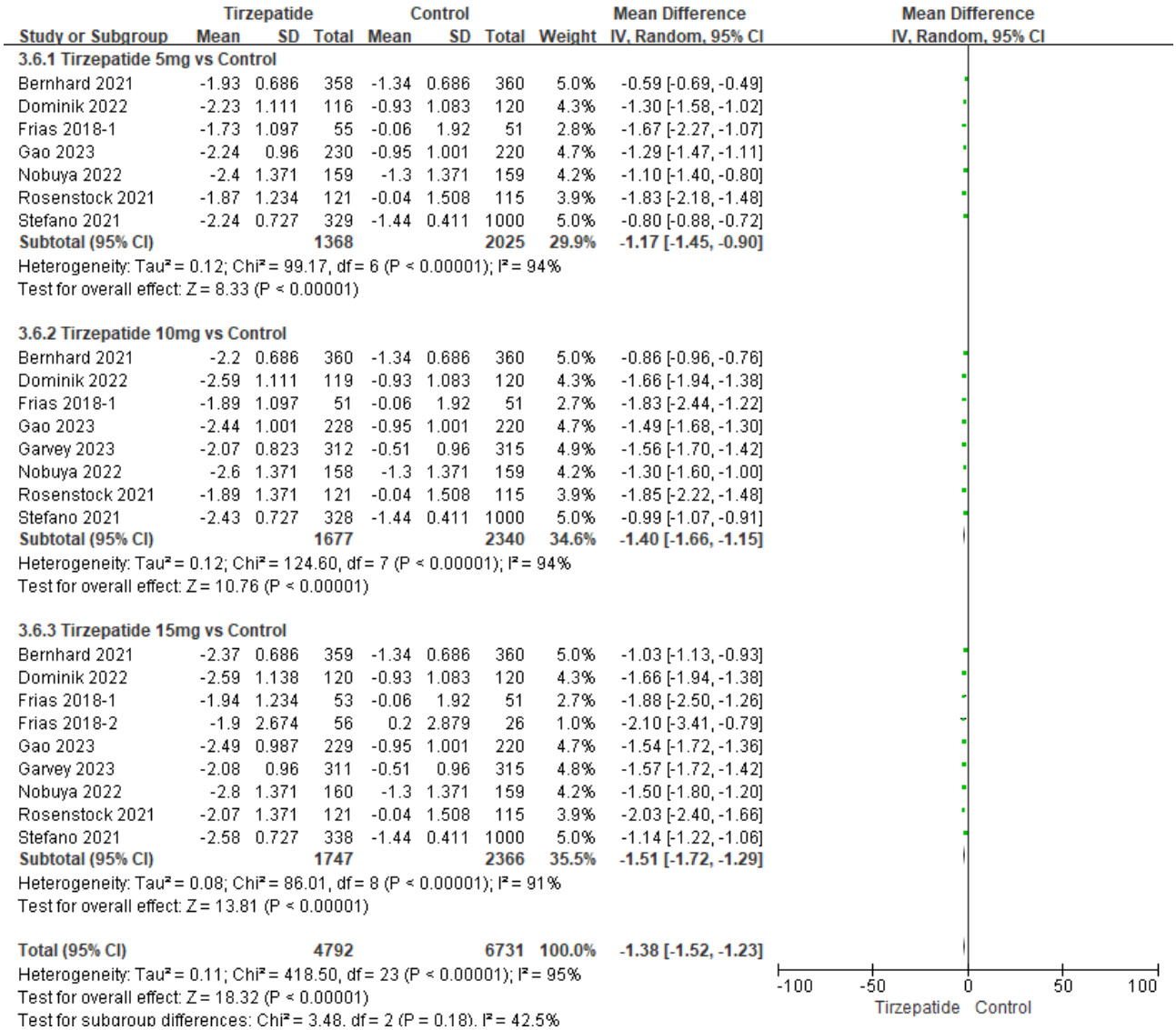

Figure 3 Forest plot of the meta-analysis for HbA1c, Tirzepatide vs Control

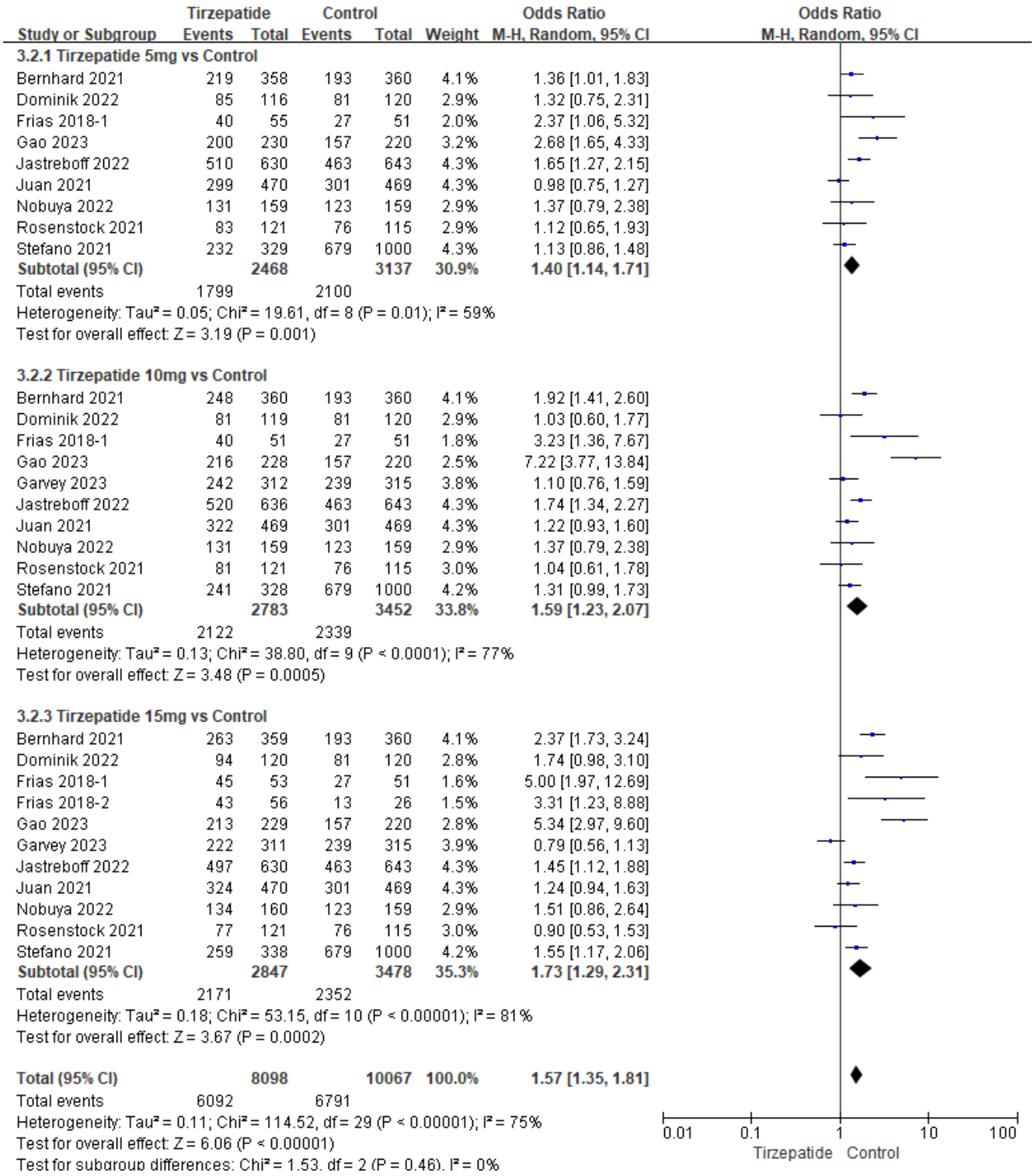

Figure 4 Forest plot of the meta-analysis for adverse event, Tirzepatide vs Control

4 Discussion

Tirzepatide is a peptide modified with fatty acids that exhibits dual agonist activity for GIP/GLP-1 receptors. It has been approved by the FDA in May 2022 and by the EMA in November 2022 for the purpose of enhancing glycemic control in adults diagnosed with T2DM [6, 7]. TZP has demonstrated the ability to enhance insulin secretion, suppress glucagon secretion, reduce hepatic glu-

coneogenesis, enhance insulin sensitivity, delay gastric emptying, decrease food intake, and promote weight loss [6, 7, 9, 20]. A recommended initial dosage of Tirzepatide, administered through once-weekly subcutaneous injections, would be 2.5 mg. This dosage may be increased to 5 mg after a period of 2 to 4 weeks, with the maximum dosage being 15 mg, also administered once weekly via subcutaneous injections [6, 7]. Our research encompasses a total of 11 randomized controlled trials, involving approximately 11,710 patients with a BMI≥28kg/m^2 and obesity. In comparison to the control group, statistically significant differences were observed. Furthermore, a subgroup analysis was conducted based on variations in treatment dosages, revealing significant differences among subgroups and indicating a dose-dependent effect.

In the long term, the reduction of weight, blood lipid levels, and blood pressure has been found to be beneficial in delaying the development of microangiopathy and macroangiopathy [21]. In recent years, there has been a significant increase in the global prevalence of obesity, leading to an annual rise in the incidence of obesity-related T2DM. GLP-1 plays a crucial role in maintaining glucose homeostasis by increasing insulin secretion and suppressing glucagon secretion in response to changes in blood glucose levels. In addition, insulin secretion is appropriately suppressed in response to hypoglycemia [8]. Furthermore, it has been observed that anorexic actions of GIP are potentially influenced by the direct stimulation of the GLP-1 receptor within the central nervous system. This stimulation results in heightened feelings of satiety and a diminished inclination to consume sweet and salty foods, thereby contributing to the anorexigenic effects of endotoxin and subsequent reduction in body weight [22]. Additionally, numerous studies have indicated that GIP functions as an insulin sensitizer in adipocytes, activating lipoprotein lipase and facilitating triglyceride hydrolysis. This process leads to a decrease in lipid overflow and the accumulation of fat in ectopic locations [20]. The findings of this study indicate that the treatment group exhibited a significantly superior effect compared to the control group. In this paper, a total of eleven studies [6, 10-19] reported on the comparison of changes in body weight between Tirzepatide and the control group, with statistically significant differences observed when compared to the control group. Additionally, nine studies [10, 11, 13-19] reported on the comparison of changes in HbA1c between Tirzepatide and the control group, with statistically significant differences observed when compared to the control group. Additionally, a total of three studies [12, 14, 17] have reported on the comparison between Tirzepatide and Duraglutide/Semaglutide/Insulin. The findings from these studies provide evidence that Tirzepatide is superior in terms of weight loss and reduction of HbA1c. Furthermore, we conducted a subgroup analysis based on the varying doses administered for the treatments, revealing significant differences among the subgroups. This analysis demonstrated a dose-dependent effect, highlighting the significance of our findings in guiding the design of clinical trials and informing clinical medication selection.

The findings of this study demonstrate statistically significant disparities in adverse reactions between the research groups and the control group when examining safety indicators. Additionally, the research group exhibited a notably higher occurrence of adverse reactions compared to the control group. Notably, new concerns regarding serious adverse effects were identified; however, there was no significant variance in the incidence of serious adverse reactions between the 5mg and 10mg groups and the control group, rendering these differences statistically insignificant. However, the 15mg group exhibited a notably higher incidence compared to the control group. Despite the elevated prevalence of adverse effects associated with this treatment, a majority of patients demonstrated tolerance towards the medication.

5 Conclusions

In terms of weight loss and reduction of HbA1c, Tirzepatide demonstrates superior efficacy, with the inhibitory effect being contingent upon dosage. Although the occurrence of adverse reactions is more frequent, severe adverse reactions are infrequent. Nonetheless, Tirzepatide holds promise as a potential therapeutic avenue for diabetic patients grappling with obesity, particularly those who have not responded favorably to conventional systemic medications or require expeditious weight loss for life-sustaining purposes.

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Author Contributions

Jingjing Zhong established the study and reviewed the manuscript. Liya Fu and Jankun Fan drafted the manuscript, reviewed the manuscript, and contributed equally to this work. Jankun Fan and Xiaohui Yue analyzed the data and edited the manuscript. Shuo Yang and Xiaoyan Xie contributed to literature searches, article selections. Liya Fu and Jankun Fan did the quality assessment and revised the manuscript.

Data Availability Statement

The original contributions presented in the study are included in the article / Appendix, further inquiries can be directed to the corresponding author.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships.

Appendix

Table A1 The results of the analysis of other outcomes

Outcomes	Interventions	Studies	0R	95%CI	P	I^2
	TZP 5 mg vs Control	9	0.90	(0.74,1.09)	0.28	11%
serious adverse event	TZP 10 mg vs Control	10	0.94	(0.78,1.13)	0.49	0%
	TZP 15 mg vs Control	11	0.70	(0.57,0.85)	0.0004	63%
	TZP 5 mg vs Control	9	2.62	(1.60,4.28)	0.0001	7%
nausea	TZP 10 mg vs Control	10	3.41	(2.10,5.54)	<0.000 01	0%
	TZP 15 mg vs Control	11	4.32	(2.75,6.79)	<0.000 01	1%
	TZP 5 mg vs Control	9	6.61	(2.31,18.99)	0.0004	59%
diarrhea	TZP 10 mg vs Control	10	6.14	(1.61,23.38)	0.008	76%
	TZP 15 mg vs Control	11	8.51	(3.17,22.82)	<0.0001	66%

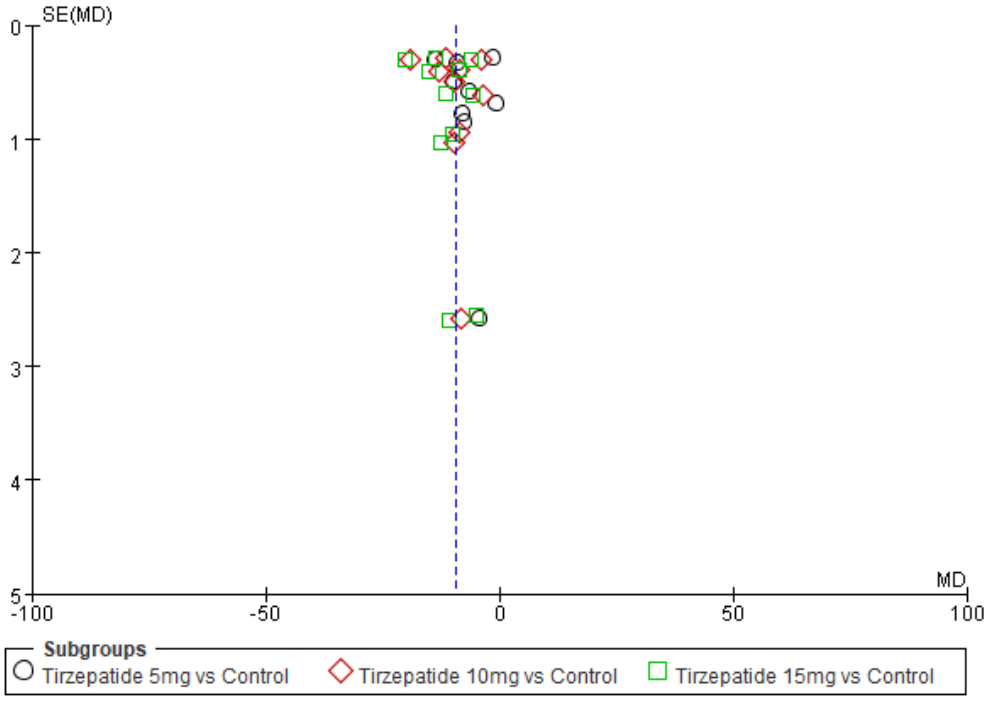

Figure A1 The funnel plots of Bodyweight, Tirzepatide vs Control

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