Real-World 1-Year Persistence to Glucagon-Like Peptide-1 Receptor Agonists by Indication Among Commercially Insured Members Without Diabetes

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Background

- In recent years, glucagon-like peptide-1 (GLP-1) receptor agonists have expanded beyond their initial use in diabetes to address a widening range of obesity-related and metabolic conditions.[1]
- Following its approval for chronic weight management in 2021, semaglutide (Wegovy) became the first weight loss therapy approved in 2024 to reduce major adverse cardiovascular events in adults with obesity or overweight and established cardiovascular disease.[2]
- Also in 2024, tirzepatide (Zepbound)—initially approved for chronic weight management in 2022—became the first FDA-approved pharmacologic treatment for obstructive sleep apnea (oSA), demonstrating clinically meaningful reductions in apnea–hypopnea index driven largely by GLP-1–mediated weight loss.[3]
- GLP-1 therapeutic expansion continued into hepatology with the August 2025 approval of semaglutide for metabolic dysfunction–associated steatohepatitis (MASH) with fibrosis—the first GLP-1 indicated for this liver disease. Clinical evidence showed improvements in steatohepatitis, fibrosis markers, and broader metabolic health, addressing a long-standing unmet need.[4]
- With GLP-1 therapies' 2025 gross annual costs exceeding $12,000 per patient, and FDA approvals continuing to expand, the utilization and financial impact of these medications is expected to increase substantially.
- Understanding real-world treatment persistence across indications is critical for optimizing outcomes and informing population-level therapeutic strategies.

Objective

- Our objective is to evaluate 1-year persistence to semaglutide (Wegovy) or tirzepatide (Zepbound) by indication in a real-world cohort of commercially insured members without diabetes.

Methods

- Prime Therapeutics' integrated medical and pharmacy claims plus enrollment data from January 1, 2023, to June 30, 2024, across 19 commercial health plans covering all regions of the United States were obtained for the study. During the study index period, the database contained an annual average of 17.9 million members with at least 1 month of eligibility.
- Data obtained for this study included medical claims (date of service, diagnoses received), pharmacy claims (fill dates, days' supply, and National Drug Code numbers), and eligibility information (member demographics and enrollment history).
- Study inclusion was limited to commercial members newly initiating a high-potency, weight loss-indicated GLP-1 medication (semaglutide [Wegovy], tirzepatide [Zepbound]) between January 1, 2024, and June 30, 2024 (index-date period).
- Members were excluded if they had a pre-period medical claim indicating a diabetes mellitus (DM) diagnosis or pharmacy claim for an antidiabetic medication during the 365-day pre-period, or less than 19 years of age at index.
- Also excluded were members with diagnoses for HIV/AIDS, hemophilia, sickle cell disease, malignant cancer, or end-stage renal disease as identified by diagnosis codes in medical claims during the 365 days before study index date.
- The primary outcome was 1-year persistence reported by indication. Indications were categorized exclusively and assigned hierarchically using pre-period medical claims in the order of MASH, oSA, and obesity.
- All members were followed until the earliest occurrence of either GLP-1 discontinuation or the end of the 365-day observation window. Persistence was defined as the absence of a treatment gap exceeding 60 days after adjusting GLP-1 claims for overlapping days' supply. Members with a gap in therapy of 60 days or more were considered to have discontinued therapy. The last day of supply before the discontinuation event gap was defined as the member's discontinuation date. Members were considered persistent if they did not have a 60-day gap in therapy and were censored at the end of the 365-day period.
- Descriptive statistics were used to compare member demographic and clinical characteristics between indications as well as for the overall study cohort. Median time to discontinuation and corresponding 95% confidence intervals (CI) were evaluated using the Kaplan-Meier method, with overall differences across indications assessed using the log-rank test.
- Persistence status at the end of 1 year was summarized as a binary outcome. Overall group differences in 1-year persistence rates across indications were assessed using a chi-square test. Pairwise comparisons of nonpersistence odds between indications were conducted using a generalized linear model (GLM) with a binomial distribution and logit link function.
- Pairwise contrasts of estimated log odds were computed between indications and derived from the model's covariance matrix, and *P* values were adjusted for multiple comparisons using the Bonferroni method to maintain a family-wise error rate of $\alpha = 0.05$ (adjusted significance threshold: $\alpha = 0.016$ for 3 comparisons). Odds ratios (OR) and 95% CIs were reported.

Table 1

Study Cohort Attrition

Study Selection Criteria for High-Potency Weight Loss-Indicated Glucagon-Like Peptide-1 Therapy	Commercially Insured Members N=17.9 million
GLP-1 naïve and initiating semaglutide (Wegovy) or tirzepatide (Zepbound) between January 1, 2024, and June 30, 2024	20,138
Medical diagnosis of obesity, obstructive sleep apnea, or MASH, and no diabetes medical or pharmacy claim (in 365 days prior to and including GLP-1 index date)	17,475
Continuously enrolled 1 year prior to index GLP-1 claim	13,542
≥19 years old at GLP-1 index claim	13,440
No malignant cancer, HIV/AIDS, hemophilia, sickle cell disease, or end-stage renal disease	12,815
Continuously enrolled 1 year after index GLP-1 claim	11,286 Final analytic cohort

GLP-1 = glucagon-like peptide-1 receptor agonists; MASH = metabolic dysfunction–associated steatohepatitis

Table 2

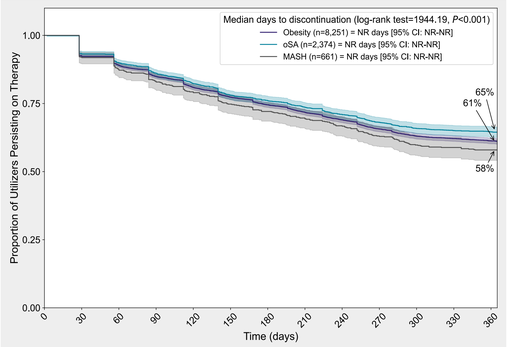
Demographic and Clinical Characteristics by Indication

	All Members[a] N=11,286	Obesity n=8,251	oSA n=2,374	MASH n=661	*P* Value[b]
Female, n (%)	8,055 (71.4)	6,471 (78.4)	1,165 (49.1)	423 (64.0)	<.001
Male, n (%)	3,304 (28.7)	1,780 (21.6)	1,209 (50.9)	238 (36.0)	
Age, mean (SD), years	45.8 (10.9)	44.8 (10.9)	49.0 (9.8)	47.0 (10.7)	<.001
Charlson Comorbidity Index Source[c], mean (SD)	0.3 (0.6)	0.2 (0.5)	0.3 (0.6)	1.3 (0.7)	<.001
Charlson Comorbidity Index Source[c] category, n (%)					
0	8,674 (76.9)	6,907 (83.7)	1,750 (73.7)	17 (2.6)	<.001
1	2,175 (19.3)	1,190 (14.4)	507 (21.4)	478 (72.3)	
2+	437 (3.8)	154 (1.9)	117 (4.9)	166 (7.1)	

[a]Commercially insured adults without diabetes newly initiating a high-potency, weight loss-indicated GLP-1 between January 1, 2024, and June 30, 2024.
[b]*P* values for continuous variables derived from one-way ANOVA; *P* values for categorical variables are derived from the chi-square test.
[c]Charlson Comorbidity Index score (Glasheen 2019) was measured in 365-day period prior to GLP-1 initiation (pre-period). Age and gender were ascertained on member's study index date.
MASH = metabolic dysfunction–associated steatohepatitis; oSA = obstructive sleep apnea.

Figure 1

High-Potency, Weight Loss-Indicated GLP-1 Agonists: Kaplan-Meier 1-Year Therapy Persistence by Indication (N=11,286)



Kaplan-Meier curve represents 11,286 commercially insured adults without diabetes initiating a high-potency, weight loss-indicated GLP-1 product defined as semaglutide (Wegovy) or tirzepatide (Zepbound) between January 1, 2024, through June 30, 2024. All persistence measurements were conducted at the GLP-1 product level. Members were considered persistent if they did not have a 60-day gap in therapy and were censored at the end of the 365-day period.
CI = confidence interval; MASH = metabolic dysfunction–associated steatohepatitis; NR = not reached; oSA = obstructive sleep apnea.

Table 3

Pairwise Comparison of 1-Year Persistence

Pairwise Comparisons	Odds Ratio	95% Confidence Interval	*P* value
oSA vs Obesity	1.16	1.06–1.27	0.005*
oSA vs MASH	1.33	1.12–1.58	0.004*
MASH vs Obesity	0.87	0.74–1.02	0.287

Odds ratio calculated from the log-odds difference. Odds ratios reflect the odds of 1-year persistence for the group listed first.
*Statistical significance after Bonferroni correction ($\alpha = 0.016$ for 3 comparisons).
Indications were categorized exclusively and assigned hierarchically using pre-period medical claims in the order of MASH, oSA, and obesity.
MASH = metabolic dysfunction–associated steatohepatitis; oSA = obstructive sleep apnea.

Results

- A total of 11,286 members without diabetes who newly initiated high-potency, weight loss-indicated GLP-1 with semaglutide (Wegovy) or tirzepatide (Zepbound) met all predefined inclusion and exclusion criteria (Table 1).
- Following indication assignment, nearly three-fourths (73%, n=8,251) of the cohort had obesity, while 21% (n=2,374) and 6% (661) had oSA and MASH, respectively.
- The mean age was 46, and 71% were female (Table 2).
- Across indications, 1-year persistence was 65% in oSA, 61% in obesity, and 58% in MASH.
- Median time to discontinuation was not reached (95% CI: NR to NR) across all indications. Figure 1 shows that fewer than 50% of members had discontinued GLP-1 therapy by the end of the observation period.
- Pairwise comparisons across indications found significantly higher odds of being persistent at the end of 1 year, with persistence being 16% higher among members with oSA compared to members with obesity (OR= 1.16, 95% CI: 1.06–1.27) and 33% higher than members with MASH (OR= 1.33, 95% CI: 1.12–1.58) (Table 3).
- There was no statistically significant difference in the odds of being persistent at the end of 1 year between members with obesity compared to members with MASH (OR= 0.87, 95% CI: 0.74–1.02).

Limitations

- Data were sourced from administrative health care claims; therefore, misclassification bias may have occurred due to using medical and pharmacy claims to exclude individuals with diabetes and to identify those with obesity, oAS, and/or MASH.
- Although outcome calculations allowed for product switching, product shortages may have impacted persistence rates.
- Individuals switching to compounded GLP-1 therapy or paying out of pocket for their GLP-1 product may have reduced observed persistence, as this utilization was not recorded in insurance claims data.
- This analysis did not account for potential differences in GLP-1 receptor agonist dosing. Specifically, the study did not assess if members achieved maximum therapy dose, describe maximum tolerated doses, or assess microdosing, which all may influence treatment persistence.
- Our study examined a commercially insured membership and therefore is not generalizable to Medicare or Medicaid populations.
- The impact of an individual's cost sharing, other diagnoses, social determinants of health, or other member characteristics are outside the scope of this analysis and are worthy of future consideration.

Conclusion

- For this analysis of commercially insured members initiating semaglutide (Wegovy) or tirzepatide (Zepbound) during the first half of 2024, persistence to GLP-1 remains challenging, with approximately 3 in 5 members remaining on therapy at the end of 1 year, and varied by indication, with an additional 1 in 14 members persistent to therapy for oSA compared to MASH.
- These findings show that real-world persistence remains below what is reported in the clinical trial setting. Additional research is needed to understand reasons for treatment discontinuation.
- These findings highlight significant investment risk due to waste and the need for indication-specific management programs to maximize GLP-1 therapy benefits and pharmaceutical manufacturer value-based contracts to mitigate financial risk.

References

1. Sheth K, Kim S, Porterfield L, Virani SS, Wadhwani S, Vaughan EM. The expanding scope of GLP-1 receptor agonists: Six uses beyond diabetes. *Curr Atheroscler Rep.* 2025 Jul 30;27(1):76. doi: 10.1007/s11883-025-01319-6. PMID: 40736924; PMCID: PMC12590185.
2. FDA approves first treatment to reduce risk of serious heart problems specifically in adults with obesity or overweight. US Food and Drug Administration. Published March 8, 2024. Accessed January 30, 2026. https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-reduce-risk-serious-heart-problems-specifically-adults-obesity-or
3. FDA approves first medication for obstructive sleep apnea. US Food and Drug Administration. Published December 20, 2024. Accessed January 30, 2026. https://www.fda.gov/news-events/press-announcements/fda-approves-first-medication-obstructive-sleep-apnea
4. FDA approves treatment for serious liver disease known as 'MASH'. US Food and Drug Administration. Published 2025. Accessed January 30, 2026. https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-treatment-serious-liver-disease-known-mash

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