Clinical Outcomes Following GLP-1 Receptor Agonist Initiation With Versus Without Background SGLT2 Inhibitor Therapy in Heart Failure with Preserved Ejection Fraction and Type 2 Diabetes: A Propensity-Matched Real-World Analysis

Abstract

Background: SGLT2 inhibitors (SGLT2i) improve heart failure outcomes, and GLP-1 receptor agonists (GLP-1 RA) confer cardiometabolic benefit. However, outcomes after GLP-1 RA initiation according to background SGLT2i use remain uncertain.

Methods: Using TriNetX, we compared GLP-1 RA initiation in patients with HFpEF and type 2 diabetes with versus without background SGLT2i. Cohorts were propensity-matched 1:1 and followed for one year, with 60-day landmark analyses.

Results: Among 27,988 matched pairs, background SGLT2i was associated with lower one-year all-cause mortality (HR 0.66, 95% CI 0.61–0.71) and major adverse cardiovascular events (MACE; HR 0.78, 95% CI 0.73–0.84; both P < 0.001). Landmark analyses were consistent for ACM (HR 0.68, 95% CI 0.63–0.75) and MACE (HR 0.83, 95% CI 0.77–0.91).

Conclusions: In HFpEF with type 2 diabetes, GLP-1 RA initiation on a background of SGLT2i therapy was associated with lower mortality and MACE than initiation without SGLT2i.

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Clinical Outcomes Following GLP-1 Receptor Agonist Initiation With Versus Without Background SGLT2 Inhibitor Therapy in HFpEF and Type 2 Diabetes: A Propensity-Matched Real-World Analysis

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ABSTRACT

Background: SGLT2 inhibitors (SGLT2i) improve heart failure outcomes, whereas GLP-1 receptor agonists (GLP-1 RA) provide cardiometabolic benefits. Outcomes following GLP-1 RA initiation according to background SGLT2i use in HFpEF and type 2 diabetes remain uncertain.

Methods: Using the TriNetX network (82 healthcare organizations; query performed October 27, 2026), we compared GLP-1 receptor agonist (GLP-1 RA) initiation among patients with HFpEF and type 2 diabetes with versus without background SGLT2 inhibitor (SGLT2i) treatment. Cohorts were propensity-score matched 1:1 and followed for one year; a 60-day landmark and a falsification outcome were assessed. Cox proportional hazards regression models were used to estimate hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). Statistical significance was defined as a two-sided p-value < 0.05.

Results: Among 27,988 matched pairs, background SGLT2i treatment was associated with lower one-year all-cause mortality (HR 0.66, 95% CI 0.61–0.71) and major adverse cardiovascular events (MACE; HR 0.78, 95% CI 0.73–0.84; both $P < 0.001$). Associations persisted in 60-day landmark analyses (mortality HR 0.68, 95% CI 0.63–0.75; MACE HR 0.83, 95% CI 0.77–0.91). The negative-control outcome was not statistically significant (HR 1.19, 95% CI 0.97–1.45).

Conclusions: Among patients with HFpEF and type 2 diabetes initiating GLP-1 RA therapy, background SGLT2i treatment was associated with lower mortality and MACE than GLP-1 RA initiation without SGLT2i. These observational findings warrant prospective confirmation.

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Introduction

Heart failure with preserved ejection fraction (HFpEF) commonly coexists with type 2 diabetes (T2DM), obesity, and chronic kidney disease. Randomized trials have demonstrated that SGLT2 inhibitors (SGLT2i) reduce worsening-heart-failure events in HFpEF, while GLP-1 receptor agonists (GLP-1 RA) improve cardiometabolic outcomes and, in obesity-related HFpEF, symptoms and physical function [1–8]. The 2023 ESC diabetes guidelines support SGLT2i in patients with T2DM and heart failure; the 2026 ESC heart failure guidelines also address incretin-based therapies for selected patients with obesity-related HFpEF [9,10].

However, these evidence streams do not directly answer whether GLP-1 RA initiation is associated with different clinical outcomes according to background SGLT2i treatment. This comparison is relevant because glucose-lowering regimens may include metformin, DPP-4 inhibitors, or sulfonylureas without the same established HF outcome evidence [10]. Our cohort was not selected using a BMI threshold, although mean BMI was high. We therefore compared one-year mortality and major adverse cardiovascular events (MACE) following GLP-1 RA initiation in patients with HFpEF and T2DM with versus without background SGLT2i.

METHODS

Data Source

We conducted a retrospective cohort study using TriNetX, a federated global research collaborative network providing de-identified electronic health record (EHR) data from 82 participating healthcare organizations (HCOs). The study query and analyses were performed on October 27, 2026. This study was exempt from institutional review board review because it used de-identified data under the HIPAA Privacy rule.

We identified adult patients (aged ≥18 years) with heart failure with preserved ejection fraction (HFpEF; ICD-10-CM I50.3), a documented left ventricular ejection fraction (LVEF) ≥50%, and type 2 diabetes mellitus (T2DM; ICD-10-CM E11) between January 1, 2015, and October 10, 2025. Patients were stratified into two cohorts based on baseline SGLT2i use: those receiving SGLT2i therapy and those not receiving SGLT2i therapy. Both cohorts subsequently initiated GLP-1 RAs therapy. The index date was defined as one day after the initiation of GLP-1 RA therapy in both cohorts. The primary outcomes of this study were all cause mortality and major adverse cardiovascular events (MACE) which includes myocardial infarction, ischemic stroke, and death. The secondary outcomes include ischemic stroke, heart failure exacerbation, all-cause hospitalization, acute kidney injury, atrial fibrillation/flutter, and pulmonary hypertension. All the outcomes were followed at one year after the index event. To reduce

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confounding, 1:1 nearest-neighbor propensity score matching (PSM) was performed on demographic, clinical, medication, and laboratory variables (Table 1). An absolute standardized mean difference <0.1 indicated adequate balance. Baseline characteristics were assessed during the 12 months before index. Cox models estimated hazard ratios (HRs) and 95% confidence intervals (CIs); two-sided P <0.05 was considered statistically significant. A 60-day landmark analysis assessed robustness after early follow-up, although it cannot fully eliminate time-related or treatment-selection bias. Open wounds of the wrist, hand, or fingers served as a negative-control outcome [11]. Analyses were conducted using TriNetX [12].

RESULTS

Before matching, 32,286 patients were in the background SGLT2i group and 44,780 in the group without background SGLT2i at GLP-1 RA initiation. After 1:1 matching, each group included 27,988 patients. Mean age was approximately 66.7 years, approximately 51% were women, and approximately 21% were Black. All reported covariates achieved standardized differences <0.1 after matching (**Table 1**).

Compared with GLP-1 RA initiation without background SGLT2i, initiation with background SGLT2i was associated with lower all-cause mortality (HR 0.66, 95% CI 0.61–0.71; P < 0.001; **Figure 1**) and MACE (HR 0.78, 95% CI 0.73–0.84; P < 0.001; **Figure 2**).

HF exacerbation (HR 0.85, 95% CI 0.77–0.93; P = 0.001) and all-cause hospitalization or emergency department visits (HR 0.84, 95% CI 0.74–0.94; P = 0.004) were less frequent in the group with background SGLT2i. No statistically significant differences were found for ischemic stroke (HR 0.95, 95% CI 0.84–1.08), acute kidney injury (HR 0.97, 95% CI 0.89–1.04), atrial fibrillation/flutter (HR 1.00, 95% CI 0.90–1.10), or pulmonary hypertension (HR 1.03, 95% CI 0.93–1.14; **Table 2**).

In 60-day landmark analyses, associations remained for mortality (HR 0.68, 95% CI 0.63–0.75) and MACE (HR 0.83, 95% CI 0.77–0.91; both P < 0.001). The negative-control outcome (open wound of wrist, hand, or fingers) was not statistically significant (HR 1.19, 95% CI 0.97–1.45; P = 0.082). Landmarking and negative controls cannot exclude residual confounding or time-related bias.

DISCUSSION

Among 27,988 propensity-matched pairs with HFpEF and T2DM initiating GLP-1 RA therapy, background SGLT2i use was associated with lower one-year all-cause mortality (HR 0.66, 95% CI 0.61–0.71) and MACE (HR 0.78, 95% CI 0.73–0.84). Associations persisted in the 60-day landmark analysis,

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while the negative-control outcome was not statistically significant. These observational associations do not establish causality or pharmacological synergy. The clinical contribution is the comparison of GLP-1 RA initiation with versus without background SGLT2i treatment. DELIVER and EMPEROR-Preserved primarily established reductions in worsening-HF outcomes with SGLT2i [3,4], whereas STEP-HFpEF trials assessed semaglutide predominantly for symptoms, function, and weight in obesity-related HFpEF [6,7]. Neither trial program directly answers our treatment-context-specific mortality and MACE question. The 2023 ESC diabetes and 2026 ESC HF guidelines support evidence-based therapy [9,10], but cannot be taken as randomized proof that the present combination reduces mortality.

Our cohort had no BMI-based eligibility threshold, extending inclusion beyond obesity-restricted trial designs. Nevertheless, mean BMI was approximately 37 kg/m², and the available aggregate data do not establish the number or outcomes of patients without obesity. The findings therefore should not be interpreted as evidence of benefit across BMI categories.

Background SGLT2i use was also associated with fewer EHR-recorded HF exacerbations (HR 0.85, 95% CI 0.77–0.93) and hospitalizations or emergency visits (HR 0.84, 95% CI 0.74–0.94). These outcomes are not equivalent to independently adjudicated trial endpoints and cannot be assumed to explain the mortality association. Other secondary outcomes were not statistically significant.

Complementary pharmacological actions provide a plausible rationale for further investigation. SGLT2i influence renal sodium handling, interstitial fluid balance, and cardiorenal stress, whereas GLP-1 RA improve weight, glycemia, and other cardiometabolic risk factors [2,5,8,13]. These effects may be relevant in our metabolically burdened cohort, in which nearly half of patients had chronic kidney disease. However, the available data do not permit mediation analyses or attribution of the mortality association to a specific mechanism. Residual confounding and treatment-selection bias remain possible despite propensity matching and sensitivity analyses, supporting the need for prospective randomized confirmation.

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Limitations

This retrospective EHR analysis remains subject to coding errors and residual confounding despite matching. HFpEF was identified using a diagnosis code and a documented LVEF ≥50%, without independent clinical adjudication. Drug dose, adherence, discontinuation, and specific GLP-1 RA agent were not fully characterized; deaths outside participating systems may be missed. The index-date definition and baseline treatment exposure require confirmation against the TriNetX export. Follow-up was limited to one year.

Clinical Implications

The findings support further evaluation of GLP-1 RA initiation in patients receiving SGLT2i and highlight the importance of evidence-based cardiometabolic treatment. Clinical decisions should continue to follow established indications; this observational comparison does not establish a causal combination effect.

CONCLUSIONS

In this retrospective cohort of patients with HFpEF and T2DM initiating GLP-1 RA therapy, concomitant background SGLT2i treatment was associated with a 34% lower hazard of all-cause mortality and a 22% lower hazard of MACE over one year compared with no background SGLT2i. These observational associations require prospective confirmation.

ACKNOWLEDGMENT:

The results of this analysis will be simultaneously presented at the American Heart Association Scientific Sessions 2026 in Chicago during the Moderated Digital Poster Session "HFpEF in CKM Syndrome: From Mechanisms to Mitigation of Risk", on November, 8th, at 3:15pm - 4:30pm (Central).

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Conflicts of Interest: Maciej Banach has received research grant(s)/support from Amgen, Daiichi Sankyo, Mylan/Viatris, and Sanofi, and has served as a consultant/received speakers fee from Adamed, Amgen, Daiichi-Sankyo, KRKA, Lilly, Mylan/Viatris, NewAmsterdam, Novartis, Novo-Nordisk, Polpharma, Sanofi, Servier, Sobe, Teva, and Zentiva (not related to current analysis); Agata Bielecka-Dabrowa has served as a consultant/received speakers fee from Lilly and Novo-Nordisk; All other authors have noting to declare.

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Table 1. Baseline Characteristics of Patients With HFpEF and Type 2 Diabetes Receiving SGLT2i + GLP-1 RA vs GLP-1 RA Alone, Before and After Propensity Score Matching

	Before Matching				After Matching			
Characteristic	**SGLT2i + GLP-1 RA**	**GLP-1 RA Alone**	**P Value**	**Std. Diff.**	**SGLT2i + GLP-1 RA**	**GLP-1 RA Alone**	**P Value**	**Std. Diff.**
No. of patients	32,286	44,780			27,988	27,988		
Demographics								
Age, y, mean ± SD	66.5 ± 11.3	66.3 ± 11.5	0.017	0.018	66.7 ± 11.2	66.7 ± 11.5	0.844	0.002
Female	15,732 (48.7)	25,519 (57.0)	<0.001	0.166	14,323 (51.2)	14,264 (51.0)	0.618	0.004
Male	15,580 (48.3)	18,208 (40.7)	<0.001	0.153	12,910 (46.1)	12,972 (46.3)	0.599	0.004
White	20,593 (63.8)	30,101 (67.2)	<0.001	0.072	18,347 (65.6)	18,418 (65.8)	0.527	0.005
Black or African American	6,947 (21.5)	9,288 (20.7)	0.009	0.019	5,837 (20.9)	5,819 (20.8)	0.851	0.002
Comorbidities								
Essential hypertension	26,761 (82.9)	36,485 (81.5)	<0.001	0.037	23,096 (82.5)	23,119 (82.6)	0.798	0.002
Ischemic heart disease	17,584 (54.5)	21,541 (48.1)	<0.001	0.127	14,579 (52.1)	14,586 (52.1)	0.953	0.001
Atrial fibrillation/flutter	10,887 (33.7)	12,935 (28.9)	<0.001	0.104	8,952 (32.0)	8,882 (31.7)	0.525	0.005

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	Before Matching				After Matching			
Characteristic	**SGLT2i + GLP-1 RA**	**GLP-1 RA Alone**	**P Value**	**Std. Diff.**	**SGLT2i + GLP-1 RA**	**GLP-1 RA Alone**	**P Value**	**Std. Diff.**
Chronic kidney disease	15,092 (46.7)	19,705 (44.0)	<0.001	0.055	12,622 (45.1)	12,605 (45.0)	0.885	0.001
End-stage renal disease	1,016 (3.1)	4,081 (9.1)	<0.001	0.251	983 (3.5)	957 (3.4)	0.548	0.005
Neoplasms	7,914 (24.5)	11,014 (24.6)	0.790	0.002	6,898 (24.6)	6,915 (24.7)	0.868	0.001
Nicotine dependence	4,339 (13.4)	5,472 (12.2)	<0.001	0.036	3,584 (12.8)	3,624 (12.9)	0.614	0.004
Socioeconomic/psychosocial risk factors (Z55–Z65)	2,152 (6.7)	2,291 (5.1)	<0.001	0.066	1,645 (5.9)	1,616 (5.8)	0.601	0.004
Heart transplant status	149 (0.5)	136 (0.3)	<0.001	0.026	110 (0.4)	122 (0.4)	0.430	0.007
Medications								
Beta-blockers	21,561 (66.8)	27,247 (60.8)	<0.001	0.124	17,886 (63.9)	17,870 (63.8)	0.888	0.001
Diuretics	23,096 (71.5)	29,203 (65.2)	<0.001	0.136	19,158 (68.5)	19,159 (68.5)	0.993	<0.001
Angiotensin II inhibitors	12,606 (39.0)	13,113 (29.3)	<0.001	0.207	9,383 (33.5)	9,367 (33.5)	0.886	0.001
ACE inhibitors	7,789 (24.1)	10,777 (24.1)	0.851	0.001	6,983 (24.9)	6,934 (24.8)	0.632	0.004
Calcium channel blockers	12,803 (39.7)	18,205 (40.7)	0.005	0.020	11,161 (39.9)	11,065 (39.5)	0.407	0.007

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	Before Matching				After Matching			
Characteristic	**SGLT2i + GLP-1 RA**	**GLP-1 RA Alone**	**P Value**	**Std. Diff.**	**SGLT2i + GLP-1 RA**	**GLP-1 RA Alone**	**P Value**	**Std. Diff.**
Sacubitril	2,861 (8.9)	770 (1.7)	<0.001	0.323	761 (2.7)	761 (2.7)	1.000	<0.001
Valsartan	4,364 (13.5)	2,636 (5.9)	<0.001	0.260	2,069 (7.4)	2,052 (7.3)	0.783	0.002
Spironolactone	8,076 (25.0)	5,719 (12.8)	<0.001	0.317	5,250 (18.8)	5,179 (18.5)	0.441	0.007
Eplerenone	400 (1.2)	190 (0.4)	<0.001	0.090	179 (0.6)	182 (0.7)	0.874	0.001
Finerenone	144 (0.4)	48 (0.1)	<0.001	0.065	57 (0.2)	46 (0.2)	0.278	0.009
Statins	22,615 (70.0)	28,452 (63.5)	<0.001	0.139	18,969 (67.8)	18,892 (67.5)	0.487	0.006
Ezetimibe	2,605 (8.1)	2,419 (5.4)	<0.001	0.107	1,910 (6.8)	1,918 (6.9)	0.893	0.001
Aspirin	11,816 (36.6)	15,949 (35.6)	0.005	0.020	9,863 (35.2)	9,817 (35.1)	0.684	0.003
Clopidogrel	4,770 (14.8)	5,985 (13.4)	<0.001	0.041	3,923 (14.0)	3,930 (14.0)	0.932	0.001
Metformin	11,458 (35.5)	12,742 (28.5)	<0.001	0.151	9,493 (33.9)	9,456 (33.8)	0.741	0.003
Insulin	18,504 (57.3)	24,709 (55.2)	<0.001	0.043	15,738 (56.2)	15,731 (56.2)	0.952	0.001
Laboratory values, mean ± SD								
BMI, kg/m²	36.8 ± 9.2	37.6 ± 9.4	<0.001	0.090	36.9 ± 9.1	37.4 ± 9.3	<0.001	0.051

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	Before Matching				After Matching			
Characteristic	**SGLT2i + GLP-1 RA**	**GLP-1 RA Alone**	**P Value**	**Std. Diff.**	**SGLT2i + GLP-1 RA**	**GLP-1 RA Alone**	**P Value**	**Std. Diff.**
HbA1c, %	7.9 ± 1.9	7.5 ± 1.9	<0.001	0.173	7.8 ± 1.8	7.8 ± 1.9	0.005	0.027
LDL cholesterol, mg/dL	77.1 ± 35.8	80.4 ± 37.0	<0.001	0.089	77.3 ± 35.7	79.7 ± 37.6	<0.001	0.066
HDL cholesterol, mg/dL	41.9 ± 15.7	42.3 ± 17.2	0.025	0.021	42.0 ± 16.0	41.7 ± 16.6	0.053	0.021
Triglycerides, mg/dL	168.7 ± 128.6	160.4 ± 110.8	<0.001	0.069	169.1 ± 128.8	162.8 ± 112.0	<0.001	0.052
C-reactive protein, mg/L	36.4 ± 57.7	38.9 ± 60.6	0.022	0.042	36.3 ± 57.7	38.0 ± 58.4	0.172	0.030
eGFR, mL/min/1.73 m²	61.9 ± 27.8	60.2 ± 30.5	<0.001	0.056	61.9 ± 27.9	61.5 ± 29.5	0.152	0.013
NT-proBNP, pg/mL	2,001.9 ± 4,636.6	2,516.6 ± 6,271.7	<0.001	0.093	1,940.9 ± 4,635.8	2,086.7 ± 5,105.5	0.123	0.030
LVEF, %	62.2 ± 6.8	62.1 ± 7.2	0.311	0.025	62.3 ± 6.8	61.9 ± 7.2	0.035	0.060

Values are n (%) unless otherwise indicated. Laboratory values are mean ± SD among patients with a recorded value. Propensity score matching (1:1) was performed on 38 baseline characteristics; a standardized difference <0.1 indicates adequate balance. Because of the large sample size, small differences can reach statistical significance despite negligible standardized differences.

ACE = angiotensin-converting enzyme; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonist; HFpEF = heart failure with preserved ejection fraction; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro–B-type natriuretic peptide; SGLT2i = sodium-glucose cotransporter 2 inhibitor; Std. Diff. = standardized difference.

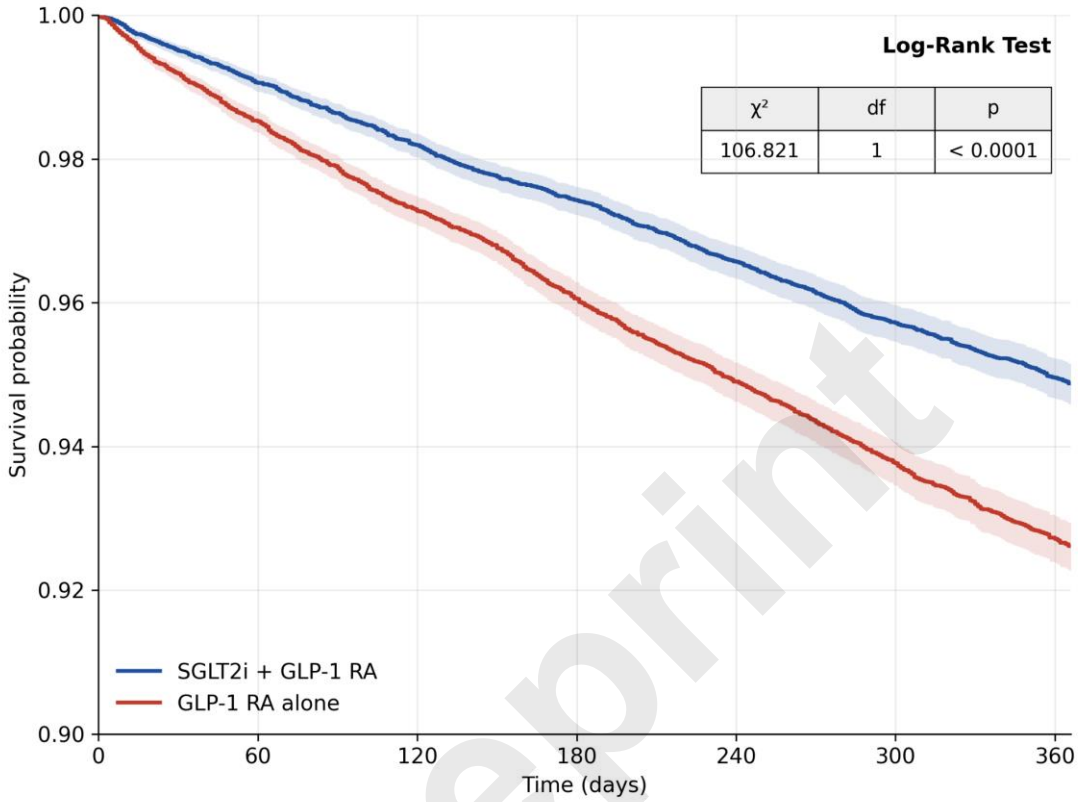
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Table 2. Outcomes of SGLT2i + GLP-1 RA vs GLP-1 RA Alone in Propensity Score–Matched Patients with HFpEF and Type 2 Diabetes

Outcome	HR (95% CI)	P Value
All-cause mortality	0.66 (0.61–0.71)	<0.001
Major adverse cardiovascular events	0.78 (0.73–0.84)	<0.001
Ischemic stroke	0.95 (0.84–1.08)	0.485
Heart failure exacerbation	0.85 (0.77–0.93)	0.001
All-cause hospitalization or ED visit	0.84 (0.74–0.94)	0.004
Acute kidney injury	0.97 (0.89–1.04)	0.432
Atrial fibrillation/flutter	1.00 (0.90–1.10)	0.990
Pulmonary hypertension	1.03 (0.93–1.14)	0.468
Falsification outcome		
Open wound of wrist, hand, and fingers	1.19 (0.97–1.45)	0.082

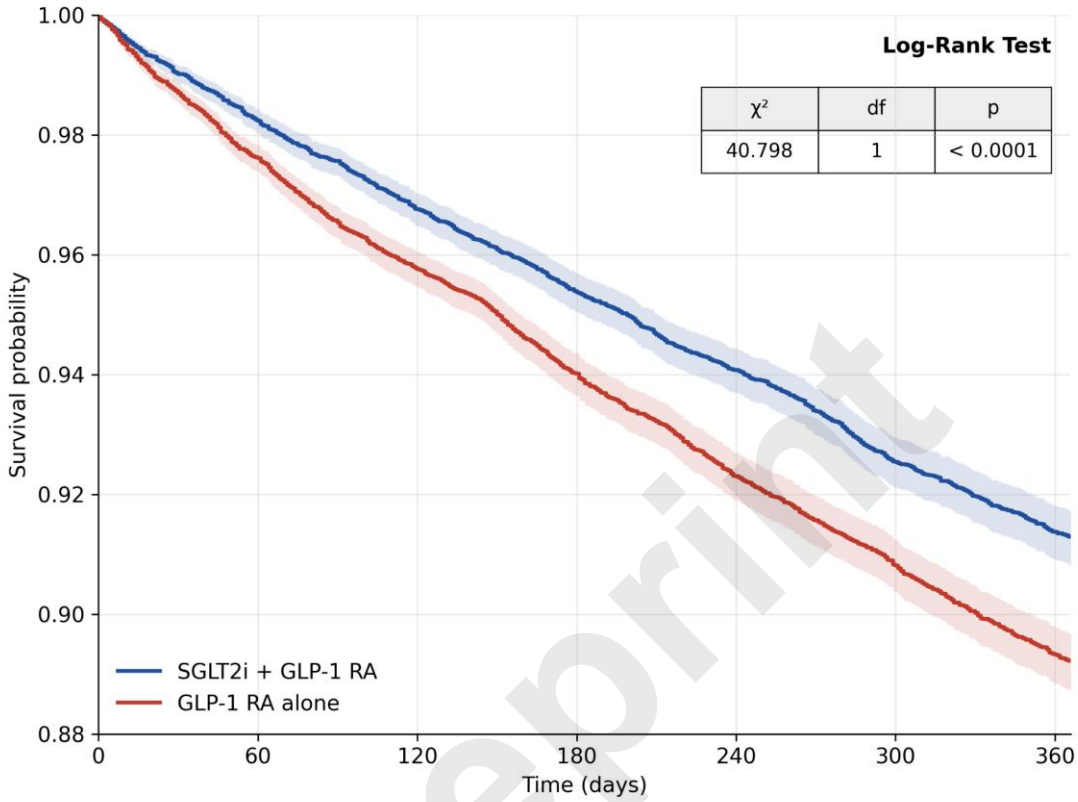
CI = confidence interval; ED = emergency department; GLP-1 RA = glucagon-like peptide-1 receptor agonist; HFpEF = heart failure with preserved ejection fraction; HR = hazard ratio; SGLT2i = sodium-glucose cotransporter 2 inhibitor.

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Figure 1. Kaplan–Meier curves for one-year overall survival (all-cause mortality) after GLP-1 RA initiation with versus without background SGLT2i therapy in propensity score–matched patients with HFpEF and type 2 diabetes. Blue: SGLT2i + GLP-1 RA; red: GLP-1 RA alone. Shaded areas indicate uncertainty intervals displayed in the supplied plots. Log-rank $\chi^2 = 106.821$, df = 1; $P < 0.0001$.



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Figure 2. Kaplan–Meier curves for one-year event-free survival for major adverse cardiovascular events (MACE) after GLP-1 RA initiation with versus without background SGLT2i therapy in propensity score–matched patients with HFpEF and type 2 diabetes. Blue: SGLT2i + GLP-1 RA; red: GLP-1 RA alone. Shaded areas indicate uncertainty intervals displayed in the supplied plots. Log-rank $\chi^2 = 40.798$, df = 1; $P < 0.0001$.

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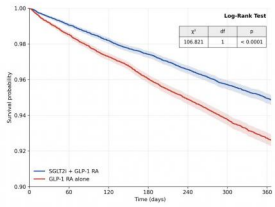
POPULATION & DESIGN

27,988
propensity-matched pairs (1:1)

- HFpEF (LVEF ≥50%) + type 2 diabetes
- All patients **initiating GLP-1 RA**
- Mean age 66.7 y • 51% women • mean BMI ≈37 kg/m²
- PSM on 38 covariates (SMD <0.1)
- Follow-up: 1 year • 60-day landmark • negative-control outcome

SGLT2i + GLP-1 RA
GLP-1 RA started on background SGLT2i

GLP-1 RA alone
GLP-1 RA started without SGLT2i



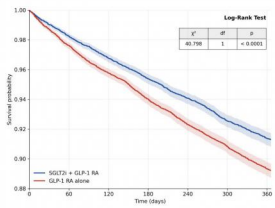
ALL-CAUSE MORTALITY

HR 0.66
95% CI 0.61–0.71 • P<0.001

▼ 34% lower risk

1-y mortality (KM): ≈5.1% vs ≈7.4%

60-day landmark: HR 0.68 (0.63–0.75)



MACE

HR 0.78
95% CI 0.73–0.84 • P<0.001

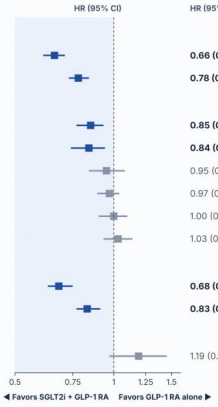
▼ 22% lower risk

1-y MACE (KM): ≈8.7% vs ≈10.7%
MI, ischemic stroke, death

60-day landmark: HR 0.83 (0.77–0.91)

ALL ENDPOINTS – HAZARD RATIOS

ENDPOINT	HR (95% CI)	HR (95% CI)	P
Primary endpoints (1 year)			
All-cause mortality		**0.66 (0.61–0.71)**	**<0.001**
MACE		**0.78 (0.73–0.84)**	**<0.001**
Secondary endpoints			
HF exacerbation		**0.85 (0.77–0.93)**	**0.001**
Hospitalization / ED visit		**0.84 (0.74–0.94)**	**0.004**
Ischemic stroke		0.95 (0.84–1.08)	0.485
Acute kidney injury		0.97 (0.89–1.04)	0.432
Atrial fibrillation / flutter		1.00 (0.90–1.10)	0.990
Pulmonary hypertension		1.03 (0.93–1.14)	0.468
Sensitivity – 60-day landmark			
All-cause mortality		**0.68 (0.63–0.75)**	**<0.001**
MACE		**0.83 (0.77–0.91)**	**<0.001**
Negative control (falsification)			
Open wound wrist/hand/fingers		1.19 (0.97–1.45)	0.082



In HFpEF + T2DM, starting a GLP-1 RA **on top of SGLT2i** was associated with **34% lower all-cause mortality**, **22% fewer MACE**, fewer HF exacerbations and hospitalizations at 1 year – with no excess AKI, AF or stroke. Consistent in 60-day landmark analysis; negative-control outcome neutral.

PRACTICAL MESSAGE

In HFpEF + T2DM, GLP-1 RA initiation **on a background of SGLT2i** was linked to better outcomes than without SGLT2i – supports evidence-based cardiometabolic therapy. Observational data; RCT confirmation needed.

AF, atrial fibrillation; AKI, acute kidney injury; CI, confidence interval; ED, emergency department; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HF, heart failure; HFpEF, HF with preserved ejection fraction; HR, hazard ratio; KM, Kaplan–Meier; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; MI, myocardial infarction; PSM, propensity score matching; SGLT2i, sodium-glucose cotransporter 2 inhibitor; SMD, standardized mean difference; T2DM, type 2 diabetes

Preprint