Real-World First Year Cost-Effectiveness Assessment of Glucagon-Like Peptide-1 Agonists to Treat Non-Diabetes Obesity

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BACKGROUND

- The National Health and Nutrition Examination Survey (NHANES) estimates U.S. obesity prevalence at 41.9% from 2017 through March 2020 with the Centers for Disease Control and Prevention (CDC) reporting U.S. total obesity-related health care costs at nearly $173 billion annually.[1]
- Glucagon-like peptide-1 agonist (GLP-1) products to treat type 2 diabetes mellitus (T2DM) have been on the market since 2005.
- In 2014, the U.S. Food & Drug Administration (FDA) approved the GLP-1 product, liraglutide injection, for obesity treatment,[2] followed by semaglutide injection in 2021.[3]
- GLP-1 clinical trials for products to treat obesity report significant weight loss (6.1%-17.4%)[4] and medication continuation through trial duration at over 90%.[5]
- GLP-1 utilization and costs during 2023 have increased dramatically in part due to increased obesity treatment and social media trends.[6]
- At an annual GLP-1 wholesale acquisition price $11,500 to $14,000, the Institute for Clinical Economic Review (ICER) cost-effectiveness analysis identified that GLP-1 weight loss therapies are two-fold overpriced to their expected value in weight loss-associated cardiovascular events reduction, diabetes development avoidance, lost work productivity and reduced quality of life over a lifetime.[5] The clinical trial data used by ICER to create their cost-effectiveness findings of GLP-1 drugs reported a medication adherence rate of 95%.
- Little real-world evidence describes the first-year GLP-1 cost-effectiveness for treating obesity without diabetes.

OBJECTIVES

To describe changes in total cost of care (TCC) one year before and one year after initiation of GLP-1 treatment among commercially insured members with obesity, without diabetes, compared to a concurrent matched control group.

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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 three-year period of Jan. 1, 2020 to Dec. 31, 2022.
- Study inclusion was limited to members newly initiating a GLP-1 (index date), defined as no use in prior year, in calendar year 2021, i.e., the identification period, with member continuous enrollment 12-months before (pre-period) and 12-months after (post-period) the index date required.
- Members were required to have a pre-period medical claim including a diagnosis code for obesity or a Z code for body mass index (BMI) ≥30.
- Members were excluded if they had a medical claim with a DM diagnosis 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 one pharmacy claim for any drug during 2021 and without a GLP-1 claim in the year prior to the 2021 index date.
- A two-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, obesity, prediabetes diagnosis among those with obesity, pregnancy, and use of statin, renin angiotensin system antagonist (RASA), and/or antidepressants at index.
  - Step 2: After the direct match, GLP-1 utilizers were matched using propensity scores on five-year age bands, month of index study date, major chronic disease medical conditions, and pre-period drug utilization of non-GLP-1 weight loss drug therapy by class (e.g., phentermine, topiramate, naltrexone, etc.).
- Total cost of care (TCC) was calculated by summing the 365-day period pre-index date TCC, and 365-day post-period included index date plus 364 days for the post-period. Costs included medical and pharmacy claim paid allowed amounts, including member share, after all network provider discounts were applied. Pharmaceutical manufacturer rebates and coupons were not included in the cost determination.
- Total cost of care for an individual in pre- or post-periods were capped at $250,000 due to stop-loss policy common threshold.
- Statistical analysis compared the pre- to post-TCC average per analyzed member cost change between the groups using a pre-period minus post-period, difference-in-difference approach.

TABLE 1

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

	Before Matching				After Matching (3 controls to 1 GLP-1 member)**			
Demographic/Clinical Characteristic*	Control n=396,103	GLP-1 n=4,073	P-value†	Standardized Mean Difference‡	Control n=11,392	GLP-1 n=3,887	P-value†	Standardized Mean Difference‡
Age, mean, years	46.5	46.3	0.2965	0.0177	47.0	46.3	<0.0001	0.0750
Age grouping into 5-year bands			<0.0001	0.2772	Propensity Match to Age Group		0.0325	0.1218
Female, n (%)	226,058 (57.1)	3,306 (81.2%)	<0.0001	0.5403	9,291 (81.6%)	3,166 (81.5%)	0.8828	0.0027
Blue Plan – 19 Blue Plans			<0.0001	0.8824	Propensity Match to Health Plan		1	0
Fully Insured, % (n)	123,805 (31.3%)	1,074 (26.4%)			2,995 (26.3%)	1,024 (26.3%)		
Health Insurance Marketplace, n (%)	123,430 (31.2%)	941 (23.1%)	<0.0001	0.2678	2,695 (23.7%)	916 (23.6%)	0.9929	0
Self-Insured, n (%)	148,868 (37.6%)	2,058 (50.5%)			5,702 (50.1%)	1,947 (50.1%)		
BMI 30 – 34.9, Z code, n (%)	142,609 (36.0%)	733 (18.0%)			2,065 (18.1%)	699 (18.0%)		
BMI 35 – 39.9, Z code, n (%)	70,502 (17.8%)	671 (16.5%)			1,875 (16.5%)	645 (16.6%)		
BMI 40 – 44.9, Z code, n (%)	37,222 (9.4%)	595 (14.6%)	<0.0001	0.4751	1,638 (14.4%)	564 (14.5%)	0.9969	0.0485
BMI 45+, Z code, n (%)	26,468 (6.7%)	574 (14.1%)			1,524 (13.4%)	524 (13.5%)		
No medical claims with Z code ≥30*, n (%)	119,302 (30.1%)	1,500 (36.8%)			4,290 (37.7%)	1,455 (37.4%)		
Prediabetes, n (%)	21,638 (5.5%)	656 (16.1%)	<0.0001	0.3483	1,595 (14.0%)	573 (14.7%)	0.2533	0.0211
Major depression, n (%)	49,285 (12.4%)	895 (22%)	<0.0001	0.2546	2,467 (21.7%)	798 (20.5%)	0.1393	0.0276
Hypothyroidism, n (%)	43,750 (11.0%)	760 (18.7%)	<0.0001	0.2154	2,019 (17.7%)	701 (18.0%)	0.6611	0.0081
Pregnancy, n (%)	8,109 (2.0%)	36 (0.9%)	<0.0001	0.0969	84 (0.7%)	30 (0.8%)	0.8294	0.004
Myocardial Infarction history, n (%)	3,567 (0.9%)	26 (0.6%)	0.0776	0.0300	84 (0.7%)	25 (0.6%)	0.5468	0.0114
Charlson Comorbidity Index (CCI), mean	0.5	0.6	<0.0001	0.1128	0.5	0.6	0.0005	0.0628
Index month Jan 2021 to Dec 2021			<0.0001	0.2295	Propensity Match to Index Month		0.9978	0.0491
Weight loss medication in pre-period, n (%)	5,628 (1.4%)	290 (7.1%)	<0.0001	0.2847	411 (3.6%)	195 (5.0%)	0.0001	0.0694
Drug therapy on index day minus 1					Propensity Score Match to Drug Therapy on Index Day Minus 1			
Statin, n (%)	48,841 (12.3%)	553 (13.6%)	0.0161	0.0371	1,398 (12.3%)	497 (12.8%)	0.4008	0.0155
Renin Angiotensin System Antagonist, n (%)	73,808 (18.6%)	930 (22.8%)	<0.0001	0.1037	2,483 (21.8%)	864 (22.2%)	0.5740	0.0104
Antidepressant, n (%)	65,130 (16.4%)	1,366 (33.5%)	<0.0001	0.4028	3,579 (31.4%)	1,248 (32.1%)	0.4241	0.0148

*All members were required to have pre-period medical claim including a diagnosis code for obesity or Z code for body mass index (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 2

Pre-Post Cost Change in Primary Endpoint Pharmacy Costs, Medical Costs and Total Care Costs Means Among New Start GLP-1 Members to Treat Obesity Without Diabetes vs. Propensity Score Matched Controls*

Mean Spending Outcome**	GLP-1 Pre-year	GLP-1 Post-year	GLP-1 Post-Pre Difference	Control Pre-year	Control Post-year	Control Post-Pre Difference	Difference-in-Difference (95% CI)‡	P-value
	N = 3,887			N = 11,392				
Pharmacy	$2,858	$9,057	**$6,199**	$2,088	$2,593	**$505**	**$5,694** ($4,810 - $6,674)	<0.0001
Medical	$9,950	$10,960	**$1,010**	$9,294	$8,818	**-$476**	**$1,487** ($576 - $2,480)	0.0007
Total (Pharmacy + Medical)	$12,776	$19,931	**$7,155**	$11,369	$11,391	**$22**	**$7,132** ($5,884 - $8,464)	<0.0001

*Eligible control group members were matched to GLP-1 treatment members on characteristics and conditions using a combined exact and propensity score matched 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 common stop-loss policy threshold
‡Difference between GLP-1 Post-Pre Difference and Control Post-Pre Difference. CI=Confidence Interval

RESULTS

- A total of 4,073 commercially insured members newly initiating GLP-1 therapy and 396,103 control group members met all study criteria. **(Table 1)**
- A 3-to-1 control member to GLP-1 treatment member ratio was used with matching replacement allowed; therefore, a control member may match to more than one GLP-1 treated member. The final unique member matching ratio was 2.9 to 1 based on approach to optimize covariate balance and matched sample size. 10,115 of controls were matched to only 1 GLP-1 treatment member, 1,086 controls to 2 treatment members, 174 controls to 3 treatment members and 5 controls to 4 treatment members.
- The final analysis cohort was 3,887 GLP-1 therapy members and 11,392 control group members.
- Standardized mean differences, a standard method for assessing covariate balance, between GLP-1 and control group demographics and characteristics was less than 0.1 for all characteristics, indicating adequate balance, except for age group which was slightly above 0.1 at 0.1218.
- Mean age for both GLP-1 utilizers and control group members was 47 years, and 82% were women.
- 14.2% of members had prediabetes.
- All members had obesity defined by either ICD-10 code claim or BMI Z code ≥30. Percent of members by BMI category was:
  - 18.1% BMI 30 – 34.9
  - 16.5% BMI 35 – 39.9
  - 14.4% BMI 40 – 44.9
  - 13.4% BMI 45+
  - 37.7% without medical claim with BMI Z code ≥30
- <1% had a history of a myocardial infarction
- Mean total cost of care for the GLP-1 group increased from $12,776 to $19,931, a $7,155 (56.0%) increase, and for controls from $11,369 to $11,391, a $22 (0.2%) increase. **(Table 2)**
- Mean medical costs for the GLP-1 group increased from $9,950 to $10,960, a $1,010 (10.1%) increase, and for controls from $9,294 to $8,818, a $476 (5.1%) decrease.
- Mean pharmacy costs for the GLP-1 group increased from $2,858 to $9,057, a $6,199 (217%) increase, and for controls from $2,088 to $2,593, a $505 (24.2%) increase.
- Difference-in-difference statistical comparison found the GLP-1 group had significantly higher per-member annual TCC $7,132 (p<0.01), medical benefit spending $1,487 (P<0.01) and pharmacy benefit spending at $5,694 (p<0.01).

LIMITATIONS

- Pharmacy costs may be overestimated because pharmaceutical manufacturer rebates and coupons were not included in the cost determination.
- Misclassification bias may have occurred due to using medical and pharmacy claims to exclude individuals without diabetes and to identify those with obesity.
- Tirzepatide products were not included in this analysis, as they were not available during the 2021 study identification period and were non-formulary during 2022.
- Our study examined a commercially insured membership and, therefore, are 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.

CONCLUSIONS

- This real-world analysis found a significant $7,132 TCC investment, in year one, for each member newly initiating a GLP-1 for weight loss without diabetes.
- No medical cost offset was observed; instead, the GLP-1 treatment medical cost increased significantly at $1,487 per member, compared to a matched control group.
- These real-world findings can aid in development of evidence-based GLP-1 weight loss management programs, pharmaceutical manufacturer value-based contracts and health insurance benefit designs.

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