

Real-World Effectiveness of Once-Weekly Semaglutide in Glycemic Control and Weight Outcomes in Type 2 Diabetes



<https://sciencehub.novonordisk.com/adces2023/Tan1.html?cid=qr-Oxiri3ny47>

Xi Tan¹, Victoria Divino², Josh Noone¹, James Amamoo¹, Lin Xie¹, Katharine Coyle², Cory L. Gamble¹, Mico Guevarra¹, Yurek Paprocki¹, Aaron A. King³

Aims

- Assess the relationships between semaglutide once weekly for type 2 diabetes (semaglutide OW T2D) and changes in glycated hemoglobin (HbA_{1c}) and weight.
- Compare the changes in HbA_{1c} and weight associated with initiating semaglutide OW T2D vs initiating dipeptidyl peptidase-4 inhibitors (DPP-4i).

Introduction

- In the SUSTAIN clinical trial program, semaglutide OW T2D achieved superior glycemic control and weight loss compared with other glucagon-like peptide-1 receptor agonists (GLP-1 RAs).¹
- However, there is limited evidence of the effectiveness of semaglutide OW T2D in achieving HbA_{1c} goals and weight loss in a real-world T2D population.

Methods

- This observational cohort database study evaluated patients during the selection window (01 Jan 2018 to 30 Apr 2021). The databases were IQVIA's PharMetrics® Plus and Ambulatory Electronic Medical Records (AEMR).
- Inclusion criteria included age ≥18 years, at least 2 filled prescription claims for semaglutide OW T2D (index date = date of first claim), continuous enrollment in PharMetrics® Plus in the pre- and post-index periods (12 months per period), a T2D diagnosis in the pre-index period, available HbA_{1c} and weight values pre- and post-index, and a baseline HbA_{1c} ≥7.0%.

Pre- and post-index analyses

- HbA_{1c} and weight of patients initiating semaglutide OW T2D were assessed descriptively during the pre-index period (baseline) and at the end of the post-index period (follow-up).

- Statistical tests were the paired t-test, Wilcoxon signed-rank test, and McNemar's test.

Inverse probability of treatment weighting (IPTW) analyses

- Patients initiating semaglutide OW T2D with no baseline DPP-4i use were compared with those initiating DPP-4i.
- IPTW adjusted for imbalances in baseline patient characteristics between the semaglutide OW T2D and DPP-4i cohorts. A standardized mean difference (SMD) ≥0.1 (absolute) between baseline characteristics indicated an imbalance.
- Post-IPTW changes in HbA_{1c} and weight were compared between the two patient cohorts. For these comparisons, weighted t-tests, Wilcoxon rank-sum test, and weighted chi-squared tests were used. To adjust for any remaining imbalanced variables, logistic regression was applied.

Results

Results of pre- and post-index analyses

- For the pre- and post-index analyses, the semaglutide OW T2D cohort comprised 354 patients. The mean age was 53.8 years, 52.5% of patients were male, and most were commercially insured (56.5%) or self-insured (42.1%).
- The mean (SD) HbA_{1c} decreased significantly from 8.8% (1.5%) in the pre-index period to 7.2% (1.4%) in the post-index period for the semaglutide OW T2D cohort (Table 1). In the post-index period, 32.2% achieved HbA_{1c} <6.5% (Table 1).

Table 1. Changes in HbA_{1c} during the pre- and post-index periods for the semaglutide OW T2D cohort

HbA _{1c}	Semaglutide OW T2D cohort (N=354)				p-value
	12-month pre-index period		12-month post-index period		
Baseline/post-index HbA _{1c} (continuous) (%)					
Mean (SD)	8.8% (1.5%)		7.2% (1.4%)		<0.0001
Median	8.4%		6.9%		<0.0001
Baseline/post-index HbA _{1c} (categorical) (n, %)					
HbA _{1c} <6.5%	0	0%	114	32.2%	<0.0001
HbA _{1c} ≥6.5% to <7.0%	0	0%	72	20.3%	
HbA _{1c} ≥7.0% to <8.0%	128	36.2%	88	24.9%	
HbA _{1c} ≥8.0% to <9.0%	97	27.4%	40	11.3%	
HbA _{1c} ≥9.0%	129	36.4%	40	11.3%	
Baseline/post-index HbA _{1c} (binary) (n, %)					
HbA _{1c} <7.0%	0	0%	186	52.5%	<0.0001
HbA _{1c} ≥7.0%	354	100%	168	47.5%	

Post-index values measured at 12 months post-index (360 days post-index ± 90 days, taking the value closest (absolute) to day 360).

- Most patients (74.9%) experienced weight loss; 34.2% achieved a reduction of ≥5.0% (Table 2).

Table 2. Changes in weight during the pre- and post-index periods for the semaglutide OW T2D cohort

Weight	Semaglutide OW T2D cohort (N=354)				p-value
	12-month pre-index period		12-month post-index period		
Baseline/post-index weight (kg) (continuous)					
Mean (SD)	108.7 (24.1)		104.5 (24.4)		<0.0001
Median	106.2		101.0		0.012
Difference between baseline and post-index weight (kg)					
Mean (SD)					-4.3 (6.7)
Median					-3.0
Patients with weight reduction (n, %)					265 74.9%
≥5.0% reduction in weight (n, %)					121 34.2%
≥10.0% reduction in weight (n, %)					48 13.6%
≥15.0% reduction in weight (n, %)					17 4.8%

Results of the IPTW analyses

- A total of 267 patients and 431 patients made up the pre-IPTW semaglutide OW T2D and DPP-4i cohorts, respectively. Post-IPTW, the totals were 251 and 417, respectively (Table 3).
- Post-IPTW mean ages were 54.3 years for the semaglutide OW T2D cohort and 54.7 years for the DPP-4i cohort, and 58.1% and 55.0% of patients in the semaglutide OW T2D and DPP-4i cohorts, respectively, were male (Table 3).
- Post-IPTW characteristics of the semaglutide OW T2D and DPP-4i cohorts were generally well balanced (Table 3).

Table 3. Pre- and post-IPTW characteristics of semaglutide OW T2D and DPP-4i cohorts

Characteristic	Pre-IPTW				Post-IPTW				SMD	
	Semaglutide OW T2D cohort (N=267)		DPP-4i cohort (N=431)		Semaglutide OW T2D cohort (N=251)		DPP-4i cohort (N=417)			
	n	%	n	%	n	%	n	%		
Age (years)										
Mean (SD)	53.4 (9.3)		55.5 (9.9)		54.3 (9.0)		54.7 (9.4)		0.045	
Gender (n, %)										
Male	138	51.7	242	56.1	0.090	146.0	58.1	229.6	55.0	-0.062
Geographic region (n, %)										
Northeast	37	13.9	111	25.8	0.302	48.8	19.4	88.5	21.2	0.044
Midwest	51	19.1	77	17.9	-0.032	47.1	18.8	80.9	19.4	0.016
South	169	63.3	227	52.7	-0.217	145.7	58.0	230.5	55.2	-0.055
West	10	3.7	16	3.7	-0.002	9.6	3.8	17.4	4.2	0.018
Payer type (n, %)										
Commercial	151	56.6	239	55.5	-0.022	143.2	57.0	238.3	57.1	0.003
All other	116	43.4	192	44.5	0.022	108.2	43.0	179.1	42.9	-0.003
CCI										
Mean (SD)	0.9 (1.7)		0.7 (1.5)		-0.084	0.7 (1.5)		0.8 (1.6)		0.063
DCSI										
Mean (SD)	1.0 (1.4)		0.8 (1.3)		-0.128	0.9 (1.3)		0.8 (1.2)		-0.032
Pre-index ADM classes* (n, % (not mutually exclusive))										
Biguanides	205	76.8	364	84.5	0.195	201.2	80.1	347.1	83.2	0.080
Sulfonylurea	71	26.6	148	34.3	0.169	79.7	31.7	135.6	32.5	0.017
Thiazolidinedione	26	9.7	32	7.4	-0.083	19.4	7.7	33.5	8.0	0.013
SGLT-2	91	34.1	93	21.6	-0.282	65.9	26.2	110.3	26.4	0.005
Insulin	73	27.3	44	10.2	-0.450	43.7	17.4	66.3	15.9	-0.040

ADM, antidiabetic medication; CCI, Charlson Comorbidity Index; DCSI, Diabetes Complications Severity Index; SGLT-2, sodium-glucose cotransporter-2.

*Only classes that were used by at least 5% of the cohorts before and after IPTW are shown.

- The mean and median decreases in HbA_{1c} were significantly greater for the semaglutide OW T2D cohort than for the DPP-4i cohort (Figure 1A).
- Significantly higher proportions of the semaglutide OW T2D cohort than the DPP-4i cohort achieved post-index HbA_{1c} goals of <7.0% and <6.5% (Figure 1B).
- Mean and median weight reductions were significantly greater for the semaglutide OW T2D cohort (Figure 2A), and this cohort had a significantly higher proportion of patients with ≥5.0% and ≥10.0% weight reductions (Figure 2B).

Figure 1. HbA_{1c} results for semaglutide OW T2D vs DPP-4i cohorts. (A) Post-index mean and median decreases in HbA_{1c} for each cohort. **(B)** Proportions of the semaglutide OW T2D and DPP-4i cohorts that achieved HbA_{1c} goals of <7.0% and <6.5%

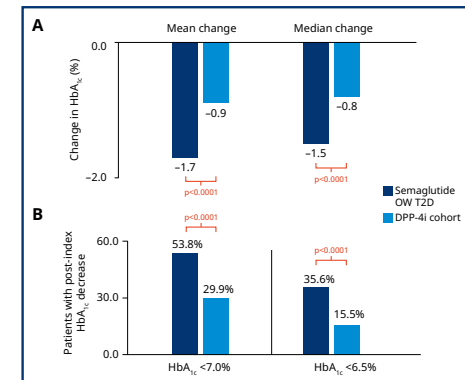
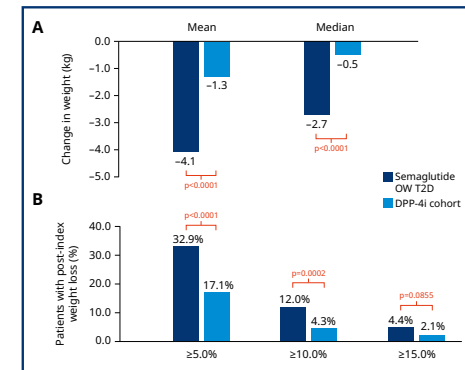


Figure 2. Weight results for semaglutide OW T2D vs DPP-4i cohorts. (A) Post-index mean and median weight changes. **(B)** Proportions with post-index weight reductions



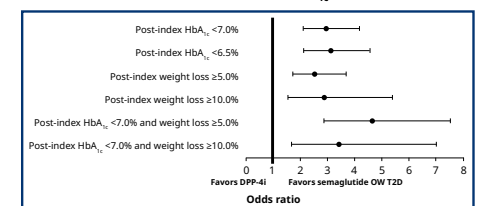
- Compared with the DPP-4i cohort, the semaglutide OW T2D cohort had a significantly greater proportion of patients who achieved composite goals of ≥5.0% and ≥10.0% reduction in weight in combination with a post-index HbA_{1c} <7.0% (Figure 3).

Figure 3. Composite HbA_{1c} and weight changes in the semaglutide OW T2D and DPP-4i cohorts



- Logistic regression analysis showed that semaglutide OW T2D index therapy was associated with higher odds of achieving HbA_{1c} goals and weight loss than DPP-4i index therapy, after adjusting for remaining imbalanced covariates (Figure 4).

Figure 4. Odds ratios from multivariate logistic regression models for post-index changes in HbA_{1c} and weight



Limitations

- The results should be interpreted in the context of limitations including the observational cohort study design, the potential for miscoding or misclassification of claims data, selection bias for patients with frequent healthcare encounters, and a lack of generalizability for Medicaid and Medicare patients.

Conclusions

- These findings demonstrate the real-world effectiveness of semaglutide OW T2D in glycemic and weight control.
- The odds of achieving HbA_{1c} goals and weight loss were more than twice as high with semaglutide OW T2D as index therapy than with DPP-4i as index therapy.
- This study may provide clinicians and diabetes educators with more evidence for incorporating once-weekly semaglutide in T2D management.