Suicidal Ideation in Patients Treated with Glucagon-like Peptide 1 Receptor (GLP1) Agonists: A Retrospective Real-World Analysis

Stevan Geoffrey Severtson PhD, Sarah Beucker MS MPH, Noa Palmon BS, Jessica R. Probst MPH, Carl Marci MD | OM1 Inc, Boston, MA, USA

Background

Glucagon-like peptide-1 receptor agonists (GLP1s) are effective in treating diabetes and assisting in weight loss yet reports of suicidal ideations (SI) among patients have raised concerns about potential side effects.[1,2] Real-word studies have not identified an association between GLP1 use and SI.[3,4]

This study utilizes clinical notes text from electronic health records (EHRs) to assess SI among patients treated with GLP1s. Electronic health records contain large amounts of structured information, which can include SI, but this information may also be recorded in unstructured clinical notes[5].

Objectives

This study examined whether the prevalence of SI increased after initiating a GLP1 and whether prevalence of SI differed by GLP1 indication.

Methods

Data were sourced from OM1 Real-World Data Cloud™ (“RWDC”, Boston, MA), a deterministically linked, multi-source dataset derived from EHR and claims records.

Patients with a diagnosis of type II diabetes (T2D) or obesity and a prescription for a GLP1 were included. The date of the first GLP1 prescription was the index date.

Patients who had a record of a previous prescription for other second-line type II diabetes or weight loss (WL) medications were excluded.

SI assessments (affirmed or denied) were identified from clinical notes using automated text extraction[6].

Patients were required to have at least one assessment for SI within the year before (baseline) and after (follow up) the index date.

Chi-square tests were used to compare prevalence of affirmed SI by GLP1 indication (diabetes or weight loss). McNemar’s test was used to assess change in affirmed SI prevalence before and after the index date.

Results

There were 2,685 patients prescribed GLP1s who met inclusion criteria.

The majority of patients were prescribed a GLP1 for type II diabetes (2,104, 78.4%); 581 (21.6%) patients were prescribed for weight loss.

Patients prescribed a GLP1 for type II diabetes were older (Med [Q1, Q3] T2DM: 54 [44, 63] vs WL: 45 [37, 54]) and less likely to have an anxiety disorder or major depressive disorder at baseline (Table 1).

The prevalence of SI before (χ^2=0.87, df=1, p=0.350) and after (χ^2=0.10, df=1, p=0.755) the index date did not differ by GLP1 indication (Table 1).

Of the 60 patients who reported SI after initiating a GLP1, 35 patients (58.3%) affirmed SI in the baseline period.

There was no statistical difference (χ^2=0.45, df=1, p=0.500) between the percentage of patients with SI during baseline (2.4%) versus follow up (2.2%) (Table 2).

When examining results by indication, there was no statistical difference between the percentage of patients with SI during baseline versus follow up among patients with T2D (χ^2=0.82, df=1, p=0.366) or WL (χ^2=0.09, df=1, p=0.763) (Table 2).

Conclusions

- No statistically significant change in SI prevalence was observed after initiation of GLP1 medications.
- SI prevalence did not differ by GLP1 indication before or after treatment initiation.
- The majority of patients who affirmed SI during follow up also affirmed SI during the baseline period.

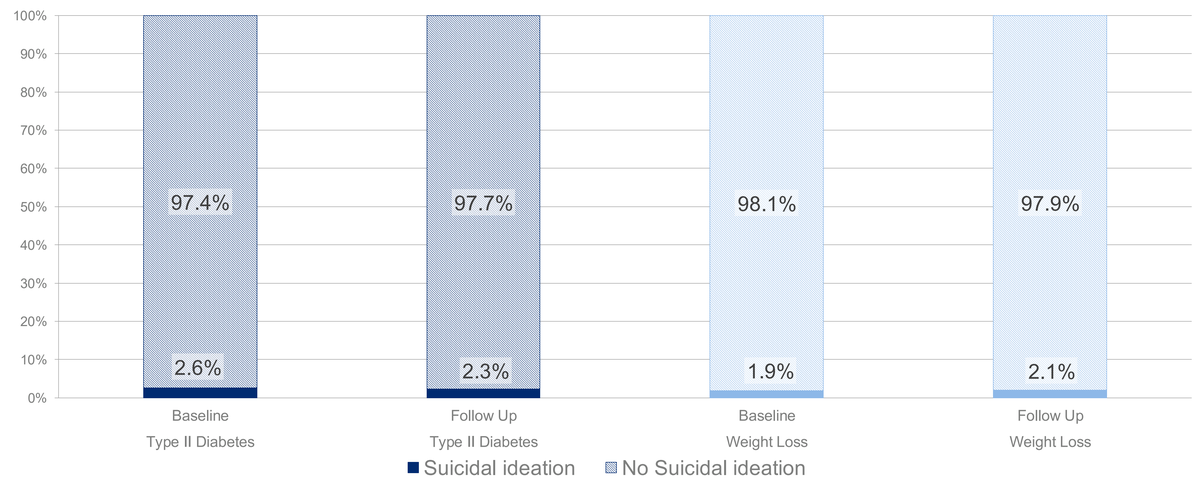
Table 1. Characteristics of Study Population

		T2DM	WL	Total	P-Value
Age at index (years)	N	2,104	581	2,685	<.001*
	Mean (SD)	53.4 (13.0)	45.2 (11.6)	51.7 (13.2)	
	Median (Q1, Q3)	54 (44, 63)	45 (37, 54)	52 (42, 61)	
Race	Black or African American	251 (11.9%)	58 (10.0%)	309 (11.5%)	0.401**
	Other Race	84 (4.0%)	26 (4.5%)	110 (4.1%)	
	White	1,207 (57.4%)	327 (56.3%)	1,534 (57.1%)	
	Unknown	562 (26.7%)	170 (29.3%)	732 (27.3%)	
Ethnicity	Hispanic or Latino	139 (6.6%)	32 (5.5%)	171 (6.4%)	0.324**
	Not Hispanic or Latino	1,406 (66.8%)	379 (65.2%)	1,785 (66.5%)	
	Unknown	559 (26.6%)	170 (29.3%)	729 (27.2%)	
Mental Health Diagnoses & Treatments at Index					
Anxiety Disorder	N (%)	889 (42.3%)	301 (51.8%)	1,190 (44.3%)	<.001**
Major Depressive Disorder	N (%)	849 (40.4%)	255 (43.9%)	1,104 (41.1%)	0.125**
Bipolar Disorder	N (%)	323 (15.4%)	83 (14.3%)	406 (15.1%)	0.525**
Anti-depressant medication	N (%)	1,310 (62.3%)	400 (68.8%)	1,710 (63.7%)	0.003**
Anti-anxiety medication	N (%)	547 (26.0%)	161 (27.7%)	708 (26.4%)	0.407**

Table 2. Prevalence of Suicidal Ideation by GLP1 Indication at Baseline and Follow Up

	SI Present at Baseline	SI Absent at Baseline	All Patients
All Patients (N=2,685)	65 (2.4%)	2,620 (97.6%)	
SI Present at Follow Up	35 (1.3%)	25 (0.9%)	60 (2.2%)
SI Absent in Follow Up	30 (1.1%)	2,595 (96.6%)	2,625 (97.8%)
T2DM Patients (N=2,104)	54 (2.6%)	2,050 (97.4%)	
SI Present at Follow Up	29 (1.4%)	19 (0.9%)	48 (2.3%)
SI Absent in Follow Up	25 (1.2%)	2,031 (96.5%)	2,056 (97.7%)
WL Patients (N=581)	11 (1.9%)	570 (98.1%)	
SI Present at Follow Up	6 (1.0%)	6 (1.0%)	12 (2.1%)
SI Absent in Follow Up	5 (0.9%)	564	569 (97.9%)

Figure 1. Change in Prevalence of Suicidal Ideation during Baseline and Follow Up, by GLP1 Indication



References

1. Salvo F, Faillie J. GLP-1 Receptor Agonists and Suicidality—Caution Is Needed. *JAMA Netw Open*. 2024;7(8):e2423335
2. McIntyre RS, Mansur RB, Rosenblat JD, Kwan ATH. The association between glucagon-like peptide-1 receptor agonists and suicidality: reports to the FDA Adverse Event Reporting System. Expert Opin Drug Saf. 2024 Jan;23(1):47-55.
3. Shapiro S B, Yin H, Yu O H Y, Rej S, Suissa S, Azoulay L et al. Glucagon-like peptide-1 receptor agonists and risk of suicidality among patients with type 2 diabetes: active comparator, new user cohort study *BMJ* 2025; 388 :e080679
4. Wang W, Volkow ND, Berger NA, Davis PB, Kaelber DC, Xu R. Association of semaglutide with risk of suicidal ideation in a real-world cohort. Nat Med. 2024 Jan;30(1):168-176. doi: 10.1038/s41591-023-02672-2. Epub 2024 Jan 5.
5. Anderson HD, Pace WD, Brandt E, et al. Monitoring Suicidal Patients in Primary Care Using Electronic Health Records. The Journal of the American Board of Family Medicine. 2015;28:65-71
6. Palmon N, Alves P, Momen S, Leavy M, Curhan G, Boussios C, Jones C, Gliklich R. Use of a Natural Language Processing-Based Approach to Extract Depression Symptom Severity and Suicide Ideation from Clinical Notes to Support Depression Research.

Conference

Presented at ISPOR Annual Conference. May 2025. Montreal, QC.