Comparing the real-world effects of once-weekly semaglutide and DPP-4is on cardiovascular outcomes, health care resource utilization, and medical costs in individuals with T2D and ASCVD

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Background and Aim

This study compared the time to occurrence of cardiovascular events, health care resource utilization (HCRU), and medical costs in patients with type 2 diabetes (T2D) and atherosclerotic cardiovascular disease (ASCVD) who initiated once-weekly semaglutide vs a dipeptidyl peptidase-4 inhibitor (DPP-4i).

Multiple guidelines and professional societies recommend GLP-1 RAs, which have demonstrated cardiovascular benefit for the treatment of people with T2D and either established ASCVD or multiple risk factors for ASCVD, independent of baseline glucose levels and glycemic control.[1-4]

Recent real-world evidence demonstrates that once-weekly GLP-1 RAs are associated with reduced risk of stroke and myocardial infarction (MI) as well as ASCVD-related and all-cause HCRU and costs compared with DPP-4is.[7]

Results

On average, patients were aged 71 years and had a 5.6-year history of T2D and a 4.3-year history of ASCVD (based on observed diagnosis codes). Average weighted follow-up duration was 10.7 months in both cohorts.

Compared with DPP-4is, semaglutide was associated with 46% lower risk of ischemic stroke (hazard ratio [HR], 0.54; *P*<0.001), 36% lower risk of MI (HR, 0.64; *P*=0.001), and 41% lower risk of their composite (HR, 0.59; *P*<0.001; **Figure 1**).

Users of semaglutide had decreased ASCVD-related and all-cause inpatient (IP) and outpatient (OP) visits but not emergency room (ER) visits (**Data Upon Request**).

- ASCVD-related IP and OP visits were reduced by 22% (HR, 0.78; *P*<0.001) and 12% (HR,0.88; *P*=0.006), respectively.
- All-cause IP and OP visits were reduced by 23% (HR, 0.77; *P*<0.001) and 4% (HR, 0.96; *P*=0.039), respectively.

Compared with DPP-4is, semaglutide was associated with significantly decreased ASCVD-related and all-cause medical costs (**Figure 3**).

- ASCVD-related IP and total medical costs were reduced by 25% (HR, 0.75; *P*<0.001) and 17% (HR, 0.83; *P*=0.009), respectively.
- All-cause IP and total medical costs were reduced by 23% (HR, 0.77; *P*<0.001) and 16% (HR, 0.84; *P*<0.001), respectively.

This study suggests that once-weekly semaglutide, relative to DPP-4is, reduces stroke and MI risks and reduces ASCVD-related and all-cause HCRU and medical costs in adults with T2D and ASCVD.

Figure 1. Clinical Outcomes: Weighted Incidence Rates, Hazard Ratios, and Cumulative Incidence Curves

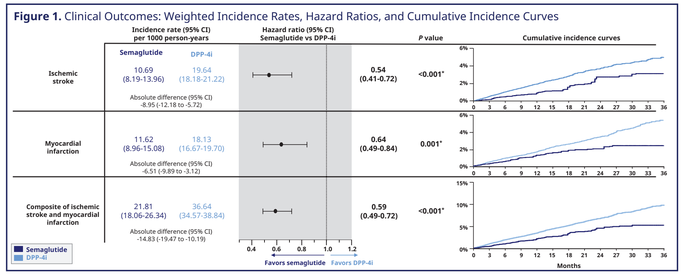
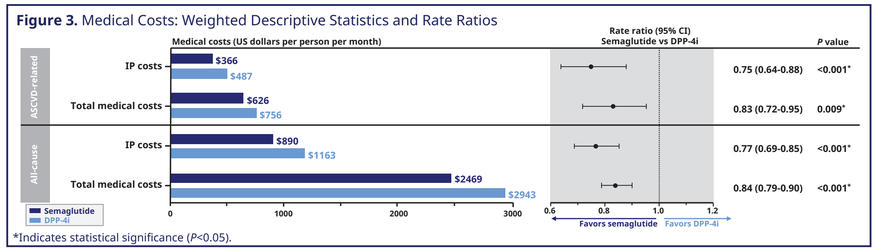


Figure 3. Medical Costs: Weighted Descriptive Statistics and Rate Ratios



*Indicates statistical significance (*P*<0.05).

This real-world evidence complements existing clinical trial results and recent real-world data on once-weekly semaglutide in reducing cardiovascular risks in patients with T2D and ASCVD.

Methods

This was an observational cohort study using data from the Optum® Clinformatics® Data Mart. The study period was from January 1, 2018, to September 30, 2022.

This study compared on-treatment time with incidence of ischemic stroke, MI, and their composite; HCRU; and medical costs in new adult users of once-weekly semaglutide or DPP-4is.

Individuals included in the study were ≥18 years of age on the index date; had a history of ASCVD; had ≥2 T2D diagnoses on different dates during the study period; had ≥1 prescription for the index drug; and used the index drug for ≥90 days (with ≤60-day gaps).

Patients were followed until drug discontinuation, enrollment end, or occurrence of an event.

Table 1. Weighted Key Baseline Characteristics

	Semaglutide (n=14,461)	DPP-4i (n=38,630)	SMD[a]
Sex, No. (%)			
Female	7201 (49.8)	19,374 (50.2)	0.007
Male	7260 (50.2)	19,255 (49.8)	0.007
Continuous variables, mean (SD)			
Age, y	70.3 (10.1)	71.0 (10.3)	0.076
ASCVD duration, y	4.31 (3.90)	4.31 (3.94)	0.002
T2D duration, y	5.64 (4.35)	5.55 (4.28)	0.022
CCI score	2.21 (1.98)	2.24 (1.97)	0.019
DCSI score	3.07 (2.10)	3.09 (2.06)	0.011

ASCVD, atherosclerotic cardiovascular disease; CCI, Charlson Comorbidity Index; DCSI, Diabetes Complications Severity Index; DPP-4i, dipeptidyl peptidase-4 inhibitor; SMD, standardized mean difference; T2D, type 2 diabetes.

[a]SMD≥0.100 is considered statistically significant.

Baseline characteristics were balanced using inverse probability of treatment weighting, generating stabilized average treatment effect weights.

Survival analyses were conducted to compare risks during exposure.

Generalized linear models with quasi-Poisson distribution and log-link function were used to compare HCRU and cost outcomes.

Discussion

In a large sample of US adults with T2D and established ASCVD, real-world data from an administrative claims database demonstrated that semaglutide was associated with a significant reduction in stroke and MI risks compared with DPP-4is.

Semaglutide use was associated with a significant decrease in ASCVD-related and all-cause HCRU and medical costs compared with DPP-4i use, suggesting improved patient outcomes and a potential decrease in health care system burden.

It is important to note that this is an observational study and is therefore limited to assessments of associations, not causality. Further, potential missing data or measurement errors (eg, misclassified billing codes) may limit the interpretation of these findings.

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