Two-Year Persistent Glucagon-Like Peptide-1 Agonist Obesity Without Diabetes Treatment: Cost-Effectiveness Among Commercially Insured

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Background

- Obesity is both highly prevalent, with 40.3% of the US adult population considered obese, and costly, with recent estimates of annual obesity-related health care costs topping $170 billion.[1,2]
- Prior to the 2014 US FDA approval of liraglutide (Saxenda), a glucagon-like peptide-1 (GLP-1) receptor agonist indicated for chronic weight management among obese patients aged 12 and older, few obesity treatment drug options were available.[3]
- In recent years, GLP-1 drugs for weight management have dominated the nationwide weight loss discussion and are driving affordability concerns.[4]
- At an annual wholesale acquisition price of $11,500 to $14,000, and 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.[5]
- Because real-world evidence indicates most patients using GLP-1 drugs for weight loss discontinue within the first year following treatment initiation,[6] it is critical to understand real-world GLP-1 treatment cost of care.
- Currently, there is scant GLP-1 weight loss treatment without diabetes mellitus (DM) real-world cost-effectiveness information beyond 1 year.

Methods

- This retrospective, observational cohort study analyzed Prime Therapeutics' integrated pharmacy and medical claims data from 16 million commercially insured members covering all regions of the United States across the 4-year period of January 1, 2020, to December 31, 2023.
- Study inclusion was limited to members newly initiating a GLP-1 (index date in calendar year 2021), defined as no GLP-1 use in prior year, i.e., the identification period, with member continuous enrollment 1 year before (pre-period) and 2 years after (post-period) the index date required.
- Members were required to have a pre-period medical claim, including a diagnosis code for obesity or Z code for body mass index (BMI) ≥30.
- 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 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 13.5 million members with at least 1 pharmacy claim for any drug during 2021 and without a GLP-1 claim in calendar year 2021 and 1 year prior to study index date.
- A 2-step matching approach was used to identify the control group.
  - **Step 1:** Direct matching on gender, health plan, line of business (i.e., fully insured, health insurance marketplace, self-insured), BMI group, prediabetes, pregnancy, and use of statin, renin-angiotensin system antagonist (RASA), and/or antidepressants at index date.
  - **Step 2:** After the direct match, GLP-1 utilizers were matched using propensity scores on 5-year age bands, month of index study date, Charlson Comorbidity Index score and conditions[7], and pre-period drug utilization of non-GLP-1 weight loss drug therapy by class (e.g. phentermine, topiramate, naltrexone, etc.).
- After matching, the cohort was limited to persistent GLP-1 users who did not have a 60-day gap in therapy during the 2-year study follow-up period and their matched controls.
- 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. Total medical benefit costs and total pharmacy benefit costs were calculated separately. Pharmaceutical manufacturer rebates and coupons were not included.
- TCC was calculated for each study period. Pre-period costs were summed across the 365 days prior to index date. Year 1 post-period costs included index date plus 364 days while year 2 post-period costs included the 365 days immediately following the last day in year 1 post-period.
- All member period cost measures were capped at $250,000, a common stop-loss policy threshold.
- Annual cost changes between groups and across periods (pre-period vs. year 1 post-period, pre-period vs. year 2 post-period) were statistically analyzed using difference-in-difference (DID) regression.

Objective

The objective is to describe changes in annual total cost of care (TCC) 1 year before and 2 years after GLP-1 obesity treatment initiation among commercially insured members without DM who were persistent to GLP-1 therapy compared to a matched control group.

Table 1

Demographics and Clinical Characteristics of Persistent Sample Post-Exact and Propensity Score Matching

	After Matching (3 Controls to 1 GLP-1 Member)**			
Demographic/Clinical Characteristic*	Control n=1,249	GLP-1 n=436	P-value†	Standardized Mean Difference‡
Age, mean, years	48.0	48.3	0.541	0.033
Age grouping into 5-year bands	Propensity Match to Age Group		0.373	0.168
Female, n (%)	1,147 (84.8%)	365 (83.7%)	0.649	0.029
Blue plan – 19 Blue plans	Propensity Match to Health Plan		<0.001	—
Fully insured, % (n)	362 (26.8%)	116 (26.6%)	0.979	0.011
Health insurance marketplace, n (%)	150 (11.1%)	47 (10.8%)		
Self-Insured, n (%)	841 (62.2%)	273 (62.6%)		
BMI 30 to 34.9, Z code, n (%)	237 (17.5%)	75 (17.2%)	0.990	0.030
BMI 35 to 39.9, Z code, n (%)	166 (12.3%)	56 (12.8%)		
BMI 40 to 44.9, Z code, n (%)	152 (11.2%)	52 (11.9%)		
BMI 45+, Z code, n (%)	149 (11.0%)	47 (10.8%)		
No medical claims with Z code ≥30 BMI*, n (%)	649 (48.0%)	206 (47.2%)		
Prediabetes, n (%)	207 (15.3%)	75 (17.2%)	0.383	0.052
Major depression, n (%)	289 (21.4%)	85 (19.5%)	0.444	0.046
Hypothyroidism, n (%)	255 (18.8%)	90 (20.6%)	0.449	0.045
Pregnancy, n (%)	7 (0.5%)	2 (0.5%)	1.000	0.008
Myocardial infarction history, n (%)	7 (0.5%)	1 (0.2%)	0.688	0.047
Charlson Comorbidity Index[7], mean	0.5	0.6	0.920	0.006
Index month Jan 2021 to Dec 2021	Propensity Match to Index Month		0.149	0.222
Weight loss medication in pre-period, n (%)	171 (12.6%)	50 (11.5%)	0.574	0.036
Prior statin, n (%)	273 (20.2%)	89 (20.4%)	0.970	0.006
Prior renin-angiotensin system antagonist, n (%)	446 (33.0%)	129 (29.6%)	0.210	0.073
Prior antidepressant, n (%)	673 (49.7%)	203 (46.6%)	0.271	0.064

*All members were required to have pre-period medical claim including a diagnosis code for obesity or Z code for BMI ≥30.
**Eligible control group members were matched to GLP-1 treatment members on characteristics and conditions using a combined exact and propensity score matching approach. Final unique member control-treatment matching ratio was 2.9:1, see Methods for more detail.
†Statistical comparisons between treatment and control group used t-tests for continuous outcomes and chi-square tests for categorical outcomes.
‡Standard mean differences assess balance in demographic and characteristics balance between groups with excellent balance defined as a value <0.1.

Table 2a

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

Mean Cost Outcome†	GLP-1 Persistent Pre-Year	GLP-1 Persistent Year 1	Year 1-Pre Difference (% change)	Matched Controls Pre-Year	Matched Controls Year 1	Year 1-Pre Difference (% change)	Annual Difference-in-Difference (95% CI)‡	P-value
	N = 436			N = 1,249				
Pharmacy	$4,029	$17,146	$13,117 (325.6%)	$2,556	$2,883	$327 (12.8%)	$12,790 ($8,807 to $17,978)	<0.0001
Medical	$10,390	$11,204	$814 (7.8%)	$10,903	$9,431	-$1,472 (-13.5%)	$2,287 (-$135 to $5,377)	0.0759
Total (pharmacy + medical) cost of care	$14,418	$28,309	$13,891 (96.3%)	$13,457	$12,314	-$1,143 (-8.5%)	$15,034 ($10,630 to $20,251)	<0.0001

Table 2b

Pre-Post Year 2 Cost Change Means, Among New Start GLP-1 Persistent Members to Treat Obesity Without Diabetes and Matched Controls*

Mean Cost Outcome†	GLP-1 Persistent Pre-Year	GLP-1 Persistent Year 2	Year 2-Pre Difference (% change)	Matched Controls Pre-Year	Matched Controls Year 2	Year 2-Pre Difference (% change)	Annual Difference-in-Difference (95% CI)‡	P-value
	N = 436			N = 1,249				
Pharmacy	$4,029	$17,302	$13,273 (329.4%)	$2,556	$3,342	$786 (30.8%)	$12,487 ($7,938 to $18,660)	<0.0001
Medical	$10,390	$10,641	$251 (2.4%)	$10,903	$10,523	-$380 (-3.5%)	$631 (-$1,660 to $3,549)	0.6315
Total (pharmacy + medical) cost of care	$14,418	$27,909	$13,491 (93.6%)	$13,457	$13,863	$406 (3.0%)	$13,085 ($8,538 to $18,516)	<0.0001

*Eligible control group members were matched to GLP-1 treatment persistent members on characteristics and conditions using a combined exact and propensity score matching approach.
†Medical and pharmacy claim paid allowed amounts, including member share, after all network provider discounts were applied. Members' annual costs capped at $250,000, a common stop-loss policy threshold.
‡Difference between GLP-1 post-pre difference and control post-pre difference. CI=Confidence Interval

Results

- A total of 3,346 commercially insured members newly initiating GLP-1 therapy, and 384,309 control group members, met all initial study criteria.
- After matching, 3,046 GLP-1 therapy members met all study criteria, and of this, 436 (14.3%) were persistent at the end of year 2 with 1,249 members matched as controls.
- Mean age for both GLP-1 utilizers and control group members was 48.2 years; 84.3% were women, 16.3% had prediabetes, and <1% had a history of myocardial infarction **(Table 1)**.
- GLP-1 group average annual TCC increased from $14,418 pre-year to $28,309 in year 1, a $13,891 (96.3%) increase, and was $27,909 in year 2, a $13,491 (93.6% over pre-year) increase. Across the same study periods, control group average annual TCC decreased from $13,457 to $12,314 in year 1, a $1,143 (-8.5%) decrease, and was $13,863 in year 2, a $406 (3.0% over pre-year) increase **(Table 2a)**.
- Difference-in-difference statistical comparison found the GLP-1 group had significantly higher per-member annual TCC $15,034 (p<0.001) in year 1 vs. pre-year, and $13,085 (p<0.0001) higher in year 2 vs. pre-year, with differences driven by higher annual per-member pharmacy cost in the GLP-1 group compared to the control group in year 1 vs. pre-year (DID: $12,790; p<0.001) and year 2 vs. pre-year (DID: $12,487; p<0.001) **(Table 2b)**.
- Per-member annual medical benefit cost trended higher but not significantly different in the GLP-1 group compared to the control group in year 1 vs. pre-year (DID: $2,287; p=0.075) or year 2 vs. pre-year (DID: $631; p=0.631).

Conclusions

- This real-world study found members without DM who were persistent with their GLP-1 obesity treatment over 2 years had a significant $28,119 average higher total cost of care compared to matched controls, indicating GLP-1 obesity therapy is an investment over the first 2 years.
- No medical cost offsets for persistent GLP-1 obesity treatment without DM were observed in the first 2 years; instead, medical cost increased by a non-significant average of $2,918 per member, compared to matched controls.
- These real-world findings highlight substantial GLP-1 obesity treatment investment during the first 2 years of therapy, with unknown future medical cost offsets. This emphasizes the need to fairly price obesity treatment GLP-1s to their real-world expected medical cost offsets.

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.
- In the full study cohort, 9% of identified new start GLP-1 obesity without DM treated members were not matched to a control, potentially resulting in an external validity threat. However, standardized mean differences in the matched analytic cohort, a standard method for assessing covariate balance, were less than 0.1 for all comparisons, indicating adequate balance, except for age group which was slightly above 0.1 at 0.168.
- Control group members may have initiated GLP-1 weight loss therapy after 2021, resulting in a potential misclassification bias.
- Pharmacy costs do not include pharmaceutical manufacturer rebates and coupons.
- Our study examined a commercially insured membership and therefore is not generalizable to Medicare or Medicaid populations.
- The impact 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.

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