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Real-World Analysis of Glucagon Like Peptide-1 (GLP-1) Agonist Obesity Treatment Year-Two Clinical and Cost Outcomes

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Introduction

U.S. Food and Drug Administration (FDA)-approved glucagon-like peptide-1 (GLP-1) products to treat diabetes mellitus (DM) have been on the market since 2005 and are known to induce weight loss. In 2015, the FDA approved the first GLP-1 drug for weight loss, liraglutide injection (Saxenda®), followed by semaglutide injection (Wegovy®) in 2022 and, in 2023, tirzepatide (Zepbound®), a dual-acting GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) product.

In the fall of 2022, social media influencers shared the benefits of GLP-1 therapies associated with weight loss attributes, which resulted in some employers experiencing substantial increases in GLP-1 utilization and associated costs. These trends in GLP-1 drug use for weight loss and associated costs have resulted in self-insured employers questioning whether they can afford to continue providing weight loss medication coverage.

In June 2023, Prime Therapeutics (Prime) released findings of a one-year pre-post real-world study of GLP-1 use among a commercially insured population with obesity and without DM. The study identified that medical costs were marginally higher in the GLP-1 treated group compared to a temporally matched cohort and that adherence/persistence was poor. Researchers presented year-one findings in a scientific poster format at the April 2024 Academy of Managed Care Pharmacy national conference and published results in the August 2024 issue of the Journal of Managed Care & Specialty Pharmacy. Prime released its year-two GLP-1 adherence and persistence results in July 2024, showing 1 in 7 members newly initiating a GLP-1 for obesity treatment without DM were persistent on therapy two years later, with 1 in 4 persistent who used a once-weekly injectable GLP-1 product. Little is known of the real-world GLP-1 obesity treatment benefits beyond one year.

Objective

To describe annual total cost of care (TCC) one year before and two years after GLP-1 obesity treatment initiation among commercially insured members without DM and to compare annual TCC and clinical outcome differences to a matched control group.

Methods

We analyzed integrated pharmacy and medical claims data from 16 million commercially insured members. Study inclusion was limited to members with a GLP-1 claim (index date) between 1/1/2021 and 12/31/2021, continuous enrollment 12 months before (pre-period) and two years after (post-period) the index date and no GLP-1 drug claim during the pre-period.

Members were required to have diagnosis of obesity and/or a body mass index (BMI) of ≥ 30 reported on a medical claim Z-code on at least one medical claim during the pre-period. Members were excluded if they had a medical claim with a DM diagnosis or a pharmacy DM drug therapy claim during the pre- period. Additional medical claim diagnosis exclusions included hemophilia, sickle cell disease, malignant cancer or end-stage renal disease.

Researchers identified a 3-to-1 matched control group using the 13.5 million members without a GLP-1 claim in 2021 and with a pharmacy claim for any drug using the same inclusion and exclusion criteria.

A two-phase matching approach was used. First, eligible GLP-1 utilizers were direct matched to control members using the following characteristics: gender, age category, Charlson comorbidity index (CCI) score category, line of business (e.g., fully-insured, health insurance marketplace, self-insured), obesity category, prediabetes diagnosis, Blue plan region, pre-period non-GLP-1 weight-loss drug therapy and pre-period pharmacy claim fills category.

Within the direct matched population, GLP-1 utilizers were further matched to controls using propensity score matching on the following characteristics: age, pre-period pharmacy claim fills count, CCI score, CCI condition indicators, pre-period non-GLP-1 weight loss drug therapy, statin drug use, renin angiotensin system antagonist (RASA) drug use, antidepressant drug use, pregnancy diagnosis, and study index month.

Three 365-day study periods were created from the member's index date: the pre-period, year-one post-index period and year-two post-index period. Annual TCC was calculated for each study period by summing medical and pharmacy claim paid allowed amounts after all network provider discounts were applied and included member share.

Obesity-related clinical outcomes included bariatric surgery, major adverse cardiovascular event (MACE), hip or knee replacement, new DM diagnosis or antidiabetic drug use, medication use change for cholesterol lowering (statin) drug and hypertension (RASA) drug categories and negative GLP-1 drug therapy outcomes. Negative outcomes were defined as one or more claims for thyroid cancer, gastroparesis, cholecystitis, intestinal obstruction, acute kidney failure, non-arteritic ischemic optic neuropathy, or acute pancreatitis.

Statistical analysis of differences in outcomes and event rates between groups and across periods were performed using the difference-in-difference method.

Results

A total of 3,346 commercially insured members newly initiating GLP-1 therapy, without DM and with a medical diagnosis of obesity and/or BMI ≥ 30, met final study criteria, and 396,103 control group members met all study criteria from which 3,046 GLP-1 utilizing members were matched to three control members for a total of 8,343 unique control members identified; 306 (3.7%) of controls matched to more than one GLP-1 utilizer.

The mean age of individuals identified was 46 years, 81% were women and 14% had a prediabetes diagnosis. Across the three study periods, TCC for GLP-1 utilizers averaged $12,695, $20,165 and $18,507, in the pre-year, year one and year two, respectively. For the same study periods, TCC in the matched control group averaged $11,406, $11,882 and $13,012. Comparing TCC between groups and across study periods, the difference-in-difference for year one vs. pre-year was $6,994 (p<.0001) higher per GLP-1 treated member compared to control. The same TCC comparison for year two vs. pre-year was $4,206 (p<.0001) higher per GLP-1-treated member compared to control. The increasing number of members who did not persist on GLP-1 therapy from year one to year two explain the observed decrease in pharmacy spend and TCC. No differences in medical spend trends were observed between groups. The rate of acute pancreatitis in year one compared to the pre-year was statistically higher for GLP-1-initiating members, with an increase from 0.1% pre-year to 0.6% in year one, compared to the matched control group, 0.3% pre-year and 0.4% in year one, for a difference-in-difference higher 0.4% GLP-1 incidence, p=0.019, translating to one additional acute pancreatitis event per 250 GLP-1 treated individuals.

GLP-1 persistence and adherence to therapy was poor with 32% still on therapy at one year and 27% adherent to therapy, defined as PDC ≥ 80%. Year-two GLP-1 persistence worsened to 15% and adherence was 17%.

Conclusions

Among GLP-1 new initiators without DM and with an obesity diagnosis, there was no health care cost reduction in the first year or second year after initiation. Instead, costs went up $6,994 per GLP-1-treated person in year one and increased in year two at $4,206, compared to the matched control group. GLP-1 treatment persistency was poor with only 1 in 3 on therapy at one year and 1 in 7 at the end of year two. No reduction in obesity-related medical events was seen over the two-year period compared to the matched control group, and in year one, there was a statistically significant higher rate of acute pancreatitis in the GLP-1-treated group, resulting in number needed to harm of 1 in 250 treated GLP-1 utilizers.

These findings indicate that in the real-world setting, for members with obesity and without diabetes treated with GLP-1s, during the first two years of therapy, no cost offsets or obesity-related medical event reductions should be expected. Instead, per individual starting a GLP-1 for obesity without DM, expect a two-year $11,200 investment at standard drug prices, prior to discounts, with a potential for higher acute pancreatitis rate and less than 1 in 4 still on GLP-1 therapy.