Real-World Adverse-Event Profile of Glucagon-Like Peptide-1 Receptor Agonists in Overweight and Obese US Adults

Rohan Vashi, PharmD, MS[1]; *Dave Iwanyckyj, BA[1]; Pablo Racana, BS[1]; Melanie Jardim, PhD[1]
[1]Amplity, Inc, Langhorne, PA, USA

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Introduction

- Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are an effective therapy for the treatment of type 2 diabetes and weight-loss management
- Although a popular treatment for both disease states, the adverse-event (AE) profile of GLP-1 RAs is unacceptable or intolerable to some patients, reducing the potential for long-term use[1]
- Common AEs of the GLP-1 RA class of medications include[2-5]:
  - Gastrointestinal (GI) AEs such as nausea, vomiting, abdominal pain, diarrhea, and constipation
  - Injection-site reactions
  - Neurological AEs including fatigue and dizziness
- The market approval of some, but not all, GLP-1 RAs in weight-loss management may result in potential off-label use in patient populations that are not indicated by the individual product label
- Coupled with potential off-label use, the increasing popularity of GLP-1 RAs in the treatment of multiple patient populations may also result in a different real-world AE profile that does not mirror what was found in the clinical trials. This research aims to determine the real-world AE profile of GLP-1 RAs

Methods

- This retrospective observational study utilized Amplity AnswerY™, which is Amplity's real-world database and platform built from HIPAA-compliant transcriptions of US prescriber–patient visits. Using AI and natural language processing (NLP), it extracts, visualizes, and summarizes treatment discussions and clinical decisions. Covering inpatient and outpatient care across 70+ specialties since 2017, AnsweY was known as *Amplity Insights*™ prior to January 2025
- NLP was used to search and analyze the AnsweY database and platform for records from 12,540 providers for patients who had received a GLP-1 RA as a class or specific agent from January 1, 2017, to October 30, 2024
- AEs were identified from a predefined list compiled from product websites or found in the AnsweY database and described as frequencies and percentages
  - AEs from the predefined list described above were manually classified as either common or serious, and this list was utilized to mine 193,193 records utilizing standardized NLP techniques. Individual patients may have multiple records
- Results were summarized for all patients utilizing GLP-1 RAs, overweight or obese patients with and without diabetes, and patients with a body mass index (BMI) <25, 25-26, 27-29, and ≥30. AEs are reported as follows:
  - Present: record was identified as having an AE, but it was not necessarily linked to the GLP-1 RA by the patient or healthcare provider (HCP)
  - Related to Treatment: record was identified as having an AE, has been related by the patient or HCP to the GLP-1 RA, but there is no known change in treatment or treatment disruption
  - Reason for Disruption: record which was identified as having an AE, has been attributed to the GLP-1 RA by the patient or HCP, and has led to a treatment disruption. A treatment disruption may include a taper, wean, dose reduction, medication hold, medication switch, and/or discontinuation of the agent

Conclusion

- In this real-world US cohort, GLP-1 RA–containing medications are used heavily in overweight and obese populations. However, within the same population, usage of GLP-1 RAs are overwhelmingly used in patients with diabetes
- Common and serious AEs were reported in 10.8% and 3.9% of patients utilizing a GLP-1 RA, in which GI issues, hypoglycemia, and acute pancreatitis were observed
  - Rates of GI issues decreased as BMI increased. As GI issues were reported as disrupting treatment for 2.2% of patients, this suggests that patients with greater BMI may be able to utilize GLP-1 RAs for a longer period
- Rates of serious AEs (as described in **Table 3** and **Figure 3**) appeared to increase with the presence of diabetes and increased BMI, suggesting an increased need for patient monitoring in these populations
- AEs observed in this real-world cohort align with the product's prescribing information, increasing confidence of safe usage in both type 2 diabetes and weight-management patients

*PRESENTING AUTHOR

DISCLOSURES
All authors are employees of Amplity, Inc.

To learn more about this study and further research by Amplity AnsweY™, please scan this code.

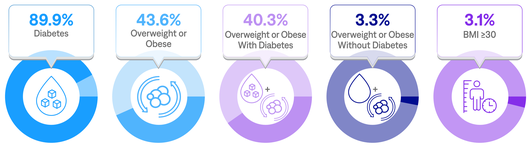
REFERENCES
1. Wang JY, Wang QW, Yang XY, et al. GLP-1 receptor agonists for the treatment of obesity: role as a promising approach. *Front Endocrinol (Lausanne)*. 2023;14:1085799. Epub February 1, 2023.
2. Novo Nordisk. WEGOVY (semaglutide) [prescribing information]. US Food and Drug Administration. Accessed April 1, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/215256s021lbl.pdf
3. Novo Nordisk. SAXENDA (liraglutide) [prescribing information]. US Food and Drug Administration. Accessed April 1, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/206321s019lbl.pdf
4. Eli Lilly. ZEPBOUND (tirzepatide) [prescribing information]. US Food and Drug Administration. Accessed April 1, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/217806Orig1s020lbl.pdf
5. Eli Lilly. TRULICITY (dulaglutide) [prescribing information]. US Food and Drug Administration. Accessed April 1, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/125469s061s062lbl.pdf

Patients utilizing GLP-1 RAs mostly have diabetes, and 43.6% are overweight or obese

Results: Patient Demographics

- AnsweY identified 124,400 patients utilizing a GLP-1 RA from 19,627 providers from January 1, 2017, to October 30, 2024
- Patients utilizing GLP-1 RAs were older (age, mean ± standard deviation [SD]: 61 ± 12.8 years), and of patients with a known race (46.8%), 11.9% of patients were African-American, 0.4% were Asian, 4.7% were Hispanic, and 82.9% were White
- Among overweight or obese patients, 92.4% of patients had diabetes, whereas 7.6% did not have diabetes. Most patients with a recorded BMI had a BMI ≥30 (68.3%)
- **Figure 1** shows market understanding of GLP-1 RA usage, and **Table 1** shows patient demographics stratified by BMI within the identified cohort utilizing the AnsweY real-world database and platform

Figure 1: Summary of GLP-1 RA Utilizing Patient Demographics (n=124,400)



BMI, body mass index; GLP-1 RA, glucagon-like peptide-1 receptor agonist.

Overweight and Obese Patients (n=53,001)

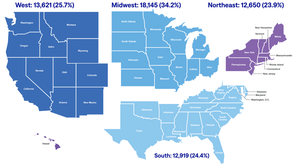


Table 1: GLP-1 RA Utilizing Patient Demographics Stratified by BMI

	BMI <25	BMI 25-26	BMI 27-29	BMI ≥30
Total Number of Patients	213	469	1,123	3,895
Age				
Patients With Record, n (%)	139 (65.3)	310 (66.1)	772 (64.3)	2,547 (65.4)
Mean (SD)	63.2 (13.4)	61.8 (12.8)	61.0 (12.8)	56.6 (13.4)
Gender				
Patients With Record, n (%)	213 (100)	468 (99.8)	1,122 (99.9)	3,887 (100)
Male, n (%)	79 (37.1)	198 (42.3)	484 (43.1)	1,650 (42.4)
Female, n (%)	134 (62.9)	270 (57.7)	638 (56.9)	2,237 (57.6)
Ethnicity				
Patients With Record, n (%)	79 (37.1)	166 (35.4)	381 (33.9)	1,302 (33.4)
African-American, n (%)	12 (15.2)	27 (16.3)	65 (17.1)	175 (13.4)
Hispanic, n (%)	3 (3.8)	11 (6.6)	30 (7.9)	68 (5.2)
White, n (%)	64 (81.0)	128 (77.1)	286 (75.1)	1,059 (81.3)

BMI, body mass index; GLP-1 RA, glucagon-like peptide-1 receptor agonist.

Gastrointestinal issues were the most experienced adverse events reported among all patients utilizing GLP-1 RAs, regardless of BMI

Results: Common AEs

- **Table 2** shows common AEs reported among all patients utilizing GLP-1 RAs
  - 10.8% of all patients utilizing a GLP-1 RA reported a common AE, and out of the patients reporting a common AE, 41.4% (5,556 out of 13,433) reported a treatment disruption
  - Among all patients reporting AEs, GI issues were the most frequently reported common AEs (7.7%), with 4.4% related to treatment and 2.2% leading to treatment disruption

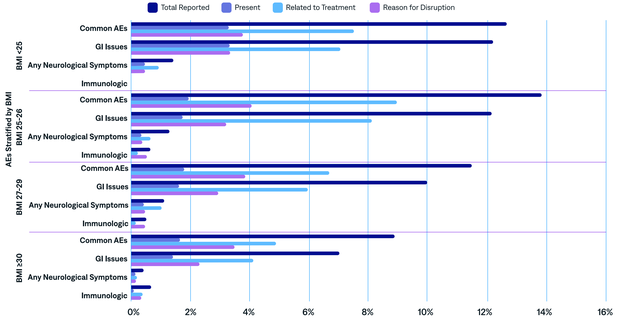
Table 2: Common AEs Among Patients Utilizing GLP-1 RAs

	*Total Reported		Present		Related to Treatment		Reason for Disruption	
	Patients	%	Patients	%	Patients	%	Patients	%
n				124,400				
Common AEs	13,433	10.80	2,751	2.21	6,518	5.24	5,556	4.47
Any GI issues	9,523	7.66	2,412	1.94	5,464	4.39	2,723	2.19
Any neurological symptom	1,040	0.84	366	0.29	537	0.43	226	0.18
Renal issues	40	0.03	11	0.01	26	0.02	6	0.00
Any metabolic and blood count change	260	0.21	72	0.06	136	0.11	63	0.05
Any nonspecific issues	0	0.00	0	0.00	0	0.00	0	0.00
Hepatic and biliary symptoms	197	0.16	25	0.02	107	0.09	75	0.06
Immunologic	559	0.45	71	0.06	240	0.19	302	0.24
Hydration issues	181	0.15	78	0.06	79	0.06	38	0.03
Intolerance	20	0.02	2	0.00	9	0.01	11	0.01
Nodules	12	0.01	0	0.00	7	0.01	5	0.00

AE, adverse event; GI, gastrointestinal; GLP-1 RAs, glucagon-like peptide-1 receptor agonists.
*AEs reported by patients may be classified as multiple categories (Present, Related to Treatment, Reason for Disruption), which may lead to an overlap in the Total Reported AEs.

- **Figure 2** shows common AEs reported among all patients utilizing GLP-1 RAs stratified by BMI
  - Common AEs were reported by 8.9–13.9% of patients utilizing GLP-1 RAs, with rates generally decreasing as BMI increases
  - GI issues were the most frequently reported common AEs across all BMI subgroups, with other common AEs being minimally reported
  - Overall, rates of GI issues decreased as BMI increased and were lower among patients with or without diabetes compared with the BMI groups (7.7%/7.4%)

Figure 2: Common AEs Among Patients Utilizing GLP-1 RAs Stratified by BMI



AE, adverse event; BMI, body mass index; GI, gastrointestinal; GLP-1 RAs, glucagon-like peptide-1 receptor agonists.

Serious adverse events were not commonly reported by patients utilizing GLP-1 RAs, regardless of BMI. Among patients who do report serious adverse events, the rate appears to increase as BMI increases

Results: Serious AEs

- **Table 3** shows serious AEs reported among all patients utilizing GLP-1 RAs, and out of patients reporting serious AEs, 70.5% (3,460 out of 4,907) reported a treatment disruption
  - Serious AEs were present in 3.9% of patients utilizing GLP-1 RAs
  - Highest rates of total reported serious AEs were for allergic reaction (2.0%), acute pancreatitis (0.9%), and hypoglycemia (0.6%)
  - Rates of serious AEs were greater in overweight or obese patients with diabetes (4.3%) compared with patients without diabetes (1.9%)

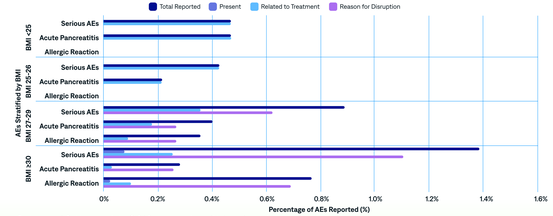
Table 3: Serious AEs Among Patients Utilizing GLP-1 RAs

	*Total Reported		Present		Related to Treatment		Reason for Disruption	
	Patients	%	Patients	%	Patients	%	Patients	%
n				124,400				
Serious AEs (Any)	4,907	3.94	512	0.41	1,307	1.05	3,460	2.78
Gallbladder disease	68	0.05	42	0.03	19	0.02	11	0.01
Acute pancreatitis	1,077	0.87	125	0.10	438	0.35	679	0.55
Allergic reaction	2,463	1.98	15	0.01	145	0.12	2,356	1.89
Hypoglycemia	759	0.61	87	0.07	479	0.39	269	0.22
Hyperglycemia	33	0.03	6	0.00	22	0.02	10	0.01
Food or liquid getting into the lungs during anesthesia or deep sedation	4	0.00	2	0.00	2	0.00	0	0.00
Vision changes	99	0.08	61	0.05	30	0.02	12	0.01
Kidney problems	154	0.12	44	0.04	76	0.06	52	0.04
Swelling of face/throat	103	0.08	17	0.01	46	0.04	52	0.04
Unusual mood changes	3	0.00	0	0.00	3	0.00	0	0.00
Thoughts of suicide/self-harm	10	0.01	6	0.00	2	0.00	3	0.00
Atrial flutter	121	0.10	66	0.05	40	0.03	27	0.02
Thyroid tumor	4	0.00	2	0.00	0	0.00	2	0.00

AE, adverse event; GLP-1 RAs, glucagon-like peptide-1 receptor agonists.
*AEs reported by patients may be classified as multiple categories (Present, Related to Treatment, Reason for Disruption), which may lead to an overlap in the Total Reported AE.

- **Figure 3** shows serious AEs reported among all patients utilizing GLP-1 RAs, stratified by BMI
  - Serious AEs were minimally reported, regardless of BMI. The highest rate of serious AEs was found in patients with a BMI of ≥30 (1.4%)
  - Overall, rates of serious AEs increased with increasing BMI, appearing to be driven by rates of acute pancreatitis and allergic reaction in patients with a BMI of ≥30. Other serious AEs were minimally reported
  - Any serious AEs were mildly attributed to treatment disruption in patients with a BMI of 27-29 (1%) and of ≥30 (1%), but there is minimal insight on the specific AE leading to treatment disruption in any of the BMI groups

Figure 3: Serious AEs Among Patients Utilizing GLP-1 RAs Stratified by BMI



AE, adverse event; BMI, body mass index; GLP-1 RAs, glucagon-like peptide-1 receptor agonists.

Strengths

- Large number of overweight and obese patients found in the AnsweY database and platform bolsters confidence in the robustness of the results
- AEs that are seen in this study generally align with what is listed in product prescribing information

Limitations

- Patients who obtain GLP-1 RAs outside of traditional healthcare channels, including online purchases, mail order, or weight-loss clinics, would not be captured in this analysis unless they provided information to their HCP
- Although 124,400 patients were identified as utilizing GLP-1 RAs, only 5,700 patients were identified as having a recorded BMI, suggesting some missing data on phrases mentioning BMI in patient records
- The list of common and severe AEs was compiled from product websites or found in the AnsweY real-world database and platform. AEs that did not fall into either of these categories may not have been captured