# Three-Year Real-World Adherence and Persistence to Glucagon-Like Peptide-1 Receptor Agonists Among Commercially Insured Adults With Obesity and Without Diabetes

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## Background

- In the clinical-trial setting, GLP-1 receptor agonists have demonstrated significant efficacy in promoting weight loss and improving cardiometabolic outcomes in individuals with obesity.[1,2]
- However, real-world evidence consistently shows suboptimal adherence and persistence to GLP-1 therapies for obesity. One-year persistence rates range from 32% to 50%, with an average proportion of days covered (PDC) between 51% and 54%.[3-6]
- A 2-year follow-up study revealed even more pronounced declines in persistence, with rates dropping to approximately 15% by the end of year 2.[7]
- High rates of discontinuation undermine both the clinical and economic value of GLP-1 therapy for obesity. Results from the STEP 1 trial extension[8] and STEP 4 trial[9] indicate that individuals discontinuing treatment after 1 year regain about two-thirds of their lost weight and reverse cardiometabolic improvements, increasing blood glucose and/or blood pressure.
- With no consensus on optimal duration of GLP-1 therapy for obesity, sustained treatment may be necessary to maintain weight loss and associated health benefits.
- Despite growing utilization, there remains a significant gap in knowledge regarding real-world GLP-1 treatment patterns beyond 2 years.

## Objective

Our objective is to evaluate adherence and persistence to GLP-1 therapy at the end of a 3-year follow-up in a real-world cohort of commercially insured members with obesity and without diabetes.

## Methods

- Prime Therapeutics' integrated medical and pharmacy claims plus enrollment data from January 1, 2020, to June 14, 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 average of 16.5 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 continuously enrolled members with obesity and without diabetes newly initiating any of the following GLP-1 medications between January 1, 2021, and March 31, 2022: semaglutide (Ozempic, Rybelsus, or Wegovy), dulaglutide (Trulicity), or liraglutide (Saxenda or Victoza).
- GLP-1 new initiation was defined as no GLP-1 claim in the 365 days prior to the member's first GLP-1 claim in the index period (pre-period).
- Continuous enrollment was defined as no more than a total of 15 days without enrollment in the pre-period and each year in the 3-year post-period.
- During the pre-period, members were required to have a medical claim with diagnosis indicating obesity, defined as ICD-10-CM codes E660-E669, except for E663, or ICD-10-CM codes Z683-Z684.
- 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 a 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-day pre-period.
- The primary outcome of persistence and secondary outcomes of adherence and GLP-1 switching were reported by the initial GLP-1 product dispensed. Switching 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 3-year follow-up period. For those considered nonpersistent, the last day of supply before the gap was defined as the member's discontinuation date.
- Adherence was measured using the PDC method endorsed by the Pharmacy Quality Alliance (PQA) and used by the Centers for Medicare & Medicaid Services (CMS) in their Part C and D Star Ratings with 3 differences: (1) all members were naive to GLP-1 therapy with no GLP-1 claim history in the prior 365 days; (2) a single GLP-1 claim allowed a member to be included in the adherence measurement, whereas CMS requires 2 claims; and (3) all members were continuously enrolled. Members with a PDC ≥80% were considered adherent, and those with a PDC <80% were defined as nonadherent. The Kaplan-Meier method with a log rank test was used to estimate median and 95% confidence interval time-to-GLP-1-discontinuation by index GLP-1 product.
- Switches between GLP-1 products were defined as changes between GLP-1 brand products from 1 claim to the next for a given member. For example, if a member initiated Ozempic and switched to Wegovy, that would count as a GLP-1 product switch, even though both are semaglutide products.
- Descriptive statistics were used to report adherence rates and the count of members with a GLP-1 product switch, by index GLP-1 product.

### Table 1

**Sample Selection**

| Study Selection Criteria – Glucagon-Like Peptide-1 (GLP-1) Obesity Therapy | 16.5 Million Average Monthly Commercially Insured Members |
|---|---|
| Newly initiated GLP-1 between January 1, 2021, and March 31, 2022 (no GLP-1 claim in the 365 days prior to index GLP-1 claim) | 174,514 |
| No diabetes medical or pharmacy claim (in 365 days prior to and including GLP-1 index date) | 36,102 |
| Obesity medical claim or Z-code BMI ≥ 30 (in past 365 days from index GLP-1 claim) | 13,148 |
| Continuously enrolled 1 year prior to index GLP-1 claim | 10,885 |
| ≥ 19 years old at GLP-1 index claim | 10,827 |
| No malignant cancer, HIV/AIDS, hemophilia, sickle cell disease, or end-stage renal disease | 10,287 |
| Continuously enrolled 1 year after index GLP-1 claim | 8,423 |
| Continuously enrolled 2 years after index GLP-1 claim | 6,967 |
| Continuously enrolled 3 years after index GLP-1 claim | 5,780 *final analytic cohort* |

Tirzepatide (Mounjaro) was FDA approved May 2022 and tirzepatide (Zepbound) was FDA approved November 2023. GLP-1 therapy = semaglutide (Ozempic), semaglutide (Rybelsus), dulaglutide (Trulicity), liraglutide (Saxenda), semaglutide (Wegovy), and liraglutide (Victoza). HIV/AIDS = human immunodeficiency virus/acquired immunodeficiency syndrome

### Table 2

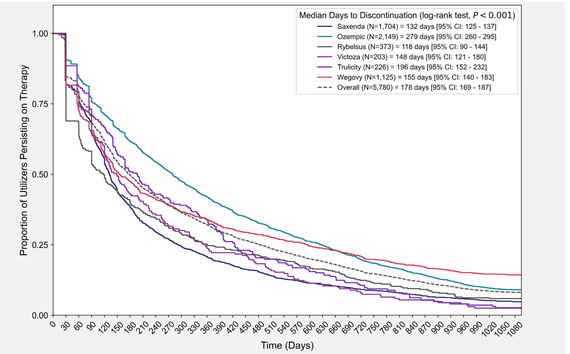
**Three-Year Glucagon-Like Peptide-1 (GLP-1) Agonists: Obesity Therapy Adherence, Persistence, and GLP-1 Product Switch Rates**

| 3-Year Obesity Treatment GLP-1 Users (N, %) | % Persistent (no 60-day gap) | % Adherent (PDC >/= 80%) | % With GLP-1 Product Switch |
|---|---|---|---|
| **Overall (N=5,780)** | **8.1%** | **12.5%** | **37.5%** |
| Wegovy (n=1,125, 19.5%) | 14.3% | 10.6% | 37.7% |
| Ozempic (n=2,149, 37.2%) | 9.0% | 14.7% | 27.5% |
| Rybelsus (n=373, 6.5%) | 5.9% | 9.9% | 38.9% |
| Saxenda (n=1,704, 29.5%) | 4.8% | 8.2% | 46.9% |
| Trulicity (n=226, 3.9%) | 2.7% | 8.8% | 45.6% |
| Victoza (n=203, 3.5%) | 2.5% | 6.4% | 53.2% |

Table 2 represents 5,780 obese commercially insured adults without diabetes initiating 1 of the following GLP-1 products between January 1, 2021, and March 31, 2022: semaglutide (Ozempic, Wegovy, or Rybelsus), dulaglutide (Trulicity), or liraglutide (Victoza or Saxenda). Members were considered persistent if they did not have a 60-day gap in GLP-1 therapy and were censored at the end of the 1,095-day period. Adherence was measured using proportion of days covered (PDC) over 3 years, which is further defined in the Methods section. All adherence and persistency measurements were conducted at the GLP-1 product level, allowing for GLP-1 product switching. Tirzepatide (Mounjaro) was FDA approved May 2022 and tirzepatide (Zepbound) was FDA approved November 2023.

### Figure 1

**Glucagon-Like Peptide-1 (GLP-1) Agonists: Kaplan-Meier 3-Year Obesity Therapy Persistence (N = 5,780) and Median Days to Discontinuation**




The Kaplan-Meier curve represents 5,780 commercially insured adults with obesity and without diabetes initiating 1 of the following GLP-1 products between January 1, 2021, and March 31, 2022: semaglutide (Ozempic, Wegovy, or Rybelsus), dulaglutide (Trulicity), or liraglutide (Victoza or Saxenda). Members were considered persistent if they did not have a 60-day gap in GLP-1 therapy and were censored at the end of the 1,095-day period. All persistency measurements allowed for GLP-1 product switching. Tirzepatide (Mounjaro) was FDA approved May 2022 and tirzepatide (Zepbound) was FDA approved November 2023.

## Results

- Among 16.5 million commercially insured members, a total of 5,780 members were identified as meeting all inclusion and exclusion criteria, including newly initiating GLP-1 obesity therapy without diabetes, and remaining continuously enrolled for 3 years after beginning their GLP-1 obesity therapy **(Table 1)**.
- The mean age of individuals included in the study was 46.7, and 79.9% were women.
- Overall, GLP-1 persistence was 31.5% at 1 year, 15.1% at 2 years, and 8.1% at 3 years **(Figure 1)**.
- The median days to discontinuation was significantly different between products, with weekly semaglutide (Ozempic) having the highest median days to discontinuation (279 days) and once-daily semaglutide (Rybelsus) having the lowest median days to discontinuation (118 days) **(Figure 1)**.
- New initiators of the weekly-injection semaglutide products (Wegovy at 14.3% and Ozempic at 9%) had the highest 3-year persistency rates, and the daily-injection liraglutide products (Trulicity at 2.7% and Victoza at 2.5%) had the lowest 3-year persistence rates **(Table 2)**.
- Overall, 12.5% were adherent to their GLP-1 obesity treatment during the 3 years, with an average adherence PDC of 37.5%. Weekly semaglutide product adherence was 14.7% for Ozempic and 10.6% for Wegovy **(Table 2)**.
- During the 3 years, 37.5% of members switched GLP-1 products **(Table 2)**.

## 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.
- Although outcome calculations allowed for product switching, product shortages may have impacted persistence and adherence rates.
- Members 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.
- Tirzepatide products were not included in this analysis as a GLP-1 new initiator group, as they were not available during the study's index date period. However, switching to tirzepatide was allowed and included in the persistence and adherence assessments.
- Our study examined a commercially insured membership and, therefore, is not generalizable to Medicare or Medicaid populations.
- The impact of a member'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.

## Conclusions

- This real-world analysis of GLP-1 products used for weight loss among obese members without diabetes found poor 3-year persistence, with 1 in 12 members remaining on GLP-1 therapy, as compared to 3-year clinical trial data of greater than 10 in 12.[1]
- Semaglutide (Wegovy) was found to have higher persistency, with approximately 1 in 7 remaining on therapy over the 3-year assessment.
- The low adherence and persistence rates, along with high prevalence of GLP-1 product switching, are likely due to drug shortages, as well as adverse effects, lack of perceived benefit, and/or member cost share.
- These findings highlight GLP-1 obesity therapy investment risk due to low persistence and subsequent loss of therapeutic gains for members who initiated in 2021 and Q1 of 2022. Participation in a comprehensive weight loss treatment program that includes a care manager may improve member experience with GLP-1 obesity treatment and time on therapy.
- 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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EVT_EXT_261001-D 10/25

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Academy of Managed Care Pharmacy (AMCP) Nexus, October 27-30, 2025, National Harbor, MD
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