Association Between Utilization of Glucagon-Like Peptide-1 Receptor Agonists and Sodium-Glucose Cotransporter-2 Inhibitors and Cardiovascular Events in Medicare Beneficiaries with Type 2 Diabetes

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BACKGROUND

- Cardiovascular disease is a leading cause of morbidity and mortality among patients with type 2 diabetes mellitus (T2DM).[1]
- Glucagon-like peptide-1 receptor agonists (GLP-1 RA) and sodium-glucose cotransporter-2 inhibitors (SGLT2i) have demonstrated significant beneficial effects in T2DM.[2, 3]
- The two classes differ in mechanism of action, administration regimen, and safety/tolerability.[4]
- Both classes have shown cardiovascular (CV) benefits in clinical trials, but it is less clear which patient-level factors are most strongly associated with CV events in the real-world Medicare population.

OBJECTIVE

- To identify clinical and medication related factors associated with cardiovascular events among Medicare beneficiaries with T2DM who initiated either an SGLT2 inhibitor or a GLP-1 receptor agonist during the study period.

METHODS

DATA SOURCE

- Navitus medical and prescription claims database

STUDY DESIGN

- Retrospective analysis of administrative claims data

STUDY POPULATION

- **Inclusion criteria:**
  - Patients with first fill of a GLP1-RA or SGLT2i between 1/1/2023 and 12/31/2024
  - Patients with type 2 diabetes mellitus diagnosis codes
  - Patients with continuous enrollment before (6 months) and during the study (24 months)
- **Exclusion criteria:**
  - Patients utilizing GLP-1 RA for weight loss or non-DM diagnosis codes
  - Patients < 65 years of age
  - Patients without continuous eligibility before and during the study
  - Patients with missing claims or diagnosis codes

OUTCOMES

- The outcomes of interest were risk factors associated with CV events occurring between 1/1/2023 and 12/31/2024 after the initiation of a GLP-1 RA or SGLT2i
- CV events were defined as cerebral infarction, transient cerebral ischemic attack, NSTEMI, STEMI, myocardial infarction, cerebrovascular disease, and intracranial thrombosis

STATISTICAL ANALYSIS

- **Descriptive statistics:** Demographic and clinical characteristics
- **Multivariable logistic regression model:** To identify factors that increase or decrease the odds of CV events among patients with newly prescribed GLP-1 RA or SGLT2i therapies

RESULTS

FIGURE 1: STUDY PERIOD AND MEASURE OF CV EVENTS

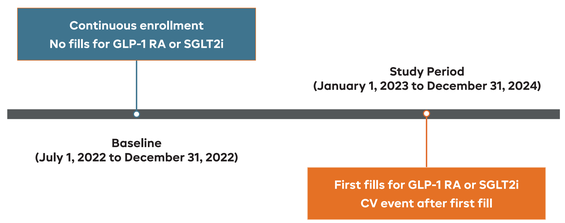


TABLE 1: BASELINE CHARACTERISTICS

	SGLT2i (n=1,211)	GLP-1 RA (n=734)
Age, mean [SD]	77 [8]	75 [7]
Female, n (%)	570 (47.1%)	425 (57.8%)
Proportion of Days Covered (PDC)	0.94 ± 0.15	0.89 ± 0.17
Duration of Therapy, mean [SD]	265 [164]	283 [186]
Average Copay, mean [SD]	9.63 [20]	11.22 [27]
Clinical Conditions		
ASCVD Event	570 (47%)	274 (37%)
Heart Failure (HF)	727 (60%)	276 (38%)
Chronic Kidney Disease (CKD)	553 (46%)	300 (41%)
Charlson Comorbidity Index (CCI)*	6.9 ± 2.3	6.8 ± 2.3

*CCI: weighted scoring system that predicts the 10-year mortality for a patient with a range of chronic health conditions such as heart disease, diabetes, and renal disease, considering a total of 16 categories

FIGURE 2: UTILIZATION OF GLP-1 RA AND SGLT2i WITH CARDIOPROTECTIVE MEDICATIONS

Comparison of GLP-1 RA and SGLT2i utilization with guideline-recommended cardioprotective therapies, including statins, ACEi/ARB agents, and P2Y12i inhibitors

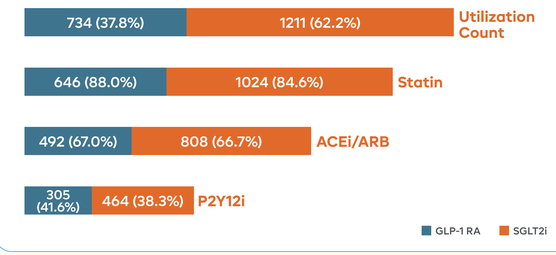


FIGURE 3: DURATION OF SGLT2i AND GLP-1 RA USE BY AGE AND GENDER

Distribution of treatment duration across demographic subgroups, with similar patterns across age groups and gender

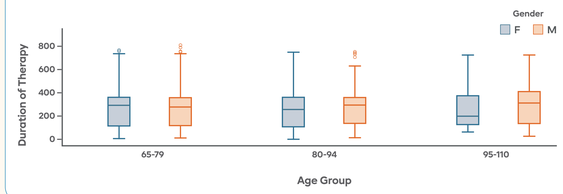


FIGURE 4: PREDICTED HOSPITALIZATION BY DURATION OF THERAPY FOR GLP-1 RA (TOP) AND SGLT2i (BOTTOM)

Early therapy is a critical period for monitoring hospitalization risk, and comorbidities such as HF and ASCVD remain strong predictors of CV outcomes

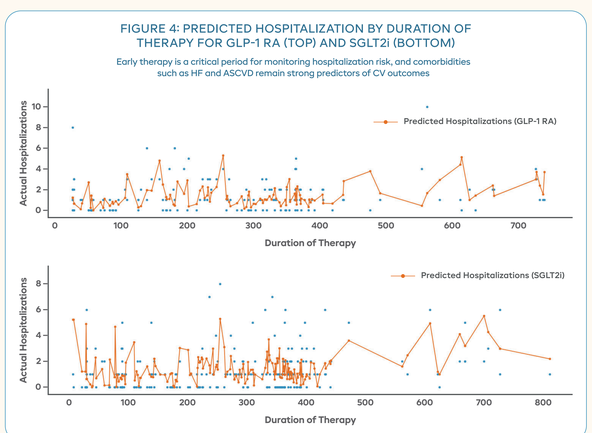
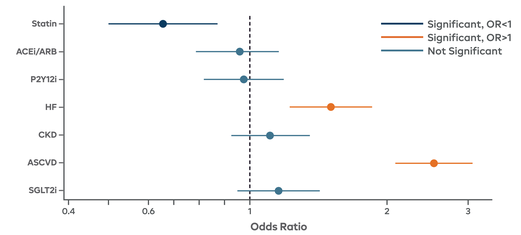


FIGURE 5: ASSOCIATION BETWEEN MEDICATION USE, COMORBIDITIES AND CV EVENTS

Statin use was associated with a **36% reduction** in the odds of a CV event. Significant risk factors include a history of heart failure (HF) and a history of ASCVD. CKD, ACEi/ARB therapy, and P2Y12i use were not significantly associated with CV outcomes. The index medication classes (SGLT2i vs GLP-1 RA) were also not significantly associated with CV events after adjustment for baseline characteristics.



CONCLUSIONS

- In the real-world Medicare population with T2DM, statin use was protective, while heart failure and ASCVD were significant predictors of increased CV event risk.
- Other factors such as ACEi/ARB, CKD, and P2Y12i use were not significantly associated with CV outcomes after adjustment for baseline characteristics.
- These findings suggest that a claims-based risk stratification approach may help managed care organizations identify high-risk patients benefiting from additional targeted interventions.
- Longer-term prospective studies are needed to generalize findings to broader populations.

LIMITATIONS

- The claim-based approach does not capture all the clinical information.
- This analysis is observational; causation cannot be inferred.
- The study results are limited to the Medicare population.

DISCLOSURE

This research was conducted by Navitus Health Solutions, LLC in Madison, WI, without external funding.

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