



A Descriptive Analysis of Weight Loss Medication Use, Including GLP-1 RA Products, and Intentional Self-Harm among Patients with Obesity in FDA’s Sentinel Distributed Database

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BACKGROUND

Select glucagon-like peptide-1 receptor agonists (GLP-1RAs) are indicated for weight reduction in persons with obesity or overweight. Postmarket reports identified a potential risk of suicidal ideation and behavior after use of GLP-1RAs.

OBJECTIVES

We assessed use of weight loss medications, including GLP-1RAs, and evaluated the occurrence of intentional self-harm among a large cohort of health plan members with obesity and without diabetes in the United States.

METHODS

Using data from 14 Data Partners in FDA’s Sentinel Distributed Database from 10/1/15 – 9/30/23, we identified health plan members 18 years or older with a diagnosis code for obesity and who initiated GLP-1RAs or nine other weight loss agents (benzphetamine, naltrexone/bupropion, diethylpropion, lorcaserin, orlistat, phendimetrazine, phentermine, phentermine-topiramate, or setmelanotide). We excluded patients with evidence of pregnancy or any diabetes. 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, and evaluated the occurrence of these events at any point after the obesity diagnosis regardless of drug exposure until either the outcome was observed or censoring occurred. We estimated the crude incidence rate (IR) of intentional self-harm among patients with obesity, regardless of medication use, and among users of the ten weight-loss medications of interest.

RESULTS

We identified 26,539,423 patients with obesity, of which 340,779 were dispensed GLP-1RAs. Use of other weight loss agents ranged from <11 users of setmelanotide to 185,145 users of phentermine. Semaglutide (62%) was the most commonly dispensed GLP-1RA, followed by liraglutide (25%). Estimated crude incidence rates (per 1000 patient-years) of intentional self-harm were highest among orlistat users (IR: 7.26, 95% confidence interval (CI): 3.02, 17.44), lower among GLP-1RA users (IR: 1.05, 95% CI: 0.89, 1.23), and lowest among users of Wegovy or Saxenda specifically (IR: 0.78, 95% CI: 0.56, 1.08). The overall incidence rate (95% CI) in patients with obesity regardless of medication use was 1.48 (95% CI: 1.47, 1.49).

Table 1. Number of Patients and Person-Years by Selected Weight Loss Medication or Obesity Diagnosis

	Number of Patients	Total Years at Risk
Any GLP-1 RA	340,779	144,003
Wegovy or Saxenda	129,942	46,026
Phentermine	185,145	58,317
Obesity	26,539,423	50,321,512

Figure 2. Selected Baseline Health Characteristics by Selected Weight Loss Medications or Obesity Diagnosis

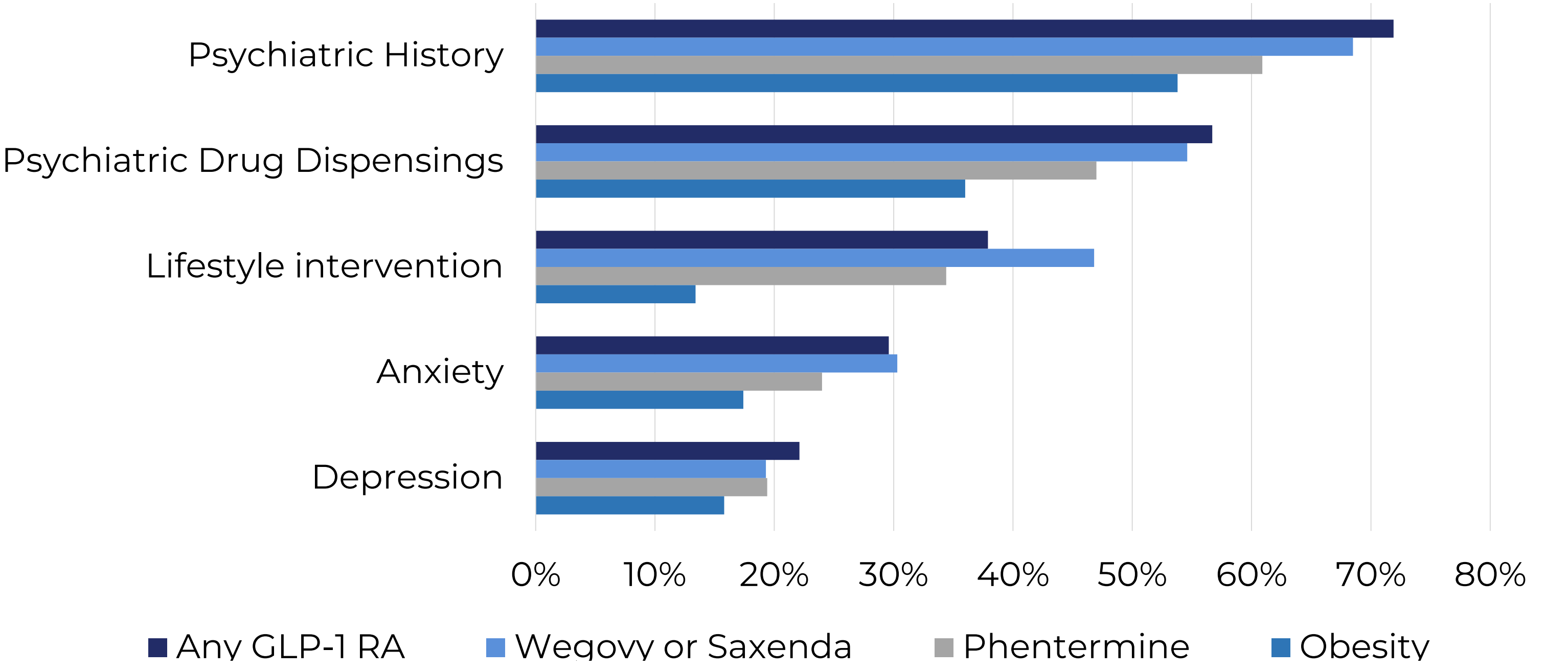


Table 2. Crude Risk and Rate of Intentional Self-Harm Events by Weight Loss Medication or Obesity diagnosis*

	Intentional Self-Harm Events	Risk per 1,000 patients (95% CI)	Rate per 1,000 person-years (95% CI)
GLP-1 RAs	151	0.44 (0.37, 0.51)	1.05 (0.89, 1.23)
Wegovy or Saxenda	36	0.28 (0.19, 0.37)	0.78 (0.56, 1.08)
Benzphetamine	0	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Combination naltrexone & bupropion	*****	*****	1.16 (0.61, 2.24)
Diethylpropion	0	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Lorcaserin	*****	*****	1.11 (0.36, 3.44)
Orlistat	*****	*****	7.26 (3.02, 17.44)
Phendimetrazine	*****	*****	2.47 (0.62, 9.88)
Phentermine	96	0.52 (0.41, 0.62)	1.65 (1.35, 2.01)
Phentermine-topiramate	*****	*****	1.01 (0.38, 2.68)
Setmelanotide	0	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Obesity	74,682	2.81 (2.79, 2.83)	1.48 (1.47, 1.49)

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

CONCLUSION

- Crude incidence rates varied by product and were found to be lowest among users of Wegovy and Saxenda.
- Additional analyses that address the limitations of descriptive analyses are needed to evaluate the association between specific weight loss medications and intentional self-harm.

LIMITATIONS

- Misclassification of intentional self-harm events is possible.
- We did not include suicidal ideation as an outcome because of the limitations of claims data to capture suicidal intent.
- Comparisons between drugs should be made with caution due to the descriptive nature of the study

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