Letter of Support

Amanda R Purcell

ESA Young Investigator Scientific Article Award

15th July 2026

Re: ESA Young Investigator Scientific Article Award – AMANDA PURCELL

Dear Endocrine Society Australia,

I am writing in support of Amanda Purcell's application for the ESA Young Investigator Scientific Article Award for her first-author publication "Tirzepatide is Associated with Improved Metabolic Outcomes in People with Type 1 Diabetes and Overweight or Obesity: A Retrospective Cohort Study," published in *Diabetes, Obesity and Metabolism* in June 2026. This study addresses an important and rapidly evolving area of clinical endocrinology: the use of incretin-based therapies in people with type 1 diabetes and overweight or obesity. The study found that tirzepatide use was associated with clinically meaningful reductions in body weight and insulin requirements in adults with type 1 diabetes and overweight or obesity, providing valuable Australian real-world evidence in a population with limited therapeutic options addressing both excess weight and insulin resistance.

Amanda made the largest individual contribution to this study. She contributed to the research question and study design, including framing the research question, then led the systematic review of electronic medical records from Royal North Shore Hospital and the Northern Sydney Endocrine Centre. She identified eligible participants, constructed and verified the dataset, and performed all statistical analyses, including propensity score matching, baseline balance assessment, outcome comparisons, correction for multiple testing and sensitivity analyses. Amanda also prepared the manuscript and led its revision, incorporating co-author feedback, responding to peer review and preparing the final accepted version.

In support of this application, Amanda is submitting her first-author systematic review and meta-analysis of GLP-1 receptor agonist therapy in people with type 1 diabetes and overweight or obesity. This work is directly relevant to the nominated paper, as it synthesised the existing evidence for incretin-based therapy in this population and provided a strong clinical rationale for investigating newer agents such as tirzepatide. Together, these publications demonstrate a coherent body of work spanning evidence synthesis and the generation of new clinical data.

Amanda is an outstanding final-year PhD candidate at the University of Sydney and a highly valued member of our team at the Kolling Institute and Royal North Shore Hospital. She is an active member of the ESA and has contributed to several studies presented at ESA scientific meetings over the past three years. These publications reflect her strong clinical research capability and emerging leadership in incretin-based therapies and type 1 diabetes.

I strongly endorse Amanda's application and recommend her without reservation. Thank you for considering this application. Please do not hesitate to contact me if you require any further information.

Yours sincerely,

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Date: 15 July 2026

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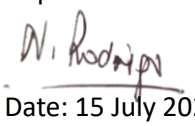

Date: 15 July 2026

Amanda R. Purcell
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Date: 15 July 2026

Submitted Article

Amanda R Purcell

ESA Young Investigator Scientific Article Award

Diabetes, Obesity and Metabolism

WILEY

ORIGINAL ARTICLE OPEN ACCESS

Tirzepatide Is Associated With Improved Metabolic Outcomes in People With Type 1 Diabetes and Overweight or Obesity: A Retrospective Cohort Study

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ABSTRACT

Aims: To evaluate the effect of tirzepatide on body weight, glycaemic control, insulin requirements, continuous glucose monitoring (CGM) metrics and cardiorenal parameters in adults with Type 1 diabetes (T1D) and overweight or obesity.

Materials and Methods: In this retrospective matched cohort study, adults with T1D, BMI ≥ 27 kg/m^2, CGM use and available baseline and follow-up electronic medical record data from Royal North Shore Hospital and the Northern Sydney Endocrine Centre between 2020 and 2025 were included. Twenty-three adults treated with tirzepatide were identified and propensity score-matched to 23 control participants. Primary outcomes included changes in percentage change in body weight, HbA1c, total daily insulin dose and CGM-derived metrics from baseline to follow-up. Exploratory outcomes included changes in blood pressure and biochemical markers.

Results: Mean follow-up duration in the tirzepatide and control groups were 28 and 31 weeks, respectively. The most common dose of tirzepatide was 5 mg/week (52.2% participants). Compared with controls, tirzepatide was associated with greater reductions in body weight (−10.01% ± 4.74% vs. +0.69% ± 3.77%, adj-$p < 0.0001$) and total daily insulin dose (−21.82 ± 16.30 vs. +5.62 ± 11.63 U/day; adj-$p = 0.002$). From baseline to end-of-study, tirzepatide was associated with a reduction in glucose management indicator, glucose SD and daily carbohydrate intake. Other CGM, blood pressure, lipid, hepatic and renal outcomes did not differ.

Conclusions: In adults with T1D and overweight or obesity, adjunctive tirzepatide treatment was associated with clinically meaningful reductions in percentage body weight and insulin requirements. Larger prospective studies are needed to confirm efficacy, ensure safety and assess broader cardiometabolic effects.

1 | Introduction

Overweight and obesity are increasingly common in adults living with Type 1 diabetes (T1D). Data from the US-based T1D Exchange Clinic Registry, a large cohort of people living with T1D receiving specialist diabetes care, indicates that approximately half of adults with T1D are living with overweight or obesity [1]. Similarly, longitudinal data from the German/Austrian DPV Registry show a sustained upward shift of body mass index (BMI) over recent decades that exceeds trends observed in the general population [2]. Importantly, excess adiposity in T1D amplifies insulin resistance, increases daily insulin requirements and contributes to an adverse cardiometabolic risk profile thereby compounding the burden of microvascular and

macrovascular disease risk in a population already vulnerable to cardiovascular complications [3]. Despite major advances in continuous glucose monitoring (CGM) and automated insulin delivery, these technologies do not directly address obesity-driven insulin resistance and its downstream metabolic and cardiovascular consequences.

Adjunctive agents such as metformin, sodium-glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists have been investigated to address insulin resistance and weight gain in T1D, but clinical benefits have varied by agent. Metformin yields modest short-term improvements in body weight and insulin dose, with limited long-term durability [4]. SGLT2 inhibitors improve weight and glycaemic outcomes but are constrained by an increased risk of diabetic ketoacidosis [5, 6]. GLP-1 receptor agonists have been associated with reductions in body weight, improvements in glycaemic outcomes and lower insulin requirements in T1D [7], but evidence for newer dual incretin agonists in T1D remains limited.

Tirzepatide, a dual GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptor agonist, has demonstrated marked reductions in glycated haemoglobin (HbA1c), body weight and several cardiometabolic risk factors in type 2 diabetes and obesity [8–11]. Emerging case reports and small observational studies in adults with T1D suggest that tirzepatide induces clinically meaningful weight loss, reduced insulin requirements and improved glycaemic variability [12, 13]. A recent small clinical trial has now demonstrated that, in 22 adults with T1D and obesity, tirzepatide produced markedly greater weight loss than placebo over a short 12-week duration, alongside reductions in HbA1c and total daily insulin dose [14]. Nonetheless, robust real-world data remains limited, particularly regarding CGM-derived glycaemic variability and the impact on other cardiometabolic measurements used in routine clinical care.

This retrospective, observational cohort study evaluated the effect of tirzepatide on body weight, HbA1c, CGM metrics and cardiometabolic parameters in adults with T1D and overweight or obesity. It was hypothesised that tirzepatide would improve metabolic outcomes in this population, including body weight, glycaemic control and insulin requirements, compared with standard care alone.

2 | Materials and Methods

2.1 | Study Design and Participants

This study was a retrospective, observational cohort study of patients with T1D, seen at Royal North Shore Hospital (RNSH), a public hospital clinic, or the Northern Sydney Endocrine Centre (NSEC), a private endocrinology clinic, between 2020 and 2025. Adults (aged ≥ 18 years) with a clinical diagnosis of T1D and overweight or obesity (BMI ≥ 27 kg/m^2) at the time of tirzepatide initiation, were eligible for inclusion in this study. Additional inclusion criteria were the use of a CGM and at least one clinic visit within 3 months before starting tirzepatide and at least one follow-up visit within the study window. Both insulin pump and multiple daily injection users were included in this study. Individuals using glucose-lowering agents known to have weight loss benefits (e.g., SGLT2 inhibitors, metformin, GLP-1 receptor agonists) or with insufficient baseline or follow-up data were excluded from the treatment and control groups.

2.2 | Comparator Cohort and Matching

A comparator cohort of adults with T1D who had not received tirzepatide was identified from the same clinic population. Controls were selected using 1:1 nearest-neighbour propensity score matching without replacement. Propensity scores were estimated using logistic regression, with baseline BMI and HbA1c included as covariates. These variables were selected as clinically relevant baseline characteristics likely to influence tirzepatide prescribing. For controls, the interval between baseline and follow-up was selected to approximate the observation period of the corresponding tirzepatide-treated participant.

2.3 | Data Collection and Outcomes

Data was obtained from electronic medical records using a standardised extraction template. Outcomes were assessed at baseline and at the final available visit within the observation window. These measures included age, sex, duration of diabetes, BMI, body weight, HbA1c, total daily insulin dose, daily carbohydrate intake, insulin-to-carbohydrate ratio, CGM metrics (percentage time in range [3.9–10.0 mmol/L], percentage time above range [> 10.0 mmol/L], percentage time below range [< 3.9 mmol/L], glucose management indicator, mean glucose, glucose standard deviation (SD) and coefficient of variation), blood pressure and a range of blood and urine measures including alanine aminotransferase, aspartate aminotransferase, total cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides, estimated glomerular filtration rate and urinary albumin-to-creatinine ratio. Daily carbohydrate intake was derived from self-reported carbohydrate entries recorded in insulin pumps for insulin dosing.

The primary outcomes were change from baseline to end-of-study in percentage change in body weight, BMI, HbA1c, total daily insulin dose, percentage time-in-range, percentage time-below-range and coefficient of variation. Secondary outcomes included change in a range of CGM- and insulin pump-derived metrics, blood pressure and biochemical markers.

2.4 | Statistical Analysis

Baseline and end-of study data are presented as mean and SD. Baseline characteristics were compared using standardised mean differences (SMD). End-of-study outcomes were analysed as change from baseline and between-group differences were compared within matched pairs using paired *t*-tests. To account for multiple testing across primary outcomes, Bonferroni-adjusted *p*-values (adj-*p*) were calculated. Sensitivity analysis using G*Power (version 3.1.9.6) indicated that, for seven primary outcomes, with 23 matched pairs, 80% power and a Bonferroni-adjusted alpha of 0.007, the study was powered to detect a large effect size (dz ≥ 0.80). Secondary outcomes were considered exploratory and were not adjusted for multiplicity. Within-group

changes from baseline to end-of-study were analysed using paired *t*-tests among participants with data available at baseline and end-of-study.

Due to incomplete data availability for some variables, the number of participants included in individual analyses varied. All analyses were performed using available data without imputation. The numbers of participants contributing to the relevant analyses are listed in Tables S1 and S2. Statistical significance was defined as $p < 0.05$, and all statistical analyses were performed using R Studio (version 2026.04.0).

2.5 | Ethics

The study protocol received approval from the Northern Sydney Local Health District Human Research Ethics Committee (#2024/ETH00590).

3 | Results

3.1 | Study Population

Searches of the RNSH and NSEC databases identified 23 individuals that met the eligibility criteria and comprised the tirzepatide cohort. An equal number of propensity score-matched participants were selected as the control group.

3.2 | Baseline Characteristics

Baseline characteristics are shown in Table 1. The tirzepatide and control groups were closely comparable for age (44.87 ± 9.35 vs. 44.83 ± 11.89 years; SMD: 0.00), T1D duration (23.35 ± 10.99 vs. 24.22 ± 12.28 years; SMD: −0.07) and baseline HbA1c (7.14% ± 0.95% vs. 7.08% ± 0.97%; SMD: 0.06). The proportion of participants using multiple daily injections was similar between groups (26.09% vs. 21.74%; SMD: 0.10), although automated insulin delivery use in those with insulin pumps was higher in the tirzepatide group than in controls (82.35% vs. 61.11%; SMD: 0.48). Mild residual imbalance remained for BMI (34.97 ± 6.34 vs. 33.90 ± 5.87 kg/m^2; SMD: 0.17) and sex, with a higher proportion of males in the tirzepatide group than in controls.

Residual imbalance was also evident for several non-matched cardiometabolic and laboratory variables, as shown in Table 1. Thus, while matching improved comparability for key baseline variables, it did not fully eliminate baseline differences across all clinical characteristics.

3.3 | Tirzepatide Treatment Is Associated With Improved Anthropometric and Glycaemic Outcomes

The most common maximum tirzepatide dose was 5 mg/week, reached by 12 participants (52.2%), followed by 2.5 mg/week in 4 participants (17.4%) and 7.5 mg/week in 3 participants (13.0%). Only 2 participants (8.7%) reached 12.5 mg/week, while 10 mg/week and 15 mg/week were each reached by 1 participant (4.3% each). Tirzepatide was generally initiated at 2.5 mg/week and up-titrated according to standard clinical practice. The average observation duration was 28.0 ± 12.8 weeks in the tirzepatide group and 31.3 ± 14.2 weeks in the control group.

In the paired primary analysis, tirzepatide treatment was associated with a 10.01% ± 4.74% decrease in body weight compared with a 0.69% ± 3.77% increase in controls (adj-$p < 0.0001$, Table 2). This equates to a BMI reduction of 3.30 ± 1.61 kg/m^2 in the tirzepatide group compared to a 0.18 ± 1.35 kg/m^2 increase in the control group (adj-$p < 0.0001$, Table 2).

There was no significant difference in HbA1c, percentage time in range, percentage time below range or coefficient of variation after adjustment for multiple comparisons. However, tirzepatide treatment was associated with a significant difference in total daily insulin dose, which decreased by 21.82 ± 16.30 U/day compared to a 5.62 ± 11.63 U/day increase in controls (adj-$p = 0.002$, Table 2). In an exploratory analysis adjusted for body weight, total daily insulin dose expressed as U/kg/day decreased with tirzepatide but increased in controls (−0.18 ± 0.21 vs. +0.05 ± 0.11 U/kg/day; $p = 0.004$, Table 3). In both groups, insulin dosing was typically reviewed at least every 3 months, with advice given and changes made as clinically indicated.

Sensitivity analyses adjusting for matched pair, sex, age and baseline outcome values produced results consistent with the primary analysis, with estimated treatment effects continuing to favour tirzepatide for change in body weight, BMI, HbA1c and total daily insulin dose (Table S3).

3.4 | Exploratory Glycaemic, Cardiometabolic and Renal Outcomes

Exploratory outcomes are shown in Table 3. Compared with controls, tirzepatide treatment was associated with a decrease in systolic blood pressure (−6.30 ± 16.35 vs. +6.00 ± 12.82 mmHg; $p = 0.015$), carbohydrate intake (−49.46 ± 47.03 vs. +11.77 ± 25.37 g/day; $p = 0.001$) and glucose SD (−0.24 ± 0.43 vs. +0.16 ± 0.35 mmol/L; $p = 0.022$). Tirzepatide treatment was associated with a higher insulin-to-carbohydrate ratio compared with controls, indicating fewer insulin units per gram of carbohydrate intake (+0.61 ± 0.99 vs. −0.07 ± 0.33 g/insulin unit; $p = 0.049$).

Within-group exploratory analyses showed a reduction in glucose management indicator ($p = 0.045$), improvement in glucose SD ($p = 0.006$) and reduced carbohydrate intake ($p = 0.007$) in the tirzepatide group. In the control group, aspartate aminotransferase decreased over follow-up ($p = 0.025$). Other exploratory cardiometabolic, renal, liver enzyme, lipid and CGM outcomes did not differ between groups (Table 3).

3.5 | Safety and Treatment Discontinuation

The reporting of safety outcomes was limited. Adverse events reported were predominantly gastrointestinal, including four reports of nausea, one report of constipation and one report of gastro-oesophageal reflux. There was one reported episode of

TABLE 1 | Baseline characteristics.

	Tirzepatide	Control	SMD
Number	23	23	
Age (years)	44.87 (9.35)	44.83 (11.89)	0.00
Duration of diabetes (years)	23.35 (10.99)	24.22 (12.28)	−0.07
Sex, male	14/23 (60.87%)	9/23 (39.13%)	0.45
Body weight (kg)	102.90 (21.47)	95.57 (13.60)	0.41
BMI (kg/m^2)	34.97 (6.34)	33.90 (5.87)	0.17
HbA1c (%)	7.14 (0.95)	7.08 (0.97)	0.06
Mode of insulin delivery and insulin pump metrics			
Multiple daily injection users	6/23 (26.09%)	5/23 (21.74%)	0.10
Insulin pump users	17/23 (73.91%)	18/23 (78.26%)	−0.10
Automated insulin delivery users	14/17 (82.35%)	11/18 (61.11%)	0.48
Total daily insulin dose (U/day)	70.42 (32.27)	66.07 (25.86)	0.15
Weight-corrected total daily insulin dose (U/kg/day)	0.70 (0.29)	0.67 (0.21)	0.12
Carbohydrate intake (g/day)	144.83 (68.12)	156.38 (63.68)	−0.18
Insulin-to-carbohydrate ratio (g/insulin unit)	2.43 (0.90)	2.27 (1.01)	0.16
Continuous glucose monitoring metrics			
Time in range (%)	64.78 (19.44)	67.95 (11.32)	−0.20
Time below range (%)	1.09 (1.00)	1.82 (2.36)	−0.40
Time above range (%)	34.13 (19.99)	30.23 (11.81)	0.24
Glucose management indicator (%)	7.24 (0.68)	7.13 (0.45)	0.18
Mean glucose (mmol/L)	9.08 (1.62)	8.82 (1.02)	0.19
Glucose SD (mmol/L)	2.79 (0.56)	2.92 (0.58)	−0.24
Coefficient of variation (%)	31.41 (4.06)	33.18 (5.13)	−0.38
Cardiorenal and hepatic measures			
Systolic blood pressure (mmHg)	128.52 (13.50)	119.95 (15.02)	0.60
Diastolic blood pressure (mmHg)	75.78 (10.00)	73.42 (12.65)	0.21
Mean arterial pressure (mmHg)	93.36 (10.49)	87.92 (10.05)	0.53
Total cholesterol (mmol/L)	4.20 (1.02)	4.73 (1.10)	−0.51
High-density lipoprotein (mmol/L)	1.32 (0.33)	1.44 (0.40)	−0.34
Low-density lipoprotein (mmol/L)	2.38 (0.97)	2.72 (0.85)	−0.38
Triglycerides (mmol/L)	1.13 (0.51)	1.35 (1.28)	−0.22
Alanine aminotransferase (U/L)	34.00 (28.11)	33.52 (21.09)	0.02
Aspartate aminotransferase (U/L)	35.79 (40.39)	29.96 (13.78)	0.19
ALT/AST ratio	1.02 (0.45)	1.10 (0.32)	−0.21
Urine albumin-creatinine ratio (mg/mmol)	14.66 (38.17)	30.86 (92.28)	−0.23
Estimated glomerular filtration rate (mL/min/1.73 m^2)	82.58 (13.74)	83.61 (17.12)	−0.07

Note: Continuous data represented as mean (SD). Categorical data represented as number/total number (%). SMD refers to standardised mean difference and ALT/AST ratio refers to alanine aminotransferase to aspartate aminotransferase ratio. For metrics in which there is missing data, the exact number of participants included in each baseline comparison is detailed in Table S1.

TABLE 2 | Primary outcome measures.

	Tirzepatide	Control	Adj-*p*	*N*
Change in body weight (%)	−10.01 (4.74)	0.69 (3.77)	**< 0.0001**	22
Change in BMI (kg/m^2)	−3.30 (1.61)	0.18 (1.35)	**< 0.0001**	22
Change in HbA1c (%)	−0.37 (0.71)	−0.02 (0.49)	0.317	21
Change in total daily insulin dose (U/day)	−21.82 (16.30)	5.62 (11.63)	**0.002**	11
Change in time in range (%)	6.45 (15.47)	−1.25 (6.76)	0.543	20
Change in time below range (%)	−0.20 (0.77)	0.35 (1.35)	1.000	20
Change in coefficient of variation (%)	−2.08 (4.02)	1.96 (4.27)	0.088	20

Note: Data represented as mean change from baseline (SD). Adjusted *p*-values (Adj-*p*) represent between-group comparisons of change from baseline to end-of-study. *N* refers to the number of matched pairs included in each paired *t*-test. Bonferroni correction was applied for multiple comparisons across the primary outcomes.

symptomatic hypoglycaemia and no reported diabetic ketoacidosis. At the time of this review, 14 participants (60.9%) were continuing tirzepatide treatment. For participants who ceased tirzepatide use, documented reasons included cost, pregnancy planning, reaching a target weight or cessation without a recorded reason.

4 | Discussion

In this retrospective, propensity score-matched cohort study of adults with T1D and overweight or obesity, adjunctive tirzepatide use was associated with clinically meaningful reductions in percentage body weight, BMI and total daily insulin dose over a mean treatment duration of approximately 28 weeks. These findings add to the limited real-world evidence for tirzepatide use in T1D.

The magnitude of weight loss observed in this cohort aligns with the limited emerging evidence for tirzepatide in T1D. This is particularly promising given the high proportion of included individuals who remained on relatively low doses (≤ 5 mg). In an observational study of 26 adults with T1D, tirzepatide was associated with approximately 10% weight loss at 8 months together with a HbA1c reduction of 0.59%. Similarly, a phase 2 placebo-controlled trial in adults with T1D and obesity demonstrated greater weight loss and improved HbA1c with tirzepatide than placebo over 12 weeks [14]. In the present study, HbA1c was not significantly different between groups. This may reflect limited statistical power as the study was powered to detect large effects only and may not have reliably detected modest differences in glycaemic outcomes. This is particularly relevant given that the observed effect size for HbA1c was smaller than that seen for body weight and insulin dose.

The reduction in total daily insulin dose observed in the subsample with available data is clinically important, particularly in adults with T1D and overweight or obesity, where high insulin requirements may reflect underlying insulin resistance and contribute to further weight gain. However, this finding should not be interpreted as evidence of a direct pharmacological effect of tirzepatide alone. Rather, the observed reduction in insulin dose likely reflects several related factors, including tirzepatide use, reduced appetite and carbohydrate intake and routine clinical insulin titration. In pump-treated individuals, changes in insulin-to-carbohydrate ratios may have further reduced prandial insulin delivery, particularly in the setting of reduced carbohydrate intake or improved postprandial glycaemia. Because insulin pump settings were adjusted as part of routine care and were not standardised for this retrospective study, the relative contribution of each factor cannot be determined. This should be considered when interpreting the insulin dose findings, particularly because insulin dose data was only available in a smaller matched subsample.

The observed associations in this study are biologically plausible and consistent with the established effects of tirzepatide in Type 2 diabetes and obesity [16, 17]. Appetite suppression, delayed gastric emptying and reduced glucagon secretion are known pharmacological mechanisms that improve postprandial glycaemia and facilitate lower exogenous insulin requirements [18]. Reduced insulin requirements may offer practical benefits in T1D, including lower insulin costs, reduced use of pump consumables and potentially less insulin-associated weight gain. This is particularly relevant given the well-established association between intensive insulin therapy and weight gain in T1D, and resultant adiposity is linked to a higher risk of cardiometabolic comorbidity in this population [19, 20].

The CGM-derived outcomes observed in this study should be interpreted cautiously. Time in range, time below range and coefficient of variation were not significantly different between groups in the primary analysis. These outcomes are clinically important, but the study may not have reliably detected smaller differences across multiple glycaemic endpoints. CGM data was incomplete for several participants, and residual baseline imbalance in some non-matched glycaemic and clinical characteristics may complicate interpretation of subsequent comparisons. Larger prospective studies with standardised CGM data capture and prespecified glycaemic endpoints are needed to determine whether tirzepatide is associated with reproducible improvements in glycaemic variability in adults with T1D.

The safety findings are descriptive and should be interpreted conservatively. One episode of symptomatic hypoglycaemia was identified on review of the clinical records, while no episodes of diabetic ketoacidosis were observed. However, given the small sample size and retrospective data collection, the low number of serious events does not permit conclusions regarding safety. Nevertheless, a recent observational study and a Phase 2 trial

TABLE 3 | Secondary outcome measures.

	Tirzepatide	Control	*p*	*N*
Weight-corrected total daily insulin dose (U/kg/day)	−0.18 (0.21)*	0.05 (0.11)	**0.004**	11
Change in time above range (%)	−3.04 (24.78)	0.90 (7.50)	0.527	20
Change in glucose management indicator (%)	−0.26 (0.59)*	0.02 (0.31)	0.126	16
Change in mean glucose (mmol/L)	−0.49 (1.34)	−0.21 (1.22)	0.541	20
Change in glucose SD (mmol/L)	−0.24 (0.43)**	0.16 (0.35)	**0.022**	16
Change in carbohydrate intake (g/day)	−49.46 (47.03)**	11.77 (25.37)	**0.001**	11
Change in insulin-to-carbohydrate ratio (g/insulin unit)	0.61 (0.99)	−0.07 (0.33)	**0.049**	10
Change in systolic blood pressure (mmHg)	−6.30 (16.35)	6.00 (12.82)	**0.015**	20
Change in diastolic blood pressure (mmHg)	−3.60 (11.20)	1.43 (14.74)	0.301	20
Change in mean arterial pressure (mmHg)	−4.50 (12.25)	4.07 (10.46)	0.054	20
Change in alanine aminotransferase (U/L)	−5.59 (19.68)	−3.12 (10.19)	0.704	17
Change in aspartate aminotransferase (U/L)	−8.35 (40.86)	−4.76 (8.74)*	0.741	17
Change in ALT/AST ratio	0.00 (0.34)	0.03 (0.28)	0.782	17
Change in total cholesterol (mmol/L)	−0.13 (0.77)	−0.16 (0.82)	0.937	18
Change in high-density lipoprotein (mmol/L)	0.02 (0.18)	0.00 (0.15)	0.823	17
Change in low-density lipoprotein (mmol/L)	−0.01 (0.75)	−0.00 (0.61)	0.960	17
Change in triglycerides (mmol/L)	−0.19 (0.49)	−0.19 (0.39)	1.000	17
Change in urine albumin-creatinine ratio (mg/mmol)	−7.75 (15.36)	−27.38 (89.97)	0.572	8
Change in estimated glomerular filtration rate (mL/min/1.73 m^2)	−0.28 (7.14)	−0.39 (4.67)	0.959	18

Note: Data represented as mean change from baseline (SD). *p*-values represent between-group comparisons of change from baseline to end-of-study. *N* refers to the number of matched pairs included in each paired between-group comparison. Bold values indicate any significant values and is intended to improve visibility for readers. *Indicates a significant within-group change from baseline to end-of-study, where *$p < 0.05$ and **$p < 0.01$. Where data was missing for within-group analyses, the number of participants included in each baseline-to-end-of-study comparison is provided in Table S2.

reported no serious adverse events during short-term follow-up [14, 21]. Further controlled clinical trials are required to appropriately assess the risks of ketoacidosis and severe hypoglycaemia in this population.

This study did not find evidence of broader cardiovascular, renal, or hepatic benefit over the study period. Similarly, in a 12-week trial of tirzepatide in adults with T1D, no significant between-group differences were seen in fasting lipids or blood pressure [14]. However, longer-term observational data of tirzepatide in adults with T1D over 21 months suggest improvement in several cardiometabolic and renal markers, including total and low-density lipoprotein, triglycerides, systolic blood pressure and estimated glomerular filtration rate [13]. Furthermore, a large target trial emulation found that GLP-1 receptor agonist therapy in T1D, including with albiglutide, dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide and tirzepatide, was associated with lower risks of major adverse cardiovascular events and end-stage kidney disease [22]. Overall, this suggests that the absence of clear cardiometabolic effects in our cohort may reflect the small sample size and short duration.

The limitations of this study must be acknowledged. First, this was a retrospective observational study and causality cannot be inferred. Although propensity score matching improved comparability for baseline BMI and HbA1c, residual baseline imbalance remained for sex and several non-matched cardiometabolic characteristics. The higher prevalence of automated insulin delivery use in the tirzepatide group represents a residual confound that may have influenced CGM-derived outcomes, including time in range and glycaemic variability and limits the interpretation of between-group differences in these endpoints. Further matching utilising additional variables relevant to tirzepatide prescription, such as total daily insulin dose, was not possible without significantly reducing the number of included participants. Second, the sample size was modest, and missing data reduced the effective sample size for several analyses. This is particularly relevant for the analysis of total daily insulin dose, which was limited to 11 matched pairs due to incomplete retrospective documentation of this outcome measure. It therefore cannot be confirmed that this subsample was representative of the full matched cohort, and this finding should be interpreted cautiously. The study was powered to detect large effects only, therefore smaller differences may have been missed. Third, although correction for multiplicity was applied across the primary outcomes, exploratory outcomes were not adjusted and should therefore be interpreted cautiously. Fourth, at the time of this study, tirzepatide was not subsidised for obesity or T1D in Australia, and access was dependent on private prescription and out-of-pocket cost. This may have introduced selection

bias and unmeasured differences in treatment access and patient characteristics such as socioeconomic status. The health institutions captured by this retrospective study include endocrine centres in a high socioeconomic health district within metropolitan Sydney, Australia. This suggests that access across both the tirzepatide and untreated populations may be higher than that of more generalised cohorts. Fifth, tirzepatide exposure was heterogeneous, with variation in maximum tolerated dose and titration schedule. These factors may have had a meaningful impact on primary outcomes, such as body weight, HbA1c and insulin dose as higher doses of tirzepatide have been associated with increased efficacy in alternative cohorts [23]. However, given the small proportion of participants receiving higher doses (> 10 mg), formal dose-response analyses for weight and glycaemic outcomes were not viable. Finally, waist circumference and waist-hip ratio were not consistently recorded, and the variables required to calculate estimated glucose disposal rate were not reliably available. The absence of formal insulin resistance measures limits mechanistic interpretation, particularly given the relevance of insulin resistance to tirzepatide use in T1D with overweight or obesity.

Future studies should include larger cohorts and randomised trials with standardised insulin-adjustment protocols, systematic adverse-event collection, and longer follow-up to assess durability and broader cardiometabolic outcomes. Mechanistic studies are also needed to clarify the extent to which glycaemic improvement is mediated by weight loss and reduced insulin resistance, as compared to direct effects of tirzepatide on gastric emptying, glucagon physiology, appetite and glycaemic variability in T1D. Importantly, tirzepatide is not approved for use in T1D, and the findings of this retrospective study should not be used to guide prescribing outside formal clinical trial settings or closely monitored specialist care. Adequately powered prospective trials with systematic safety ascertainment are required before clinical adoption of tirzepatide in T1D can be recommended.

Overall, adjunctive tirzepatide use was associated with reduced percentage body weight and reduced insulin requirements in adults with T1D and overweight or obesity. These findings are encouraging but should be interpreted in the context of a small retrospective study with limited power for smaller effects and no formal safety assessment. Larger prospective studies and randomised trials are now warranted to confirm these findings, better define safety and determine which individuals are most likely to benefit from adjunctive tirzepatide therapy.

Author Contributions

A.R.P., M.S.G.L. and S.J.G. conceptualised the research question for this study. All authors contributed to the preparation of the human ethics application associated with this study. A.R.P. performed data collection, conducted the statistical analysis and prepared the manuscript. M.S.G.L., N.R. and S.J.G. reviewed and edited the manuscript. S.J.G. is the guarantor of this work.

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The authors have nothing to report.

Conflicts of Interest

S.J.G. has received honoraria and travel support from pharmaceutical companies including Lilly, Novo Nordisk, and Sanofi. The other authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Peer Review

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References

1. N. C. Foster, R. W. Beck, K. M. Miller, et al., "State of Type 1 Diabetes Management and Outcomes From the T1D Exchange in 2016-2018," *Diabetes Technology & Therapeutics* 21, no. 2 (2019): 66–72.

2. A. Welters, S. R. Tittel, K. Laubner, et al., "Long-Term Trends of BMI and Cardiometabolic Risk Factors Among Adults With Type 1 Diabetes: An Observational Study From the German/Austrian DPV Registry," *Diabetes Research and Clinical Practice* 178 (2021): 108973.

3. H. Hamasaki, "Obesity Paradox in Individuals With Type 1 Diabetes," *Frontiers in Clinical Diabetes and Healthcare* 6 (2025): 1670312.

4. M. M. Masouri, R. Ebrahimi, and S. Noori, "An Updated Systematic Review and Meta-Analysis on the Efficacy and Safety of Metformin as Add-On Therapy to Insulin in Patients With Type 1 Diabetes," *Endocrinology, Diabetes and Metabolism* 8, no. 4 (2025): e70060.

5. P. Maffei, S. Bettini, L. Busetto, and F. Dassie, "SGLT2 Inhibitors in the Management of Type 1 Diabetes (T1D): An Update on Current Evidence and Recommendations," *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy* 16 (2023): 3579–3598.

6. J. Chen, F. Fan, J. Y. Wang, et al., "The Efficacy and Safety of SGLT2 Inhibitors for Adjunctive Treatment of Type 1 Diabetes: A Systematic Review and Meta-Analysis," *Scientific Reports* 7, no. 1 (2017): 44128.

7. A. R. Purcell, X. M. Zhen, J. Wong, and S. J. Glastras, "Glucagon-Like Peptide-1 Receptor Agonist Treatment Reduces Body Weight and Improves Glycaemic Outcomes in Patients With Concurrent Overweight/Obesity and Type 1 Diabetes: A Systematic Review and Meta-Analysis," *Diabetes, Obesity and Metabolism* 28, no. 1 (2025): 296–305.

8. M. A. Nauck and D. A. D'Alessio, "Tirzepatide, a Dual GIP/GLP-1 Receptor Co-Agonist for the Treatment of Type 2 Diabetes With Unmatched Effectiveness Regrading Glycaemic Control and Body Weight Reduction," *Cardiovascular Diabetology* 21, no. 1 (2022): 169.

9. J. P. Frías, M. J. Davies, J. Rosenstock, et al., "Tirzepatide Versus Semaglutide Once Weekly in Patients With Type 2 Diabetes," *New England Journal of Medicine* 385, no. 6 (2021): 503–515.

10. E. R. Hankosky, J. Lebrec, C. J. Lee, et al., "Tirzepatide and the 10-Year Predicted Risk of Cardiovascular Disease and Type 2 Diabetes in Adults With Obesity and Prediabetes: A Post Hoc Analysis From the

Three-Year SURMOUNT-1 Trial," *Diabetes, Obesity & Metabolism* 27, no. 12 (2025): 7385–7394.

11. P. Dutta, Y. Kumar, A. T. Babu, et al., "Tirzepatide: A Promising Drug for Type 2 Diabetes and Beyond," *Cureus* 15, no. 5 (2023): e38379.

12. F. Mendoza and R. Parsiani, "Impact of Tirzepatide in a Patient With Type 1 Diabetes and Obesity: A Case Report," *Journal of the American Pharmacists Association* 63, no. 6 (2023): 1821–1825.

13. S. K. Garg, G. Kaur, D. Renner, et al., "Cardiovascular and Renal Biomarkers in Overweight and Obese Adults With Type 1 Diabetes Treated With Tirzepatide for 21 Months," *Diabetes Technology & Therapeutics* 27, no. 3 (2025): 152–160.

14. J. R. Snaith, R. Frampton, D. Samocha-Bonet, and J. R. Greenfield, "Tirzepatide in Adults With Type 1 Diabetes: A Phase 2 Randomized Placebo-Controlled Clinical Trial," *Diabetes Care* 49, no. 1 (2026): 161–170.

15. H. K. Akturk, F. Dong, J. K. Snell-Bergeon, K. E. Karakus, and V. N. Shah, "Efficacy and Safety of Tirzepatide in Adults With Type 1 Diabetes: A Proof of Concept Observational Study," *Journal of Diabetes Science and Technology* 19, no. 2 (2024): 292–296.

16. A. V. Fanshier, B. K. Crews, M. C. Garrett, and J. L. Johnson, "Tirzepatide: A Novel Glucose-Dependent Insulinotropic Polypeptide/Glucagon-Like Peptide 1 Receptor Agonist for the Treatment of Type 2 Diabetes: The First Twincretin," *Clinical Diabetes* 41, no. 3 (2023): 367–377.

17. N. Alfaris, S. Waldrop, V. Johnson, B. Boaventura, K. Kendrick, and F. C. Stanford, "GLP-1 Single, Dual, and Triple Receptor Agonists for Treating Type 2 Diabetes and Obesity: A Narrative Review," *EClinicalMedicine* 75 (2024): 102782.

18. J. R. Snaith, P. Narongkiatikhun, P. Bjornstad, J. R. Greenfield, and K. L. Tommerdahl, "Advancing Type 1 Diabetes Management: Integrating Novel Therapies, Technologies, and Adjunctive Approaches," *Diabetes Care* 49, no. 1 (2025): 7–21.

19. J. Q. Purnell, J. E. Hokanson, S. M. Marcovina, M. W. Steffes, P. A. Cleary, and J. D. Brunzell, "Effect of Excessive Weight Gain With Intensive Therapy of Type 1 Diabetes on Lipid Levels and Blood Pressure: Results From the DCCT. Diabetes Control and Complications Trial," *JAMA* 280, no. 2 (1998): 140–146.

20. B. Van der Schueren, D. Ellis, R. N. Faradji, E. Al-Ozairi, J. Rosen, and C. Mathieu, "Obesity in People Living With Type 1 Diabetes," *Lancet Diabetes & Endocrinology* 9, no. 11 (2021): 776–785.

21. H. K. Akturk, K. E. Karakus, D. Cengiz, et al., "Glucose Control and Continuous Glucose Monitoring Metrics During 12 Months of Treatment With Tirzepatide in Overweight or Obese Patients With Type 1 Diabetes," *Diabetes Technology & Therapeutics* 28, no. 3 (2026): 193–200.

22. Y. Xu, N. D. Malek, A. R. Chang, et al., "Glucagon-Like Peptide-1 Receptor Agonists for Major Cardiovascular and Kidney Outcomes in Type 1 Diabetes," *Nature Medicine* 32 (2026): 1682–1685.

23. H. S. Rangwala, H. Fatima, M. Ali, et al., "Evaluating the Effectiveness and Safety of Various Tirzepatide Dosages in the Management of Type 2 Diabetes Mellitus: A Network Meta-Analysis of Randomized Controlled Trials," *Journal of Diabetes & Metabolic Disorders* 23, no. 1 (2024): 1199–1222.

Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Number of participants included in analyses in Table 1. **Table S2:** Number of participants included in paired *t*-tests for within-group analyses for change from baseline to end-of-study in Table 3. **Table S3:** Sensitivity analyses for primary outcomes.

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ORIGINAL ARTICLE

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Glucagon-like peptide-1 receptor agonist treatment reduces body weight and improves glycaemic outcomes in patients with concurrent overweight/obesity and type 1 diabetes: A systematic review and meta-analysis

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Abstract

Aims: This systematic review and meta-analysis evaluated the long-term efficacy and safety of glucagon-like peptide-1 receptor agonists (GLP-1RAs) as adjunctive therapies for individuals with type 1 diabetes (T1D) and overweight or obesity.

Materials and Methods: A literature search was conducted in June 2023 and updated in June 2025. Eligible studies included adults with T1D, body mass index ≥25 kg/m^2, and GLP-1RA treatment alongside insulin for ≥12 weeks. Changes in body weight, HbA1c, and insulin dose were expressed as mean differences (MDs) with 95% confidence intervals (CIs). Safety outcomes were assessed using odds ratios (ORs) with 95% CIs. Data were pooled using random-effects models.

Results: Exactly 13 studies met the inclusion criteria. GLP-1RA treatment was associated with a body weight reduction of 4.31 kg (95% CI: 3.61–5.00 kg) and a HbA1c reduction of 0.25% (95% CI: 0.18–0.32%). Across all studies, insulin dosage was reduced by 9.24 U/day (95% CI: 7.04–11.45 U/day). Subgroup analysis identified that semaglutide achieved the greatest reductions in all outcome measures. Hypoglycaemic episodes were increased (OR = 1.34; 95% CI: 1.02–1.76), while hyperglycaemic episodes decreased (OR: 0.69, 95% CI: 0.56–0.87). Gastrointestinal adverse events, including nausea and vomiting, were significantly more frequent with GLP-1RA treatment, though no increase in serious adverse events was observed.

Conclusions: GLP-1RAs are effective for body weight reduction and glycaemic improvement in individuals with T1D and overweight/obesity, with acceptable safety profiles. These findings provide evidence that GLP-1RAs can be effectively and safely used as adjunctive therapy to insulin in people with T1D, but additional robust randomised clinical trials are needed.

KEYWORDS
antiobesity drug, dose–response relationship, hypoglycaemia, incretin therapy

1 | INTRODUCTION

Type 1 diabetes (T1D) is characterised by the autoimmune destruction of pancreatic β-cells, necessitating lifelong exogenous insulin therapy. Despite advancements in insulin formulations and delivery, only 34% of adults with T1D achieve target HbA1c levels of <7% (53 mmol/mol).[1] Once regarded as a condition predominantly affecting lean individuals, T1D is now increasingly associated with overweight and obesity. Recent data reported rates of 62% among American adults with T1D, mirroring rates observed in the general population.[2] Insulin therapy itself may promote weight gain by increasing energy storage.[12] Progressive weight gain subsequently elevates insulin requirements, perpetuating a cycle of further weight gain. The Diabetes Control and Complications Trial (DCCT) demonstrated this association, with participants receiving intensive insulin therapy gaining an average of 4.6 kg over 5 years.[3]

Although limited, available evidence links weight gain in T1D to higher rates of cardiovascular and renal complications. In the Epidemiology of Diabetes Interventions and Complications follow-up study, excessive weight gain during the DCCT was associated with worsening insulin resistance, dyslipidaemia, hypertension, and a significantly increased risk of cardiovascular events.[4] Obesity is also associated with an increased risk of chronic kidney disease in people with T1D.[5]

Despite the rising prevalence of obesity in T1D and the subsequent cardiometabolic risks, structured lifestyle and weight management interventions are less frequently implemented in this population than in type 2 diabetes (T2D) or the general population.[2] Few studies have rigorously evaluated strategies to address obesity in T1D, leaving clinicians with little guidance beyond insulin adjustment and general weight management recommendations. Adjunctive therapies that target both glycaemic control and weight are essential.

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are established treatment options in T2D, reducing HbA1c, promoting substantial weight loss, and conferring robust cardiovascular and kidney protection in large outcome trials.[6–9] While these benefits have not been definitively demonstrated in T1D, their potential utility is compelling given the high burden of cardiometabolic risk in individuals with T1D and overweight or obesity.

Previous meta-analyses in T1D primarily evaluated first-generation GLP-1RAs, including liraglutide, exenatide, and albiglutide. They demonstrated modest benefits, with a mean weight loss of 4.9 kg and HbA1c reduction of 0.28%.[10] These findings were limited by the inclusion of studies of short duration, for example, 4–6 weeks, and likely underestimate the benefits of newer, more potent GLP-1RAs such as semaglutide. Early retrospective analyses in T1D suggest semaglutide may offer substantially greater benefits, demonstrating weight reductions of ∼16 kg and HbA1c reductions of 0.66% over 12 months,[11] but no systematic review to date has evaluated the longer-term efficacy of newer second-generation GLP-1RAs, such as semaglutide, in individuals with T1D and overweight or obesity.

This systematic review and meta-analysis aims to assess the longer-term efficacy and safety of GLP-1RAs, including newer-generation agents, in individuals with T1D and overweight or obesity.

2 | METHODS

A systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[13] This protocol is registered in PROSPERO (registration ID: CRD42023429281).

2.1 | Eligibility criteria

Studies were eligible for inclusion if they were randomised controlled trials. Retrospective or prospective cohort studies, case-controlled, observational studies, editorial comments, and letters were not included. Studies met the eligibility criteria if they included adult subjects (age ≥18 years) with a body mass index (BMI) ≥25 kg/m^2 and a clinical diagnosis of T1D. Studies were included if they investigated an intervention with any drug classed as a GLP-1RA in conjunction with insulin treatment, administered for a duration ≥12 weeks, as compared with insulin treatment alone. Studies were excluded if study participants had a clinical diagnosis of diabetes other than T1D, if the drug intervention involved a combination with any other drug class, or the intervention was for less than 12 weeks. Studies were eligible if they reported data on any of the following: body weight, HbA1c, daily insulin requirements, episodes of hypoglycaemia, or episodes of hyperglycaemia. For consistency, hyperglycaemia was defined as ≥10.0 mmol/L (180 mg/dL) while hypoglycaemia was defined as blood glucose ≤3.9 mmol/L (71 mg/dL) across all studies.

2.2 | Search Strategy

The literature search was completed in June 2023 and updated in June 2025 in MEDLINE (1946 to present), Embase (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL) (1991 to present), and Scopus databases (1970 to present). The search terms were 'type 1 diabetes mellitus' and 'glucagon-like peptide-1 receptor agonist' (including liraglutide, dulaglutide, exenatide, Trulicity, Bydureon, Byetta, semaglutide, Ozempic, Saxenda, Victoza, lixisenatide, Adlyxin, Rybelus, and Wegovy). The full search strategy can be found in Supporting Information 1 in Data S1.

2.3 | Study selection

Results from the database searches were imported into Covidence software, which detected and removed duplicates. The remaining results were independently screened by two authors by title and abstract. The full text of relevant articles was subsequently assessed against the eligibility criteria. Any discrepancies between the two reviewers were resolved by consensus. In cases where consensus could not be reached, a third reviewer was consulted to adjudicate the disagreement.

2.4 | Quality assessment

The risk of bias in each study was evaluated by two independent authors. Trials were assessed using the Cochrane Risk of Bias assessment tool (RoB 2.0).[14] Assessments were made on the following criteria: (D1) randomisation process, (D2) deviation arising from the intended interventions, (D3) missing outcome data, (D4) measurement of the outcome, and (D5) selection of the reported result. In the case of a crossover trial, (DS) bias arising from period and carryover effects was also assessed.

2.5 | Data extraction

Data extraction from studies that met the inclusion criteria was conducted using a proforma based on predetermined outcomes. For studies reporting outcome measures at multiple time points, only the outcome measured closest to the study's active treatment endpoint was included. In the case where multiple publications reported data from the same study, all reports were analysed. To address missing data, the ClinicalTrials.gov registry was consulted, and study authors were contacted when necessary. For data presented exclusively in graphical format, numerical values were extracted by pixel counting using WebPlotDigitizer (https://automeris.io/wpd/).

Baseline means and standard deviations (SDs) for body weight (kg), HbA1c (%), and total daily insulin (U/day) were extracted to define prespecified smallest effects of interest (SIEs) and to calculate optimal information size (OIS) thresholds for each outcome (see Section 2.6). Mean changes from baseline to the endpoint and their corresponding SDs were also extracted. If SDs were not explicitly reported, they were estimated using the following approaches: from the standard error of the mean (SEM), SD was calculated as $SD = SEM \times \text{sqrt}(n)$, where sqrt($n$) is the square root of the total number of participants; from interquartile range (IQR), SD was calculated as $SD = (Q3 - Q1)/1.35$, where Q3 and Q1 are the third and first quartiles, respectively. If the SD of the mean change was not available numerically or graphically, it was imputed using a correlation coefficient from Dejgaard et al.,[15] following the method outlined in Section 6.5.2.8 of the Cochrane Handbook[16] (Data S2). Data extraction was conducted independently by two reviewers to ensure objectivity and accuracy.

2.6 | Data synthesis and analysis

For this meta-analysis, clinically relevant SIEs for continuous outcomes were defined as a body weight reduction of 4.40 kg (5% of the mean baseline 87.98 kg), a HbA1c reduction of 0.50%, and a total daily insulin dose reduction of 9.00 U/day (15% of the mean baseline 59.93 U/day). Using pooled SDs (weight 16.80 kg, HbA1c 0.75%, insulin 20.19 U/day), the OIS was computed as the conventional two-arm sample size to detect each SIE at $\alpha = 0.05$ (two-sided) with 80% power. To account for heterogeneity ($I^2 = 50\%$, a priori), the OIS was inflated by $1/(1 - I^2)$. The resulting thresholds for weight, HbA1c, and insulin were 917, 142, and 316 participants, respectively.

The primary analyses focused on the continuous outcomes of change in body weight, HbA1c, and total daily insulin dose. A random-effects model was employed due to the expected heterogeneity among studies to pool effect sizes, with the restricted maximum likelihood (REML) method used to estimate between-study variance. Subgroup analyses were conducted to explore the effect of different doses of GLP-1RAs. Results were reported as mean differences (MD) with 95% confidence intervals (CI), and overall statistical significance was assessed using a Z test. Publication bias was assessed using funnel plots, supplemented by the Egger and Begg–Mazumdar tests, provided that 10 or more studies met the eligibility criteria for inclusion.

Further analyses evaluated the safety of GLP-1RAs, compared with placebo. The Mantel–Haenszel method was used to calculate pooled odds ratios (OR) for each safety outcome, providing a weighted estimate of treatment effects. A random-effects model was applied to account for heterogeneity, using the inverse variance method to consider study size and variance. Results were presented as ORs with 95% CIs. All analyses were performed using the 'meta' and 'metafor' packages in R Statistical Software (version 4.4.0), and all R code can be seen in Supporting Information 2 in Data S1.

3 | RESULTS

3.1 | Search results and study characteristics

The search strategy identified a total of 1623 articles (Figure 1). Thirteen trials were deemed eligible for inclusion in this review. The weighted mean age of participants across the studies was 43.9 ± 2.4 years, with an average diabetes duration of 21.7 ± 1.8 years. The gender distribution was balanced, with an average of 50.7% ± 9.4% female participants (Table 1). The mean body weight and BMI at baseline were 86.3 ± 3.4 kg and 29.5 ± 1.2 kg/m^2, respectively. The mean baseline HbA1c was 8.1% ± 0.2%, and the average total daily insulin dose was 54.5 ± 8.9 units/day (Table 1).

3.2 | Quality assessment

The risk-of-bias assessment was conducted using the ROB 2.0 tool (Table 3.1 in Data S1). Overall, 12 out of 13 RCTs included in this review were of high quality. The study by Kuhadiya et al.[17] was identified as having methodological limitations specifically related to the randomisation process.

3.3 | Treatment efficacy

The meta-analysis revealed that GLP-1RAs significantly reduced body weight compared with placebo. The overall mean weight reduction

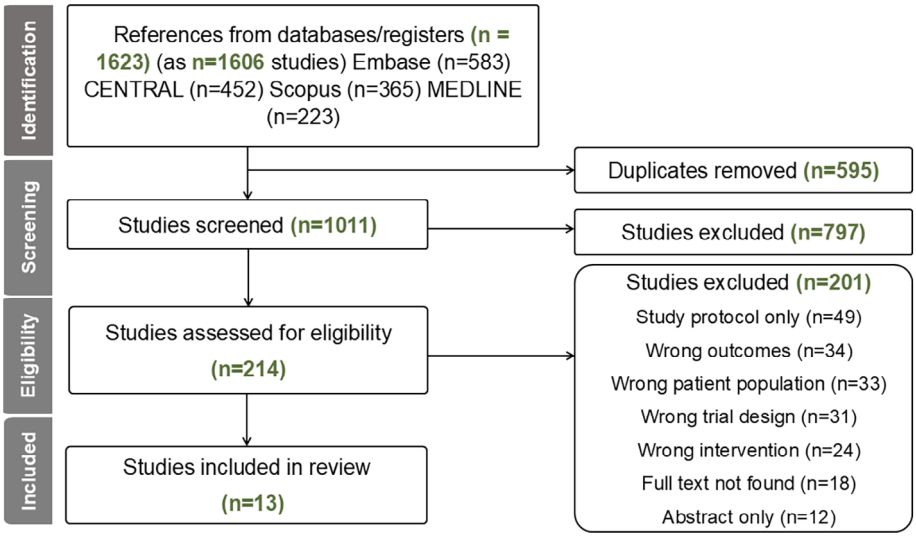

FIGURE 1 PRISMA diagram of study selection.

was 4.31 kg (95% CI: 3.61–5.00 kg, $p < 0.01$; Figure 2). Notably, semaglutide exhibited the most pronounced effect, achieving a reduction in mean body weight loss of 6.05 kg (95% CI: 3.47–8.64 kg; Figure 2). Liraglutide 1.8 mg also demonstrated significant efficacy, reducing body weight by 4.77 kg when compared with control (95% CI: 4.10–5.44 kg; Figure 2). Exenatide treatment resulted in a notable body weight reduction of 3.70 kg compared with control (95% CI: 1.57–5.83 kg; Figure 2). Substantial heterogeneity was observed across all studies ($I^2 = 90\%$, $p < 0.01$; Figure 2), indicating variability in treatment effects.

GLP-1RA treatment led to significant, albeit modest, reductions in HbA1c levels, compared with placebo. The overall mean reduction in HbA1c was 0.25% (95% CI: 0.18%–0.32%, $p < 0.01$; Figure 3A). Treatment with semaglutide 1 mg was associated with the most significant HbA1c reduction of 0.33% (95% CI: 0.19%–0.47%; Figure 3A). A dose–response relationship was observed with liraglutide: the dosage of 1.8 mg resulted in the largest mean HbA1c reduction of 0.29% (95% CI: 0.14%–0.45%), followed by 0.20% with 1.2 mg (95% CI: 0.12%–0.29%), and 0.15% with 0.6 mg (95% CI: 0.04%–0.27%; Figure 3A). There was no statistically significant difference between exenatide treatment and control, as the mean difference was −0.16% (95% CI: −0.32% to 0.01%; Figure 3A). Moderate heterogeneity was observed overall ($I^2 = 48\%$, $p = 0.01$; Figure 3A); however, subgroup analyses reduced this variability to non-significant levels in all groups except for liraglutide 1.8 mg, which persistently exhibited significant heterogeneity ($I^2 = 63\%$, $p < 0.01$; Figure 3A).

In individuals with T1D and overweight or obesity, GLP-1RAs led to significant reductions in total daily dose of insulin. The pooled estimate showed a reduction of 9.24 U/day (95% CI: 7.04–11.45 U/day, $p < 0.01$; Figure 3B). Due to limited data on insulin requirements across the studies included in this meta-analysis, the subgroup analysis excluded liraglutide at the 1.2 and 0.6 mg doses, focusing instead on analysis by drug rather than by dose. Semaglutide treatment exhibited the greatest impact, reducing insulin requirements by 14.95 U/day (95% CI: 6.31–23.58 U/day; Figure 3B). Liraglutide and exenatide treatment resulted in a reduction of 8.34 U/day (95% CI: 7.18–9.51 U/day) and 8.89 U/day (95% CI: 7.95–9.84 U/day), respectively (Figure 3B). Substantial heterogeneity was observed across all studies ($I^2 = 63\%$, $p < 0.01$; Figure 3B).

3.4 | Safety

The safety profiles of GLP-1RAs were assessed across 11 studies reporting adverse event outcomes. GLP-1RA treatment was associated with a higher incidence of adverse events (AEs) compared with placebo (OR = 1.91; 95% CI: 1.51–2.42), but no increased incidence of serious adverse events (SAEs) was observed (OR = 1.02; 95% CI: 0.82–1.28). Adverse events leading to discontinuation were more frequent in the GLP-1RA group compared with placebo (OR = 4.23; 95% CI: 2.13–8.40). Gastrointestinal side effects such as nausea (OR = 7.61; 95% CI: 3.36–17.23) and vomiting (OR = 4.60; 95% CI: 2.70–7.63) were significantly increased with GLP-1RA treatment. Although the odds of diarrhoea and constipation were also higher in the GLP-1RA group compared with control, these differences were not statistically significant (diarrhoea: OR = 1.56; 95% CI: 0.89–2.73; constipation: OR = 2.02; 95% CI: 0.81–5.03).

The risk of hypoglycaemic episodes was modestly increased with GLP-1RA treatment (OR = 1.34; 95% CI: 1.02–1.76), while GLP-1RAs significantly reduced the risk of hyperglycaemic episodes compared with placebo (OR = 0.69; 95% CI: 0.56–0.87). Notably, significant heterogeneity was observed in some adverse events, such as nausea ($I^2 = 86.3\%$, $p < 0.0001$) and adverse events leading to discontinuation ($I^2 = 73.3\%$, $p < 0.05$).

3.5 | Publication bias

There was no evidence of publication bias in the assessment of body weight reduction, as indicated by Egger test ($p = 0.3951$) and

TABLE 1 Characteristics of the included trials and baseline characteristics of participants.

Study reference	Study type	Study title	GLP-1RA	Dose	Frequency[a]	Duration of study (weeks)	Participants in GLP-1RA group	Participants in control group	Female (%)	Age (years)	Duration of diabetes (years)	BMI (kg/m^2)	Body weight (kg)	HbA1c (%)	Total daily insulin dose (U/day)
Pasqua et al.[29]	RCT (crossover)	SEMA-AP	Semaglutide	1 mg	QW	15	28	28	61	45.0	28.0	32.2	91.3	7.5	63.9
Shah et al.[23]	RCT	ADJUST-T1D	Semaglutide	1 mg	QW	26	36	36	21	40.2	22.7	35.4	102.0	7.8	72.9
Navodnik et al.[30]	RCT	ENDIS	Semaglutide	1 mg	QW	12	30	29	39	47.8	20.4	27.6	83.6	7.2	N/A
Dejgaard et al.[15]	RCT	Lira Pump	Liraglutide	1.8 mg	QD	26	22	22	68	46.5	20.5	29.5	86.5	8.2	51.0
Ghanim et al.[31]	RCT	N/A	Liraglutide	1.8 mg	QD	26	37	27	62	46.2	27.5	31.7	88.8	7.9	56.9
Herold et al.[32]	RCT	N/A	Exenatide	2 mg	QW	24	40	39	68	36.1	19.6	29.4	83.9	7.8	49.5
Johansen et al.[33]	RCT	MAG1C	Exenatide	10 μg	TID	26	52	53	28	50.3	21.1	28.3	87.9	8.2	59.8
Brock et al.[34]	RCT	TODINELI	Liraglutide	1.8 mg	QD	26	19	20	20	50.5	31.5	29.0	92.5	8.2	49.5
Dubé et al.[35]	RCT (crossover)	LIDO	Liraglutide	1.8 mg	QD	24	15	15	53	35.8	20.3	30.5	89.0	7.4	70.9
Ahren et al.[27]	RCT	ADJUNCT TWO	Liraglutide	1.8 mg	QD	26	205 (1.8 mg)	206	54	43.2	21.0	28.9	83.9	8.1	53.5
				1.2 mg			209 (1.2 mg)								
				0.6 mg			211 (0.6 mg)								
Dejgaard et al.[36]	RCT	Lira-1	Liraglutide	1.8 mg	QD	24	50	50	35	48.0	22.5	30.1	93.7	8.7	59.7
Kuhadiya et al.[17]	RCT	N/A	Liraglutide	1.8 mg	QD	12	16 (1.8 mg)	17	56	44.8	24.1	28.8	84.8	7.6	54.5
				1.2 mg			16 (1.2 mg)								
				0.6 mg			14 (0.6 mg)								
Matthieu et al.[28]	RCT	ADJUNCT ONE	Liraglutide	1.8 mg	QD	52	346 (1.8 mg)	347	52	43.6	21.4	29.5	86.2	8.2	55.9
				1.2 mg			346 (1.2 mg)								
				0.6 mg			250 (0.6 mg)								

[a]QD, daily administration; QW, weekly administration; RCT, randomised controlled trial; TID, three times daily administration.

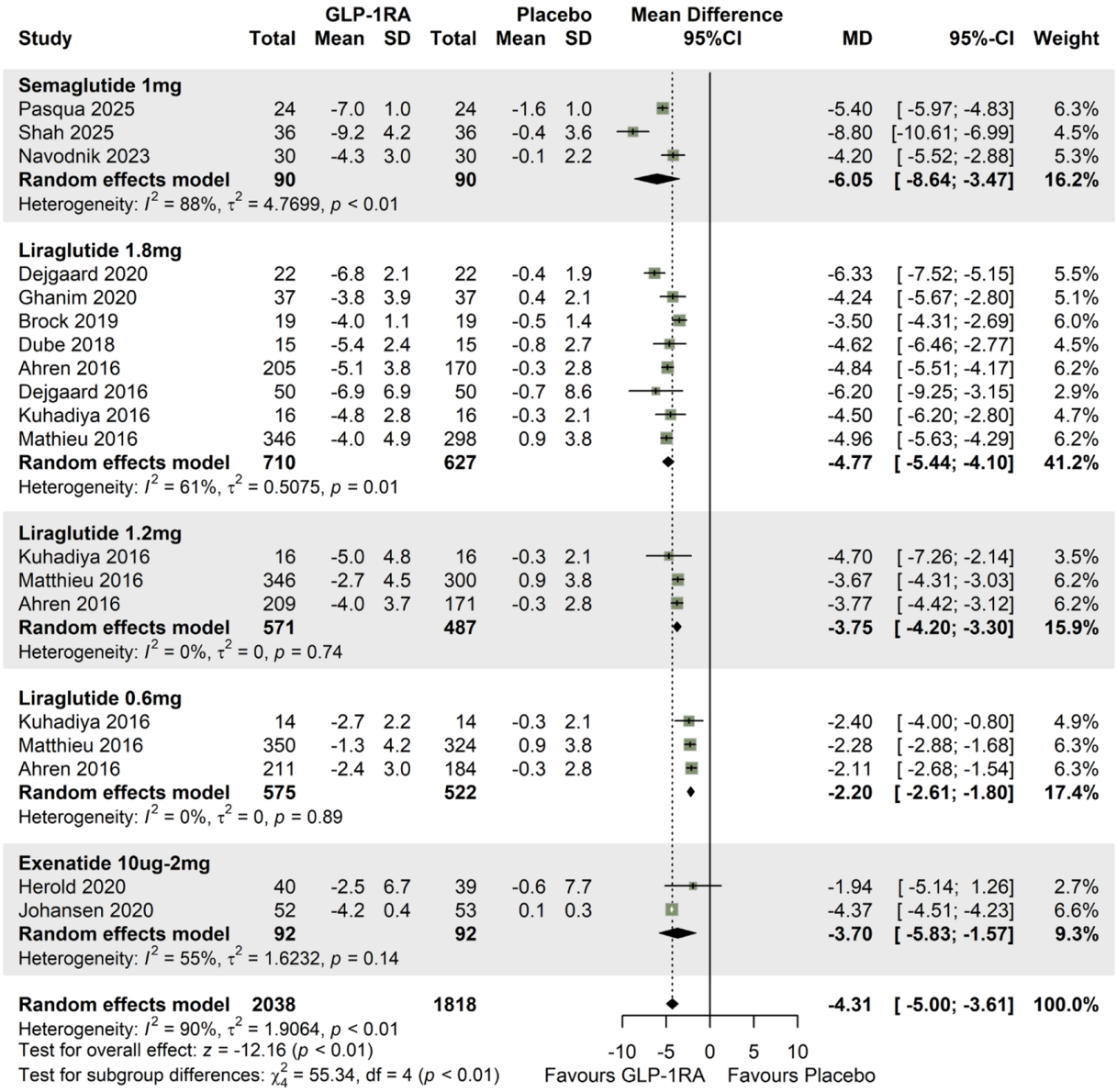

FIGURE 2 Forest plot comparing GLP-1RAs and placebo for change in body weight (kg) in patients with type 1 diabetes and overweight or obesity. The mean difference (MD) indicates the average weight change between groups, with negative values favouring GLP-1RAs.

Begg–Mazumdar test ($p = 0.4893$; Figure 4.1 in Data S1). While the funnel plot shows some visual asymmetry with some studies falling outside the funnel, this most likely reflects study heterogeneity rather than systematic bias.

There was no significant evidence of publication bias in the assessment of HbA1c and TDD reduction, as indicated by Egger test (HbA1c: $p = 0.8908$, TDD: $p = 0.2763$) and Begg–Mazumdar test (HbA1c: $p = 0.7263$, TDD: $p = 1.0000$) (Figures 4.2 and 4.3 in Data S1).

4 | DISCUSSION

This meta-analysis demonstrates that GLP-1RA therapy for >3 months' duration in individuals with T1D and overweight or obesity leads to clinically meaningful reductions in body weight, HbA1c, and insulin requirements. Semaglutide shows the greatest efficacy among the therapeutic agents included in this analysis. These findings highlight the potential of newer second-generation GLP-1RAs as adjunctive therapies to insulin for people with T1D, a population in which overweight or obesity and suboptimal glycaemic control remain ongoing therapeutic challenges.

Semaglutide, at a maximum dose of 1.0 mg, produced the most pronounced benefits, including body weight reduction of 6.05 kg, HbA1c reduction of 0.33%, and insulin reduction of 14.95 U/day. These results are consistent with the established potency of semaglutide in T2D and obesity.[18,19] In the STEP-1 trial, conducted in individuals with obesity without diabetes, semaglutide 2.4 mg resulted in an average weight loss of 15.3 kg (15%), a magnitude exceeding that

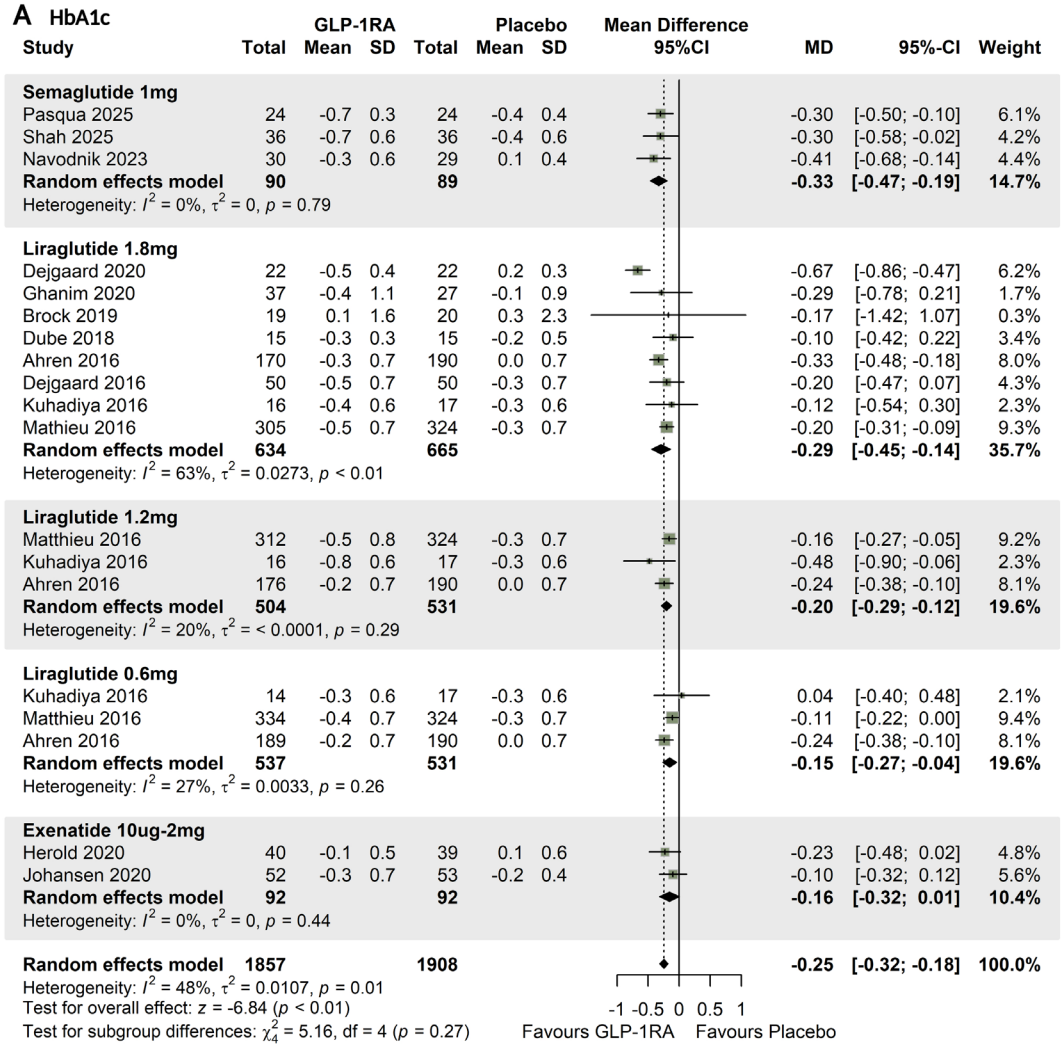

FIGURE 3 Legend on next page.

observed here.[20] Whether similar benefits can be realised in individuals with T1D remains uncertain due to a paucity of published studies evaluating the 2.4 mg dosage of semaglutide in this population. This evidence gap is now being addressed by the ongoing OBES1TY trial (NCT06909006), which will assess semaglutide 2.4 mg in adults with T1D and obesity.

This meta-analysis showed that the most significant therapeutic advantage of GLP-1RAs in T1D was weight reduction rather than HbA1c lowering. Although GLP-1RAs significantly reduced HbA1c in this analysis, the mean post-treatment HbA1c remained at 7.5%, above the American Diabetes Association's recommended target of <7%.[21] It remains unclear whether higher doses of semaglutide or newer dual incretin therapies can achieve greater HbA1c improvements. Beyond HbA1c, however, other indices of glycaemic control may better capture therapeutic benefit. Continuous glucose monitoring (CGM)–derived metrics, particularly time-in-range and measures of glycaemic variability, are increasingly recognised as critical markers of glycaemic management.[22] Shah et al.[23] reported that semaglutide increased the time-in-range (70–180 mg/dL) by 8.8% compared with placebo. In this meta-analysis, insufficient CGM data prevented pooled evaluation, highlighting the need for future trials to incorporate CGM endpoints as primary outcomes.

Interestingly, our analysis revealed a reduction in insulin requirements by more than 9 U/day despite modest HbA1c changes. This finding suggests that GLP-1RAs may improve glycaemic control through mechanisms such as enhancing peripheral insulin sensitivity, suppressing glucagon secretion, or delayed gastric emptying. An alternative explanation is reduced carbohydrate intake leading to lower bolus insulin requirements, though dietary data and distribution of insulin usage between basal and meal-related bolus administration were unavailable in the included studies.

Looking forward, the use of more potent GLP-1RAs and dual or triple incretin-based therapies may amplify the clinical benefits observed in this meta-analysis. Tirzepatide is a dual agonist of the GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptors that have demonstrated exceptional efficacy in T2D and obesity, yet evidence for its use in T1D remains limited to early case reports.[24,25] Ongoing trials will provide further clarity on dual agonist safety and efficacy in this population.

Safety remains a key consideration. Gastrointestinal adverse events such as nausea and vomiting were common in the included trials, but the risk of serious adverse events was not increased. The risk of hypoglycaemia was slightly elevated, though the reported incidence was low overall, and hyperglycaemic episodes were notably reduced. Importantly, as GLP-1RAs increase insulin sensitivity and suppress glucagon secretion, they may heighten hypoglycaemia risk if insulin adjustments are inadequate. Careful titration, ideally in conjunction with automated insulin delivery systems, may mitigate this risk. Despite reduced insulin dosing, no study reported an increased incidence of diabetic ketoacidosis (DKA), although routine ketone testing was not always described. Future trials should systematically assess ketone dynamics in this context. Furthermore, no trial reported pancreatitis, retinopathy progression, or psychiatric adverse events, but the relatively short duration of studies mandates caution.

This study is not without limitations. First, significant heterogeneity was observed, particularly in trials involving liraglutide 1.8 mg, likely reflecting differences in design, study populations, and trial duration (12–52 weeks). Such variability is important to consider due to changes in treatment effects over time. For example, the SUSTAIN 2 trial, which evaluated semaglutide in T2D and obesity over 56 weeks, demonstrated progressive weight loss until week 30 before weight plateaued, whereas HbA1c declined until week 23 before stabilising.[26] Thus, the magnitude of weight and HbA1c reductions observed in shorter-duration studies included in this meta-analysis may underestimate or misrepresent longer-term effects. Second, most available RCTs assessed liraglutide, while semaglutide was underrepresented, limiting conclusions on class-wide effects. Evidence for dulaglutide in T1D is particularly sparse, precluding meaningful analysis. Finally, HbA1c was the dominant glycaemic outcome, while CGM-derived endpoints such as time-in-range and glycaemic variability were insufficiently reported to allow meta-analysis. Additional limitations typical of systematic reviews should be acknowledged, including restriction to English language publications and potential publication bias.

These limitations highlight the need for longer-duration RCTs in T1D that evaluate emerging incretin-based therapies, including higher-dose semaglutide (2.4 mg), and systematically incorporate CGM-derived endpoints alongside traditional HbA1c and insulin outcomes. Finally, whether GLP-1RAs and dual incretin therapies provide the cardiovascular and kidney protection established in T2D remains an open question, as no dedicated cardiorenal outcome trials exist for T1D. An area warranting further study is the potential influence of residual beta-cell function on GLP-1RA efficacy. In the ADJUNCT ONE and ADJUNCT TWO trials, liraglutide showed greater efficacy in participants with preserved C-peptide levels, suggesting that baseline beta-cell reserve may modulate therapeutic response.[27,28] Incorporating C-peptide stratification in future studies may refine patient selection.

In summary, this meta-analysis demonstrates that GLP-1RAs offer clinically meaningful benefits for individuals with T1D with overweight or obesity, most notably through reductions in body weight and insulin requirements. Semaglutide, even at a maximum dose of 1.0 mg, emerged as the most potent agent, producing the largest reductions in weight, HbA1c, and insulin dose. Although HbA1c improvements were modest and did not reduce the population HbA1c to meet ADA targets, GLP-1RAs nonetheless offered

FIGURE 3 Forest plot comparing GLP-1RAs and placebo for change in (A) HbA1c (%) and (B) total daily insulin dose (U/day) in patients with type 1 diabetes and overweight/obesity. The mean difference (MD) indicates the average value change between groups, with negative values favouring GLP-1RAs.

complementary benefits that extend beyond HbA1c alone. These include reductions in glycaemic variability and enhancements in time-in-range, as reported in selected trials.[23,29] Importantly, the observed insulin-sparing effect of over 9 units/day suggests that GLP-1RAs improve the metabolic environment in T1D through mechanisms beyond HbA1c reduction. These benefits were achieved without an increase in serious adverse events. The absence of reported episodes of DKA despite insulin reduction, lack of reported pancreatitis or psychiatric harms, and limited evidence for dulaglutide and oral GLP-1RAs all underscore the importance of ongoing and future high-dose semaglutide (2.4 mg) and incretin-therapy trials. Looking forward, ongoing trials of higher-dose semaglutide (2.4 mg) and newer incretin therapies such as tirzepatide will be essential to determine whether greater efficacy can be achieved safely, with the potential to reshape treatment strategies for people with T1D.

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AUTHOR CONTRIBUTIONS

Amanda R. Purcell, Xi May Zhen, Jencia Wong, and Sarah J. Glastras were responsible for the design of the research question. Amanda R. Purcell and Xi May Zhen were responsible for the literature search and data extraction. Amanda R. Purcell was responsible for writing the original draft. Amanda R. Purcell, Xi May Zhen, Jencia Wong, and Sarah J. Glastras were responsible for reviewing and editing the paper.

CONFLICT OF INTEREST STATEMENT

Sarah J. Glastras has received honoraria and travel support from pharmaceutical companies including Lilly, Novo Nordisk, and Sanofi. All other authors have no conflicts of interest to declare.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in the supplementary files of this publication.

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REFERENCES

1. Ebekozien O, Noor N, Dimeglio L, et al. 1456-P: 2022 state of type 1 diabetes in the U.S.—real world T1D exchange multicenter data from over 60,000 people. *Diabetes*. 2023;72:1456-P.
2. Fang M, Jeon Y, Echouffo-Tcheugui JB, Selvin E. Prevalence and management of Obesity in U.S. adults with type 1 diabetes. *Ann Intern Med*. 2023;176:427-429.
3. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329:977-986.
4. Purnell JQ, Zinman B, Brunzell JD. The effect of excess weight gain with intensive diabetes mellitus treatment on cardiovascular disease risk factors and atherosclerosis in type 1 diabetes mellitus: results from the diabetes control and complications trial/epidemiology of diabetes interventions and complications study (DCCT/EDIC) study. *Circulation*. 2013;127:180-187.
5. Wallace AS, Chang AR, Shin JI, et al. Obesity and chronic kidney disease in US adults with type 1 and type 2 diabetes mellitus. *J Clin Endocrinol Metab*. 2022;107:1247-1256.
6. Vanderheiden A, Harrison L, Warshauer J, Li X, Adams-Huet B, Lingvay I. Effect of adding liraglutide vs placebo to a high-dose insulin regimen in patients with type 2 diabetes: a randomized clinical trial. *JAMA Intern Med*. 2016;176:939-947.
7. Sorli C, Harashima SI, Tsoukas GM, et al. Efficacy and safety of once-weekly semaglutide monotherapy versus placebo in patients with type 2 diabetes (SUSTAIN 1): a double-blind, randomised, placebo-controlled, parallel-group, multinational, multicentre phase 3a trial. *Lancet Diabetes Endocrinol*. 2017;5:251-260.
8. Aroda VR, Rosenstock J, Terauchi Y, et al. PIONEER 1: randomized clinical trial of the efficacy and safety of oral semaglutide monotherapy in comparison with placebo in patients with type 2 diabetes. *Diabetes Care*. 2019;42:1724-1732.
9. Perkovic V, Tuttle KR, Rossing P, et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. *N Engl J Med*. 2024;391:109-121.
10. Park J, Ntelis S, Yunasan E, et al. Glucagon-like peptide 1 analogues as adjunctive therapy for patients with type 1 diabetes: an updated systematic review and meta-analysis. *J Clin Endocrinol Metabol*. 2024;109:279-292.
11. Garg SK, Kaur G, Haider Z, Rodriquez E, Beatson C, Snell-Bergeon J. Efficacy of semaglutide in overweight and obese patients with type 1 diabetes. *Diabetes Technol Ther*. 2024;26:184-189.
12. Vilarrasa N, San Jose P, Rubio M, Lecube A. Obesity in patients with type 1 diabetes: links, risks and management challenges. *Diabetes Metab Syndr Obes*. 2021;14:2807-2827.
13. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
14. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898.
15. Dejgaard TF, Schmidt S, Frandsen CS, et al. Liraglutide reduces hyperglycaemia and body weight in overweight, dysregulated insulin-pump-treated patients with type 1 diabetes: the lira pump trial-a randomized, double-blinded, placebo-controlled trial. *Diabetes Obes Metab*. 2020;22:492-500.
16. Higgins JPT, Li T, Deeks JJ. Chapter 6: Choosing effect measures and computing estimates of effect [last updated August 2023]. In: Higgins JPT, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, eds. *Cochrane Handbook for Systematic Reviews of Interventions*. Cochrane; 2024.
17. Kuhadiya ND, Dhindsa S, Ghanim H, et al. Addition of liraglutide to insulin in patients with type 1 diabetes: a randomized placebo-controlled clinical trial of 12 weeks. *Diabetes Care*. 2016;39:1027-1035.
18. Davies M, Færch L, Jeppesen OK, et al. Semaglutide 2–4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. *Lancet*. 2021;397:971-984.
19. Kosiborod MN, Petrie MC, Borlaug BA, et al. Semaglutide in patients with obesity-related heart failure and type 2 diabetes. *N Engl J Med*. 2024;390:1394-1407.
20. Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384:989-1002.

21. Chiang JL, Kirkman MS, Laffel LMB, Peters AL. Type 1 diabetes through the life span: a position statement of the American Diabetes Association. *Diabetes Care*. 2014;37:2034-2054.
22. Monnier L, Colette C, Owens DR. The application of simple metrics in the assessment of glycaemic variability. *Diabetes Metab*. 2018;44:313-319.
23. Shah VN, Akturk Halis K, Kruger D, et al. Semaglutide in adults with type 1 diabetes and obesity. *NEJM Evid*. 2025;4(8): EVIDoa2500173.
24. Ahmed K, Koubeh S, Ahmed A, Hussain S. Cardiorenal benefit of tirzepatide in type 1 diabetes: a case report. *J Diabetol*. 2024;15(4):447–451.
25. Mendoza F, Parsiani R. Impact of tirzepatide in a patient with type 1 diabetes and obesity: a case report. *J Am Pharm Assoc*. 2023;63:1821-1825.
26. Ahrén B, Masmiquel L, Kumar H, et al. Efficacy and safety of once-weekly semaglutide versus once-daily sitagliptin as an add-on to metformin, thiazolidinediones, or both, in patients with type 2 diabetes (SUSTAIN 2): a 56-week, double-blind, phase 3a, randomised trial. *Lancet Diabetes Endocrinol*. 2017;5:341-354.
27. Ahrén B, Hirsch IB, Pieber TR, et al. Efficacy and safety of liraglutide added to capped insulin treatment in subjects with type 1 diabetes: the ADJUNCT TWO randomized trial. *Diabetes Care*. 2016;39:1693-1701.
28. Mathieu C, Zinman B, Hemmingsson JU, et al. Efficacy and safety of liraglutide added to insulin treatment in type 1 diabetes: the ADJUNCT ONE treat-to-target randomized trial. *Diabetes Care*. 2016;39:1702-1710.
29. Pasqua M-R, Tsoukas MA, Kobayati A, Aboznadah W, Jafar A, Haidar A. Subcutaneous weekly semaglutide with automated insulin delivery in type 1 diabetes: a double-blind, randomized, crossover trial. *Nat Med*. 2025;31:1239-1245.
30. Navodnik MP, Janež A, Žuran I. The effect of additional treatment with empagliflozin or semaglutide on endothelial function and arterial stiffness in subjects with type 1 diabetes mellitus—ENDIS study. *Pharmaceutics*. 2023;15:1945.
31. Ghanim H, Batra M, Green K, et al. Liraglutide treatment in overweight and obese patients with type 1 diabetes: a 26-week randomized controlled trial; mechanisms of weight loss. *Diabetes Obes Metab*. 2020;22:1742-1752.
32. Herold KC, Reynolds J, Dziura J, et al. Exenatide extended release in patients with type 1 diabetes with and without residual insulin production. *Diabetes Obes Metab*. 2020;22:2045-2054.
33. Johansen NJ, Dejgaard TF, Lund A, et al. Efficacy and safety of meal-time administration of short-acting exenatide for glycaemic control in type 1 diabetes (MAG1C): a randomised, double-blind, placebo-controlled trial. *Lancet Diabetes Endocrinol*. 2020;8:313-324.
34. Brock C, Hansen CS, Karmisholt J, et al. Liraglutide treatment reduced interleukin-6 in adults with type 1 diabetes but did not improve established autonomic or polyneuropathy. *Br J Clin Pharmacol*. 2019;85:2512-2523.
35. Dubé MC, D'Amours M, Weisnagel SJ. Beyond glycaemic control: a cross-over, double-blinded, 24-week intervention with liraglutide in type 1 diabetes. *Diabetes Obes Metab*. 2018;20:178-184.
36. Dejgaard TF, Frandsen CS, Hansen TS, et al. Efficacy and safety of liraglutide for overweight adult patients with type 1 diabetes and insufficient glycaemic control (Lira-1): a randomised, double-blind, placebo-controlled trial. *Lancet Diabetes Endocrinol*. 2016;4:221-232.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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