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GLP-1 Therapy to Treat Obesity Among Members Without Diabetes: Three-Year Persistence and Year-Over-Year Persistence Rate Change

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Introduction

As of 2024, 1 in 8 U.S. adults had used a glucagon-like peptide-1 (GLP-1) agonist product,[1] and nearly 4 in 10 users reported they took a GLP-1 for obesity. Clinical trial evidence has shown use of newer GLP-1 products results in a 10% to 20% reduction in weight,[2] and a four-year trial following patients without diabetes using semaglutide to treat obesity and cardiovascular disease demonstrated a reduction in major adverse cardiovascular events.[3]

Despite the effectiveness of GLP-1 products for the treatment of obesity, persistence remains low with a large portion of members discontinuing therapy within one year of initiation. In 2023, Prime Therapeutics (Prime) published a one-year, real-world study following members without diabetes using a GLP-1 for obesity treatment, and it found adherence and persistence of 27% and 32%, respectively,[4] and a follow-up research study found persistence of 15% at two years.[5] Initiators of weekly injection semaglutide products had the highest two-year persistence rates — Wegovy® at 24% and Ozempic® at 22%.[5] Prime's findings have been confirmed by other published literature,[6, 7] and the medical community has expressed concern over these high discontinuation rates.[2]

While there are no clear guidelines on the length of therapy for GLP-1 obesity treatment, clinical trial evidence has found individuals stopping GLP-1 therapy at one year regained two-thirds of their prior weight loss with similar changes in loss of cardiometabolic benefits.[2,8]

As many individuals will need long-term GLP-1 obesity therapy to achieve the benefits and maintain weight loss, it's important to understand real-world GLP-1 obesity treatment adherence and persistence rates. Factors affecting GLP-1 therapy persistence are numerous and include GLP-1 supply chain issues, member cost, adverse effects, meeting of clinical or personal weight-loss goals and more. Little is known of real-world GLP-1 obesity treatment adherence and persistence beyond two years. In addition, with supply chain issues largely resolving for obesity-indicated GLP-1 products in 2024, understanding

persistence patterns for members who started therapy in more recent years may make the impact of supply chain issues more clear.

Objectives

This study had two objectives:

1. To describe three-year GLP-1 obesity treatment adherence and persistence among commercially insured members without diabetes who newly initiated GLP-1 treatment in 2021 and the first quarter of 2022 (1Q2022).
2. To compare year-over-year persistence to obesity-indicated, high-potency GLP-1 products, semaglutide (Wegovy) and tirzepatide (Zepbound®), among new initiators by year of initiation.

Methods

Detailed methods have been published in the Journal of Managed Care & Specialty Pharmacy with a minor change to the member continuous enrollment definition and GLP-1 index date period.[5] Briefly, data for this analysis come from Prime's integrated pharmacy and medical claims data, which include an average of 16.5 million commercially insured lives during any given month. For the first objective, members with obesity and without diabetes who newly initiated GLP-1 obesity treatment between Jan. 1, 2021, and March 31, 2022 (index period) were identified. GLP-1 new initiation was defined as no GLP-1 claim from Jan. 1, 2020, through the first GLP-1 claim in the index period (index GLP-1 claim). Study inclusion was limited to members with continuous enrollment during the 365 days pre-period prior to their index GLP-1 claim, defined as no more than a total of 15 days without enrollment. Members were also required to have continuous enrollment for each year in the three-year treatment period. During the pre-period, members were required to have a medical claim indicating obesity without a diabetes diagnosis or diabetes drug claim, and aged 19 years or older on the day of index. Adherence was measured as the proportion of days covered (PDC) during the treatment period, and members with a PDC ≥ 80% for the entire three-year evaluation period were considered adherent. Persistence was defined as no ≥ 60-day gap between a claim days' supply ending and a subsequent claim fill date in the treatment period. GLP-1 product switching was allowed during the assessment period, and switch rates were descriptively assessed.

For the second objective, comparing one-year GLP-1 persistence by year of initiation, four GLP-1 obesity without diabetes treatment cohorts were identified using the methods above, with the exception that members were not required to have an obesity medical claim as the GLP-1 products assessed were limited to semaglutide (Wegovy) and tirzepatide (Zepbound) — the only high-potency GLP-1 products indicated for the treatment of obesity. The four cohort index periods were comprised of calendar years

2021, 2022 and 2023 and the first calendar quarter of 2024 (Jan. 1, 2024, through March 31, 2024).

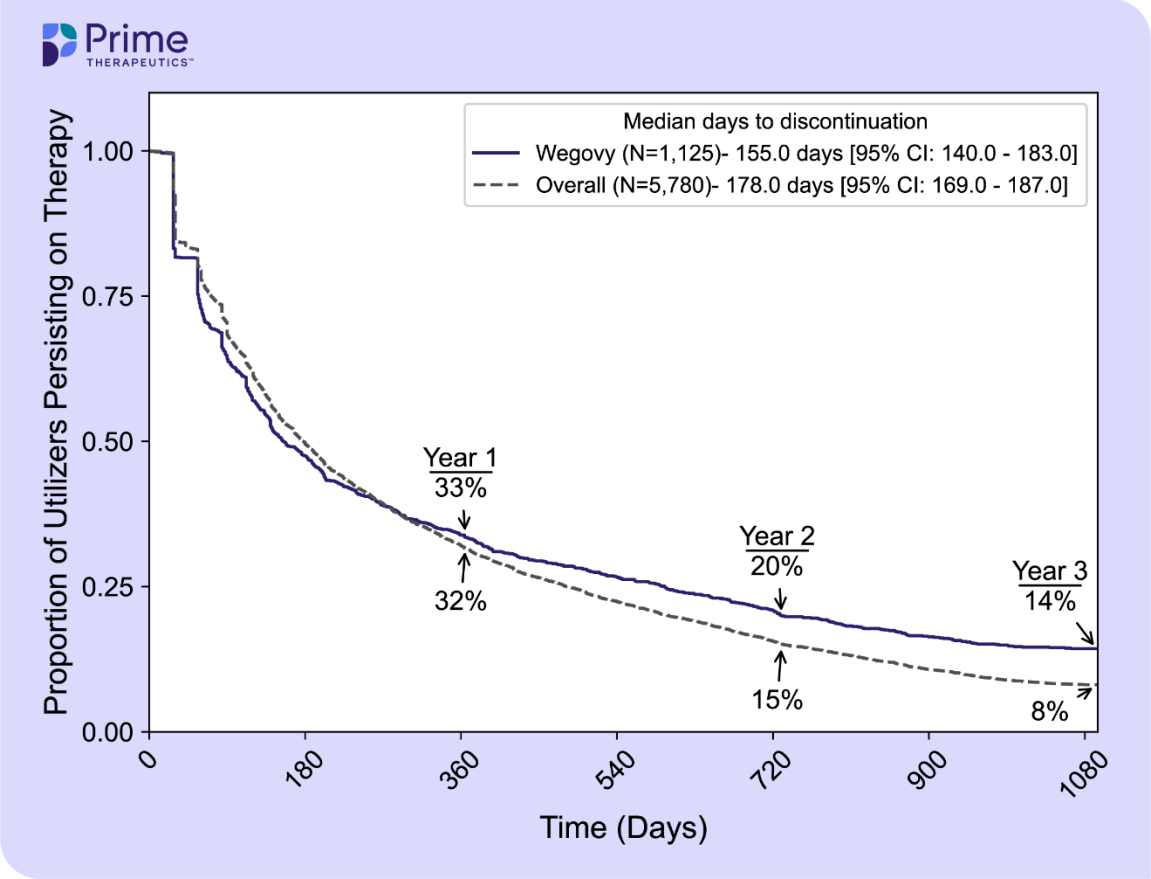
Limitations

Data were sourced from administrative health care claims; therefore, misclassification bias may have occurred due to using medical and pharmacy claims to exclude individuals without 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. This study examined commercially insured members, and therefore, results are not generalizable to Medicare or Medicaid populations. The impact of cost sharing, other diagnoses, social drivers of health or other member characteristics are outside the scope of this analysis; however, they are worthy of future consideration.

Results

Of the 174,519 members who had a GLP-1 claim between Jan. 1, 2021, and March 31, 2022, 10,292 (5.9%) met eligibility criteria, including evidence of obesity in medical claims and no diabetes diagnosis or drug therapy in the 365 days from starting a GLP-1. Of these 10,292 members, the final analyzable population were the 5,780 (56.2%) continuously enrolled for three years after starting their GLP-1. The primary reason members were removed from the analysis was a diabetes diagnosis in the pre-period (138,412 removed, 79.3%). The mean age was 46.7 years and 79.9% identified as female. Overall GLP-1 persistence was 1 in 12 (8.1%) at three years. The highest and lowest persistence rates at three years were observed for weekly semaglutide (14.3%; Wegovy) and daily liraglutide (2.5%; Victoza®), respectively. Average GLP-1 PDC over three years was 37.5%, with 12.5% of members adherent using the PDC at or above 80% definition, and 37.5% switched GLP-1 drugs at least once during the three years.

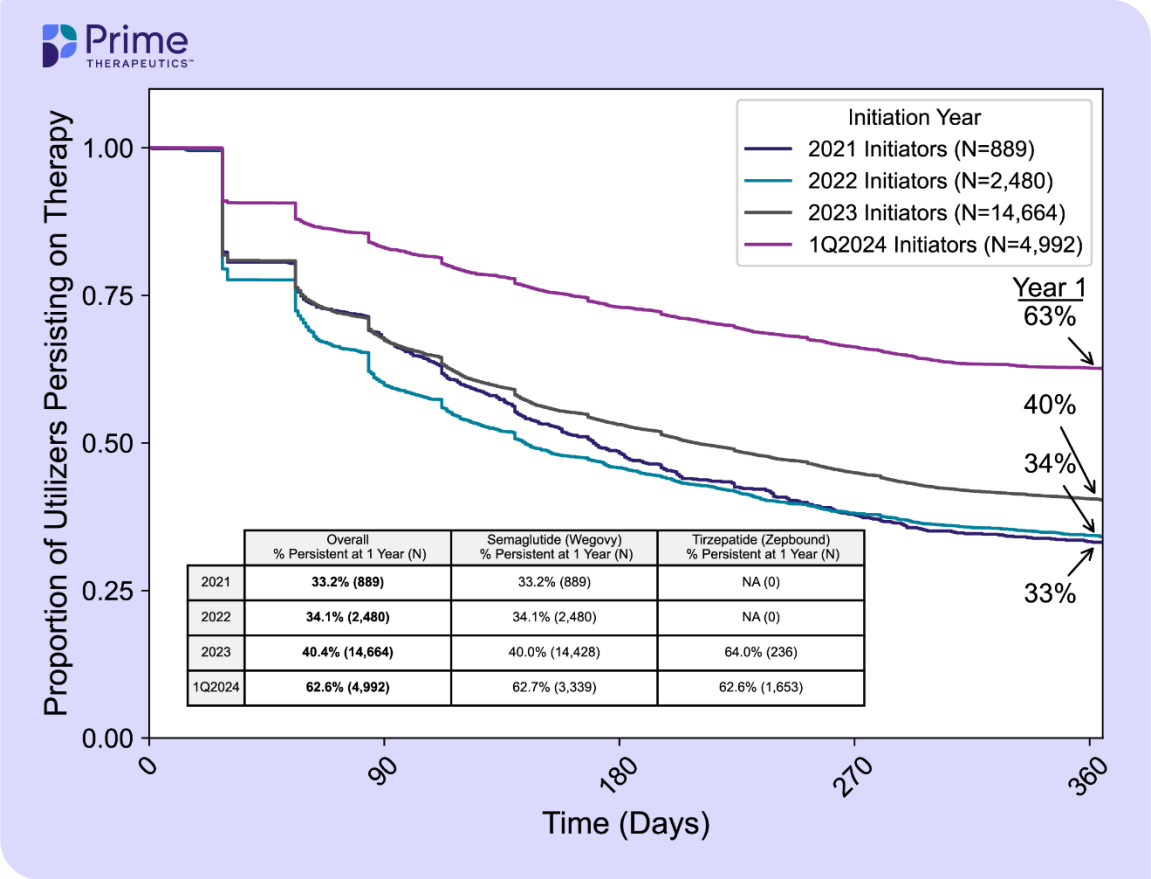
Figure 1. Obesity Treatment GLP-1 Agonists: Kaplan-Meier Three-Year Therapy Persistence (N = 5,780)



Kaplan-Meier curve represents 5,780 obese commercially insured adults without diabetes, initiating a GLP-1 product between January 1, 2021, and March 31, 2022. GLP-1 product switching was allowed. Members were considered persistent if they did not have a 60-day gap in GLP-1 therapy and were censored at the end of their 1,095-day (three year) period following their index GLP-1 claim.

For the year-over-year obesity-indicated, high-potency GLP-1 one-year persistence trend analysis, 43,427 members without diabetes newly initiated semaglutide (Wegovy) or tirzepatide (Zepbound) during the study period and 23,025 (53.0%) met full study criteria. The mean age was 46.3 years, and 76.7% were female. Across the index years, persistence to obesity-indicated, high-potency GLP-1 products increased from 33.2% in 2021, 34.1% in 2022, 40.4% in 2023 and 62.6% in 2024. Semaglutide (Wegovy) one-year persistence rates from 2021 to 2024 were 33.2%, 34.1%, 40.0%, and 62.7% across respective years. With tirzepatide (Zepbound), the product was available beginning in November 2023, and one-year persistence rates were 64.0% and 62.6% for 2023 and 2024.

Figure 2. Obesity-Indicated High-Potency GLP-1 Agonists (Wegovy and Zepbound): Kaplan-Meier One-Year Therapy Persistence (N=23,025)



NOTE: Wegovy became available in June 2021 and Zepbound in November 2023. NA = not applicable.

Kaplan-Meier curve represents 23,025 commercially insured adults without diabetes newly initiating an obesity-indicated, high-potency GLP-1 product (Wegovy or Zepbound) between January 1, 2021, and March 31, 2024. Persistence was measured over a one-year period, allowing for switching between all dosage strengths of GLP-1 products. Members were considered persistent if they did not have a 60-day gap in GLP-1 therapy and were censored at the end of their one-year follow-up period, following their index GLP-1 claim.

Conclusions

Three-year GLP-1 obesity treatment persistence was poor, with 1 in 12 members remaining on therapy, and while persistence was better for the Wegovy initiators, it was still 1 in 7. These findings highlight GLP-1 obesity therapy investment risk due to poor persistence leading to unachieved clinical benefits for members who initiated in 2021 and early in 2022. However, the year-over-year, one-year persistence

analysis of obesity-indicated, high-potency GLP-1 products found one-year persistence nearly doubling from 33.2% in 2021 to 62.7% in 2024. Obesity-indicated, high-potency GLP-1 supply chain issues, including product shortages, were largely resolving in 2024 and likely explain improved persistence. Other potential explanations include improved GLP-1 dose escalation and side-effect management, as well as care and lifestyle management programs. The extremely low, three-year GLP-1 obesity treatment persistence seen among individuals initiating in 2021 and early 2022 may not be reflective of the current state as one-year persistence has nearly doubled between 2021 and the first quarter of 2024. Additional research is still needed to understand reasons for treatment discontinuation and the long-term cost-effectiveness.

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