

Non-Diabetic Patients on GLP-1 Medications Have an Increased Likelihood of GI Side Effects Compared to Patients on Other Weight Loss Medications

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Key Findings:

- Non-diabetic patients prescribed liraglutide have an increased likelihood of experiencing delayed gastric emptying and ileus compared to those on a weight loss medication not classified as a glucagon-like peptide-1 receptor agonist (GLP-1).
- Non-diabetic patients prescribed semaglutide have an increased likelihood of delayed gastric emptying and gallstones compared to those on other weight loss medications.

We [recently noted](#) that diabetic patients prescribed a glucagon-like peptide-1 receptor agonist (GLP-1) medication have an increased likelihood of delayed gastric emptying, also known as gastroparesis, and a reduced likelihood of gallstones and ileus compared to diabetic patients not on a GLP-1.¹ To understand whether non-diabetic patients prescribed GLP-1 medications experience similar rates of these gastrointestinal (GI) side effects, we studied 367,439 non-diabetic patients, including 170,842 who were on a GLP-1 medication and 196,597 who were on other weight loss medications.

We adjusted for factors including patient sex, social vulnerability, BMI classification, race, ethnicity, and age. We limited our analysis for this study to liraglutide and semaglutide medications as they are FDA-approved for weight loss, while other GLP-1 medications are not. Tirzepatide, while FDA-approved for weight loss, was not included because the recency of that approval limited the data available for analysis.²

For non-diabetic patients prescribed liraglutide, we observed an increased likelihood of delayed gastric emptying (139%) and ileus (32%), but no difference in likelihood of gallstones when compared to those on a non-GLP-1 weight loss medication. For patients prescribed semaglutide, the likelihood of delayed gastric emptying and gallstones increased 39%, but we found no statistically significant change in the likelihood of ileus.

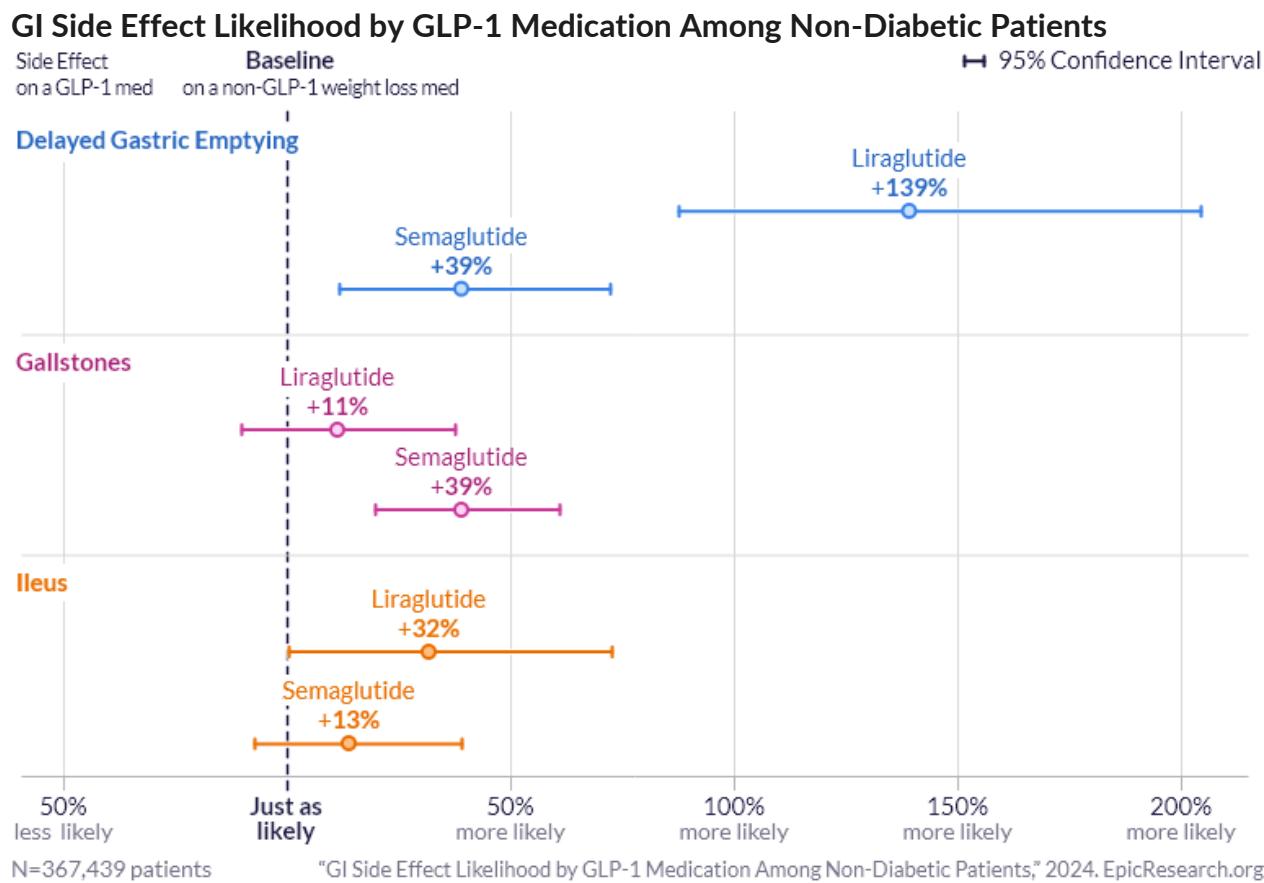


Figure 1. The likelihood of GI side effects for non-diabetic patients prescribed GLP-1 medications.

These data come from *Cosmos*, a dataset created in collaboration with a community of Epic health systems representing more than 246 million patient records from 1,400 hospitals and more than 32,800 clinics from all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Bartelt K, Deckert J, Allen S, Joyce B. Delayed Gastric Emptying More Likely, Gallstones and Ileus Less Likely for Diabetic Patients on GLP-1 Medications Compared to Diabetics on Other Treatments. Epic Research. <https://epicresearch.org/articles/delayed-gastric-emptying-more-likely-gallstones-and-ileus-less-likely-for-diabetic-patients-on-glp-1-medications-compared-to-diabetics-on-other-treatments>. Accessed on May 1, 2024.
2. FDA Approves New Medication for Chronic Weight Management. U.S. Food and Drug Administration. Published November 8, 2023. <https://www.fda.gov/news-events/press-announcements/fda-approves-new-medication-chronic-weight-management>. Accessed March 7, 2024.

Data Definitions

Term	Definition
Study period	1/1/2017 to 9/1/2023
Study population	Patients with an index event between 1/1/2017 and 3/1/2023.
Excluded patients with any of the outcomes before their index event.	

Case population	A medication order for a patient for either a GLP-1 drug or another weight management drug. Patients with both were excluded. Patients with diabetes were excluded. Patients without a documented starting BMI in the year prior to or up to 30 days following the start of the semaglutide or liraglutide classifying them as obese were excluded.
Control populations	Patients taking other weight management drugs.
Index event	Date of the medication order.
Outcomes	A diagnosis or delayed gastric emptying, ileus, or gallstones between 14 and 180 days following beginning of treatment.
Delayed gastric emptying	A diagnosis with ICD-10-CM code K31.84.
Ileus	A diagnosis with ICD-10-CM code K56.0 or K56.7.
Gallstones	A diagnosis with ICD-10-CM code K81.
Obesity class	Not Obese: BMI <30 Class 1 Obesity: BMI between 30 and 35 Class 2 Obesity: BMI between 35 and 40 Class 3 Obesity: BMI 40+
Diabetes	A diagnosis with SNOMED CT code 44054006.
GLP-1	Any drug with one of the following pharmaceutical classes: ANTI-OBESITY GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST ANTIHYPERGLY, INCRETIN MIMETIC(GLP-1 RECEPTOR AGONIST) ANTIHYPERGLY, INCRETIN, LONG ACT-GLP-1 RECEPTOR AGONIST
GLP-1 drugs of interest	A drug in the GLP-1 group with a simple generic name like: Semaglutide Liraglutide
Other weight management drugs	Orders with one of the following pharmaceutical classes and not associated with any GLP-1 simple generics: ANTI-OBESITY SEROTONIN 2C RECEPTOR AGONISTS ANTI-OBESITY-OPIOID ANTAGONIST, DOPAMINE RU INHIB ANTI-OBESITY - ANOREXIC AGENTS ANTI-OBESITY - MELANOCORTIN 4 RECEPTOR AGONISTS

Table 1. GI Side Effect Likelihood by GLP-1 Medication Among Non-Diabetic Patients - Delayed Gastric Emptying

	Odds Ratio	Lower CI	Upper CI
semaglutide	1.386	1.115	1.722
liraglutide	2.391	1.877	3.045
Male	0.471	0.353	0.629
Age	1.005	0.999	1.012
SVI	2.499	1.777	3.515
BMI Class 2 Obesity	1.392	1.094	1.770
BMI Class 3 Obesity	1.104	0.870	1.400
Black	0.201	0.048	0.837
Hispanic	0.427	0.103	1.775
White	0.527	0.131	2.124

Table 2. GI Side Effect Likelihood by GLP-1 Medication Among Non-Diabetic Patients - Gallstones

	Odds Ratio	Lower CI	Upper CI
semaglutide	1.387	1.197	1.609
liraglutide	1.109	0.895	1.374
Male	0.450	0.362	0.559
Age	0.989	0.984	0.994
SVI	1.132	0.885	1.447
BMI Class 2 Obesity	1.043	0.871	1.249
BMI Class 3 Obesity	1.175	0.996	1.386
Black	1.030	0.143	3.406
Hispanic	1.900	0.595	6.067
White	1.840	0.590	5.736

Table 3. GI Side Effect Likelihood by GLP-1 Medication Among Non-Diabetic Patients - Ileus

	Odds Ratio	Lower CI	Upper CI
semaglutide	1.134	0.926	1.388
liraglutide	1.316	1.003	1.725
Male	1.457	1.191	1.782
Age	1.034	1.027	1.041
SVI	1.615	1.161	2.246
BMI Class 2 Obesity	1.001	0.787	1.271
BMI Class 3 Obesity	1.157	0.928	1.444
Black	0.646	0.089	4.687
Hispanic	0.948	0.129	6.935
White	0.949	0.133	6.774