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# Impact of 1-Year Tirzepatide Use on Glycemic and Metabolic Profile in Overweight to Obese People with Type 1 Diabetes: A Systematic Review and Meta-Analysis

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## Abstract

**Background:** Currently, tirzepatide is not approved for use in type 1 diabetes (T1D). Several studies have reported the clinical benefit of tirzepatide use in T1D. However, no systematic review and meta-analysis (SRM) has been published on this topic; this SRM was conducted to evaluate the impact of tirzepatide use in T1D.

**Methods:** Electronic databases were searched for articles evaluating the use of tirzepatide in overweight and obese adults with T1D. Coprimary outcomes were the percent reduction in body weight and glycated hemoglobin (HbA1c). Secondary outcomes included percent change in total daily dose (TDD) of insulin requirement, glycemic variability, and side effects after 6, 9, and 12 months of tirzepatide therapy.

**Results:** Data from six studies (221 patients) were analyzed. A >10% reduction in body weight was noted with 6- [mean difference or MD -10.39% (95% confidence interval or CI: -10.66, -10.12);  $I^2 = 17\%$ ], 8- to 9- [MD -13.20% (95% CI: -19.79, -6.60);  $I^2 = 93.6\%$ ], and 12-month [MD -15.70% (95% CI: -22.99, -8.41);  $I^2 = 73.4\%$ ] tirzepatide therapy. A more than half-a-percent reduction in HbA1c was noted with 6- [MD -0.60% (95% CI: -0.67, -0.53);  $I^2 = 41.3\%$ ], 8- to 9- [MD -0.78% (95% CI: -1.25, -0.31);  $I^2 = 95.6\%$ ], and 12-month [MD -0.58% (95% CI: -0.62, -0.55);  $I^2 = 0\%$ ] tirzepatide therapy. A >30% reduction in TDD insulin requirement was noted with 6- [MD -33.59% (95% CI: -46.00, -21.17);  $I^2 = 92.6\%$ ], 8- to 9- [MD -36.01% (95% CI: -57.91, -14.11);  $I^2 = 97.7\%$ ], and 12-month [MD -36.19% (95% CI: -52.87, -19.50);  $I^2 = 80.5\%$ ] tirzepatide therapy. Significant improvement in glycemic variability was noted.

**Conclusions:** Tirzepatide is effective in adults with T1D and obesity for improving glycemic control and promoting weight loss. It leads to a significant reduction in both insulin requirements and glycemic variability. The benefits observed at 6 months were durable and continued to improve further after 12 months of therapy, particularly with regard to weight reduction, which warrants longer follow-up studies.

**Keywords:** type 1 diabetes; tirzepatide; weight loss; insulin requirement; glycemic variability

## Introduction

Type 1 diabetes (T1D) is primarily an autoimmune disorder that destroys beta cells of the pancreas, necessitating lifelong insulin therapy.<sup>1</sup> Generally, it has become

increasingly challenging for patients and their treating physicians to sustain adequate glycemic control in individuals diagnosed with T1D.<sup>2</sup> Several factors may contribute; the requirement for intricate insulin therapy

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Artificial intelligence was not used in any form in the planning as well as the execution of the study and article preparation.

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regimens, along with stricter adherence to dietary and lifestyle factors than those needed for type 2 diabetes (T2D), could be among these reasons.<sup>2</sup> The worsening of the obesity pandemic in this century has affected not only people living with T2D but also those with T1D. Obesity is linked to insulin resistance, which subsequently decreases the effectiveness of insulin administered in T1D. This is akin to the existence of T2D in individuals living with T1D, hence often called “double diabetes.”<sup>3</sup> Weight loss in individuals with T1D who have obesity improves glycemic control, along with a reduction in total daily dose (TDD) of insulin requirement. A recent systematic review and meta-analysis (SRM) has shown that glucagon-like peptide-1 receptor agonists (GLP-1RAs), such as liraglutide, are effective for weight loss, improving glycemic control, and reducing insulin requirements in patients with T1D who have obesity.<sup>4</sup>

Tirzepatide is a twincretin (a dual GLP-1 and GIP receptor agonist) with glycemic and weight-loss properties superior to GLP-1RAs in treating T2D and/or obesity.<sup>5,6</sup> Tirzepatide is currently not approved for use in T1D. Several studies have been published evaluating the use in T1D, particularly among individuals with obesity.<sup>3</sup> The literature review revealed that, to date, no SRM has been published evaluating the efficacy and safety of tirzepatide use in T1D. Therefore, this SRM was conducted to address this knowledge gap.

## Methods

### Ethical compliance

This SRM was conducted according to the procedures outlined in the Cochrane Handbook for Systematic Reviews of Interventions and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.<sup>7</sup> The SRM is registered with PROSPERO (CRD420251025973), and the protocol summary can be accessed online.

### Search strategy

We conducted an extensive literature search across databases including PubMed, Ovid Embase, Ovid Medline, Cochrane Library, ClinicalTrials.gov, CNKI, ctri.nic.in, and Google Scholar. All studies published up to March 31, 2025, were examined. The search strategy utilized combinations of key terms such as “tirzepatide” and “type 1 diabetes.” The search terms were implemented in the titles and abstracts of the documents. The goal was to find published and

unpublished full-length journal articles and abstracts for the conference proceedings in English. Additionally, the search entailed examining references in the published articles obtained for this study and in relevant journals.

### Eligibility criteria

The PICOS criteria were utilized to screen and select the studies. The population (P) included people living with T1D. The intervention (I) consisted of the use of tirzepatide along with the standard of care insulin therapy for managing T1D. The control (C) group (if available) used the standard of care insulin therapy only or a placebo/any other approved medication in addition to the standard of care insulin therapy for T1D. In addition, studies without a control group were considered for single-arm and proportion meta-analysis. The outcomes (O) focused on percent weight reduction, glycated hemoglobin (HbA1c), total daily insulin requirement (units/day), time in range (TIR) (70–180 mg/dL), time above range (TAR) (>180 mg/dL), time below range (TBR) (<70 mg/dL), hypoglycemia, and side effects. The study type (S) comprised randomized controlled trials (RCTs), cohort studies, case-control studies, and case series.

Cross-sectional studies, case reports, reviews, expert opinions, editorials, letters to the editor, and duplicate reports were excluded from the analysis. Duplicates were removed before screening articles by title and abstract, followed by full-text screening to confirm eligibility.

### Study outcomes

The primary outcomes analyzed were the percent reduction in body weight and HbA1c after 6 months of tirzepatide therapy compared with baseline. Secondary outcomes included percent change in TDD of insulin requirement, TIR, TAR, TBR, hypoglycemia, ketoacidosis, and side effects after 6, 9, and 12 months of tirzepatide therapy. Secondary outcomes also included changes in body weight and HbA1c after 9 and 12 months of tirzepatide therapy.

### Study selection

Two reviewers independently screened the titles and abstracts of the identified studies. They reviewed the full text to determine if a study could not be excluded based solely on the title and abstract. Any disagreements concerning the study's eligibility were resolved by consulting a third author.



### Data extraction

Two review authors independently extracted data using standardized forms for data extraction. When multiple publications from a single study group were identified, the results were consolidated, and relevant data from each article were included in the analyses. The following data were extracted from all eligible studies and included in the review: first author, year of publication, the country where the study was conducted, study design, major inclusion and exclusion criteria, sample size, proportions of female and male subjects, mean age, and body-weight body mass index (BMI) of the participants, duration of T1D, HbA1c, TDD of insulin, proportions of study subjects using different insulin delivery methods, and the outcomes as mentioned above. Any disagreements were resolved by consensus.

### Data synthesis and statistical analysis

The extracted data were analyzed using the “meta” and “metafor” packages in RStudio for R Statistics programming (Version 2025.4.5.0).<sup>8</sup> Continuous variables were presented as mean/standard deviation, whereas categorical variables were presented as frequency/proportion. The outcomes were measured as mean differences (MD) for the continuous variables and odds ratios (OR) or risk ratios (RR) for the categorical variables, along with 95% confidence intervals (CI). For the studies with a non-tirzepatide control group, the MDs for the changes from baseline values of the continuous outcomes in the tirzepatide versus control groups for the categorical variables were calculated. For the single-arm studies using tirzepatide only, the mean changes from baseline values of the continuous outcomes were pooled to generate the effect sizes. The random-effects model was chosen to address the anticipated heterogeneity resulting from population characteristics in the included studies. The inverse variance statistical method was applied for all instances. Details of the meta-analysis included using the restricted maximum-likelihood estimator for tau,<sup>2</sup> the Q-profile method for confidence interval of tau<sup>2</sup> and tau. Calculation of  $I^2$  was based on Q statistics using untransformed (raw) means. Forest plots were generated with the same software. Forest plots were generated for visualization in RStudio.

### Assessment of heterogeneity and publication bias

The assessment of heterogeneity was initially performed by examining forest plots. Subsequently, Chi-squared

tests were conducted using N-1 degrees of freedom and a significance level of 0.05 to assess statistical significance. The  $I^2$  test was also used in the subsequent analysis. Thresholds for  $I^2$  values were defined as follows: 25% for low heterogeneity, 50% for moderate heterogeneity, and 75% for high heterogeneity.<sup>9</sup>

### Assessment of the quality of the included studies

Two independent reviewers meticulously evaluated the risk of bias in the included studies using the Risk of Bias in Non-randomized Studies of Interventions, Version 2 (ROBINS-I V2) for the RCTs and non-RCTs.<sup>10</sup> The ROBINS-I V2 tool covers seven domains through which bias might be introduced. Based on these responses to the signaling questions, which aim to elicit information relevant to the RoB judgment for the domain, the options for a domain-level RoB judgment are “Low,” “Moderate,” “Serious,” or “Critical” risk of bias, with an additional option of “No information.” The judgments within each domain are carried forward to an overall RoB judgment across bias domains for the outcome being assessed. In discrepancies, the sixth and seventh authors acted as arbitrators to achieve consensus. The Risk-of-bias VISualization (ROBVIS) web app was used to create risk-of-bias plots.<sup>11–13</sup>

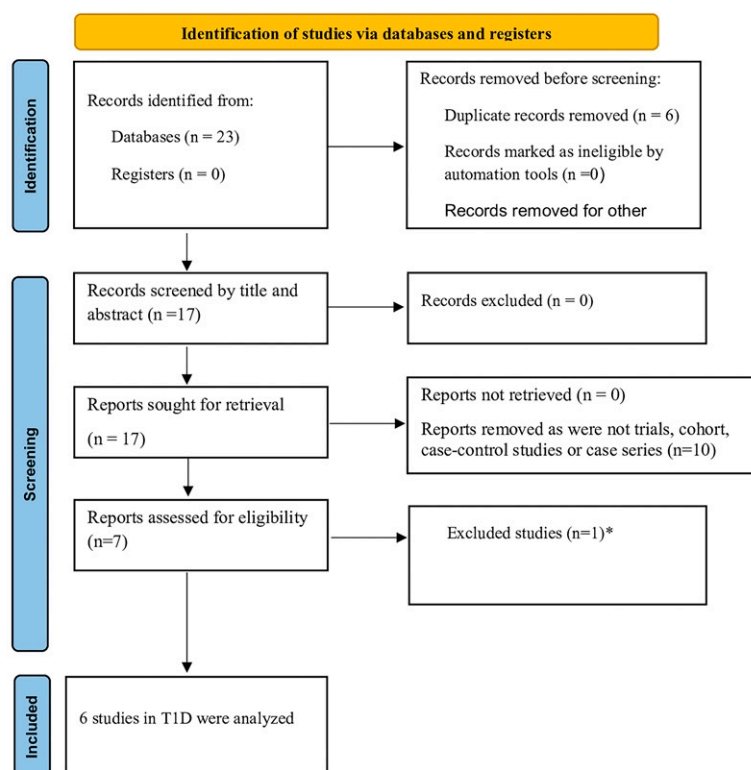
### Results

An initial search yielded 23 articles. After removing six duplicates, the remaining 17 articles were further reviewed in detail. The details have been elaborated in Figure 1. A total of seven articles were found on our topic of interest, of which six articles, including 221 patients with T1D on standard of care and receiving tirzepatide (fulfilled all the inclusion and exclusion criteria), were included in the analysis.<sup>14–19</sup> One study focused on people with latent onset diabetes of adults (LADA) and not T1D—hence excluded from analysis.<sup>20</sup>

### Study characteristics

The characteristics of the patients evaluated in different studies analyzed in our SRM have been elaborated in Table 1. The majority of the study participants were women. The mean age of the study participants living with T1D was more than 40 years, having a diabetes duration of more than 20 years, and a mean BMI of more than 35 kg/m<sup>2</sup>, suggestive of the presence of obesity with T1D (double diabetes) (Table 1). The dose of tirzepatide received by the study participants has been elaborated in Table 1. The characteristics of the





\*One study focused on people with latent onset diabetes of adults (LADA) and not type 1 diabetes (T1D), hence excluded from analysis

**FIG. 1.** Flowchart elaborating on study retrieval and inclusion in this systematic review.

patients in the excluded study on LADA have been elaborated in Supplementary Table S1.

### Risk of bias and quality assessment of the included studies

The risk of bias was calculated to be low among the studies analyzed in this systematic review and meta-analysis. Details have been elaborated in the Supplementary Figure S1.

### Primary outcomes

**Body weight and HbA1c (post 6-month therapy).** All six studies (221 patients) reported on percent body-weight reduction and HbA1c reduction from baseline following 6 months of tirzepatide therapy. Six-month tirzepatide therapy in T1D was associated with a >10% reduction in body weight from baseline [MD −10.39% (95% CI: −10.66, −10.12);  $I^2 = 17\%$  (low heterogeneity); Fig. 2A]. Six-month tirzepatide therapy in T1D was associated with a greater than half-a-

percent reduction in HbA1c on the background standard insulin therapy for T1D [MD −0.60% (95% CI: −0.67, −0.53);  $I^2 = 41.3\%$  (low heterogeneity); Fig. 2B].

### Secondary outcomes

**Body weight and HbA1c (post 9- and 12-month therapy).** Four studies (187 patients) reported on percent body-weight reduction from baseline following 8–9 months of tirzepatide therapy. Eight to 9 months of tirzepatide therapy in T1D were associated with a >10% reduction in body weight from baseline [MD −13.20% (95% CI: −19.79, −6.60);  $I^2 = 93.6\%$  (considerable heterogeneity); Fig. 2C]. Three studies (155 patients) reported the percent body-weight reduction from baseline following 12 months of tirzepatide therapy. Twelve-month tirzepatide therapy in T1D was associated with a >10% reduction in body weight from baseline [MD −15.70% (95% CI: −22.99, −8.41);  $I^2 = 73.4\%$  (considerable heterogeneity); Fig. 2D].



**Table 1. Baseline Characteristics of the Included Studies and Participants**

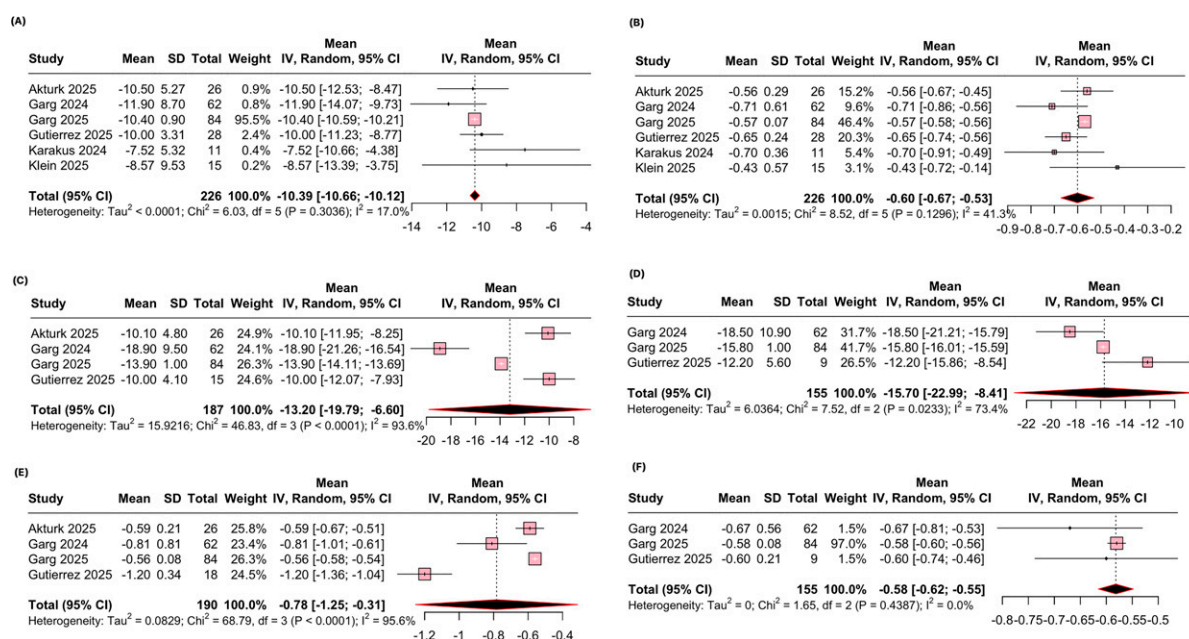
Study ID [ref]; Type of study; Study place	Major inclusion criteria	N	Female (%)	Duration of diabetes (years), mean $\pm$ SD or median (IQR)	Age (years), mean $\pm$ SD or median (IQR)	BW (kg), mean $\pm$ SD or median (IQR)	BMI (kg/m <sup>2</sup> ), mean $\pm$ SD or median (IQR)	HbA1c (%), mean $\pm$ SD or median (IQR)	Insulin TDD (units/day), mean $\pm$ SD or median (IQR)	Insulin delivery method (%)	Study duration	Tirzepatide dose at the end of the study
Akturk 2025 <sup>14</sup> ; Retrospective observational study; Single center in the United States	-Adults with T1D -Not on OAD -Prescribed with tirzepatide between June 15, 2022, and January 30, 2023	26	54	NR	42 $\pm$ 8	108.1 $\pm$ 21.2	36.7 $\pm$ 5.3	7.3 $\pm$ 0.7	83.9 $\pm$ 44.7	MDI: 27%; Insulin pump: 73%	8 months	7.5 mg (n = 7) 10 mg (n = 7) 5–15 mg (n = 12)
Garg 2024 <sup>15,a</sup> ; Retrospective real-world study; Single center in the United States	-Adults (age 18–80) with T1D on tirzepatide for at least 3 months -BMI $\geq$ 27 kg/m <sup>2</sup> -On IIT, using either MDIs or on an insulin pump or an HCL system -Were using a CGM	62	63	24 $\pm$ 13	40 $\pm$ 10	103.8 $\pm$ 19.4	35.6 $\pm$ 5.5	7.0 $\pm$ 0.9	76 $\pm$ 40	MDI: 16%; Insulin pump/HCL: 84%	12 months	Mean: 9.7 $\pm$ 3.3 mg
Garg 2025 <sup>16,a</sup> ; Retrospective real-world study; Single center in the United States	-Adults (age $\geq$ 18) with T1D on tirzepatide for at least 6 months -BMI $\geq$ 27 kg/m <sup>2</sup> -On IIT, using either MDIs or on an insulin pump or an AID or an HCL system -Were using a CGM	84	63	27 $\pm$ 13	41 $\pm$ 7	103.4 $\pm$ 18.6	35.2 $\pm$ 4.8	7.0 $\pm$ 0.9	78 $\pm$ 47	MDI: 14%; Insulin pump/HCL: 86%	21 months	Median: 10 mg
Gutierrez 2025 <sup>17</sup> ; Retrospective study; Single center in the United States	-Adults (age $\geq$ 18) with T1D on tirzepatide for at least 3 months -BMI $\geq$ 30 or 27 kg/m <sup>2</sup> with at least one adiposity-associated disease	51	58.8	24.0 (14.5–34.3)	50 (39–58)	111 (93.6–129)	36.1 (32–42.6)	7.6 (6.8–8.3)	68.6 (49.1–102.0)	MDI: 21.6%; Insulin pump/HCL: 78.4%	Median: 8 months	2.5–5 mg (n = 12) 7.5–10 mg (n = 21) 12.5–15 mg (n = 18)
Karakus 2024 <sup>18</sup> ; Retrospective observational study; Single center in the United States	Adults with T1D who were using AID and initiated tirzepatide adjunct therapy for clinical indications	11	63.6	24 (15–35)	37 (34–49)	114.3 (94.8–129.3)	39.6 (35.6–40.7)	7.0 (6.7–7.4)	63.7 (43.2–114)	AID (Control IQ): 100%	8 months	5 mg (n = 2) 7.5 mg (n = 1) 10 mg (n = 3) 12.5 mg (n = 3) 15 mg (n = 2)
Klein 2024 <sup>19,b</sup> ; Retrospective observational study; Single center in the United States	-Adults (age $\geq$ 18) with T1D -BMI $\geq$ 40 kg/m <sup>2</sup> -History of early-onset, severe obesity	15	45.5	24 (15.3–42.7)	45.8 (34.9–48.0)	109.7 (92.1–117.3)	38.7 (33.7–41.5)	7.2 (6.9–7.6)	0.46 U/(kg-d) (0.42–0.64)	MDI: 53.3%; AID: 46.7%	6 months	NR

<sup>a</sup>These two studies have a control group that did not take tirzepatide. As the number of studies is small, we did not include them in the meta-analysis.

<sup>b</sup>This study has two groups of patients with T1DM: patients tested positive for obesity-related mutation(s) and patients either tested negative for obesity-related mutation(s) or were not eligible for genetic testing (thus low probability of genetic obesity). We have included the latter group for our analysis.  
AID, automated insulin delivery; BMI, body mass index; BW, body weight; CGM, continuous glucose monitoring; HbA1c, glycated hemoglobin; HCL, hybrid closed loop; IIT, intensive insulin treatment; IQR, interquartile range; MDI, multiple daily injections; NR, not reported; OAD, oral anti-hyperglycemic drugs; SD, standard deviation; T1D, type 1 diabetes; T1DM, type 1 diabetes mellitus.







**FIG. 2.** Forest plot highlighting the impact of tirzepatide therapy in type 1 diabetes on (A) percent weight reduction at 6 months; (B) HbA1c reduction at 6 months; (C) percent weight reduction at 9 months; (D) percent weight reduction at 12 months; (E) HbA1c reduction at 9 months; and (F) HbA1c reduction at 12 months. HbA1c, glycated hemoglobin.

Four studies (190 patients) reported HbA1c reduction from baseline following 8–9 months of tirzepatide therapy. Eight to 9 months of tirzepatide therapy in T1D were associated with a greater than half-a-percent reduction in HbA1c from baseline [MD  $-0.78\%$  (95% CI:  $-1.25, -0.31$ );  $I^2 = 95.6\%$  (considerable heterogeneity); Fig. 2E]. Three studies (155 patients) reported HbA1c reduction from baseline following 12 months of tirzepatide therapy. Twelve-month tirzepatide therapy in T1D was associated with a greater than half-a-percent reduction in HbA1c from baseline [MD  $-0.58\%$  (95% CI:  $-0.62, -0.55$ );  $I^2 = 0\%$  (low heterogeneity); Fig. 2F].

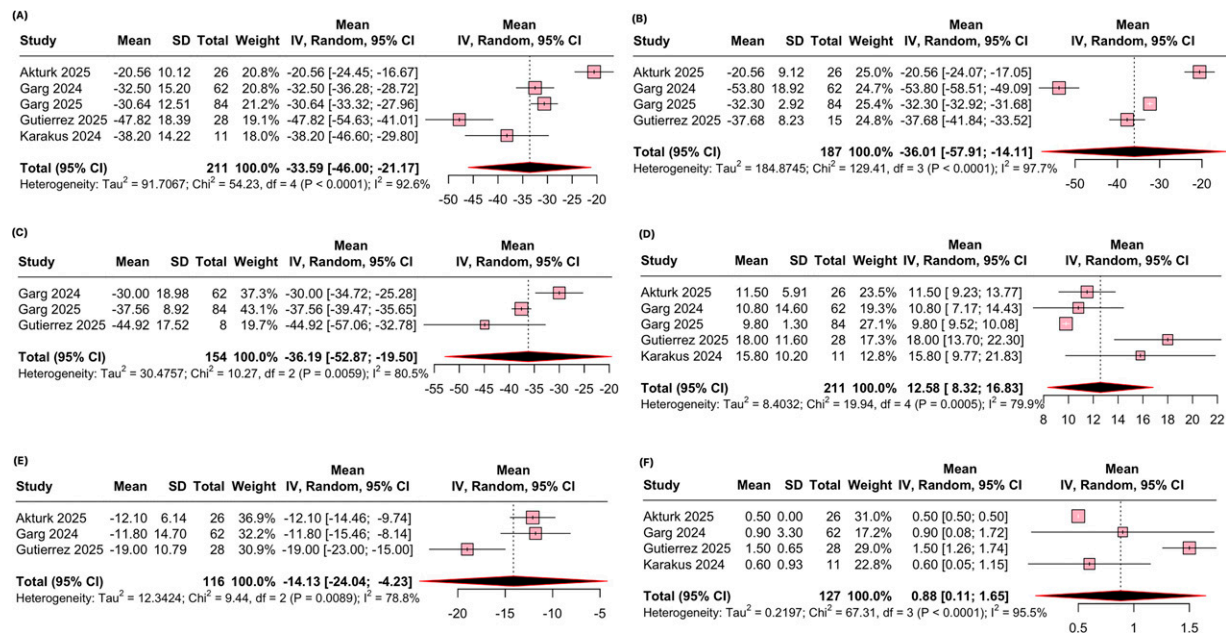
**Percent change in TDD of insulin therapy.** Five studies (211 patients) reported the percent change in TDD of insulin therapy from baseline following 6 months of tirzepatide therapy. Six-month tirzepatide therapy in T1D was associated with a  $>30\%$  reduction in TDD of insulin therapy from baseline [MD  $-33.59\%$  (95% CI:  $-46.00, -21.17$ );  $I^2 = 92.6\%$  (considerable heterogeneity); Fig. 3A]. Four studies (187 patients) reported the percent change in TDD of insulin therapy from

baseline following 8–9 months of tirzepatide therapy. Eight to 9 months of tirzepatide therapy in T1D were associated with a  $>30\%$  reduction in TDD of insulin therapy from baseline [MD  $-36.01\%$  (95% CI:  $-57.91, -14.11$ );  $I^2 = 97.7\%$  (considerable heterogeneity); Fig. 3B].

Three studies (154 patients) reported the percent change in TDD of insulin therapy from baseline following 12 months of tirzepatide therapy. Twelve-month tirzepatide therapy in T1D was associated with a  $>30\%$  reduction in TDD of insulin therapy from baseline [MD  $-36.19\%$  (95% CI:  $-52.87, -19.50$ );  $I^2 = 80.5\%$  (considerable heterogeneity); Fig. 3C].

**Changes in continuous glucose monitoring parameters.** Five studies (211 patients) reported changes in TIR (70–180 mg/dL) from baseline following 6 months of tirzepatide therapy. Six-month tirzepatide therapy in T1D was associated with a  $>10\%$  increase in TIR [MD  $12.58\%$  (95% CI:  $8.32, 16.83$ );  $I^2 = 79.9\%$  (considerable heterogeneity); Fig. 3D]. Three studies (116 patients) reported on changes in TAR ( $>180$  mg/dL) from baseline following 6 months of tirzepatide therapy.





**FIG. 3.** Forest plot highlighting the impact of tirzepatide therapy in type 1 diabetes on (A) percent change in total daily dose (TDD) of insulin requirement at 6 months; (B) percent change in TDD of insulin requirement at 9 months; (C) percent change in TDD of insulin requirement at 12 months; (D) change in time in range (TIR) at 6 months; (E) change in time above range (TAR) after 6 months; and (F) change in time below range (TBR) at 6 months.

Six-month tirzepatide therapy in T1D was associated with a >10% decrease in TAR [MD -14.13% (95% CI: -24.04, -4.23);  $I^2 = 78.8\%$  (considerable heterogeneity); Fig. 3E]. Four studies (127 patients) reported on changes in TBR (<70 mg/dL) from baseline following 6 months of tirzepatide therapy. Six-month tirzepatide therapy in T1D was associated with a mild increase in TBR [MD 0.88% (95% CI: 0.11, 1.65);  $I^2 = 95.5\%$  (considerable heterogeneity); Fig. 3F].

**Adverse events.** Gastrointestinal adverse events are the common and well-known adverse events associated with the use of tirzepatide, with maximum data available from people living with T2D.<sup>5,6</sup> Among the six studies analyzed in this SRM, details of gastrointestinal adverse events were available from only one study.<sup>17</sup> The most common gastrointestinal adverse events in T1D were reported to be nausea, loss of appetite, and heartburn, with an occurrence of 3.9%–13.7%.<sup>17</sup> There were no reports of ketoacidosis in any of the 221 patients analyzed in this SRM. Hypoglycemia was

defined as a blood glucose value <70 mg/dL. Severe hypoglycemia was defined as a blood glucose value <54 mg/dL or hypoglycemia needing hospital admission. There were 17 and 5 reports of hypoglycemia and severe hypoglycemia, respectively, among the cohort of patients analyzed in this SRM.

## Discussion

The prevalence of overweight to obesity in adults living with T1D in the United States, Brazil, and Europe has been reported to be 62%, 40.7%, and 29.6%–33%, respectively.<sup>21–23</sup> The problem is only going to worsen with the global pandemic of metabolic syndrome and obesity. Tirzepatide has established itself as a potent and efficient anti-obesity and anti-diabetes medication with good hepatobiliary,<sup>24</sup> pancreatic,<sup>25</sup> and renal safety<sup>26</sup> without increasing malignancy risk.<sup>27</sup> This is the first SRM to evaluate the impact of tirzepatide use in people living with T1D on their body weight, glycemic control, insulin requirement, and glycemic variability. Our analysis shows that tirzepatide use in



adults with T1D and obesity on standard of care insulin therapy was associated with, on average, more than 10% reduction in body weight, around half a percent additional reduction in HbA1c, more than 30% reduction in TDD of insulin requirement, and a reduction in glycemic variability. Improvements in glycemic control noted after 6 months of tirzepatide therapy in T1D were found to be durable and sustained after 1 year of tirzepatide therapy. Similarly, the >30% reduction in insulin requirement noted after 6 months of tirzepatide therapy was durable even after 1 year of treatment. However, regarding weight loss, the >10% weight loss seen after 6 months of tirzepatide therapy in T1D continued to improve and was >15% after 12 months of tirzepatide therapy. Hence, a plateau was not reached with regard to weight loss and thus warrants longer follow-up studies. The benefits seen with use of tirzepatide in obese T1D may be considered somewhat akin to bariatric surgery in obese T1D. In a systematic review analyzing data from 648 obese patients with T1D, bariatric surgery was associated with lowering of BMI from  $42.6 \pm 4.7$  kg/m<sup>2</sup> to  $29.4 \pm 4.7$  kg/m<sup>2</sup>, reduction in TDD insulin requirement by  $-0.2$  units/(kg·d), along with a reduction in HbA1c by on an average 0.71%.<sup>28</sup> Post-hoc analysis of data from 120 patients with anti-GAD antibody positive from the Survey Using Randomized Procedures and Systematic Studies (SURPASS) 2–5 trials, who can be considered to be having latent onset autoimmune diabetes of adults (LADA); use of tirzepatide was associated with similar reduction in body weight (as seen in T1D in this SRM) along with an impressive reduction in HbA1c, highlighting the potential adjective role of tirzepatide in patients with LADA and obesity (Supplementary Table S1).<sup>20</sup>

It was reassuring to see that this reduction in insulin requirement with use of tirzepatide was not associated with increased ketoacidosis. Since the TDD of insulin requirement depends on the individual's weight, significant weight loss with tirzepatide use in T1D would have contributed to the reduction in TDD of insulin requirement. Tirzepatide use in T1D was associated with a substantial improvement (increase) in TIR along with a significant decrease in TAR. However, there was also a small but significant increase in TBR. A few reports of severe hypoglycemia were also noted.

Hence, tirzepatide initiation in T1D should be closely monitored using more intensive self-monitoring of blood glucose in the initial few weeks and months so that the insulin doses can be more effectively reduced to prevent hypoglycemia as well as glycemic variability. A good clinical practice on the “sick days” in people living with T1D would be to have a low threshold for temporarily withholding tirzepatide during the sick days, with more frequent blood glucose monitoring along with intensification of the insulin regimen to reduce the risk of ketoacidosis.

In a pilot real-world study of 50 patients, Garg et al. noted that semaglutide use in overweight/obese patients with T1D was associated with a lowering of body weight and BMI, along with improvement in glycemic metrics.<sup>29</sup> In a systematic review of five trials (2445 randomized T1D patients), liraglutide 1.8 mg/day use was associated with a mild HbA1c reduction ( $-0.24\%$ ) and mild weight reduction ( $-4.87$  kg), with a decrease in TDD of insulin requirement.<sup>30</sup> Gastro-intestinal problems were the predominant side effects, without any increased occurrence of ketoacidosis.<sup>30</sup> Previously, mild weight reduction has been documented with the use of sodium glucose cotransporter-2 inhibitors and metformin in obese people with T1D.<sup>31</sup> In contrast, the quantum of weight, HbA1c, and TDD of insulin reduction in T1D were much greater with tirzepatide in our SRM. This is in accordance with the quantum of body weight and HbA1c reduction with tirzepatide in T2D and obesity, which was much more than other anti-diabetes medications such as GLP-1RAs.<sup>5</sup>

The limitations of our SRM were that only single-arm (pre- and post-treatment) SRM could be done, as most of the studies on tirzepatide in T1D did not have a valid matched control group. In addition, both the number of studies and the size of the studied population were limited. All the studies were single-centered and lacked global representation. All the studies included adults with overweight or obesity. We do not have any efficacy and safety data on use of tirzepatide in lean or normal weight T1D. Currently, there are also no data on the use of tirzepatide in children and adolescents with T1D and obesity/metabolic syndrome. These should be areas of further investigation.





## Conclusions

Tirzepatide is effective for adults with long-standing T1D and obesity. It improves glycemic control and aids in weight loss, significantly reducing insulin requirements and glycemic variability. The benefits observed at 6 months were enduring and continued to improve further after 12 months of therapy, particularly with regard to weight reduction, warranting longer follow-up studies.

## Authors' Contributions

The study was conceptualized by D.D. and A.B.M.K.-H. Literature search was done by D.D., R.M., and N.R. Data entry was done by D.D., A.B.M.K.-H., and R.M. Analysis was done by D.D. and A.B.M.K.-H. All authors contributed equally to article preparation.

## Author Disclosure Statement

All authors declare no conflicts of interest.

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## Supplementary Material

Supplementary Figure S1  
 Supplementary Table S1

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### Abbreviations Used

CI = Confidence Interval  
 GAD = Glutamic Acid De-carboxylase  
 RoB = Risk of Bias  
 SRM = Systematic Review and Meta-analysis  
 TAR = Time Above Range  
 TBR = Time Below Range  
 TIR = Time In Range  
 T1D = Type 1 Diabetes  
 T2D = Type 2 Diabetes

