



Risk of Intentional Self-Harm After GLP-1 RA Use Among Patients with Type 2 Diabetes in FDA’s Sentinel Distributed Database

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BACKGROUND

Many glucagon-like peptide-1 receptor agonists (GLP-1RA) are indicated to improve glycemic control in patients with type 2 diabetes mellitus. Postmarketing reports identified a potential risk of suicidal ideation and behavior after use of GLP-1RAs.

OBJECTIVES

We assessed the association between GLP-1RA use and intentional self-harm among a large cohort of health plan members with a diagnosis of type 2 diabetes mellitus in the United States.

METHODS

Using data from 10 Data Partners in the Sentinel Distributed Database from October 1, 2015, through September 30, 2023, we identified health plan members 18 years or older with a diagnosis of type 2 diabetes mellitus who were dispensed GLP-1RAs, sodium-glucose cotransporter-2 inhibitors (SGLT-2i), or dipeptidyl peptidase-4 inhibitors (DPP-4i). We defined treatment episodes based on the number of days supplied per product dispensed with an allowable treatment episode gap of 30 days. We defined intentional self-harm using a validated, administrative claims-based algorithm. To control for confounding, we estimated propensity scores, trimmed distribution areas of non-overlap, truncated scores symmetrically at 1%, and applied inverse probability of treatment weighting of propensity scores. We estimated hazards ratios (HR) and 95% confidence intervals (CI) of the risk of self-harm in users of GLP-1RAs compared to SGLT-2is or DPP-4is, and among subgroups of patients with and without a history of 1) psychiatric events or 2) self-harm.

RESULTS

We identified 1,161,983 GLP-1 RA users, 1,081,155 SGLT-2i users, and 1,396,382 DPP-4i users. After trimming, weighting, and truncating, overall incidence rates of self-harm were 1.13, 1.22, and 1.37 per 1,000 person-years, respectively. Incidence rates were much higher among the subgroup of patients with a history of self-harm(251.80, 397.91, and 234.32 per 1,000 person-years) in the GLP-1 RA, SGLT-2i, and DPP-4i cohorts, respectively. After controlling for confounding, results did not show an increased risk of intentional self-harm among users of GLP-1RAs compared to SGLT-2is (HR: 0.93, 95% CI: 0.81, 1.08) or DPP-4is (HR: 0.94, 95% CI: 0.82, 1.07). Patterns were similar among patients with a history of psychiatric events, a history of self-harm, comorbid obesity, or diabetes.

Figure 1. Number of Users, Person-Years, and Events by Antidiabetic Class

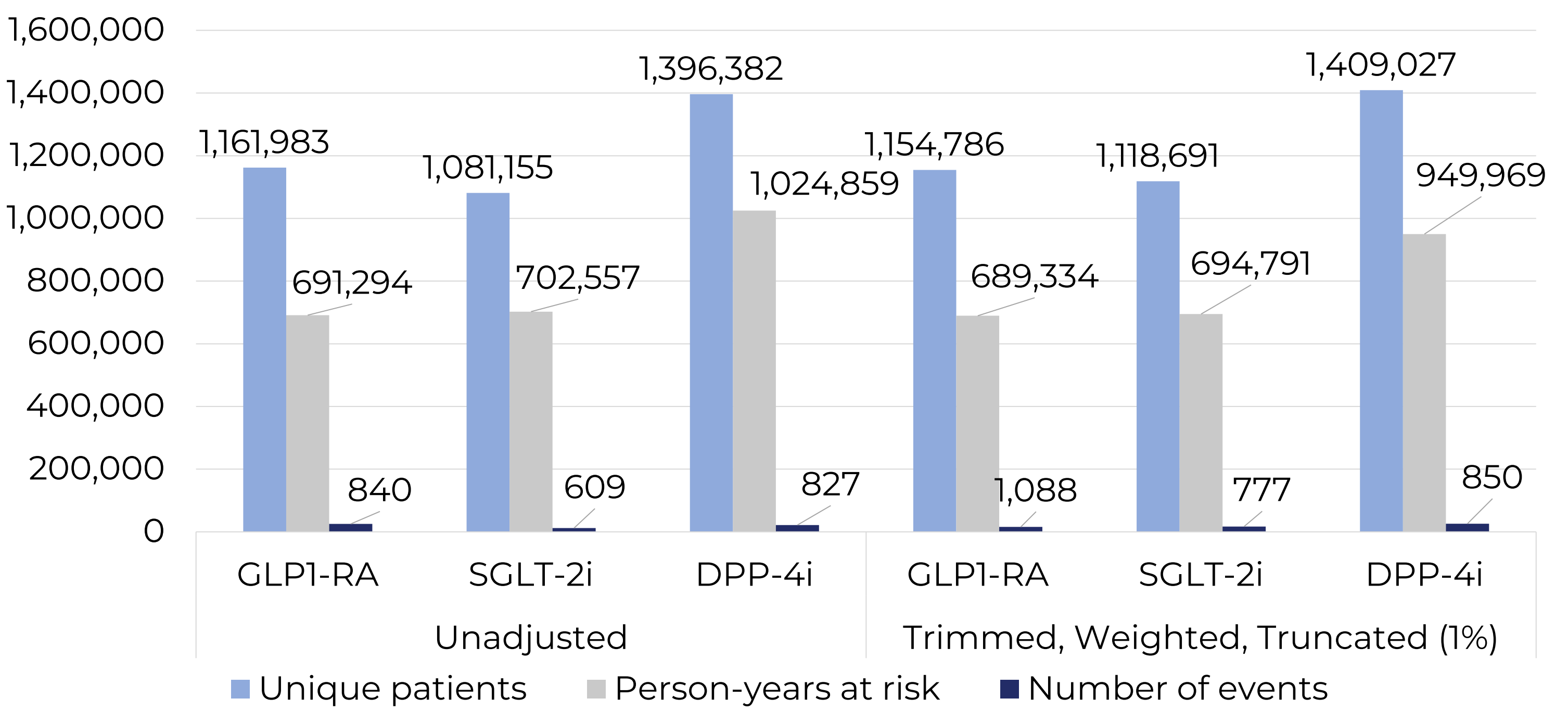
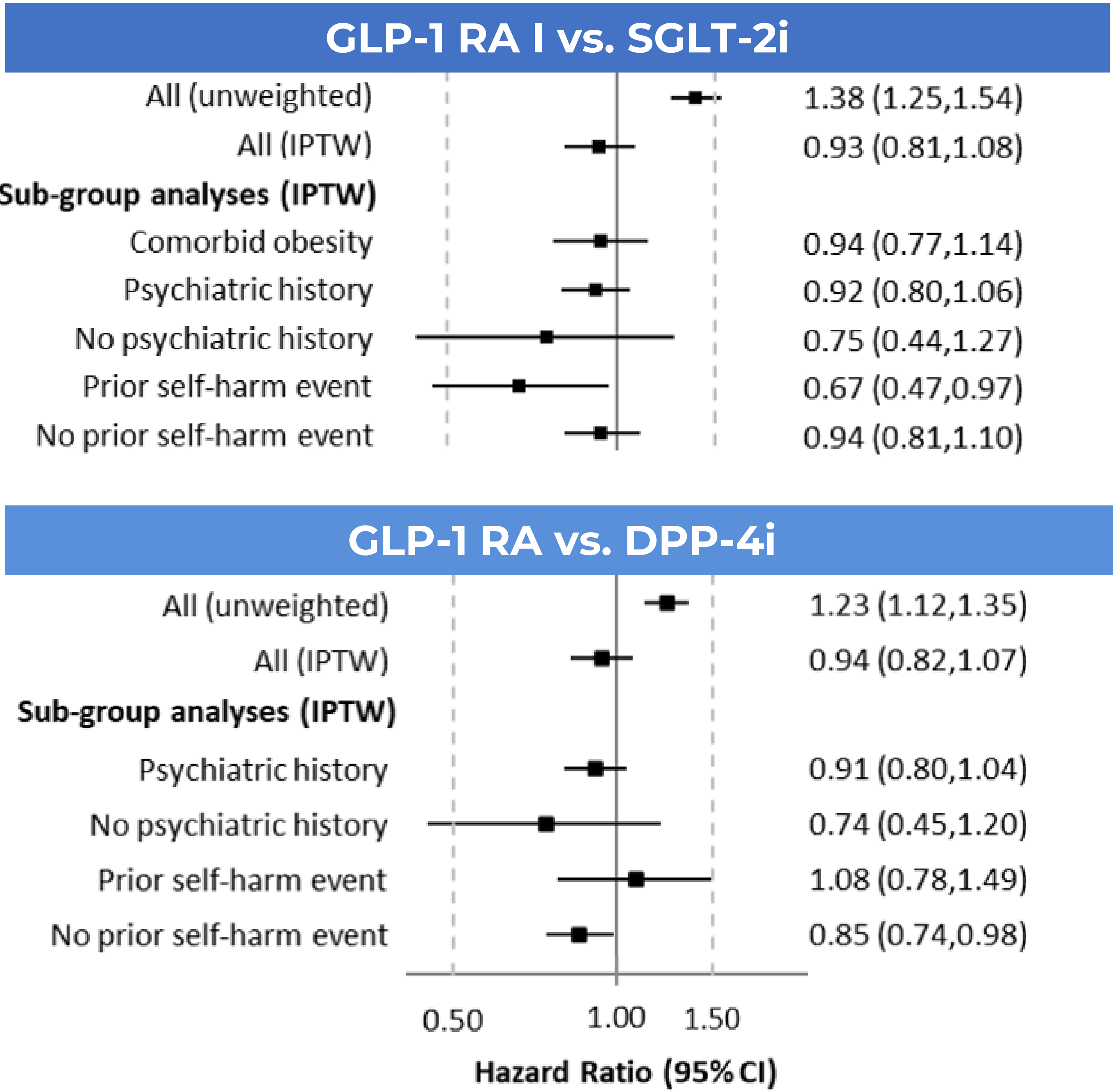


Figure 2. Hazard Ratios (95% CI)* of the Association Between GLP1-RA use vs. SGLT-2i or DPP-4i Use and Intentional Self-Harm



*Propensity score trimmed, inverse probability of treatment weighted and truncated (1%)

CONCLUSION

- Use of GLP-1 RAs in patients with type 2 diabetes mellitus did not show increased risk of intentional self-harm.
- Subgroup analyses were consistent with overall findings
- Propensity score weighting controlled for a comprehensive set of potential confounders, which helped to minimize bias from confounding

LIMITATIONS

- We lacked data to assess the risk with extended use.
- Our study population was limited to patients with health insurance and did not include patients with type 1 diabetes.
- Unmeasured confounders, such as socio-economic factors or educational level, could bias results.
- The healthcare claims data provided incomplete data on race and ethnicity.

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