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**ABSTRACT**

Glucagon-like peptide-1 receptor agonists (GLP-1s) represent a major improvement in treatment of diabetes, obesity, and cardiovascular risk reduction, but they are also among the most expensive drugs in widespread use and the subject of significant policy debate. The high price of these drugs may overstate their net cost if the health improvements they produce lead to reduced downstream health care use and medical spending, that is, cost offsets. We estimate such offsets using insurance claims data, examining the effects of GLP-1 initiation on subsequent GLP-1 use and spending, and on other non-GLP-1 spending. We use a stacked difference-in-differences design, comparing patients initiating GLP-1 medication to not-yet-treated controls who initiate GLP-1s several months or years later, allowing us to control for underlying time trends and baseline characteristics. Overall, we do not find a reduction in downstream medical spending. Although GLP-1 initiation reduces spending on other diabetes medications, total non-GLP-1 spending increases, driven by higher outpatient health care use; GLP-1 drug spending rises mechanically. For health care payers, the relevant cost of GLP-1 initiation therefore extends beyond the sticker price of the drug. We find similar results across subgroups of GLP1 initiators including those with prior cardiovascular disease and those without diabetes (consistent with obesity indication). Our main results examine spending responses over the first year after initiation. However, we also estimate longer run effects in a smaller sample and find no cost offsets even five years after GLP-1 initiation. Taken together, these results suggest that payers facing the costs of GLP-1 coverage are unlikely to see large savings from reduced spending on other care. If GLP-1 therapies ultimately yield cost savings, they are likely to occur only over longer horizons or through non-medical channels.

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## 1 – Introduction

Obesity and diabetes are major drivers of poor health in the United States and around the world (Mokdad et al. 2018; Hay et al. 2025). The prevalence of both conditions has continued to rise in recent years (Centers for Disease Control and Prevention 2024; Fryar, Carroll, and Afful 2020). However, a new class of drugs has recently proven highly effective for weight loss and diabetes management: glucagon-like peptide-1 receptor agonists (GLP-1s).<sup>1</sup> But these drugs are associated with very high prices.

The high price of GLP-1s, combined with the high prevalence of obesity, has made insurance coverage an important fiscal challenge for insurers and policy makers. In an op-ed, Deese, Gruber, and Cummings (2024) argued that making GLP-1s available to all Americans with obesity could cost the government over a trillion dollars per year, an amount approaching total annual Medicare spending. However, the procurement costs of these drugs may overstate their true cost to insurers because their effectiveness in treating obesity and diabetes may reduce downstream spending on related health conditions. Clinical trials show that GLP-1s improve glycemic control in type 2 diabetes (Yao et al. 2024), produce substantial and sustained weight loss (Wilding et al. 2021; Jastreboff et al. 2022), and reduce heart attacks and strokes (Steven P. Marso, Gary H. Daniels, et al. 2016; Steven P. Marso, Stephen C. Bain, et al. 2016b; Lincoff et al. 2023). Whether these health improvements translate into meaningful cost offsets remains an open question because clinical trials do not measure health care costs, trial populations may differ from real-world users, and offsets depend critically on whether patients persist with treatment, since health gains appear to fade after discontinuation (Wilding et al. 2022).

In this paper, we measure cost offsets associated with GLP-1 use by estimating how initiating GLP-1 treatment affects subsequent spending on both GLP-1s and non-GLP-1 health care, accounting for non-adherence and discontinuation through an intent-to-treat design. We study past and future insurance claims for approximately 537,000 patients initiating GLP-1 treatment between 2017 and 2022, using a staggered difference-in-difference design that compares patients who initiate in a given month to patients who initiate at a later date. Our main result is that GLP-1 initiation does not lead to reductions in other health care spending and in fact increases it. This result holds across subpopulations of patients with a wide range of baseline health conditions and persists for at least five years after initiation. The modal patient in our sample has a type 2 diabetes diagnosis, but our

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1. During our study period (2017 to 2023), GLP-1 therapies were indicated primarily for type 2 diabetes and weight management. Because type 2 diabetes and obesity share key behavioral and metabolic risk factors, we consider both conditions in this study, despite differences in dosing, formulation, and insurer coverage across indications and over time.

results are informative about cost effects of GLP-1 use for obesity as well. Obesity is highly prevalent in our sample and key GLP-1 therapies for diabetes and obesity rely on the same active molecules, despite differences in dosing and regulatory labeling.

These results are central to ongoing discussions about insurance coverage of obesity treatment medications, particularly GLP-1s. Currently, public and private payers generally cover GLP-1s for type 2 diabetes and certain cardiovascular indications while coverage for obesity treatment is less common. By statute, Medicare Part D excludes coverage for obesity treatment medications ([Social Security Act 2003](#)). In Medicaid, 38 states do not cover GLP-1 medications for obesity treatment ([Williams, Rudowitz, and Bell 2024](#)). Among employers with 200+ employees, about 20% of plans cover GLP-1s for obesity, and coverage has grown substantially among large employers ([Claxton et al. 2025](#)). There is increasing pressure to expand coverage. Federal employee health plans are required to cover GLP-1s for obesity ([U.S. Office of Personnel Management 2014, 2022](#)), and the National Conference of Insurance Legislators has encouraged regulators to facilitate coverage of anti-obesity treatments ([National Conference of Insurance Legislators \(NCOIL\) 2015](#)). In late 2024, CMS proposed requiring Medicaid coverage and permitting Medicare Part D to cover obesity treatment medications ([Centers for Medicare & Medicaid Services 2024](#)); the National Association of Medicaid Directors recommended against the change, citing fiscal concerns ([National Association of Medicaid Directors 2025](#)). Concerns about cost are the central reason payers have resisted broader coverage.

Cost offsets are a potentially important source of savings, but existing approaches to estimating offsets rest on strong assumptions. Several papers use simulation methods to project cost offsets implied by health improvements observed in clinical trials ([Ward et al. 2023](#); [Atlas et al. 2022](#); [Hwang et al. 2025](#)). The Congressional Budget Office adopts a similar approach ([Congressional Budget Office 2024](#)). These simulations model healthcare spending as a function of health status. GLP-1s are assumed to affect spending primarily by changing the probability of transitioning to more acute health states. As a result, these models require assumptions about how GLP-1s affect health state transitions, how health states translate into health care spending, and how long patients persist in GLP-1 treatment

Our approach avoids these challenges by directly estimating the spending effects of GLP-1 initiation, following patients for up to five years post initiation. We implement a patient-level staggered adoption design. For our one-year follow-up analysis, we compare patients who initiate GLP-1 treatment in a given month-year to a control group of patients who initiate GLP-1 treatment 12 months later. In our five year follow up, each monthly GLP-1 initiation cohort is compared to a control group that initiates GLP-1 treatment 60 months later. Using [Wing, Freedman, and Hollingsworth \(2024\)](#), we combine all initiation cohorts

using a stacked difference-in-differences (DID) estimator. This study design leverages patients who will eventually initiate GLP-1s as a comparison group for those who initiate earlier. The DID design has advantages over cross-sectional matching designs because it is robust to confounding from time invariant differences between treatment and control groups that are hard to adjust for using measured covariates. It also removes confounding from factors that could bias a simple pre-post comparison, including secular trends, maturation and aging, and regression-to-the-mean effects, yielding a more credible causal estimate. To account for non-adherence, we take an intent to treat approach in our main analysis, tracking subsequent spending of all GLP-1 initiators, including those who discontinue therapy. The stacked DID design relies on the standard assumption that absent initiation, early and later adopters would have followed parallel trends, and that there are no anticipation effects around the timing of initiation.

We implement this design using 2016-2023 insurance claims from the Merative MarketScan database, extracting a sample of 750,000 patients initiating GLP-1 therapy and continuously enrolled over the pre- and post-initiation period under study. Patients initiating GLP-1 treatment earlier (the treatment group) have higher baseline health care spending and greater prevalence of chronic conditions. Consistent with our identification assumptions, we find parallel trends in health care spending in the months leading up to initiation.

We make two main contributions with these data. First, we provide real-world evidence on the dynamics of spending and utilization following GLP-1 initiation in routine clinical practice. In the month of initiation, patients spend nearly \$1000 on GLP-1s. In the following months, however, many patients do not renew their prescription, and the share of initiators remaining on treatment stabilizes at about 60 percent. Accounting for this limitation continuation, cumulative GLP-1 spending in the year following initiation totals \$6500, which is roughly half of *total* medical spending in the year prior to initiation. Five years post-initiation, cumulative GLP-1 spending totals \$22,000 per initiator. This finding is important because clinical trials—which are designed to promote medication adherence—nevertheless report high rates of side effects, especially gastrointestinal discomfort (Steven P. Marso, Gary H. Daniels, et al. [2016](#); Steven P. Marso, Stephen C. Bain, et al. [2016b](#); Lincoff et al. [2023](#)). How these side effects translate into medication adherence is not well understood, which matters for assessing cost offsets because non-adherence reduces the health effects of GLP-1 use as well as GLP-1 spending. Simulation studies of GLP-1 offsets must make assumptions about treatment adherence (Ward et al. [2023](#); Ippolito and J. Levy [2023](#); Congressional Budget Office [2024](#); Hwang et al. [2025](#)). Our study provides direct real-world evidence that discontinuation is important in practice.

Our second contribution is to show that GLP-1 initiation does not reduce other health

care spending and, indeed, increases it. While initiation does produce savings in the form of reduced spending on other diabetes drugs, these savings are more than countered by a large increase in outpatient spending, which drives the overall positive result in GLP-1 spending. Increased outpatient spending likely reflects monitoring costs of GLP-1 use as patients check in with their prescriber to manage and adapt to side effects and dosing. While our main results look at spending effects after one year, we find no evidence for cost offsets even five years post-initiation, where we estimate a cumulative \$6800 increase in non-GLP-1 spending, again driven by increased outpatient spending. When we explore subpopulations defined by baseline health, we see similar results. Among patients with pre-initiation diagnoses of diabetes, indicators of cardiovascular disease, or neither condition, GLP-1 initiation increases non-GLP-1 health care spending. However, when we look at newer-generation GLP-1s for which we can apply our research design, we find statistically insignificant estimates of partial offsets.

Our results have two important limitations. First, we are only able to examine spending for five years after initiation; it is possible that important offsets materialize over a longer horizon. Even so, these five-year effects are important for the cost of coverage. Second, much of our data predates the widespread approval, uptake, and coverage of GLP-1s specifically indicated for obesity. It is possible that future molecules will produce large offsets or that patients with obesity will eventually show larger cost offsets. We expect, however, that short and medium term cost offsets would be greater for patients with diabetes, who have worse baseline health and higher health care spending.

Overall, our results show that the cost of covering GLP-1s exceeds the already substantial direct costs of drug procurement. These results contrast with the impressive reductions in stroke and heart attacks observed in clinical trials. (Steven P. Marso, Gary H. Daniels, et al. 2016; Steven P. Marso, Stephen C. Bain, et al. 2016b), and contrast with simulation studies suggesting substantial offsets by five years post initiation (Hwang et al. 2025; Congressional Budget Office 2024). Our study does not fully identify the mechanisms underlying the divergence between the simulation-based projections and our results. However, we highlight two channels that may be important. First, in clinical trials establishing that GLP-1s reduce rates of major adverse cardiac events, the patients were substantially sicker than the typical patient in our population, leading to greater scope for improving health and reducing spending. Second, simulation studies may not be designed to account for extra outpatient visits required for monitoring GLP-1 use, the primary source of the increased spending we observed.

**Related literature**—Our paper provides among the first quasi-experimental evidence on how GLP-1 initiation affects health care spending. Two contemporaneous studies examine closely related questions using different data and identifying strategies.<sup>2</sup> Bock, Moshfegh, and Zhang (2025) use electronic medical records to study the addition of semaglutide to the Veterans Health Administration formulary in 2020. They use an event study framework with the 2021-2022 GLP-1 prescribing rate of the patient's 2018 primary care provider as a “bite” variable. They find patients of high-prescribing providers lost 2.45% more weight and realized better glycemic control (A1C fell 0.11 points), but they find no significant changes in non-GLP-1 spending or utilization. Like ours, their research design allows for selection on unobservables into GLP-1 treatment. Wennberg et al. (2025) use a selection-on-observables identification strategy to analyze commercial claims, defining treated patients as GLP-1 initiators (2017–2024) and constructing matched controls by assigning pseudo index dates to non-users, exact matching on pseudo index date, basic demographics and obesity and diabetes diagnoses, and then propensity score matching on a rich set of diagnoses and prior medications. They find non-GLP-1 medical spending is 5.8% higher for all GLP-1 initiators, and 8.9% higher for GLP-1 initiators without diabetes.

Despite differences in methods, data, and patient populations, all three studies find little evidence that GLP-1 drugs substantially reduce other health care utilization and spending. The matching study by Wennberg et al. (2025) relies on the strong assumption that GLP-1 use is as good as random in their matched sample; our stacked DID design uses future adopters as controls and accounts for common time trends and time-invariant differences. Our design estimates treatment effects as a function of time since patient-level GLP-1 initiation. This matters because discontinuation rates vary with side effects and other factors, and because health benefits and potential cost offsets may take time to materialize. In contrast, Bock, Moshfegh, and Zhang (2025) index effects to calendar time following the 2020 formulary change and use provider prescribing intensity for exposure. As a result, their post-2020 coefficients blend outcomes for patients starting, continuing, or discontinuing GLP-1 therapy rather than isolating trajectories relative to each patient's initiation. However, Bock, Moshfegh, and Zhang (2025) demonstrate health benefits in a real-world setting, which we cannot measure in claims data.

Our study also contributes to broader research on cost offsets in health insurance and the economics of obesity treatment. Glazer and McGuire (2012) argue that cost offsets rep-

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2. In addition, Akpan et al. (2026) use MEPS data and regression adjustment to find substantial spending increases for GLP-1 users with diabetes, inclusive of GLP-1 spending. Michalak et al. (2025) use claims data to study a highly selected sample of 770 adherent semaglutide 2.4mg users with cardiovascular disease and overweight/obesity, match them to 3,080 controls via propensity scores, and find 22% lower non-pharmaceutical spending in the treatment group.

resent a fiscal externality relevant for the welfare consequences of changing insurance coverage, and Starc and Town (2020) study the role of externalities created by standalone drug plans in Medicare Part D. Prior work finds substantial cost offsets from prescription drugs in some contexts, but not in others. Chandra, Gruber, and McKnight (2010) and Gaynor, Li, and Vogt (2007) show that increased drug cost-sharing led to substantial increases in other forms of medical care. Lichtenberg (2007) estimates that newer drug vintages substantially reduce non-drug expenditures, with estimated offsets exceeding 100 percent. Several studies find that the introduction of Medicare Part D increased utilization of prescription drugs and reduced other health care spending and utilization (Kaestner, Schiman, and Alexander 2019; Afendulis et al. 2011; Zhang et al. 2009), though others find limited offsets from Part D or other expansions (Liu et al. 2011; Kaestner and Khan 2012; Duggan 2005). Weiner et al. (2013) find that bariatric surgery does not reduce overall health care costs in the long term; in a similar analysis, Crémieux et al. (2008) find bariatric surgery recovers initial costs within two to four years. Our study adds to this literature by examining cost offsets for GLP-1 medications, a costly but highly effective new treatments for obesity and diabetes.

On the economics of obesity, Cutler, Glaeser, and Shapiro (2003) and Lakdawalla and Philipson (2009) argue that rising obesity is rooted in technological changes that have reduced food prices and time costs of calories. A natural policy response is to tax calories, and in particular sugar-sweetened beverages. Allcott, Lockwood, and Taubinsky (2019) analyze the efficiency and incidence of such taxes, Dubois, Griffith, and O'Connell (2020) study their targeting, and many papers study their consumption effects (e.g. Fletcher, Frisvold, and Tefft (2015) and Cawley et al. (2019)). Research by economists and other social scientists has focused on the social and behavioral determinants of obesity, in part because few pharmaceutical and medical interventions have been effective at weight loss and chronic weight management. The development of new GLP-1 drugs may represent an important shift towards more medicalized responses to obesity. Cawley and Meyerhoefer (2012) argue that obesity has a large causal effect on health care spending, an externality because these costs are borne by public and private insurers. Bhattacharya and Bundorf (2009) show that obese workers with employer-sponsored health insurance pay for their higher expected medical expenditures through lower wages, suggesting that labor markets partially internalize obesity-related health costs. Our study shows that GLP-1 drugs increase rather than decrease total healthcare spending. Covering these drugs may further increase the costs of providing insurance to people with obesity or diabetes, potentially amplifying wage responses.

## 2 – Background

GLP-1s were originally developed to treat type 2 diabetes, a disease characterized by insulin resistance and eventually insulin deficiency.<sup>3</sup> Insulin enables cells to take up glucose from the bloodstream, regulating blood glucose levels. Insulin resistance means that cells do not respond to insulin and are slow to take up blood glucose. Glycemic control refers to the regulation of blood glucose and is commonly assessed using hemoglobin A1c (HbA1c), which reflects average blood glucose over the prior 2–3 months. HbA1c levels of 5.7–6.4 percent are classified as prediabetes, and levels of 6.5 percent or higher meet diagnostic criteria for diabetes (American Diabetes Association 2014). Poorly managed diabetes can lead to numerous severe health problems, including nerve damage, heart disease and stroke, kidney disease, and low vision or blindness (National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health 2025).

Prior to the development of GLP-1s, the main drug for managing type 2 diabetes was metformin (American Diabetes Association 2010), which reduces both HbA1c levels and diabetes-related mortality (UK Prospective Diabetes Study (UKPDS) Group 1998). A series of clinical trials has established that GLP-1s are highly effective for glycemic control (Yao et al. 2024) in patients with Type 2 Diabetes. Since the first GLP-1, exenatide, was brought to market in 2005, successive generations have been developed, with increasing effectiveness. Next generation GLP-1s liraglutide (approved in 2008) and semaglude (approved in 2017, marketed as Ozempic for diabetes and Wegovy for weight loss) have also been shown to reduce major adverse cardiac events—heart attack, stroke, or death—among patients with type 2 diabetes at high risk for these events (Steven P Marso, Gilbert H Daniels, et al. 2016; Steven P Marso, Stephen C Bain, et al. 2016a). Although GLP-1s were developed to treat diabetes, clinical trial participants noticed weight loss of 2-5 percent, prompting investigators to consider whether higher-dose GLP-1s could produce larger weight loss (Drucker 2024). Subsequent trials found weight loss of 10-15 percent in patients with and without type 2 diabetes (Wilding et al. 2021). GLP-1s for weight loss have been shown to reduce cardiovascular outcomes for patients without diabetes and with a risk of cardiovascular disease (Lincoff et al. 2023). Treating pre-diabetic patients with GLP-1 substantially reduces transition to diabetes (Le Roux et al. 2017; Kahn et al. 2024; Jastreboff et al. 2025).

In light of their impressive clinical performance, GLP-1s are now widely prescribed, and spending on them is rapidly growing. Figure 1 shows that spending on GLP-1s has become a major component of overall pharmaceutical spending, in Medicaid, Medicare, and especially

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3. There are two major variants of diabetes. Type 1 diabetes is relatively rare and occurs when the body is unable to produce insulin.

commercial insurance (as measured in Marketscan), where one in every eight dollars of pharmaceutical spending goes to GLP-1s. Over most of this period, the rapid spending growth primarily reflects the widespread adoption of GLP-1s as a treatment for diabetes. More recent growth in the commercial sector reflects additional growth due to GLP-1s as treatment for obesity. Indeed, GLP-1s have become part of the standard of care for managing diabetes – typically in combination with metformin – as an initial therapy for patients (especially those at risk of chronic kidney disease or cardiovascular disease) and as a secondary therapy for low risk patients for whom metformin is inadequate for glycemic control goals (American Diabetes Association Professional Practice Committee 2025).

Beyond cost, the main barriers to GLP-1 use are delivery mechanism and side effects. Currently available GLP-1s are delivered via injection.<sup>4</sup> More than half of trial participants report experiencing gastro-intestinal distress (Drucker 2024). In clinical trials this is often a reason for discontinuation (Wilding et al. 2021). In practice, these side effects may limit treatment persistent, but they may also prompt patients and physicians to adjust dosage rather than discontinue.

The potential for downstream cost savings from GLP-1s is somewhat ambiguous, given existing research. On the one hand, reductions in major adverse cardiac events might be expected to reduce hospitalizations and follow up health care use, generating savings. In the longer run, it is possible that weight loss, better glycemic control, and reduced diabetes incidence could prevent more severe health conditions, which might lead to substantial savings. On the other hand, treatment discontinuation implies that some payment for GLP-1s does not produce long-term health improvements. In addition, the required follow-up care to adjust dosage and monitor the side effects of GLP-1s could even increase spending. We therefore turn to estimating the downstream cost consequences of GLP-1 use.

### 3 – Empirical Strategy

We estimate the causal effects of GLP-1 initiation on subsequent health care spending and GLP-1 persistence using a person-level staggered adoption design implemented using commercial health insurance claims data. The design is organized around a sequence of monthly GLP-1 initiation cohorts: groups of patients who start taking GLP-1s for the first time in a specific calendar month and year. For each cohort, we construct a “not-yet-treated” control group of patients who first initiate GLP-1 treatment in the same calendar month in a subsequent year. We follow both groups for a fixed window before and after the focal treated cohort’s initiation date, taking care to ensure that the entire post-period occurs be-

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4. Early generations of GLP-1s required daily injections but the current generation requires weekly injections, and an oral GLP-1 has recently been approved.

fore the control group begins GLP-1 treatment. Each monthly GLP-1 initiation cohort and its not-yet-treated clean control represents a sub-experimental DID design with no staggering. We combine the family of sub-experiments into a single stacked analytic file and estimate treatment effects using a weighted stacked event study regression, following the approach developed in Wing, Freedman, and Hollingsworth (2024). We implement two versions of the design: a short-run analysis with one year of follow-up and a longer-run analysis with five years of follow-up. This section develops notation and lays out key inclusion criteria, identifying assumptions, causal effects, and econometric estimators. We discuss the insurance claims data we used to operationalize the design in section 4.

### 3.1. Dynamic Treatment Effects of GLP-1 Initiation

The spending consequences of GLP-1 initiation are likely to be dynamic because GLP-1 costs are frontloaded and benefit may be backloaded. Since some patients will initiate but not persist in treatment, direct costs in the first few months post-initiation are likely to be especially high. GLP-1 induced reductions in downstream spending — if there are any — would likely take time to appear because they require health improvements which do not necessarily occur immediately. Indeed, microsimulation models of GLP-1 effects generally point to benefits which grow over time (Atlas et al. 2022; Hwang et al. 2025). Therefore an important feature of any estimator of the effect of GLP-1s on downstream spending is that it account for dynamic treatment effects. Our estimator does so because it lets us recover causal effects of GLP-1 initiation in each post-initiation time period.

To see how, use  $i$  to index individuals in our study population and  $t$  to index calendar months.  $A_i$  is the month-year of the person's first GLP-1 prescription.  $Y_{it}(a)$  is a potential outcome that represents person  $i$ 's health care expenditures or GLP-1 utilization in calendar period  $t$  if she had first initiated GLP-1 therapy in period  $a$ .  $Y_{it}(0)$  is the same person's outcome in the absence of GLP-1 therapy. Person  $i$ 's realized outcome is  $Y_{it}^{obs} = Y_{it}(0) + \sum_a 1(A_i = a) \times [Y_{it}(a) - Y_{it}(0)]$ .

We focus on the average causal effect of initiating GLP-1 treatment at a particular date on downstream health care spending and GLP-1 use using an event time perspective. For GLP-1 initiation in period  $a$ , let  $e = t - a$  measure event time in months relative to initiation. From the event time point of view,  $ATT(a, a + e) = E[Y_{i,a+e}(a) - Y_{i,a+e}(0)|A_i = a]$  represents the average treatment effect of initiating GLP-1 therapy in period  $a$  on outcomes experienced in period  $t = a + e$  among people who actually start taking a GLP-1 in period  $a$ . This parameter is the so-called group-time average treatment effect on the treated for people who started taking a GLP-1 at  $a$  measured  $e$  months the initial dose. For example,  $ATT(a, a)$  is the effect of initiating GLP-1 treatment in the month of initiation,  $ATT(a, a+11)$

is the effect a year later, and  $ATT(a, a + 59)$  is the effect five years later.

### 3.2. Estimation via Differences in Differences

Although these group-time ATTs are not directly identified because they depend on counterfactual outcomes, we can recover group-time ATTs using difference-in-difference identification assumptions. To do so, it is helpful to define a sub-experimental data set for each initiation cohort. In sub-experiment  $a$ , the treatment group consists of people with  $A_i = a$  and the *clean control group* consists of not-yet-treated people with  $A_i = a + \delta$ , where  $\delta$  is a positive integer measuring how many months downstream the control group will initiate treatment. In other words, the control group consists of people initiating exactly  $\delta$  months after the focal treatment group. Each sub-experimental data sets is perfectly balanced in event time. In the 12 month design, for example, each individual member of the treatment group and clean control is observed for exactly 24 event time periods: 12 pre-treatment periods, and 12 post treatment periods.

We face a trade-off in selecting a value for  $\delta$  because it determines the maximum post-period over which the clean controls will remain untreated. A larger value of  $\delta$  allows us to estimate event studies with a longer follow up window. But a longer follow up also results in smaller sample size because more recent GLP-1 initiation cohorts will not have a feasible control group that can be followed for the full post-period. To balance this trade-off, we work with two extreme values for  $\delta$ : 12 months and 60 months. The  $\delta = 12$  month case means that the January-2018 initiation cohort is paired with the January-2019 cohort, and monthly outcomes in both groups are followed from January 2017 to December 2018. The same logic applies to each of the 72 monthly initiation cohorts from January-2018 to December-2023, collectively yielding a large sample size and improving statistical precision. Since our claims data end in 2024, in the  $\delta = 60$  months design, we are limited to the 12 monthly cohorts that initiate GLP-1 treatment in 2018. Each of these groups is paired with initiators from the corresponding month in 2024. Although the 60 month design produces a smaller sample size, it allows us to examine treatment effects up to five years after GLP-1 initiation.

To identify the group-time ATTs of a given sub-experiment, we require three standard difference in differences (DID) assumptions: no spillovers, no anticipation, and common trends. The *no spillovers assumption* implies that GLP-1 utilization in treatment group does not affect health care spending among members of the clean control group. The *no-anticipation assumption* requires that the average causal effect of initiating GLP-1 treatment in period  $a$  on health care expenditures in periods  $t < a$  is equal to zero. Formally, this implies that  $E [Y_{i,a+e}(a)|A_i = a] = E [Y_{i,a+e}(0)|A_i = a]$  for all  $e < 0$ . In practice, we guard against limited

anticipation by setting the baseline pre-period in our DID estimator to be two periods prior to treatment exposure. The *common trend assumption* requires that in the absence of GLP-1 initiation, the treatment group and clean control group would have followed a common trend so that  $E [Y_{i,a+e}(0) - Y_{i,a-2}(0)|A_i = a] = E [Y_{i,a+e}(0) - Y_{i,a-2}(0)|A_i = a + \delta]$ .

Under these assumptions, a standard DID applied to observed outcomes for a specified event time period and sub-experiment identifies the group-time ATT:

$$\begin{aligned}\theta_{(a,e)}^{DID} &= E [Y_{i,a+e}^{obs} - Y_{i,a-2}^{obs}|A_i = a] - E [Y_{i,a+e}^{obs} - Y_{i,a-2}^{obs}|A_i = a + \delta] \\ &= ATT(a, a + e)\end{aligned}$$

Together, the common trends and no-anticipation assumptions imply that group-time ATTs from pre-treatment time periods estimates should equal zero. Diverging trends in the pre-period would suggest a violation of the no anticipation and/or common trend assumptions. In our empirical work, we estimate event studies that examine DID comparisons across each period of the pre-treatment window, providing a partial test of the core identifying assumptions.

### 3.3. Aggregation and Stacked Estimation

The staggered adoption DID design identifies group-time ATT for multiple initiation cohorts at multiple follow up time periods. But these group-time estimates are apt to be noisy. Rather than study each sub-experiment in isolation, we combine the sub-experiments and focus on estimating an aggregate ATT parameter. Use  $\Omega$  to represent the set of sub-experimental initiation cohorts in our analysis, and let  $N_a^{GLP} = \sum_i 1(A_i = a)$  be the number of individuals initiating a GLP-1 in period  $a \in \Omega$ . Then  $N^{GLP} = \sum_{a \in \Omega} N_a^{GLP}$  is the total number of people who initiate a GLP-1 in any of our sub-experimental initiation cohorts. We focus on the following aggregate ATT:

$$\theta_e = \sum_{a \in \Omega} ATT(a, a + e) \frac{N_a^{GLP}}{N^{GLP}}$$

In words,  $\theta_e$  is a event-time specific weighted average of underlying group-time ATTs. Each of group-time ATTs is weighted by its share of the overall treated sample. Larger initiation cohorts get more weight in the aggregate than smaller initiation cohorts.

To estimate the aggregate ATT parameter, we vertically concatenate the collection sub-experimental datasets into a single *stacked* analytic data set. In the stacked data set  $Y_{iae}^{obs}$

represents the observed outcome for person  $i$  in sub-experiment  $a$  measured at event time  $e = t - a$ . We let  $GLP_{ia} = 1[A_i = a]$  be a dummy variable set to 1 if the person is a member of the treatment group in sub-experiment  $a$ , and set to 0 if the person is a clean control for that sub-experiment. Then  $N_a^{GLP} = \sum_i 1[GLP_{ia}]$  gives the number of treated units in sub-experiment  $a$ , and  $N_a^C = \sum_i (1 - GLP_{ia})$  gives the number of clean controls in sub-experiment  $a$ . The total number of treated and control subjects in the stacked data are  $N^{GLP}$  and  $N^C$ , and the stacked data set is balanced in the sense that each of subjects is observed in each of the event time periods.<sup>5</sup>

We estimate the aggregate ATT effects using a saturated event study regression fitted to the stacked data set:

$$Y_{iae} = \alpha_0 + \alpha_1 GLP_{ia} + \sum_{\substack{h=-12\dots\delta \\ h \neq -2}} \theta_e \cdot GLP_{ia} \times 1[e = h] + m_e + u_{iae},$$

In the equation,  $m_e$  represents a full set of event time main effects. Throughout, the pre-period covers the 12 months leading up the GLP-1 initiation and we make event time period -2 to be the reference group, allowing some limited anticipation in the month immediately preceding GLP-1 initiation.

If the share of treated and control observations was the same in each sub-experiment, the coefficients from the saturated event study would equal the aggregate ATT parameter presented above. In practice, the share of treated and control observations differs across sub-experiments and so the simple stacked event study does not quite recover the aggregate ATT parameter. To account for these different shares, we use the following corrective sample weight:

$$Q_{ia} = \begin{cases} 1 & \text{if } GLP_{ia} = 1 \\ \frac{N_a^{GLP}/N^{GLP}}{N_a^C/N^C} & \text{if } GLP_{ia} = 0 \end{cases}$$

Wing, Freedman, and Hollingsworth (2024) show that under the common trend and no-anticipation assumptions, the interaction terms in this weighted regression identify the aggregate ATT parameter evaluated at each event time. The post-period coefficients are intent to treat estimates that capture the spending effects of initiating GLP-1 therapy over

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5. Concatenating multiple sub-experiment data sets means that many people will be in our data set twice, once as in a treatment group and once in a control group. Our cluster-robust standard errors allow for within-person dependence, accounting for this.

the follow up period without making any assumptions about whether or how much each person actually ends up continuing or discontinuing GLP-1 use. Under the common trends and no-anticipation assumptions, the pre-period event study coefficients should be equal to 0, providing a partial test of the core identifying assumptions needed to give the results a causal interpretation. We estimate standard errors and confidence intervals for the event study coefficients using a cluster robust variance matrix that allows for heteroskedasticity and dependence at the person level.

### 3.4. Spending offsets

We use the event study coefficients to construct measures of GLP-1 spending offsets, understood as the per-dollar impact of cumulative GLP-1 spending on cumulative non-GLP-1 spending. This is sometimes called a cost offset since it answers the question, how much of each \$1 of GLP-1 spending is offset by reductions in other spending (e.g. Chandra, Gruber, and McKnight (2010)). To see the idea, let  $\theta_e^{GLP}$  be the aggregate ATT of GLP-1 initiation on GLP-1 spending measured  $e$  months after initiation and estimated using a weighted stacked event study regression in which monthly GLP-1 spending is the dependent variable. Similarly, let  $\theta_e^{spend}$  be the aggregate ATT of GLP-1 initiation on a measure of monthly non-GLP-1 health care spending. Our measure of the spending offset is the ratio of the cumulative sum of monthly spending effects to the cumulative sum of monthly GLP-1 spending:

$$\text{Offset} = \frac{\sum_{e=1\dots\delta} \theta_e^{spend}}{\sum_{e=0\dots\delta} \theta_e^{GLP}}.$$

An offset of  $\text{Offset} = -1$  would imply that the direct costs of the GLP-1 medications is fully offset by reduced health expenditures in other domains so that each dollar of GLP-1 spending is matched by a one dollar reduction on non-GLP-1 health care spending. In practice, we start the numerator sum in event month  $e = 1$  rather than  $e = 0$  because we find that GLP-1 initiation is associated with a run-up in spending in month  $e = 0$ , reflecting medical visits required to obtain a prescription. This is a conservative choice in the sense that we do not allow the pure start up costs to drive the results.

To perform statistical inference on the offset statistic, we jointly estimate the GLP-1 spending and non-GLP-1 spending event study regressions as a stacked system. This stack of stacked regressions yields the identical point estimates of the event study coefficients as separately estimated regressions, but it also provides a joint cluster robust variance matrix for the coefficients in the two equations. We use the delta method and the joint covariance matrix to estimate standard errors and confidence intervals on the offset statistic.

## 4 – Data

Our primary data source is the Merative MarketScan Commercial database covering calendar years 2016–2023. MarketScan is a large administrative sample of individuals with employer-sponsored commercial health insurance in the United States and includes enrollment records and adjudicated claims for inpatient and outpatient services as well as outpatient prescription drugs. It has been widely used in health economics (e.g. Kowalski (2016), Dickstein (2017), Sacks (2018), Guo and Zhang (2019), Dickstein et al. (2021), and Dunn, Hall, and Dauda (2022)). Marketscan's large sample size and claims history allows us to follow hundreds of thousands of patients who fill GLP-1 prescriptions. We use the enrollment data and outpatient pharmacy claims to identify GLP-1 medication fills and to define each individual's GLP-1 initiation month. Then we construct longitudinal person-month panels of outcomes and covariates. These person-month panels are the key input to our stacked staggered-adoption difference in difference study design.

**Sample Construction** Our staggered adoption research design requires us to identify patients who initiate GLP-1 therapy in a specific month and then follow them over a period extending 12 months pre-initiation to 12 months (or more) post-initiation. Appendix Figure A.1 shows how we construct our study population by applying a series of inclusion criteria. We start with the full set of 75,193,282 unique individuals who were enrolled in a Marketscan plan at any point between 2016 and 2023, which are the years of Marketscan we have available. We restrict our attention to the 1,258,542 patients who fill at least one GLP-1 prescription during this time period. To make sure that we can consistently track spending and utilization, we restrict the sample to the patients who have a single enrollment spell during the study period, yielding a sample of 1,079,241 individuals. Because our analyses require at least a 12 month pre-initiation period, we limit the sample to people whose first GLP-1 claim occurs in 2017 or later. This sample of  $N = 952,503$  people who initiate GLP-1 therapy between January 2017 and December 2023 forms the donor pool for our quasi-experimental design. After restricting to patients enrolled throughout our event-study window and limiting to people ages 18-64, we end up with  $N = 768,231$  unique patient-cohorts, corresponding to  $N = 537,743$  unique enrollees.

**Forming Sub-Experiments** Our research design is organized around a sequence of monthly GLP-1 initiation cohorts running from January 2017 to December 2022. We draw on the donor pool to build a separate sub-experimental data set for each GLP-1 initiation cohort. For a generic sub-experiment  $a$ , the treatment group consists of people whose first GLP-1

claim occurs in month-year  $a$ , and the control group consists of people whose first GLP-1 claim occurs in month-year  $a+12$  for the one year follow up study and month-year  $a+60$  for the five year follow up. Once people have been assigned to treatment and control groups for a specific sub-experiment, we restrict the sub-experiment sample to people who were continuously enrolled in a MarketScan plan and were ages 18-64 for the 24 month event window centered on period  $a$ . Once all of the sub-experimental data sets have been constructed, we vertically concatenate them into a single stacked analytic data file. In our main analysis of our 12 month design, the stacked data file has  $N = 18,437,544$  person month observations spread over 72 sub-experiments that are each made up of a balanced sample of treated and clean control individuals observed for 24 event time periods.

**GLP-1 initiation, use, and spending** Our focus is on patients who filled a GLP-1 prescription. Appendix Table A.1 lists the set of 172 National Drug Codes (NDC) referring to GLP-1 receptor agonists or related medications that we examine in this study. We classify a prescription drug claim as a GLP-1 claim if it has an NDC code corresponding to any of the 172 medications. Among patients with at least one GLP-1 claim, we define the patient's GLP-1 initiation date as the date of the first GLP-1 claim following at least 12 months with no GLP-1 claim. We use information on days supply and date of claim to construct measures of utilization/adherence over time, defined as having at least one day supply of GLP-1 medication supply available during the month. Supply from earlier refills is carried forward, and the leftover days are applied to future months. We define GLP-1 spending as the (monthly) sum of spending on the 172 listed drugs.

**Health Conditions** We identify certain health conditions using ICD-10-CM codes. We classify individuals as having a type 2 diabetes diagnosis if they have any inpatient or outpatient claim with an ICD-10-CM diagnosis code beginning with E11. We identify obesity using ICD-10-CM codes E660, E661, E662, E663, E668, E669, E66811, E66812, E66813, and E6689, and BMI codes in the range Z683-Z685. We classify individuals with a cardiovascular disease (CVD) diagnosis if they have any inpatient or outpatient claims with a diagnosis code indicating myocardial infarction (I21-I22, I25.2), ischemic stroke (I63), hemorrhagic stroke (I61-I62), transient ischemic attack or prior stroke (G45, Z86.73), chronic ischemic heart disease (I20, I25.1, I25.7, I25.8), peripheral arterial disease (I70.2, I73.8-I73.9), carotid artery stenosis/occlusion (I65.2-I65.3), or heart failure (I50). We additionally flag chronic kidney disease (N18.3-N18.6, N18.9) as part of this composite cardiovascular comorbidity indicator. To assess individual baseline health status, we create indicators for whether each condition was observed at least once during the 12 months before GLP-1 initiation.

**Expenditure Measures** We measure five main forms of healthcare expenditures at the person-month level: (1) total GLP-1 spending, (2) total spending on non-GLP 1 care, (3) spending on non-GLP-1 diabetes drugs, (4) outpatient spending, and (5) inpatient spending. Total non-GLP-1 spending is the sum of inpatient, outpatient, and non-GLP-1 prescription drug claims.

**Summary statistics** Table 1 shows pre-adoption baseline characteristics for GLP-1 adopters and their not-yet-treated clean controls. We measure baseline characteristics with demographics and diagnoses codes, medical events, and spending in event months -12 to -1 (i.e. before the treated group adopts). The statistics in the table are weighted averages of the full stack of sub-experiments using the same corrective weights used in the event study regressions. The treatment group (earlier adopters) are slightly older and in worse health than the control group (later adopters), with higher rates of type 2 diabetes and obesity and prior major cardiac events. They have higher health care spending in inpatient, outpatient, and overall. These differences in baseline health may partly explain their early adoption. These differences are not a threat to the validity of our design as long as the treated and control group satisfy the parallel trends and no anticipation assumption, a condition we verify in our analysis.

## 5 – Results

### 5.1. Validating identification assumptions

Our empirical strategy relies on the no-anticipation and parallel trends assumptions. To validate these assumptions, we present standard tests of pre-event parallel trends by showing event study plots for each category of non-GLP-1 spending. For reference, Figure 2 shows results from the one year follow up design, and Figure 3 shows results from the five year follow up design. Panels (a) shows how the treatment group accumulates GLP-1 spending over the post-initiation period, and Panel (b) shows how GLP-1 use tapers off over the post-initiation period. The remaining panels (c) to (f) are central for assessing our identification assumptions. They show event-month specific effects of GLP-1 adoption on non-GLP-1 health care spending. Under our identification assumptions, event-study coefficients should be approximately zero during the pre-initiation periods. The results show that the estimated pre-event effects are typically small, insignificant, and not increasing or decreasing systematically prior to GLP-1 initiation. Our main outcome metric, overall non-GLP-1 spending, is flat through the month prior to initiation. Outpatient spending and inpatient spending show similar patterns. There are some differences in the pre-period in

non-GLP-1 diabetes-related prescription spending, but no generally increasing trend. Overall, the event-study evidence supports the parallel trends and no-anticipation assumptions.

The event study plots show a temporary elevation in non-GLP-1 spending around the time of GLP-1 initiation, but this does not indicate a violation of our identification assumptions. Specifically, relative to two months before initiation, non-GLP-1 spending increases by a statistically significant \$75 in the month before initiation and by \$225 in the month of initiation, before falling back to trend in the first month after initiation. This increase in spending likely reflects true costs of initiating GLP-1 coverage - namely, patients will typically have a health care encounter prior to receiving a prescription. Given delays in filling prescriptions, some of these encounters occur in the month before initiation. For this reason, we normalize the event-time coefficient at -2 to zero and treat event months -1 and 0 as part of the treatment period.

While it is conceivable that the pre-event increase in spending is driven by worsening health of the treated patients, this explanation would imply that spending should continue to diverge rather than revert to trend immediately after initiation, as shown in the figure. By post-period month 1, patients are treated, so it is conceptually possible that the zero spending effect in month 1 reflects a combination of cost offsets from GLP-1 use and worsening health. This explanation is unlikely because the health effects of GLP-1 therapy do not materialize immediately. For example, four weeks into the weight loss trial of semaglutide, treated patients had lost roughly two percent of their body weight, compared to 14 percent at 36 weeks (Wilding et al. 2022). Likewise the efficacy of semaglutide for A1C management was much greater at 16 weeks than at 4 weeks (Sorli et al. 2017). More generally, we see flat spending prior to initiation, and a level shift in spending beginning about 2 months post initiation, not the pattern we would expect if gradually worsening health drove initiation.

Additional evidence rules out the possibility that initiation of GLP-1 therapy is driven by suddenly worsening health. In our heterogeneity analysis below, we condition on diagnoses of diabetes or (separately) cardiovascular disease prior to the early initiation. In these analyses, the treated and control samples both have a diagnosis before initiation among the treated group. If newly arriving diagnoses were driving GLP-1 initiation, we would expect different spending dynamics and pre-trends in these subpopulations than in the full sample. Instead, the estimated spending effects and pre-event trends are very similar across these subgroups.

## 5.2. GLP-1 initiation raises GLP-1 spending with limited cost offsets

We now turn to the effects of GLP-1 initiation. We begin by showing that GLP-1 initiation leads to steadily growing GLP-1 spending, driven by sustained use of GLP-1s. Panel (a) of Figure 2 plots the event study estimates for cumulative GLP-1 spending, which is mechanically zero prior to initiation. Spending in the month of initiation is about \$1000. Panel (b) shows how the share of the treatment group sample that has at least one day of available GLP-1 supply during the month evolves over the year after initiation. The line jumps from 0 to 100% in the first post-period month because, by construction, all of our treatment group patients fill a prescription for a GLP-1 in their initiation month. The fraction with an active supply of GLP-1 medication declines over the first few months after initiation, likely because some patients do not tolerate the side effects of GLP-1s. After falling to 75 percent in one month after initiation and roughly 65 percent in month 3, continued GLP-1 use falls slowly for the remaining 9 months, ending up at 56 percent one year after initiation. Spending on GLP-1 accumulates accordingly, growing by about \$500 per month and reaching \$6,400 total by month 11.

**Total Expenditures** The remaining panels of Figure 2 show event study plots for total non-GLP-1 spending and components of total spending. We begin in panel (c) with total non-GLP-1 spending, an overall measure that captures the net effect of offsets across all categories healthcare spending. We see an immediate increase in non-GLP-1 spending in the month before initiation, and a larger increase in the initiation month. These increases may reflect triggering events as well as the outpatient visit required for a new prescription. The spending effects return to 0 in event month 1 and then increase slightly, averaging about \$70 over event months 1-11, reaching a cumulative total of \$585 by month 11 (standard error: \$162); see Table 2. This represents about 4 percent of the treated group's counterfactual mean total spending of \$14,000.<sup>6</sup> On net, we find no offsets.

**Diabetes-related prescription expenditures** The lack of offsets may seem surprising because one might expect diabetes-related spending on non-GLP-1 drugs to fall as patients switch to GLP-1s. Indeed we do see such offsets. Panel (d) of Figure 2 shows that spending on diabetes-related prescriptions (exclusive of GLP-1 spending) falls by about \$17 per month, for first year savings of \$189 (standard error: \$11). This fall is reassuring as it shows our design has the power to detect offsets when they are present. It is also small—\$189 is small relative to GLP-1 spending (about \$6400) or overall non-GLP-1 spending (about

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6. To calculate the counterfactual mean, we find the actual mean outcome among the treated group in the post initiation period, and then we subtract off the average treatment effect.

\$13,000). The small offset in diabetes drug spending is insufficient to generate large overall offsets.

**Outpatient spending** Panel (e) shows that GLP-1 initiation increases overall outpatient spending. After the spike in month 0 spending (likely driven by the office visit required for a GLP-1 prescription), outpatient spending remains persistently elevated by about \$40 per month, or \$438 over months 1-11 (standard error: \$75). Higher outpatient spending is consistent with the possibility that GLP-1 use requires dose titration and monitoring of side effects. If GLP-1 use does not reduce other office visits sufficiently, this additional care shows up as increased outpatient spending overall.

**Inpatient Expenditures** Finally, panel (f) of Figure 2 shows the effects of GLP-1 initiation on inpatient health care spending. Here we find insignificant and noisy monthly effects, consistent with the very high variance of inpatient spending. Despite the larger standard errors, when we aggregate across months, we end up with an overall fairly precise effect of \$252 (standard error: \$136), which is not significantly positive, but rules out meaningfully negative cost reductions.

### 5.3. Quantifying offsets

In the second row of Table 2, Panel A, we report the offsets implied by our spending effects. Recall that we find GLP-1 initiation leads to \$6,400 in GLP-1 spending over the next 12 months. This direct cost might be offset by reductions in other health care spending. We have found, instead, spending increases in all categories except non-GLP-1 diabetes medicine. Scaling the overall spending increase of \$585 by the \$6,400 increase in GLP-1 spending, we end up with an offset of about 9 percent. This means that over the first year after initiation, every \$1 of GLP-1 spending generates an extra \$0.09 of non-GLP-1 spending. The standard error of the estimated offset is about 2.5 percent, meaning our confidence intervals rule out negative offsets, which would imply cost reductions. (Below we compare our estimates to predictions from the literature and to offsets estimated in other contexts.)

### 5.4. Long run estimates do not point to large offsets

Although some clinical trials of GLP-1s include follow up periods up to 5 years, our small offset is not a consequence of our shorter, 12 month follow-up period. To show this, we present estimates from an alternative event study which matches GLP-1 initiators with controls who initiate 60 months later. To implement this design, we limit the sample to

patients with 72 months of continuous enrollment (from 12 months pre to 60 months post), which requires that we look at 2017 and 2018 initiators only (matching them to 2022 and 2023 initiators). The results from the five year follow up are in Figure 3. Panel (c) shows the event study for total non-GLP-1 spending. The smaller sample size results in wider monthly confidence intervals. Nonetheless the figure gives no indication that a longer follow-up period would result in spending reductions. The spending effects in the first year are similar to our baseline estimates, and then increase in subsequent years, becoming significantly positive after year 2. We report the cumulative spending effects and implied offsets in Table 2, Panel B. After 5 years, GLP-1 initiation leads to \$22,500 in GLP-1 spending. We find a statistically significant increase in non-GLP-1 spending over this time period, amounting to \$6,800. These five year results imply that cumulative GLP-1 spending increases non-GLP-1 medical by 30 percent of the GLP-1 spending. The standard error of the offset is about 8.5 percent. Although noisier than the one year estimates, these are still precise enough to rule out a negative cost offset that might help justify GLP-1 spending on fiscal grounds. The five year increase in spending is driven by both outpatient and inpatient spending. We find neither increases nor decreases in spending on other diabetes medicines. Thus over a 5 year time horizon, we find no evidence of cost savings, and indeed continued evidence that GLP-1s lead to additional spending beyond the direct costs.

### 5.5. Survivorship bias does not explain our findings

Our main research design compares patients who initiate GLP-1 treatment on a particular date to those who initiate a year later. A concern with this design is that it conditions on survival, which itself may be influenced by GLP-1s. To understand the problem, suppose that GLP-1 utilization increases survival, and spending in the last year of life is especially high. Untreated patients may have a higher risk of mortality and therefore higher risk of having very high end-of-life spending. Our research design would differentially exclude these non-GLP-1 using deceased patients from our *control* group, resulting in too-low spending in the controls group and biasing our treatment effects upward.

Although conceptually plausible, this concern is unlikely to be quantitatively important in our results, for multiple reasons. First, our treatment group is sicker at baseline than our control group, making extra survival in the treatment group relatively unlikely. Second, mortality effects of GLP-1s are small even in more medically complex populations. Accounting for these effects, a conservative back-of-the-envelope calculation suggests that survivorship bias can account for less than half of our positive spending effect.<sup>7</sup> A final observation

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7. Specifically, we assume a differential survival rate of 0.5 percent per year, which is conservative given clinical trial evidence. Looking at effects of GLP-1s among patients with diabetes, Steven P. Marso, Gary H.

confirms that survivorship is quantitatively unimportant. When we look at long run effects, we focus on cohorts that survive for at least 60 months post initiation. If survivorship bias is important, it should be especially large here. However the first-year effects are smaller for this cohort than for our main cohort.

## 5.6. Heterogeneous effects

So far we have estimated overall effects, looking at the entire sample of GLP-1 initiators. Although this group shows small offsets, it is possible that there are subgroups with larger offsets. We might expect larger offsets for more medically complex patients, for whom there is more scope to reduce spending. However, we find no offsets across several important subgroups of patients: patients with diabetes or with prior diagnoses of cardiovascular disease. We also find no offsets among patients *without* diabetes indications, as well as patients with obesity indications. Those subgroups are important because they perhaps more closely resemble the patients who would use GLP-1s for obesity treatment only, a large population that is more closely the subject of coverage debates. To analyze these subgroups, we look at subgroups of initiators who have a diagnosis for type 2 diabetes or for cardiovascular disease in the 12 months prior to initiation. We then match them to a control group who initiates 12 months later, and who has a diagnosis of the given disease in the same window (i.e. 12 to 1 month before the early initiation).

**Patients with type 2 diabetes** We show event studies for patients with diabetes in Figure 4. These patients represent about 55 percent of our sample. Patients with diabetes show a very similar pattern of GLP-1 spending and adherence (panels (a) and (b)) as our main sample, and they also show a similar pattern of total non-GLP-1 spending effects. Adherence falls slightly in the first few months and then more slowly over the next few months. We find large month 0 spending increases which fall to small but positive and significant levels for the rest of the year. Spending on diabetes-related medication (exclusive of GLP-1 spending) falls in month 1 and remains lower throughout. The fall here is larger than in our main sample, unsurprisingly, as spending on diabetes-related medication is higher for patients with diabetes diagnoses. Finally we see the same pattern of persistently elevated outpatient spending and noisy but positive effects on inpatient spending. Thus we find

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Daniels, et al. (2016) do not find any significant reduction in mortality from semaglutide use, and Steven P. Marso, Stephen C. Bain, et al. (2016b) find 0.4 fewer deaths per 100 patient years. Effects in our sample are likely to be smaller as our sample is healthier than the clinical trial population. We next assume that spending in the last year of life is 5 times as large as usual, given that 5 percent of Medicare patients die in a year and their spending accounts for 25 percent of all spending (Riley and Lubitz 2010; Einav et al. 2018). Thus we might expect an extra 4 fold in spending among 0.5 percent of patients, or an extra 2 percent of spending overall. Our actual effect is 4.5 percent.

overall slightly positive spending effects for diabetics. Table 3, Panel A, reports cumulative effects and implied percent offsets. After a year, GLP-1 use increases non-GLP-1 spending by \$770 (standard error: \$228), despite reducing non-GLP-1 diabetes drug spending by \$301.

**Patients with cardiovascular disease** Patients with cardiovascular disease represent an especially medically complex subgroup for whom we might expect to see the most important offsets. These patients represent about 17 percent of our sample. We show event studies for this subgroup in Figure 5. The pattern of results is very similar to our baseline estimates. We estimate insignificant monthly overall offsets. Clear reductions in spending on non-GLP-1 diabetes prescriptions are roughly matched by clear increases in outpatient spending. There is also a noisy increase in inpatient spending. Even this medically vulnerable sample shows no sign of substantial cost offsets. Table 3, Panel B, reports cumulative effects and implied percent offsets. These estimates are noisier because fewer patients have a history of cardiovascular disease. Even so the 95% confidence interval for the estimated offset, -0.07 to 0.35, rules out large offsets.

**Patients without diabetes** We show event studies for a subgroup who are relatively less medically complex, patients without diabetes prior to GLP-1 initiation, who represent about 45 percent of our sample.<sup>8</sup> Figure 6 shows no overall offsets but slight reductions in diabetes-related spending. Here we see no clear increase in outpatient spending, but a slight increase in inpatient spending after several months, which works out to \$654 after a year (Table 3, Panel C). For this group we also estimate a positive and significant effect on overall spending.

**Patients with obesity diagnosis** Next we show event studies for patients with an obesity diagnosis. Figure 7 shows no clearly elevated non-GLP-1 spending beginning two months post initiation and, if anything, growing with time since initiation. This increase is driven by both outpatient and inpatient spending, and slightly offset by falling spending on diabetes medication. Overall, GLP-1 initiation results in a large increase in non-GLP-1 spending, equal to about a month of counterfactual spending (Table 3, Panel D).

**Patients initially prescribed semaglutide** So far we have pooled all patients regardless of which GLP-1 they were initially prescribed. However, more recent generations of GLP-1s

8. We consider these patients to be less medically complex because they do not have a diabetes diagnosis. As further evidence of their relative health, note that they have lower counterfactual health care spending than patients with diabetes or cardiovascular disease.

may produce different spending consequences due to differences in patient persistence or health effects, with corresponding implications for downstream health care spending. We therefore study the subsample of patients who were prescribed semaglutide as their initial GLP-1. This subsample is especially relevant because semaglutide is the ingredient in Ozempic and Wegovy, which are widely prescribed today. As semaglutide was not approved until 2017, we have relatively few prescriptions in the early years of our data, limiting the length of the follow-up period we can consider. We therefore use a follow-up period of  $\delta = 24$  months.

We show the event study coefficients in Figure 8 and the cumulative effects and offsets in Table 4. Spending and persistence patterns for semaglutide are similar to our baseline results, with spending averaging roughly \$500 per month and the fraction of patients with active supply falling to about 60 percent after a year and then leveling off. Total non-GLP-1 spending falls by about \$40 per month or a statistically insignificant \$900 in total. The 95 percent confidence interval for the offset is consistent with an increase in spending of \$0.04 or a decrease in spending of \$0.20 per dollar of GLP-1 spend.

### 5.7. Comparison to other studies of GLP-1 offsets

So far we have found that GLP-1 use results in higher non-GLP-1 health care spending in the first year of use, for our overall patient population and among patients with or without prior diabetes diagnoses, and even with prior cardiovascular disease, albeit with some uncertainty for this last group. Looking up to five years out, our estimated cumulative spending effects are significantly positive, ruling out any cost reductions.

These estimates are arguably disappointing given existing research on potential spending consequences of patients using or insurers covering GLP-1 medicines. Much of the existing research on offsets from GLP-1s has focused on simulating the consequences of Medicare covering anti-obesity medicine. That literature does not directly measure spending effects. Instead it uses multiple methodologies and assumptions to project health effects from clinical trials into spending changes. Ippolito and J. F. Levy (2024), for example, assume that sustained GLP-1 use reduces the body mass (obesity) index classification by one category (e.g. from obese to overweight) and, drawing on evidence from Suehs et al. (2017), assume that each reduction in obesity category reduces annual spending by \$970. More sophisticated approaches draw on microsimulation methods which model health spending as a function of health status (e.g., hypertensive with diabetes) and model health status transitions as a Markov process. To use these models to simulate spending effects of GLP-1 use (or insurance coverage thereof), authors must also make assumptions about how GLP-1 use affects health status transition rates. Clinical trials provide only imper-

fect guidance. The literature reports a range of estimates. For example Ward et al. (2023) estimate that Medicare coverage of GLP-1s would, over 10 years, save \$176 billion in non-GLP-1 cost. (They assume all eligible patients would use GLP-1s and they do not estimate direct costs.) Atlas et al. (2022) estimate that semaglutide coverage would cost, on a life time basis, \$274,000 in direct drug costs, with a 23% offset. Costs and offsets for liraglutide would be lower (14% offsets life time). Hwang et al. (2025) estimate \$18 billion in offsets against \$66 billion in spending (i.e. 27% offsets) at a 10 year frequency.

To compare our results to these simulations, we need to align time horizons. Many of the simulations report effects at 10 year horizons or later, which is beyond the scope of our study. However some simulation studies report shorter run effects. Ippolito and J. Levy (2023) do not consider time horizons but their methods imply effects could show up within a year because weight loss happens quickly. Hwang et al. (2025) report effects by years since initiation. They find savings from reduced non-GLP-1 spending in all years, a projection that is not consistent with our year 1 impacts. At year 5 they report \$8 billion in savings on \$32 billion in spending, a 25% offset. Congressional Budget Office (2024), drawing on simulations conducted by Atlas et al. (2022), finds \$4.3 billion in direct costs and \$0.3 billion in offsets, five years after Medicare coverage of anti-obesity medicine. Our 95% confidence intervals reject these estimates.

Our estimates therefore rule out offsets as large as those predicted by the simulation studies. Two factors likely explain this difference. First, we find that GLP-1 use actually increases certain aspects of non-drug spending. This finding drives our offset estimates, and other studies do not account for the increase in outpatient spending caused by GLP-1s. Second, the microsimulation approach requires strong assumptions about both how short-run improvements in weight and diabetes management affect health status transitions, and about the impact of health status on health spending. Our results do not impose these assumptions and so they suggest these some of the assumptions involved in the microsimulation projections may not be valid in practice.

While our results are not consistent with projections from microsimulation models, they are broadly consistent with two contemporaneous papers that take an approach that is similar in spirit to our work: (Bock, Moshfegh, and Zhang 2025) and (Wennberg et al. 2025). These studies uses different data and methods (Veterans Affairs and a provider propensity-to-prescribe design in (Bock, Moshfegh, and Zhang 2025) and private Blue Health Intelligence claims with untreated matched controls in Wennberg et al. (2025) ) but nonetheless also find no evidence of cost offsets.

## 6 – Discussion

GLP-1 receptor agonists represent a major clinical advance for diabetes, obesity, and related cardiometabolic disease, but they are also among the most expensive drugs in widespread use. A central question in insurance coverage debates is whether their procurement costs are partly or fully offset by downstream reductions in other health care spending. We directly estimate the real-world spending consequences of GLP-1 initiation using MarketScan commercial claims and a stacked difference-in-differences design that compares earlier initiators to later initiators.

Our findings provide little support for the idea that GLP-1s “pay for themselves” in reduced downstream medical spending, at least over the five years after initiation. Even accounting for substantial discontinuation rates, people who initiate GLP-1 therapy accrue substantial GLP-1 spending of approximately \$6,500 in the first year and \$22,000 over five years. Despite these high procurement costs, non-GLP-1 spending does not fall and instead increases modestly on net. We find some evidence that GLP-1 initiation reduces spending on other diabetes medications, but these savings are more than offset by higher outpatient spending, consistent with increased levels of monitoring and follow-up care associated with GLP-1 use in practice. Our estimates imply that each dollar of GLP-1 spending increases other medical care spending by 9 cents over the first year and by 30 cents over five years. The confidence intervals around both estimates rule out net savings from GLP-1 utilization. When we focus on the most recent generation of GLP-1s for which we have adequate data, we find savings effects that are statistically insignificant. It remains possible that more recent molecules will produce offsets.

These results do not call into question the health benefits of GLP-1 therapy documented in randomized trials. They do, however, suggest that the fiscal case for broad coverage should not rest on expectations of near-term medical cost savings. Indeed, because GLP-1 initiation increases outpatient utilization, the medical spending associated with these drugs may exceed the sticker price of the prescriptions alone. Cost savings, if they arise, may materialize only over longer horizons than we can observe in these data or through non-medical channels.

Looking ahead, key priorities include (i) evaluating longer-run spending and health trajectories as more cohorts age into sustained treatment, (ii) assessing whether newer molecules, dosing regimens, and use for new indications generate different expenditure dynamics, and (iii) clarifying the mechanisms behind increased outpatient spending and the potential role of care-management and adherence interventions.

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**Table 1 – Weighted Baseline Characteristics (12-Month Pre-Adoption) by Treatment Status, Weighted by Q-weights**

Variable	GLP-1 Adoption	Control
Birth Year (Mean [SD])	1970.4 (9.7)	1971.0 (10.0)
Age (Mean [SD])	49.2 (9.4)	48.5 (9.7)
Female (%)	61.7	62.1
Obesity (%)	67.7	60.1
Type 2 DM (%)	68.0	53.6
CVD (%)	18.8	16.3
Inpatient Spending (\$)	2517 (17238)	2508 (18528)
Outpatient Spending (\$)	6095 (17320)	5852 (17799)
Non-GLP1 Spending (\$)	13083 (31211)	12147 (32461)
Non-GLP1 DM Rx Spending (\$; Mean [SD])	1777 (3788)	1278 (3319)
Unique Enrollees (N)	307,616	460,615

Notes: Table reports weighted baseline characteristics measured during the 12 months prior to initiation (event time –12 to –1). The GLP-1 Adoption group includes early adopters; the Control group includes matched individuals who initiate one year later (not-yet-treated). Summary statistics are weighted using Q-weights to balance control group sizes across stacked sub-experiments. Unique Enrollees in each column reports the number of distinct enrollment IDs that have ever been observed in the treated and control groups, respectively, while the total number of distinct enrollees represented in the stacked sample is  $N = 537,743$ . Standard deviations are shown in parentheses for continuous variables.

**Table 2 – Cumulative effects of GLP-1 initiation and implied spending offsets**

Outcome:	Spending on ....			
	Non-GLP-1	Diabetes (excl. GLP-1)	Outpatient	Inpatient
<b>Panel A. Full sample, 12 month follow-up</b>				
<i>Cumulative GLP-1 spending (periods 0-11): 6,452.1 (SE: 7.12)</i>				
Cumulative effect	585.2 (162.33)	-189.0 (10.87)	438.4 (74.81)	252.2 (136.17)
Offset	0.0907 (0.02516)	-0.0293 (0.00168)	0.0679 (0.01160)	0.0391 (0.02110)
Counterfactual mean	1182.2	165.0	548.0	209.1
<b>Panel B. Full sample, 60 month follow-up</b>				
<i>Cumulative GLP-1 spending (periods 0-59): 22,542.1 (SE: 96.26)</i>				
Cumulative effect	6773.3 (1934.28)	237.1 (196.81)	2792.3 (802.47)	2941.7 (1645.83)
Offset	0.3005 (0.08584)	0.0105 (0.00873)	0.1239 (0.03561)	0.1305 (0.07303)
Counterfactual mean	1231.2	234.8	533.3	192.3

Notes: Each panel is for a different sample and each column for a different outcome. For each panel, we report cumulative GLP-1 spending as the sum of monthly GLP-1 spending over periods 0-11 for the 12-month follow-up, and periods 0-59 for the 60-month follow-up. We then report the cumulative effect on each outcome (sum over periods 1-11 or 1-59), and the offset (the ratio of cumulative spending effects and cumulative GLP-1 spending). The last row shows the counterfactual monthly mean outcome, the average outcome in the absence of GLP-1 initiation computed over periods 1-11 or 1-59. Robust standard errors clustered on patient are in parentheses.

**Table 3 – Cumulative effects of GLP-1 initiation and implied spending offsets, by patient subgroup**

Outcome:	Spending on ....			
	Non-GLP-1	Diabetes (excl. GLP-1)	Outpatient	Inpatient
<b>Panel A. Patients with diabetes</b>				
<i>Cumulative GLP-1 spending (periods 0-11): 6,430.0 (SE: 7.84)</i>				
Cumulative effect	768.3 (228.14)	-301.4 (17.33)	783.6 (100.54)	161.8 (194.22)
Offset	0.1169 (0.03580)	0.0461 (0.00269)	0.1215 (0.01568)	0.0207 (0.03053)
Counterfactual mean	1297.7	240.8	539.2	256.4
<b>Panel B. Patients with cardiovascular disease</b>				
<i>Cumulative GLP-1 spending (periods 0-11): 6,526.5 (SE: 15.96)</i>				
Cumulative effect	866.5 (724.64)	-395.8 (33.69)	892.1 (264.53)	315.2 (653.97)
Offset	0.1368 (0.11213)	-0.0606 (0.00518)	0.1405 (0.04077)	0.0468 (0.10131)
Counterfactual mean	2034.3	272.8	893.4	476.9
<b>Panel C. Patients without diabetes</b>				
<i>Cumulative GLP-1 spending (periods 0-11): 6,423.4 (SE: 14.65)</i>				
Cumulative effect	575.5 (202.09)	-41.2 (4.78)	-48.6 (112.93)	653.8 (154.75)
Offset	-0.0867 (0.03036)	0.0065 (0.00073)	0.0082 (0.01732)	-0.1012 (0.02299)
Counterfactual mean	902.7	12.2	544.4	89.4
<b>Panel D. Patients with obesity</b>				
<i>Cumulative GLP-1 spending (periods 0-11): 6,603.5 (SE: 8.88)</i>				
Cumulative effect	1183.4 (210.54)	-175.1 (13.04)	642.6 (99.75)	640.5 (175.25)
Offset	0.1780 (0.03184)	-0.0266 (0.00197)	0.0964 (0.01508)	0.0969 (0.02650)
Counterfactual mean	1188.0	148.1	574.3	188.8

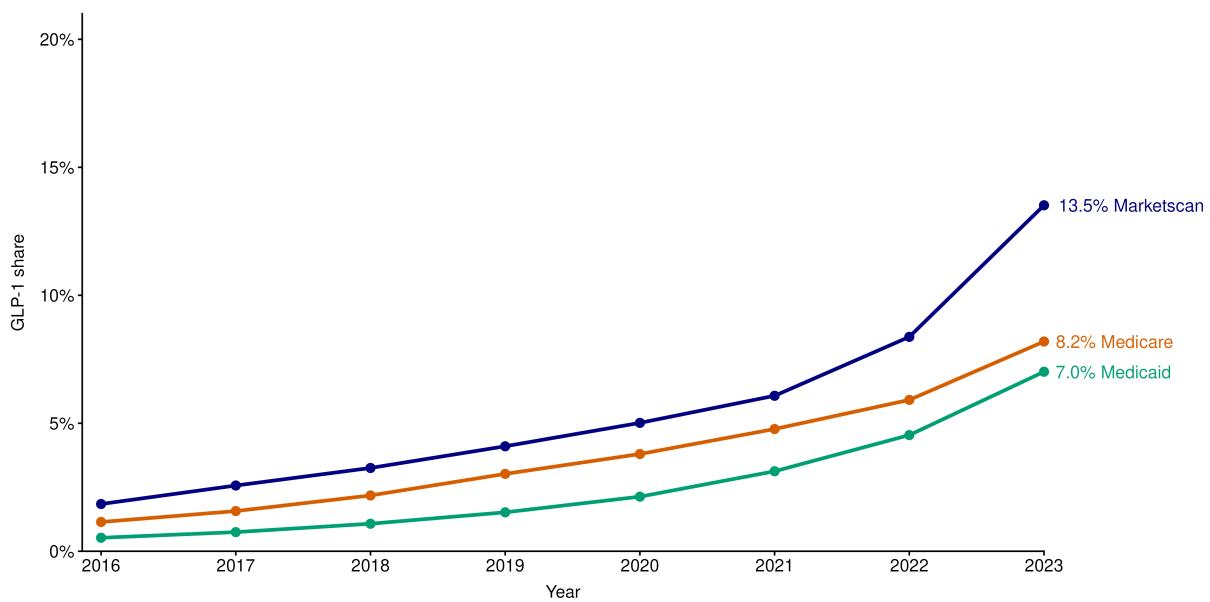
Notes: See notes to Table 2. This table is identical but it focuses on the 12 months of follow-up only and each panel reports results from the indicated subsample.

**Table 4 – Cumulative effects of Semaglutide initiation and implied spending offsets**

Outcome:	Spending on ....			
	Non-GLP-1	Diabetes (excl. GLP-1)	Outpatient	Inpatient
<b>Semaglutide sample, 24 month follow-up</b>				
<i>Cumulative GLP-1 (Semaglutide) spending (periods 0-23): 11709.8 (SE: 30.90)</i>				
Cumulative effect	-902.8 (685.25)	-635.2 (50.49)	-97.7 (296.55)	-429.9 (587.12)
Offset	-0.0771 (0.05852)	-0.0542 (0.00431)	-0.0083 (0.02533)	-0.0367 (0.05014)
Counterfactual mean	1303.8	194.8	587.0	246.6

Notes: Each column reports results for a different spending outcome using the Semaglutide first-adoption stacked event-study sample with event time defined relative to the month of first observed Semaglutide fill. We report cumulative GLP-1 spending as the sum of monthly GLP-1 spending over event-time periods, and the offset (the ratio of cumulative spending effects and cumulative Semaglutide spending). The last row shows the counterfactual monthly mean outcome, the average outcome in the absence of Semaglutide initiation computed over periods 1-23. Robust standard errors clustered on patient are in parentheses.

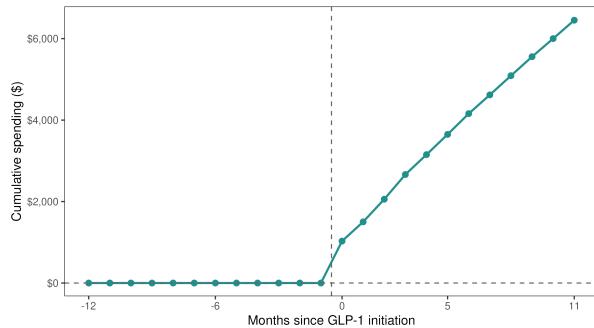
**Figure 1 – Share of prescription drug spending attributable to GLP-1 medications, 2016–2023.**



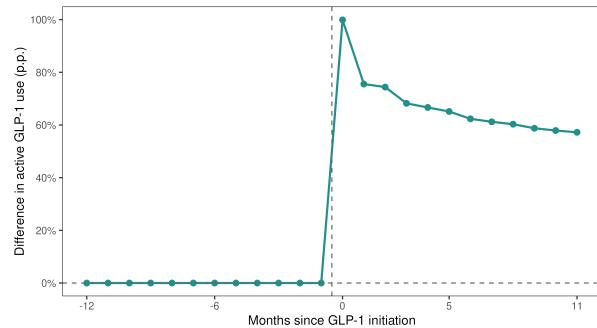
**Notes:** The figure plots, by year, the share of total prescription drug spending attributable to GLP-1 medications for each payer group (commercial payers in our Marketscan data, Medicare, and Medicaid). For each payer group-year, the GLP-1 spending share is calculated as GLP-1 prescription drug spending divided by total prescription drug spending.

**Figure 2 – Effects of GLP-1 Initiation on Downstream Health Care Spending – 12 month follow up**

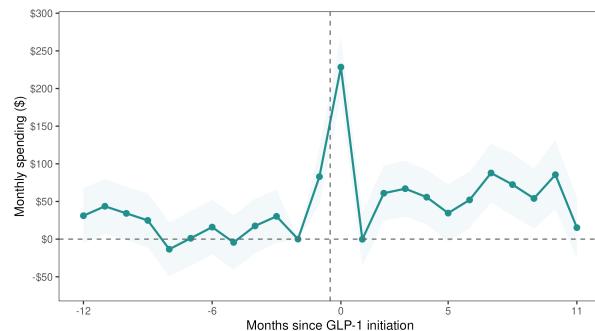
(a) Cumulative GLP-1 Spending



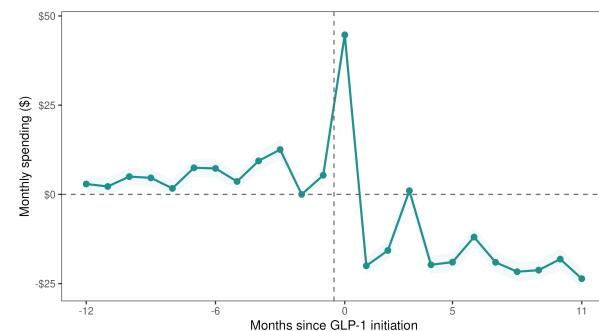
(b) Fraction with Active GLP-1 Supply



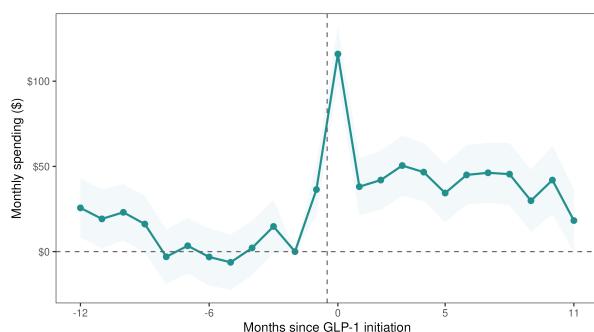
(c) Total Spending (non-GLP)



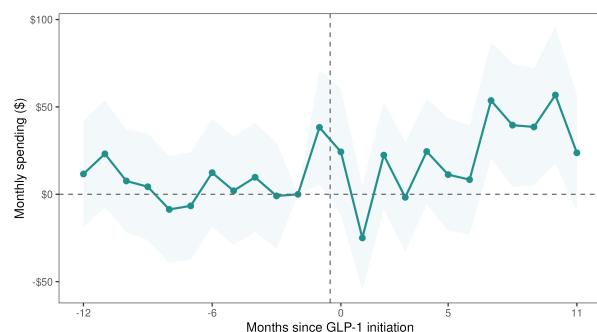
(d) Diabetes Rx Spending (non-GLP)



(e) Outpatient Spending



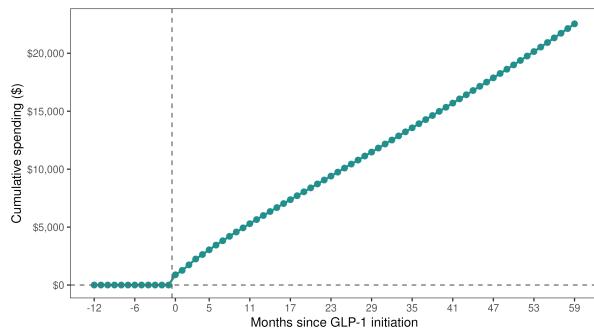
(f) Inpatient Spending



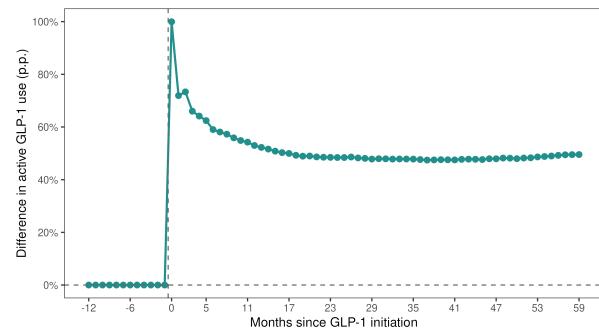
Notes: Each graph reports event-study coefficients from a stacked saturated specification estimated using weighted least squares with weights to correct for control group sizes across sub-experiment. The reference month is event time period -2. Each regression is based on the same balanced panel of N = 18,571,850 person-month observations. Error bars show 95% confidence intervals.

**Figure 3 – Effects of GLP-1 Initiation on Downstream Health Care Spending – 60 month follow up**

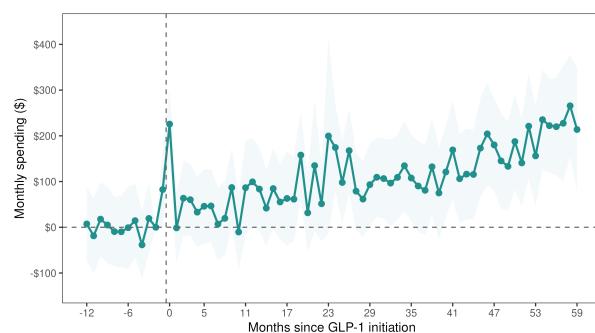
(a) Cumulative GLP-1 Spending



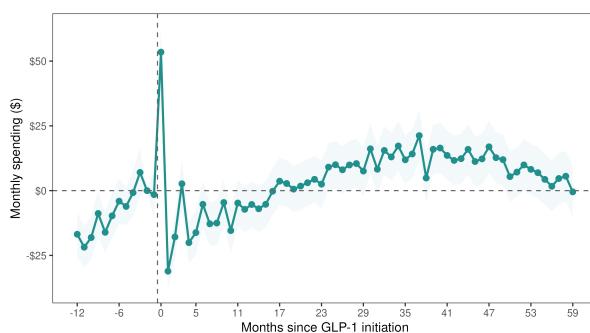
(b) Fraction with Active GLP-1 Supply



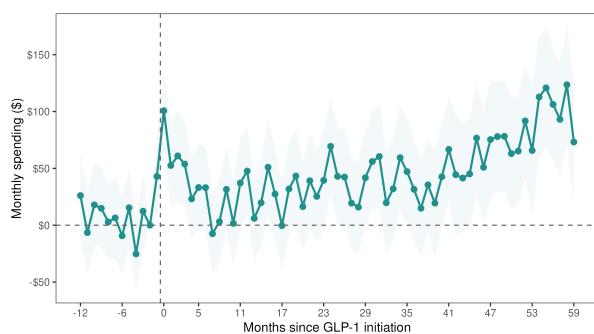
(c) Total Spending (non-GLP)



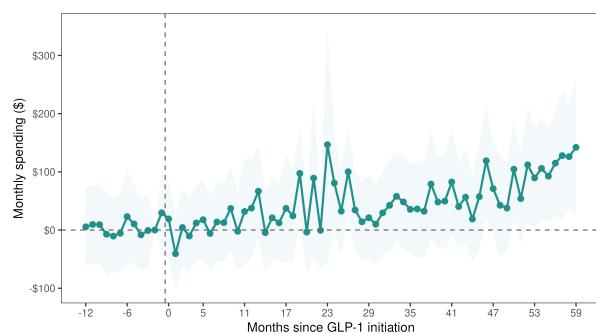
(d) Diabetes Rx Spending (non-GLP)



(e) Outpatient Spending



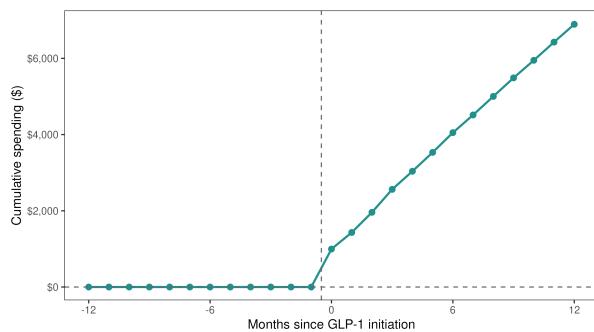
(f) Inpatient Spending



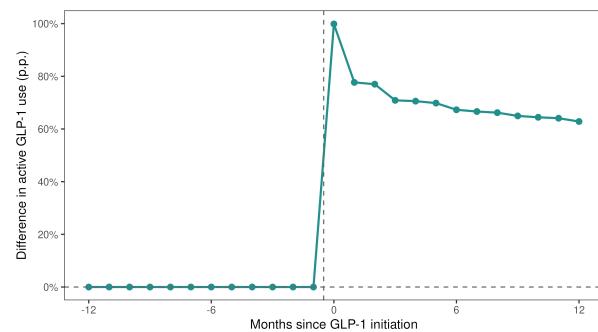
Notes: Each graph reports event-study coefficients from a stacked saturated specification estimated using weighted least squares with weights to correct for control group sizes across sub-experiment. The reference month is event time period -2. Each regression is based on the same balanced panel of N = 18,437,544 person-month observations. Error bars show 95% confidence intervals.

**Figure 4 – Effects of GLP-1 Initiation on Downstream Health Care Spending Among People With Diabetes**

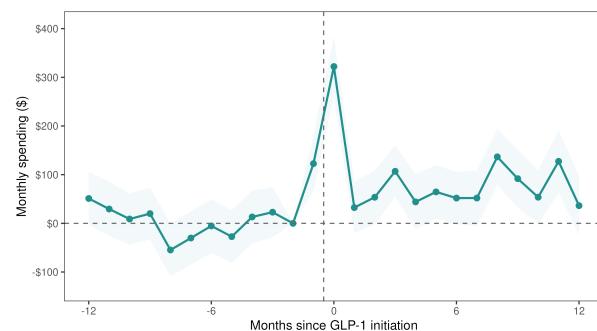
(a) Cumulative GLP-1 Spending



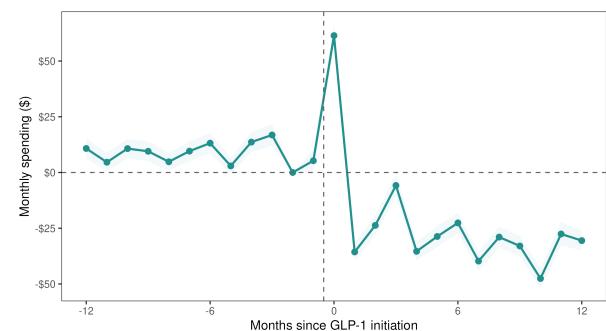
(b) Fraction with Active GLP-1 Supply



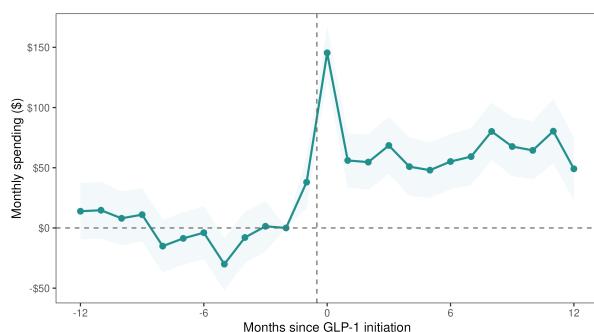
(c) Total Spending (non-GLP)



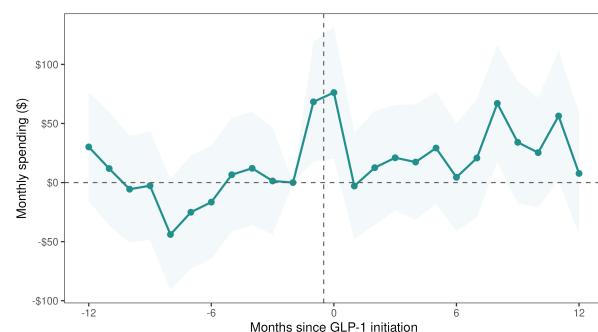
(d) Diabetes Rx Spending (non-GLP)



(e) Outpatient Spending



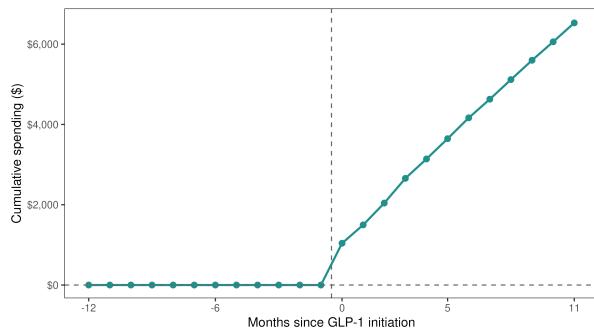
(f) Inpatient Spending



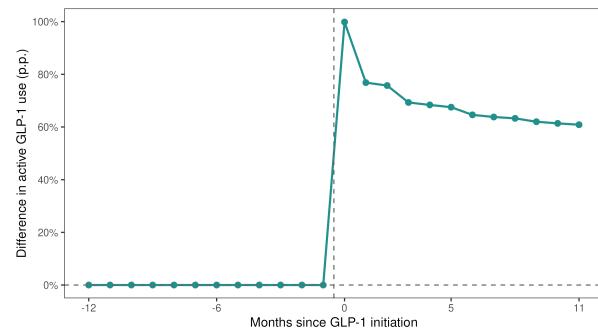
Notes: Each graph reports event-study coefficients from a stacked saturated specification estimated using weighted least squares with weights to correct for control group sizes across sub-experiment. The reference month is event time period -2. Each regression is based on the same balanced panel of  $N = 10,533,936$  person-month observations. Error bars show 95% confidence intervals.

**Figure 5 – Effects of GLP-1 Initiation on Downstream Health Care Spending Among People With Cardiovascular Disease**

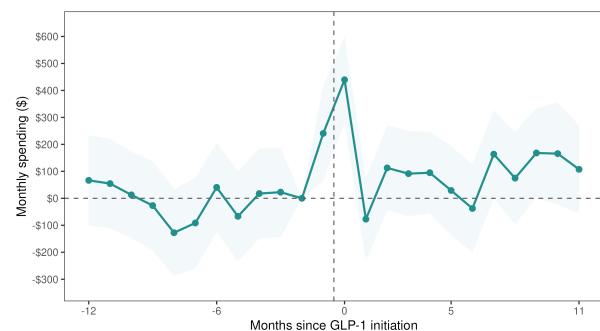
(a) Cumulative GLP-1 Spending



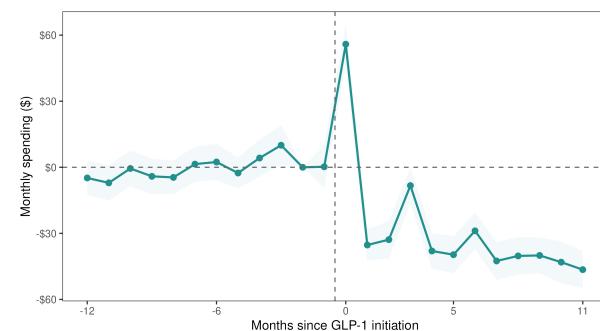
(b) Fraction with Active GLP-1 Supply



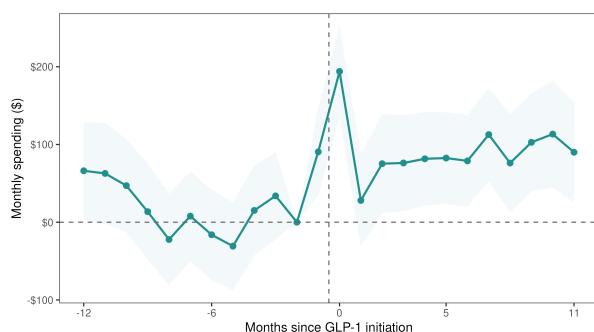
(c) Total Spending (non-GLP)



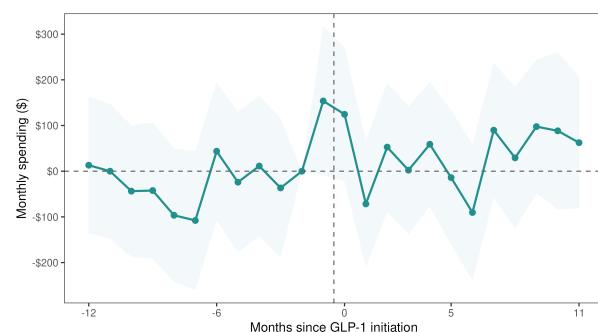
(d) Diabetes Rx Spending (non-GLP)



(e) Outpatient Spending



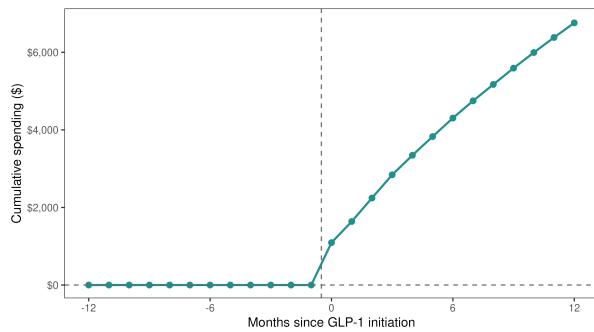
(f) Inpatient Spending



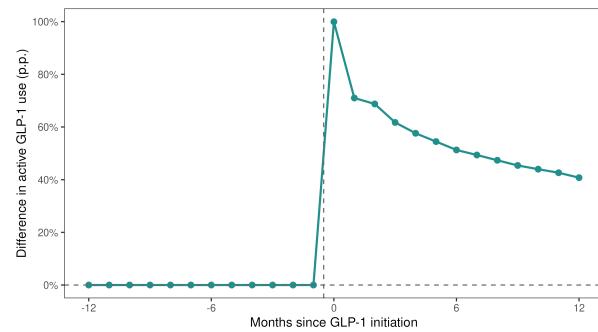
Notes: Each graph reports event-study coefficients from a stacked saturated specification estimated using weighted least squares with weights to correct for control group sizes across sub-experiment. The reference month is event time period -2. Each regression is based on the same balanced panel of  $N = 3,136,944$  person-month observations. Error bars show 95% confidence intervals.

**Figure 6 – Effects of GLP-1 Initiation on Downstream Health Care Spending Among People Without Diabetes**

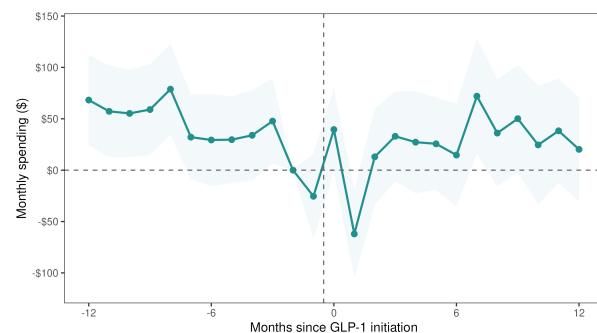
(a) Cumulative GLP-1 Spending



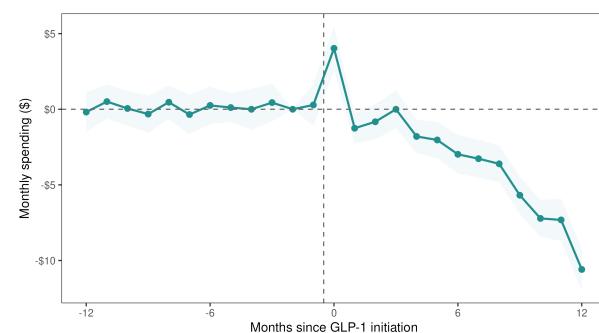
(b) Fraction with Active GLP-1 Supply



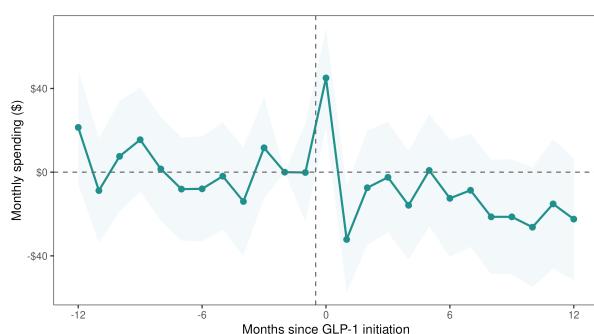
(c) Total Spending (non-GLP)



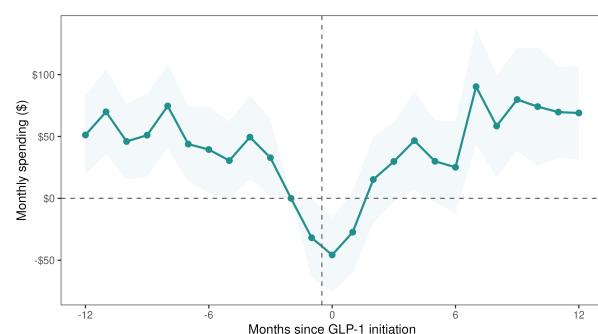
(d) Diabetes Rx Spending (non-GLP)



(e) Outpatient Spending



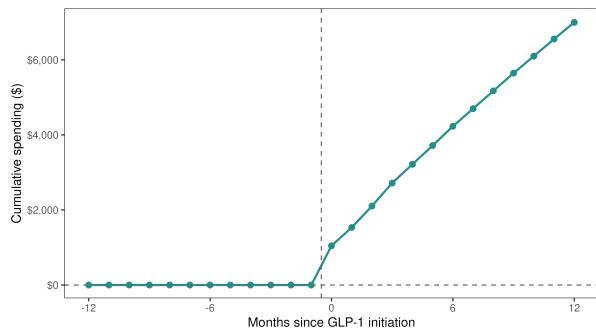
(f) Inpatient Spending



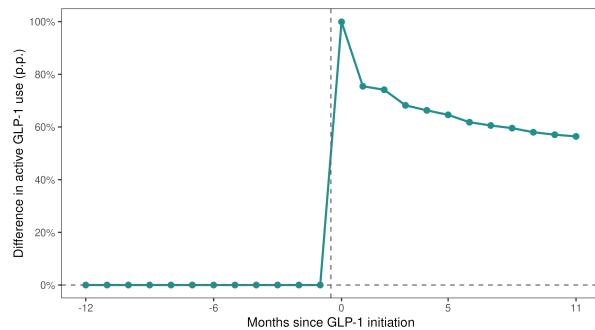
Notes: Each graph reports event-study coefficients from a stacked saturated specification estimated using weighted least squares with weights to correct for control group sizes across sub-experiment. The reference month is event time period -2. Each regression is based on the same balanced panel of N = 7,903,608 person-month observations. Error bars show 95% confidence intervals.

**Figure 7 – Effects of GLP-1 Initiation on Downstream Health Care Spending Among People With Obesity**

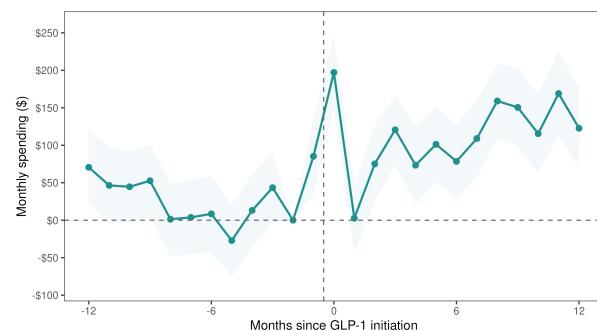
(a) Cumulative GLP-1 Spending



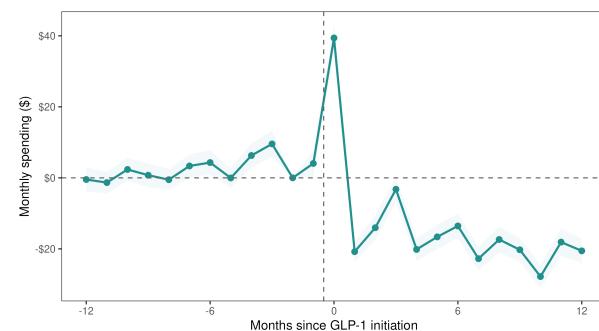
(b) Fraction with Active GLP-1 Supply



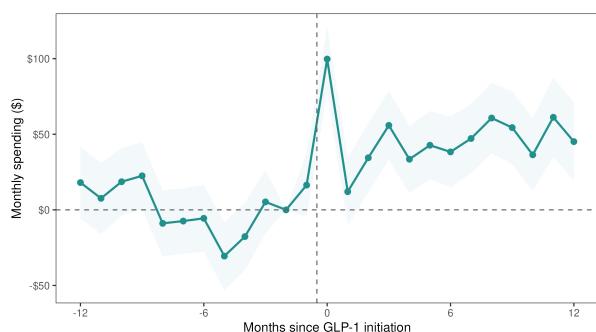
(c) Total Spending (non-GLP)



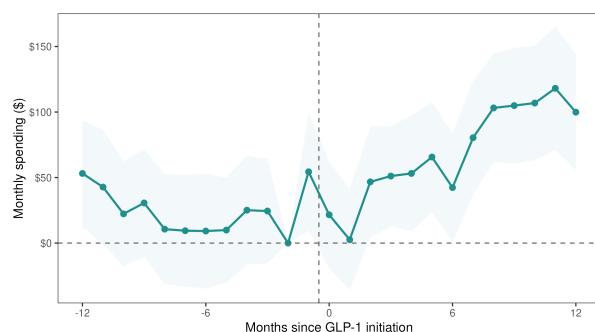
(d) Diabetes Rx Spending (non-GLP)



(e) Outpatient Spending



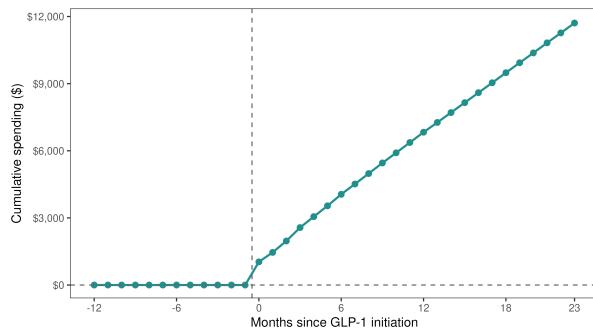
(f) Inpatient Spending



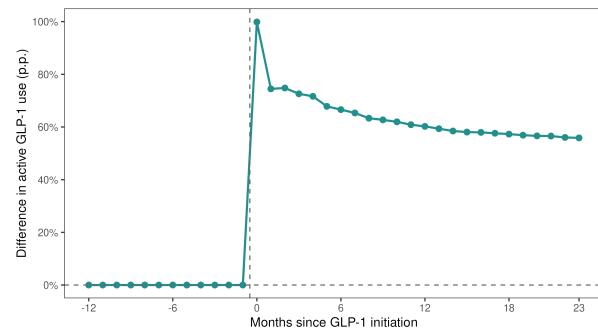
Notes: Each graph reports event-study coefficients from a stacked saturated specification estimated using weighted least squares with weights to correct for control group sizes across sub-experiment. The reference month is event time period -2. Each regression is based on the same balanced panel of  $N = 11,811,168$  person-month observations. Error bars show 95% confidence intervals.

**Figure 8 – Effects of GLP-1 Initiation on Downstream Health Care Spending among Patients with an Initial Prescription for Semaglutide Adoption- 24 month follow up**

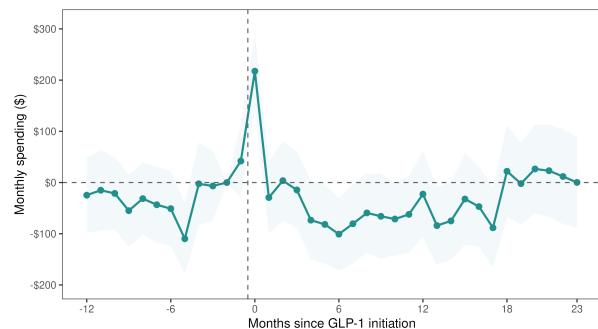
(a) Cumulative GLP-1 Spending



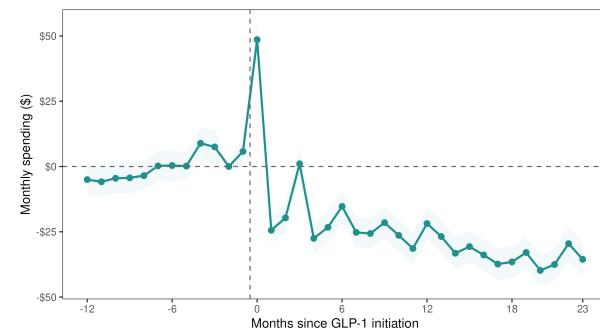
(b) Fraction with Active GLP-1 Supply



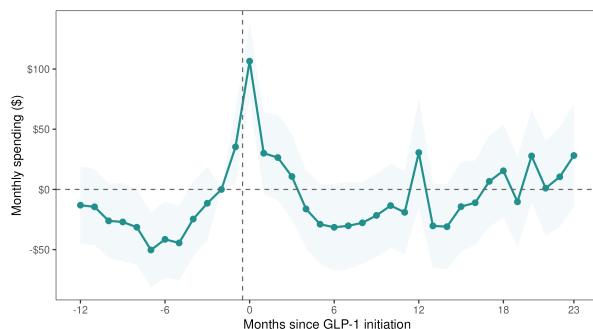
(c) Total Spending (non-GLP)



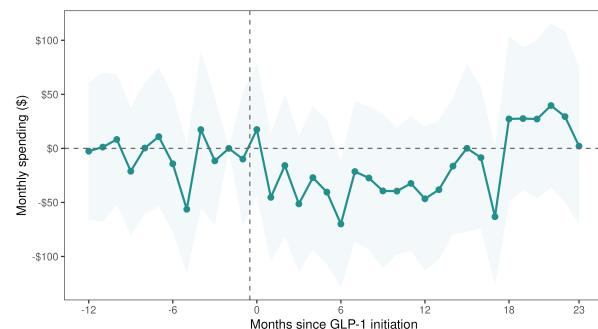
(d) Diabetes Rx Spending (non-GLP)



(e) Outpatient Spending

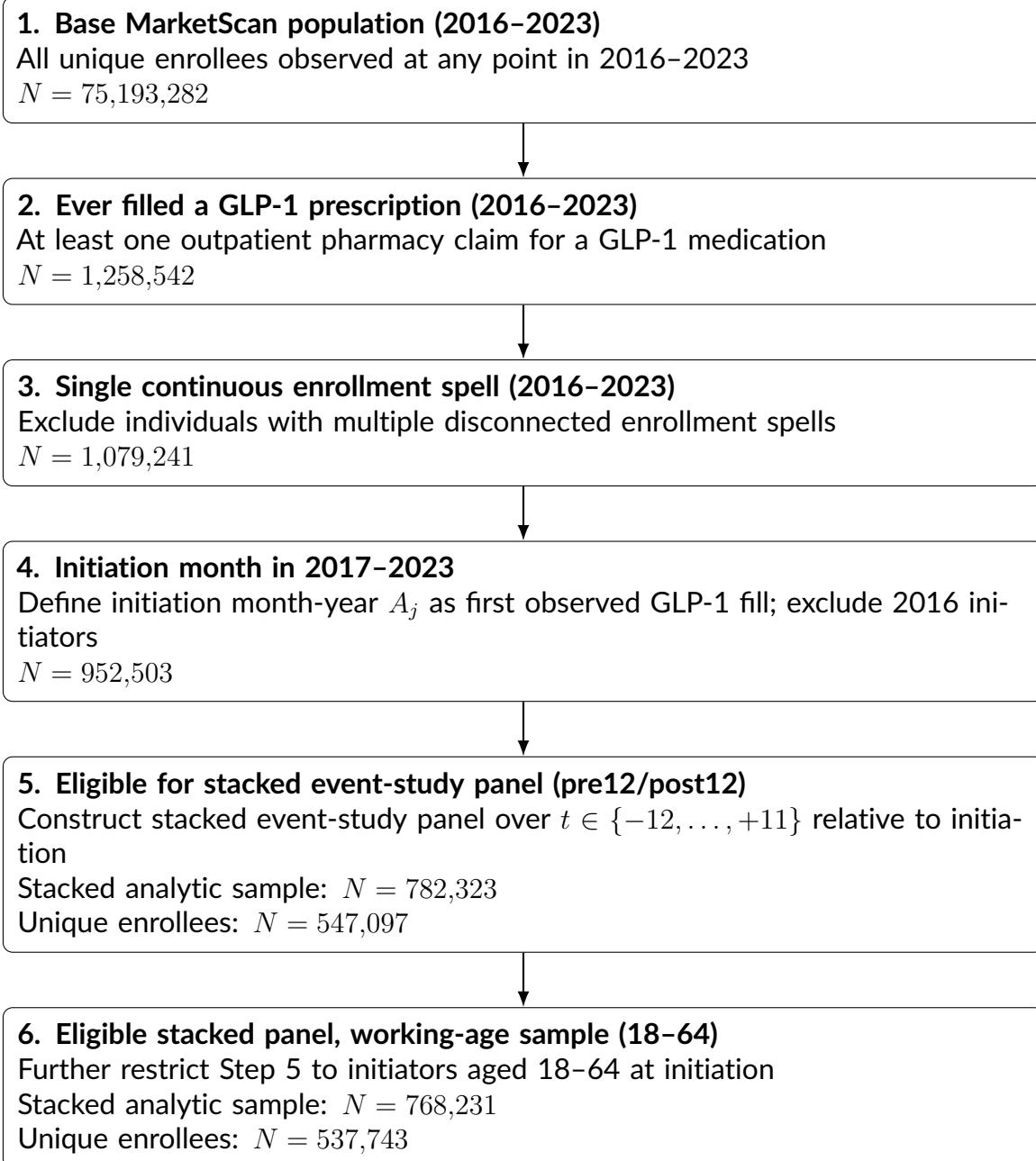


(f) Inpatient Spending



Notes: Each graph reports event-study coefficients from a stacked saturated specification estimated using weighted least squares with weights to correct for control group sizes across sub-experiment. The reference month is event time period -2. Each regression is based on the same balanced panel of N = 9,680,364 person-month observations. Error bars show 95% confidence intervals.

**Figure A.1 – Sample construction and eligibility for stacked event-study analysis**



Notes: Counts reflect sequential restrictions applied to the MarketScan population. The final eligible pool consists of people aged 18–64 with a single MarketScan enrollment spell who started taking a GLP-1 medication between January 2017 and December 2022 and had complete observation of the pre12/post12 event window. Because the analysis stacks multiple sub-experiments, people may appear more than once and may contribute observations as treated in their own initiation cohort and as controls in earlier cohorts; therefore, we report both the stacked analytic sample size and the number of unique enrollees represented in the stacked panel.

**Table A.1 – GLP-1 Receptor Agonists and NDC Codes**

<b>GLP-1 Type</b>	<b>NDC Numbers</b>
Lixisenatide	24576302, 24576105, 24576102, 24576101, 24574702, 24574502, 24574101, 24574000
Dulaglutide	2143301, 2143361, 2143380, 2143401, 2143461, 2143480, 2223601, 2223661, 2223680, 2318201, 2318261, 2318280, 50090348300, 50090348400, 50090546700, 50090645300, 50090645600, 50090657100, 54568043363, 54568043371, 54568043463, 54568043471
Semaglutide	169413001, 169413013, 169413211, 169413212, 169413290, 169413297, 169413602, 169413611, 169418103, 169418113, 169418190, 169418197, 169430301, 169430313, 169430330, 169430390, 169430393, 169430399, 169430701, 169430713, 169430730, 169431401, 169431413, 169431430, 169450101, 169450114, 169450501, 169450514, 169451701, 169451714, 169452401, 169452414, 169452501, 169452514, 169452590, 169452594, 169477211, 169477212, 169477290, 169477297, 50090513800, 50090513900, 50090582400, 50090594900, 50090605100, 70518214300
Exenatide	2021007, 2021008, 2021009, 310651201, 310651285, 310652004, 310652401, 310653001, 310653004, 310654001, 310654004, 310654085, 54868538400, 54868538401, 54868538402, 66029021007, 66029021008, 66780021007, 66780021008, 66780021009, 66780021201, 66780021902, 66780021904, 66780022601, 66914103504, 66914103505, 68258894701, 68258894802, 70121168501, 70121168601
Tirzepatide	2015201, 2015204, 2024301, 2024304, 2115201, 2121401, 2124301, 2134001, 2142301, 2145701, 2145780, 2146001, 2146080, 2147101, 2147180, 2148401, 2148480, 2149501, 2149580, 2150601, 2150661, 2150680, 2200201, 2221401, 2234001, 2242301, 2245701, 2245780, 2246001, 2246080, 2247101, 2247180, 2248401, 2248480, 2249501, 2249580, 2250601, 2250661, 2250680, 2300201
Liraglutide	143914402, 143914403, 169280013, 169280015, 169280090, 169280097, 169291115, 169291190, 169291197, 169406012, 169406013, 169406090, 169406097, 169406098, 169406099, 480366719, 480366720, 480366722, 14403340001, 14403340002, 14403340003, 50090285300, 50090425700, 50090450300, 54569650700