Trends in Real-World Persistence to Weight-Loss-Indicated Glucagon-Like Peptide-1 Receptor Agonists from 2021 to 2024 Among Commercially Insured Adults Without Diabetes

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Background

- Obesity affects approximately 40% of adults in the United States, with an estimated economic and societal impact of $1.39 trillion dollars annually.[1,2]
- Once-weekly, high-potency glucagon-like peptide-1 (GLP-1) formulations—semaglutide (Wegovy) and tirzepatide (Zepbound)—are highly efficacious pharmacologic options for weight loss and weight management. Semaglutide, approved by the Food and Drug Administration (FDA) in June 2021, demonstrated average weight reductions of 15% in clinical trials, while tirzepatide, approved by the FDA in November 2023, demonstrated average weight reductions between 15% and 20.9%.[3,4]
- Driven by surging demand for GLP-1 therapies, formulations of semaglutide and tirzepatide faced supply shortages beginning in 2022. These shortages persisted through early 2025, creating widespread access barriers and disrupting prescribed treatment regimens.[5,6]
- Real-world studies report poor persistence and adherence to GLP-1 therapies for obesity, with 1-year persistence rates ranging from 32% to 50%, and average proportion of days covered (PDC) ranging from 51% to 54%.[7-10]
- With GLP-1 therapies' gross annual costs exceeding $12,000 per patient, GLP-1s for obesity pose challenges to cost effectiveness and sustained pharmacy benefit affordability, particularly given the growing scale of use.

Objectives

Our objective is to evaluate 1-year persistence and adherence to high-potency, weight-loss-indicated GLP-1 therapy among commercially insured adults without diabetes, stratified by year of treatment initiation from January 1, 2021, through March 31, 2024.

Methods

- Prime Therapeutics' integrated medical and pharmacy claims plus enrollment data from January 1, 2020, to June 30, 2025, across 19 commercial health plans covering all regions of the United States were used 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, and procedures performed), pharmacy claims (fill dates, days' supply, and National Drug Code numbers), and eligibility information (member demographics and enrollment history).
- Study inclusion was limited to members newly initiating a high-potency, weight-loss-indicated GLP-1 medication (semaglutide [Wegovy], tirzepatide [Zepbound]) between January 1, 2021, and March 31, 2024.
- Members were excluded if they had a pre-period medical claim indicating a diabetes mellitus (DM) diagnosis (type 1, type 2, gestational, due to underlying condition, chemical-induced, and other specified) or pharmacy claim for an antidiabetic medication during the 365-day pre-period, or were 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 the study index date.
- The primary outcome of persistence and the secondary outcome of adherence were reported by the index GLP-1 product by index year. Switching to any GLP-1 product, including diabetes-indicated GLP-1 products, was allowed and persistency and adherence measurements were calculated at the GLP-1 category 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. The last day of supply before the gap was defined as the member's discontinuation date for those considered nonpersistent.
- Adherence was measured using the PDC method endorsed by the Pharmacy Quality Alliance and used by the Centers for Medicare & Medicaid Services in their Part C & D Star Ratings. Members with a PDC ≥80% were considered adherent, and those with a PDC <80% were defined as nonadherent.
- The Kaplan-Meier method was used to estimate median and 95% confidence interval time-to-GLP-1 discontinuation by index GLP-1 product by index year.
- Descriptive statistics compared member demographic and clinical characteristics between study index years, as well as for the overall study cohort. Analysis of variance (ANOVA) and chi-square tests were used to evaluate differences in demographic and clinical characteristics across products.

Table 1
Study Cohort Attrition

Study Selection Criteria for High-Potency Weight-Loss-Indicated Glucagon-Like Peptide-1 (GLP-1) Therapy	Commercially Insured Members*
GLP-1 naïve and initiating semaglutide (Wegovy) or tirzepatide (Zepbound) between Q1 2021 and Q1 2024	43,427
No diabetes medical or pharmacy claim (in 365 days prior to and including GLP-1 index date)	37,981
Continuously enrolled 1 year prior to index GLP-1 claim	29,006
≥ 19 years old at GLP-1 index claim	28,807
No malignant cancer, HIV/AIDS, hemophilia, sickle cell disease, or end-stage renal disease	27,521
Continuously enrolled 1 years after index GLP-1 claim	23,025 final analytic cohort

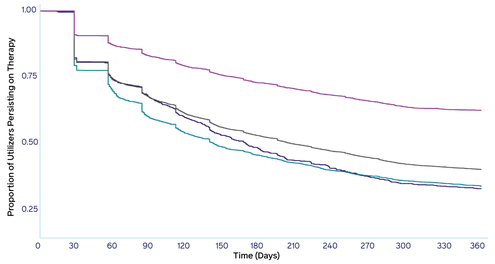
*Study based on 16.5 million average monthly commercially insured members. Rare or debilitating disease is defined as HIV/AIDS, hemophilia, sickle cell disease, malignant cancer, or end-stage renal disease. Discontinuation was defined as a gap in therapy of 60 days or more. GLP-1 product switching was allowed. Wegovy was FDA approved June 4, 2021, and Zepbound was FDA approved November 8, 2023. NA = not applicable

Table 2
One-Year Persistence Rates to High-Potency, Weight-Loss-Indicated Glucagon-Like Peptide-1 (GLP-1) Products: 2021 to First Quarter 2024

	Overall N = 23,025	Semaglutide (Wegovy) N = 21,136	Tirzepatide (Zepbound) N = 1,889
2021 Initiators, % (n)	33.2% (889)	33.2% (889)	NA (0)
2022 Initiators, % (n)	34.1% (2,480)	34.1% (2,480)	NA (0)
2023 Initiators, % (n)	40.4% (14,664)	40.0% (14,428)	64.0% (236)
Q1 2024 Initiators, % (n)	62.6% (4,992)	62.7% (3,339)	62.6% (1,653)

Data represents 23,025 commercially insured adults without diabetes initiating 1 of the following high-potency, weight-loss-indicated GLP-1 products between January 1, 2021, and March 31, 2024: semaglutide (Wegovy) or tirzepatide (Zepbound).
Discontinuation was defined as a gap in therapy of 60 days or more. GLP-1 product switching was allowed.
Wegovy was FDA approved June 4, 2021, and Zepbound was FDA approved November 8, 2023. NA = not applicable

Figure 1
High-Potency, Weight-Loss-Indicated Glucagon-Like Peptide-1 (GLP-1) Agonists: Kaplan-Meier 1-Year Therapy Persistence by Year of Initiation (n = 23,025)



Kaplan-Meier curve represents 23,025 commercially insured adults without diabetes initiating 1 of the following high-potency, weight-loss-indicated GLP-1 products between January 1, 2021, and March 31, 2024: semaglutide (Wegovy) or tirzepatide (Zepbound). Discontinuation is defined as a gap in therapy of 60 days or more. GLP-1 product switching was allowed.

Table 3
Demographics, Clinical Characteristics, and Outcomes by Index Year[a]

	All Members N = 23,025 (100%)	2021 Initiators n = 889 (3.9%)	2022 Initiators n = 2,480 (10.8%)	2023 Initiators n = 14,664 (63.7%)	Q1 2024 Initiators n = 4,992 (21.7%)	*P* value[e]
Characteristic[b]						
Female, n (%)	17,654 (76.7)	704 (79.2)	1981 (79.9)	11283 (76.9)	3686 (73.8)	<.001
Age, mean (SD), years	46.3 (10.4)	45.9 (10.2)	46.7 (9.9)	46.1 (10.4)	46.6 (10.6)	0.006
Charlson Comorbidity Index, mean (SD)	0.2 (0.5)	0.2 (0.5)	0.2 (0.5)	0.2 (0.5)	0.2 (0.5)	0.662
Category						
0	19,615 (85.2)	761 (85.6)	2,113 (85.2)	12,509 (85.3)	4,234 (84.8)	0.904
1	2,856 (12.4)	107 (12.0)	314 (12.7)	1,796 (12.2)	639 (12.8)	
2+	554 (2.4)	21 (2.4)	53 (2.1)	359 (2.4)	121 (2.4)	
Sleep apnea, n (%)	2,537 (11.0)	105 (11.8)	285 (11.5)	1,569 (10.7)	578 (11.6)	0.235
Prediabetes, n (%)	1,723 (7.5)	60 (6.7)	154 (6.2)	1,063 (7.2)	446 (8.9)	<0.001
GLP-1 Outcome[d]						
Persistent without 60-day gap, n (%)	10,187 (44.2)	295 (33.1%)	846 (34.1)	5,919 (40.4)	3,127 (62.6)	<0.001
Adherence (PDC), mean (SD)	59.9 (33.2)	52.6 (33.0)	51.6 (34.0)	57.3 (33.3)	72.7 (28.7)	<0.001
Adherent (PDC ≥80%), n (%)	9,127 (39.6)	271 (30.5)	769 (31.0)	5,304 (36.2)	2,783 (55.7)	<0.001

[a]Commercially insured adults without diabetes newly initiating a high-potency, weight-loss-indicated GLP-1 between January 1, 2021, and March 31, 2024. [b]Clinical characteristics measured in 365-day period prior to GLP-1 initiation (pre-period). Age and gender ascertained at index date. [c]Giasheen WP, et al. Charlson comorbidity index: ICD-9 update and ICD-10 translation. *Am Health Drug Benefits*. 2019;12(4):188–97. https://pubmed.ncbi.nlm.nih.gov/31428236/. [d]Measured in 365-day post GLP-1 initiation (post-period). [e]*P* values for continuous variables is the F-test resulting from ANOVA; *P* values for categorical variables is derived from the chi-square test. SD = standard deviation. GLP-1 = glucagon-like peptide-1 agonist. PDC = proportion of days covered

Results

- A total of 23,025 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 2).
- The mean age was 46.3 years, 76.7% were female, and the prevalence of sleep apnea or pre-diabetes was 11% and 7.5%, respectively (Table 3).
- Across the index years, high-potency weight-loss GLP-1 persistence across all products increased from 33.2% in 2021 to 62.6% in 2024 (Table 2).
- Semaglutide 1-year annual persistence rates from 2021 to 2024 were 33.2%, 34.1%, 40%, and 62.7%, respectively.
- For tirzepatide, 1-year persistence rates in 2023 and 2024 (the only years the product was available) were 64% and 62.2%.
- Median time to discontinuation ranged from 143 days (95% confidence interval [CI]: 134 to 154) in 2022 to not reached (95% CI: NR to NR) in the first quarter of 2024 (Figure 1).
- Mean PDC was lowest in 2022 (52.4 [SD=32.9]) and highest in Q1 2024 (72.6 [SD=28.8]).
- Across index years, 39.3% (range: 30.2% to 55.5%) of members were adherent to GLP-1 during follow-up. (Table 3).

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.
- Although outcome calculations allowed for product switching, product shortages may have impacted persistence and adherence rates.
- Individuals switching to compounded GLP-1 therapy or paying out of pocket for their GLP-1 product may have reduced observed persistence and adherence, as this utilization was not recorded in insurance claims data.
- Additionally, while persistence and adherence were evaluated, this analysis did not account for potential differences in GLP-1 receptor agonist dosing. Specifically, the study did not assess if members achieved the maximum therapy dose, describe maximum tolerated doses, or assess microdosing, which all may influence treatment persistence, adherence, and switching.
- Using medical and pharmacy claims to exclude individuals without a diabetes diagnosis or by drug therapy may misclassify cohort members.
- 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 is outside the scope of this analysis and is worthy of future consideration.

Conclusion

- This real-world analysis of high-potency, weight-loss-indicated GLP-1 products among individuals without diabetes found 1-year treatment persistence nearly doubled, from 1 in 3 individuals initiating therapy in 2021 to almost 2 of 3 initiating therapy in the first quarter of 2024.
- This improvement likely reflects the resolution of GLP-1 supply chain issues, including product shortages, which were addressed throughout 2024 and into 2025. Other potential explanations include improved GLP-1 dose escalation and side effect management, as well as increasing availability of lifestyle management programs over the same period.
- The extremely low, 1-year GLP-1 obesity treatment persistence seen among individuals initiating in 2021 and early 2022 may not be reflective of the current state, as 1-year persistence has nearly doubled between 2021 and the first quarter of 2024.
- Additional research is needed to understand reasons for treatment discontinuation and the long-term cost effectiveness of these products.
- Understanding real-world persistence and adherence to current GLP-1 products when used for weight loss will aid in assessing product cost-effectiveness, understanding obesity care management program needs, forecasting future GLP-1 utilization and cost trends, and negotiating GLP-1 pharmaceutical manufacturer value-based purchasing agreements.

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