PHARMACY SYSTEMS OUTCOMES AND POLICY COLLEGE OF PHARMACY

Acute Pancreatitis Risk Associated with Glucagon-Like Peptide-1 Receptor Agonists Used for Weight Loss: A Retrospective Cohort Study in the United States

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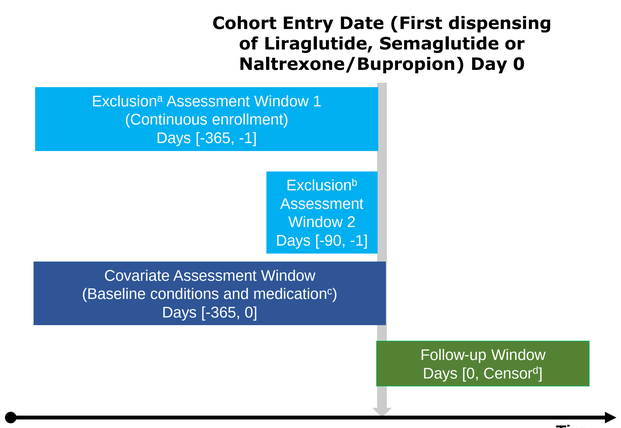
OBJECTIVES

- To evaluate the risk of incident acute pancreatitis (AP) associated with the use of GLP-1 receptor agonists (GLP-1 RAs) liraglutide and semaglutide used for weight loss compared to naltrexone/bupropion fixed dose combination.

METHODS

- We used data from the Merative MarketScan Commercial Claims and Encounters, and Medicare Supplemental databases.
- The study involved adults (≥18years) who began using GLP-1 RAs or naltrexone/bupropion from October 2016 to September 2021.
- We included individuals with an obesity diagnosis and no diabetes diagnosis or dispensing record in the preceding year.
- Also, those with diagnoses of AP, chronic pancreatitis, or pancreatic cancer within past 90 days were excluded.

FIGURE 1. Study design diagram

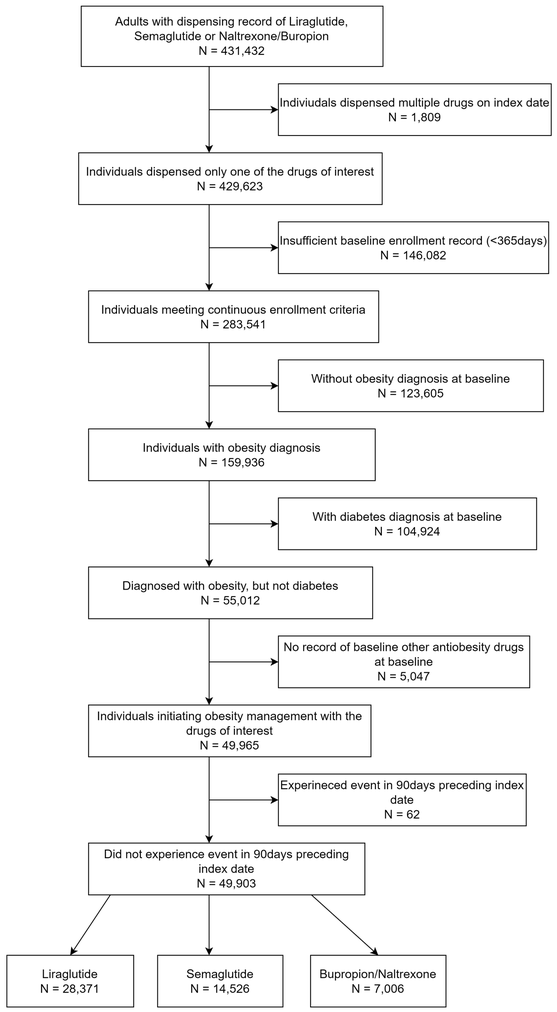


a. Exclusion: Diabetes diagnosis, any anti-obesity medication dispensing
b. Exclusion: Acute pancreatitis, chronic pancreatitis, pancreatic cancer
c. Baseline conditions: hyperlipidemia, hypertension, ischemic heart disease, non-alcoholic fatty liver disease, chronic kidney disease, congestive heart failure, cholecystitis, cholecystectomy, abdominal pain, tobacco use, alcohol use
d. Earliest of: outcome of interest (acute pancreatitis), treatment switching, discontinuation, disenrollment, or study end

METHODS (CONT.)

- Patients were followed from treatment initiation until the onset of AP, treatment switching, discontinuation, disenrollment, or study end.
- We used inverse probability of treatment weighting (IPTW) to balance demographic and clinical factors across groups.
- Using a Cox proportional hazard model, we compared the association of AP between naltrexone/bupropion and GLP-1 RAs.
- We also performed separate evaluations for assessing AP risk in users of liraglutide and semaglutide.

FIGURE 2. Sample selection



RESULTS

TABLE 1. Baseline characteristics (weighted)

	GLP-1 RA	Na/Bu	SMD
N	35,372	14,524	
Age, Mean (SD)	45.26 (10.52)	45.38 (10.53)	0.012
Age group (%)			0.005
18-34	5822 (16.5)	2375 (16.3)	
35-44	10216 (28.9)	4185 (28.8)	
45-54	11926 (33.7)	4913 (33.8)	
55-64	6961 (19.7)	2873 (19.8)	
>=65	448 (1.3)	178 (1.2)	
Sex (%)			<0.001
Male	6698 (18.9)	2751 (18.9)	
Region			0.001
North Central	6994 (19.8)	2877 (19.8)	
Northeast	7332 (20.7)	3007 (20.7)	
South	19132 (54.1)	7852 (54.1)	
West	1897 (5.4)	780 (5.4)	
Unknown	19 (0.1)	8 (0.1)	
Plan type			0.012
PPO	20553 (58.1)	8442 (58.1)	
CDHP	5508 (15.6)	2265 (15.6)	
HDHP	341 (9.6)	1413 (9.7)	
HMO	1957 (5.5)	795 (5.5)	
POS	1928 (5.5)	766 (5.3)	
Comprehensive	1185 (3.3)	492 (3.4)	
EPO	122 (0.3)	48 (0.3)	
POS with capitation	114 (0.3)	45 (0.3)	
Basic/major medical	3 (0.0)	1 (0.0)	
Missing	592 (1.7)	258 (1.8)	
Hyperlipidemia	12424 (35.1)	5108 (35.2)	0.001
Hypertension	14483 (40.9)	5961 (41.0)	0.002
IHD	1037 (2.9)	429 (2.9)	0.001
NAFLD	1831 (5.2)	758 (5.2)	0.002
CKD	448 (1.3)	187 (1.3)	0.002
CHF	472 (1.3)	198 (1.4)	0.002
Cholecystitis	218 (0.6)	89 (0.6)	<0.001
Cholecystectomy	376 (1.1)	155 (1.1)	<0.001
Abdominal pain	5700 (16.1)	2340 (16.1)	<0.001
Tobacco use	3035 (8.6)	1249 (8.6)	0.001
Alcohol use	381 (1.1)	157 (1.1)	<0.001

GLP-1 RA = Glucagon-like Peptide 1 Receptor Agonist, Na/Bu = Naltrexone/Bupropion fixed dose combination, PPO =Preferred Provider Organizations, CDHP = Consumer Driven Health Plans, HDHP = High-Deductible Health Plan, HMO = Health Maintenance Organizations, POS = Point of Service, EPO = Exclusive Provider Organizations, IHD = Ischemic Heart Disease, NAFLD = Non-alcoholic Fatty Liver Disease, CKD = Chronic Kidney Disease, CHF = Congestive Heart Failure

RESULTS (CONT.)

- We identified 35,377 users of GLP-1 RA (28,371 liraglutide; 7,006 semaglutide) and 14,526 users of the naltrexone/bupropion.
- Mean age was 45 years and 81% were female.
- Per 100,000 patient-year incidence of first AP event was 358 for GLP1 RA and 170 for naltrexone/bupropion users.
- The hazard ratio (HR) for AP among GLP-1 RA users compared to naltrexone/bupropion was 1.93 (95%CI 1.39, 2.67).
- When comparing individual GLP-1 RAs to bupropion/naltrexone, the HR for liraglutide was 2.02 (95%CI 1.46, 2.81) and was 1.42 (95%CI 0.80, 2.60) for semaglutide.

FIGURE 3. Risk of acute pancreatitis in obese individuals treated with GLP-1 RAs compared to Naltrexone/Bupropion fixed dose combination

CONCLUSION

- GLP-1 RAs are associated with a higher risk of AP compared to the naltrexone/bupropion, which becomes particularly significant as the use of GLP-1 RAs continues to grow.
- The risk of AP varies among liraglutide and semaglutide, suggesting that the safety profile is not similar within this class of medication.
- With the expanding use of GLP-1 RAs, careful consideration is crucial, especially when prescribing these drugs to patients with a high risk of AP.

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