



# Real-World Clinical Experience of Semaglutide in Secondary Care Diabetes: A Retrospective Observational Study

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## ABSTRACT

**Introduction:** The glucagon-like peptide-1 receptor analogue (GLP-1RA) semaglutide is associated with improvements in glycaemia and cardiovascular risk factors in clinical trials. The aim of this study was to examine the real-world impact of semaglutide administered by injection in people with type 2 diabetes (T2D) across three secondary care sites in Wales.

**Methods:** A retrospective evaluation of 189 patients with T2D initiated on semaglutide between January 2019 and June 2020 with at least one follow-up visit was undertaken.

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**Results:** At baseline, participants had a mean age of 61.1 years, mean glycated haemoglobin (HbA1c) of 77.8 mmol/mol (9.3%) and mean body weight of 101.8 kg. At 6 and 12 months of follow-up, mean HbA1c reductions of 13.3 mmol/mol (1.2%) and 16.4 mmol/mol (1.5%), respectively, were observed, and mean weight loss at 6 months was 3.0 kg (all  $p < 0.001$ ). At 12 months, there were significant reductions in total cholesterol (0.5 mmol/L) and alanine transaminase (4.8 IU/L). Patients naïve to GLP-1RAs or with higher baseline HbA1c at baseline had greater glycaemic reductions, although clinically significant HbA1c reductions were also observed in those who switched from other GLP-1RAs, whose body mass index was  $< 35.0$  and  $> 35.0$  kg/m<sup>2</sup> or who had lower baseline HbA1c. Semaglutide was generally well tolerated, although adverse-effects limited use in 18 patients (9.5%).

**Conclusion:** Semaglutide provided clinically and statistically significant reductions in HbA1c, body weight, lipids and liver enzymes.

**Keywords:** Glucagon-like peptide-1 receptor analogues; Glycaemic control; Semaglutide; Type 2 diabetes; Weight loss

## Key Summary Points

### Why carry out this study?

The glucagon-like peptide-1 receptor analogue (GLP-1RA) semaglutide is associated with improved glycated haemoglobin (HbA1c) and metabolic risk factors in clinical trials; however, the real-world impact of semaglutide in people with type 2 diabetes has not been well studied.

This retrospective observational study investigated changes in HbA1c, body weight and other clinical and biochemical variables associated with semaglutide use.

### What was learned from the study?

Semaglutide use was associated with significant reductions in body weight and HbA1c over 6–12 months. There were also significant reductions in total cholesterol and alanine transaminase at 12 months.

Patients naïve to GLP-1RAs or with higher baseline HbA1c had greater HbA1c reductions. However, clinically significant HbA1c reductions were also observed in those who switched from other GLP-1RAs, had body mass index of < 35.0 and > 35.0 kg m<sup>2</sup> or had lower baseline HbA1c.

## DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.13651214>.

## INTRODUCTION

Type 2 diabetes (T2D) is a complex metabolic disorder associated with obesity, hypertension,

dyslipidaemia and complications that include cardiovascular, hepatic and renal disease; these complications impart significant morbidity and premature mortality [1, 2]. Whilst pharmacotherapies for T2D have largely focussed on glycaemic control, there is growing clinical and regulatory interest in optimising modifiable risk factors for complications of T2D. The importance of dietary and pharmacological interventions on cardiovascular outcomes in persons with T2D is highlighted by the benefits of risk factor modification [3, 4] and adverse cardiovascular consequences of some previous pharmacological therapies for T2D [5]. Pharmacological interventions to reduce cardiovascular disease will reduce the financial burden associated with T2D treatment, since the cost of treating the complications of T2D is greater than treating the disease itself [6]. Hence diabetes therapies which have a multifactorial approach to reduce complications (e.g. glucose, weight, blood pressure, lipids) are of major interest.

Cardiovascular outcome trials (CVOTs) have reported reduced major adverse cardiovascular events, including cardiovascular death, non-fatal stroke or myocardial infarction, in association with glucagon-like peptide-1 receptor analogue (GLP-1RA) therapy [7]. Indeed, there is strong rationale for the use of GLP-1RAs in people with T2D and obesity, and these drugs are generally recommended in a subgroup of people with poorly controlled T2D and obesity as a second- or third-line therapy [8, 9]. These agents enhance the incretin effect to augment glucose-mediated insulin release from the pancreatic  $\beta$ -cells and to diminish glucagon release from the  $\alpha$ -cells, thereby reducing blood glucose levels. Furthermore, GLP-1RAs delay gastric emptying and enhance centrally mediated hypothalamic satiety, two factors which may account for the observed weight loss associated with these agents. The once-weekly GLP-1RA semaglutide is the most recently licenced injectable GLP-1RA and is associated with clinically significant improvements in metabolic and cardiovascular risk factors [10]. In the SUSTAIN-6 trial, these benefits included a reduction in body weight (2.9–4.4 kg), systolic blood pressure (SBP) (3.4–5.4 mmHg) and

glycated haemoglobin (HbA1c; 11.9–15.4 mmol/mol [1.1–1.4%]), along with reductions in total cholesterol and serum triglycerides [11]. Whilst semaglutide is sometimes associated with gastrointestinal disturbance, it is generally well tolerated [11, 12].

Clinical trial and real-world evidence do not always correlate as there may be differences in patient selection (e.g. HbA1c, body weight) and medication adherence [13]. Within clinical practice, real-world experience and the experience of peers adds to the contribution of clinical trial data. Our aim was to examine the real-world impact of injectable semaglutide on glucose control and cardiovascular risk factor control in people with T2D treated in secondary care diabetes clinics.

## METHODS

A total of 189 people with T2D initiated on semaglutide between January 2019 and June 2020 with at least one follow-up visit were identified using a local electronic database. These patients attended clinical follow-up visits in local diabetes secondary care clinics across three hospital sites (Morrison hospital, Neath Port Talbot hospital and Singleton hospital). Original analysis of these data was performed in November 2020.

We examined changes in routinely collected clinical variables, including SBP, diastolic blood pressure (DBP), body weight and body mass index (BMI), and biochemical variables, including HbA1c, lipids (total cholesterol, triglycerides, high-density lipoprotein [HDL]), alanine transaminase (ALT) and serum creatinine, at follow-up visits. As patients were not initiated on semaglutide at the same time, 63 of the 189 patients had a 12-month follow-up visit at which time biochemical data were collected. All patients with at least one follow-up visit were included in the analysis. Clinic letters were used to determine the reason for clinician choice of semaglutide and diabetes medication.

We compared the effects of semaglutide in three subgroups defined by (1) previous GLP-1RA usage (GLP-1RA groups); (2) baseline glycaemic control (glycaemic control groups); and

(3) baseline BMI (BMI groups). In the GLP-1RA groups, we compared the effects of semaglutide in patients with previous GLP-1RA usage versus those naïve to GLP-1 therapy. In the glycaemic control groups, we compared patients with baseline poor control versus moderate control using a HbA1c  $\geq 75$  mmol/mol (9.0%) cutoff to define patients with poor glycaemic control. The HbA1c cutoff of 75 mmol/mol (9.0%) was used because this is a level above which physicians would usually consider insulin therapy rather than additional oral agents. The National Institute for Health and Care Excellence (NICE) in the UK recommend considering insulin therapy if HbA1c is  $\geq 75$  mmol/mol (9.0%) [9]. In the BMI groups, we compared patients with a baseline BMI  $< 35.0$  kg/m<sup>2</sup> with those with a baseline BMI  $\geq 35.0$  kg/m<sup>2</sup>. The BMI cutoff 35.0 kg/m<sup>2</sup> was used in line with NICE guidance which recommends considering GLP-1RA therapy for those persons with BMI  $\geq 35.0$  kg/m<sup>2</sup> [9].

### Compliance with Ethics Guidelines

Ethics committee approval was not required as this analysis was conducted as part of a service-based evaluation project to examine the effects of semaglutide therapy, which is routine in our local practice following the introduction of new diabetes therapies.

### Statistical Analysis

Statistical analysis was performed using SPSS version 26 (IBM Corp., Armonk, NY, USA). Results for continuous variables are presented as the mean and standard deviation (SD). The paired *t*-test was used to compare mean changes in clinical and biochemical measures at the 6-month follow-up. Repeated measure analysis of variance (ANOVA) with post-hoc analysis was used to compare biochemical measures at the 6- and 12-month visits. Baseline parameters in the subgroup analysis were compared by independent sample *t* test. The effects of semaglutide in the subgroup analysis were examined using one-way ANOVA (general linear model). Change in each group over time was tested

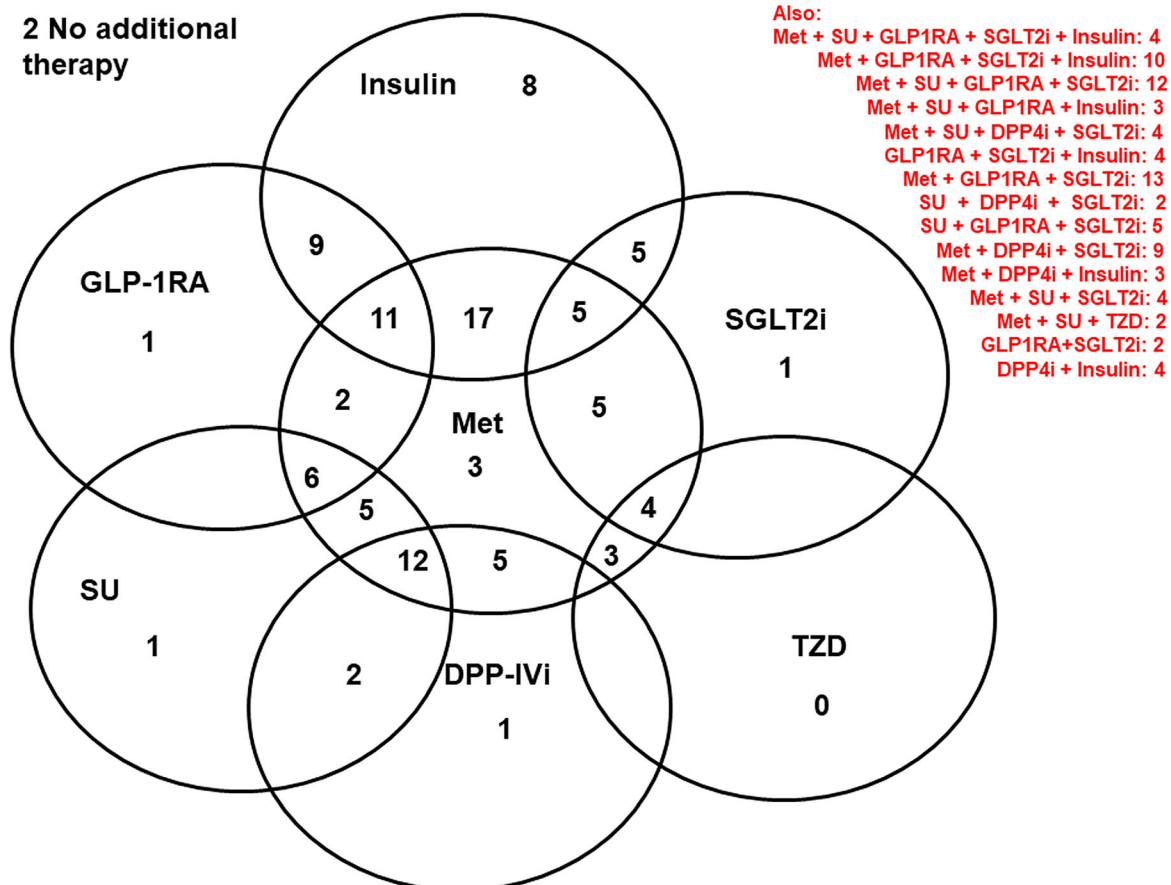
separately if the interaction was significant.  $p \leq 0.05$  was considered to be statistically significant.

## RESULTS

### Baseline Characteristics

Pre-semaglutide therapy, 87 (46.0%) of the participants were male, with a mean age ( $\pm$  SD) of 61.1 ( $\pm$  11.2) years, HbA1c of 77.8 ( $\pm$  17.9) mmol/mol (9.3 [ $\pm$  1.8%]), body weight of 101.8 ( $\pm$  19.5) kg, BMI of 35.6 ( $\pm$  6.6) kg/m<sup>2</sup> and serum creatinine of 83.8 ( $\pm$  35.0)  $\mu$ mol/L. Prior to commencing semaglutide, 142 (75.1%) patients were prescribed metformin, 66 (34.1%)

a sulphonyurea, nine (4.8%) pioglitazone, 43 (22.2%) a dipeptidyl peptidase-4 (DPP-4) inhibitor, 89 (47.1%) a sodium-glucose co-transporter-2 (SGLT-2) inhibitor and 83 (43.9%) insulin. Interestingly, 82 (43.4%) patients were previously prescribed a different GLP-1RA (60 liraglutide, 17 dulaglutide, 4 exenatide once-weekly, 1 lixisenatide). Pharmacological therapies for T2D prescribed to patients prior to semaglutide initiation is presented in Fig. 1. As a result of initiating semaglutide, pre-existing GLP-1RA therapy and DPP-4 inhibitor therapies were discontinued in 82 (43.4%) and 43 (22.2%) participants, respectively. Reasons for initiating or switching to semaglutide included: fewer injections (11.6%), the need for weight loss (17.5%), inadequate glycaemic control (38.1%)



**Fig. 1** Diabetes therapies used by patients prior to the initiation of semaglutide. *DDP-IVi* Dipeptidyl peptidase IV inhibitor, *GLP-1RA* glucagon-like peptide-1 receptor analogue, *Met* metformin, *SGLT2i* sodium-glucose co-

transporter-2 inhibitor, *SU* sulphonyureas, *TZD* thiazolidinediones

or both the need for weight loss and inadequate glycaemic control (32.8%).

### Changes in Metabolic Risk Factors

At 6 months following semaglutide initiation, there were significant improvements in mean HbA1c of 13.3 mmol/mol (1.2%) and a mean weight loss of 3.0 kg (both  $p < 0.001$ ). There were statistically significant reductions in the mean SBP (1.8 mmHg) and serum triglycerides (0.4 mmol/L) (both  $p = 0.04$ ). There were no significant changes in the DBP, total cholesterol, HDL, ALT or serum creatinine at the 6-month follow-up visit. These data are shown in Table 1.

Following 12 months of therapy with semaglutide, there were only limited data available to evaluate changes in SBP, DBP and body weight. Exploratory analysis of the available biochemical follow-up data revealed significant reductions in HbA1c (16.4 mmol/mol [1.5%],  $p < 0.001$ ), total cholesterol (0.5 mmol/L,  $p < 0.001$ ) and ALT (4.8 IU/L,  $p = 0.02$ ). These data are presented in Table 2.

### Subgroup Analyses

#### GLP-1RA Groups

There were no statistically significant differences in baseline characteristics (age, BMI, weight, blood pressure, HbA1c and lipid profile) between the two GLP-1RA groups. Patients naïve to GLP-1RA at baseline had a mean HbA1c reduction of 15.3 mmol/mol (12.1–18.4 mmol/mol [1.4%]) at 6 months compared with a reduction of 10.6 mmol/mol (7.2–14.0 mmol/mol [1.0%]) in those switched from a different GLP-1RA. The ANOVA showed an interaction ( $p < 0.04$ ), indicating significantly greater response in patients with no previous exposure to GLP-1RA. At 6 months, there was a mean reduction in the BMI of 1.7 (0.8–2.7) kg/m<sup>2</sup> in those with previous GLP-1RA use compared with a reduction of 1.1 (0.7–1.5) kg/m<sup>2</sup> in those naïve to GLP-1RA therapy (interaction not significant,  $p = 0.14$ ). These data are shown in Fig. 2.

#### Glycaemic Control Groups

We chose a priori to divide participants into glycaemic control groups based on a HbA1c cutoff of 75 mmol/mol (9.0%), with the aim to

**Table 1** Changes in metabolic risk factors at 6 months

Metabolic risk factors	Baseline ( <i>n</i> = 151)	3–6 months ( <i>n</i> = 151)	Mean difference from baseline	<i>p</i> value
HbA1c (mmol/mol)	77.2 ± 17.8	63.9 ± 16.9	– 13.3	< 0.001**
SBP (mmHg)	132.7 ± 18.0	130.9 ± 15.4	– 1.8	0.04*
DBP (mmHg)	76.9 ± 10.5	79.1 ± 10.9	+ 2.2	0.29
Body weight (kg)	100.5 ± 15.4	97.5 ± 16.2	– 3.0	< 0.001**
Total cholesterol (mmol/L)	4.2 ± 1.1	4.2 ± 3.4	0.0	0.91
Triglycerides (mmol/L)	2.8 ± 2.1	2.4 ± 2.2	– 0.4	0.04*
HDL (mmol/L)	1.2 ± 0.5	1.1 ± 0.4	– 0.1	0.17
ALT (IU/L)	30.2 ± 19.9	28.2 ± 16.8	– 2.0	0.17
Creatinine (µmol/L)	81.0 ± 31.7	82.8 ± 32.5	+ 1.8	0.20

This table summarises changes in metabolic risk factors observed at 6 months following initiation of semaglutide therapy. Data are presented as the mean ± standard deviation (SD).

ALT Alanine transaminase, DBP diastolic blood pressure, HbA1c glycated haemoglobin, HDL high-density lipoprotein, SBP systolic blood pressure

\*Statistically significant at  $p \leq 0.05$ , \*\*Statistically significant at  $p \leq 0.001$ , paired *t* test

**Table 2** Changes in metabolic risk factors over 12 months of follow-up

Metabolic risk factors	Baseline	6 months	12 months	<i>p</i> value
HbA1c (mmol/mol) ( <i>n</i> = 63)	77.3 ± 18.9	62.8 ± 16.1	60.9 ± 17.0	< 0.001**
Total cholesterol (mmol/L) ( <i>n</i> = 53)	4.2 ± 1.1	3.7 ± 0.9	3.7 ± 0.9	< 0.001**
Triglycerides (mmol/L) ( <i>n</i> = 53)	2.8 ± 1.7	2.6 ± 3.0	2.1 ± 1.4	0.15
HDL (mmol/L) ( <i>n</i> = 53)	1.2 ± 0.5	1.1 ± 0.4	1.1 ± 0.4	0.22
ALT (IU/L) ( <i>n</i> = 37)	30.3 ± 15.6	25.0 ± 12.5	25.5 ± 14.5	0.02*
Creatinine (μmol/L) ( <i>n</i> = 59)	84.2 ± 32.2	85.8 ± 34.1	85.3 ± 36.4	0.75

This table summarises changes in metabolic risk factors at 6 and 12 months following initiation of semaglutide  
Data presented as the mean ± SD

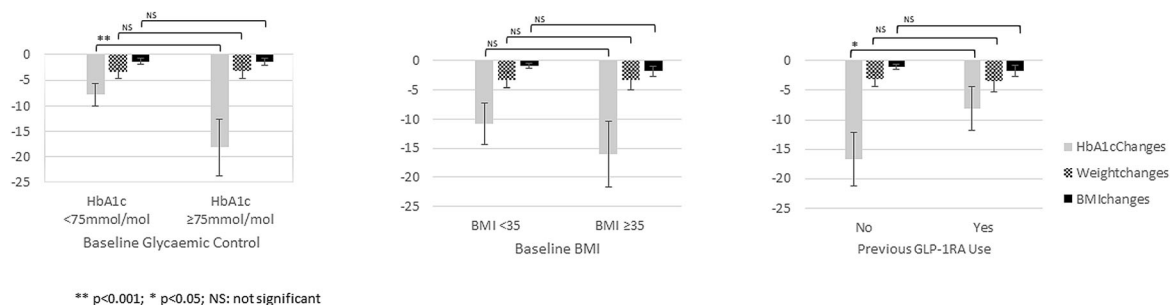
\*Statistically significant at  $p \leq 0.05$ , \*\*Statistically significant at  $p \leq 0.001$ , repeated-measures analysis of variance (ANOVA)

compare changes in clinical measurements, as this cutoff is the HbA1c threshold recommended by NICE to consider insulin initiation [9] and previous studies have observed greater HbA1c reductions in those with a greater baseline HbA1c [14]. Patients with a pre-treatment HbA1c  $\geq 75$  mmol/mol (9.0%) demonstrated significant reductions in HbA1c of 17.7 (13.9–21.5) mmol/mol (1.6%) at 6 months, compared with a mean reduction of 8.4 (6.4–10.4) mmol/mol (0.8%) in those with a baseline HbA1c  $< 75$  mmol/mol (9.0%) (interaction  $p < 0.001$ ). At 6 months, there was a mean weight loss of 3.3 (1.7–5.0) kg in those with HbA1c  $\geq 75$  mmol/mol (9.0%) and 3.4 (2.1–4.7) kg in those with HbA1c  $< 75$  mmol/mol (9.0%) (interaction not

significant,  $p = 0.93$ ). At 6 months, there was also a mean BMI reduction of 1.4 (0.6–2.1) kg/m<sup>2</sup> in those with baseline HbA1c  $\geq 75$  mmol/mol (9.0%) and 1.3 (0.8–1.8) kg/m<sup>2</sup> in those with baseline HbA1c  $< 75$  mmol/mol (9.0%) (interaction not significant,  $p = 0.91$ ). These data are shown in Fig. 2.

### BMI Groups

We examined changes in clinical measurements grouped by pre-treatment BMI in 144 subjects with available baseline BMI and follow-up data. Participants were divided into two groups defined by baseline BMI of 35.0 kg/m<sup>2</sup>. This BMI cutoff was selected as people with diabetes and a BMI  $\geq 35.0$  kg/m<sup>2</sup> are generally recommended to commence GLP-1RA therapy [9] and the



**Fig. 2** Mean changes in glycated haemoglobin (*HbA1c*), body weight and body mass index (*BMI*) in the between-group comparison (general linear model)

median baseline BMI of this cohort was 34.9 kg/m<sup>2</sup>. At baseline, patients with BMI < 35.0 kg/m<sup>2</sup> were older than those with BMI ≥ 35.0 kg/m<sup>2</sup> (63.0 ± 10.6 vs. 58.5 ± 11.5 years, *p* = 0.02), but there were no significant differences in blood pressure, HbA1c and lipid profiles. At 6 months, patients with a baseline BMI ≥ 35.0 kg/m<sup>2</sup> had a mean reduction in HbA1c of 15.4 (11.5–19.3) mmol/mol (1.4%), compared with a mean reduction of 11.8 (9.1–14.6) mmol/mol (1.1%) in those with a baseline BMI < 35.0 kg/m<sup>2</sup> (interaction not significant, *p* = 0.14). Patients with BMI < 35.0 kg/m<sup>2</sup> had a mean weight loss of 3.2 (1.9–4.5) kg at 6 months, compared with 3.6 (1.9–5.2) kg in those with a baseline BMI ≥ 35.0 kg/m<sup>2</sup> (interaction not significant, *p* = 0.77). Those with a baseline BMI < 35.0 kg/m<sup>2</sup> had a mean BMI reduction of 1.0 (0.5–1.4) kg/m<sup>2</sup> compared with a mean reduction of 1.8 (1.0–2.6) kg/m<sup>2</sup> in those with baseline BMI ≥ 35.0 kg/m<sup>2</sup> (interaction not significant, *p* = 0.06). These data are presented in Fig. 2.

### Safety and Acceptability

Of the 189 patients with at least one follow-up visit, semaglutide was discontinued in 18 patients (9.5%) because of nausea and vomiting (*n* = 12), diarrhoea (*n* = 4), abdominal cramps (*n* = 1) or tiredness (*n* = 1). Dose increases were limited in 11 patients (5.8%) by nausea and vomiting (*n* = 5), dyspepsia (*n* = 4), abdominal cramps (*n* = 1) and diarrhoea (*n* = 1). The remaining 160 patients (84.7%) continued to use semaglutide without significant side-effects.

In participants who switched from an alternative GLP-1RA, semaglutide was started at a dose of 0.25 mg weekly in 21 (25.6%) people, 0.5 mg weekly in 52 (63.4%) people and 1.0 mg weekly in nine (11.0%) people. In those who switched from an alternative GLP-1RA, semaglutide was discontinued in five (6.1%) people compared with 13 (12.1%) of those previously naïve to GLP-1RA. Dose increases were limited by side-effects in three (3.7%) people switching GLP-1RA and in eight (4.4%) people naïve to GLP-1RA treatment.

## DISCUSSION

The focus of pharmacological therapy for T2D extends beyond glycaemic control, to reduce cardiovascular and renal morbidity and mortality. Previous trial data support benefits in glucose control, weight reduction, cardiovascular risk factors and outcomes associated with once-weekly injectable semaglutide in people with T2D. Indeed, superiority for improved HbA1c and weight loss has been observed for semaglutide versus placebo [11, 15], DPP-4 inhibitors [16], SGLT-2 inhibitors [17], basal insulin [18, 19] and other GLP-1RAs [20–22]. Whilst CVOT results are supportive of a favourable effect of semaglutide (and other GLP-1RAs) on cardiovascular and renal outcomes [23], there is a lack of real-world and published peer-based experience to corroborate this impact in routine diabetes clinical practice.

In this clinically based analysis of 189 patients with T2D, semaglutide was associated with clinically important improvements in HbA1c of 13.3 mmol/mol (1.2%) and 16.4 mmol/mol (1.5%) at 6 and 12 months, respectively, and a mean weight loss of 3.0 kg at 6 months. Additionally, significant reductions in blood pressure and triglycerides were noted at 6 months and in total cholesterol and ALT at 12 months. These results are comparable with those observed in the SUSTAIN-6 trial which noted a HbA1c reduction of 11.9–15.4 mmol/mol (1.1–1.4%), a weight loss of 2.9–4.4 kg and a reduction in SBP of 3.4–5.4 mmHg [11]. As a result of a considerable amount of missing data for body weight, BMI, SBP and DBP at 12 months, directly attributable to the reduced face-to-face consultations during the COVID-19 pandemic, statistical analysis at the 12-month follow-up visit was limited. At the 6-month follow-up visit, however, we noted a statistically significant reduction in SBP of 1.8 mmHg.

Further findings from this analysis include a significant reduction in total cholesterol (0.5 mmol/L) at 12 months. Similar findings were noted in the SUSTAIN-6 trial, with significant reductions in total cholesterol in those taking semaglutide 0.5 mg and triglycerides in

those taking semaglutide 1.0 mg [23]. The present analysis also noted a 4.8 IU/L reduction in serum ALT associated with semaglutide use, representing a 15.8% reduction from baseline. This is comparable to results from a previous study investigating the impact of semaglutide on liver enzymes, which reported an ALT reduction of 6–21% in those with elevated baseline ALT. Given our population had a normal baseline mean ALT, it will be interesting to see the effect of semaglutide and other GLP-1RAs in more specific populations, such as those with non-alcoholic steatohepatitis (NASH) in the ongoing SEMA-NASH study [24].

Previous real-world analyses of semaglutide in patients with T2D have shown significant benefits. One study of 107 American patients with T2D found that semaglutide improved HbA1c by 14 mmol/mol (1.3%), with the greatest improvements in those with no previous GLP-1RA use or worse glycaemic control [25]. A more recent and larger study of 937 Canadian patients with T2D observed an improvement of 11.3 mmol/mol (1.03%) and a weight loss of 3.9 kg over 6 months [26]. Similarly, the findings in this analysis found greater improvements in HbA1c in people naïve to GLP-1RA and in those with worse baseline glycaemic control. However, these results also demonstrate that clinically significant reductions in HbA1c and body weight were noted in people who switched from other GLP-1RAs and with relatively well-controlled HbA1c. Interestingly, we observed important reductions in HbA1c in those with baseline BMI  $\geq 35.0$  kg/m<sup>2</sup> or  $< 35.0$  kg/m<sup>2</sup>, although there was not a significant difference in HbA1c reduction between the groups. As expected, those with baseline BMI  $\geq 35.0$  kg/m<sup>2</sup> demonstrated a greater reduction in BMI, although this did not reach statistical significance ( $p = 0.06$ ). Consistent with previous studies [14], these results demonstrate that semaglutide initiation in those with poorer baseline HbA1c  $\geq 75$  mmol/mol (9.0%) resulted in a greater HbA1c reduction, in a population who would have traditionally required insulin therapy. However, a clinically important reduction in HbA1c of 8.4 mmol/mol (0.7%) was noted in those even with relatively well-controlled

HbA1c  $< 75$  mmol/mol (9.0%). Our findings therefore support the initiation of semaglutide in people who have used other GLP-1RAs, have a BMI  $< 35.0$  kg/m<sup>2</sup> and have HbA1c  $< 75$  mmol/mol (9.0%) in addition to the already known benefits in those with poorly controlled HbA1c, significant obesity or naivety to GLP-1RA therapy. In the UK, this finding challenges current NICE guidance which generally recommends the use of GLP-1RAs in those with a BMI  $> 35.0$  kg/m<sup>2</sup> or obesity-related comorbidity and initiation of insulin when HbA1c  $> 75$  mmol/mol (9.0%) [9]. The results of the present analysis support published findings and add further to the analysis of changes in ALT, lipids and serum creatinine.

Semaglutide was generally well-tolerated, though side-effects including nausea and vomiting, diarrhoea and abdominal cramps limited use in 18 patients (9.5%). This is lower than the discontinuation rate observed in the SUSTAIN-6 trial in which 216 participants (13.1%) discontinued semaglutide due to gastrointestinal or other side effects; the period of drug exposure in SUSTAIN-6 was, however, longer at 2 years. We did not identify any patient admitted to hospital due to semaglutide use including pancreatitis or for any other reason. Further real-world studies to evaluate semaglutide adherence and acceptability would be important and of clinical interest.

## Limitations

This study has some important limitations. Given the restrictions associated with the Covid-19 pandemic there was limited follow-up and therefore less data collected with respect to variables such as body weight and blood pressure in this cohort. However, biochemical monitoring continued over this period, and the limited follow-up did not significantly limit the analysis of changes in HbA1c or other serum tests. Given the retrospective nature of this analysis, the study is prone to the biases affecting this type of study and was also limited by a lack of a control group. Real-world assessment of the impact of semaglutide on major adverse cardiovascular events, such as myocardial



infarction, stroke or cardiovascular death, and assessment of impact on microvascular outcomes, including ophthalmic and renal disease, were limited by the 12-month duration of follow-up and would be an important observation in future studies with longer follow-up.

## CONCLUSIONS

In this retrospective observational study of people with T2D treated in secondary diabetes clinics, semaglutide use was associated with clinically and statistically important reductions in HbA1c, body weight, BMI, total cholesterol and ALT. Our results support the addition of semaglutide in all patients with T2D and no contraindication, especially in those with poorer glycaemic control, greater body weight and/or naivety to GLP-1RA use.

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**Compliance with Ethics Guidelines.** Ethics committee approval was not required as this article is based on routinely collected clinical data as part of a service-based evaluation project performed regularly in our local practice following the introduction of new diabetes therapies.

**Data Availability.** All data generated or analysed during this study are included in this published article.

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