diabetesresearchandclinicalpractice 236 (2026) 113244

Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.journals.elsevier.com/diabetes-research-and-clinical-practice

# Oral semaglutide reduces diabetes-related distress in adults with type 2 diabetes mellitus switching from DPP-4 inhibitors. The DOORS prospective real-world Italian study

Andrea Giaccari [a,*], Francesca Borroni [b], Marco Dauriz [c], Daniela Gioia [d], Paris Baptiste [e], Alessandro Bisio [f], Giusi Lastoria [f], Keerthana Udupa [g], Mario Barbagallo [h]

[a] Università Cattolica del Sacro Cuore and Center for Endocrine and Metabolic Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[b] Ospedale Generale Provinciale di Macerata, Macerata, Italy
[c] Section of Endocrinology and Diabetes, Department of Internal Medicine, South-Tyrolean Healthcare System (SABES-ASDAA), Bolzano General Hospital, Via Lorenz Böhler 5, 39100 Bolzano, Italy
[d] Casa di cure Triolo Zancla, Palermo, Italy
[e] Novo Nordisk LTD, Gatwich, UK
[f] Novo Nordisk s.p.a., Rome, Italy
[g] Novo Nordisk A/S, Bangalore, India
[h] A.O.U. Policlinico Giaccone, Palermo, Italy

ARTICLE INFO

*Keywords:*
Type 2 diabetes mellitus
Glycemic control
Weight management
Patient-reported outcomes (PROs)
Diabetes-related distress
Real world evidence
Oral semaglutide

ABSTRACT

*Aims:* To evaluate glycemic control, weight management, and patient-reported outcomes (PROs) in adults with type 2 diabetes mellitus who transitioned to oral semaglutide (OS) after inadequate glycemic control on dipeptidyl peptidase-4 inhibitors (DPP-4i).
*Methods:* This 40-week, observational, prospective study included three visits: baseline (V1, OS initiation), intermediate visits (V2.X), and final visit (V3, week 40 ± 4). The primary endpoint was change in glycated haemoglobin (HbA1c) from V1 to V3. Secondary endpoints included changes in body weight (BW), PROs – assessed by the Diabetes Distress Scale (DDS) and the Dutch Eating Behaviour Questionnaire (DEBQ) – and anthropometric/clinical parameters.
*Results:* 281 patients were enrolled (mean age 67.5 ± 12.0 years; 55.9% male). In the in-study set (all patients initiating OS, regardless of discontinuation), mean HbA1c decreased by − 0.7 ± 0.05% ($p < 0.0001$), and mean BW decreased by − 3.6 ± 0.22 kg ($p < 0.0001$) from V1 to V3. Scores on the DDS domains and the DEBQ (emotional and external eating domains) decreased, indicating reduced diabetes-related distress and improved eating behaviours. Adverse events were reported by 23.1% of patients, with no hypoglycaemic episodes observed.
*Conclusions:* OS was safe and effective in improving glycemic control, reducing BW, and alleviating diabetes-related distress and unhealthy eating behaviors in patients with type 2 diabetes mellitus switched from DPP-4i.

## 1. Introduction

The PIONEER (Peptide InnOvatioN for Early diabEtes tReatment) program – comprising ten randomized Phase III clinical trials – was designed to evaluate the safety and efficacy of once-daily oral semaglutide (OS) in over 9,000 patients with type 2 diabetes mellitus [1–10].

Among these trials, PIONEER 7 specifically demonstrated the superior efficacy of OS, administered with flexible dose adjustment, in achieving glycemic control and weight reduction compared to sitagliptin 100 mg over a 52-week treatment period [7]. In the subsequent 52-week extension phase, a third treatment arm was introduced in which patients previously treated with sitagliptin were switched to OS. While this group experienced additional reductions in HbA1c, the

* Corresponding author at: Università Cattolica del Sacro Cuore and Center for Endocrine and Metabolic Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy.
*E-mail address:* andrea.giaccari@unicatt.it (A. Giaccari).

https://doi.org/10.1016/j.diabres.2026.113244
Received 12 December 2025; Received in revised form 20 March 2026; Accepted 5 April 2026
Available online 6 April 2026

difference between switchers and non-switchers did not reach statistical significance (−0.2% for OS vs. 0.1% for sitagliptin; p = 0.079) [11]. Therefore, although a significantly greater proportion of patients in the OS group achieved HbA1c levels < 7.0% after the switch compared to the sitagliptin group (p = 0.0011), fewer required rescue medication (9.0% vs. 23.5%), and a greater mean reduction in body weight was observed (between-group difference −1.5 kg; p = 0.0321) [11], the question of possible superior efficacy of OS after the switch remained unresolved.

A specific study aiming to re-evaluate the efficacy of OS after a switch from a dipeptidyl peptidase-4 inhibitors (DPP-4i) (after confirmed DPP-4 failure) was therefore necessary. Since failure with a DPP-4i was the primary inclusion criteria, we considered a significant HbA1c reduction following the switch to be sufficient, rather than requiring comparison with a placebo group. Therefore, instead of repeating the extension period of the PIONEER 7 in a new trial, we opted to initiate a prospective observational study that, unlike retrospective studies, offers the advantage of a complete data collection. Although randomized controlled trials remain the gold standard for establishing efficacy and safety under controlled conditions, real-world evidence is essential for assessing therapeutic effectiveness in broader, more heterogeneous populations that reflect routine clinical practice. It also plays a critical role in capturing outcomes that matter to patients and incorporating their perspectives – an approach aligned with the principles of evidence-based medicine, which emphasize integrating the clinical expertise with patient preferences to support optimal decision-making [12].

In light of these considerations, the present study aimed to evaluate the real-world safety and effectiveness of OS in improving glycemic control and promoting weight loss in patients with type 2 diabetes mellitus who had inadequate glycemic control on DPP-4i and subsequently switched to OS, in line with current national and international clinical guidelines [13–16]. Importantly, given their growing role in shaping individualized diabetes management, patient-reported outcomes (PROs) were also assessed.

## 2. Materials and Methods

### 2.1. Study design

This was a 40-week, Italian multicentre, observational, prospective, single-arm study designed to evaluate glycemic control, weight management, and PROs – including diabetes-related distress and eating behaviour – in adults with type 2 diabetes mellitus who had inadequate glycemic control on DPP-4i and subsequently transitioned to OS. The decision to switch to OS was made at the discretion of the treating physician in accordance with local clinical practice and current national and international clinical guidelines [13–16], and was entirely independent of the decision to include participants in the study.

The study was approved by the relevant Independent Ethics Committees and conducted in accordance with the Declaration of Helsinki, the Guidelines for Good Pharmacoepidemiology Practice (GPP), and Good Pharmacovigilance Practices (GVP), Module VI. All participants provided written informed consent to participate.

### 2.2. Patients

Inclusion criteria were: providing written informed consent; the decision to switch from DPP-4i treatment to OS made by the patient (or legally acceptable representative) and the treating physician prior to, and independently of, the decision to include the patient in the study; documentation, at the time of enrolment, of the last HbA1c measurement with a value ≥ 7.5% (a measurement obtained within 90 days prior to enrolment was also considered valid); and being treatment-naïve to insulin, with the exception of short-term insulin use for acute illness lasting fewer than 14 days.

Exclusion criteria were: age under 18 years at the time of enrolment; previous participation in this study, defined as having provided informed consent for it; participation in any clinical trial involving an approved or unapproved investigational medicinal product within 30 days prior to enrolment and throughout the duration of the study, with the exception of trials whose primary objective was the prevention or treatment of COVID-19 disease or post-infectious conditions, provided that the last dose of the investigational medicinal product had been received more than 30 days before signing the informed consent; diagnosis of type 1 diabetes; pregnancy, planned pregnancy, or becoming pregnant during the study period; and mental incapacity, unwillingness, or language barriers that could preclude adequate understanding or cooperation.

### 2.3. Visit schedule and data collection

The study began in February 2023 and concluded in October 2024. Each participant was followed for a total of 40 ± 4 weeks from the time of enrolment.

Over the course of the observational period, patients attended three visits. The first visit (V1), conducted at week 0, marked the initiation of OS treatment in accordance with local clinical practice. At this time, patients who met the eligibility criteria and provided written informed consent were formally enrolled in the study. A comprehensive set of baseline data was collected during this visit, including demographic characteristics, medical and diabetes history (with associated complications), current and previous diabetes treatments, concomitant medications, the rationale for switching to OS, and the prescribed starting dose.

The second visit (V2.X) referred to any intermediate visit occurring between the first and the final visits, specifically between weeks 1 and 36. These visits were conducted according to the routine clinical practice at each site, were not mandatory, and varied in timing and frequency across patients and centres.

The final visit (V3) corresponded to the end-of-study assessment and was conducted at 40 ± 4 weeks following the enrolment.

At each visit (V1, V2.X when applicable, and V3), data were collected on the number and dates of visits, OS dosage, any discontinuation of OS (including dates and reasons), and concomitant medications. HbA1c, body weight, waist circumference, body mass index (BMI), and blood pressure (systolic and diastolic) were also assessed at each visit, while lipid and renal profile were assessed at V1 and V3.

PROs diabetes-related distress and eating behaviour were obtained at V1 and V3 using the Diabetes Distress Survey (DDS) [17] and the Dutch Eating Behaviour Questionnaire (DEBQ) [18,19], respectively. Specifically:

- The DDS [17] is a 17-item self-report survey designed to measure the diabetes-related emotional distress, which refers to the negative emotional experiences and challenges that arise from living with and managing diabetes on a daily basis. Each item is scored on a 6-point Likert scale, ranging from 1 (no problem) to 6 (serious problem). The DDS encompasses four key domains: emotional burden, which reflects feelings of being overwhelmed by the disease; physician-related distress, which captures frustrations when concerns are not adequately addressed by healthcare providers; regimen-related distress, which assesses difficulties adhering to treatment plans; and interpersonal distress, which relates to perceptions of insufficient support from family and friends [17]. To facilitate interpretation of DDS scores, three categories have been established: little or no distress (DDS < 2.0), moderate distress (DDS 2.0–2.9), and high distress (DDS ≥ 3.0) [20].
- The DEBQ [18,19] is a 33-item self-report instrument designed to assess eating behaviours using a 5-point Likert scale ranging from 1 (never) to 5 (very often). The questionnaire is divided into three subscales: emotional eating, external eating, and restrained eating.

Emotional eating captures the tendency to eat in response to negative emotions, external eating assesses responsiveness to external food cues such as sight and smell, independent of hunger, and restrained eating measures conscious efforts to restrict food intake in order to control or reduce body weight.

Adverse events (AEs), self-reported episodes of severe hypoglycaemia, and pregnancies were recorded throughout the entire study period.

### 2.4. Objectives and endpoints

The primary objective of the study was to evaluate glycemic control in a real-world clinical setting in adult patients with type 2 diabetes mellitus who had inadequate control on DPP-4i therapy and switched to OS. The corresponding primary endpoint was the absolute change in HbA1c from V1 to V3.

Secondary objectives included the evaluation of changes in body weight, perceived diabetes-related distress, and eating behaviour. Accordingly, secondary endpoints comprised the absolute and relative changes in body weight, the absolute change in DDS scores, and the absolute change in DEBQ scores from V1 to V3.

Additional endpoints included absolute changes from V1 to V3 in waist circumference; BMI; systolic and diastolic blood pressure; lipid parameters, including total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides; serum creatininemia and estimated glomerular filtration rate (eGFR).

Glycemic outcomes were further evaluated at V3 by assessing the proportion of patients who achieved the following targets: HbA1c $< 7\%$, HbA1c $< 6.5\%$, a reduction in HbA1c $\geq 1\%$, a weight reduction $\geq 3\%$, a weight reduction $\geq 5\%$, a concomitant reduction in HbA1c $\geq 1\%$ and body weight $\geq 3\%$, and a concomitant reduction in HbA1c $\geq 1\%$ and body weight $\geq 5\%$.

Safety endpoints included AEs, self-reported episodes of severe hypoglycaemia, and pregnancies, all of which were recorded throughout the study period.

### 2.5. Statistical analysis

Continuous variables were described using means, standard deviations (SD), medians, and ranges, while categorical variables were described as absolute counts and percentages.

The sample size needed to assess the primary endpoint of the study – the mean change in HbA1c from V1 to V3 – was calculated using a one-sample *t*-test ($\alpha = 0.05$, power = 90%), based on an expected mean change in HbA1c of 0.46% and a standard deviation of 1.7%. Under these assumptions, 146 patients were required for the primary analysis. Given the observational design and the likelihood of missing data in routine clinical practice it was anticipated that only 75% of patients would have HbA1c data available at V3. Therefore, a total of 195 patients were required to ensure that at least 146 would provide complete data for the primary endpoint.

Analyses were conducted using the Full Analysis Set (FAS), which included all eligible patients who provided informed consent and initiated treatment with OS. Within this population, two pre-defined observation periods were established: the in-study period and the on-treatment period. The in-study period referred to the time during which patients were considered part of the study, regardless of treatment discontinuation ("in-study set"). It began at V1 and ended at the earliest occurrence of either the final visit (V3), withdrawal of informed consent, the last documented contact between the patient and physician (as determined by the investigator for those lost to follow-up), death, or closure of the study site. The on-treatment period, a subset of the in-study period, referred to the time during which patients were actively receiving OS ("on-treatment set"). It also began at V1 and concluded either on the date of the last recorded dose of OS, or upon the occurrence of any of the aforementioned criteria that marked the end of the in-study period, whichever came first. To minimize missing data, a 14-day grace period following treatment discontinuation was applied, allowing clinical measurements collected within this window to be included in the on-treatment period.

Demographic and baseline characteristics, as well as safety were described in the FAS population. Analyses of the primary endpoint and the secondary endpoint of body weight were conducted for both the "in-study" and "on-treatment" sets using a linear mixed model for repeated measurements (MMRM). The model included baseline HbA1c, baseline BMI, visit timing, and age as covariates, and sex, diabetes duration, and concomitant use of anti-hyperglycaemic or weight management medications as fixed effects. Study site was included as a random effect when appropriate. An unstructured covariance matrix was used to model within-subject variability; if the model failed to converge, a compound symmetry structure was applied. Results were presented as estimated mean changes from baseline with corresponding two-sided 95% confidence intervals (CI) and p-values. All statistical tests were two-sided with a significance threshold of 0.05. No adjustments were made for multiple comparisons.

All remaining endpoints were summarized descriptively in the FAS population. Missing data were not imputed. All analyses were conducted using SAS, Version 9.4 (SAS Institute, Cary, NC).

## 3. Results

### 3.1. Study disposition

Study disposition is illustrated in Fig. 1. Briefly, a total of 300 patients were screened for the study. Of these, 3 patients did not sign the informed consent form, and 16 did not meet the eligibility criteria. Consequently, 281 patients were enrolled and included in the FAS population.

Within the FAS, 14 patients (5.0%) did not complete the study, and 32 patients (11.4%) discontinued OS treatment. Of those who discontinued treatment, 27 patients nonetheless completed the study by attending the V3.

Accordingly, a total of 267 patients (95.0%) completed the study, and 240 patients were still on OS treatment at V3. Additionally, a total of 238 intermediate visits (V2.X) were conducted, with an average of two intermediate visits per patient.

### 3.2. Patient characteristics at baseline

At baseline (V1), patients in the FAS population had a mean (±SD) age of 67.5 years (±12.0; range 27.0–91.0), and the majority were male (55.9%). The mean duration of type 2 diabetes mellitus was 13.2 years (±8.3), with slightly more than 60% of patients had been living with the disease for over ten years.

The mean HbA1c at baseline was 8.2% (±0.8), and the mean body weight was 77.7 kg (±15.6). On the basis of the BMI, more than 70% of patients were classified as overweight or obese.

In terms of diabetes-related distress, 34.5% of patients reported high levels, 21.0% moderate levels, and 44.6% low levels of distress in the total domains of DDS. When analyzing subdomains, the emotional burden and treatment regimen categories showed a higher percentage of patients reporting high distress with respect to those reporting moderate or low levels. Conversely, in the domains related to physician interaction and interpersonal relationships, the majority of patients reported low distress, suggesting a greater impact of the emotional and therapeutic regimen-related factors on diabetes-related distress.

All baseline characteristics are detailed in Table 1.

### 3.3. Concomitant diabetes medication and OS dosage

Prior to switching to OS, all patients were receiving DPP-4i, either as

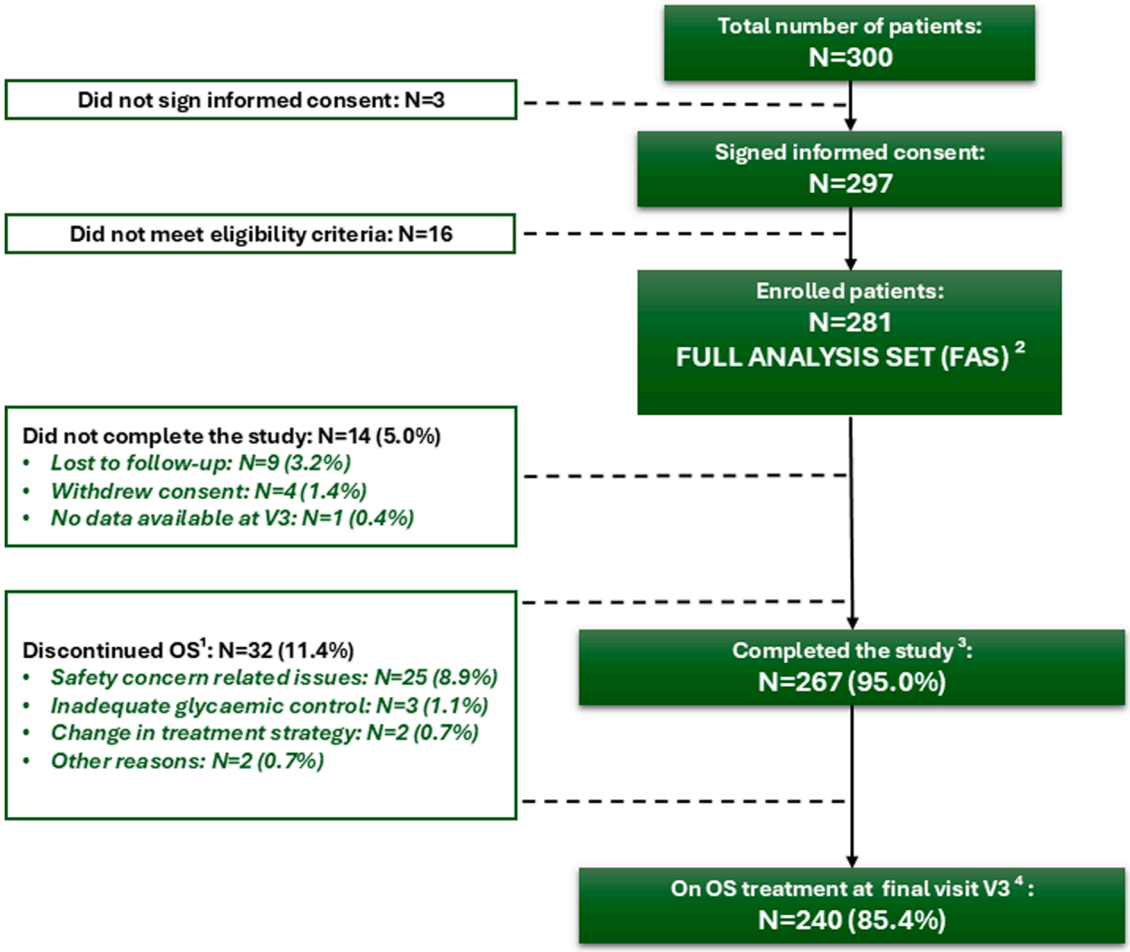


**Fig. 1. Study disposition.** Note: [1] Discontinuation of OS treatment does not imply non-completion of the study (27 patients who discontinued OS completed the study, while 5 patients did not). [2] FAS included all eligible patients who signed the informed consent and initiated treatment with OS. [3] Includes patients who started OS and attended V3, regardless of treatment discontinuation. Five patients attended V3 slightly outside the protocol-defined window (36–44 weeks), but as the deviations were only by a few days, they were included in the analysis. [4] Includes patients who started OS and were still on treatment at V3. All percentages are based on FAS. Abbreviations: OS, oral semaglutide; FAS, Full analysis set.

monotherapy or in combination with other antidiabetic agents, administered as free or fixed-dose regimens (Supplemental Table S1). Concomitant glucose-lowering therapies included biguanides (27.0%), sulfonylureas (11.7%), sodium-glucose cotransporter-2 inhibitors (SGLT2i) (7.5%), thiazolidinediones (3.2%), meglitinides (1.4%), alpha-glucosidase inhibitors (0.4%), and fixed-dose combinations (46.3%) (Supplemental Table S1).

At the time of switching, all 281 patients initiated OS treatment at a dose of 3 mg/day, in accordance with the Summary of Product Characteristics (SmPC). After one month, all patients were escalated to 7 mg/day, except for 20 patients who remained on 3 mg/day. Following at least one month on 7 mg/day, 73 patients were further escalated to 14 mg/day, while the remaining 187 patients continued on 7 mg/day. One patient reported an intermediate dose by alternating daily doses between 3 mg and 7 mg. Consequently, at V3, 187 patients (66.5%) were receiving 7 mg/day, 73 patients (26.0%) were on 14 mg/day, 20 patients (7.1%) remained on 3 mg/day, and one patient maintained an alternating dosing schedule. The primary reason for switching was to improve glycemic control (N = 274, 97.5%), followed by weight reduction (N = 98, 34.9%), management of cardiovascular risk factors (N = 93, 33.1%), management of hypoglycaemia associated with previous therapies (N = 20, 7.1%), and simplification of the existing treatment regimen (N = 4, 1.4%).

### 3.4. HbA1c and body weight

HbA1c significantly decreased ($p < 0.0001$) from V1 to V3 in both the "in-study set" and the "on-treatment set", with a change of –0.7% ±0.05 and –0.7%±0.06, respectively (Fig. 2A, 2B).

Body weight also significantly decreased ($p < 0.0001$) in both sets, with an absolute change of –3.6 ± 0.22 kg in the "in-study set", and –3.9 ± 0.28 kg in the "on-treatment set" (Fig. 2C, 2D).

The percentage of patients achieving predefined HbA1c and body weight targets are presented in Fig. 2E.

### 3.5. Patient-reported outcomes: DDS and DEBQ

Mean DDS scores decreased across all domains of the survey from V1 to V3, including the total score and the subscales of emotional burden, physician-related distress, regimen-related distress, and interpersonal distress, suggesting a reduction in diabetes-related distress across multiple aspects of life (Supplemental Table S2). Importantly, when DDS scores were categorized into low (<2.0), moderate (2.0–2.9), and high distress (≥3.0), the proportion of patients in the low and moderate distress categories increased from V1 to V3, while the proportion in the high distress category decreased. This trend was observed in both the total score and all DDS subscales, appearing most marked in the emotional burden and regimen-related distress domains (Fig. 3).

**Table 1**
Baseline patient characteristics in FAS population.

| Characteristic | | Statistics N = 281 |
|---|---|---|
| Gender | Female | 124 (44.1) |
| | Male | 157 (55.9) |
| Age, years | Mean (SD) | 67.5 (12.0) |
| | Median (Min, Max) | 70.0 (27.0, 91.0) |
| Age groups, years | <45 | 16 (5.7) |
| | [45–65) | 79 (28.1) |
| | [65–75) | 100 (35.6) |
| | ≥75 | 86 (30.6) |
| Type 2 diabetes mellitus duration, years | Mean (SD) | 13.2 (8.3) |
| | Median (Min, Max) | 12.4 (0.0, 38.8) |
| Type 2 diabetes mellitus duration, categorized, years | ≤ 1 | 9 (3.2) |
| | (1 – 5] | 43 (15.3) |
| | (5–10] | 56 (19.9) |
| | >10 | 173 (61.6) |
| Patients with medical history | | 252 (89.7) |
| | CV related medical history [a] | 232 (82.6) |
| | Chronic kidney disease | 51 (18.1) |
| Diabetes-related complications | Diabetic Retinopathy | 20 (7.1) |
| | Diabetic Neuropathy | 21 (7.5) |
| Other disease | | 91 (32.4) |
| HbA1c, % | Mean (SD) | 8.2 (0.8) |
| | Median (Min, Max) | 7.9 (7.5, 12.0) |
| HbA1c, mmol/mol | Mean (SD) | 66.1 (8.5) |
| | Median (Min, Max) | 62.8 (58.5, 107.7) |
| Body weight, kg | Mean (SD) | 77.7 (15.6) |
| | Median (Min, Max) | 76.0 (41.7, 139.0) |
| Height, cm | Mean (SD) | 165.6 (9.3) |
| | Median (Min, Max) | 165.0 (140.5, 193.0) |
| BMI, kg/m$^2$ | Mean (SD) | 28.3 (4.9) |
| | Median (Min, Max) | 27.4 (18.0, 45.9) |
| BMI categories, kg/m$^2$ | < 18.5 | 1 (0.4) |
| | [18.5 – 25) (Normal weight) | 73 (26.0) |
| | [25.0–30) (Overweight) | 118 (42.0) |
| | ≥ 30.0 (Obesity) | 89 (31.7) |
| Waist circumference, cm, N = 244 | Mean (SD) | 100.7 (13.8) |
| | Median (Min, Max) | 100.0 (68.0, 147.0) |
| Systolic Blood Pressure, mmHg, N = 279 | Mean (SD) | 130.8 (15.3) |
| | Median (Min, Max) | 130.0 (90.0, 200.0) |
| Diastolic Blood Pressure, mmHg, N = 279 | Mean (SD) | 77.7 (8.6) |
| | Median (Min, Max) | 80.0 (50.0, 100.0) |
| Total cholesterol, mg/dL, N = 259 | Mean (SD) | 163.1 (38.7) |
| | Median (Min, Max) | 161.0 (83.0, 287.0) |
| LDL, mg/dL, N = 241 | Mean (SD) | 86.9 (34.1) |
| | Median (Min, Max) | 82.0 (14.4, 196.0) |
| HDL, mg/dL, N = 253 | Mean (SD) | 51.4 (15.9) |
| | Median (Min, Max) | 49.0 (17.0, 165.0) |
| Triglycerides, mg/dL, N = 259 | Mean (SD) | 138.3 (68.3) |
| | Median (Min, Max) | 122.0 (35.0, 462.0) |
| Serum creatinine, mg/dL, N = 266 | Mean (SD) | 0.9 (0.3) |
| | Median (Min, Max) | 0.9 (0.5, 2.3) |
| eGFR, mL/min/1.73 m$^2$, N = 266 | Mean (SD) | 78.8 (20.0) |
| | Median (Min, Max) | 82.0 (27.9, 131.8) |
| eGFR categories, mL/min/1.73 m$^2$, N = 266 | <30 | 3 (1.1) |
| | [30 – 60) | 47 (17.7) |
| | [60 – 90) | 136 (51.1) |
| | ≥ 90 | 89 (30.1) |
| DDS total score, N = 267 | Mean (SD) | 2.6 (1.4) |
| | Median (Min, Max) | 2.2 (1.0, 6.0) |
| - *DDS emotional burden score, N = 267* | Mean (SD) | 2.7 (1.4) |
| | Median (Min, Max) | 2.4 (1.0, 6.0) |
| - *DDS physician distress score, N = 267* | Mean (SD) | 2.5 (1.8) |
| | Median (Min, Max) | 1.8 (1.0, 6.0) |
| - *DDS regimen distress score, N = 267* | Mean (SD) | 2.6 (1.3) |
| | Median (Min, Max) | 2.4 (0.8, 6.0) |
| - *DDS interpersonal score, N = 266* | Mean (SD) | 2.4 (1.4) |
| | Median (Min, Max) | 2.0 (1.0, 6.0) |
| DDS total score, categorized [b], N = 267 | Low distress | 119 (44.6) |
| | Moderate distress | 56 (21.0) |
| | High distress | 92 (34.5) |
| - *DDS emotional burden score, categorized [b], N = 267* | Low distress | 97 (36.3) |
| | Moderate distress | 61 (22.8) |
| | High distress | 109 (40.8) |
| - *DDS physician distress score, categorized [b], N = 267* | Low distress | 137 (51.3) |
| | Moderate distress | 40 (15.0) |
| | High distress | 90 (33.7) |
| - *DDS regimen distress score, categorized [b], N = 267* | Low distress | 98 (36.7) |
| | Moderate distress | 66 (24.7) |
| | High distress | 103 (38.6) |
| - *DDS interpersonal score, categorized [b], N = 266* | Low distress | 125 (47.0) |
| | Moderate distress | 53 (19.9) |
| | High distress | 88 (33.1) |
| DEBQ total score, N = 267 | Mean (SD) | 2.5 (0.7) |
| | Median (Min, Max) | 2.4 (1.1, 4.9) |
| - *DEBQ restrained eating score, N = 267* | Mean (SD) | 2.5 (0.8) |
| | Median (Min, Max) | 2.5 (1.0, 5.0) |
| - *DEBQ emotional eating score, N = 267* | Mean (SD) | 2.2 (1.0) |
| | Median (Min, Max) | 2.0 (1.0, 5.0) |
| - *DEBQ external eating score, N = 267* | Mean (SD) | 2.7 (0.9) |
| | Median (Min, Max) | 2.8 (1.0, 4.8) |

Data are presented as: mean (SD) and median (Min, Max) for continuous variables; N (%) for categorical variables, with percentages based on FAS (N = 281 patients, except where indicated). Percentages may not total 100% due to rounding. Notes: *a.* Includes: arteriosclerosis of the coronary arteries, atrial fibrillation, chronic cardiac failure, cardiac valve disease, coronary artery disease, myocardial ischaemia, tachycardia, haemoglobinopathy, dyslipidaemia, hyperuricaemia, cerebrovascular accident, cardiac valve prosthesis, carotid revascularisation, coronary revascularisation, peripheral revascularisation, hypertension, and peripheral arterial occlusive disease. *b* Low distress: DDS score < 2.0, Moderate distress: DDS score 2.0–2.9, High distress: DDS score ≥ 3.0. Abbreviations: FAS, Full Analysis Set; CV, cardiovascular; HbA1c, glycated hemoglobin; BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; eGFR, estimated glomerular filtration rate; DDS, Diabetes Distress Survey; DEBQ, Dutch Eating Behaviour Questionnaire; SD, Standard Deviation; Min, minimum; Max, Maximum.

Mean DEQS scores also decreased from V1 to V3 in the total domain and in the emotional eating and external eating subdomains, suggesting a reduction in eating behaviours triggered by emotions and external cues. In contrast, the restrained eating subdomain remained unchanged between the two visits (Supplemental Table S2).

### 3.6. Other endpoints

Between V1 and V3, patients exhibited several reductions in anthropometric and clinical parameters. Mean waist circumference

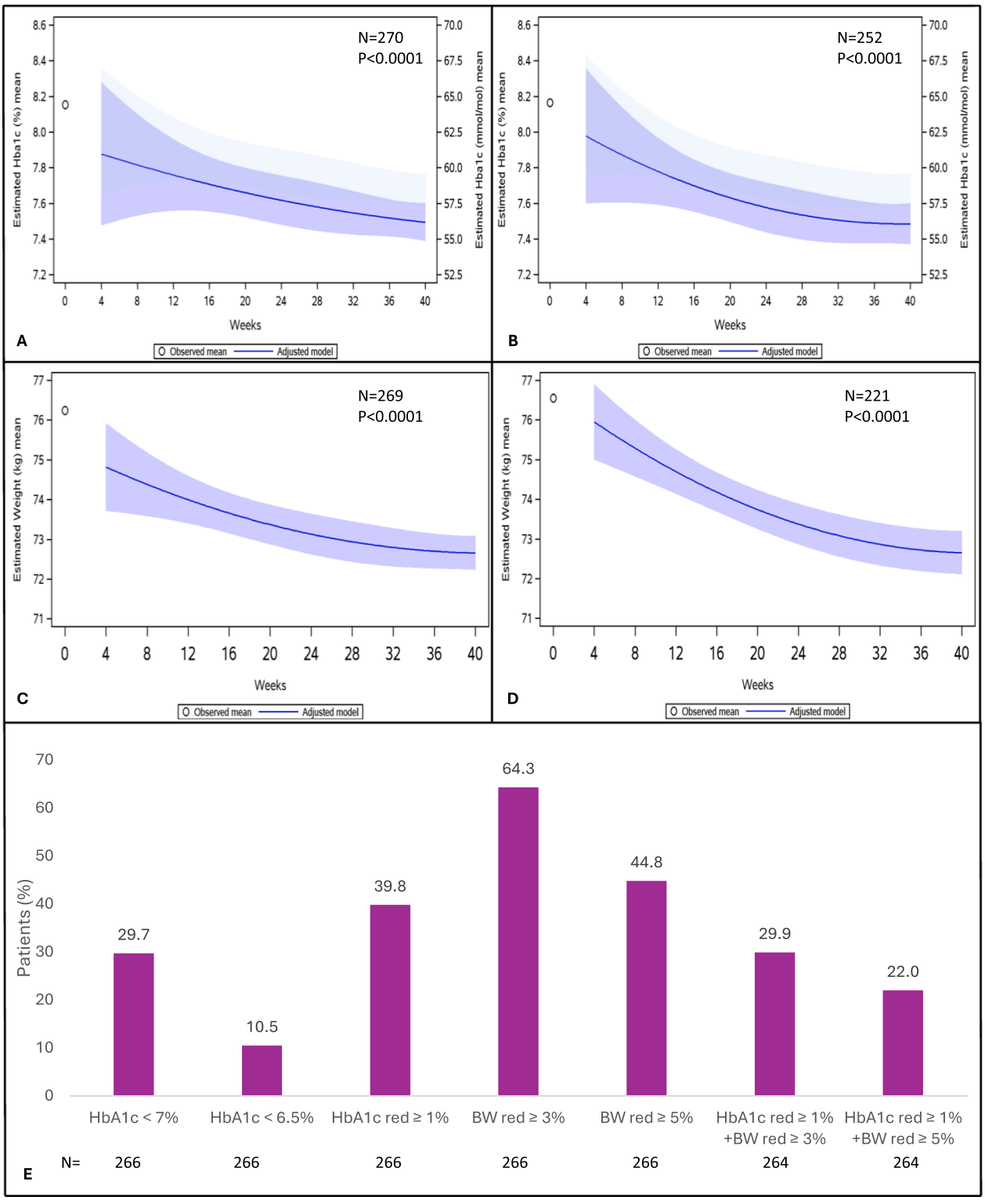


**Fig. 2.** **(A-B)** Estimated mean values of HbA1c from V1 to V3 (week 0 to week 40) in **(A)** the "in-study set" (HbA1c decreased from 8.2%±0.74 [65.9 ± 8.04 mmol/mol] to 7.5% [58.4 mmol/mol]) and **(B)** in the "on-treatment set" (HbA1c decreased from 8.2%±0.74 [66.0 ± 8.13 mmol/mol] to 7.5% [58.3 mmol/mol]). **(C-D)** Estimated mean values of body weight from V1 to V3 in **(C)** the "in-study set" (body weight decreased from 77.5 ± 15.1 kg to 72.7 kg, with relative change of –4.6% ±0.29 [95% CI: –5.21,–4.07]) – and **(D)** in the "on-treatment set" (body weight decreased from 77.3 ± 15.2 kg to 72.7 kg with relative change of –5.0%±0.34 [95% CI: –5.71,–4.35]). The symbol "o" indicates the estimated mean at V1 for patients with at least one post-baseline measurement. The blue line represents the adjusted model, and the outer lines of the band indicate the 95% CI. The model was adjusted for baseline HbA1c, age, baseline BMI, time, and time-squared as covariates, and sex, baseline use of oral antidiabetics, diabetes duration, and site as fixed factors, with random intercept and time (slope). **(E)** Percentage of patients achieving the predefined targets for HbA1c and body weight. Abbreviations: HbA1c, glycated haemoglobin; BW, body weight; BMI, body mass index; CI, confidence interval; red, reduction. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article)

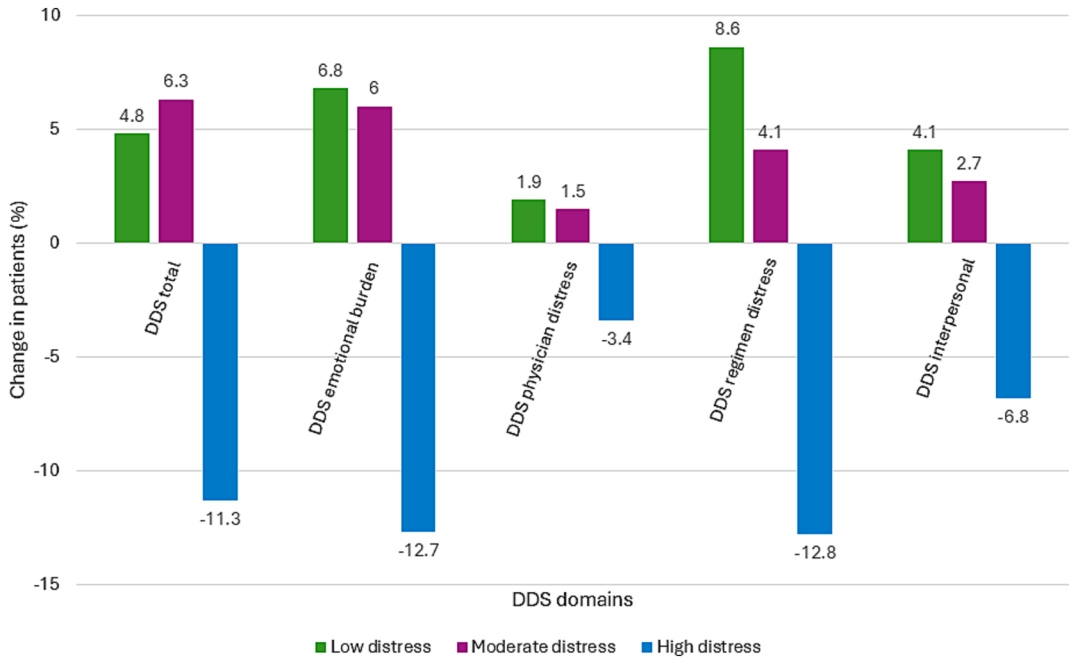


**Fig. 3.** Percentage change in patients from V1 (week 0) to V3 (week 40) within the distress categories (low, moderate, and high) of the DDS domains. Low distress: DDS score < 2.0, Moderate distress: DDS score 2.0–2.9, High distress: DDS score ≥ 3.0. Abbreviations: DDS, Diabetes Distress Survey.

decreased by 3.0 ± 8.6 cm (N = 227), and mean BMI decreased by 1.4 ± 1.4 kg/m$^2$, (N = 266). Systolic and diastolic blood pressure showed mean decreases of 3.2 ± 15.7 mmHg (N = 265) and 1.3 ± 9.6 mmHg (N = 265), respectively. Lipid profiles also improved, with mean reductions in total cholesterol of 13.4 ± 35.5 mg/dL (N = 225), LDL-C of 10.5 ± 31.7 mg/dL (N = 211), and triglycerides of 16.0 ± 55.3 mg/dL (N = 225). Renal function markers remained largely unchanged, with mean serum creatinine showing no change (0.0 ± 0.14 mg/dL, N = 244) and mean eGFR decreasing by 0.4 ± 9.5 mL/min/1.73 m$^2$ (N = 244).

### 3.7. Safety

During the study, 23.1% of patients (N = 65) reported a total of 99 AEs, with only one event classified as a serious AE. In terms of severity, 76 events were mild, 21 events were moderate, and 2 events were severe. Treatment discontinuations due to AEs occurred in 25 patients (8.9%). The most frequently affected system organ class (SOC) was "gastrointestinal disorders", reported in 14.9% of participants (N = 42; 59 events), with the most common events being nausea (26 events), vomiting (13 events), and abdominal pain (5 events). This was followed by SOC "injury, poisoning and procedural complications" (N = 11; 3.9%), "general disorders and administration site conditions" (N = 5; 1.8%), and "metabolism and nutrition disorders" (N = 5; 1.8%).

No severe hypoglycaemia episodes occurred, and no pregnancies were reported during the study.

## 4. Discussion

The effectiveness of OS in glycemic control and body weight reduction has been consistently demonstrated in both randomized controlled trials [1–10] and real-world studies [21–29]. The DOORS study contributes further evidence by specifically evaluating OS effectiveness in adults with type 2 diabetes mellitus inadequately controlled on DPP-4i, who subsequently switched to OS.

The PIONEER 7 trial [7] and its extension [11], which comprised patients switching from sitagliptin to OS in a controlled setting, reported a mean HbA1c reduction of 0.2%, with no significant difference between treatment arms. However, a significantly greater proportion of patients in the OS group achieved HbA1c < 7.0% compared with those continuing sitagliptin (52.6% vs 28.6%), and achieved significantly greater mean weight loss (–2.4 kg vs –0.9 kg). Although without a comparator group, the DOORS study extends these findings in a real-world context. After 40 weeks of treatment, mean HbA1c decreased by 0.7% ($p < 0.0001$), with 64% of patients reaching the < 7.0% threshold, and mean body weight decreased by 3.6 kg ($p < 0.0001$). When compared with data from the PIONEER REAL program [23–27], which documented reductions in HbA1c ranging from –0.7% to –1.2% after 34–44 weeks of OS therapy, the HbA1c reduction observed in our study is positioned at the lower bound of this range. This finding may be related to the specific prior therapy. Bonora et al. [21] demonstrated that the absence of previous DPP-4i treatment is associated with greater HbA1c reductions when switching to OS. Accordingly, more modest glycemic improvements can be anticipated in patients transitioning from DPP-4i therapy. In line with this, Candido et al. [22] found HbA1c significantly decreased by –0.4% over 6 months in patients switching from DPP-4i to OS. However, both these studies were retrospective and may be limited by incomplete data collection and selection bias (e.g., missing data, exclusion of patients not tolerating OS).

Beyond clinical outcomes, the DOORS study explored patient-reported outcomes, highlighting important psychosocial aspects of diabetes care. In this study, DDS and DEBQ questionnaires provided valuable insights. Reductions were observed across all domains of diabetes distress (emotional burden, physician-related distress, regimen-related distress, and interpersonal distress), with particularly marked improvements in emotional burden and regimen-related distress. Patients classified as highly distressed at baseline decreased in number, while those in moderate or low categories increased, indicating an overall improvement in psychological well-being.

Such improvements are of critical importance. Indeed, high levels of diabetes distress are known to correlate with poor glycemic control, suboptimal self-care, reduced diabetes self-efficacy, impaired quality of life, increased cardiovascular risk, and higher mortality [20,30,31].

Importantly, many patients with type 2 diabetes mellitus experience significant distress due to the challenges of managing their condition [20,32,33]. In turn, high distress levels have been shown to be predictors of lower medication adherence [34]. Interestingly, the greatest

reduction in this study was observed in regimen-related distress, with a 12.8% decrease in patients classified as highly distressed at V3 compared with V1, suggesting greater acceptance of OS therapy over prior treatment and potentially improved adherence, which may in turn support more favourable clinical outcomes. This finding is in line with the PIONEER 7 trial, which showed higher treatment satisfaction and a preference for OS over sitagliptin. It confirms that, even though both DPP-4i and OS are oral therapies, patients showed a preference for OS, further reinforced by the observed reduction in distress after the switch.

Eating behaviour also improved. Specifically, emotional and external eating scores decreased, suggesting reduced susceptibility to food intake triggered by emotions or external stimuli, while restrained eating remained unchanged. This pattern may be attributed to the mechanism of action of OS, which, by mimicking endogenous GLP-1, modulates central appetite regulation by increasing satiety, suppressing appetite and food cravings, and reducing the preference for high-fat, energy-dense foods [35].

From our perspective, these findings are highly relevant, as they suggest that treatment may influence psychological and behavioural factors, which in turn could contribute to improved clinical outcomes. Notably, the American Diabetes Association [36,37] recommends routine assessment and management of diabetes distress and disordered eating as part of clinical practice to guide targeted interventions, such as diabetes self-management education and support, ultimately fostering more patient-centred diabetes care.

Consistent with expectations [21–29], favourable changes were also observed in anthropometric and cardiometabolic parameters, including waist circumference, BMI, blood pressure, and lipid profiles. Although no inferential statistical analyses were conducted, these improvements are particularly relevant for patients with type 2 diabetes mellitus, in whom hypertension, dyslipidaemia, and obesity substantially contribute to cardiovascular risk [38].

Safety findings were consistent with prior studies, in which AE rates ranged from 10% to 58% [21–29]; in our cohort, approximately 23% of patients reported AEs, predominantly gastrointestinal in nature. Importantly, no episodes of hypoglycaemia were observed.

Although novel, of clinical value, and with the unique advantage of a prospective design, this study has some limitations. First, its observational, single-arm design without a control group may have introduced bias, making it difficult to exclude the influence of factors other than treatment on the observed outcomes. Indeed, because the decision to switch to OS preceded enrolment, patients included in the study may have had specific clinical characteristics, motivations, or personal preferences that influenced the magnitude of the observed improvements. Moreover, baseline HbA1c levels and regression to the mean may also have contributed to the observed changes. Second, data were collected during routine clinical practice, which may have introduced variability and missing data. Third, hypoglycaemic events were recorded based on patient recall, potentially resulting in recall bias. Finally, some endpoints – including DDS, DEBQ, and clinical parameters other than HbA1c and body weight – were not subjected to inferential statistical testing, reducing the strength of conclusions in these outcomes. Nonetheless, the broad inclusion criteria improved the representativeness of this real-world population, enhancing the generalizability of the findings, especially on amelioration of diabetes distress.

## 5. Conclusion

In conclusion, OS demonstrated a favourable safety profile and effectiveness in glycemic control, weight reduction, and cardiometabolic parameters in patients with type 2 diabetes mellitus switching from DPP-4i in a real-world scenario. Importantly, improvements in diabetes-related distress and eating behaviours were also observed, suggesting a potential role of treatment also in psychological well-being of patients with type 2 diabetes mellitus.

## 6. Data and Resource Availability

The data that support the findings of this study are available from Novo Nordisk A/S but restrictions apply to the availability of these data, which were used under license for the current study and therefore are not publicly available. Data are however available from the authors upon reasonable request and with permission of Novo Nordisk A/S.

## Author Contributions

A.Giaccari contributed to conceptualization, methodology, data curation, investigation, data interpretation, supervision and the preparation and original draft preparation. F.Borroni, M.Dauriz, D.Gioia, M. Barbagallo contributed to investigation and validation. P.Baptiste contributed to methodology, data curation and validation. A.Bisio contributed to conceptualization, methodology, funding acquisition and resources. K.Udupa contributed to methodology and formal analysis. All authors have read and approved the final manuscript.

## Funding and Assistance

This study has been funded by Novo Nordisk S.p.A.

## CRediT authorship contribution statement

**Andrea Giaccari:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Francesca Borroni:** Validation, Investigation. **Marco Dauriz:** Validation, Investigation. **Daniela Gioia:** Validation, Investigation. **Paris Baptiste:** Validation, Methodology, Data curation. **Alessandro Bisio:** Resources, Methodology, Funding acquisition, Conceptualization. **Giusi Lastoria:** Resources, Methodology, Funding acquisition, Conceptualization. **Keerthana Udupa:** Methodology, Formal analysis. **Mario Barbagallo:** Validation, Investigation.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: A. Giaccari has received speaker honoraria from Abbott, AstraZeneca, Lilly, Novo Nordisk, and Sanofi. F.Borroni, M.Dauriz, D.Gioia, M.Barbagallo have no competing interests to declare that are relevant to the content of this article. P.Baptiste, G.Lastoria, K.Udupa work at Novo Nordisk, and A.Bisio worked at Novo Nordisk at the time of study conduct and manuscript development.

## Acknowledgement

**Personal Thanks:** The authors sincerely thank Cristina Romano (ASST Sette Laghi, Varese), Uberto Pagotto (IRCCS Policlinico S. Orsola, Bologna), Paolo Marzullo (A.O.U. Maggiore della Carità, Novara), Rocco Bulzomì (Casa della Salute Santa Caterina della Rosa, Roma), Gianluca De Morelli (P.O. Praia a Mare, Cosenza), Fabio Vescini (Ospedale S. Maria della Misericordia, Udine), Roberto Anichini (Ospedale San Jacopo, Pistoia), Loredana Rizzo (Ospedale della Misericordia di Grosseto), Luigia Miretto (ASL Caserta), Daniele Pantaleo (Centro Diabetologico ASL Lecce, Nardò), Gianluigi Vendemiale (A.O.U. "Policlinico Riuniti", Foggia), Massimiliano Anzaldi (A.O. Emergenza Cannizzaro, Catania), Fabrizio Querci (Ospedale Pesenti Fenaroli, Alzano Lombardo), Giancarla Meregalli (Ospedale di Treviglio, Bergamo), and Elena Tortato (INRCA, Ancona) for their contribution. The authors also thank Clariscience S.r.l. for their assistance with medical writing, and Amale Chalfoun for believing in this project.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2026.113244.

## References


[1] 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;42:1724–32. https://doi.org/10.2337/dc19-0749.

[2] Rodbard HW, Rosenstock J, Canani LH, et al. Oral Semaglutide Versus Empagliflozin in patients with Type 2 Diabetes Uncontrolled on Metformin: the PIONEER 2 Trial. Diabetes Care 2019;42:2272–81. https://doi.org/10.2337/dc19-0883.

[3] Rosenstock J, Allison D, Birkenfeld AL, et al. Effect of additional Oral Semaglutide vs Sitagliptin on Glycated Hemoglobin in adults with Type 2 Diabetes Uncontrolled with Metformin Alone or with Sulfonylurea: the PIONEER 3 Randomized Clinical Trial. J Am Med Assoc 2019;321:1466. https://doi.org/10.1001/jama.2019.2942.

[4] Pratley R, Amod A, Hoff ST, et al. Oral semaglutide versus subcutaneous liraglutide and placebo in type 2 diabetes (PIONEER 4): a randomised, double-blind, phase 3a trial. Lancet 2019;394:39–50. https://doi.org/10.1016/S0140-6736(19)31271-1.

[5] Mosenzon O, Blicher TM, Rosenlund S, et al. Efficacy and safety of oral semaglutide in patients with type 2 diabetes and moderate renal impairment (PIONEER 5): a placebo-controlled, randomised, phase 3a trial. Lancet Diabetes Endocrinol 2019;7:515–27. https://doi.org/10.1016/S2213-8587(19)30192-5.

[6] Husain M, Birkenfeld AL, Donsmark M, et al. Oral Semaglutide and Cardiovascular Outcomes in patients with Type 2 Diabetes. N Engl J Med 2019;381:841–51. https://doi.org/10.1056/NEJMoa1901118.

[7] Pieber TR, Bode B, Mertens A, et al. Efficacy and safety of oral semaglutide with flexible dose adjustment versus sitagliptin in type 2 diabetes (PIONEER 7): a multicentre, open-label, randomised, phase 3a trial. Lancet Diabetes Endocrinol 2019;7:528–39. https://doi.org/10.1016/S2213-8587(19)30194-9.

[8] Zinman B, Aroda VR, Buse JB, et al. Efficacy, Safety, and Tolerability of Oral Semaglutide Versus Placebo added to Insulin with or without Metformin in patients with Type 2 Diabetes: the PIONEER 8 Trial. Diabetes Care 2019;42:2262–71. https://doi.org/10.2337/dc19-0898.

[9] Yamada Y, Katagiri H, Hamamoto Y, et al. Dose-response, efficacy, and safety of oral semaglutide monotherapy in Japanese patients with type 2 diabetes (PIONEER 9): a 52-week, phase 2/3a, randomised, controlled trial. Lancet Diabetes Endocrinol 2020;8:377–91. https://doi.org/10.1016/S2213-8587(20)30075-9.

[10] Yabe D, Nakamura J, Kaneto H, et al. Safety and efficacy of oral semaglutide versus dulaglutide in Japanese patients with type 2 diabetes (PIONEER 10): an open-label, randomised, active-controlled, phase 3a trial. Lancet Diabetes Endocrinol 2020;8:392–406. https://doi.org/10.1016/S2213-8587(20)30074-7.

[11] Buse JB, Bode BW, Mertens A, et al. Long-term efficacy and safety of oral semaglutide and the effect of switching from sitagliptin to oral semaglutide in patients with type 2 diabetes: a 52-week, randomized, open-label extension of the PIONEER 7 trial. BMJ Open Diab Res Care 2020;8:e001649. https://doi.org/10.1136/bmjdrc-2020-001649.

[12] Evidence-Based Medicine - StatPearls - NCBI Bookshelf. Accessed July 22, 2025. https://www.ncbi.nlm.nih.gov/books/NBK470182/.

[13] Davies MJ, Aroda VR, Collins BS, Management of hyperglycaemia in type 2 diabetes,, et al. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia 2022;2022(65):1925–66. https://doi.org/10.1007/s00125-022-05787-2.

[14] Mannucci E, Candido R, Monache LD, et al. 2023 update on italian guidelines for the treatment of type 2 diabetes. Acta Diabetol 2023;60:1119–51. https://doi.org/10.1007/s00592-023-02107-x.

[15] Mannucci E, Candido R, Monache LD, et al. Italian guidelines for the treatment of type 2 diabetes. Acta Diabetol 2022;59:579–622. https://doi.org/10.1007/s00592-022-01857-4.

[16] Published online 2022.

[17] Polonsky WH, Fisher L, Earles J, et al. Assessing Psychosocial Distress in Diabetes. Diabetes Care 2005;28:626–31. https://doi.org/10.2337/diacare.28.3.626.

[18] Dakanalis A, Zanetti MA, Clerici M, Madeddu F, Riva G, Caccialanza R. Italian version of the Dutch Eating Behavior Questionnaire. Psychometric proprieties and measurement invariance across sex, BMI-status and age. Appetite 2013;71:187–95. https://doi.org/10.1016/j.appet.2013.08.010.

[19] Van Strien T, Frijters JER, Bergers GPA, Defares PB. The Dutch Eating Behavior Questionnaire (DEBQ) for assessment of restrained, emotional, and external eating behavior. Int J Eat Disord 1986;5:295–315. https://doi.org/10.1002/1098-108X(198602)5:2%3C295::AID-EAT2260050209%3E3.0.CO;2-T.

[20] Fisher L, Hessler DM, Polonsky WH, Mullan J. When is Diabetes Distress Clinically Meaningful? Diabetes Care 2012;35:259–64. https://doi.org/10.2337/dc11-1572.

[21] Bonora BM, Russo G, Leonetti F, et al. Effectiveness of oral semaglutide on glucose control and body weight up to 18 months: a multicenter retrospective real-world study. J Endocrinol Invest 2024;47:1395–403. https://doi.org/10.1007/s40618-024-02309-2.

[22] Candido R, Gaiotti S, Giudici F, et al. Real-World Retrospective Study into the Effects of Oral Semaglutide (As a Switchover or Add-on Therapy) in Type 2 Diabetes. JCM 2023;12:6052. https://doi.org/10.3390/jcm12186052.

[23] Catrina SB, Amadid H, Braae UC, et al. PIONEER REAL Sweden: a Multicentre, prospective, Real-World Observational Study of Oral Semaglutide Use in adults with Type 2 Diabetes in Swedish Clinical Practice. Diabetes Ther 2024;15:2079–95. https://doi.org/10.1007/s13300-024-01614-6.

[24] Jain AB, Reichert SM, Amadid H, et al. Use of once-daily oral semaglutide and associated clinical outcomes among adults with type 2 diabetes in routine clinical practice in Canada: a multicentre, prospective real-world study (PIONEER REAL Canada). Diabetes Obes Metab 2024;26:1799–807. https://doi.org/10.1111/dom.15493.

[25] Kick A, M'Rabet-Bensalah K, Acquistapace F, et al. Real-World use of Oral Semaglutide in adults with Type 2 Diabetes: the PIONEER REAL Switzerland Multicentre, prospective. Observational Study Diabetes Ther 2024;15:623–37. https://doi.org/10.1007/s13300-023-01525-y.

[26] Van Houtum W, Schrömbges P, Amadid H, et al. Real-World use of Oral Semaglutide in adults with Type 2 Diabetes in the PIONEER REAL Netherlands Multicentre, prospective. Observational Study Diabetes Ther 2024;15:1749–68. https://doi.org/10.1007/s13300-024-01588-5.

[27] Saravanan P, Bell H, Braae UC, et al. PIONEER REAL UK: a Multi-Centre, prospective, Real-World Study of Once-Daily Oral Semaglutide Use in adults with Type 2 Diabetes. Adv Ther 2024;41:4266–81. https://doi.org/10.1007/s12325-024-02973-z.

[28] Yabe D, Hamamoto Y, Kawanami D, et al. PIONEER REAL Japan: Primary results from a multicenter, prospective, real-world study of oral semaglutide in adults with type 2 diabetes in Japanese clinical practice. J Diabetes Investig 2024;15:1566–77. https://doi.org/10.1111/jdi.14291.

[29] Suzuki R, Amadid H, Major-Pedersen A, Yabe D. PIONEER REAL Japan: Baseline characteristics of a multicenter, prospective, real-world study of oral semaglutide in adults with type 2 diabetes in clinical practice in Japan. J of Diabetes Invest 2024;15:1047–56. https://doi.org/10.1111/jdi.14219.

[30] Winchester RJ, Williams JS, Wolfman TE, Egede LE. Depressive symptoms, serious psychological distress, diabetes distress and cardiovascular risk factor control in patients with type 2 diabetes. J Diabetes Complications 2016;30:312–7. https://doi.org/10.1016/j.jdiacomp.2015.11.010.

[31] Owens-Gary MD, Zhang X, Jawanda S, Bullard KM, Allweiss P, Smith BD. The Importance of addressing Depression and Diabetes Distress in adults with Type 2 Diabetes. J Gen Intern Med 2019;34:320–4. https://doi.org/10.1007/s11606-018-4705-2.

[32] Fisher L, Skaff MM, Mullan JT, et al. Clinical Depression Versus Distress among patients with Type 2 Diabetes. Diabetes Care 2007;30:542–8. https://doi.org/10.2337/dc06-1614.

[33] Fisher L, Skaff MM, Mullan JT, Arean P, Glasgow R, Masharani U. A longitudinal study of affective and anxiety disorders, depressive affect and diabetes distress in adults with Type 2 diabetes. Diabet Med 2008;25:1096–101. https://doi.org/10.1111/j.1464-5491.2008.02533.x.

[34] Brown SA, García AA, Brown A, et al. Biobehavioral determinants of glycemic control in type 2 diabetes: a systematic review and meta-analysis. Patient Educ Couns 2016;99:1558–67. https://doi.org/10.1016/j.pec.2016.03.020.

[35] Blundell J, Finlayson G, Axelsen M, et al. Effects of once-weekly semaglutide on appetite, energy intake, control of eating, food preference and body weight in subjects with obesity. Diabetes Obes Metab 2017;19:1242–51. https://doi.org/10.1111/dom.12932.

[36] American Diabetes Association. 4. Lifestyle Management. Diabetes Care 2017;40(Supplement_1):S33-S43. doi:10.2337/dc17-S007.

[37] Young-Hyman D, De Groot M, Hill-Briggs F, Gonzalez JS, Hood K, Peyrot M. Psychosocial Care for People with Diabetes: a Position Statement of the American Diabetes Association. Diabetes Care 2016;39:2126–40. https://doi.org/10.2337/dc16-2053.

[38] Cebrián-Cuenca AM, Mata-Cases M, Franch-Nadal J, Mauricio D, Orozco-Beltrán D, Consuegra-Sánchez L. Half of patients with type 2 diabetes mellitus are at very high cardiovascular risk according to the ESC/EASD: data from a large Mediterranean population. Eur J Prev Cardiol 2022;28:e32–4. https://doi.org/10.1093/eurjpc/zwaa073.