ISSUE BRIEF: MAY 2024

Real-World Trends in GLP-1 Treatment Persistence and Prescribing for Weight Management

KEY TAKEAWAYS

The adoption rate of prescribing GLP-1s for weight management has been exponential.

30% of patients stopped treatment within four weeks, before reaching the targeted dose.

Many people discontinued use of GLP-1 therapy before achieving clinically meaningful weight loss.

Individuals age 35 and older were more likely to stay on GLP-1 treatment for at least 12 weeks.

Regular visits to healthcare providers improved medication persistence.

Issue Brief by Blue Health Intelligence® (BHI®)
for Blue Cross Blue Shield Association

AON Center
200 East Randolph, Suite 3050
Chicago, Il 60601
(312) 540-5151
Bluehealthintelligence.com

EXECUTIVE SUMMARY

The introduction of GLP-1 agonist (GLP-1) drugs significantly disrupted traditional approaches to weight and obesity management. Since the U.S. Food and Drug Assocation (FDA) approval of semaglutide (Wegovy®) for weight management in June 2021, net sales of all anti-obesity medications in the United States have increased, amounting to an estimated $1.1 billion in the second quarter of 2023.[1] A better understanding of how these new weight management medications are prescribed and what issues may be impacting medication persistence will inform strategies around ensuring the success of GLP-1 therapies for patients, while limiting ineffective care and unnecessary healthcare spending.

This study was performed to explore if patients prescribed GLP-1s for weight loss are dropping out of treatment too quickly to attain the health benefits of these drugs.

BACKGROUND

- In the United States, seven out of 10 adults and three out of 10 children have overweight or obesity.[2]
- When weight management interventions are used successfully, they have the potential to lower the healthcare costs and health risks associated with obesity. Adults with obesity average a total of $1,861 more in medical costs annually than people who are a healthy weight, and severe adult obesity was linked to $3,097 in excess annual costs per person.[3] Additional research is needed to understand if GLP-1 interventions lead to lower medical costs in the longer term.
- The average monthly list price for semaglutide is over $1,000.
- Nearly half of U.S. adults are interested in taking a weight loss drug[4], and a recent report by the Institute for Clinical and Economic Review shows that if just 0.1% of the 142 million qualifying Americans took GLP-1s, the impact on the nation's healthcare spending would be significant.[5]
- Patients on GLP-1 drugs should complete at least 12 weeks of continuous treatment to be able to achieve clinically meaningful weight loss that will positively impact their health.[6,7]

[1] Congressional Budget Office, "A Call for New Research in the Area of Obesity." Retrieved 20 March 2024.
[2] Centers for Disease Control and Prevention, National Center for Health Statistics. "Obesity and Overweight." Retrieved 25 March 2024.
[3] Kaiser Family Foundation, "KFF Health Tracking Poll July 2023: The Public's Views of New Prescription Weight Loss Drugs and Prescription Drug Costs." Retrieved 25 March 2024.
[4] Institute for Clinical and Economic Review. "Medications for Obesity Management: Effectiveness and Value." Final Evidence Report, October 20, 2022.
[5] Varanasi, A, 2021. "Obesity Epidemic Accounts for More than $170 Billion in Surplus Medical Costs Per Year in the United States: Study." Forbes. 31 Retrieved 25 March 2024.
[6] Pi-Sunyer, X., Astrup, A., Fujioka, K., Greenway, F., Halpern, A., Krempf, M., Lau, D. C. W., le Roux, C. W., Violante Ortiz, R., Jensen, C. B., & Wilding, J. P. H. (2015). A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management. New England Journal of Medicine, 373(1), 11–22.
[7] Wilding, J. P. H., Batterham, R. L., Calanna, S., Davies, M., Van Gaal, L. F., Lingvay, I., McGowan, B. M., Rosenstock, J., Tran, M. T. D., Wadden, T. A., Wharton, S., Yokote, K., Zeuthen, N., & Kushner, R. F. (2021). Once Weekly Semaglutide in Adults with Overweight or Obesity. New England Journal of Medicine, 384(11), 989–1002.

APPROACH

To learn more, Blue Health Intelligence® (BHI®) used a nationally representative, commercially insured data set to answer the following questions:

1. Is there evidence that patients prescribed GLP-1s for weight management drop out of treatment too soon to see a clinically significant effect?
2. Is premature GLP-1 treatment discontinuation more likely for certain patients or if certain types of providers oversee the treatment?

FINDINGS

- More than 30% of patients dropped out of treatment after the first four weeks, when the dose was still being increased to reach the targeted dose.
- When looking at patients using GLP-1 drugs for weight management, our findings show that most individuals did not stay on their prescribed treatment for a minimum of 12 weeks, suggesting that they were unlikely to achieve clinically meaningful weight loss.
- Younger patients, age 18 to 34, were more likely to drop out of treatment sooner.
- Gender had no impact on dropout rates within the first 12 weeks.
- Patients who were prescribed GLP-1s by providers with expertise in weight management and obesity, like endocrinologists and obesity specialists, were more likely to complete 12 weeks of treatment.
- Individuals who completed 12 weeks of treatment saw their providers more frequently after the prescription of GLP-1s than those who dropped out of treatment sooner.
- People who had health inequities or lived in underserved health regions were also less likely to complete 12 weeks of treatment.

INTRODUCTION

Nearly three out of every four Americans over the age of 20 are overweight,[8] and 42% of Americans are affected by obesity.[2] The health risks of obesity are considerable and the U.S. Centers for Disease Control and Prevention (CDC) estimates that healthcare costs related to obesity exceed $170 billion annually.[5] People with obesity are more likely to suffer from heart disease, liver disease, cancer, diabetes, and arthritis than individuals who maintain a normal body weight. Additionally, the stigma associated with obesity significantly impacts the emotional well-being of people unable to lose weight or maintain weight loss.

The introduction of GLP-1 drugs for the management of obesity has significantly disrupted traditional weight management approaches. The momentum of adoption of GLP-1s increased in June 2021 with the FDA approval of semaglutide (Wegovy®) for weight management. The rapid growth in the number of prescriptions issued and filled for GLP-1s for weight management has, at times, led to shortages of the formulations for patients who are intended to use these therapies to manage Type 2 diabetes.[9]

GLP-1s represent the first, at-scale, therapeutic drug success for weight management. Historically, the emphasis of weight management programs has been on integrated diet and exercise programs – which have shown some success, but where most participants fail to lose any significant weight or regain most, if not all, of it.[10]

[8] Axios. "42% of Americans are Living with Obesity." Retrieved 20 March 2024.
[9] American Journal of Managed Care, "An Ongoing Crisis: Semaglutide Shortage Raises Dual Concerns for Obesity and Diabetes Treatment." Retrieved 20 March 2024.
[10] Fildes A, Charlton J, Rudisill C, Littlejohns P, Prevost AT, Gulliford MC. Probability of an Obese Person Attaining Normal Body Weight: Cohort Study Using Electronic Health Records. Am J Public Health. 2015 Sep;105(9):e54-9. doi: 10.2105/AJPH.2015.302773. Epub 2015 Jul 16. PMID: 26180980; PMCID: PMC4539812.

GLP-1s are game changers. The first licensed GLP-1 for weight loss, a daily formulation, liraglutide (Saxenda®), resulted in a 5% weight loss for most people who used it during clinical trials. This level of weight loss is clinically significant and has measurable effects on conditions associated with obesity.[6,7] Some of the GLP-1-type drugs that are now in the late phases of development can help people lose in excess of 25% of their starting body weight, rivaling the amount of weight loss achieved after most bariatric surgeries.

Even at modest levels of sustained weight loss (5% or more for people that meet threshold GLP-1 therapy-eligible body mass index (BMI) numbers), there are significant benefits to their health and well-being. Health conditions related to obesity, such as diabetes, hypertension, heart disease, stroke, liver disease, sleep apnea, and increased wear and tear on joints are improved. For example, in a trial of 529 people with obesity and heart failure, people who were on the GLP-1 semaglutide (Wegovy®) had nearly double the improvement in symptoms as measured on a standard heart failure questionnaire after one year when compared to people that were treated in the standard way.[11] In another large study, the Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity (SELECT) trial, people with both excess weight and cardiovascular disease who took semaglutide (Wegovy®) had a 20% lower risk of heart attacks and strokes than those on placebo.[12]

To achieve these important health benefits, it is critical that people taking GLP-1s continue taking the drug long enough to achieve clinical success. This means that, on average, patients should complete at least 12 weeks of continuous treatment[6,7] to achieve a level of weight loss that will positively impact their health. Weight management strategies should be in place to continue maintaining weight loss after initial success and may include long-term use of GLP-1s and healthy eating and exercise. Like all therapies, GLP-1s can cause side effects. Some of these may be serious enough, even if rare, that result in patient harm. There are also unanswered questions about the safety of long-term high-dose use, costs to the healthcare system, and equity that still need to be answered.

Almost all new users of GLP-1 drugs suffer from some gastrointestinal side effects. This nausea, vomiting, and diarrhea can be disruptive enough that people stop GLP-1 treatment. Because the dose of the drug is increased at regular intervals, this drop-out challenge is common, unless effective coping strategies are identified and discussed with patients before treatment starts. For patients treated with GLP-1s, side effects can be a considerable treatment persistence challenge. For individuals who are unable to develop side effect coping strategies that work for them or who do not have access to support that can help them manage through this challenge, initiating therapy that will not result in positive clinical or personal outcomes, leading to treatment failure and wasted expense.

RESEARCH QUESTIONS

BHI examined the persistence patterns in the utilization of GLP-1 products for weight management by Blue Cross Blue Shield members participating in Plans that provided coverage of these products. We assessed the initiation and continued use of these products, as well as the prescribers of the medication and the association between the provider and the patient, in a national data set of commercial members' pharmacy and medical benefit claims. We specifically evaluated if members were maintaining use of GLP-1 medications for a time period associated with clinically meaningful weight loss (a minimum of 12 weeks) and identified characteristics associated with successful use.

[11] Kosiborod MN, Abildstrøm SZ, Borlaug BA, Butler J, Rasmussen S, Davies M, Hovingh GK, Kitzman DW, Lindegaard ML, Møller DV, Shah SJ, Treppendahl MB, Verma S, Abhayaratna W, Ahmed FZ, Chopra V, Ezekowitz J, Fu M, Ito H, Lelonek M, Melenovsky V, Merkely B, Núñez J, Perna E, Schou M, Senni M, Sharma K, Van der Meer P, von Lewinski D, Wolf D, Petrie MC; STEP-HFpEF Trial Committees and Investigators. Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity. N Engl J Med. 2023 Sep 21;389(12):1069-1084. doi: 10.1056/NEJMoa2306963. Epub 2023 Aug 25. PMID: 37622681.

[12] Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, Hardt-Lindberg S, Hovingh GK, Kahn SE, Kushner RF, Lingvay I, Oral TK, Michelsen MM, Plutzky J, Tornøe CW, Ryan DH; SELECT Trial Investigators. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. N Engl J Med. 2023 Dec 14;389(24):2221-2232. doi: 10.1056/NEJMoa2307563. Epub 2023 Nov 11. PMID: 37952131.2023 Dec 14;389(24):2221-2232. doi: 10.1056/NEJMoa2307563. Epub 2023 Nov 11. PMID: 37952131.

This analysis explored two questions:

1. Is there evidence that patients prescribed GLP-1s for weight management drop out of treatment too soon to see a clinically significant effect?
2. Is premature GLP-1 treatment discontinuation more likely for certain patients or if certain types of providers oversee the treatment?

METHODOLOGY

To understand GLP-1 utilization for weight management and identify characteristics of clinically successful users, BHI examined national pharmacy and medical claims data between January 2014 (when the earliest GLP-1, liraglutide (Saxenda®) was approved for weight management) and December 2023. The study population was comprised of members who resided in the United States and had medical and pharmacy benefits through a large commercial insurance provider. Coverage of GLP-1 products for weight loss was determined by the Plan having fully adjudicated and paid for at least 10 unique weight management GLP-1 claims per month for the six-month period from January 2023 to June 2023; all individuals participating in these Plans were eligible for inclusion.

Uptake of semaglutide (Wegovy®) increased exponentially during that time, and it was for this reason that we chose it as a baseline period to ensure the largest sampling of Plans possible. Included members were prescribed semaglutide (Wegovy®) and/or liraglutide (Saxenda®) between July 2014 and December 2023. To ensure comprehensive insight into their healthcare engagement and other clinical features, these members had to have at least six months of continuous enrollment both before and after beginning their GLP-1 product for weight management. Users of tirzepatide (Zepbound®), a newer GLP-1 product available for weight management in November 2023, were not included in this study, as the new availability of this product did not allow us to study users for a period long enough to adequately assess 12-week persistence.

How did we define GLP-1 users?

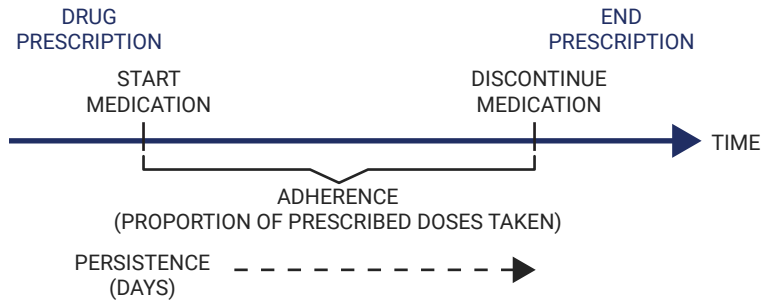
INCLUSION CRITERIA	EXCLUSION CRITERIA
▪ Aged between 18-64 at the time of their first GLP-1 prescription. ▪ Primary medical and drug coverage is a Blue Cross Blue Shield Plan that covered GLP-1 use for weight management on or prior to 6/1/23. ▪ Prescribed a GLP-1 indicated by the FDA for weight management (BMI ≥30 or BMI ≥ 27 with at least one related comorbidity) between 7/1/14 and 12/31/23. ▪ Continuously enrolled in Blue Cross Blue Shield medical and drug coverage for at least six months before and after their first GLP-1 prescription.	▪ Patients with dementia, active cancer, psychosis, on dialysis, and transplant recipients. ▪ Primary medical and drug coverage is managed Medicaid or Medicare Advantage. ▪ Prescribed a GLP-1 that is not indicated by the FDA for weight management.

The following characteristics were examined:

- Characteristics of GLP-1 users (overall, persistent, and non-persistent)
  - General demographics (age, gender, rural/urban status, and geographic region)
  - Charlson Comorbidity Index (CCI), an overall indicator of a patient's health status

- Comorbidities of interest
  - Diabetes mellitus Type 2
  - Dyslipidemia (high cholesterol)
  - Hypertension (high blood pressure)
  - Migraine
  - Gastroesophageal reflux disease (GERD)
  - Osteoarthritis
  - Obstructive sleep apnea
  - Chronic pain
  - Coronary artery disease
  - Nonalcoholic fatty liver disease
- Potentially ineffective prescribing: There were high rates of weight management GLP-1 prescribing by providers whose scope of practice does not typically include obesity management (such as cardiologists and obstetricians/gynecologists). Due to this, we hypothesized that there were characteristics of the patient-provider interaction that led to poor persistence and sought to characterize these features.
- Length of time to GLP-1 discontinuation.
- Medication persistence: Continuous dispensing, with non-persistence defined as a gap following the most recent prescription that is two or more times the expected duration of that prescription (e.g., for a four-week dose autoinjector, discontinuation would be met if not refilled within eight weeks). How persistence is measured is detailed in **Figure 1** below.

Figure 1: Medication-taking behavior definitions[13]



[13] Michel Burnier, Medication Adherence and Persistence as the Cornerstone of Effective Antihypertensive Therapy, American Journal of Hypertension, Volume 19, Issue 11, November 2006, Pages 1190–1196, https://doi.org/10.1016/j.amjhyper.2006.04.006

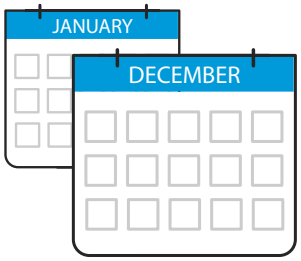
GLP-1 Medication for Weight Loss: Profile of Users and Prescribers

169,250
unique GLP-1 users for weight loss

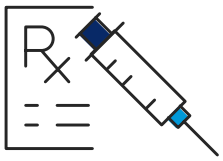
79%
female on average

45 years
average age

TIME PERIOD

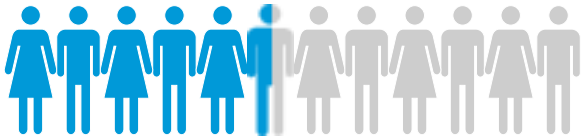


JANUARY 2014
through
DECEMBER 2023



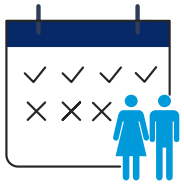
Majority of GLP-1 prescriptions for weight loss were provided by PRIMARY CARE PROVIDERS over endocrinologists or obesity medicine specialists.

GLP-1 Medication Persistence: Factors Affecting Discontinuation

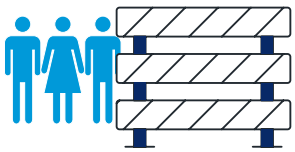


LESS THAN HALF of those prescribed stay on the medication for 12 weeks or more.

Those who receive their medication from an endocrinologist or obesity medicine specialist were MORE LIKELY to continue longer.



Gender DID NOT impact 12-week discontinuation rate.



Members with the highest barriers to care were LEAST likely to continue medication.

AGE

18 to 34

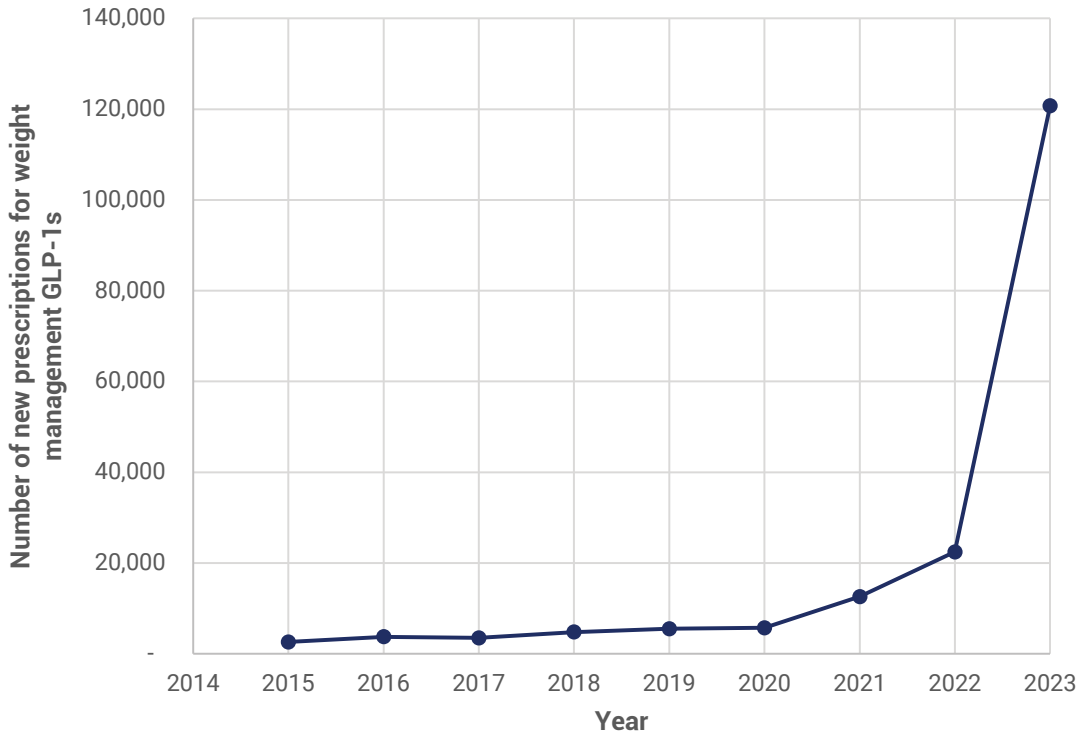
Younger adults were LESS likely to continue on the drug.

RESULTS

- About half of all individuals who used GLP-1s for weight management stayed on treatment for a minimum of 12 weeks, suggesting that they were likely to achieve clinically meaningful weight loss.
- Those who visited their provider more often during the first 12 weeks of treatment were more likely to be persistent.
- Persistence, also known as taking the medication as prescribed for a long enough period to be effective, was higher in individuals seeing endocrinologists or obesity medicine specialists.
- These results were observed in GLP-1 users regardless of the type of GLP-1 medication treatment used.

We found that use of GLP-1 products for weight management has escalated over the past several years (**Figure 2**). From 2014 to 2021, liraglutide (Saxenda®), a product requiring daily injections, was the only GLP-1 product available for weight management. During that time, use of these products was largely consistent and fewer than 6,000 individuals began on the medication each year. The 2021 introduction of semaglutide (Wegovy®), which necessitated only weekly injections, accelerated use of these products, with an increase from 5,717 new users in 2020 to 120,763 in 2023 (an increase of over 2,000%).

Figure 2: Trends in use of GLP-1 products for weight management 2014-2023



The majority of weight management GLP-1 users in our study were female, between the ages of 35 and 54 years, resided in the Northeast, and received their GLP-1 prescription from a primary care provider (**Table 1**). Nearly two-thirds of the group had low social vulnerability (i.e., had a score in the 4th quartile), as indicated by the Social Vulnerability Index, a CDC-developed measure of a community's vulnerability based on external factors such as sociodemographic status.

The most common obesity-related comorbidities observed included dyslipidemia, hypertension, and GERD.

Table 1: Descriptive statistics (categorical): Sociodemographic and clinical characteristics of weight management GLP-1 users in the BHI closed claims data set, July 2014 to December 2023 (n=169,250).

	n (%)
Gender	
Male	34,949 (20.6)
Female	134,301 (79.4)
Age	
18-34 years	27,887 (16.5)
35-54 years	107,244 (63.4)
55-64 years	34,119 (20.2)
Overall Social Vulnerability Index (SVI) score	
1st quartile (least vulnerable)	57,457 (33.9)
2nd quartile	45,761 (27.0)
3rd quartile	36,124 (21.3)
4th quartile (most vulnerable)	21,437 (12.7)
Unassigned	8,471 (5.0)
Census region	
Northeast	71,211 (42.1)
South	49,935 (29.5)
West	18,752 (11.1)
Midwest	29,352 (17.3)
Obesity-related comorbidities*	
Diabetes mellitus Type 2	18,189 (10.0)
Hypertension	86,869 (47.8)
Dyslipidemia	87,944 (48.4)
Migraine	48,916 (26.9)
Gastroesophageal reflux disease	72,561 (39.9)
Osteoarthritis	48,300 (26.6)
Obstructive sleep apnea	49,873 (27.5)
Chronic pain	6,870 (3.8)
Non-alcoholic fatty liver disease	17,742 (9.8)
Coronary artery disease	8,819 (4.9)
Prescribing provider specialty	
Primary care providers	93,321 (55.1)
Endocrinologists/obesity medicine specialists	7,121 (4.2)
Other specialists	62,446 (36.9)
Uncategorized	6,362 (3.8)

*Diagnosed in at least one medical claim in the six months prior to GLP-1 initiation

Medication persistence, also known as the amount of time an individual stays on the drug, is detailed in **Table 2** below by GLP-1 product and by prescribing provider.

Table 2: Medication persistence* in weight management GLP-1^ users in the BHI closed claims dataset, July 2014 to December 2023.

	n (%)
Persistence by product^	
<4 weeks	1,389 (0.8)
4 to <8 weeks	75,572 (41.6)
8 to <12 weeks	27,996 (15.4)
≥12 weeks	76,676 (42.2)
Persistence by prescribing provider specialty	
Primary care providers	
<4 weeks	912 (0.9)
4 to <8 weeks	39,468 (39.9)
8 to <12 weeks	14,818 (15.0)
≥12 weeks	43,671 (44.2)
Endocrinologists/obesity medicine specialists	
<4 weeks	84 (1.1)
4 to <8 weeks	2,705 (35.3)
8 to <12 weeks	1,026 (13.4)
≥12 weeks	3,843 (50.2)
Other specialists	
<4 weeks	130 (1.1)
4 to <8 weeks	4,637 (40.0)
8 to <12 weeks	1,548 (13.3)
≥12 weeks	5,284 (45.6)

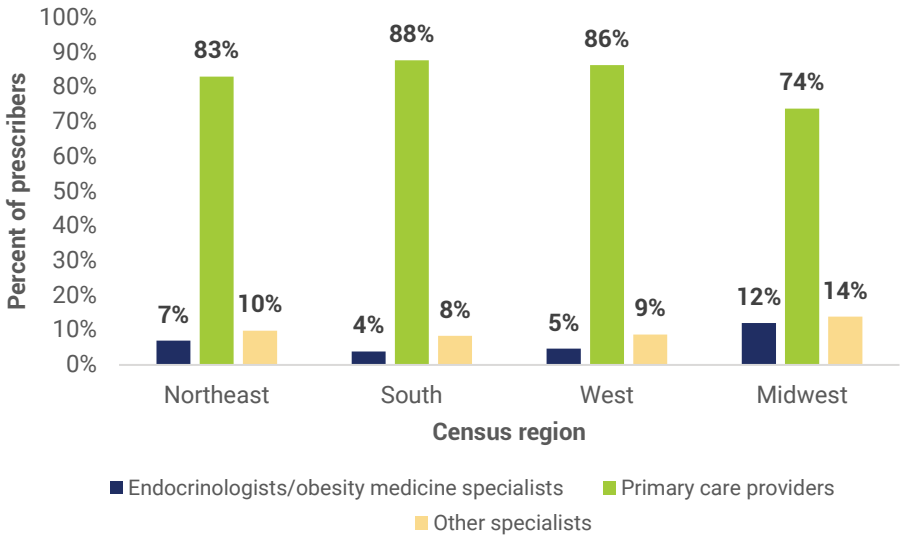
*A GLP-1 user is considered non-persistent when discontinuation is reached. Discontinuation will be defined – as in previous GLP-1 studies – as a gap in dispensing following the most recent prescription that is two or more times the expected duration of that prescription (e.g., for a four-week dose autoinjector, discontinuation would be met if not refilled within eight weeks).

^Tirzepatide, which was approved by the US FDA for weight management indications in November 2023, was not included in this iteration of the analysis due to limited accumulation of utilization data in BHI's data source.

More than two-thirds of GLP-1 prescriptions occurred in the Northeast (42.1%) and South (29.5%). Prescribing providers were identified via provider information associated with an individual's first fill of a GLP-1 product for weight management. Endocrinologists and obesity medicine specialists were grouped together, as they are uniquely equipped to assess patients and prescribe medications for weight management such as semaglutide (Wegovy®) and liraglutide (Saxenda®). Family nurse practitioners and family medicine, internal medicine, pediatric, prevention specialist physicians were included in the primary care provider (PCP) group. Other providers, such as obstetrician/gynecologists, cardiologists, and nutritionists, and non-office locations like hospitals, emergency rooms, and managed care settings, were categorized in an 'other provider' group. Individuals from some Plans, where prescribing provider information were not readily available, were excluded from this portion of our analysis.

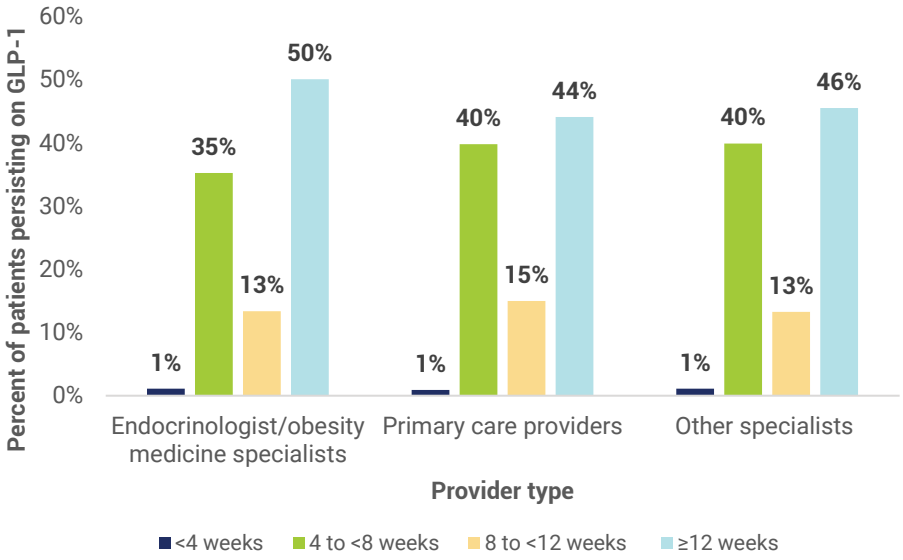
Across all parts of the U.S., individuals were most likely to be prescribed GLP-1 products for weight management by PCPs (**Figure 3**). There was regional variance in prescriptions written by endocrinologists and obesity medicine specialists, with a greater proportion of prescriptions generated by these types of physicians in the Northeast and Midwest (7% and 12% of prescriptions, respectively) versus the South and West (2% and 3%).

Figure 3: Proportions of weight management GLP-1 prescriptions by initiating provider type across regions of the U.S.



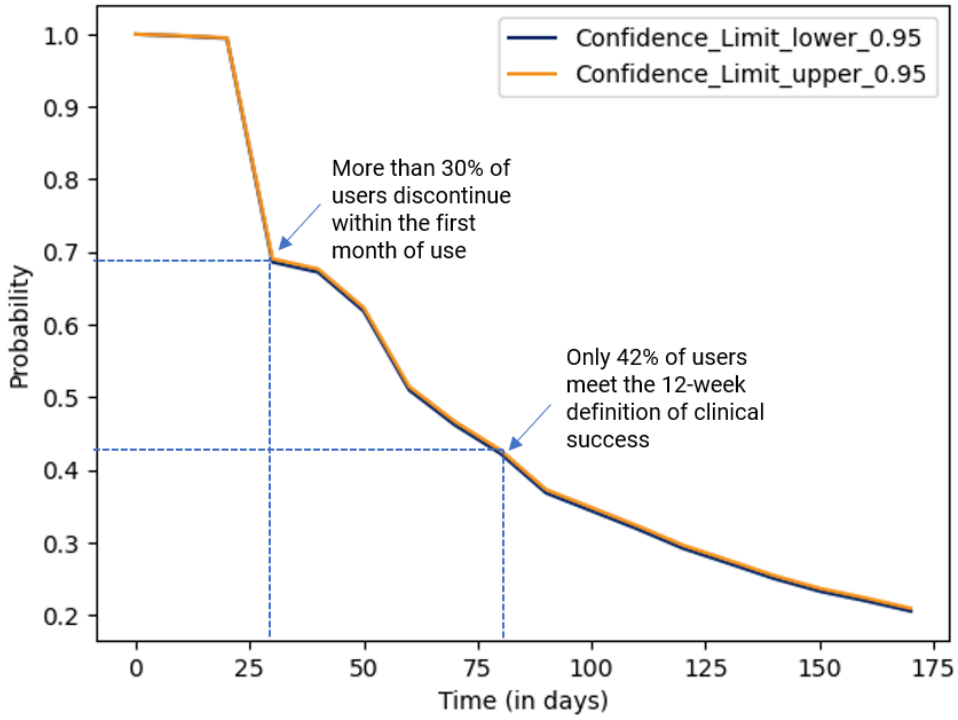
Endocrinologists and obesity medicine specialists were associated with better medication persistence (**Figure 4**). While half of GLP-1 users remained on treatment beyond 12 weeks when prescribed by endocrinology and obesity medicine specialists, only 44% of patients prescribed weight management GLP-1s by PCPs and 46% of those prescribed by other specialists reached that time point.

Figure 4: Weight management GLP-1 persistence by prescribing provider specialty.



In this study, the maximum number of days we followed individuals was 180 days. This is plotted in **Figure 5**, where the horizontal axis represents the number of days they completed treatment, and the vertical axis represents the probability of discontinuing treatment. The probability of discontinuing treatment decreases drastically between zero and six weeks, which may be due to the intolerability of early GLP-1 side effects (such as nausea) outweighing the patient's perception of the benefits of remaining on the drug. Beyond six weeks, persistence decreased at a slower rate.

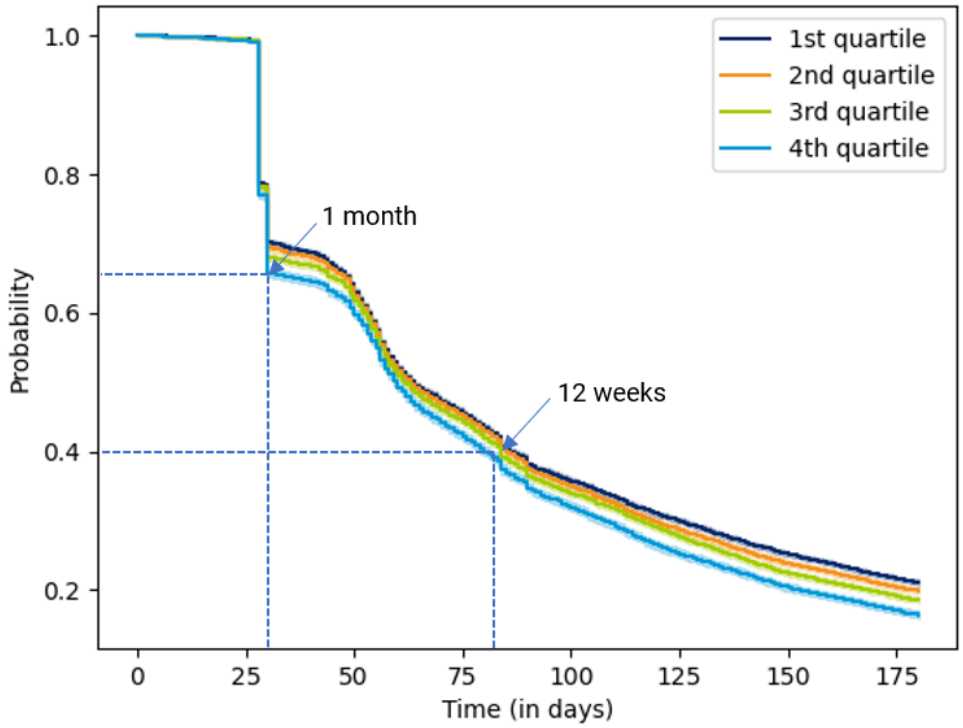
Figure 5: Overall time to treatment discontinuation in GLP-1 users for weight management.



The probability of staying on a GLP-1 drug drops drastically between zero and six weeks. These individuals are not on a GLP-1 long enough to see a clinically meaningful benefit.

The SVI is a measure originally designed by the CDC's Agency for Toxic Substances and Disease Registry (ASTDR) to measure a community's resilience to disasters.[14] In research, it is used more broadly to quantify the vulnerability of a community in relation to socioeconomic factors. The SVI score includes four themes (socioeconomic status, household characteristics, racial and ethnic minority status, housing type and transportation).[15] In this analysis, we looked at the time to treatment discontinuation by overall SVI score, which is a combination of all four themes (**Figure 6**). We found that individuals in the fourth quartile (most vulnerable and likely to have the highest limitations in terms of access to healthcare, such as cost, transportation, and language barriers) showed the lowest persistence on GLP-1s.

Figure 6: Time to treatment discontinuation by SVI score.

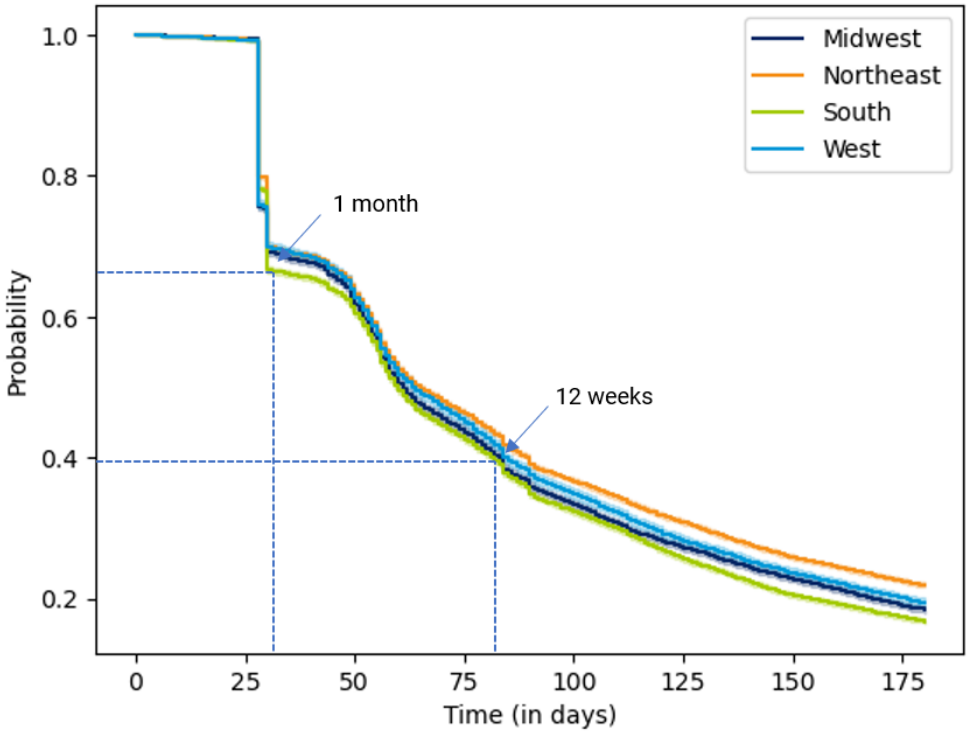


Individuals with the highest barriers to care, including cost, transportation, and language barriers, were least likely to stay on GLP-1s.

[14] Agency for Toxic Substances and Disease Registry, "CDC/ATSDR Social Vulnerability Index." Retrieved 20 March 2024.
[15] Agency for Toxic Substances and Disease Registry, "CDC SVI Documentation 2020." Retrieved 20 March 2024.

Medication persistence was also found to vary by region, particularly in those persisting beyond 12 weeks (**Figure 7**). Those in the South were the least persistent.

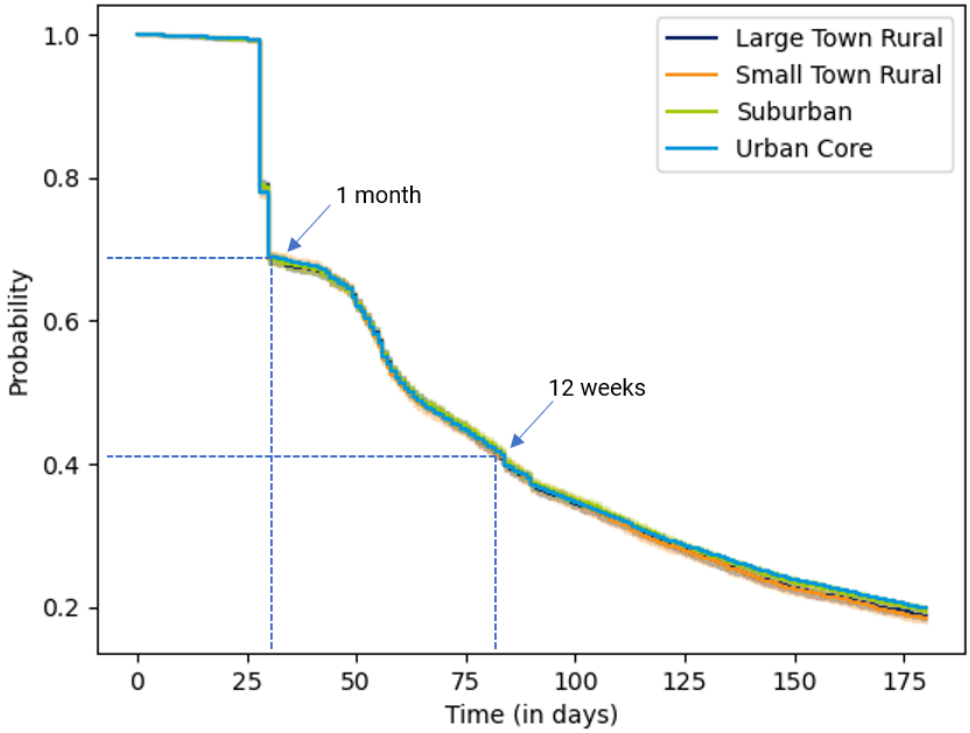
Figure 7: Time to treatment discontinuation by census region.



Individuals in the Northeast region of the United States were most likely to stay on GLP-1s, while those in the South were least likely.

Variation was less prominent across people located in rural and urban regions (**Figure 8**). Individuals located in large and small rural towns had somewhat lower persistence compared to their urban and suburban counterparts.

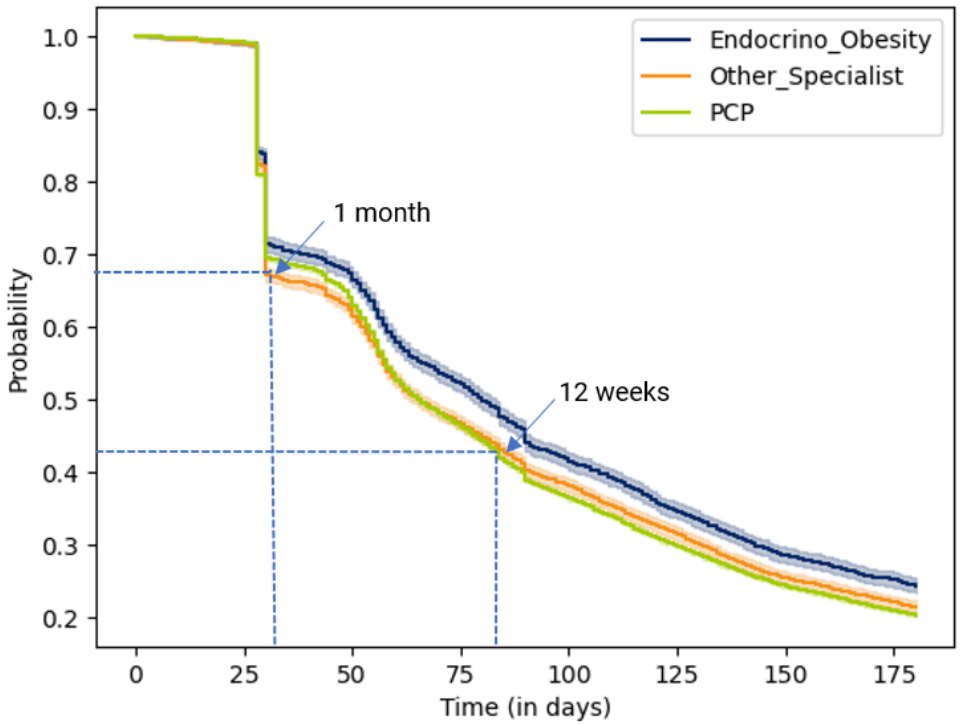
Figure 8: Time to treatment discontinuation by rural/urban status.



Individuals in urban and suburban regions were more likely to stay on GLP-1s than their rural counterparts.

When assessing the amount of time individuals remained on weight management GLP-1s by provider specialty, we found that those prescribed these products by endocrinologists and obesity medicine specialists were more likely to stay on medications than those prescribed by other types of providers (**Figure 9**). Relative to all prescriptions, fewer than 10% of prescriptions for GLP-1s are issued by obesity medicine specialists or endocrinologists.

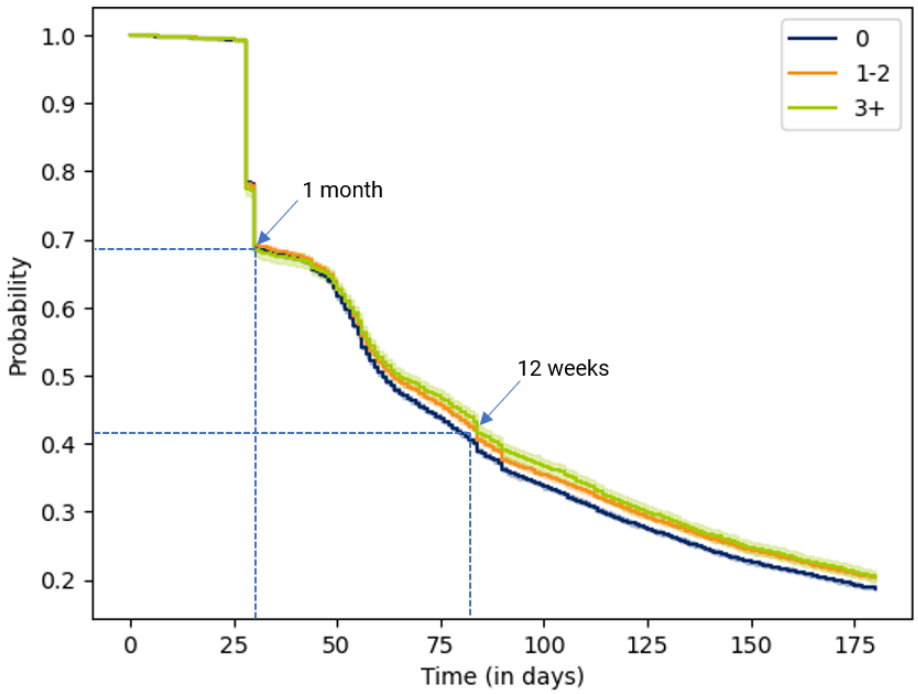
Figure 9: Time to treatment discontinuation by provider specialty.



Individuals who were prescribed their GLP-1 from an endocrinologist or obesity medicine specialist were more likely to stay on the drug.

The Charlson Comorbidity Index (CCI), an indicator of individual health, was also found to be associated with persistence (**Figure 10**). Individuals with coexisting health conditions, such as peripheral vascular disease and diabetes, and particularly those with three or more of these comorbidities, were more likely to maintain continuous use of GLP-1 products than those with zero CCI conditions.

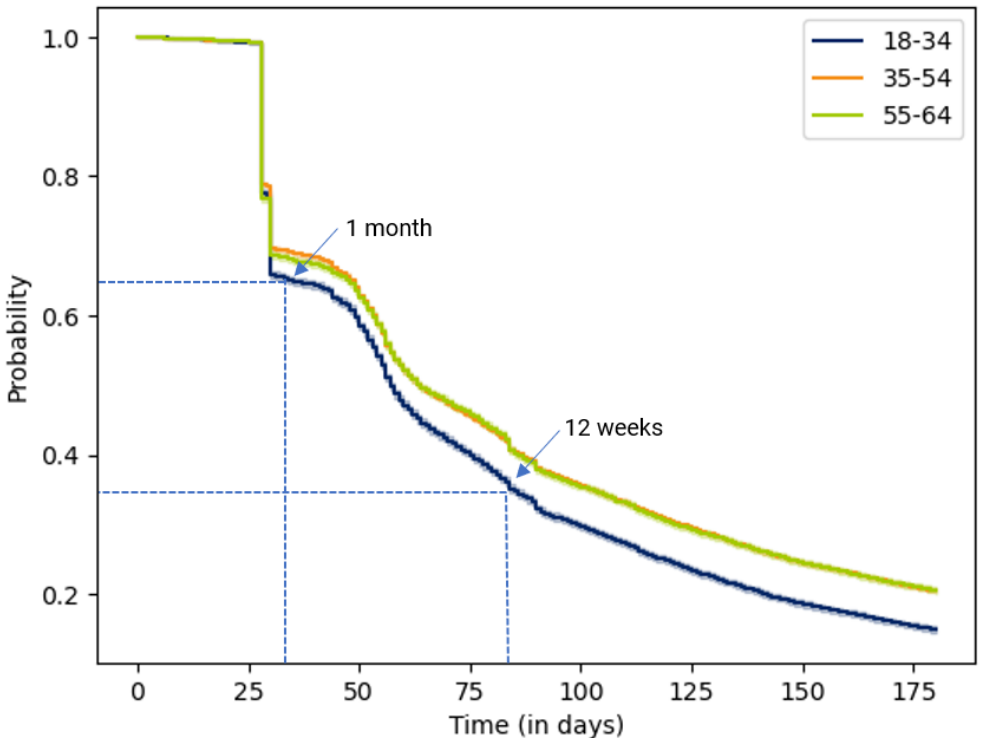
Figure 10: Time to treatment discontinuation by CCI score.



Individuals with coexisting health conditions, such as diabetes and liver disease, were more likely to stay on treatment.

Relationships were also observed between patients' ages and persistence: While individuals ages 35 to 54 and 55 to 64 years were similarly persistent on GLP-1s for weight management, those between 18 and 34 years had notably earlier treatment discontinuation (**Figure 11**).

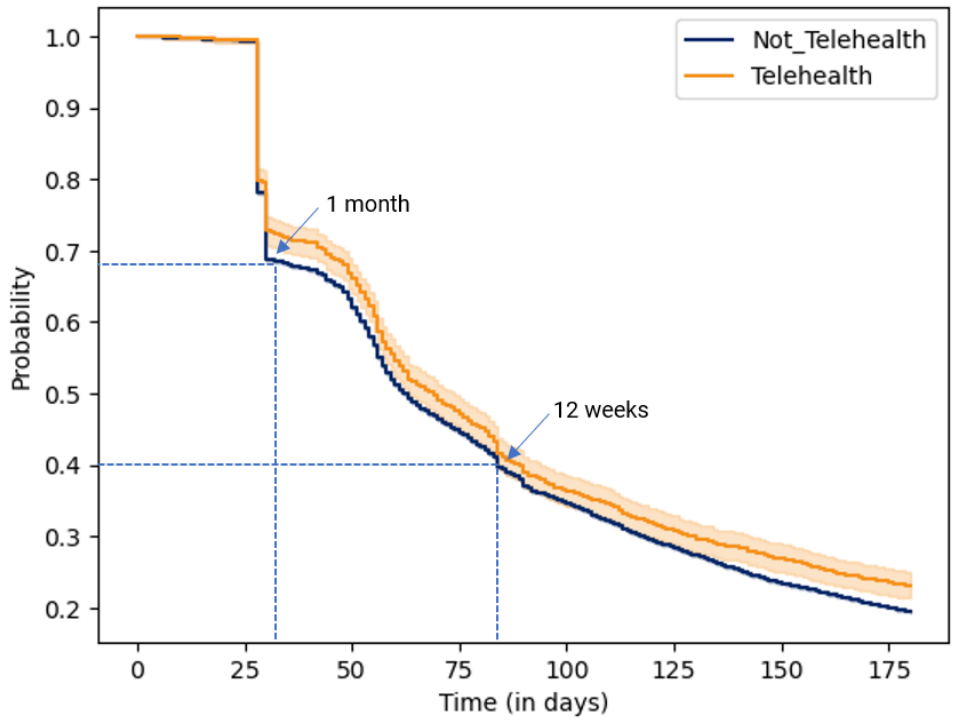
Figure 11: Time to treatment discontinuation by age category.



Individuals age 18-34 were more likely to drop out of treatment sooner than any other age group examined.

Procedure modifier codes were used to identify appointments provided using telehealth measures versus those conducted in person. We found that those with telehealth appointments had higher but more variable rates of persistence than those prescribed at in-person appointments (**Figure 12**).

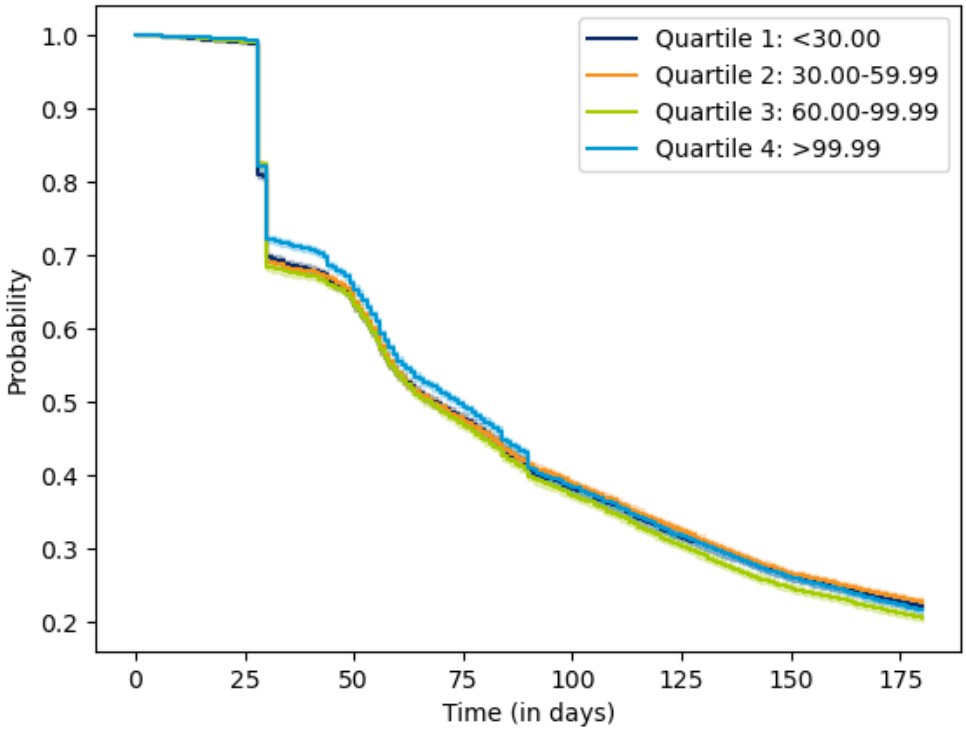
Figure 12: Time to treatment discontinuation by appointment type (in-person vs. telehealth).



Telehealth visits for GLP-1 prescribing were associated with more variable rates of persistence.

Costs to patients in the form of copayments and coinsurance also influenced persistence on GLP-1 medications (**Figure 13**). Individuals with monthly costs lower than $60.00 were significantly more likely to stay on these products than their counterparts paying costs above $60.00 each month. Those paying at least $100.00 per month were slightly more likely to persist than those paying $60.00 to $99.00, which may be attributable to motivation related to substantial monetary investment in their treatment.

Figure 13: Time to treatment discontinuation by copayment quartile.



Individuals with lower copayments were more likely to stay on treatment.

A logistic regression method was used to assess the relationship between persistence to a minimum of 12 weeks (when clinically significant weight loss is likely to have occurred) and other potentially related factors, such as patient and provider characteristics. As shown in **Table 3** and **Figure 14**, those ages 35 to 54 and 55 to 64 years were 41% and 48% more likely, respectively, to persist on weight management GLP-1s in comparison to those aged 18-34 years. Sociodemographic characteristics were also found to influence persistence to 12 weeks: The most socially vulnerable individuals, ranked in the 4th quartile for SVI, were 9% less likely than those with less vulnerability to stay on GLP-1 medication for at least 12 weeks. Individuals prescribed GLP-1s by obesity medicine specialists and endocrinologists were much more likely to persist beyond 12 weeks. Those receiving medications from endocrinologists and obesity medicine specialists were 22% more likely to persist beyond 12 weeks compared to those prescribed by PCPs, but relatively few patients (<10%) are managed by these specialists. Provider engagement was also an important contributor to persistence: With each additional provider visit, the likelihood of reaching 12 weeks of GLP-1 treatment increases by about 60%.

In line with existing literature on GLP-1 persistence in patients with diabetes and obesity, we found that those with coexisting conditions were less likely to reach 12 weeks of medication use.[16,17,18,19] Patients with three or more CCI comorbidities, which are conditions with high mortality risk, were 14% less likely to persist to 12 weeks than those with no CCI comorbidities. An analysis of other comorbidities related to overweight and obesity, including hypertension and high cholesterol, found that those with one, two, and three or more comorbidities were 9% and 20% less likely to reach 12 weeks than their counterparts with no related comorbidities.

Table 3: Logistic regression assessing factors influencing medication persistence to 12 weeks in weight management GLP-1 users with all available data in the BHI closed claims data set, July 2014 to December 2023 (n=100,106).

Characteristics		Odds ratio	P-value
Intercept		0.39	0.000
Gender (Reference=Male)	Female	0.88	0.000
Social Vulnerability Index (SVI) (Reference=1st_quartile)	2nd_quartile	1.02	0.340
	3rd_quartile	1.00	0.926
	4th_quartile	0.91	0.000
Age (in years) (Reference=18-34)	35-54	1.41	0.000
	55-64	1.48	0.000
Region (Reference=Northeast)	West	0.94	0.008
	Midwest	0.96	0.056
	South	0.94	0.000
Rural Urban Community Area (RUCA) (Reference=Urban Core)	Suburban	1.09	0.000
	Rural_Large_Town	1.07	0.002
	Rural_Small_Town	1.09	0.001
Prescribing Provider Type (Reference=PCP)	Other_Specialist	1.03	0.163
	Endocrinologist or Obesity Specialist	1.22	0.000
Charlson Comorbidity Index (CCI) Score (Reference= No comorbidity)	1 to 2 comorbidities	0.99	0.548
	3+ comorbidities	0.86	0.000
Other Comorbidies (Reference= No comorbidity)	1 to 2 comorbidities	0.91	0.000
	3+ comorbidities	0.80	0.000
GI_Conditions		0.89	0.000
Visits_during_Treatment		1.57	0.000

*Signifies that the odds ratio is statistically significant from 1.0. This indicates a significant relationship between the characteristic and weight management GLP-1 persistence to a minimum of 12 weeks. Odds ratios below 1.0 indicate that a characteristic is associated with decreased persistence to 12 weeks, while odds ratios above 1.0 indicate that the characteristic is predictive of improved persistence to 12 weeks. P-values are a statistical measurement used in research to validate hypotheses against observed data, and values <0.05 identify significant associations.

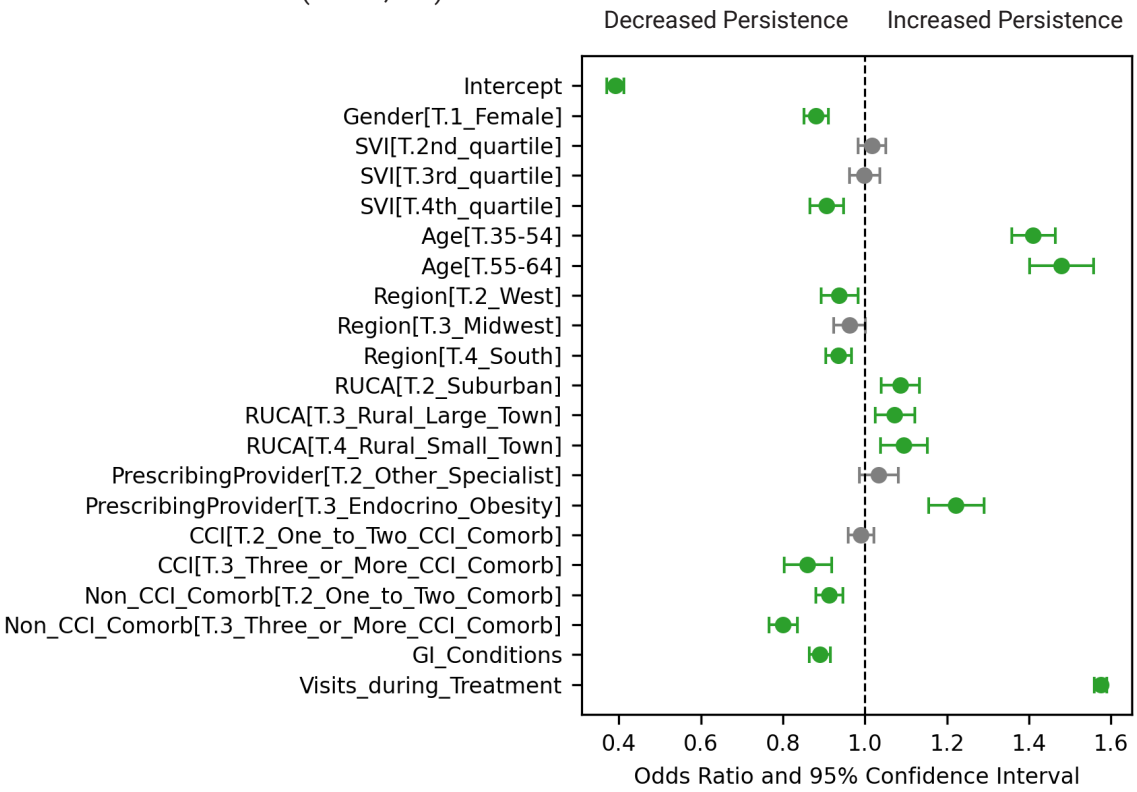
[16] Gasoyan H, Pfoh ER, Schulte R, Le P, Rothberg MB. Early- and Later-Stage Persistence with Antiobesity Medications: A Retrospective Cohort Study. Obesity (Silver Spring). 2024 Mar;32(3):486-493. doi: 10.1002/oby.23952. Epub 2023 Dec 6. PMID: 38053443.

[17] Wilke T, Mueller S, Groth A, Berg B, Fuchs A, Sikirica M, Logie J, Martin A, Maywald U. Non-Persistence and Non-Adherence of Patients with Type 2 Diabetes Mellitus in Therapy with GLP-1 Receptor Agonists: A Retrospective Analysis. Diabetes Ther. 2016 Mar;7(1):105-24. doi: 10.1007/s13300-015-0149-4. Epub 2015 Dec 22. PMID: 26695499; PMCID: PMC4801815.

[18] Lin J, Lingohr-Smith M, Fan T. Real-World Medication Persistence and Outcomes Associated with Basal Insulin and Glucagon-Like Peptide 1 Receptor Agonist Free-Dose Combination Therapy in Patients with Type 2 Diabetes in the U.S. Clinicoecon Outcomes Res. 2016 Dec 22;9:19-29. doi: 10.2147/CEOR.S117200. PMID: 28053550; PMCID: PMC5192057.

[19] Uzoigwe C, Liang Y, Whitmire S, Paprocki Y. Semaglutide Once-Weekly Persistence and Adherence Versus Other GLP-1 RAs in Patients with Type 2 Diabetes in a U.S. Real-World Setting. Diabetes Ther. 2021 May;12(5):1475-1489. doi: 10.1007/s13300-021-01053-7. Epub 2021 Apr 10. PMID: 33837922; PMCID: PMC8099966.

Figure 14: Forest plot depicting factors influencing medication persistence to 12 weeks in weight management GLP-1 users with all available data in the BHI closed claims data set, July 2014 to December 2023 (n=100,106).



Note: Odds ratios of significant value are displayed in green.
SVI = Social Vulnerability Index
RUCA = Rural/urban indicator
CCI = Charlson Comorbidity Index

APPENDICES

Appendix 1: National Drug Codes GLP-1 weight management products.

National Drug Code	Generic name	Brand name
00169280015	Liraglutide	Saxenda
00169280090	Liraglutide	Saxenda
00169280097	Liraglutide	Saxenda
50090425700	Liraglutide	Saxenda
00169450514	Semaglutide	Wegovy
00169451714	Semaglutide	Wegovy
00169452414	Semaglutide	Wegovy
00169452514	Semaglutide	Wegovy
00169450101	Semaglutide	Wegovy
00169450501	Semaglutide	Wegovy
00169451701	Semaglutide	Wegovy
00169452401	Semaglutide	Wegovy
00169452501	Semaglutide	Wegovy
00169452590	Semaglutide	Wegovy
00169452594	Semaglutide	Wegovy
50090582400	Semaglutide	Wegovy

Appendix 2: Comorbidities included in Charlson Comorbidity Index

Comorbidity	ICD-9 code(s)	ICD-10 code(s)
Myocardial infarction	410.x-412.x	121.x, 1.22.x, 125.2
Congestive heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4-425.9, 428.x	I09.9, I11.0, I13.0, I13.2, I25.5, I 42.0, I42.5-I42.9, I43.x, I50.x, P29.0
Peripheral vascular disease	093.0, 437.3, 440.x, 441.x, 443.1-443.9, 447.1, 557.1, 557.9, V43.4	I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Cerebrovascular disease	362.34, 430.x-438.x	G45.x, G46.x, H34.0, 160.x-169.x
Dementia	290.x, 294.1, 331.2	F00.x-F03.x, F05.a, G30.x, G31.1
Chronic pulmonary disease	416.8, 416.9, 490.x-505.x, 506.4, 508.1, 508.8	I27.8, I27.9, J40.x-J47.x, J60.x-J67.x, J68.4, J70.1, J70.3
Rheumatic disease	446.5, 710.0-710.4, 714.0, 714.2, 714.8, 725.x	M05.x, M06.x, M31.5, M32.x-M34.x, M35.z, M35.5, M36.0
Peptic ulcer disease	531.x-534.x	K25.x-K28.x
Mild liver disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 570.x, 571.x, 573.3, 573.4, 573.8, 573.9, V42.7	B18.x, K70.0-K70.3, K70.9, K71.2-K71.5, K71.7, K73.x, K74.x, K76.0, K76.2-K76.4, K76.8, K76.9, Z94.4
Diabetes without chronic complication	250.0-250.3, 250.8, 250.9	E10.0, E10.1, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13,9, E14.0, E14.1, E14.6, E14.8, E14.9
Diabetes with chronic complication	250.4-250.7	E10.2-E10.5, E10.7, E11.2-E11.5, E11.7, E12.2-12.5, E12.7, E13.2-13.5, E13.7, E14.2-E14.5, E14.7
Hemiplegia or paraplegia	334.1, 342.x, 343.x, 344.0-344.6, 344.9	G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0-83.4, G83.9
Renal disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.x, 583.0-583.7, 585.x, 586.x, 588.0, V42.0, V45.a, V56.x	I12.0, I13.1, N03.2-N03.7, N05.2-N05.7, N18.x, N19.x, N25.0, Z49.0-Z49.3, Z94.0, Z99.2
Any malignancy, except malignant neoplasm of the skin	140.x-172.x, 174.x-195.8, 200.x-208.x, 238.6	C00.x-C26.x, C30.x-C34.x, C37.x-C41.x, C43.z, C45.x-C58.x, C60.x-C76.x, C81.x-C85.x, C88.x, C90.x-C97.x
Moderate or severe liver disease	456.0-456.2. 572.2-572.8	I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7
Metastatic solid tumor	196.x-199.x	C77.x-C80.x
AIDS/HIV	042.x-044x	B20.x-B22.x, B24.x

Appendix 3: Comorbidities of interest related to obesity

Comorbidity of interest	ICD-9 code(s)	ICD-10 code(s)	Healthcare Common Procedure Coding System (HCPCS) code(s)
Coronary artery disease	414*	I20.0-I20.1, I23.7*, I25.1*, I25.7*	N/A
Chronic pain	338.4	G89.4	N/A
Type 2 diabetes mellitus	250.x*	E11.*	N/A
Dyslipidemia	272*	E78.*	G8767, G9782, 82465, 0342T, G8585
Gastroesophageal reflux disease (GERD)	530.81	K21.*	N/A
Hypertension	401*	H35.03*, I10.*, I11.*, I12.*, I13.* I15.*	N/A
Migraine	346*	G43.*, G43.A*, G43.B*, G43.C*, G43.D*, G44.*	N/A
Nonalcoholic fatty liver disease (NAFLD)	571.5, 571.8, 571.9	K76.0	N/A
Obstructive sleep apnea	327.23	G47.33	N/A
Osteoarthritis	715*	M15.*, M16.*, M17.*, M18.*, M19.*	N/A