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# Sodium–Glucose Cotransporter-2 Inhibitors Versus Glucagon-like Peptide-1 Receptor Agonists and the Risk for Cardiovascular Outcomes in Routine Care Patients With Diabetes Across Categories of Cardiovascular Disease

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## Visual Abstract. SGLT2 Inhibitors Versus GLP-1 RAs in Patients With and Without CVD.

In this population-based cohort study, sodium–glucose cotransporter-2 (SGLT2) inhibitors were found to have greater reduction in heart failure admissions than glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in patients with and without cardiovascular disease. There was no difference in benefit between both drugs on the outcomes of myocardial infarction or stroke. The findings suggest that preferential use of SGLT2 inhibitors over GLP-1 RAs in patients with diabetes—regardless of presence of cardiovascular disease—can reduce hospitalization for heart failure.

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## Background:

Both sodium–glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have shown cardiovascular benefits in placebo-controlled trials of patients with type 2 diabetes (T2D) and established cardiovascular disease (CVD).

**Objective:**

To evaluate whether SGLT2 inhibitors and GLP-1 RAs are associated with differential cardiovascular benefit among T2D patients with and without CVD.

**Design:**

Population-based cohort study.

**Setting:**

Medicare and 2 U.S. commercial claims data sets (April 2013 to December 2017).

**Participants:**

1:1 propensity score–matched adult T2D patients with and without CVD (52 901 and 133 139 matched pairs) initiating SGLT2 inhibitor versus GLP-1 RA therapy.

**Measurements:**

Primary outcomes were myocardial infarction (MI) or stroke hospitalization and hospitalization for heart failure (HHF). Pooled hazard ratios (HRs) and

rate differences (RDs) per 1000 person-years were estimated, with 95% CIs, controlling for 138 preexposure covariates.

## **Results:**

The initiation of SGLT2 inhibitor versus GLP-1 RA therapy was associated with a slightly lower risk for MI or stroke in patients with CVD (HR, 0.90 [95% CI, 0.82 to 0.98]; RD, -2.47 [CI, -4.45 to -0.50]) but similar risk in those without CVD (HR, 1.07 [CI, 0.97 to 1.18]; RD, 0.38 [CI, -0.30 to 1.07]). The initiation of SGLT2 inhibitor versus GLP-1 RA therapy was associated with reductions in HHF risk regardless of baseline CVD in patients with CVD (HR, 0.71 [CI, 0.64 to 0.79]; RD, -4.97 [CI, -6.55 to -3.39]) and in those without CVD (HR, 0.69 [CI, 0.56 to 0.85]; RD, -0.58 [CI, -0.91 to -0.25]).

## **Limitation:**

Treatment selection was not randomized.

## **Conclusion:**

Use of SGLT2 inhibitors versus GLP-1 RAs was associated with consistent reductions in HHF risk among T2D patients with and without CVD, although the absolute benefit was greater in patients with CVD. There were no large differences in risk for MI or stroke among T2D patients with and without CVD.

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