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Real-World Comparison of Cardiovascular Benefits Between Sodium-Glucose Cotransporter 2 Inhibitors (SGLT-2i) and Glucagon-like Peptide-1 Receptor Agonist (GLP-1RA) Inhibitors in Patients with Type 2 Diabetes (T2D)

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INTRODUCTION

- Type 2 Diabetes (T2D) is a chronic condition that affects millions of people worldwide and is associated with an increased risk of cardiovascular complications, including congestive heart failure, stroke, and peripheral artery disease.[1]
- Sodium-glucose cotransporter-2 inhibitors (SGLT-2i) and glucagon-like peptide-1 receptor agonists (GLP-1RA) are two classes of medications commonly prescribed for the management of T2D.[2]
- While both have been shown to improve glycemic control, studies suggest that they may also have distinct cardioprotective benefits.[3] However, the comparative cardiovascular benefits of these two drug classes remain unclear.

OBJECTIVE

This study examined cardiovascular benefits among patients with T2D newly initiated on SGLT-2i or GLP-1RA using real-world claims data.

METHODS

- **Design:** Retrospective new-user active comparator cohort study comparing GLP-1RA (liraglutide, dulaglutide and semaglutide) users versus SGLT2i (empagliflozin, canagliflozin) users. The index date was defined as the date of the first prescription claim for GLP-1RA or SGLT2i.
- **Data:** The IBM® MarketScan® Commercial Claims Database, which includes comprehensive medical and pharmacy claims data for U.S. residents with employer-sponsored health insurance.
- **Study Population:** Adult patients (≥18 years) with a diagnosis of T2D ([ICD-10-CM] code : E11) who newly initiated either an SGLT-2i or a GLP-1RA between Jan. 1, 2017, and Dec. 31, 2018. Patients were required to have continuous health plan enrollment for at least one year prior to the index date and have no prior use of either study drug class during this period.
- **Time-to-Event Outcome and Censoring**
  - The primary study outcome was the time to the occurrence of a hospitalization for a cardiovascular (CVD) event, which was a composite outcome that included congestive heart failure, stroke, or peripheral artery disease during the two-year follow-up period.
  - Follow-up was censored for the end of the study period (December 31, 2020), index drug discontinuation, switching to the other study drug class, or end of MarketScan enrollment.
- **Statistical Analysis**
  - Baseline patient characteristics, including demographics, comorbidities, and medication use, were measured during the one-year period before the index date.
  - Crude rates for each group were calculated as the number of events per 100 person-years of person-time in follow-up.
  - Cox proportional hazards models were used to compare the rates of cardiovascular events between the two treatment groups. Models were adjusted for demographic characteristics, CVD history, and baseline medication use.

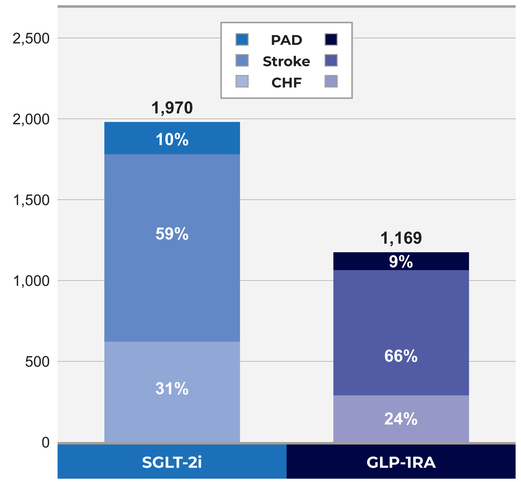
RESULTS

Table 1. Baseline Characteristics

	SGLT-2 Inhibitors (N = 33,189)	GLP-1 Receptor Agonists (N = 52,246)
Mean Age	**54.2**	**53.2**
Sex (%)		
Male	58.5	47.1
Female	41.5	52.9
CVD History (%)		
Congestive Heart Failure	2.3	2.7
Stroke	13.5	11.0
Peripheral artery disease	2.4	2.6
Prior Medication History (%)		
Diuretics	33.1	37.4
Beta-blockers	24.3	24.8
ACEi or ARBs	70.3	70.0
Statins	67.27	64.62
Metformin	74.67	73.02
NOACs	0.83	1.03

Abbreviations: ACEi: Angiotensin-converting enzyme inhibitor; ARBs: Angiotensin II receptor blockers; CVD: Cardiovascular Disease; GLP-1RA: Glucagon-like Peptide-1 Receptor Agonist; NOACs: Non-Vitamin K antagonist oral anticoagulants; SGLT-2i: Sodium Glucose Cotransporter 2 Inhibitors

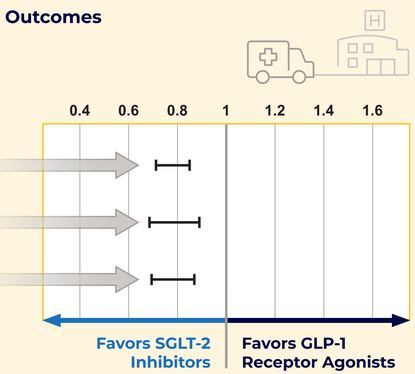
Figure 1. Breakdown of Composite Cardiovascular Events for Patients taking SGLT-1 or GLP-1RA



Abbreviations: CHF: Congestive Heart Failure; GLP-1RA: Glucagon-like Peptide-1 Receptor Agonist; SGLT-2i: Sodium Glucose Cotransporter 2 Inhibitors; PAD: Peripheral artery disease

Table 2. Regression Adjusted Hazard Ratio for Composite Cardiovascular Outcomes

	Incidence rate (per 100 person-years)		HR (95% CI) P-value
	SGLT-2i	GLP-1RA	
Total Population	1.07	1.56	**0.78** (0.71-0.85) **P<0.0001**
Patients without CVD History	2.35	2.7	**0.78** (0.69-0.89) **P<0.0002**
Patients with CVD History	9.34	10.28	**0.77** (0.69-0.87) **P<0.0001**



Abbreviations: CVD: Cardiovascular Disease; CI: Confidence Interval; GLP-1RA: Glucagon-like Peptide-1 Receptor Agonist; HR: Hazard Ratio; SGLT-2i: Sodium Glucose Cotransporter 2 Inhibitors

DISCUSSION

- Baseline characteristics were similar between the two groups except for the difference in gender distribution.
- This real-world study demonstrated a greater cardioprotective benefit for patients with T2D initiating SGLT-2i compared to those initiating GLP-1RA, with a lower rate of cardiovascular events observed in the SGLT-2i group.
- This finding was consistent regardless of patients' prior cardiovascular disease history. The results are in line with previous observational studies, suggesting that SGLT-2i may offer additional cardiovascular benefits beyond glycemic control.

LIMITATIONS

- A significant limitation of real-world evidence (RWE) is its inability to establish strong causal relationships due to the presence of confounding factors.
- The MarketScan databases primarily consist of data from beneficiaries under large commercial health plans, with a majority of participants in the study being under 65 years of age. Therefore, the applicability of the study's conclusions to individuals over 65 years old, particularly those insured through Medicare, necessitates further investigation.
- The study assumed that different drugs within the same class had identical treatment effects; however, further research is needed to determine if certain drugs within the same class have unique cardioprotective effects.
- Due to the lack of mortality information in MarketScan data, the classic major cardiovascular adverse event (MACE) metric, which includes cardiovascular death, cannot be used as the primary outcome.

CONCLUSIONS

- The real-world data suggest greater cardioprotective benefit for SGLT-2i versus GLP-1RA users.
- These findings may be useful for clinical decision-making but should also be weighed against the potential risk of adverse events associated with SGLT-2i.

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DISCLOSURES

The authors have no financial disclosures.