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ABSTRACT

In a pervasive but controversial practice, drug firms frequently make monetary or in-kind payments to physicians in the course of promoting prescription drugs. We use a federal database on the universe of such interactions between 2013 and 2015 linked to prescribing behavior in Medicare Part D. We account for the targeting of payments with fixed effects for each physician-drug combination. In an event study, we show that physicians increase prescribing of drugs for which they receive payments in the months just after payment receipt, with no evidence of differential trends between paid and unpaid physicians prior to the payment. Using hand-collected efficacy data on three major therapeutic classes, we show that those receiving payments prescribe lower-quality drugs following payment receipt, although the magnitude is small and unlikely to be clinically significant. In addition, we examine five case studies of major drugs going off patent. Physicians receiving payments from the firms experiencing the patent expiry transition their patients just as quickly to generics as physicians who do not receive such payments.

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1 Introduction

More than 85 percent of drug firms' marketing expenditures are targeted at influencing physicians as the key prescribing decision-maker (Pew Charitable Trust, 2013). Such marketing expenditures include face-to-face "detailing" visits from pharmaceutical sales representatives that commonly involve purchases of food and beverage for physicians, as well as high-dollar speaking fees or travel reimbursements. These financial interactions are commonly thought to distort physician's prescribing decisions; Consumer Reports declares that "a major conflict of interest is at work when a physician has accepted payments from a drug company whose products he or she then prescribes" (Consumer Reports, 2014). However, the fact that drug firms target payments at physicians who are *ex ante* most likely to prescribe the drug makes it difficult to establish the causal effect of payments. In addition, even if payments influence a physician's behavior, it is an empirical question whether patients' outcomes are helped or harmed. Defenders of the practice argue that payments facilitate education on a fast-changing evidence base: "Pharma reps provide timely access to balanced, FDA-approved research and information. This 'delivery mechanism' organically complements and reinforces the information they receive from medical journals and conferences" (Flewell, 2006).

In this paper, we use rich microdata to evaluate how financial interactions between drug firms and physicians affect prescribing outcomes such as expenditures, the number of patients taking the drug, transitions to generic versions of branded drugs, and the quality of prescribed drugs. Our analysis links the Open Payments dataset—the universe of monetary or in-kind payments that drug firms made to physicians between 2013 and 2015—to prescription data for a large panel of Medicare Part D enrollees. We examine prescribing behavior at the monthly level to identify abrupt changes in a physician's prescribing of a drug that occur right after a physician receives a payment related to that drug. This "event study" approach permits physician by drug fixed effects, allowing us to overcome the empirical challenge that physicians who receive payments tend to be *ex ante* higher-volume physicians than those who do not. Our approach also allows us to examine the trends of paid and unpaid physicians prior to the payment's receipt and to confirm that paid physicians are not on different trends prior to the payment, and that they diverge in their prescribing behavior only after the payment is received. These patterns support the claim that our analysis captures the causal impact of payments on prescribing behaviors.

We find that over the years 2013-2015, more than one-fifth of branded expenditure in Part D comes from a physician who has recently received a payment for the drug, and 29 percent of Part D physicians are paid for at least one drug over the sample period. If the payments have substantial causal impacts on prescribing behavior, the prevalence of the

practice implies that the financial impacts are economically large.

In our primary specification, we find that paid and unpaid physicians are trending similarly prior to receiving a payment. However, beginning in the month the payment is received, paid physicians increase the number of patients taking the drug for which they received a payment and increase the total amount of expenditures on that drug. Our results suggest that a single payment raises expenditures on the paying drug[1] by $121 during the first year, or 4 percent, with effects peaking approximately six months after the payment is made and declining after that. Scaling up this effect to the full prescription drug market, and dividing through by the best-available estimates of the cost of the marginal visit to a doctor, we find that drug firms can expect $2.64 in returns for another dollar spent in these marketing efforts. Although large, this is considerably smaller than existing estimates (Narayanan et al., 2004; Schwartz and Woloshin, 2019).

We next explore heterogeneity by type of payment and market structure. Firstly, we characterize payments by the type and dollar value. The majority of payments are an in-kind meal, while others signify a deeper relationship, e.g. fees for speaking or conducting continuing medical education. Eighty percent of payments are less than $20. We find that our overall effects are driven by food payments and low-dollar payments. We also show how the impact of a drug's payment varies with its competitive setting. If a doctor receives a payment from two drugs in the same therapeutic class, the second payment partially offsets the impact of the first payment. In addition, we show that payments have a higher estimated impact in therapeutic classes with five or fewer drugs making payments as compared to all classes.

We conduct two exercises to assess the impact of these payments not only on prescribing behavior, but on welfare-relevant quality outcomes. Payments from drug firms may increase expenditures without decreasing patient well-being if these payments also improve the quality of the drug prescribed. We use hand-collected data on drug efficacy for three major therapeutic classes where there is a common and well-defined clinical endpoint for drug therapy. For each therapeutic class, we obtain a unidimensional efficacy measurement for every molecule from the medical literature. Using this drug quality measure, we find that paid and non-paid physicians prescribe drugs of a similar quality prior to receiving a payment, but that relative drug quality falls among drugs prescribed by paid physicians after the payment. Although these reductions in drug quality are statistically significant, they are very small; our confidence intervals allow us to rule out reductions in drug efficacy larger than about 1/100th of a standard deviation. Thus, we conclude that, on average, there are

[1]For ease of exposition, we describe instances in which a firm makes a payment to a physician related to a particular drug as the drug "paying" the physician.

no clinically meaningful changes in prescribing quality.

As a second evaluation of prescribing quality, we examine five case studies in which a major drug went off patent. If paid physicians do not transition their patients to a generic version of a drug following a patent expiry, this behavior would financially reward the drug firms and increase patients' cost-sharing, suggesting the physicians are poor agents for their patients. We find that paid physicians move patients just as quickly to the generic version of the drug as unpaid physicians, contradicting some media reports (e.g. Gold, 2001). At the same time, we observe that paid physicians also tend to switch patients to the (still patent protected) extended release version of a molecule that has lost patent protection. Extended release versions commonly cost substantially more but only improve on the original version in convenience. Taken together, we find that payments to physicians do not impede the transition to generics in the general case, but can help a drug firm implement a "line extension" with potentially low benefits for patients.

Our paper contributes to the literature that explores whether pharmaceutical detailing affects the quantity and cost of physicians' prescribing. The majority of past work in the medical literature has found a positive relationship between a physician's exposure to pharmaceutical companies' sales representatives and the quantity and cost of prescribed drugs. However, most of these studies have not addressed the selection of payments to physicians[2] or are studying the impacts of other types of pharmaceutical firm marketing (Adair and Holmgren, 2005; Dolovich et al., 1999; Freemantle et al., 2000). Some recent analyses in economics and marketing have used longitudinal data to explore the effect of payments on prescribing, but are limited to a small number of drugs (e.g. Mizik and Jacobson, 2004; Datta and Dave, 2017; Grennan et al., 2018; Agha and Zeltzer, 2019). Grennan et al. (2018) use variation in hospitals' policies that ban pharmaceutical sales representatives from the premises and find that a meal increases cardiologists' prescribing of detailed statins by roughly 70 percent. Shapiro (2018a) and Agha and Zeltzer (2019) use fixed-effect approaches similar to ours and find that a detailing visit increases prescribing of an antipsychotic by 14 percent in the following twelve months[3] and that small payments increase prescribing of blood thinners by

[2]See Spurling et al. (2010) and Henry (2010) for a review and discussion of the medical literature on this topic. Overall, the review concludes that "the limitations of studies reported in the literature mentioned above mean that we are unable to reach any definitive conclusions about the degree to which information from pharmaceutical companies increases, decreases, or has no effect on the frequency, cost, or quality of prescribing" (Spurling et al., 2010, p. 19).

[3]The estimates from Shapiro (2018a) are not immediately comparable to ours. He assumes that a detailing visit adds to a detailing stock that depreciates over time. We convert his estimates to a year-long percentage increase in prescribing as follows. We compute the implied increase in prescriptions over a one year period and then divide by average prescribing in a year. Mathematically, this is $\frac{\sum_{t=0}^{11}\delta^t\beta}{\overline{Rx}}$ where $\delta = 0.6$ is the speed at which the detailing stock depreciates, $\beta = 0.1224$ is the estimated impact of a unit increase in the detailing stock on total prescriptions in a month (from his Table 5), and $\overline{Rx} = 5.124$ is the average

approximately 10 percent, respectively.[4]

We contribute to this literature in three ways. First, we exploit the detailed timing of payments to address concerns about selection of payments to physicians. Second, we estimate the impacts of detailing for all drugs that pharmaceutical firms were promoting, rather than focusing on a single drug or drug class. By examining the universe of drugs, we are able to improve on the external validity of estimates based on a narrow set of drugs and establish new descriptive facts about the prevalence of detailing in the Part D market overall. And third, because it is becoming increasingly difficult for sales representatives to gain access to physicians,[5] past estimates of detailing's effects may no longer reflect its current impacts. Our estimates are based on the immediate past and so may better reflect detailing's changing influence. To our knowledge, this is the first paper that shows the trajectory of prescribing behavior for physicians before and after a payment, for *all* detailed drugs, in a recent time period.

Our paper also contributes to the literature assessing whether payments from pharmaceutical firms affect the quality of physicians' prescribing. Past work has used a number of different measures of prescribing quality: reviews of prescribing by other physicians (Becker et al., 1972; Haayer, 1982), the variance in the number of prescriptions a particular physician made (de Bakker et al., 2007), and adherence to certain treatment guidelines (Muijrers et al., 2005).[6] These analyses have tended to find that physicians who had greater interaction with pharmaceutical sales representatives had lower quality prescribing. Our results complement this literature by addressing the selection of payments to physicians and using a clinical measure of quality. Our results using patent expirations also contribute to this literature by showing how a sharp change in benefits to patients differentially affects paid and unpaid physicians' choices.[7]

yearly prescriptions (twelve times the 0.427 monthly average from Table 2).

[4]Mizik and Jacobson (2004) use a fixed-effect approach to study the impact of detailing on *new* prescriptions for three different drugs. Their estimates suggest that detailing increases new prescriptions by between 3.6 percent and 11.8 percent over a six month horizon.

[5]For example, a growing number of academic medical centers forbid pharmaceutical sales representatives from visiting physicians on their campuses (Larkin et al., 2017).

[6]The impacts of information from the government (Soumerai et al., 1987), "dear doctor" letters (Kazmierczak and Coley, 1997), the presentation of information during grand rounds (Spingarn et al., 1996), and being involved in a clinical trial (Andersen et al., 2006) on similar measures of quality have also been explored with mixed results.

[7]Our results on quality are also related to a long literature in marketing that models physician learning about drugs via detailing or other sources in a Bayesian framework (e.g. Narayanan et al., 2005; Narayanan and Manchanda, 2009; Ching and Ishihara, 2010, 2012; Chintagunta et al., 2012). This is discussed further in Section 2.

2 Background

According to Pew Charitable Trusts, in 2012 pharmaceutical firms spent more than $27 billion in marketing with 85 percent of that sum spent on marketing direct to physicians (Pew Charitable Trust, 2013). The three major categories of marketing to physicians are face-to-face promotional activities ($15 billion), expenditures on educational opportunities for physicians such as conferences ($2.1 billion), and drug samples for physicians to distribute to patients free of charge (imputed value of $5.7 billion). These expenditures are targeting a population of approximately one million physicians. Given such large expenditures on physician marketing, it is no surprise that relationships between drug firms and physicians are commonplace (Campbell et al., 2007).

In the 2000s, there were a number of efforts to curb these physician-industry relationships for fear that they influenced prescribing at the cost of patient welfare. For example, in 2008, the Association of American Medical Colleges called on all academic medical centers to ban acceptance of industry gifts by doctors, faculty, students, and residents (Sears, 2008). In 2007, Senator Chuck Grassley proposed the "Sunshine Act" to force drug firms to publicly disclose interactions with physicians and it passed as part of the Affordable Care Act in 2010. As of August 1, 2013, all drug and medical device firms were compelled by the Sunshine Act to start tracking these payments and were required to report them for public release to the Center for Medicare and Medicaid Services.

There is a long theoretical literature in economics about the varied impacts of advertising.[8] The "persuasive" view goes back at least as far as Robinson (1933). She discusses how advertising increases demand for a particular product, tending to increase prices and reduce social welfare. On the other hand, proponents of the "information" view (beginning with Stigler, 1961) outline how advertising notifies consumers of products' existence, prices, or other qualities. This information tends to increase welfare via reduced search costs and increased competition. Because the theories have opposing predictions, how pharmaceutical firms' marketing affects the costs, quantity, and quality of prescribing is an empirical question.

Past work from the medical literature has shown a positive association between receiving a payment and awareness of the paying firm's drug, prescribing the firm's drug, and adding the firm's drug to the hospital formulary (Wazana, 2000; Spurling et al., 2010). Although these correlations are suggestive, they are not able to account for the fact that pharmaceutical firms direct payments to physicians with patient populations most likely to use the drug. However, a small number of studies have estimated the impacts of pharmaceutical

[8]For a thorough review of this literature, see Bagwell (2007).

marketing on physicians' behavior using randomized controlled trials or quasi-experimental variation. In a study of 29 medical residents, Adair and Holmgren (2005) randomized letters to half the residents that discouraged the use of free samples and found that the letters did reduce residents' use of samples. This suggests that the standard practice of firms providing samples might affect physicians' choices. Epstein and Ketcham (2014) randomly provide IT to physicians that conveys information about patients' cost-sharing for specific drugs, but also reports the hassle costs of prescribing particular drugs (e.g. prior authorization). They find that physicians' choices are more influenced by hassle costs than they are by payments from pharmaceutical sales representatives. Shapiro (2018b) and Sinkinson and Starc (2019) use quasi-experimental designs to study the impacts of direct-to-consumer advertising on prescribing with a focus on the market-expanding and business-stealing aspects of advertising. While both studies find important market-expanding effects, Sinkinson and Starc (2019) also find business-stealing effects. Ching and Ishihara (2012) exploit co-marketing agreements to show that the informative and persuasive roles of advertising are important in medical marketing.

There is also an extensive literature that models physician learning about the underlying quality of a particular drug. Narayanan et al. (2005) finds that medical marketing is primarily informative for the first 6-14 months of a drug's life and then primarily persuasive thereafter. Chintagunta et al. (2009) and Chintagunta et al. (2012) find that physicians learn about drug quality from both pharmaceutical sales representatives and feedback from patients. While these findings are very suggestive, they only indirectly speak to the quality of physicians' prescribing since they are focused more on physician learning about the underlying quality of a drug. Additional work has found that there are diminishing returns to detailing (Manchanda and Chintagunta, 2004), that firms' advertising decisions take account of how learning about drug quality affects the dynamics of price-sensitivity (Ching, 2010), that there is important heterogeneity across physicians in how much detailing affects their prescribing (Janakiraman et al., 2008), and that historically, detailing tended to have stronger business-stealing than market-expanding effects (Fischer and Albers, 2010). The data used in these studies is often from previous decades and focuses on very few drugs; because of the change in medical professionals' attitudes towards industry interactions, there could be important differences in the impacts of payments today.

3 Data

3.1 Medicare Part D

We assess prescribing behavior using the prescription drug claims of a 20% random sample of enrollees in Medicare Part D from 2013 through 2015; both enrollees in Medicare Advantage Part D plans and free-standing Part D plans are included. Over the sample period, Medicare Part D provided subsidized private insurance for outpatient prescription drugs to about 37 million elderly and disabled enrollees per year and represents approximately 30% of US retail prescription drug expenditure (Kaiser Family Foundation, 2019). An advantage of this dataset over a commercial claims dataset is that nearly all individuals continue in the sample once enrolled, minimizing changes in the composition of a particular physician's patient pool.

For each Part D claim, we observe the exact drug purchased (ingredients, strength, drug form, brand/generic status, extended release if applicable), the date of the pharmacy fill, the days supplied, the full drug price paid by the patient's insurer to the drug firm (prior to discounts or rebates),[9] and the National Provider Identifier of the prescriber.[10] We define a "drug" for the purposes of our analyses as an ingredient (or ingredient combination) in either branded or generic status. We do not differentiate between prescriptions of the same ingredients in different strengths (10mg, 50mg) or drug forms (oral, injectable). This definition reflects the level of specificity in the Open Payments database, which generally does not distinguish between strengths and drug forms of the same ingredients. We do, however, distinguish between the original and "extended release" formulation of a drug. Versions of drugs with extended release properties may be introduced prior to patent expiry and are often promoted independently from the non-extended release version. Open Payments commonly reports payments for both the original and extended release formulations of an ingredient, so we consider these as distinct drugs and examine a case study of Namenda and Namenda XR in Section 5.2.

We observe 2,513 drugs over our sample period, of which one-quarter are branded drugs that account for 69% of Part D expenditure. We acknowledge the competitive structure of

[9]Like most research in prescription drug markets, our measure of "expenditure" does not reflect post-market rebates paid from drug firms back to insurers. The expenditures reported in Part D are closer to "list prices" announced for all drugs than the "net prices" that represent the true income to a drug firm. According to an analysis by Milliman of rebates in Part D in 2016, rebates represented 22% of branded expenditure (16% of all expenditure) in that year (Johnson et al., 2018). We use number of patients as a key outcome that is not subject to this weakness, but focus on expenditure in order to facilitate our calculation of drug firms' returns from payments.

[10]While some prescribers in Part D are non-physician nurse practitioners or physician assistants, we describe all prescribers as "physicians" in what follows.

prescription drugs by assigning each drug to one of 159 therapeutic classes using the 2011 and 2014 Formulary Reference Guides provided to Medicare Part D plans. Drugs in the same therapeutic class are not perfect substitutes, but there is much higher substitutability within classes than between them.

We aggregate these prescription drug claims to the physician × calendar month × drug level, measuring the total pre-rebate expenditure incurred for that drug, the number of patients the physician treats with the drug, and total days supply consumed by those patients. Our use of the month as our unit of time allows us to illustrate in our event-study design the sharp change in behavior at the exact month of payments.

3.2 Open Payments

Our data on payments made by drug firms to physicians come from the Open Payments database. Under the Affordable Care Act, drug firms must report to the Open Payments database any payment or in-kind "transfer of value" they make to physicians. These transfers of value include the meals, travel, and educational expenses that direct-to-physician marketing activities commonly entail. Although the database does not record free samples, the encounters recorded may involve the distribution of free samples. Open Payments separately collects information on payments that drug firms make to physicians for participation in clinical trials ("research payments"); however, these data do not describe the drug being researched and so we do not include them in this analysis. The database contains information beginning August 2013.

For each encounter between drug firms and medical professionals, Open Payments records the individual's name, address, and other identifying information, the drug or drugs discussed, the dollar amount of in-kind or cash payments, and a coarse description of the purpose of the encounter. We find the National Provider Identifier for each professional named in Open Payments using the publicly-available National Plan and Provider Enumeration System. We refer to each encounter as a "payment."[11] We remove payments for medical devices and Part B drugs, and for physicians who we never observe prescribing any drug in Part D. The median payment is small, at about $10, reflecting the typical purpose of the encounter (a meal). We will distinguish food payments from all others. The non-food payments are most commonly for continuing medical education, consulting, education, or travel. There are very small numbers of payments described as gift, grant, honoraria, royalty, entertainment, charity, or own investment.

In Figure 1, we show how the number and value of payments in each of the categories

[11] When an encounter includes multiple drugs being promoted, we divide the total dollar value of the payment equally among each of the promoted drugs.

over the time period. The first column shows that more than 95% of the payments are for food and about 5% are in the "other" category. However, the average encounter where there is only a food payment represents about $16 of value, while the "other" category transfers are much larger, averaging $1,239.[12] Thus, the second column in the figure shows that the other payment types constitute the majority of the dollar value of payments.

The next two columns in Figure 1 show the distribution of payments by amount. The vast majority of payments are less than $50, and about 80 percent are less than $20. However, the rare, very large payments dominate the distribution by value. In our primary analysis, we define our independent variable of interest as a binary indicator that a physician has received a payment for a drug by that month. We consider payment size in a separate analysis.

Payments to at least one Part D physician are reported in Open Payments for 574 distinct Part D drugs in 128 of the 159 therapeutic classes. It is clear that encounters with physicians are a core part of marketing and promotion activities for prescription drugs over the time period. For our main analyses, only drugs with at least some payments contribute to identification in our empirical strategy. Consequently, we retain only drugs for which at least one physician receives a payment.

Between 2013 and 2015, there are nearly four million payments, totaling almost one billion dollars, related to the 574 distinct Part D drugs. We merge payments to a physician for a drug to the physician's monthly prescribing history. In some cases, a Part D physician receives a payment for a drug that they never prescribe over the three years.[13] We retain these payments, imputing zeroes for the physician's prescribing of the drug in all months, as long as the physician ever prescribes in the drug's therapeutic class over the time period. We rectangularize the dataset to include an observation for every physician $\times$ drug combination in all 36 months, to facilitate our event study research design. The resulting dataset has more than 446 million observations, reflecting 991,380 physicians' prescribing of 574 drugs for 36 months each.

3.3 Summary Statistics

It is common for Part D physicians to receive payments related to the drugs they prescribe. In the first row of Table 1, we describe the prevalence of payments overall. Our sample of

[12]The low average amount of food payments can reflect the Open Payments reporting rules for cases where non-physician office staff and physicians both participate in a meal brought by a drug firm (Federal Register, 2013). If only front office staff consume the meal, drug firms are not required to report this interaction. If any physicians eat the meal, the meal is apportioned equally among all participants (including non-physicians), and then the physician's portion is reported.

[13]Some of these payments may arise due to scattershot marketing strategies, for example at medical conferences, or efforts to simply instill brand awareness.

drugs with some payments, equal to 63 percent of total Part D expenditure, captures 92 percent of overall Part D branded expenditure, implying the vast majority of branded drugs are using direct-to-physician marketing captured by Open Payments. Of all expenditure on drugs making payments, 21 percent has been "affected by payments," in that the physician has received a related payment prior to prescribing. By the end of the time period, more than one-fifth (22 percent) of physician × drug combinations have a payment. Overall, 29% of Part D physicians are paid for at least one drug over the sample period. Clearly, even after the required disclosure represented by Open Payments, drug firms are reaching substantial numbers of physicians with their marketing efforts.

The next rows of Table 1 report the same statistics for the top twenty drugs by total expenditure over the sample period. Together, these drugs account for nearly one-third of all Part D expenditure. Payments are common across nearly all of these drugs, which span a number of distinct indications and include both long-standing drugs (Crestor and Zetia) and new entrants (Harvoni and Sovaldi). The percent of expenditure that comes from physicians who had received a related payment by the time of prescribing ranges from 2 percent for Namenda to close to half for Humira and Xarelto. Generic competition was imminent for both Namenda and Gleevec, which explains why payments were less common for those drugs. We examine generic onset during our sample period, including for Namenda, in Section 5.2.

We know, however, that drug firms commonly monitor physicians' prescribing and specifically target high-volume physicians for payments (Fugh-Berman and Ahari, 2007). Consequently, our empirical strategy, detailed below, exploits variation within a physician × drug combination over time. To ensure we have a sufficient "pre" period for each paid physician × drug, we will exclude from our analysis in Section 4 physician × drug pairs whose first observed payment occurs in 2013. The last column of Table 1 describes the share of physicians who are first paid in 2014 or 2015. The relationships described in Open Payments are commonly ongoing frequent interactions, so on average about 40 percent of the physicians who are ever paid got a payment in 2013.

Our research is unique in describing the universe of payments instead of focusing on a single class. Thus, we are able to explore some dimensions of how competitive structure affects the impact of payments. In heterogeneity analyses, we will explore how the impact of payments varies by the number of drugs in a class making payments. Across the 128 therapeutic classes, we observe as few as one and as many as 26 different drugs making payments to Part D physicians. In Figure 2, the x-axis counts the number of drugs in a therapeutic class making payments. The y-axis measures, for drugs in each x-axis category, the average share of expenditure where a physician has received a payment at the time of prescribing (the same measure as the fourth column of Table 1). The size of the marker

denotes the total expenditure represented. The two measures are positively related, such that going from one paying drug in the therapeutic class to eleven paying drugs in the class would raise the percent of branded expenditure affected by payments by 17 percentage points.

Given how often multiple drugs are engaged in competing payments in a therapeutic class, we find, perhaps surprisingly, that 81% of our physician × drug observations are paid by only one drug in the therapeutic class. We propose in the next section an empirical specification to test how payments from a second drug in the therapeutic class affect the physician's behavior. However, we exclude cases where a physician is paid by more than two drugs in a therapeutic class, which amounts to about six percent of all observations.

4 How Do Payments Affect Prescribing?

4.1 Empirical Strategy

Because drug firms commonly monitor physicians' prescribing and specifically target high-volume physicians for payments, the cross-sectional correlation between a physician's payments and her patients' expenditures overstates the impact of payments on prescribing. To address this targeting of payments to physicians, we use a difference-in-differences design that compares outcomes for physicians who are paid to those who are not paid, before and after the payment.[14] This research design relies upon a physician's changes over time and so is able to account for time-invariant characteristics of physicians that lead a drug firm to target them for payments. For physician p, drug d, and year-month t, we estimate the event-study specification

$$y_{pdt} = \sum_{r \neq -1} PresPaid_{pd} \beta_r + \sum_{r \neq -1} PresPaidOth_{pd} \alpha_r + \delta_{pd} + \delta_{dt} + \epsilon_{pdt} \tag{1}$$

Our outcomes, y_{pdt}, are total expenditures, number of patients, or total days supply for a physician-drug-month. $PresPaid_{pd}$ indicates whether the physician will be paid for drug d at some point in our sample, and r denotes the time period relative to the time the physician is paid (if ever). $PresPaidOth_{pd}$ indicates whether the physician will be paid for a drug d' in the same therapeutic class as d (a competitor) at some point in our sample. Including this variable both controls for the effects of a competitor payment and allows us to directly

[14] We use a linear model to represent a physician's supply of each drug in each month. While a discrete-choice model such as logit might be appropriate for a patient's choice of drugs, the typical physician is prescribing five different branded drugs in a therapeutic class over the time period, and even in a single month a physician is prescribing an average of 1.5 distinct branded drugs in each therapeutic class.

observe their time pattern, measured by the α coefficients. We estimate β_r and α_r for every event period and report a 25-month window around the time of payment in the figures. Because we have prescribing information beginning in January 2013 but only use payments that take place in January 2014 or later, we observe 12 pre-event months for all physician-drug pairs that are paid. We normalize β_{-1} and α_{-1} to zero, making the month preceding the payment the reference period.

The fixed effect δ_{pd} allows a different intercept for each combination of physician and drug. The drug $\times$ year-month fixed effect δ_{dt} adjusts for changes in each drugs' prescribing over time, including the overall effects of direct-to-consumer advertising. Both the paid and the never-paid physician $\times$ drugs contribute to this fixed effect. With these sets of fixed effects, we are effectively running the event-study specifications separately for each drug and then aggregating across the different drugs. Finally, we cluster errors at the physician level, which accounts for serial autocorrelation in the errors as well as the possibility of correlation in a physician's behavior across drugs.

We weight observations by the physician's average number of patients in drug d's therapeutic class. By weighting by the number of patients, our coefficients are representative of patients' experiences rather than physicians'. We use the average number of patients across all periods because we find that the treatment affects the number of patients directly. And finally, we use the average number of patients in the entire therapeutic class because we wish to include with positive weight cases where a physician is paid for a drug but never prescribes it.

In order to provide a summary of the impact of payments on outcomes over different time periods, we also report linear combinations of β_r and α_r. Because we observe dynamic treatment effects, we report two estimates, reporting the average coefficient and its standard error in months 0 through 5 as well as months 6 through 12.

We make three edits to our dataset prior to estimation. As discussed, we drop physician-drug pairs that receive a payment in 2013; this gives us twelve pre-period months for all payments. We drop physician-drug pairs where the physician is paid by more than three drugs in the therapeutic class. Finally, to reduce the computational burden of the analysis, we conduct our main analyses using a random 50 percent sample of physicians, retaining all of their prescribing and payment information. These changes result in 494,525 physicians and 190,511,352 physician $\times$ drug $\times$ month observations.

4.2 Effect of Payments on Prescribing

Figure 3 presents the event study results from equation (1) where the dependent variable is the total expenditure by a physician's patients on a drug in a given month. Shortly after the payment, expenditures begin to increase, remain elevated, and then decline a bit. This pattern is consistent with empirical findings that physicians forget advertising over time (Iizuka and Jin, 2005). On average, expenditures are approximately $9 greater per month in the year following the payment. Relative to average monthly expenditures, $238, this is slightly less than a 4 percent increase. There is no obvious trend in the twelve months leading up to the payment that would suggest our estimated increase in expenditures is due to differential underlying trends.

Our estimated impact is considerably smaller than some recent findings. Grennan et al. (2018) study how payments for statins affect cardiologists' prescribing and find that payments increase prescribing by 73 percent. Shapiro (2018a) studies prescribing of an antipsychotic, Seroquel, between 2001 and 2006 and finds that a detailing visit increases prescribing by 14 percent in the following twelve months. Agha and Zeltzer (2019) study anticoagulants ("blood thinners") and find that small payments increase prescribing by 10 percent while large payments increase prescribing by 65 percent. Although a full reconciliation of results is beyond the scope of this article, some portion of the differences are likely due to the specific therapeutic classes studied (all classes with payments vs. a subset of classes with payments), differences in the variation exploited by the empirical designs, and differences in the effects of detailing over time. We further discuss the implied magnitude and estimate a return-on-investment in Section 4.4.

To assess whether our estimated increases in expenditures are due to more patients being put on a drug, we estimate our event study specification with the physician's number of patients as the dependent variable and present the results in Figure 4. As with expenditures, there is no systematic differential trend prior to the payment. Upon receiving the payment, the number of patients increases immediately, remains elevated for approximately six months, and then returns to pre-payment levels; Mizik and Jacobson (2004) find a similar, short-lived increase following detailing visits. The number of patients does increase shortly after the payment, although the magnitude is relatively small. We note that an increase in the number of patients taking the drug could arise both from physicians deciding to start a new patient on the drug after an encounter with the drug firm or physicians differentially continuing current patients on the drug (instead of switching to another drug).

Table 2 summarizes the event study estimates. As seen in column (1), expenditures increase by $5.67 on average in the first six months after a payment; in months 6 - 12, expenditures are an average of $12.47 greater per month than in the month prior to the

payment. In column (2), we present analogous results for the number of patients. Payments increase the number of patients significantly in months 0-5 by 0.016 patient, on average (about 1.3%), but the effect is not significant in months 6-12.

To further examine the margins of adjustment, we examine the impact of payments on the total days supplied of the drug by the physician in the month (results provided in Appendix Figure A.1 and Appendix Table A.1). We find that the days supplied increases by 1.4 percent after a payment. Since expenditure increases by 4 percent and expenditure is the product of days supply and expenditure per day, our findings imply increases in the expenditure per day.[15] A potential explanation is that some individuals are using newer or stronger formulations of the drug that have a higher price.

Whereas most previous studies on the impacts of payments have only had information on the detailing or drug samples for a very small subset of drugs (usually one to three), our data contain this information for all detailed drugs. This allows us to not only control for other firms' activities, but to also directly estimate the impact of a being paid for both a drug and its competitor. Figure 5 presents the event study estimates that show how prescribing changes when a physician who has been paid for one firm's drug also receives a payment from the drug's competitor. Figure 5a suggests that expenditures for drug d fall after the physician gets a second payment for a competing drug d' in the therapeutic class, although the individual event study estimates are somewhat noisy. In the first 6 months after the competitor's payment, expenditures on drug d fall by a (statistically insignificant) \$1.91 per month on average (see Table 3). In the following 6 months, expenditures on drug d decrease significantly by \$10.53 on average. Figure 5b provides the corresponding figure for the number of patients as the dependent variable. There appears to be a somewhat steady downward trend in the number of patients preceding a competing firm's payment and this trend continues after the payment is made. We conclude that payments by other firms do not appear to have large, lasting impacts on the number of patients taking drug d.

4.3 Heterogeneity of Payment Impact

Different types of payments might have different impacts on physicians' choices. If payments are part of a "quid pro quo" in which physicians exchange prescribing volume for a payout, impacts would likely be strongest for the high-value payments and small for very low-dollar payments. As we saw in Section 2, there is tremendous heterogeneity in the dollar value of the payment.

In Figures 6a to 6d, we present the event-study results for payments below \$500 and

[15] We cannot test this finding directly because we cannot calculate an implied expenditure per day for physician-drug combinations with zero prescribing in a month.

payments of at least $500. The results for payments less than $500 closely mirror those for payments overall. Given that the vast majority of payments have a small dollar value, the results for payments of at least $500 are considerably more noisy. There appears to be a slight upward trend in the pre-payment period and little increase in expenditures until eight months after the payment. We summarize the event-study figures by grouping the estimates from months 0-5 and 6-12; these are presented in Table 4.

We also present results for payments under $20, $20-$49, $50-$99, and $100-$499 in Appendix Figure A.2. Generally, the payments below $50 appear to be driving the results seen in the under $500 figure. The fact that we observe meaningful changes in prescribing even for these small payments, which are trivial relative to the average income of a physician, suggests that a simple "quid pro quo" model of physician-pharmaceutical company interactions is unsatisfying in describing the purpose and impact of these payments.

If prestigious (and lucrative) speaking or consulting opportunities are used as rewards to encourage high levels of prescribing, then these types of payments might have very different impacts on expenditures. Figure 7 shows the event-study results for payments for food (7a and 7c) and for other relationships such as consulting or speaking at a continuing medical education event (7b and 7d). The estimates are summarized in Table 4. We show the estimates for food because it is by far the most common type of payment and provides a baseline against which we can compare the estimates for other activities (see Figure 1). Food payments appear to closely resemble our overall estimates with a small increase in the number of patients taking the drug and a larger increase in expenditures. However, other types of payments do not appear to have clear impacts on either the number of patients or expenditures, although our conclusions are limited by the large size of the confidence intervals. Figure 7b and 7d appear to show somewhat elevated expenditures in the months prior to a promotional payment (though for expenditure we can not reject that the individual estimates are different from zero at conventional levels). That might suggest that firms are using promotional payments as rewards for past prescribing. However, that strategy seems unlikely since these payments do not appear to increase expenditures going forward at all.

We might also think that a payment has different impacts depending on the underlying competitive structure of the therapeutic class. For example, in classes with very few branded drugs, a payment might be more effective than in a class where there are many different drugs being promoted. In our data, among therapeutic classes with at least one promoted drug, the median number of drugs being promoted is five. Figure 8 show the estimated impacts of a payment in classes with five or fewer promoted drugs ("low competition"). Again, we see increases in expenditures following a payment. In the first year after a payment, expenditures increased by an average of approximately $25 per month (see

Table 4). Given the $206 average monthly expenditure in these classes, this translates to a 12 percent increase. Because our overall estimate was a 4 percent increase in expenditures, this suggests a potentially important role for the competitive structure of the class in determining the impacts of payments. This may, in part, explain differences between our main results that use data on drugs in all therapeutic classes and other papers that focus only on classes with relatively few detailed drugs; e.g., Grennan et al. (2018). In contrast, in high competition classes (those with more than 5 drugs making payments), we observe that firms make payments to prescribers who were cutting back on that firm's drug even prior to the payment (reported in Appendix Figure A.3), suggesting that in these classes, firms may be attempting to stem losses rather than spur new revenue. However, the pre-existing trend observed in these high competition classes makes the causal interpretation of the event study coefficients more difficult.

4.4 Gauging the Magnitude of our Estimates

To gauge the magnitude of our main estimates, we estimate a firm's return on investment for its payments. The following calculation should be treated as speculative because there are many important determinants excluded from the analysis or not measured precisely.

Because the vast majority of the payments in our data are small, they are likely made in the context of a detailing visit. Given that, the relevant measure of marginal costs should include the sales representative's time cost, travel costs, and the dollar cost of the payment.[16] Liu et al. (2015) presents a range of estimates related to the sales representative's costs. Using their structural model, they estimate that the marginal cost of a visit is $195.[17] Based on the Open Payments data, the average payment on these visits is approximately $18.[18] Then a rough estimate of the marginal cost of a single detailing visit is $213.[19]

To estimate the increased expenditures from a detailing visit, we must scale our estimates to account for multiple relevant factors. Medicare Part D accounts for approximately 30 percent of retail prescription expenditures in the United States (Kaiser Family Foundation, 2019). In addition, our data only include 20 percent of Part D patients. Together, these

[16]Here we abstract away from issues of divisibility such as whether the firm would need to hire an additional sales representative. Instead, we assume that we could simply increase an existing sales representative's wages without any negotiation or administrative costs.

[17]The Liu et al. (2015) estimate is $153 based on data from 2002-2004; we assume their estimate is in 2003 dollars and convert it to 2015 dollars to arrive at $195.

[18]Consulting, speaking at medical events, research, and other payments unlikely to be associated with a standard detailing visit have been excluded from this average.

[19]This estimate of the marginal cost of a single detailing visit is likely an underestimate of the average cost. Descriptive statistics from Pew Charitable Trust (2013) suggest that the average cost of a detailing visit might be as much as an order of magnitude larger.

factors suggest we need to scale up our estimates.[20] On the other hand, our measure of expenditures is not the expenditures that the pharmaceutical firms get to keep. Rebates are common and in 2016 accounted for 22 percent of raw Part D drug spending measures (Johnson et al., 2018). Consequently, we scale our estimates down by 22 percent.

In order to facilitate our calculation, we must specify a time period over which the costs and benefits are realized. For simplicity, we assume that the relevant time frame is one year. Our estimates indicate that a payment increases Part D expenditures among the 20% sample by \$121 in the first year after the payment.[21] After applying the scaling discussed previously, this suggests that expenditures to the pharmaceutical firm increased by \$1,573. Conditional on receiving a payment, physicians receive 2.8 payments in the following twelve months (including the original payment). A rough, back-of-the-envelope calculation suggests that the return on investment (ROI) is approximately 164 percent. Although this might seem quite large, it is smaller than available estimates in the literature which range from 200 - 1,700 percent (Narayanan et al., 2004; Schwartz and Woloshin, 2019). We also note that the increase in expenditure we find (about 4 percent) is smaller than that found by most previous research (e.g. 10 percent by Agha and Zeltzer (2019), 14 percent by Shapiro (2018a), or 73 percent by Grennan et al. (2018)) and so implies a smaller ROI overall than their class- or drug-specific estimates.

There are factors that would cause this estimate to be an underestimate, as well as factors that would cause it to be an overestimate. To the degree that physicians' behaviors are affected for longer than 12 months, we will underestimate the additional expenditures the firm receives in response to the detailing visit. Agha and Zeltzer (2019) find that spillovers to non-paid physicians via physician social networks contribute one-quarter of the overall impact of payments in the blood-thinner class; if this effect holds for all classes, the ROI we calculate would be an underestimate. On the other hand, it is possible that the marginal treatment effect of the next physician to be detailed would be lower than our estimates. If so, our ROI comparing estimated benefits to the marginal cost of another detailing visit will be an overestimate.

[20] More specifically, if the impact on expenditures is the same for a physician's Medicare and non-Medicare patients, we should scale our estimate up by 10/3. To account for the fact our data are a 20 percent random sample of Part D patients, we scale up by a factor of 5.

[21] This is calculated by multiplying the estimates in Table 2 by the number of months covered in each period (i.e., \$5.67 $\times$ 6 months + \$12.47 $\times$ 7 months). Because the first month is only partially treated, this time period represents somwhere between 12 and 13 months.

5 How to Payments Affect Drug Quality?

5.1 Payments and the Efficacy of Prescribed Drugs

Industry representatives have claimed that regular contact with drug firm representatives helps to keep physicians up to date on the availability and quality of new drugs. If these interactions do result in physicians having better information about which drugs are most efficacious, they may lead to an overall improvement in the quality of drugs prescribed. Alternatively, if the payments mislead physicians into incorrectly assessing the quality of drugs available, we may find a negative relationship between payment receipt and drug quality.

We evaluate whether payments lead physicians to choose more efficacious drugs using a novel dataset on drug efficacy. Together with an MD/PhD student, we identified three major therapeutic classes where there is a common and well-defined clinical endpoint for drug therapy. For each therapeutic class, we obtained a unidimensional efficacy measurement for every molecule (including generics) from the medical literature. Within the drug class of statins, our measure of efficacy for each drug is the percent reduction in LDL cholesterol associated with use of that drug observed in clinical trials; for ARBs (Angiotensin II Receptor Blockers), the outcome is the reduction in systolic blood pressure; and for atypical antipsychotics, the outcome is the reduction in the Positive and Negative Syndrome Scale.

This measure of efficacy is imperfect along a number of dimensions. First, it is a single measure of efficacy for all patients and yet there is almost certainly heterogeneity in a given drug's efficacy for different patients.[22] Because efficacy will be our dependent variable, this could bias our estimates if physicians who receive payments differentially increase use of the paid drug in patients for whom it is least effective. Second, bad clinical trial results might be censored by pharmaceutical firms (Turner et al., 2008). If firms that pay physicians censor their clinical trial results more (or less) than firms that do not pay physicians, our estimates will be biased.

Despite these drawbacks, our measures largely capture efficacy as viewed by physicians. Sullivan et al. (2014) show that when asked about drug efficacy, physicians seek information about clinical studies. In addition, a 2012 survey of more than 250 physicians found that physicians want more information about clinical studies and evidence-based medicine from their interactions with pharmaceutical sales representatives (Publicis Touchpoint Solutions, 2012). In 2011, a nationally representative survey of more than 500 physicians found that in addition to a physician's clinical knowledge and experience, one of the most important factors

[22] High-efficacy drugs may still have adverse effects on patients. Alpert et al. (2019) show the relationship between Oxycontin detailing and subsequent overdose deaths.

in drug prescribing decisions was clinical practice guidelines, which are based on clinical trial results (KRC Research, 2011). Together, these studies suggest that physicians view clinical trial results as important indicators of efficacy and actively seek this information from drug firms' representatives.

We adjust our empirical strategy to evaluate how payments affect the efficacy of prescribed drugs.[23] In particular, we allow payments to affect the physician's decision among both branded and generic drugs. The physician's generic choice could be affected either by more information about generic molecules or by increased valuation of efficacy relative to other drug characteristics. Thus, our key dependent variable is a weighted average of the efficacy of drugs the physician prescribes in the class (including generics), where the weights are the days supply of that drug by that physician in that month. This measure characterizes the overall efficacy of a physician's prescribing in a therapeutic class.

Since we are interested in the overall efficacy of prescribing in a therapeutic class, we use as our key independent variable an indicator for whether the physician has received a payment from *any* drug in the therapeutic class.[24] We find that 36% of antipsychotics prescribing arises from prescribers who have received a payment from at least one of the drugs in that class. The corresponding figures for statins and ARBs are 21% and 16% respectively.[25]

Our estimation equation is given by

$$\textit{efficacy}_{pct} = \sum_{r \neq -1} \textit{DocPaid}_{pc} \beta_r + \delta_{pc} + \delta_{ct} + \epsilon_{pct} \tag{2}$$

where $\textit{efficacy}_{pct}$ is our measure of efficacy, $\textit{DocPaid}_{pc}$ indicates whether physician p will be paid by some drug in therapeutic class c at some point in our sample, r denotes the time period relative to the time the physician is paid (if ever), δ_{pc} is a set of fixed effects for each combination of physician and therapeutic class, δ_{ct} is a set of class by month fixed effects, and ϵ_{pct} is a random error term. We normalize β_{-1} to zero, making the month preceding the

[23] We cannot use our original model, Equation (1), for this question because efficacy is a time-invariant property of a molecule. In Appendix Figure A.4 and Table A.2, we evaluate the impact of payments on expenditure and the number of patients using the three therapeutic classes where we have efficacy measures. We confirm that overall, physicians respond to payments in these TCs much as they do in the general case – by increasing total expenditure on the paying drug and increasing the number of patients taking the paying drug.

[24] In the statin and ARB classes, most of the payments over the time period arise from Crestor and Benicar, respectively. In the antipsychotics class, there are six drugs actively making payments over the time period.

[25] As in our main equation, only physicians who receive a first payment in 2014 or 2015 contribute to identification. As in the overall sample, about half of the physicians who are paid at all are paid for the first time in 2014 or 2015.

payment the reference period. With these sets of fixed effects, we are effectively running the event-study specifications separately for each therapeutic class and then aggregating across the different classes. To create a measure of efficacy comparable across classes, we standardize each therapeutic class's efficacy measure to a z-score and interpret our point estimates, β_r, as standard deviation changes in the efficacy measure.[26] In addition to estimating equation (2) with all three classes, we also estimate the equation independently for each therapeutic class. Because we need only focus on the three classes for which we have efficacy information, we are able to estimate this model using the full dataset, rather than the 50% random sample of physicians used in the expenditure analysis.

We present our main event study results in Figure 9, with summary coefficients in Appendix Table A.3. Prior to the payment, there does not appear to be any differential trend in efficacy. Immediately after the payment, there appears to be a small decline in efficacy which is sustained in the following twelve months. However, the economic magnitude is extremely small. Based on these estimates, we can reject an average effect in the twelve months following a payment any larger than a 0.01 standard deviation reduction in average efficacy.

To explore whether there is important heterogeneity in these effects across our three classes, we present the class-by-class event study results in Figure A.5. In each case, the estimates suggest that there were not large changes in average efficacy following a payment from a pharmaceutical firm. Although there is some evidence of a pre-trend in two of the figures, there is no large deviation from that trend following the payment that might suggest a reduction in efficacy.

Overall, we do not find evidence that payments lead to economically large reductions in the average quality of drugs that patients are prescribed. Nor do we find meaningful increases in average quality following a payment. Although we can not rule out the possibility that no patients were put onto less (or more) effective drugs, we can rule out large average negative (or positive) effects of payments on the quality of prescribing.

5.2 Payments and the Transition to Generics

In Part D, patients typically pay higher out-of-pocket prices for a branded drug when there exists a generic equivalent; therefore, physicians acting as good agents for their patients should transition patients to generics as soon as possible. At the same time, patent expiries represent substantial revenue losses to branded drug firms. Finding that physicians who receive payments from a drug firm disproportionately keep patients on the firm's brands

[26]More specifically, for the therapeutic class, we subtract the average efficacy (weighted by total days supply in Part D) of drugs within that class and then divide by the standard deviation of that measure.

would be evidence that physicians were privileging the drug firms' interests over their patients.[27] Previous research using distance to a drug firm's headquarters as an instrument for a physician's detailing exposure found that detailing causes physicians to shift away from generic drugs and towards branded versions of the same molecule (Engelberg et al., 2014). Such behavior would be clear evidence of payments reducing patient welfare and increasing public costs with no corresponding benefit.

We choose five major drugs that lost patent protection and faced new generic competition over our sample period: Abilify, Namenda, Celebrex, Evista, and Zyvox. Details of the five drugs are recorded in Table 5. These five drugs alone accounted for 5.5 percent of Medicare Part D expenditure in 2013, and all five were making payments to physicians over the time period. We use the full sample of physicians for this analysis because we only need to incorporate information about these five drugs and their competitors. As reported in Huckfeldt and Knittel (2011), we confirm that drug firms dramatically reduce the number of physicians receiving payments prior to generic entry.[28]

We calculate the generic efficiency rate for physicians who ever receive payments for the branded version of the drug and those who never did in the first six months after the onset of generic competition. The generic efficiency rate is the standard measure of the penetration of generic drugs in a market and is simply the ratio of the days supply from generic suppliers and the total days supply of the molecule. Generic efficiency is zero prior to generic entry and generally rises quickly as generic substitution takes place.

Figure 10 shows the generic efficiency rate over the first six months of generic competition for the five case studies. For example, in panel (a), we see that the share of the days supplied of aripiprazole that is generic rises sharply from 0 in April 2015, leveling out at about 70 percent six months later. Panels (b)-(e) show similar findings for the four other drugs which lost patent protection during our sample. While we do not attempt to explain why generic efficiency does not rise to one,[29] it is clear that generic efficiency rises at least as quickly among paid physicians as it does among physicians who were never paid. In four of five

[27]Physicians can override automatic substitutions of a generic for the name-brand drug by marking the prescription "Dispense as Written" (see Hellerstein, 1998). Patients can also elect to override generic subsitution at the pharmacy.

[28]The number of payments over the entire sample period is reported for all five drugs in Appendix Figure A.6. For Celebrex, Evista, and Zyvox, payments drop sharply to zero right around the time of generic entry. For Namenda, which as discussed below was trying to extend its drug line via Namenda XR, payments for original Namenda fell to essentially zero about a year earlier. While payments for Abilify fall by about three-quarters, they do not reach zero over the sample period. Over the sample period Otsuka Pharmaceuticals was promoting a once-monthly injectable formulation of aripiprazole, Abilify Maintena, and it is possible that some encounters related to Abilify Maintena were described as Abilify in the Open Payments dataset.

[29]Generic efficiency may remain below one if either patients or physicians do not view the generic as perfectly substitutable.

cases, paid physicians transition more quickly than physicians who were never paid.

A drug firm facing generic entry will sometimes use direct-to-physician marketing to support a "line extension" strategy by which they heavily promote a newly-introduced distinct drug formulation just prior to generic entry in the original drug. Individuals who are taking the new formulation are not subject to automatic generic substitution at the pharmacy. For example, Actavis[30] introduced an extended-release formulation of Namenda (Namenda XR) prior to the expiry of the original Namenda (Capati and Kesselheim, 2016). Namenda XR needed to be taken only once per day, while the original formulation needed to be taken twice per day.[31] While promotional activities were greatly reduced for original Namenda over our sample period, leading to a low share of detailed physicians at expiry, Actavis detailed heavily for Namenda XR. More than 11% of Namenda XR physicians received a payment related to the drug over the sample period.

We provide suggestive evidence on the line extension strategy for Namenda XR in Figure 11. We add the days supply of Namenda XR to the denominator of the generic efficiency rate and report the share of all memantine prescribing that is generic memantine (Figure 11a) and the share that is Namenda XR (Figure 11b). These figures show that those who were ever paid for Namenda or Namenda XR indeed prescribe more Namenda XR, and also prescribe less generic memantine. By the end of 2015, the prescribing of those who were never paid for Namenda or Namenda XR is approximately 6% branded Namenda, 37% Namenda XR, and 57% generic menantine. Those who were paid for Namenda or Namenda XR are actually prescribing less branded Namenda (3%), but are prescribing much more Namenda XR (64%).

This analysis does not use the physician fixed effects we used in our other analyses to account for the targeting of payments to physicians. However, Figure 11 does not compare the overall prescribing volume of physicians who receive payments to those that do not; instead, the figure shows how the composition of prescribing varies among three potential forms (original brand, generic, and extended release brand). The higher prescribing of Namenda XR among those who receive related payments could only be attributable to selection if Actavis targeted physicians with an especially high preference for the convenience of a once-daily formulation. Thus, we conclude that those who were ever paid for Namenda or Namenda XR were more likely to prescribe extended formulations, consistent with the line extension

[30]Forest Pharmaceuticals was the original maker of Namenda and introduced Namenda XR in 2014. Actavis acquired Forest Pharmaceuticals later that year. For simplicity, we refer to Actavis, since they were the patent holder at the time of memantine generic entry.

[31]As noted, there was also an extended-release version of Abilify, Abilify Maintena. However, a once-monthly injectable formulation does represent a distinct advantage over an oral daily formulation for a drug where adherence is a significant challenge. Consequently, we focus our analysis on Namenda XR which still required daily dosing.

strategy.

6 Conclusion

Activists who favor limiting physician and pharmaceutical industry interactions characterize these relationships as "bribes and kickbacks," while industry advocates simultaneously describe such interactions as educational tools that benefit patients. Our analysis in this papers suggests neither characterization is wholly accurate.

Using detailed information on the timing of payments and accounting for the selection of payments to physicians, we find that physicians who are paid by a drug firm have similar prescribing trends to unpaid physicians prior to the payment, but increase the number of patients and expenditures on the marketed drug after the payment occurs. This increase in drug usage that occurs after a payment is substantial, representing a 4% increase in expenditures. If a physician receiving a payment for one drug also receives a payment for a competing drug, it partially offsets the estimated increase.

We examine whether these expenditure changes are accompanied by reductions in drug quality. First, for three large classes of drugs, we collected data from the medical literature on a unidemensional quality measure, such as the reduction in LDL cholesterol observed in clinical trials, for each drug. Using this efficacy measure, we find that drug firm interactions reduce drug quality, but that this effect is very small. Our confidence intervals allow us to rule out reductions in quality larger than 1/100th of a standard deviation, indicating that such quality changes are unlikely to be clinically meaningful. We also examine whether physicians who are paid by a pharmaceutical company keep their patients on the branded version of a molecule even when a generic version becomes available. We find no evidence that paid physicians transition their patients to generics more slowly, although we do see that they are more likely to put their patients on (branded) extended release versions of a molecule when a patent expiry occurs for the original version.

Overall, our results suggest that costs do increase as a result of marketing encounters between drug firms and physicians. At the same time, our results on drug quality are mixed; we do not find clear evidence that such payments are harmful to patients, only that they do not seem to be obviously helpful. The extent to which physician and drug firm interactions are actually welfare reducing represents a potentially useful area for future research.

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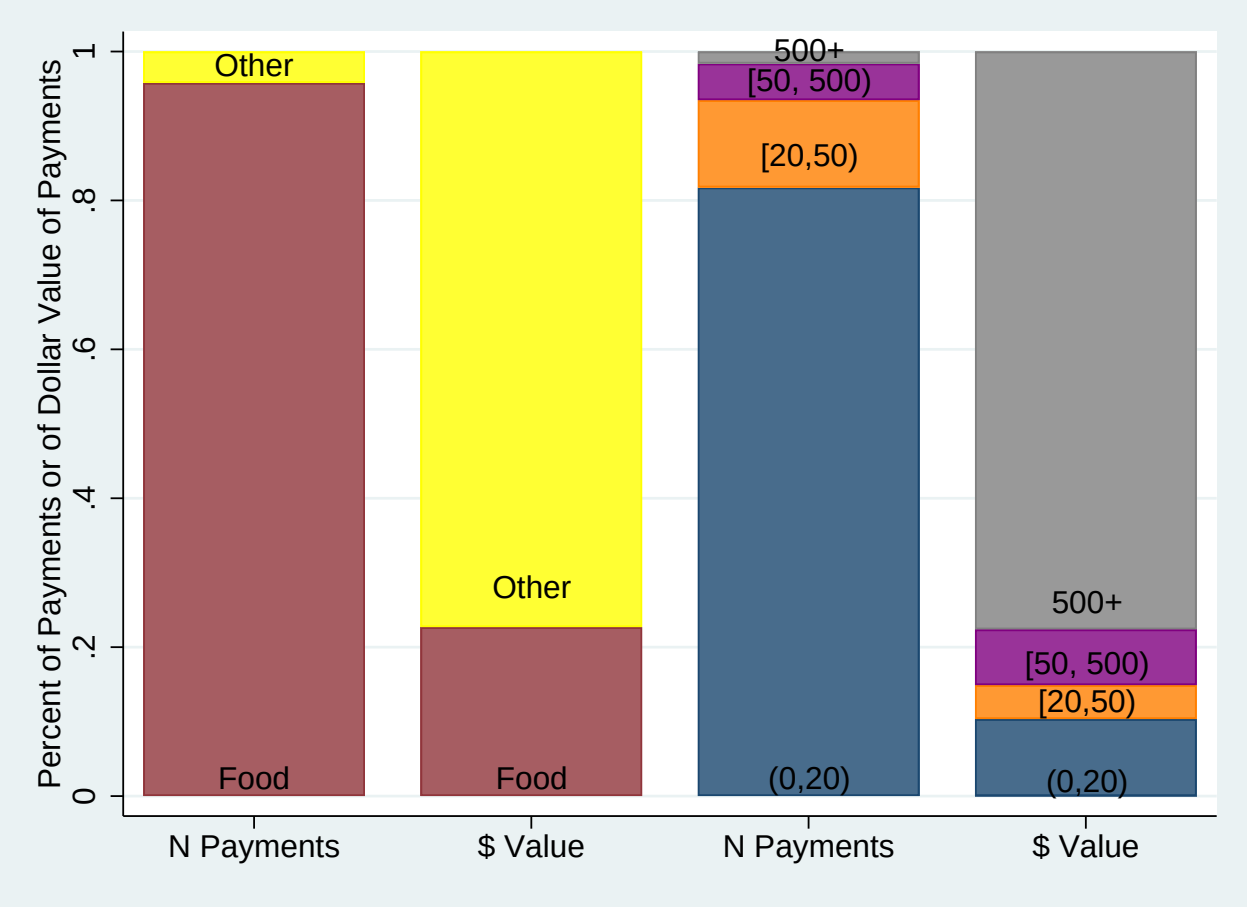
Figure 1: Summary Statistics: Distribution of Payments by Type and Amount



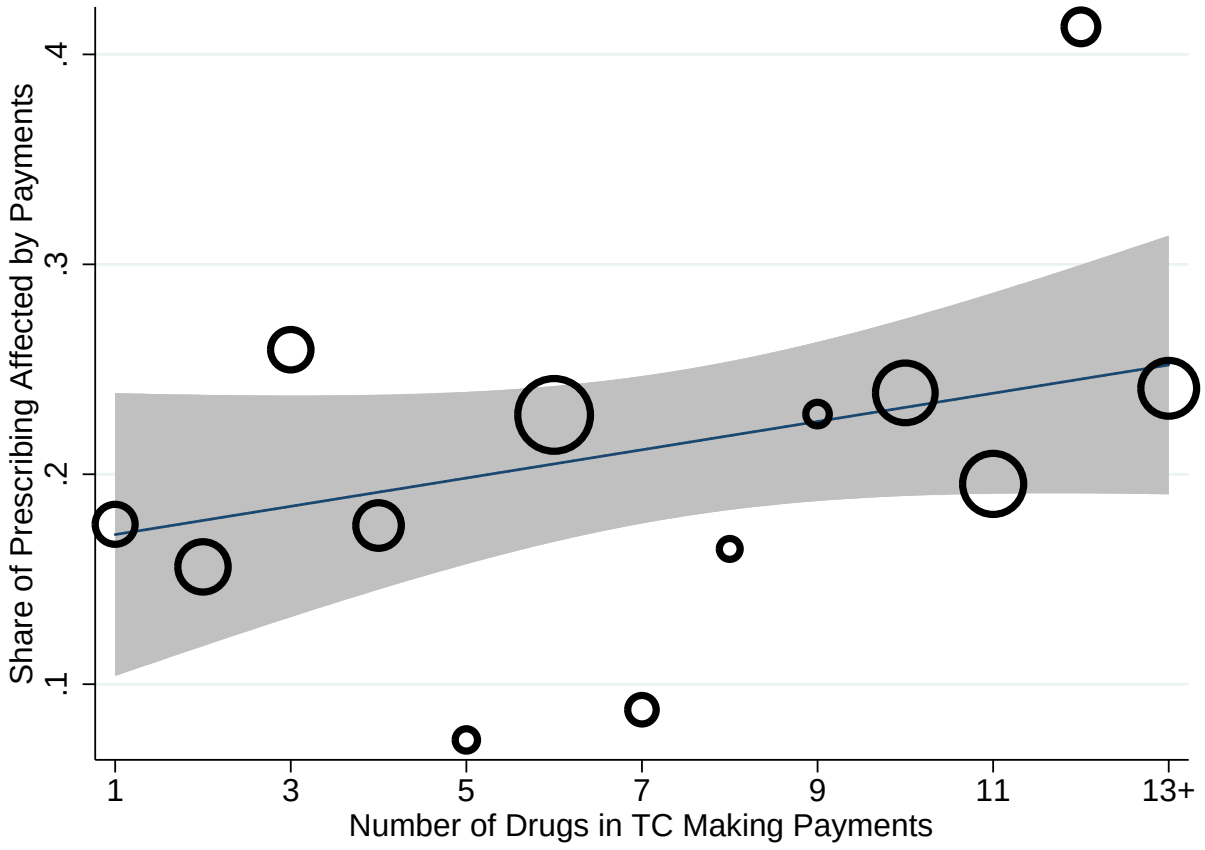
This figure depicts the share of payments that are an in-kind transfer of food or beverage (first bar) vs. all other payment types. The second bar weights the payments by the dollar value. The third bar shows the share of payments in each of four size categories, and the fourth bar shows the same shares when weighted by dollar value.

Table 1: Summary Statistics

Drug	Indication	% of Part D Expenditure	% of Expenditure Affected by Payments	% of Prescribing Physicians Ever Paid	% of Prescribing Physicians First Paid in 14 or 15
All Drugs In Analytic Dataset		63	21	22	14
Lantus	Diabetes	3.3	24	16	9
Harvoni	Hep C	2.3	18	23	23
Crestor	High Cholesterol	2.3	23	18	9
Advair	Asthma/COPD	2.2	10	10	10
Spiriva	Asthma/COPD	1.9	26	21	11
Abilify	Mental Illness	1.9	28	24	8
Januvia	Diabetes	1.6	19	21	15
Sovaldi	Hep C	1.3	21	21	9
Lyrica	Nerve Pain	1.3	25	18	9
Novolog	Diabetes	1.2	27	27	17
Levemir	Diabetes	1.2	37	37	21
Humira	Immune Conds	1.1	45	66	27
Namenda	Dementia	1.1	2	1	0
Enbrel	Immune Conds	1.1	39	50	19
Xarelto	Blood Clots	1	44	45	24
Zetia	High Cholesterol	1	16	18	13
Gleevec	Cancer	.9	6	13	5
Symbicort	Asthma/COPD	.9	30	28	15
Oxycontin	Pain	.8	23	21	12
Humalog	Diabetes	.8	26	29	15

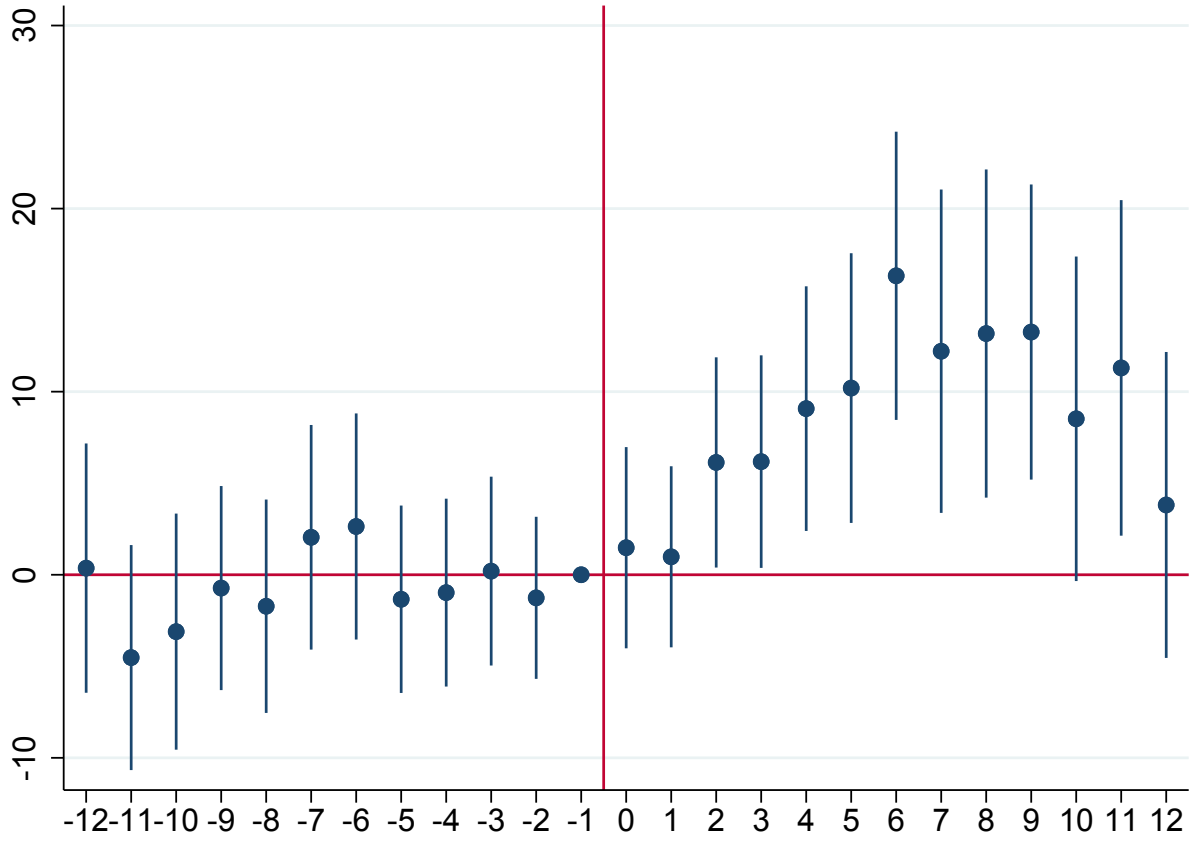
This table describes the prevalence of payments in Part D overall and for the twenty drugs with the largest total expenditure over the sample period. The third column describes the share of Part D expenditure. The next column describes the share of expenditure where the physician has received a payment for the drug at the time of prescribing. The next column describes the share of those who ever prescribe the drug who ever receive a payment for the drug. Finally, we report the share of prescribing physicians who are first paid in 2014 or 2015, since these physicians identify our estimates given fixed effects.

Figure 2: Summary Statistics: Share of Prescribing Affected by Payments and Number of Paying Products in the Therapeutic Class



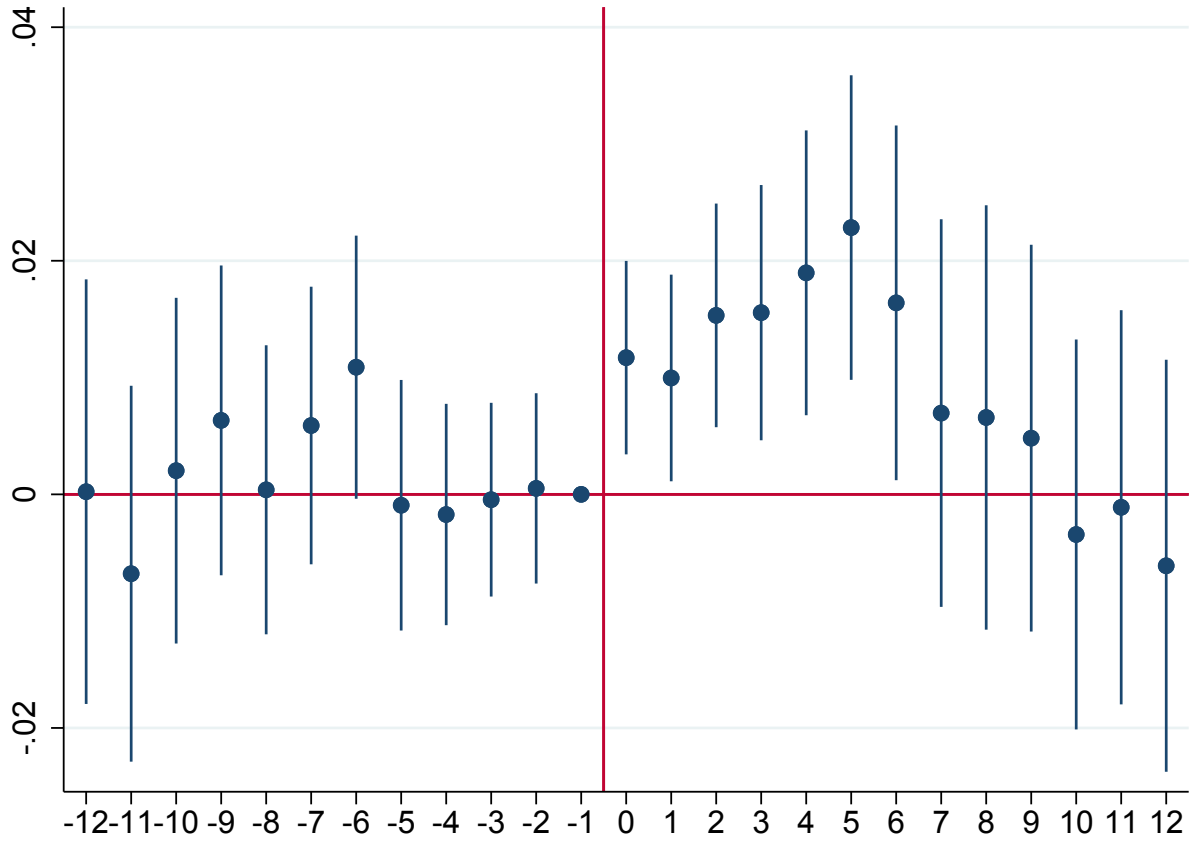
The x-axis in this figure counts the number of drugs in each therapeutic class that are making payments to any prescriber. The y-axis in this figure measures the average share of prescribing of those drugs that is affected by payments (i.e., where a prescriber has received a payment prior to prescribing). The size of the marker is the total expenditure represented by the observation. The least squares line (weighted by expenditure) and its 95% CI (shaded area) are also reported.

Figure 3: Impact of a Payment on Drug Expenditure



Coefficients and 95% confidence intervals from estimation of Equation 1 are presented. The dependent variable is the total expenditure by a physician's patients on a drug in a given month. The omitted time period is the month prior to the payment.

Figure 4: Impact of a Payment on Number of Patients Taking the Drug



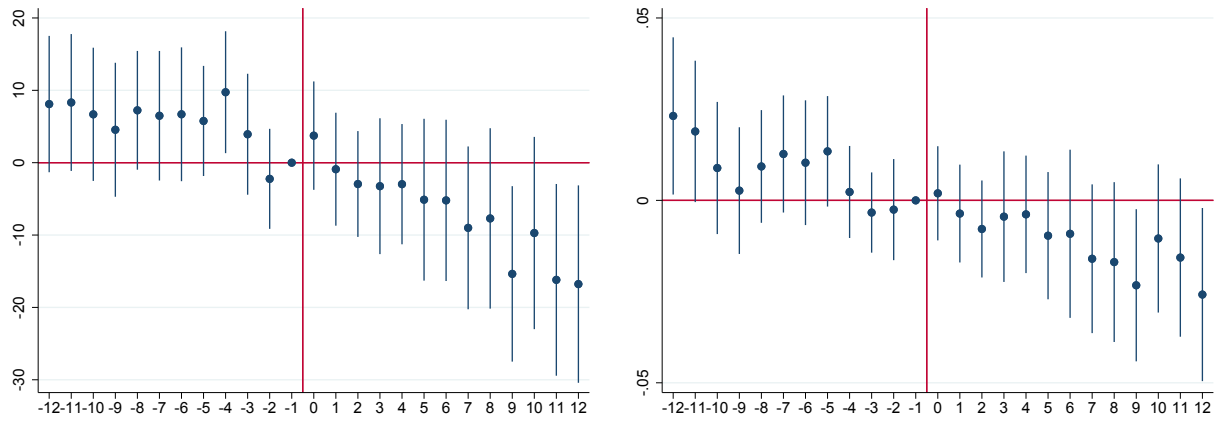
Coefficients and 95% confidence intervals from estimation of Equation 1 are presented. The dependent variable is the physician's number of patients filling a prescription for a drug in a given month. The omitted time period is the month prior to the payment.

Table 2: Estimated Impacts of Payments

	Expenditure	Number of Patients
	(1)	(2)
Months 0 - 5	5.67**	0.016***
	(2.42)	(0.004)
Months 6 - 12	12.47***	0.005
	(3.68)	(0.008)
Mean dep. var.	$238	1.25
No. physicians	494,525	494,525
Observations	190,511,352	190,511,352

Dependent variable is given in column heading. Estimates are linear combinations of event study estimates presented in Figures 3 and 4. The month prior to the payment is the reference group. Standard errors are clustered by physician.

Figure 5: Impact of a Payment by Competing Drug



(a) Expenditure

(b) Number of Patients

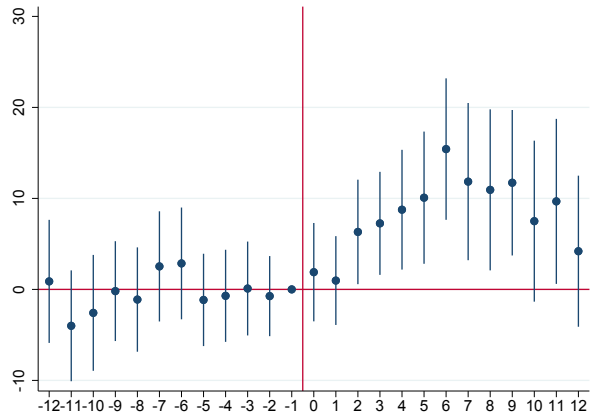
This figure reports the impact on drug d outcomes of receiving a payment from a competing drug d' in the therapeutic class, represented by the α coefficients in Equation 1. The dependent variables are total expenditure on drug d (Panel a) and number of patients taking drug d (Panel b). The x-axis measures the months before and after the payment from drug d'. Estimated coefficients and 95% confidence intervals are presented. The omitted time period is the month prior to the payment.

Table 3: Estimated Impacts on Drug d of a Competing Drug's Payment

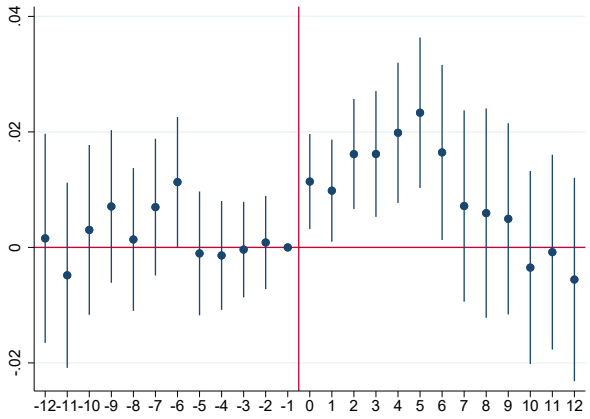
	Expenditure	Number of Patients
	(1)	(2)
Months 0 - 5	-1.91	-0.005
	(3.52)	(0.006)
Months 6 - 12	-10.53***	-0.015
	(5.30)	(0.009)
Mean dep. var.	$238	1.25
No. physicians	494,525	494,525
Observations	190,511,352	190,511,352

Dependent variable is given in column heading. Estimates are linear combinations of event study estimates presented in Figure 5. The month prior to the payment is the reference group. Standard errors are clustered by physician.

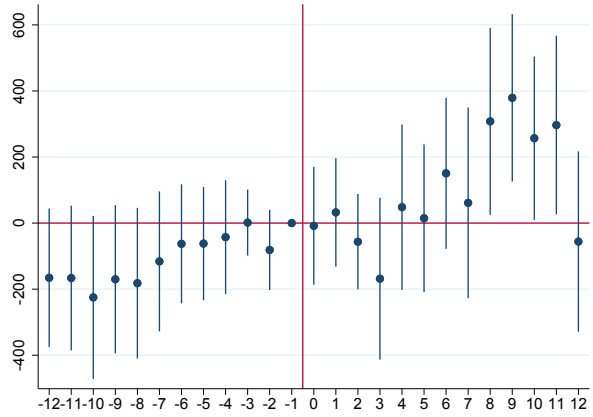
Figure 6: Impact of a Payment on Drug Expenditure by Payment Size



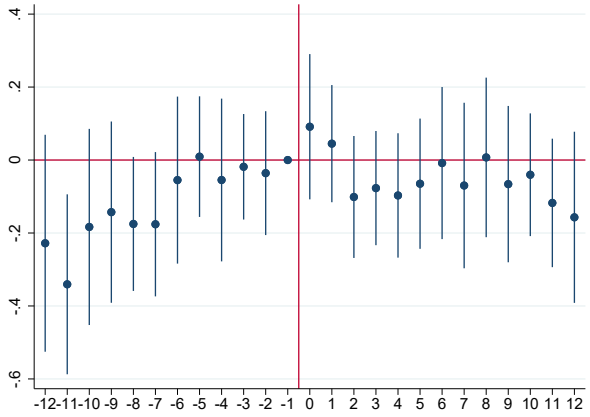
(a) Expenditures, Payment $<$ \$500



(b) # Patients, Payment $<$ \$500



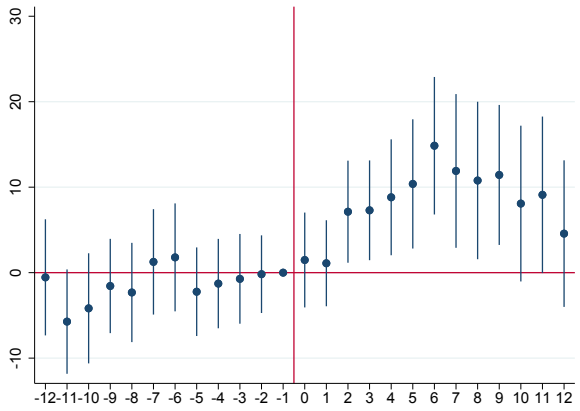
(c) Expenditures, Payment $\geq$ \$500



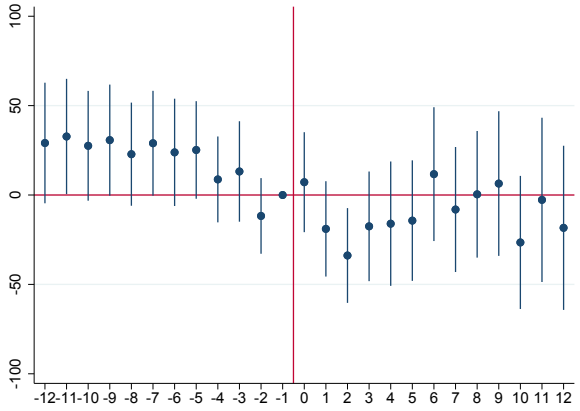
(d) # Patients, Payment $\geq$ \$500

Coefficients and 95% confidence intervals from the estimation of Equation 1 are presented. The dependent variable is the total expenditure by a physician's patients on a drug in a given month. The omitted time period is the month prior to the payment. Estimates based on payments that were less than \$500 are presented in panel (a); estimates based on payments that were at least \$500 are presented in panel (b).

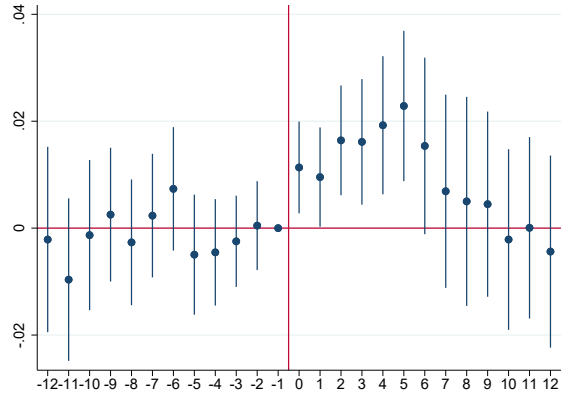
Figure 7: Impact of a Payment by Payment Type



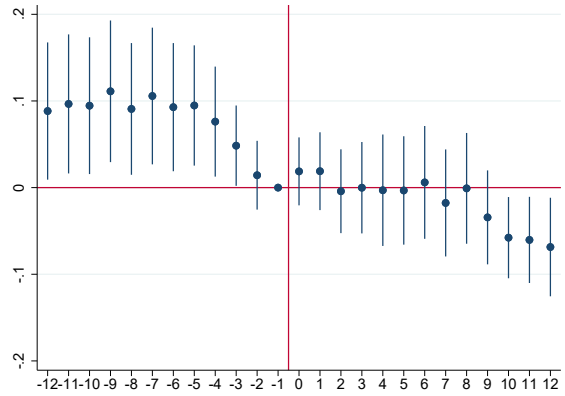
(a) Impact of Food Payment on Expenditure



(b) Impact of Other Payment on Expenditure



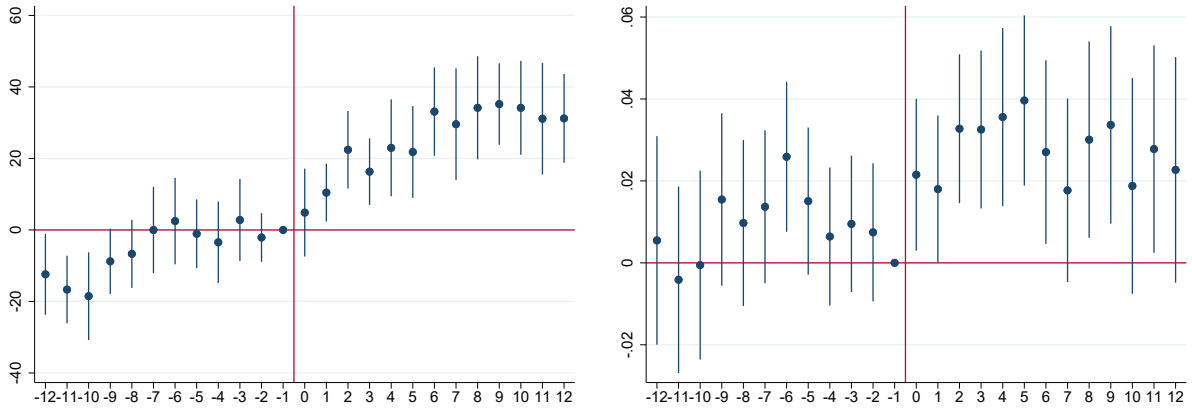
(c) Impact of Food Payment on # Patients



(d) Impact of Other Payment on # Patients

Coefficients and 95% confidence intervals from the estimation of Equation 1 are presented. The dependent variable is the total expenditure (panels a and b) or number of patients (panels c and d) for a physician-drug-month. The omitted time period is the month prior to the payment. Panels a and c report estimates based on food-related payments. Panels b and d report estimates based on all other payments excluding food, primarily speaking at continuing medical education events, consulting, and travel.

Figure 8: Impact of a Payment in Low Competition Classes



(a) Expenditure

(b) Number of Patients

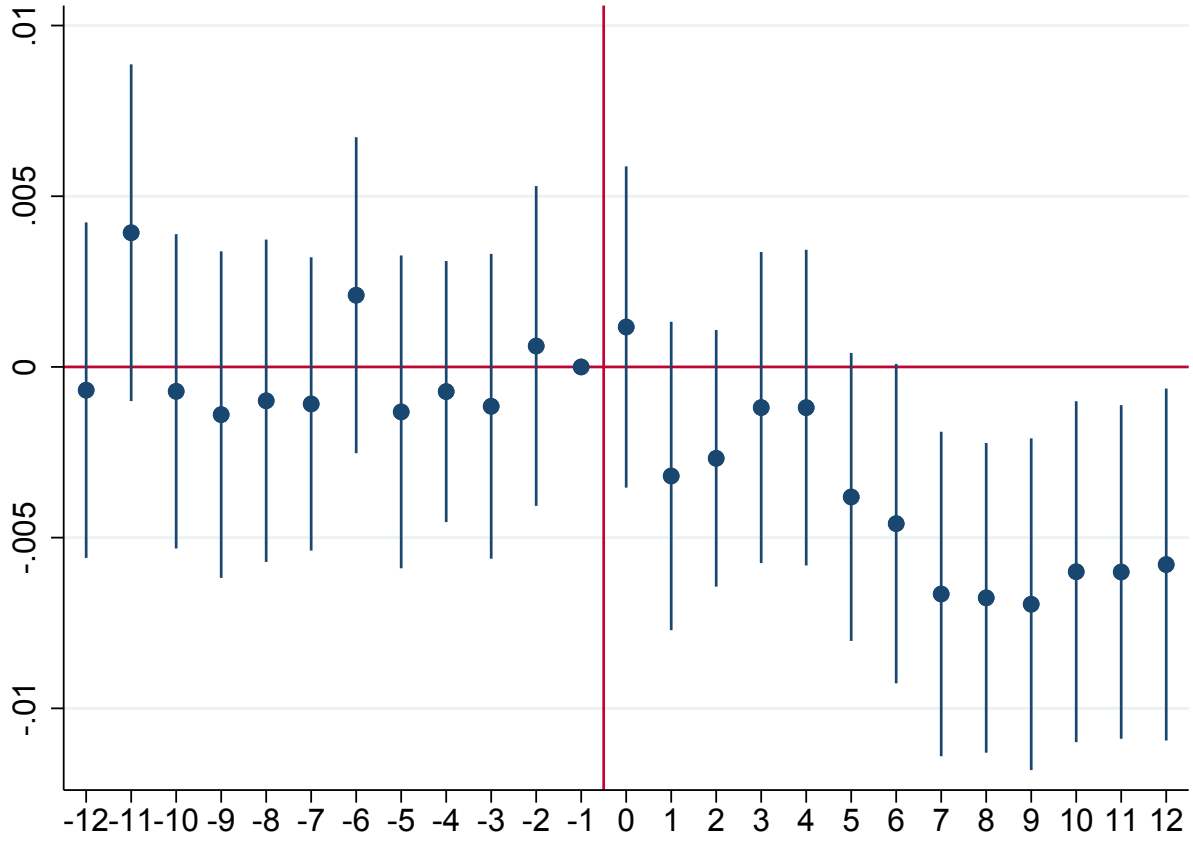
Estimated coefficients and 95% confidence intervals are presented. The dependent variable is the total expenditure by a physician's patients on a drug in a given month. The omitted time period is the month prior to the payment. Estimates based on payments made in therapeutic classes where few (five or fewer) other products are marketed.

Table 4: Heterogeneity in Estimated Impacts of Payments

	Expenditure	Number of Patients
	(1)	(2)
Panel A: Payment $<$ \$500		
Months 0 - 5	5.88**	0.016**
	(2.39)	(0.004)
Months 6 - 12	11.18***	0.005
	(3.66)	(0.008)
Mean dep. var.	\$236	1.24
Panel B: Payment $\geq$ \$500		
Months 0 - 5	-22.95	-0.03
	(82.57)	(0.06)
Months 6 - 12	242.10***	-0.05
	(91.60)	(0.08)
Mean dep. var.	\$233	1.31
Panel C: Food payment		
Months 0 - 5	6.03**	0.016***
	(2.47)	(0.005)
Months 6 - 12	11.03***	0.005
	(3.78)	(0.008)
Mean dep. var.	\$238	1.24
Panel D: Other payment		
Months 0 - 5	-15.57	0.005
	(12.54)	(0.024)
Months 6 - 12	-3.14	-0.028
	(16.07)	(0.024)
Mean dep. var.	\$236	1.29
Panel E: Low competition class (5 or fewer paying drugs)		
Months 0 - 5	16.46***	0.030***
	(4.28)	(0.008)
Months 6 - 12	32.88***	0.026***
	(5.13)	(0.011)
Mean dep. var.	\$206.18	1.76

Dependent variable is given in column heading. Estimates are linear combinations of event study estimates presented Figures 6, 7, and 8.

Figure 9: Impact of a Payment on Average Efficacy



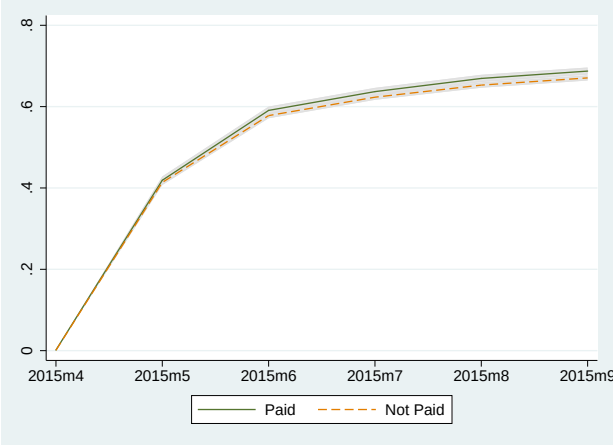
Estimated coefficients and 95% confidence intervals are presented. The dependent variable is the standardized efficacy measure for a physician in a given therapeutic class and month. The omitted time period is the month prior to the payment.

Table 5: Generic Entry Case Studies

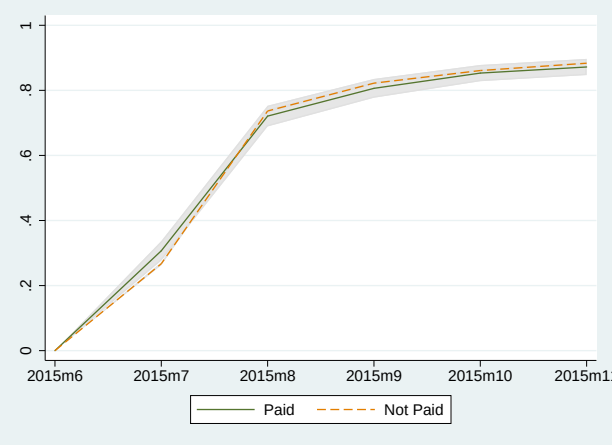
Brand Name	Molecule	Drug Maker	Indication	% of 2013 Part D Expenditure	% Physicians Ever Paid	Generic Onset
Abilify	aripiprazole	Otsuka	Mental Illness	2.2	18.3	2015m4
Namenda	memantine	Actavis	Dementia	1.7	1.4	2015m6
Celebrex	celecoxib	Pfizer	Pain	1.0	16.7	2014m11
Evista	raloxifene	Eli Lilly	Osteoporosis	0.5	1.0	2014m3
Zyvox	linezolid	Pfizer	Bacterial Infection	0.1	11.5	2015m5

This table provides details for the five case studies of generic entry evaluated in Section 5.2.

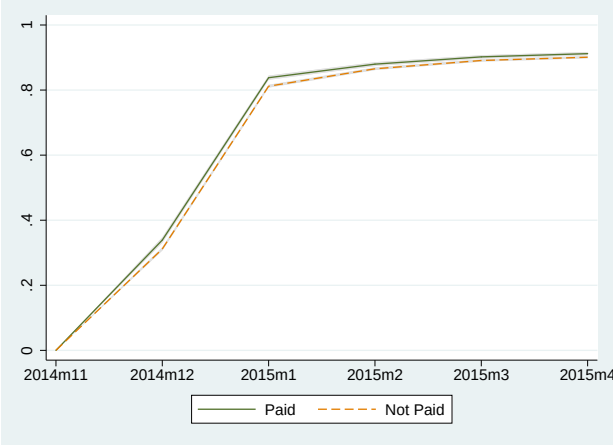
Figure 10: Generic Efficiency in the First Six Months After Patent Expiry



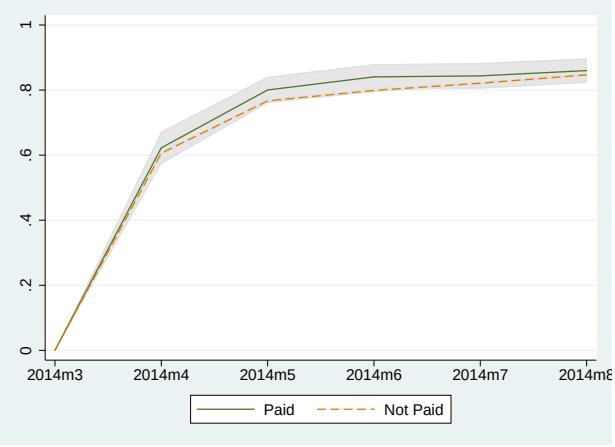
(a) Abilify



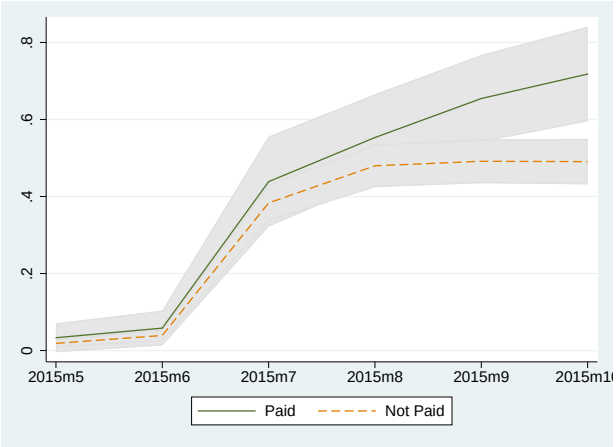
(b) Namenda



(c) Celebrex



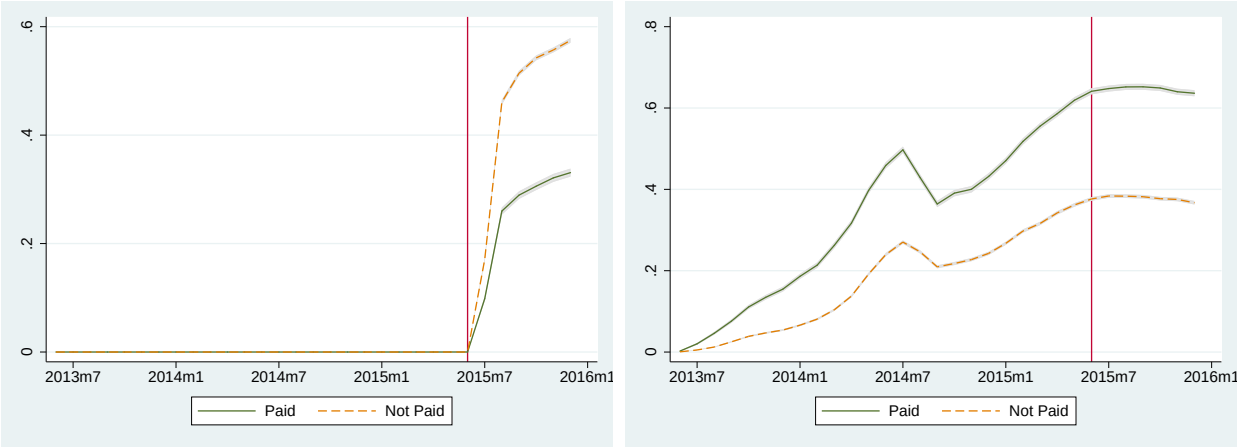
(d) Evista



(e) Zyvox

Each figure shows the generic efficiency, measured as the share of days supply for each molecule supplied in the generic form, for the first six months of generic competition for each of five molecules experiencing generic entry during the sample period. Physicians who previously received a payment for the branded drug are represented by the solid green line; physicians who never received a related payment are represented by the dashed gold line. 95% confidence intervals are reported in gray.

Figure 11: Generic Memantine and Namenda XR as a Share of All Memantine



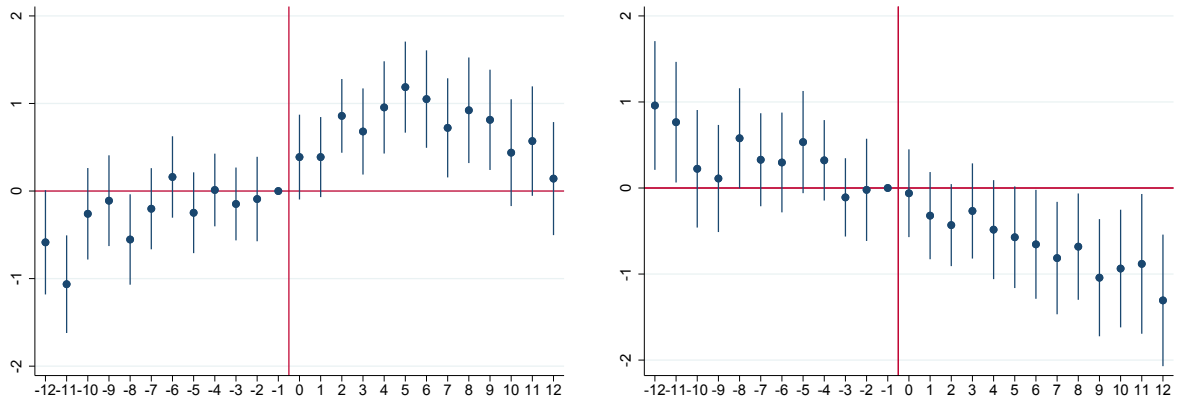
(a) $\frac{\text{generic Memantine}}{\text{generic Memantine+ Namenda + Namenda XR}}$ (b) $\frac{\text{NamendaXR}}{\text{generic Memantine+ Namenda + Namenda XR}}$

This figure reports the distribution of all days supplied of the molecule memantine across three forms: branded Namenda, branded Namenda XR, and generic memantine. Panel a reports the share of days of generic memantine in the total prescribing of the molecule, separately for physicians ever receiving a payment for Namenda or Namenda XR (solid green) and physicians who never receive such a payment (dashed gold). Panel b reports the share of days of Namenda XR in the total days supplied of the molecule, separately for paid and unpaid physicians. 95% confidence intervals are reported in gray.

Appendices

A. Additional Figures and Tables

Figure A.1: Impact of a Payment or Competing Firm's Payment on the Total Days Supplied of the Drug



(a) Impact of Own Payment

(b) Impact of Competing Firm's Payment

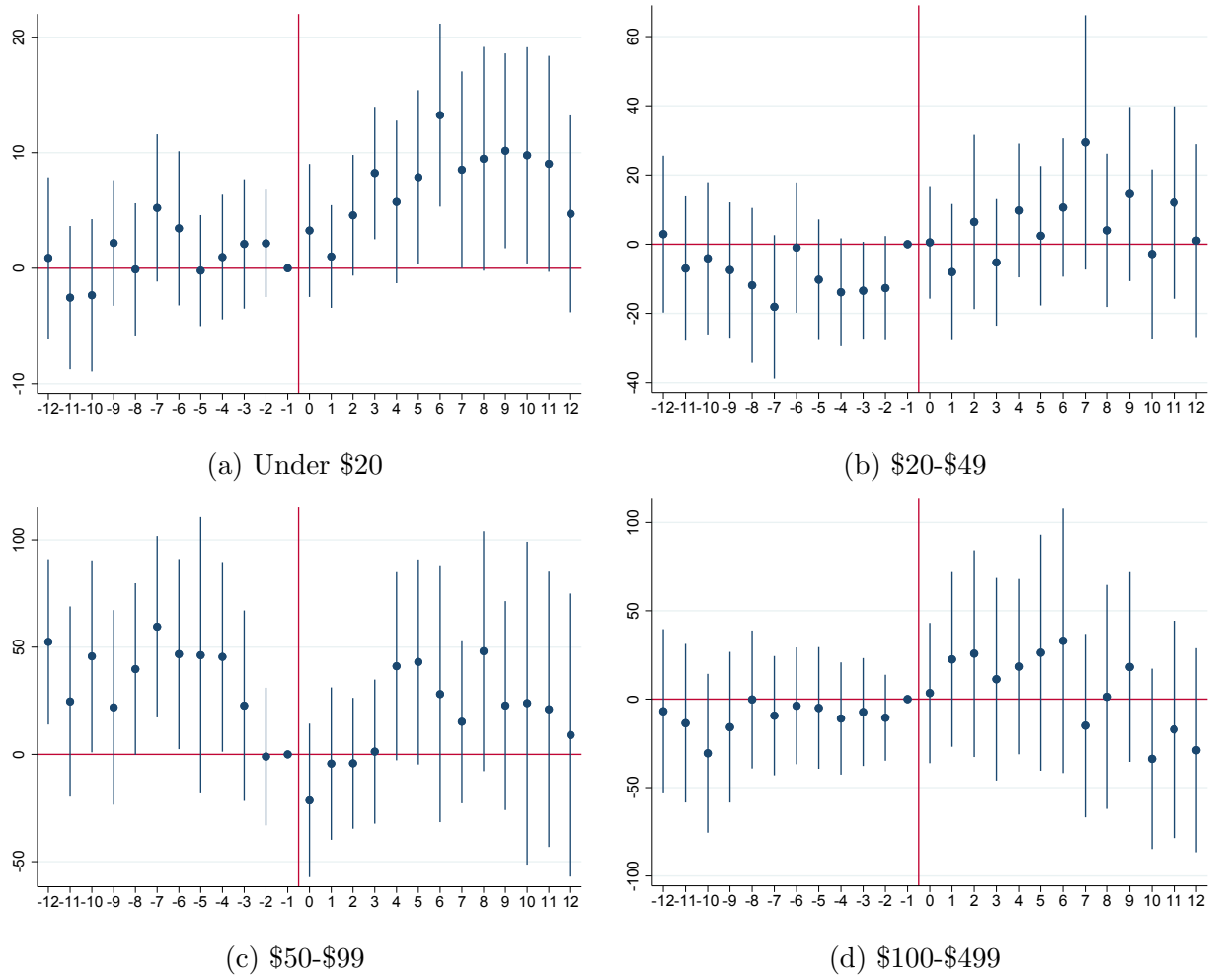
Coefficients and 95% confidence intervals from the estimation of Equation 1 are presented. The dependent variable is the physician's total number of days of the drug supplied in a given month. The omitted time period is the month prior to the payment.

Table A.1: Estimated Impacts of Payments on Total Days Supplied

	Impact of Own Payment	Impact of Rival Payment
Months 0 - 5	0.743***	-0.356*
	(0.194)	(0.210)
Months 6 - 12	0.753***	-0.835***
	(0.244)	(0.285)
Mean dep. var.	53.42	53.42
No. physicians	494,525	494,525
Observations	190,511,352	190,511,352

Dependent variable is physician's total number of days of the drug supplied in a given month. Estimates are linear combinations of event study estimates presented in Figure A.1. The month prior to the payment is the reference group. Standard errors are clustered by physician.

Figure A.2: Impact of a Payment on Drug Expenditure by Payment Value



(a) Under $20

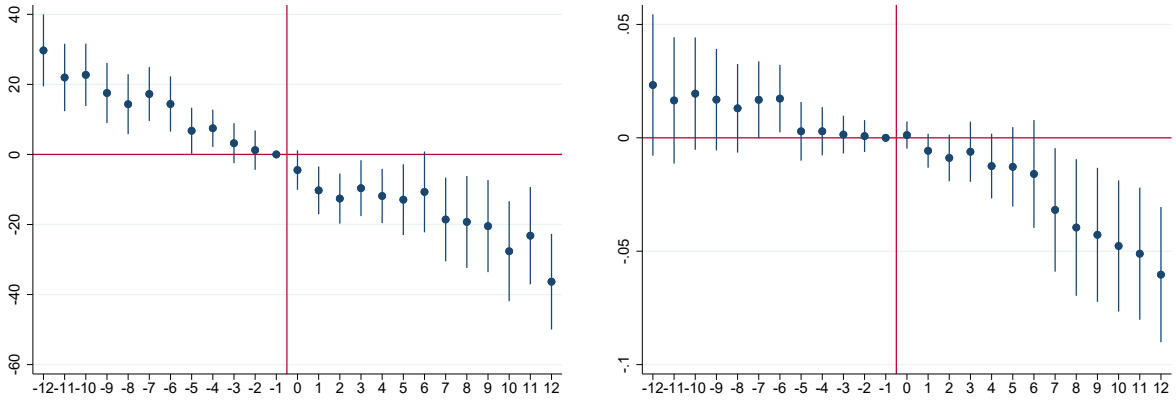
(b) $20-$49

(c) $50-$99

(d) $100-$499

Coefficients and 95% confidence intervals from the estimation of Equation 1 are presented. Each panel compares physician-drug pairs receiving a payment in the stated range with those receiving no payment. The dependent variable is the total expenditure by a physician's patients on the drug in a month. The omitted time period is the month prior to the payment.

Figure A.3: Impact of a Payment on Expenditure and Patients: High Competition Classes

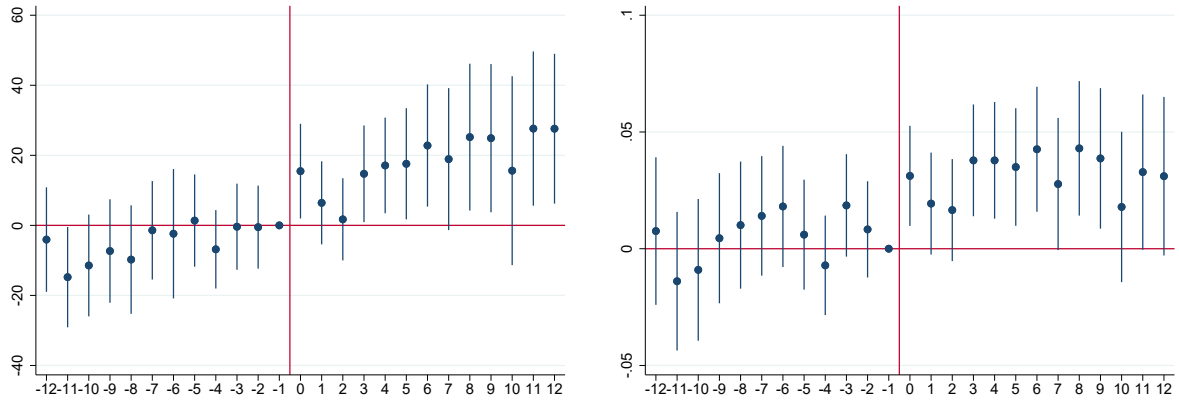


(a) Expenditure

(b) Number of Patients

Estimated coefficients and 95% confidence intervals from the estimation of Equation 1 are presented are presented for therapeutic classes with more than five drugs making payments over the sample period. The dependent variable is the total expenditure of a physician's patients on a drug (panel (a)) and the number of patients on that drug (panel (b)) in a given month. The omitted time period is the month prior to the payment.

Figure A.4: Impacts of Payments on Expenditure and Patients: Therapeutic Classes for Efficacy Analysis



(a) Expenditure (b) Number of Patients

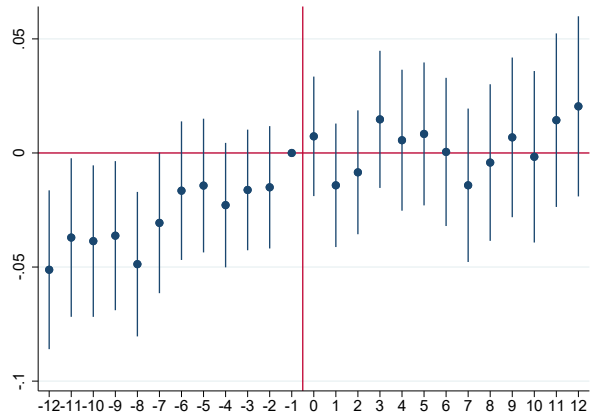
Coefficients and 95% confidence intervals from the estimation of Equation 1 are presented for the three therapeutic classes used in the efficacy analysis in Section 5.1. The dependent variable is the total expenditure of a physician's patients on a drug (panel (a)) and the number of patients on that drug (panel (b)) in a given month. The omitted time period is the month prior to the payment.

Table A.2: Impacts of Payments on Expenditure and Patients: Therapeutic Classes for Efficacy Analysis

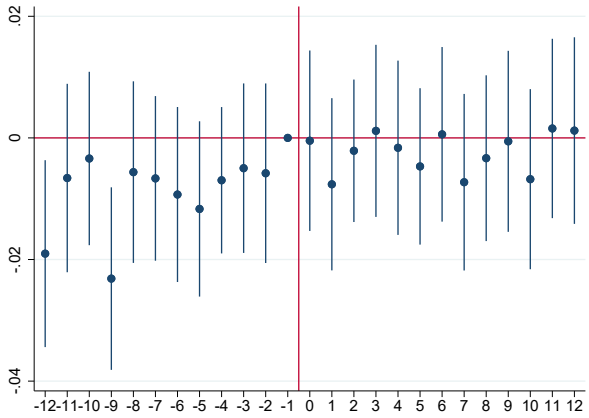
	Expenditure	Number of Patients
	(1)	(2)
Months 0 - 5	12.17**	0.0296***
	(5.02)	(0.009)
Months 6 - 12	22.51**	0.034***
	(9.77)	(0.013)
Mean dep. var.	$249.3	1.90
No. physicians	228,261	228,261
Observations	20,932,596	20,932,596

Dependent variable is given in column heading. Estimates are linear combinations of event study estimates presented in Figure A.4. The month prior to the payment is the reference group. Standard errors are clustered by physician.

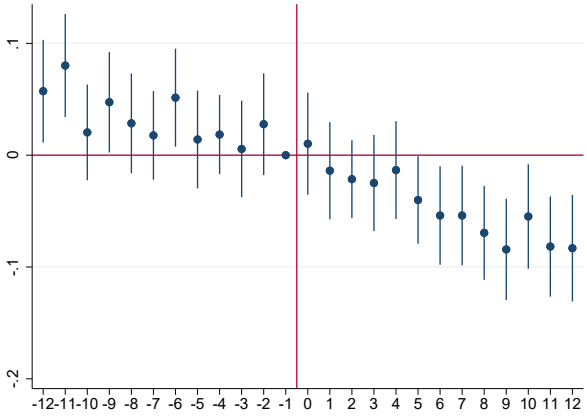
Figure A.5: Impact of a Payment on Average Efficacy by Individual Therapeutic Class



(a) Antipsychotics



(b) ARBs



(c) Statins

Coefficients and 95% confidence intervals from the estimation of Equation 2 are presented independently for each therapeutic class. The dependent variable is the raw efficacy measure for each therapeutic class (PANSS for antipsychotics, reduction in blood pressure for ARBs, and reduction in LDL for statins). The omitted time period is the month prior to the payment.

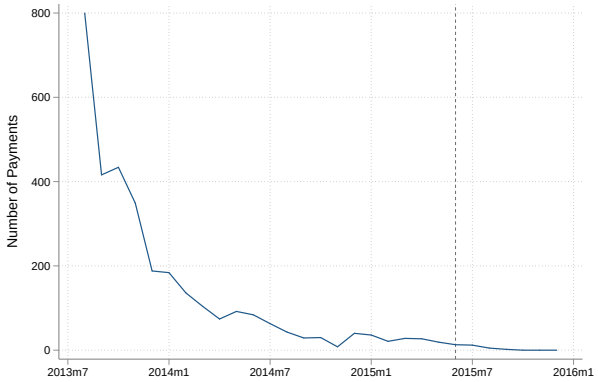
Table A.3: Impact of Payments on Drug Efficacy

	Overall Drug Efficacy (Std Deviations)	Anti-psychotics (Improvement in PANSS)	Statins (% Reduction in LDL)	Angiotensin II Receptor Blockers (Reduction in Systolic BP)
Months 0 - 5	-0.0018	0.0022	-0.0172	-0.0026
	(0.0017)	(0.0115)	(0.0161)	(0.0053)
Months 6 - 12	-0.0062***	0.00027	-0.0663***	-0.0026
	(0.0019)	(0.0149)	(0.0176)	(0.0.0058)
Mean dep. var.		13.92	37.44	9.22
No. physicians	496,834	210,249	421,989	316,760
Observations	18,128,779	3,172,059	8,672,558	6,284,162

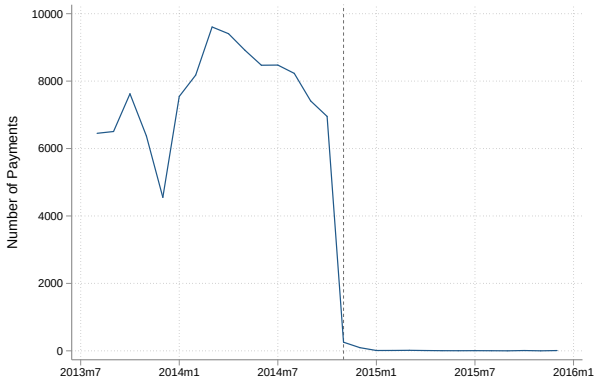
Dependent variable is given in column heading. Estimates are linear combinations of event study estimates presented in Figure A.5. The month prior to the payment is the reference group. Standard errors are clustered by physician.

Figure A.6: Number of Payments Around Patent Expiries

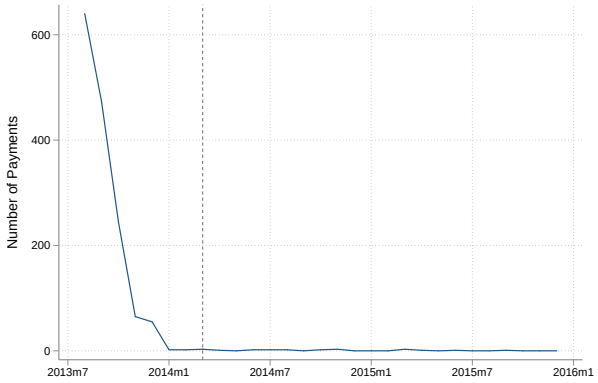
(a) Abilify



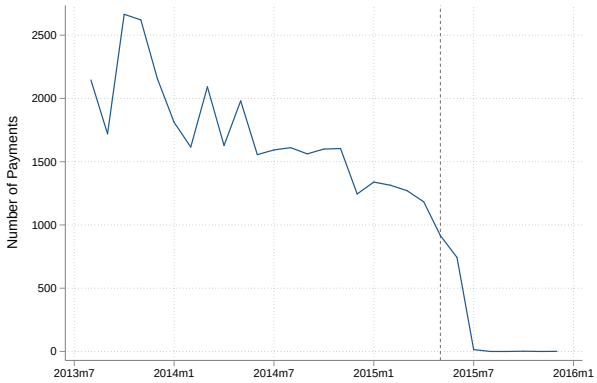
(b) Namenda



(c) Celebrex



(d) Evista



(e) Zyvox

Each figure shows the number of payments recorded for five molecules experiencing generic entry over the full sample period. The vertical dashed line denotes the month of patent expiry.