Real-World 3-Year Cost Impact Assessment of Glucagon-Like Peptide-1 Receptor Agonists to Treat Obesity Among Commercially Insured Members Without Diabetes

J. Tran, PharmD, PhD[1]; B.Y. Urick, PharmD, PhD[1]; L.Z. Marshall, PharmD, PhD[1]; J.F. Farley, PhD[2]; M. McCann[1]; P.P. Gleason, PharmD[1,2] [1]Prime Therapeutics LLC, Eagan, MN, United States [2]University of Minnesota College of Pharmacy, Minneapolis, MN, United States

Background

- Obesity, which affects 41.9% of the US adult population, creates more than $170 billion in annual health care spending.[1]
- In recent years, glucagon-like peptide-1 receptor agonists (GLP-1s) for weight management have dominated the nationwide weight loss discussion and are driving affordability concerns.[2]
- At a historic annual wholesale acquisition price of $11,500 to $14,000, and with a meteoric rise in popularity, the increase in GLP-1 weight loss treatment is contributing to unprecedented health care spend growth for US employers covering weight loss medications.[3]
- Because real-world evidence indicates discontinuation is common within the first year following treatment initiation,[4] it is critical to understand the real-world GLP-1 treatment cost of care.
- Real-world evidence finds GLP-1 products, when used for obesity among a population without diabetes, do not result in cost offsets within the first 2 years of therapy.[5,6]
- Longer-term studies are needed to assess the potential for GLP-1 products to reduce medical spending after 2 years.

Objective

Our objective is to describe changes in annual medical spending and total cost of care (TCC) 1 year before and 3 years after GLP-1 obesity treatment initiation among commercially insured members without diabetes, as compared to a matched control group, regardless of treatment persistence.

Methods

- This retrospective, observational cohort study analyzed Prime Therapeutics' integrated pharmacy and medical claims data from 16 million commercially insured members from all regions of the United States across the 4+ years between January 1, 2020, and March 31, 2025.
- Study inclusion was limited to members newly initiating a GLP-1, as defined as no GLP-1 use in the prior year, between January 1, 2021, and March 31, 2022.
- Inclusion criteria were continuous enrollment in the 12 months prior to index for a new GLP-1 therapy start date (pre-period), an obesity diagnosis on 1 or more medical claims during the pre-period, age 19 or more years at index, and no GLP-1 use or evidence of diabetes mellitus (DM) during the pre-period.
- Members were excluded if they had a DM diagnosis medical claim or a pharmacy DM drug therapy claim during the pre-period, or medical claim diagnosis in the pre-period for HIV/AIDS, hemophilia, sickle cell disease, malignant cancer, or end-stage renal disease.
- Using the same inclusion and exclusion criteria, a control group was identified using 10 million members with at least 1 new pharmacy claim for a maintenance medication between January 1, 2021, and March 31, 2022. Each distinct chronic medication fill date was considered as a potential index date.
- A 2-step matching approach was used to identify a 3:1 matched control group.
  - Step 1: Direct match on gender, 10-year age bands, region, line of business (i.e., fully insured, health insurance marketplace, self-insured), Charlson Comorbidity Index score band[7], pre-period pharmacy claim fill band, quarter and year of index date, hospitalization in the 91-day period before index, prediabetes, severe obesity, sleep apnea, and any weight loss medication use.
  - Step 2: After the direct match, GLP-1 utilizers were matched using propensity scores on age, month of index study date, body mass index (BMI) grouping, Charlson Comorbidity Index score and conditions[8], pre-period pharmacy claim fill rates, pregnancy, and pre-period utilization of non-GLP-1 weight loss drug therapy by class (e.g., phentermine, topiramate, naltrexone), statins, renin-angiotensin system antagonists and/or antidepressants. Replacement and direct-matched control group members with the smallest absolute difference were selected for the final sample.
- Balance across cohorts was evaluated using standardized mean differences (SMDs), with differences less than 0.1 considered balanced.
- Spending was calculated using rolling 91-day periods relative to index. All members had 4 pre-period and up to 12 post-period measurements, depending on eligibility. Controls who initiated a GLP-1 were censored beginning with the period of initiation. Annual spending estimates were derived from quarterly averages multiplied by 4.
- Spending amounts were adjusted to first-half 2025 dollars using the medical component of the consumer price index (CPI) and capped at the 99th percentile.
- TCC was calculated for each study period by summing medical and pharmacy costs. Costs are from claim paid allowed amounts, after all network provider discounts were applied, and included member share. Total medical benefit cost and total pharmacy benefit cost were calculated separately. Pharmaceutical manufacturer rebates and coupons were not included.
- Time series analysis was used to compare the quarterly spending trend before and after index between the 2 groups. Cost changes between groups and across annual periods (e.g., pre-period vs. Year 3 post-period) were statistically analyzed using difference-in-difference (DID) regression.

Table 1

Selected Demographics and Clinical Characteristics of Study Sample After Matching

Demographic or Clinical Characteristic	After Matching** Control (N = 29,570)	GLP-1 Obesity Treatment (N = 10,094)	SMD†	*P* value‡
Age in years, mean (SD)	45.6 (10.5)	45.7 (10.3)	0.004	0.731
Gender–female, N (%)	23,844 (80.6%)	8,129 (80.5%)	0.003	0.833
Index year & quarter, N (%)				
Q1 2021	3,160 (10.7%)	1,079 (10.7%)	0.002	1
Q2 2021	4,850 (16.4%)	1,664 (16.5%)		
Q3 2021	5,707 (19.3%)	1,946 (19.3%)		
Q4 2021	6,845 (23.1%)	2,332 (23.1%)		
Q1 2022	9,008 (30.5%)	3,073 (30.4%)		
Severe obesity*, N (%)	12,152 (41.1%)	4,178 (41.4%)	0.006	0.611
BMI Z-code category, N (%)				
30–34.9	5,322 (18.0%)	1,868 (18.5%)	0.035	0.058
35–39.9	4,772 (16.1%)	1,677 (16.6%)		
40–44.9	4,397 (14.9%)	1,418 (14.0%)		
45+	3,893 (13.2%)	1,393 (13.8%)		
No obesity BMI Z-code	11,186 (37.8%)	3,738 (37.0%)		

SD = standard deviation; SMD = standardized mean difference

*Severe obesity is defined as BMI ≥ 40 using ICD-10-CM codes of E66.01 or Z68.4. The number of members with severe obesity exceeds the number of members categorized with BMI of 40 or more due to coding of E66.01 and under-coding of Z-codes for BMI, which are not billable ICD-10-CM codes.

**Eligible control group members were matched to GLP-1 treatment members on characteristics and conditions using a combined exact and propensity score matching approach, as described in Methods. Final unique member control-treatment matching ratio was 2.9:1.

†SMDs assess balance in demographic and characteristics balance between groups with excellent balance defined as a value <0.1.

‡Statistical comparisons between treatment and control group used t-tests for continuous outcomes and chi-square tests for categorical outcomes.

Table 2

Year 3 Versus Pre-Year Cost Change Means Among New-Start GLP-1 Members to Treat Obesity Without Diabetes and Matched Controls*

Mean Cost Outcome†	GLP-1 Obesity Treatment Pre-Year	GLP-1 Obesity Treatment Year 3	Year 3-Pre Difference (% change)	Matched Controls Pre-Year	Matched Controls Year 3	Year 3-Pre Difference (% change)	Annual Difference-in-Difference (95% CI)‡	*P* value
	N = 10,094			N = 29,570				
Pharmacy	$2,788	$7,371	$4,583 (164.4%)	$2,643	$3,588	$945 (35.8%)	$3,639 (3,344 to 3,933)	<0.001
Medical	$9,043	$11,045	$2,002 (22.1%)	$8,828	$9,900	$1,072 (12.1%)	$930 (411 to 1,449)	<0.001
Total cost of care (pharmacy + medical)	$12,177	$18,961	$6,784 (55.7%)	$11,872	$14,166	$2,294 (19.3%)	$4,490 (3,842 to 5,139)	<0.001

CI = confidence interval

*Eligible control group members were matched to GLP-1 treatment members on characteristics and conditions using a combined exact and propensity score matching approach; see Methods.

†Medical and pharmacy claim paid allowed amounts were adjusted to first-half 2025 dollars using the medical component of the consumer price index and capped at the 99th percentile. Annual spending estimates were derived from quarterly averages multiplied by 4. Costs are from the claim paid allowed amounts, after all network provider discounts were applied, and included member share. Total medical benefit cost and total pharmacy benefit costs were calculated separately. Pharmaceutical manufacturer rebates and coupons were not included.

‡Difference between GLP-1 post-pre difference and control post-pre difference.

Figure 1a

Pharmacy Benefit Spending Trend

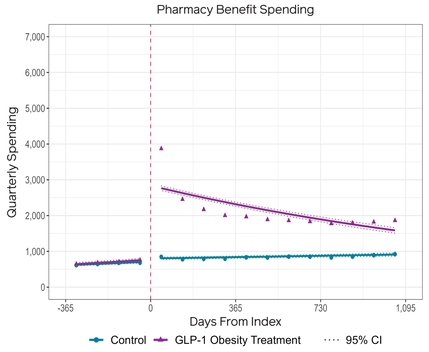


Figure 1b

Medical Benefit Spending Trend

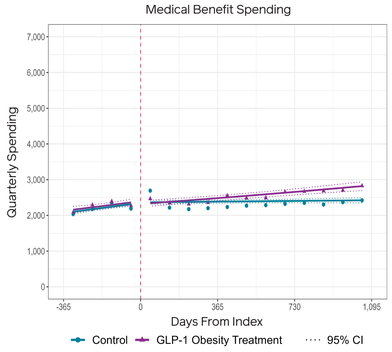
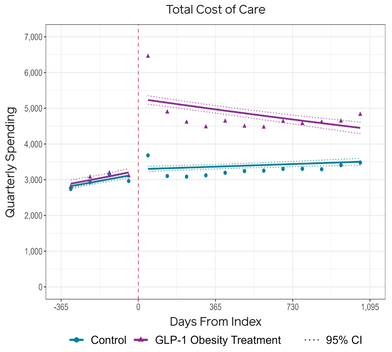


Figure 1c

Total Cost of Care Trend



Three-Year post-index trends: pharmacy benefit spending -7.2% (95% CI: -9.1% to -5.3%); medical benefit spending 1.7% (95% CI: -0.5% to 3.9%); total cost of care -2.1% (95% CI: -3.8% to -0.4%).

Results

- Out of an initial pool of 5,112,150 control member-index date combinations and 10,686 GLP-1 obesity treatment without diabetes members, 29,570 (28,378 distinct) controls were matched to 10,094 treatment members.
- The cohorts were well balanced after matching (SMD<0.1; Table 1).

Spending trends varied by outcome:

- Pharmacy benefit spending increased immediately following GLP-1 initiation and then decreased substantially over 3 years among GLP-1 users compared to controls (Figure 1a).
- Medical benefit spending trends were similar between GLP-1 initiators and control patients after treatment initiation (Figure 1b).
- TCC spending increased immediately after treatment initiation and then decreased over 3 years due to reductions in pharmacy benefit spending among GLP-1 users compared to controls (Figure 1c).

- Pharmacy spending, medical spending, and TCC for the GLP-1 obesity treatment population remained greater than the control population in Year 3 compared to the pre-year (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 without diabetes and to identify those with obesity. Similarly, claims-based identification of GLP-1 utilization may have failed to appropriately classify utilizers of compounded GLP-1 products, individuals procuring GLP-1 through direct-to-consumer programs, or other individuals with non-adjudicated GLP-1 utilization.
- Pharmacy costs do not include pharmaceutical manufacturer rebates and coupons.
- Our study examined a commercially insured membership; therefore, results are not generalizable to Medicare or Medicaid populations.
- The impacts of an individual's cost sharing, other diagnoses, social determinants of health, or other member characteristics are outside the scope of this analysis and are worthy of future consideration.

Conclusion

- For members without diabetes using GLP-1 products to treat obesity, this real-world, intent- to-treat study found TCC remained $4,490 higher in Year 3 compared to controls.
- No trend toward medical spending reduction among the GLP-1 treatment group was observed.
- Long-term, sustained weight loss will be essential to deliver future medical cost offsets.
- The large GLP-1 drug-cost investment without medical-cost offset over the first 3 years of therapy creates an even greater need for value-based pharmaceutical manufacturer contracting to help ensure recouping of GLP-1 costs among those not persisting with therapy.

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2900 Ames Crossing Road, Eagan, MN 55121

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Ben Urick
Ben.Urick@PrimeTherapeutics.com