Observed Cardiovascular Diagnosis Outcome Comparison Among Adult Obese and Type 2 Diabetes Patients With and Without GLP-1 Treatment (2021-2024)

EPH138

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Objective: To describe real-world cardiovascular diagnosis prevalence following treatment index among obese and/or type 2 diabetes (T2D) patients treated with glucagon-like peptide-1 (GLP-1) therapies compared with patients not treated with GLP-1s.

Background

Glucagon-like peptide-1 (GLP-1) agonists are used to treat type 2 diabetes mellitus (T2DM) and obesity by enhancing insulin secretion via the incretin effect. Cardiovascular disease (CVD) remains the leading cause of death in the United States (~20%) [1], and T2DM is associated with a 2–4× higher CVD risk [2]. Randomized trials have shown reduced major adverse cardiovascular events with GLP-1 receptor agonists [3,4], but real-world evidence is limited. This study evaluated real-world cardiovascular outcomes among GLP-1–treated and untreated patients.

Methods

A retrospective analysis of U.S. claims data identified adults with obesity and/or type 2 diabetes (T2D) with claims activity from 2021–2024. Patients were stratified into 2.5 million GLP-1–treated and 13.9 million non–GLP-1–treated cohorts. The index date for GLP-1 patients was the first observed GLP-1 claim; non–GLP-1 patients were assigned imputed index dates based on mean time from diagnosis to GLP-1 initiation within strata of state, age, and sex. All patients required ≥24 months of post-index claims activity. Cohort sizes were balanced using exact stratification matching across sex, age group, state and exact diagnosis (obesity, T2D or both). Cardiovascular outcomes (CO) were defined by diagnosis claims for myocardial infarction, coronary insufficiency, angina, ischemic or hemorrhagic stroke, transient ischemic attack, peripheral artery disease, or heart failure. Demographics, hazard ratios, and per-patient-per-month (PPPM) CO rates were compared between cohorts.

Results

The final matched study population included approximately 2.5 million patients in each group (GLP-1–treated and non–GLP-1).. The cohort was predominantly middle-aged (40–64), female, and located in the Southeast. Hazard ratios indicated a 3% increase per additional year of age (HR 1.03, 95% CI 1.03–1.04) and a lower risk for females (HR 0.82, 95% CI 0.82–0.83; reference = female). Comorbidities of T2D and obesity showed the highest risk (reference = T2D only). Regional hazard ratios (reference = Southeast) were close to 1 with narrow confidence intervals. PPPM CO visits were higher in the control group by 0.044 visits ($p<0.05$). Kaplan–Meier analysis showed a higher probability of CO events in the control vs target group, with a median time to event.

Conclusions

This large real-world study of over 5 million matched patients showed that GLP-1–treated individuals experienced modestly better cardiovascular outcomes than non–GLP-1 users. Despite similar baseline characteristics after matching, GLP-1 use was associated with lower cardiovascular event rates, reduced PPPM visits, and improved event-free survival on Kaplan–Meier analysis. These findings support potential cardioprotective effects of GLP-1 therapies in routine care and are consistent with prior trial evidence, highlighting the value of continued real-world evaluation to further characterize long-term benefits.

Figure 1. Unmatched Cohort Demographics
GLP1 Group younger, with higher female proportion than Non-GLP1 group

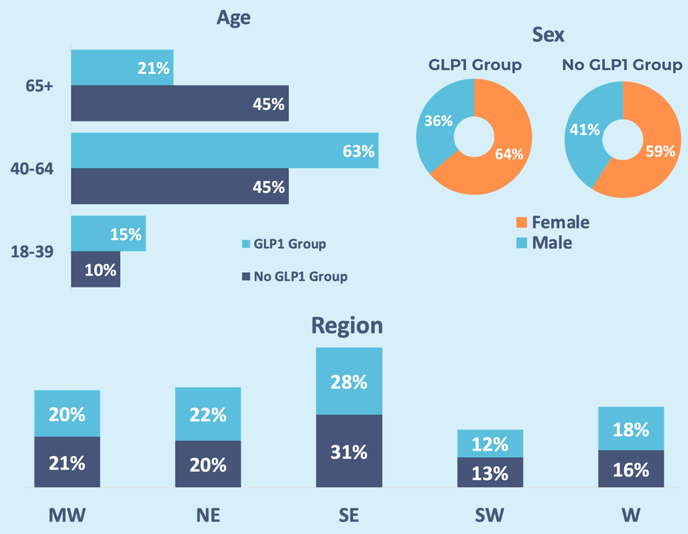


Figure 2. Demographic Comparison Hazard Ratio

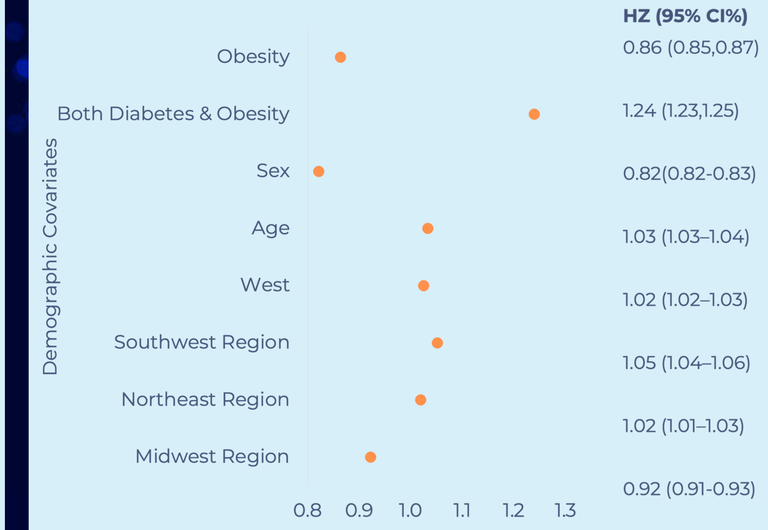
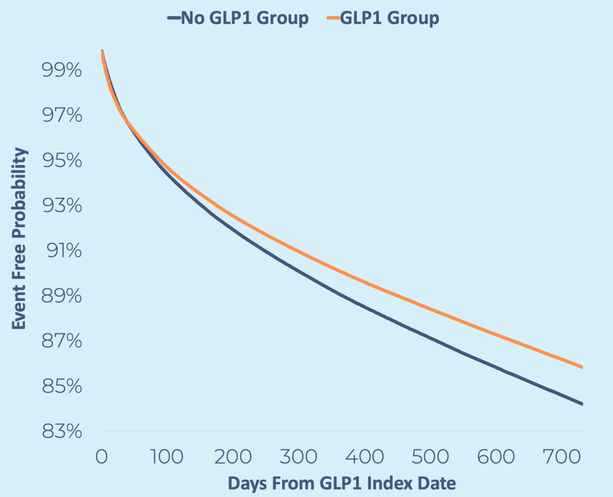


Figure 3. Per Patient Per Month (PPPM) Diagnosis: 2-Year Post–GLP-1 Index Follow-Up

Indication	PPPM (GLP-1 Group)	PPPM (Non-GLP1 Group)	p-value
Atrial Fibrillation/Flutter	0.569	0.624	<0.0001
Hypertension	0.498	0.533	<0.0001
Heart Failure	0.593	0.642	<0.0001
Ischemic Stroke	0.324	0.356	<0.0001
Hemorrhagic Stroke	0.270	0.290	<0.0001
Coronary Artery Disease	0.413	0.424	<0.0001
Peripheral Artery Disease	0.247	0.254	<0.0001
All Indications Above	**0.690**	**0.734**	**<0.0001**

Figure 4. Kaplan Meier Curve: Heart Failure Event-Free Probability Over Time



*Survival curves differ significantly over the 2-year follow-up period (log-rank $p < 0.05$)

Citations

1. Centers for Disease Control and Prevention. Heart Disease Facts. CDC; 2024.
2. Sarwar N, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis. Lancet. 2010.
3. Marso SP, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2016.
4. Marso SP, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2016.