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

Ben Urick, PharmD, Ph.D.; Jacinda Tran, PharmD, Ph.D.; Landon Marshall, PharmD, Ph.D.; Michelle McCann; Marci Chodroff, M.D., Chief Medical Officer; David Lassen, PharmD, Chief Clinical Officer; and Patick Gleason, PharmD, Assistant Vice President, Health Outcomes

All authors are employees of Prime Therapeutics.

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Introduction

The obesity epidemic continues to represent a significant public health and economic challenge in the United States.[1-4] This chronic, progressive disease affects approximately 40% of U.S. adults[3] with an estimated economic impact of $1.39 trillion dollars annually.[4] Since 2021, the therapeutic landscape for obesity has evolved with the introduction of new anti-obesity medications, including glucagon-like peptide-1 (GLP-1) receptor agonist and dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 receptor co-agonist medications.

As a direct result of GLP-1 weight-loss treatment demand, GLP-1 spending has become a major cost driver for plan sponsors who provide weight-loss drug coverage.[5-7] With current annual gross GLP-1 costs exceeding $12,000 per patient, plan sponsors face mounting pressure to balance clinical benefit with budgetary constraints. For every 1 percentage point increase in the population using a weight-loss GLP-1, there is an approximately $10 increase in per-member-per-month expense, equating to an approximate 3% to 5% increase in the entire drug budget.[8]

While the cost of these products is substantial, treating obesity will likely improve health outcomes and reduce medical spending, which could offset some of the cost from these products.[4] However, real-world evidence supporting this possibility is both limited and mixed. Reports from consulting firms and industry-sponsored studies have shown modest outcome improvement and medical-cost offsets over one to two years following GLP-1 initiation.[9-12] However, these analyses have largely focused on highly selective cohorts — such as patients who are adherent or have coexisting diabetes — rather than evaluating the full population of utilizers. Other studies have found that GLP-1 initiation can lead to meaningful improvements in key cardiometabolic measures, including weight reduction, lower A1C, reduced blood pressure and improved lipid profiles.[13] However, use does not appear to change overall outcomes or reduce health care spending among patients with obesity alone during the initial few years of treatment.[13-17] Low persistence and

adherence to products, particularly when initiated prior to 2024, reduce the observed effectiveness of GLP-1 products in the real world.

Prior work by Prime Therapeutics (Prime) has established that, among commercially insured members with obesity and without diabetes, initiating a GLP-1 in 2021 does not reduce medical spending over two years of therapy compared to matched controls.[14, 15] This analysis expands on that prior work by adding GLP-1 initiators into 2022, identifying more members who initiated high-potency GLP-1 products (semaglutide or tirzepatide) and increasing the post-period to three years. This work provides valuable information to payers and plan sponsors considering the real-world GLP-1 therapy investment costs, member GLP-1 therapy persistence and medical-cost offset from obesity-indicated products.

Objectives

To describe changes in annual pharmacy benefit spending, medical benefit spending and total cost of care (TCC) one year before and three years after GLP-1 obesity treatment initiation among commercially insured members without diabetes compared to a matched control group among the full population as well as among a subset who have remained adherent to GLP-1 therapy.

Methods

Prime's integrated medical and pharmacy claims plus enrollment data from Jan. 1, 2020, to Sept. 14, 2025 across 19 commercial health plans covering all regions of the United States were obtained for this study. During the study index period, the database contained an average of 17.9 million members with at least one month of eligibility. The study population consisted of new initiators of a GLP-1 (“treatment”) or a chronic medication (“control”) between Jan. 1, 2021 and March 31, 2022. Inclusion criteria were continuous enrollment in the 12 months prior to index (“pre-period”), an obesity diagnosis on one or more medical claims during the pre-period, aged 19 or more years at index and no GLP-1 use or evidence of diabetes during the pre-period.

For the adherence subanalysis, adherence was measured using the proportion of days covered (PDC) method. Unlike the standard PDC methodology used by the Centers for Medicare and Medicaid Services,[18] which requires a minimum of two claim fills, Prime’s approach included members with one or more fills. This methodological difference allowed adherence to be assessed beginning with the member’s index GLP-1 claim. All prescription fill dates within the 1,092 days (91-day period * 12 periods) following each member’s study index date were included in the PDC calculation. Members with a PDC at 80% or greater were classified as adherent; those with a PDC of less than 80% were considered nonadherent.

Members were matched 3:1 on gender, age category, Charlson comorbidity index (CCI) score,[19] line of business (i.e., fully-insured, health insurance marketplace, self-insured), obesity severity, prediabetes diagnosis, Blue plan region, pre-period non-GLP-1 weight loss drug therapy, pre-period pharmacy claim fills and presence or absence of an inpatient visit in the 91 days prior to index.

Annual spending was calculated using rolling 91-day periods, representing approximately one-quarter of a year relative to the index date. Members could contribute up to three years of spending data, depending on continuous enrollment and censoring, allowing for longitudinal assessment of cost trends. All spending was calculated from allowed amounts and excluded rebates or other post-adjudication discounts. To ensure comparability over time, spending was inflation-adjusted to first-half 2025 dollars using the medical component of the Consumer Price Index.[20]

All members had four 91-day quarter pre-period measurements. Controls who initiated a GLP-1 were censored beginning with the period of initiation. For the primary assessment with the full population, members had up to 12 post-period quarter measurements depending on eligibility. For the adherent-only subanalysis, both treatment and control members were required to have continuous eligibility. All treatment members for the subanalysis had 12 quarter periods of eligibility, and control members had fewer than 12 if they initiated GLP-1 treatment. Difference-in-differences (DID) regressions with a gamma distribution and log link were used to compare differences in health care spending by annual periods and trend over time.

Results

Out of an initial pool of 5,112,150 control member and 10,686 treatment member index date combinations, 29,570 (29,234 distinct) control member-index dates were matched to 10,094 treatment members who met eligibility criteria and were matched for the full population analysis. The adherent-only subanalysis resulted in 1,864 distinct control member-index dates matched to 644 treatment members.

Continuous eligibility was applied on a 91-day quarter period-by-period basis, allowing members to come in and out of the cohort during the post period depending on benefit enrollment. By the end of the three-year post-period, 61.3% (6,193) treatment members and 60.5% (17,892) control members remained enrolled. Censoring control members who initiated GLP-1 therapy resulted in an additional 2,281 control members dropping for a final retained percentage of 51.0%.

The cohorts were well balanced after matching, with standardized mean differences for matching variables all less than 0.1 for both the full population and adherent-only cohort. For the full population, 80.6% were women. The mean age of 45.6 years old, and 41.2% had severe obesity, or a body mass index of 40 or higher. For the adherent-only cohort, 79.1% were women. The mean age was 48.3 years old, and 42.5% of the sample had severe obesity.

Assessing changes in spending for the primary analysis with the full population, total pharmacy benefit spending for the GLP-1 treatment group increased from $758 in the 91 days immediately prior to index to $3,871 for the 91-day period beginning with the index date. After this substantial increase, and as treatment members discontinued GLP-1 therapy, total pharmacy benefit spending decreased at a rate of -7.2% (95% CI -9.1 to -5.3%) throughout the three-year post-period compared to the one-year pre-period for treatment members compared to controls (Figure 1). Despite this downward trend, total pharmacy benefit spending remained significantly elevated across post-periods, with an annualized difference-in-difference of $3,639 (95% CI $3,344 to $3,933) for Year 3 compared to pre-period (Table 1).

Non-GLP-1 pharmacy benefit spending, which excludes the cost of GLP-1 products from total pharmacy benefit spending, was similar between GLP-1 treatment and control groups after index. For treatment members compared to controls, quarterly trend difference-in-difference was -0.3% (95% CI -2.4 to 1.9%) for the post-period compared to pre-period (Figure 2). Despite this slightly negative trend, per member per year (PMPY) was $249 (95% CI -$10 to $508) for treatment compared to control members in Year 3, compared to the pre-period (Table 1).

Medical benefit spending, by contrast, did not change substantially in the first year of therapy for GLP-1 treatment members compared to controls. Medical benefit spending did, however, trend up in the three-year post-period at a rate of 1.7% (95% CI -0.1 to 3.9%) for treatment members compared to controls (Figure 3). This resulted in a difference-in-difference of $695 (95% CI $251 to $1,139) for treatment members compared

to controls in Year 2 compared to the pre-period and $930 (95% CI $411 to $1,449) for the Year-3 comparison.

TCC, which is a combination of medical benefit spending and pharmacy spending, reflects the combined trend of these two spend components. TCC rose from $3,107 in the quarter period before index to $6,554 the quarter period after index and decreased at a rate of -2.1% (95% CI -3.8 to -0.4%) in the post-period. Across the three post-period years, the difference in spending for Years 1, 2 and 3 compared to the pre-period was $7,071, $4,777 and $4,490.

The adherent-only subanalysis found total pharmacy spending among the treatment group increased immediately from $948 in the 91-day period before index to $5,020 in the first 91 days post index (Figure 1.). Total pharmacy benefit spending remained elevated throughout, with a nonsignificant downward trend of -2.2% (95% CI -9.1 to 5.3%) over the three years post-index. Total pharmacy benefit spending difference-in-difference compared to the pre-year varied from $13,577 (95% CI $13,002 to $14,151) in Year 1 to $13,076 (95% CI $12,396 to $13,755) in Year 2 and $12,489 (95% CI $11,613 to $13,366) in Year 3 (Table 1). By contrast, non-GLP-1 pharmacy spending trends (Figure 2) and annual differences (Table 1) remained similar between the groups, with non-GLP-1 pharmacy benefit spending remaining $774 (95% CI -$50 to $1,599) higher for treatment members compared to controls in Year 3 compared to the pre-period.

Medical benefit spending trend among the adherent group was not different between groups during the three years post-index, and medical spending did not differ between groups in Year 1 or Year 2 (Figure 2, Table 1). In Year 3, medical spending means appeared higher for the treatment group than controls, driven by unusually high spending in the final study quarter in the treatment group. None of these differences in medical spending were statistically significant. A sensitivity analysis excluding the final quarter finds trends to be essentially flat with only a $149 (95% CI -$1,058 to $2,254; p=0.479) difference in difference for Year 3 compared to the Pre-period. TCC showed an immediate increase in spending, driven by increased prescription drug spending, which remained elevated throughout the study period at $13,308 to $14,017 greater annual spending for adherent treatment members compared to controls.

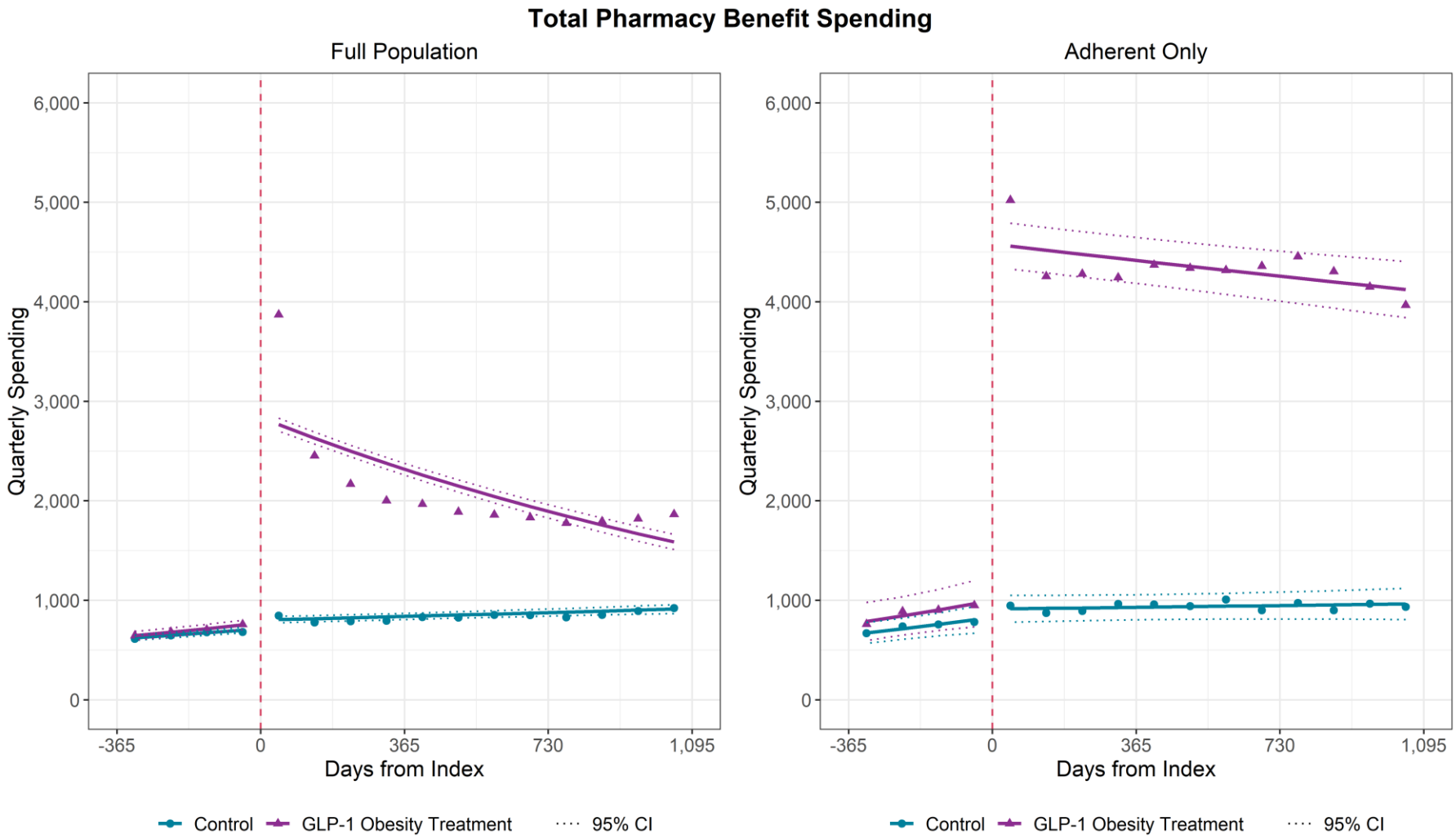
Conclusions

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 with no indication of a trend toward medical spending reductions. The lack of medical-spend offsets holds when limiting the analysis to members who are adherent to therapy for three years. Annual total pharmacy benefit spending among the adherent group remains more than $12,000 greater than baseline for every year in the post-period.

Trends in pharmacy benefit spending were driven almost entirely by increases in GLP-1 spending among the treatment group. Excluding GLP-1 spending results in similar trends between groups, with treatment group non-GLP-1 pharmacy benefit spending remaining above, but not statistically different from, controls in Year 3 compared to the pre-year. For the real-world intent-to-treat study population, a pro-forma assessment using $350 per GLP-1 28-day supply instead of allowed amounts results in a Year-3 pharmacy benefit spending and TCC difference-in-difference estimates of $1,365 (95% CI $1,101 to $1,629) and $2,213 (95% CI $1,574 to $2,852) compared to the pre-period for treatment members compared to controls. Under the same assumptions, the post-period trend quarterly differences for pharmacy benefit spending and TCC were -4.6% (95% CI -6.6% to -2.6%) and -0.3% (95% CI -2.1% to 1.5%).

These real-world findings indicate substantial ongoing investment over the first three years of GLP-1 therapy for obesity without diabetes among a commercially insured population. Medical trends were slightly lower among the adherent population than the nonadherent population, suggesting adherence may be important in supporting health benefits which result in lower healthcare spending. Obesity care management programs have been shown to support adherence and could plan a role in promoting sustained weight loss and maximizing benefit from these products.

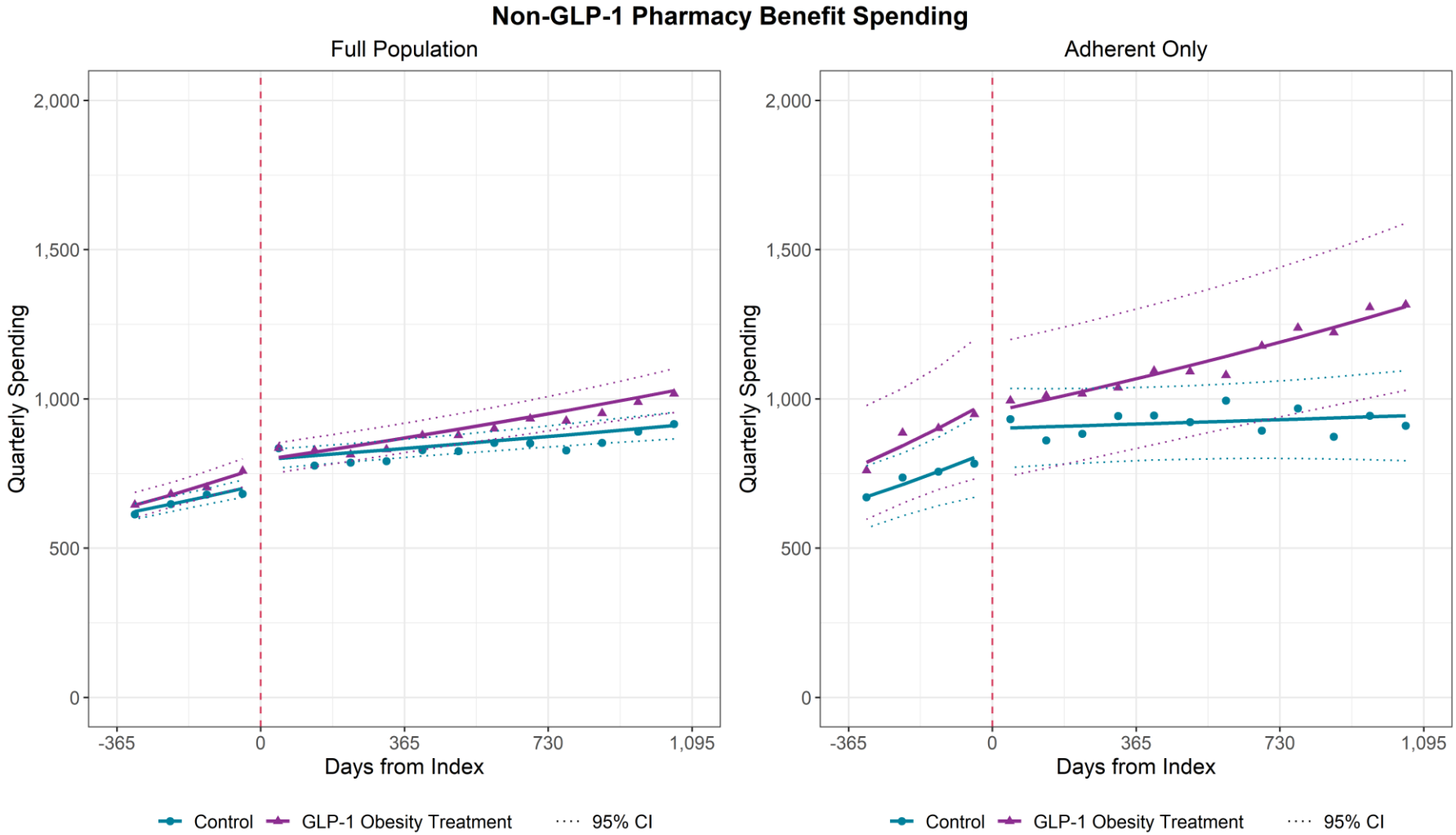
Figure 1. Total Pharmacy Benefit Spending Trends Over Time Among Members Without Diabetes Treated With a GLP-1 Product for Obesity Compared to Matched Controls, Full Population and Adherent Only



Pre-period full population GLP-1 obesity treatment (N = 10,094) and control (N = 29,570). Pre-period adherent population GLP-1 obesity treatment (N = 644) and control (N = 1,864). Index dates covered Jan 1., 2021 and March 31,2022. The points represent the mean observed spending for each 91-day quarter period, relative to the index. All costs are allowed amounts reported 2025 U.S. dollars. Model estimates were derived from difference-in-differences regressions with a gamma distribution and log-link. For treatment members in the full population, pharmacy spending trended down at a rate of -7.2% (95% CI: -9.1 to -5.3%) per quarter over three years post-index compared to control members. In the adherent-only population, the change in pharmacy spending for treatment members decreased at a rate of -2.2% (95 CI: -9.1 to 5.3%) per quarter compared to controls.

Figure 2. Non-GLP-1 Pharmacy Benefit Spending Trends Over Time Among Members Without Diabetes Treated With a GLP-1 Product

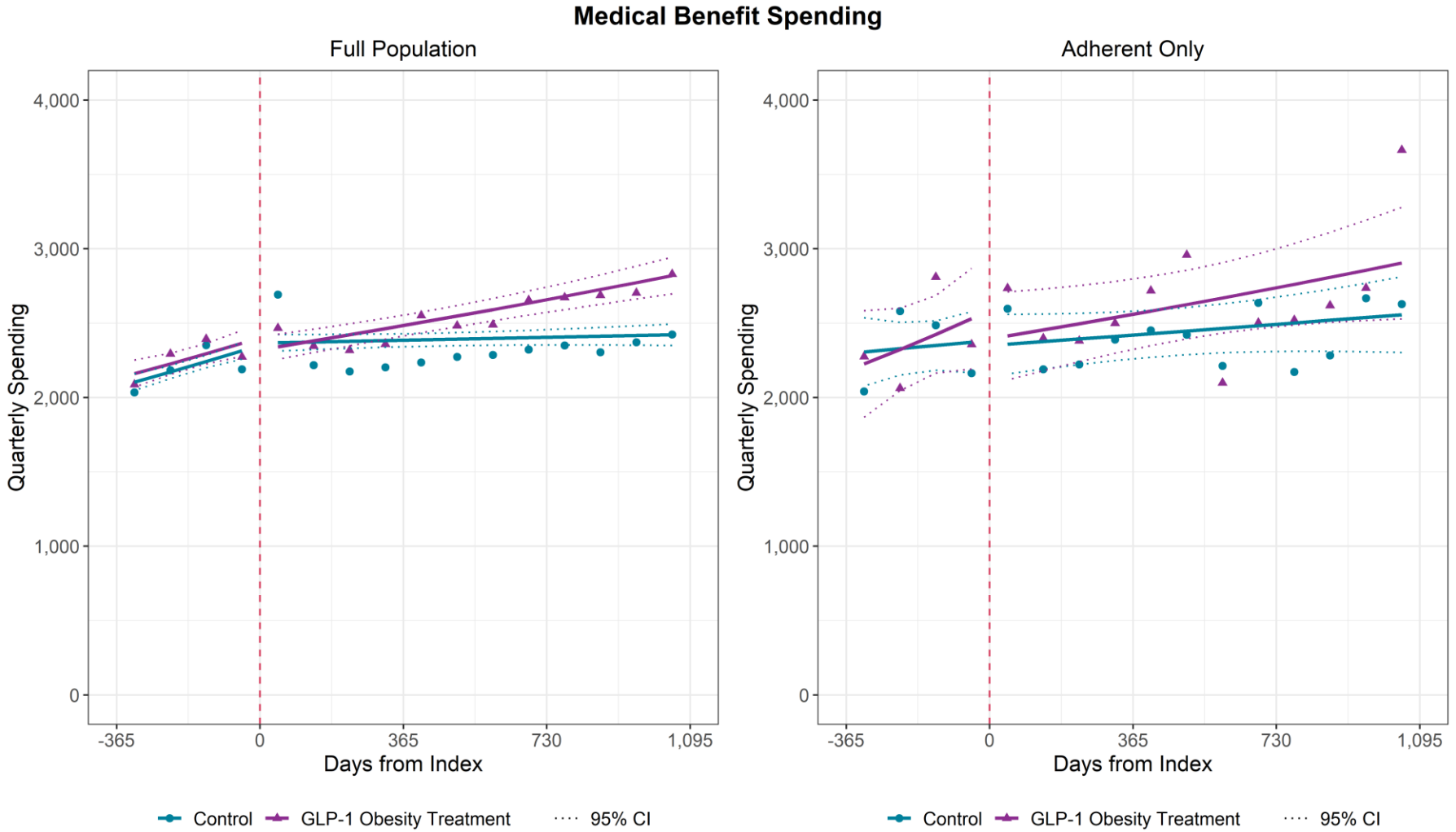
for Obesity Compared to Matched Controls, Full Population and Adherent On



Pre-period full population GLP-1 obesity treatment (N = 10,094) and control (N = 29,570). Pre-period adherent population GLP-1 obesity treatment (N = 644) and control (N = 1,864). Index dates covered Jan 1., 2021 and March 31,2022. The points represent the mean observed spending for each 91-day quarter period, relative to the index. All costs are allowed amounts reported in 2025 U.S. dollars. Model estimates were derived from difference-in-differences regressions with a gamma distribution and log-link. For treatment members in the full population, non-GLP-1 pharmacy spending trended down at a rate of -0.3% (95% CI: -2.4 to 1.9%) per quarter over three years post-index compared to control members. In the adherent-only population, the change in non-GLP-1 pharmacy spending for treatment members increased at a rate of 1.5% (95 CI: -5.8 to 9.4%) per quarter compared to controls.

Figure 3. Medical Spending Trends Over Time Among Members Without Diabetes Treated With a GLP-1 Product for Obesity Compared

to Matched Controls, Full Population and Adherent Only



Pre-period full population GLP-1 obesity treatment (N = 10,094) and control (N = 29,570). Pre-period adherent population GLP-1 obesity treatment (N = 644) and control (N = 1,864). Index dates covered Jan 1., 2021 and March 31, 2022. The points represent the mean observed spending for each 91-day quarter period, relative to the index. All costs are allowed amounts reporte 2025 U.S. dollars. Model estimates were derived from difference-in-differences regressions with a gamma distribution and log-link. For treatment members in the full population, medical spending trended upward at a rate of 1.7% (95% CI: -0.5 to 3.9%) per quarter over three years post-index compared to control members. In the adherent-only population, the change in medical spending for treatment members decreased at a rate of -2.4% (95 CI: -9.9 to 5.9%) per quarter compared to controls.

Table 1. Annual Spending and Difference-In-Difference Estimates Among Members Without Diabetes Treated With a GLP-1 Product for

Obesity Compared to Matched Controls, Full Population and Adherent Only

Spending Type	Period	Full Population			Adherent Only		
		Annual Spending (95% CI)		DID Estimate vs. Pre-Period (95% CI; p-value)	Annual Spending (95% CI)		DID Estimate vs. Pre-Period (95% CI; p-value)
		GLP-1 Obesity Treatment (N=10,094)	Control (N=29,570)		GLP-1 Obesity Treatment (N=644)	Control (N=1,864)	
Total Pharmacy Benefit	Pre-period	$2,788 (2,621 to 2,955)	$2,643 (2,540 to 2,746)	--	$3,496 (2,705 to 4,287)	$2,945 (2,510 to 3,381)	--
	Year 1	$10,648 (10,413 to 10,883)	$3,266 (3,141 to 3,390)	$7,238 (7,050 to 7,425)***	$17,797 (16,884 to 18,709)	$3,668 (3,141 to 4,196)	$13,577 (13,003 to 14,151)***
	Year 2	$7,646 (7,382 to 7,911)	$3,426 (3,286 to 3,567)	$4,075 (3,839 to 4,311)***	$17,386 (16,423 to 18,350)	$3,760 (3,220 to 4,300)	$13,076 (12,396 to 13,755)***
	Year 3	$7,371 (7,071 to 7,672)	$3,588 (3,426 to 3,749)	$3,639 (3,344 to 3,933)***	$16,873 (15,766 to 17,979)	$3,832 (3,242 to 4,423)	$12,489 (11,613 to 13,366)***
Non-GLP1 Pharmacy Benefit	Pre-period	$2,788 (2,621 to 2,955)	$2,643 (2,540 to 2,746)	---	$3,496 (2,705 to 4,287)	$2,945 (2,509 to 3,380)	---
	Year 1	$3,305 (3,110 to 3,500)	$3,247 (3,124 to 3,370)	-$87 (-214 to 40)	$4,059 (3,148 to 4,970)	$3,613 (3,101 to 4,125)	-$105 (-622 to 412)
	Year 2	$3,642 (3,415 to 3,869)	$3,420 (3,280 to 3,560)	$77 (-116 to 270)	$4,441 (3,465 to 5,417)	$3,706 (3,182 to 4,231)	$183 (-454 to 820)
	Year 3	$3,971 (3,707 to 4,236)	$3,578 (3,417 to 3,738)	$249 (-10 to 508)	$5,082 (4,003 to 6,162)	$3,756 (3,190 to 4,323)	$774 (-50 to 1,599)
Medical Benefit	Pre-period	$9,043 (8,777 to 9,310)	$8,828 (8,664 to 8,991)	--	$9,501 (8,476 to 10,526)	$9,354 (8,693 to 10,015)	--
	Year 1	$9,527 (9,206 to 9,848)	$9,499 (9,297 to 9,701)	-$187 (-560 to 185)	$10,010 (8,863 to 11,158)	$9,554 (8,807 to 10,300)	$310 (-1,115 to 1,734)
	Year 2	$10,291 (9,921 to 10,661)	$9,381 (9,153 to 9,609)	$695 (251 to 1,139)**	$10,273 (9,077 to 11,469)	$9,919 (9,098 to 10,739)	$207 (-1,334 to 1,748)
	Year 3	$11,045 (10,606 to 11,484)	$9,900 (9,632 to 10,167)	$930 (411 to 1,449)***	$11,536 (10,197 to 12,875)	$9,972 (9,079 to 10,865)	$1,417 (-254 to 3,087)
Total Cost of Care	Pre-period	$12,177 (11,817 to 12,536)	$11,872 (11,651 to 12,094)	--	$13,381 (11,881 to 14,880)	$12,869 (11,954 to 13,784)	--
	Year 1	$20,678 (20,234 to 21,121)	$13,302 (13,029 to 13,576)	$7,071 (6,639 to 7,503)***	$28,229 (26,563 to 29,895)	$13,787 (12,737 to 14,838)	$13,930 (12,291 to 15,570)***
	Year 2	$18,481 (17,967 to 18,995)	$13,400 (13,092 to 13,707)	$4,777 (4,242 to 5,312)***	$28,096 (26,335 to 29,857)	$14,276 (13,149 to 15,403)	$13,308 (11,490 to 15,127)***
	Year 3	$18,961 (18,361 to 19,562)	$14,166 (13,808 to 14,525)	$4,490 (3,842 to 5,139)***	$29,050 (26,968 to 31,132)	$14,521 (13,260 to 15,782)	$14,017 (11,880 to 16,155)***

* < 0.05; ** <0.01; *** <0.001. CI: Confidence interval; DID: Difference in difference. Index dates covered 1/1/2021 and 3/31/2022. Annual estimates reflect the mean 91-day quarter spending across all quarters in a given year period multiplied by 4. All costs are allowed amounts reported in 2025 US dollars. DID model estimates were derived from difference-in-differences regressions with a gamma distribution and log-link. Adherence defined as >= 80% proportion of days covered.

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