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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 payments 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. Next, 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. In addition, using hand-collected efficacy data on three major therapeutic classes, we show that drug quality is largely unaffected by the receipt of payments.

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1 Introduction

More than 85 percent of drug firms' marketing expenditures are targeted at influencing physicians (Pew Charitable Trust, 2013). These marketing expenditures fund face-to-face 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 physicians' prescribing decisions. "The doctors are manipulated by... what amounts to bribery from the drug companies," states the influential critic Marcia Angell; "there is a conflict of interest there"(PBS Frontline, 2002). However, drug firms may target payments at physicians who are *ex ante* most likely to prescribe the drug, making 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 these marketing encounters inform physicians about 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 interactions between drug firms and physicians affect the amount the promoted drug is prescribed, transitions to generic versions of branded drugs, and the quality of prescribed drugs. Our analysis links the Open Payments dataset—a comprehensive database of monetary and in-kind payments that drug firms made to physicians between 2013 and 2015[1]—to prescription data for a large panel of Medicare Part D enrollees. 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.

We examine prescribing behavior at the monthly level to identify abrupt changes in prescribing that occur right after a physician receives a payment related to the promoted drug. We use an event study approach that 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 (Homer et al., 2009; Fugh-Berman

[1]To ease exposition, we will refer to all monetary and in-kind transfers of value recorded in Open Payments as "payments." These payments primarily arise because of a face-to-face marketing encounter, known as a detailing visit. But detailing visits can occur without any transfer of value, and a transfer of value could occur without any face-to-face encounter if, for example, a physician was unavailable for a meeting but still accepted lunch.

and Ahari, 2007). 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 both the number of patients taking the promoted drug as well as the days supply prescribed. In the first six months, the number of patients taking the marketed drug each month increases significantly by about 0.03 (2.2% relative to the mean), the number of days supplied increases by about 0.9 (1.6%), and the total monthly expenditure prescribed by the physician increases by about $12 (5.2%). We find similar results when we restrict our analysis to small payments, suggesting that policies which cap the dollar value of payments will not substantively change how payments affect prescribers' behaviors.

We then conduct two tests that look for evidence of patient harm. First, 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 without a corresponding health benefit, suggesting the physicians are poor agents for their patients. We find that paid physicians move patients to the generic version of the drug just as quickly as unpaid physicians, contradicting some media reports (e.g. Gold, 2001). Second, we study the effect of payments on prescribing quality using hand-collected data on drug efficacy for three major therapeutic classes. For each therapeutic class, we obtain a unidimensional efficacy measurement for every molecule from the medical literature. We find that paid and non-paid physicians prescribe drugs of a similar efficacy both prior to and after receiving a payment; our confidence intervals allow us to rule out reductions in drug efficacy larger than about 0.007 standard deviations. While this simple measure of drug efficacy is unable to speak to more complicated measures of quality (e.g. the quality of patient-drug matches), it does allow us to rule out a narrow hypothesis that payments induce providers to switch patients to drugs that appear to have lower average quality. Overall, our results find that prescribing is indeed affected by marketing encounters between drug firms and physicians; however, we rule out two hypothesized pathways in which the prescribing changes might harm patients.

Our paper contributes to the literature that explores whether interactions between prescribers and pharmaceutical firms affect 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

[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

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 the promoted statin by roughly 70 percent. Agha and Zeltzer (2019) use a fixed-effect approach similar to ours and find that small payments increase prescribing of blood thinners by approximately 10 percent.[3]

We contribute to this literature in three ways. First, we exploit high-frequency data on the timing of payments and prescribing to address concerns about selection of payments to physicians. Second, we estimate the impacts of payments for all Part D drugs that pharmaceutical firms promoted, rather than focusing on a single drug or drug class.[4] Although Part D is not the entire market for pharmaceuticals, and in particular will under-represent drugs targeted to younger patients, it is a substantial share of the overall US pharmaceutical market and one of great policy interest. And third, because it is becoming increasingly difficult for sales representatives to gain access to physicians,[5] the impacts of a payment have likely changed in recent years. Our estimates are based on the immediate past and so may better reflect payments' changing influence.

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

prescribing" (Spurling et al., 2010, p. 19).

[3]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.

[4]As emphasized in Shapiro et al. (2020), impacts of marketing can very widely across products. Because many policies that regulate pharmaceutical marketing do not target individual drugs or therapeutic classes, it can be important to have estimates based on all drugs to understand likely impacts of broad policies.

[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; Sacarny et al., 2018), "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.

measure of quality. Our results using patent expirations also contribute to this literature by showing how a sharp change in patient costs affects paid and unpaid physicians' choices.[7]

2 Background: Direct-to-Physician Marketing

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.

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 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, suggesting that providing samples might affect physicians' choices.

[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.

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 the impact of hassle costs on physicians' choices exceeds the difference in prescribing between physicians who did and did not receive a marketing encounter in the past month. 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 in the data. A limitation is that the data excludes non-disabled, younger adults who represent a sizeable portion of the market for prescription drugs.

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),[8] and the National Provider Identifier of the prescriber.[9] 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 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 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 $\times$ calendar month $\times$ drug level, measuring the total expenditure incurred for that drug, the number of patients the physician treats with the drug, and total days supply consumed by those patients.[10] Our use of the month as our unit of time allows us to illustrate in our event-study design any changes in behavior that might occur right after payments are received.

[8]Like most research in prescription drug markets, our measure of "expenditure" does not reflect post-market rebates paid from drug firms back to insurers or pharmacy benefit managers. 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 and days supply as key outcomes that are not subject to this weakness, but focus on expenditure in order to facilitate our calculation of drug firms' returns from payments.

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

[10]We note as a data limitation that we cannot observe if a prescription was written by a physician but never filled by the patient.

3.2 Open Payments

Our data on financial transfers from drug firms to physicians come from the Open Payments database. Open Payments reports payments and in-kind "transfers of value" drug firms make to physicians.[11] These transfers include the meals, travel, and educational expenses that are made during direct-to-physician marketing. The database contains information beginning August 2013.

For each transfer between drug firms and physicians, Open Payments records the physicians's name, address, and other identifying information, the drug or drugs discussed, the dollar amount of in-kind or cash transfers, and a coarse description of the nature of the transfer. 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 transfer, whether cash or in-kind, as a "payment."[12] 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 in-kind transfer of a meal. The non-food payments are most commonly for continuing medical education, consulting, education, or travel. Very few payments are described as a gift, grant, honoraria, royalty, entertainment, charity, or own investment.

In Figure 1, we describe the number and value of payments in each of the categories. 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 meal-related payment represents only $16 of value, while the "other" category transfers are much larger, averaging $1,239.[13] The second column 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.

[11] There are a few notable exceptions. First, pharmaceutical sales representatives may leave free samples of their drug firms' products with a physician. This behavior is not recorded in the Open Payments database. Second, information on payments that drug firms make to physicians for participation in clinical trials ("research payments") is recorded in a separate database; however, these data do not describe the drug being researched and so we do not include them in this analysis. Finally, firms are only required to report payments if they exceed about $10 in a given encounter, or if the cumulative value over a calendar year exceeds about $100. However, perhaps in order to ensure compliance with the cumulative $100 reporting threshold, firms commonly track and report to Open Payments payments that are less than $10.

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

[13] 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.

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 between 2013 and 2015. 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 she never prescribes over the three years.[14] 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. The 574 drugs with any associated Open Payments record comprise 63 percent of total Part D expenditure and 92 percent of branded Part D expenditure, implying the vast majority of branded drugs are using direct-to-physician marketing captured by Open Payments. Of all expenditure on drugs promoted to physicians, 21 percent is incurred after the prescribing doctor has received a related payment. By the end of the time period, more than one-fifth (22 percent) of physician $\times$ 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 after physicians

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

had received a related payment ranges from 2 percent for Namenda to close to half for Humira and Xarelto. Generic competition was imminent for both Namenda and Gleevec, likely explaining why payments were less common for those drugs. We examine generic onset during our sample period, including for Namenda, in Section 5.

Drug firms commonly monitor physicians' prescribing and specifically target high-volume physicians for payments (Homer et al., 2009; Fugh-Berman and Ahari, 2007). This targeting is evident in our data. Physicians who will later get paid for a drug are already prescribing $460 more in monthly expenditures *prior* to the payment than those who will never get a payment, a 9% difference.[15] Thus, a cross-sectional comparison between paid and unpaid physicians will tend to overstate the effect of the payment.

Because of the pre-period differences in paid and unpaid physicians, our empirical strategy, detailed below, exploits variation within a physician $\times$ drug combination over time. To ensure we have a full 12 month "pre" period for each paid physician $\times$ drug, we will exclude from our analysis in Section 4 physician $\times$ drug pairs whose first observed payment occurs prior to August 2014.[16] The last column of Table 1 describes the share of physicians who are first paid in August 2014 or later.

In 88 of the 128 classes with any payments, there are multiple drugs being promoted to doctors over the sample period. On average, each therapeutic class has 4 drugs making payments. Given how often multiple drugs are engaged in competing payments in a therapeutic class, we find, perhaps surprisingly, that among physicians receiving a payment, 81% of our physician $\times$ drug observations are paid by only one drug in the therapeutic class.

Although physicians are usually only receiving payments for one drug in a therapeutic class, drug firms commonly market to physicians repeatedly. Conditional on getting any payment for a drug in August 2014 or later, physicians average 2.8 payments (including the first) for the drug over the next twelve months. Figure 2 plots the average value of payments received in each month for a given drug for physicians who receive payments, relative to the first month a payment from that firm is received. This figure demonstrates that, while the largest exposure to payments occurs in the first month, on average there are positive payment amounts throughout the sample period. The average amount received in later months from the same firm is lower than what is observed at the initial payment, due to the fact that some physicians only receive one payment, and have zero payments at subsequent event times. Similarly, exposure to payments from rival firms may also occur over time. Figure A.2 shows the average amount received in each month from the first firm paying within a

[15] While this is a simple comparison of means, the difference is very similar ($425) if we instead net out the drug $\times$ month fixed effects we use in our main specification.

[16] However, our results are very similar if we instead include these observations in the analysis; see Figure A.1 and Table A.1 in the Appendix.

therapeutic class (solid line) and all other firms paying within a therapeutic class (dashed line). Over time, the physician is exposed both to additional payments from the first paying firm and, to a lesser extent, payments from competing firms within the class.

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 (Fugh-Berman and Ahari, 2007). 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. This research design relies upon a physician's changes over time and so is able to account for time-invariant characteristics that lead a drug firm to target specific physicians for payments. For physician p, drug d, and year-month t, we estimate the event-study specification

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

Our primary outcomes, y_{pdt}, are number of patients, total days supply, and expenditures 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 for d (if ever). We estimate β_r for every event period and report a 25-month window around the time of payment in the figures. We normalize β_{-1} to zero, making the month preceding the payments the reference period.

There are two important factors which affect the interpretation of these coefficients. First, physicians can be paid multiple times for the same drug. Our event study estimates are based on the first payment the physician received for that drug and as a result, the effects of any additional payments within the next twelve months are captured by our estimates. Thus, we should not interpret the βs as the effect of receiving a single payment, but the total effect of the initial and any subsequent payments over the observed time frame. Second, our estimates could be affected by unpaid interactions not recorded in Open Payments. To the degree paid and unpaid interactions are positively correlated, our estimates reflect the impacts of both types of interactions. If physicians with unpaid interactions are less likely to have payments, then these treated physicians are included in our control group and our

estimates are likely biased towards zero.

For those who have received a payment for drug d, we flexibly control for payments for other drugs within the therapeutic class. In particular, we include event-time dummies, analogous to $PresPaid_{pd}$, based on the timing of a payment for a competing drug. These controls are captured in X_{pdt}. 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 the prescribing of each drug 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. Because we observe dynamic treatment effects, we report the average coefficient (and the average's standard error) in two time periods: months 0 through 5 and months 6 through 12.

We make three edits to our dataset prior to estimation. As mentioned previously, we drop physician-drug pairs that receive a payment prior to August 2014. We also drop the 6 percent of physician-drug pairs where the physician is paid by three or more drug firms in the therapeutic class to avoid computational issues that arise from over-saturating the specification with payment variables.[17] To reduce the computational burden of the analysis, we conduct our main analyses using a 50 percent random sample of physicians, retaining all of their prescribing and payment information. These changes result in 492,767 physicians and 179,255,484 physician $\times$ drug $\times$ month observations.

[17]We have conducted our main analyses including all physician-drug pairs and added controls for up to two additional payments from competing drug firms. Our results are very similar to those presented in the text.

4.2 Effect of Payments on Prescribing

We estimate our event study specification with the physician's number of patients being prescribed the promoted drug as the dependent variable and present the results in Figure 3a. There are no systematic differential trends prior to the payment, but upon receiving the payment, the number of patients begins to increase. Our estimates remain elevated for approximately nine months before returning to pre-payment levels. The gradual increase in a physician's number of patients reflects the fact that, even if a physician decides to prescribe the drug to all her patients, prescriptions are commonly only issued at patient office visits, and so it would take a few months for all her patients to begin taking the drug. The apparent reversion of effects to pre-payment levels is consistent with past empirical findings that suggest physicians forget advertising or that the impacts of interactions with pharmaceutical firms fade over time (e.g. Iizuka and Jin, 2005; Mizik and Jacobson, 2004). Over the first year post-payment, the number of patients is approximately 0.024 greater per month. That corresponds to a 1.8 percent increase over the average number of patients over the year after the first payment.

Our second outcome of interest, days supply, captures not only the extensive margin change of the number of patients, but potential increases on the intensive margin as well (e.g. patients filling their prescriptions more regularly or being prescribed more frequent dosing). The results for this outcome are presented in Figure 3b. The general shape of the impacts is very similar to that found for the number of patients, though our estimates are somewhat less precise. Over the first year after the payment, the days supply is approximately 0.843 greater per month, a 1.5 percent increase.

Figure 3c presents the event study results where the dependent variable is the expenditure by a physician's patients on a drug in a given month. Again, we see the same general pattern observed for our quantity measures: a gradual increase in the months following the payment followed by reversion to pre-payment levels roughly twelve months after the payment. On average, expenditures are \$17.64 greater per month in the year following the payment. Relative to average monthly expenditures, \$230, this is a 7.6 percent increase.[18] 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.

Table 2 summarizes the event study estimates. As seen in column (1), relative to the month preceding the payment, the number of patients increases by 0.029 on average in the

[18]We find a larger increase in percentage terms for expenditure than for our two quantity measures, number of patients and days supply. Appendix Figure A.3 suggests that this pattern is due to heterogeneity in treatment effect by monthly per-patient expenditure. We find that our overall effects are driven by more expensive drugs, those with a monthly per-patient expenditure exceeding the median of \$225.

first six months after a payment; in months 6 - 12, it is an average of 0.018 greater per month, though not statistically distinguishable from zero at conventional levels. In column (2), we present analogous results for total days supply. Payments increase the total days supply by 0.89 in months 0-5 and by 0.79 in months 6-12, though again, we lose precision on our estimate for months 6-12 and can not reject the null. In column (3), we present our expenditure results. On average, expenditures rise by $12 in months 0-5 and by $23 in months 6-12.

Our estimated impact is somewhat smaller than some recent related findings. Grennan et al. (2018) study how payments in the form of meals affect cardiologists' prescribing of statins and find that payments increase prescribing by 73 percent. Shapiro (2018a) finds that a detailing visit (which may or may not involve a payment) increases prescribing of the antipsychotic Seroquel over the years 2001 to 2006; his estimates imply an increase of about 14 percent in the following twelve months.[19] 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, the variation exploited by the empirical designs, the types of physician-industry interactions that are studied, and the sample periods (given large changes in physician-industry relationships over the past decades). We further discuss the implied magnitude and estimate a return-on-investment in Section 4.3.

There is a perception among policymakers that large-dollar payments are particularly influential. This has led some states like Minnesota and Massachusetts to ban and the American Medical Association[20] to strongly discourage payments above a certain dollar amount. We assess whether the remaining small payments have an impact on physicians' prescribing by re-estimating our main specification for payments of no more than $20. The results are presented in Figures 4a - 4c and summarized in Table 3. Again, we see the same general patterns that were observed for the entire sample of payments: a gradual increase in the post-payment estimates which peaks approximately 6-9 months after the payment and then decreases towards zero thereafter.[21]

[19]The author models detailing as a stock subject to depreciation. We convert his estimates to a year-long percentage increase in prescribing by computing the implied increase in prescriptions over a one year period and then dividing by average prescribing in a year. Mathematically, this is $\frac{\sum_{t=0}^{11} \delta^t \beta}{\overline{Rx}} = 0.14$ 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 yearly prescriptions (twelve times the 0.427 monthly average from Table 2).

[20]See the association's Code of Ethics.

[21]Although the majority of payments in the data are less than $20, it was not a foregone conclusion that these figures would look very similar to those that include payments of all sizes. Because OLS produces a sample weighted average of heterogenous treatment effects (Angrist and Krueger, 1999), it could have been

We find that expenditures rise by an average of $11 per month in the first six months after the payment and by $22 per month in the remainder of the year, only slightly smaller than our estimate for the full sample. Overall, our results show that banning large payments will prevent payments from pharmaceutical firms from affecting physicians' prescribing.

4.3 Pharmaceutical Firms' Return on Investment

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 visit from a pharmaceutical sales representative. 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.[22] 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.[23] Based on the Open Payments data, the average payment on these visits is approximately $18.[24] Then a rough estimate of the marginal cost of a single detailing visit, including the payment, is $213.[25]

To estimate the increased expenditures from a 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 factors suggest we need to scale up our estimates by 50/3.[26] 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 branded expenditure (Johnson et al., 2018). Consequently, we scale our estimates down by 22 percent.

that the large dollar value payments were leading to very large increases in the number of patients, total days supply, and expenditures while smaller payments had little or no effect.

[22]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.

[23]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.

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

[25]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.

[26]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.

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 $235 in the first year after the payment.[27] After applying the scaling discussed previously, this suggests that expenditures to the pharmaceutical firm increased by $3,051. Conditional on receiving a payment, physicians receive 2.8 payments in the following twelve months (including the original payment), implying that firms incur $596 (=$213*2.8) in marketing expenses. A rough, back-of-the-envelope calculation suggests that the return on investment (ROI) is approximately 412 percent. Although this might seem quite large, it is on the smaller end of available estimates in the literature which range from 200 - 1,700 percent (Narayanan et al., 2004; Schwartz and Woloshin, 2019).

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 or that our estimates for the Part D population overstate the impacts for the non Part D population. If so, our ROI comparing estimated benefits to the marginal cost of another detailing visit will be an overestimate.

5 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 they are available. 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 would be evidence that physicians were privileging the drug firms' interests over their patients' interests. Previous research using distance to a drug firm's headquarters as an instrument for a physician's likelihood of getting a payment from a firm found that

[27] This is calculated by multiplying the estimates in Table 2 by the number of months covered in each period (i.e., $12.18 $\times$ 6 months + $23.09 $\times$ 7 months). Because the first month is only partially treated, this time period represents somewhere between 12 and 13 months.

payments cause physicians to shift away from generic drugs and towards branded versions of the same molecule (Engelberg et al., 2014). Such behavior would be fairly clear evidence of payments reducing patient welfare and increasing public costs with no corresponding benefit.

There were 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 Appendix Table A.2. These five drugs alone accounted for 5.5 percent of Medicare Part D expenditure in 2013, and all five were promoted to physicians over the time period. Because we only need to incorporate information about these five drugs and their competitors, we use the full sample of physicians for this analysis rather than a 50 percent sample of physicians as before.

We measure the degree to which a physician prescribes a generic or branded drug with the standard measure of generic drug penetration, generic efficiency. It 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. We calculate the generic efficiency rate for physicians who ever receive payments for the branded version of the drug and for physicians who had not received a payment for the drug up through six months after a generic drug entered the market.[28] It is important to note two factors that likely play a role in the generic efficiency rate. First, states' generic substitution laws allow, or even force, pharmacists to substitute an equivalent generic for a branded drug. However, these laws can be overridden by a physician or the patient herself (see Hellerstein, 1998). Secondly, Part D formularies can exclude or set high cost-sharing to disincentivize the use of brands with exact generics. However, Carey (2020) reports that the rate of coverage among branded drugs with exact generics is 84% in Part D. Therefore, although both generic substitution laws and formulary design may play a role in increasing generic efficiency, prescribers and patients retain the ability to choose a branded drug even after its generic equivalent becomes available.

Figure 5 shows the generic efficiency rate over the first six months of generic competition for the five case studies. In Panel 5a, 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

[28] As reported in Huckfeldt and Knittel (2011), we confirm that drug firms dramatically reduce the number of physicians receiving payments prior to generic entry. The number of payments over the entire sample period is reported for all five drugs in Appendix Figure A.4. For Celebrex, Evista, and Zyvox, payments drop sharply to zero right around the time of generic entry. For Namenda, which tried 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.

later. Panels 5b-5e show similar findings for the four other drugs which lost patent protection during our sample. It is clear that generic efficiency rises at least as quickly among paid physicians as it does among physicians who were not paid for the drug. In four of the five cases, paid physicians appear to transition patients to generics *more quickly* than physicians who were never paid for the branded drugs, though in general we can not reject the null that the generic efficiency is the same overall across the paid and unpaid physicians. These results do not suggest that payments are leading physicians to harm patients through this channel.

6 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 indeed 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 less 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: statins, Angiotensin II Receptor Blockers (ARBs), and atypical antipsychotics.[29] For each therapeutic class, we obtained a unidimensional efficacy measurement for every molecule (including generics) from the medical literature. For statins, our measure is the percent reduction in LDL cholesterol; for ARBs, our measure is the reduction in systolic blood pressure; and for atypical antipsychotics, our measure is the reduction in the Positive and Negative Syndrome Scale. We report our raw efficacy measures, the details of their measurement, and the sources from the medical literature in Appendix Tables A.3-A.5. Using these clinical measures, we calculate the weighted average of the efficacy of drugs the physician prescribes in each class and month (including generics). The weights in the average are the days supply of that drug prescribed by the physician in the 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

[29] Appendix Figure A.5 and Appendix Table A.6 show that our main findings from Section 4 hold within the three therapeutic classes studied in this section, although the point estimates are somewhat less precisely estimated.

use as our key independent variable an indicator for whether the physician has received a payment from *any* drug in the therapeutic class. Our estimating equation is

$$efficacy_{pct} = \sum_{r \neq -1} DocPaid_{pc}\beta_r + \delta_{pc} + \delta_{ct} + \epsilon_{pct} \tag{2}$$

where $efficacy_{pct}$ is our measure of efficacy, $DocPaid_{pc}$ indicates whether physician p will be paid for a drug in therapeutic class c at some point in our sample, r denotes the time period relative to the first time the physician is paid (if ever) in class c, δ_{pc} is a set of fixed effects for each combination of physician and therapeutic class, δ_{ct} is a set of class $\times$ month fixed effects, and ϵ_{pct} is a random error term. We normalize β_{-1} to zero, making the month preceding the 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.[30] 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 6, with summary coefficients in Appendix Table A.7. Prior to the payment, there does not appear to be any differential trend in efficacy. There does not appear to be any statistically or economically meaningful effect in the year after the payment: Based on our estimates, we can reject an average effect in the twelve months following a payment that is any larger than a 0.007 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 Appendix Figure A.6. In each case, the estimates suggest that there were not large changes in average efficacy following a payment from a pharmaceutical firm.[31]

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

[30] 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.

[31] Although there might be a slight pre-trend in some of the figures, there is no large deviation from that trend following the payment that might suggest a reduction in efficacy.

(or positive) effects of payments on the apparent efficacy of drugs prescribed.

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.[32] If physicians who receive payments differentially increase use of the paid drug in patients for whom it is least or most effective, then our estimates will be biased. 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. Third, these efficacy measures capture intensive-margin changes in drug quality among patients taking drugs within these classes. We have no information about other changes to clinical treatment patterns.

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 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.

7 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 quantity of and expenditures on the marketed drug after the payment occurs. This increase in drug usage

[32]High-efficacy drugs may still have adverse effects on patients. For example, Alpert et al. (2019) suggests that Oxycontin's physician-directed marketing played an important role in the large increase in overdose deaths that began in the late 1990s.

that occurs after a payment is substantial, representing a 7.6% increase in expenditures. These patterns are present even for small-value payments that are trivial compared to a physician's annual income.

We examine whether these expenditure changes are likely to harm patients. First, we 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. Second, for three large classes of drugs, we collected clinical measures of drug effectiveness from the medical literature for each drug. Using these efficacy measures, we do not find evidence that drug firm interactions reduce the efficacy of drugs prescribed. Our confidence intervals allow us to rule out even very small reductions in efficacy.

Overall, our results suggest that drug costs do increase as a result of marketing encounters between drug firms and physicians, but we do not find any direct evidence that the payments to doctors are systematically harming or helping patients. It is important to stress that our estimates do not rule out the possibility that some patients are being helped or harmed by these payments; however, on average, it does not appear to be the case that patients are moved to drugs that are obviously less efficacious. The extent to which physician and drug firm interactions are actually welfare reducing represents a challenging, but important, area for future research.

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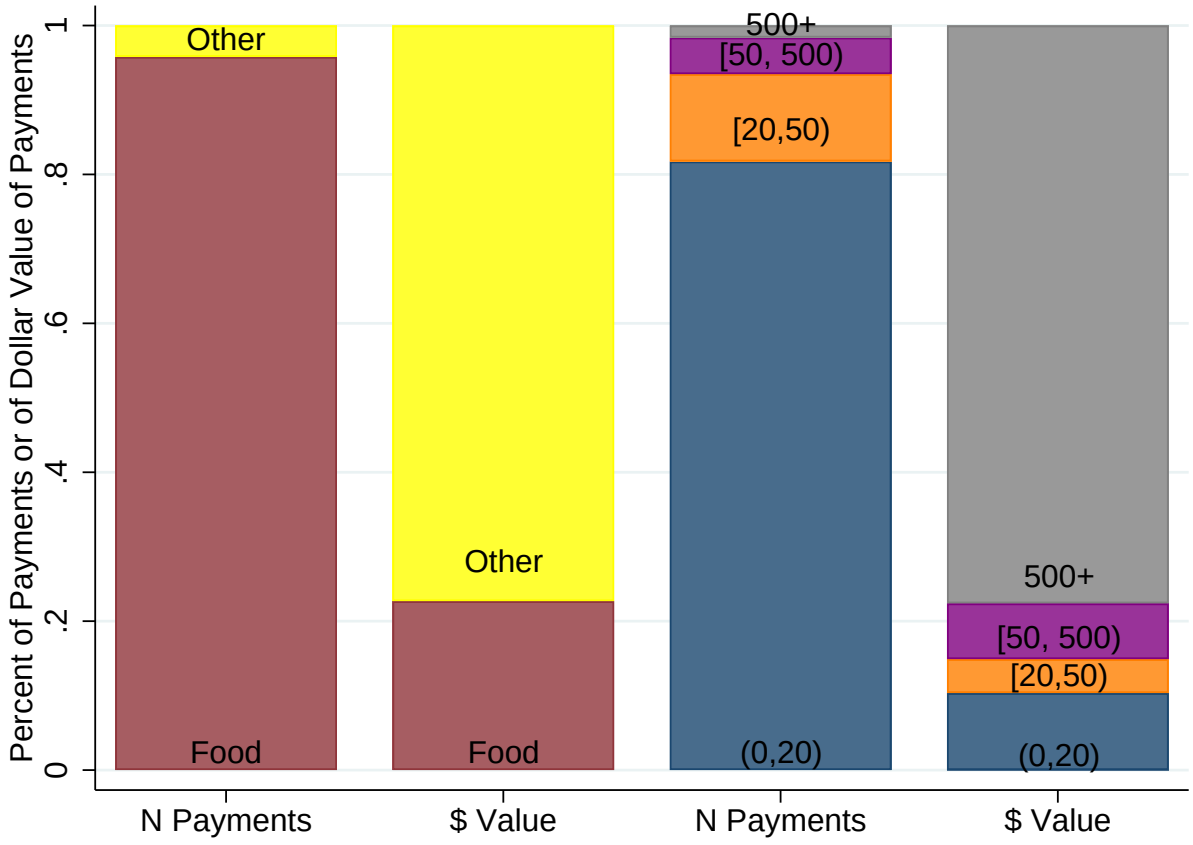
Figure 1: Summary Statistics: Distribution of Payments by Type and Amount



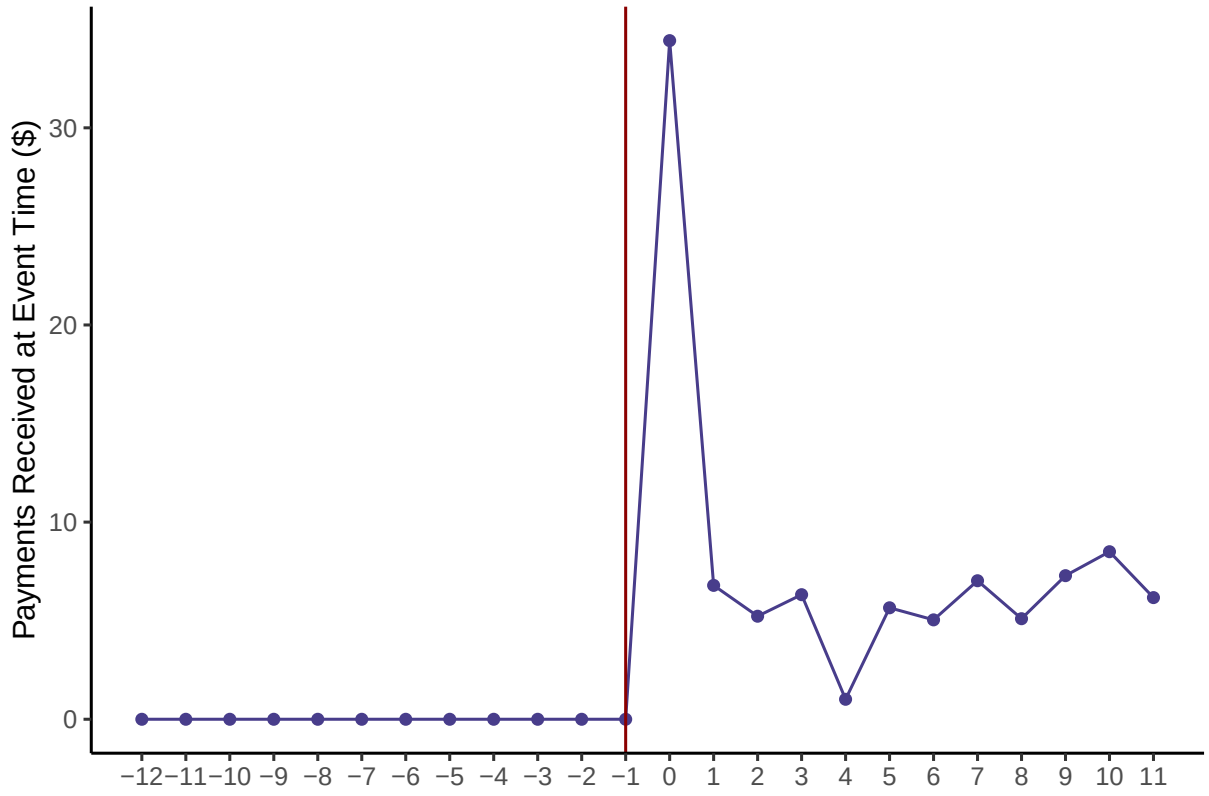
This figure depicts the share of payments that are an in-kind transfer of food or beverage (first bar) vs. all other payment types. The second bar weights the payments by their dollar values. The third bar shows the share of payments in each of four size categories, and the fourth bar shows the same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

Table 1: Summary Statistics: Prevalence of Payments

Drug	Indication	% of Part D Expenditure	% of Expenditure After Payments	% of Prescribing Physicians Ever Paid	% of Prescribing Physicians First Paid in or after Aug 2014
All Drugs In Analytic Dataset		63	21	22	8
Lantus	Diabetes	3.3	24	16	3
Harvoni	Hep C	2.3	18	23	23
Crestor	High Cholesterol	2.3	23	18	4
Advair	Asthma/COPD	2.2	10	10	4
Spiriva	Asthma/COPD	1.9	26	21	5
Abilify	Mental Illness	1.9	28	24	4
Januvia	Diabetes	1.6	19	21	7
Sovaldi	Hep C	1.3	21	21	1
Lyrica	Nerve Pain	1.3	25	18	4
Novolog	Diabetes	1.2	27	27	7
Levemir	Diabetes	1.2	37	37	7
Humira	Immune Conds	1.1	45	66	17
Namenda	Dementia	1.1	2	1	0
Enbrel	Immune Conds	1.1	39	50	10
Xarelto	Blood Clots	1	44	45	13
Zetia	High Cholesterol	1	16	18	7
Gleevec	Cancer	.9	6	13	2
Symbicort	Asthma/COPD	.9	30	28	7
Oxycontin	Pain	.8	23	21	6
Humalog	Diabetes	.8	26	29	10

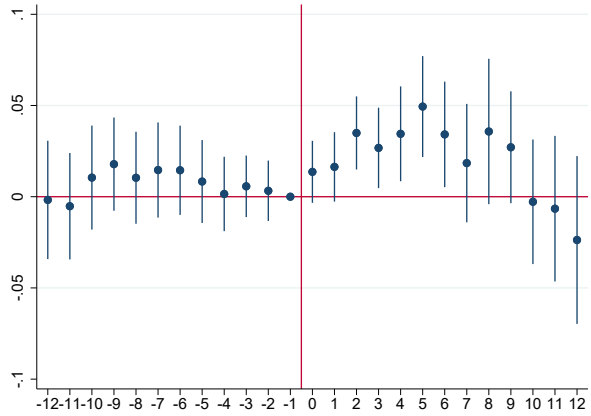
This table describes the prevalence of payments in Part D overall and for the twenty drugs with the largest total expenditure over the sample period. The third column describes the share of Part D expenditure. The next column describes the share of expenditure where the physician has received a payment 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 or after August 2014.

Figure 2: Average Payment Amount Received in Each Event Time

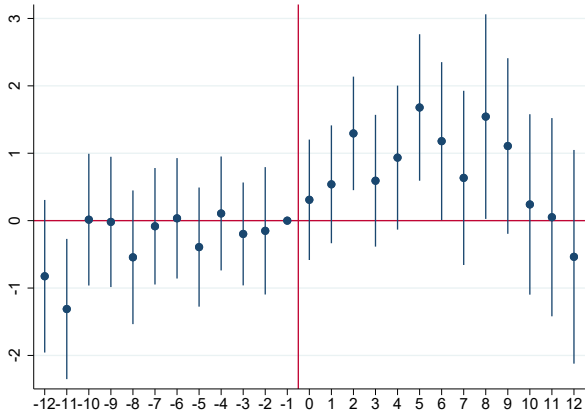


The x-axis denotes event time in months, defined relative to the first observed payment received by a physician for a given drug. The y-axis reports the average amount (in dollars) received by paid physicians for the drug, at both the first observed payment (event 0) and in subsequent months.

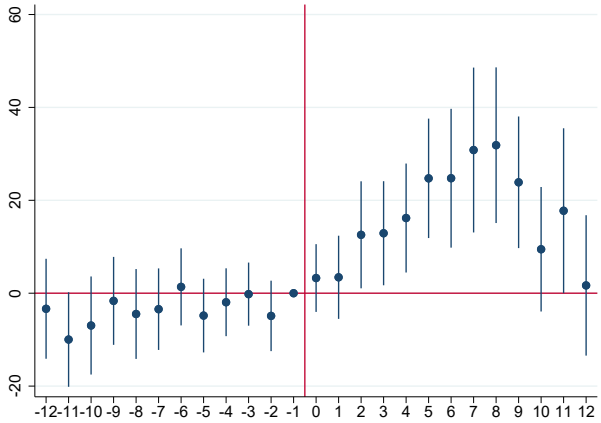
Figure 3: Impact of Payments on Quantity and Expenditure



(a) Number of Patients



(b) Days Supply



(c) Expenditure

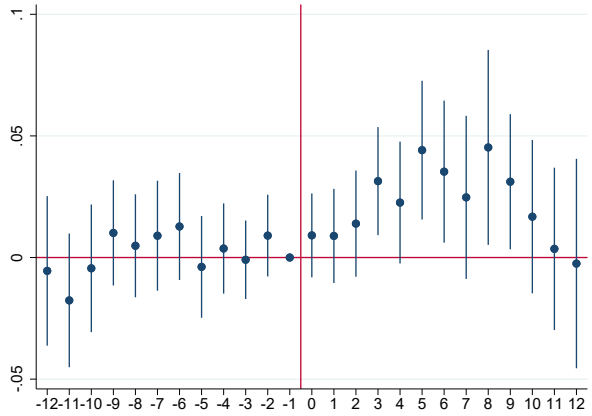
Estimated coefficients and 95% confidence intervals from estimation of Equation 1 are presented. The dependent variable is (a) the number of patients, (b) the total days supply, or (c) total expenditure for a physician-drug-month. The month prior to the payment is the reference group. Controls for other payments in the therapeutic class as well as physician-drug and drug-month fixed effects are always included. Standard errors are clustered by physician.

Table 2: Impact of Payments on Quantity and Expenditure

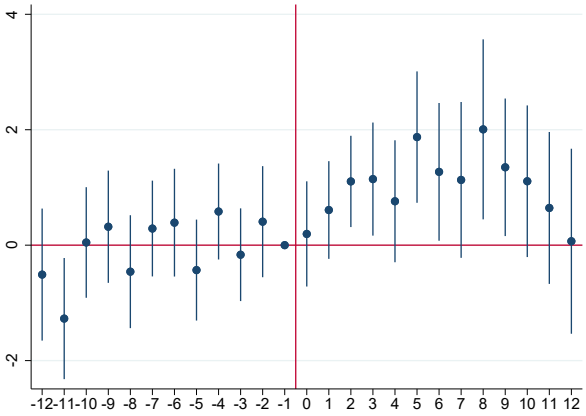
	Number of Patients	Days Supply	Expenditure
	(1)	(2)	(3)
Months 0 - 5	0.029***	0.892**	12.18**
	(0.010)	(0.384)	(4.43)
Months 6 - 12	0.018	0.793	23.09***
	(0.014)	(0.538)	(6.36)
Mean dep. var.	1.30	56.23	$230
No. physicians	492,767	492,767	492,767
Observations	179,255,484	179,255,484	179,255,484

Dependent variable is given in column heading. Estimates are linear combinations of event study estimates presented in Figures 3a, 3b, and 3c. The month prior to the payment is the reference group. Controls for other payments in the therapeutic class as well as physician-drug and drug-month fixed effects are always included. Standard errors are clustered by physician.

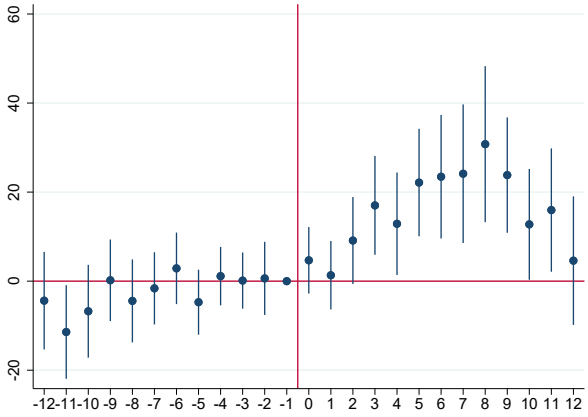
Figure 4: Impact of Low Dollar ($20 and Less) Payments on Quantity and Expenditure



(a) Number of Patients



(b) Days Supply



(c) Expenditure

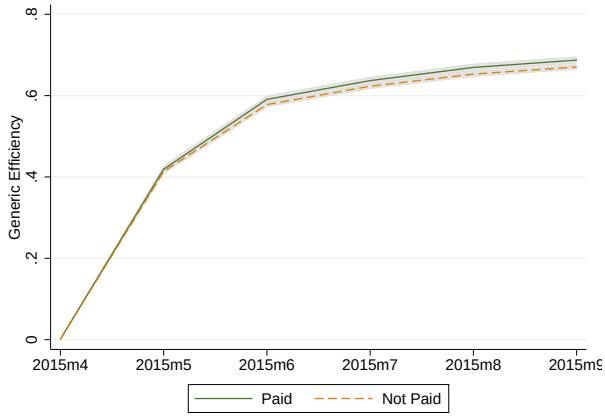
Coefficients and 95% confidence intervals from the estimation of Equation 1 are presented. Each panel only uses physician-drug pairs where the payment was no more than $20 (or the physician was not paid for that drug). The dependent variable is (a) the number of patients, (b) the total days supply, or (c) total expenditure for a physician-drug-month. The month prior to the payment is the reference group. Controls for other payments in the therapeutic class as well as physician-drug and drug-month fixed effects are always included. Standard errors are clustered by physician.

Table 3: Impact of Low Dollar ($20 and Less) Payments on Quantity and Expenditure

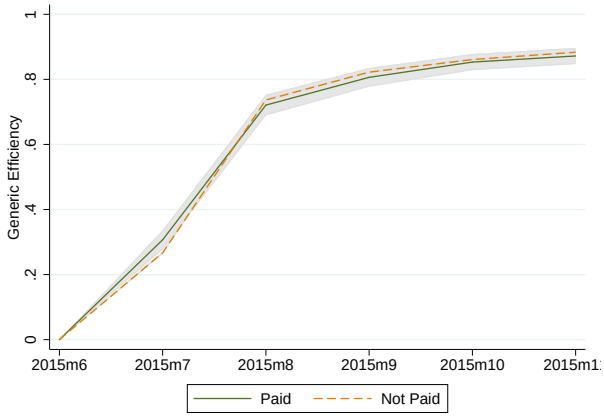
	Number of Patients	Days Supply	Expenditure
	(1)	(2)	(3)
Months 0 - 5	0.022**	0.948**	11.20**
	(0.0098)	(0.379)	(4.33)
Months 6 - 12	0.026*	1.25**	21.82***
	(0.014)	(0.523)	(6.02)
Mean dep. var.	1.30	56.30	$228.52
No. physicians	492,086	492,086	492,086
Observations	177,483,968	177,483,968	177,483,968

This analysis only uses physician-drug pairs where the payment was no more than $20 (or the physician was not paid for that drug). Dependent variable is given in column heading. Estimates are linear combinations of event study estimates presented in Figures 4a, 4b, 4c. The month prior to the payment is the reference group. Controls for other payments in the therapeutic class as well as physician-drug and drug-month fixed effects are always included. Standard errors are clustered by physician.

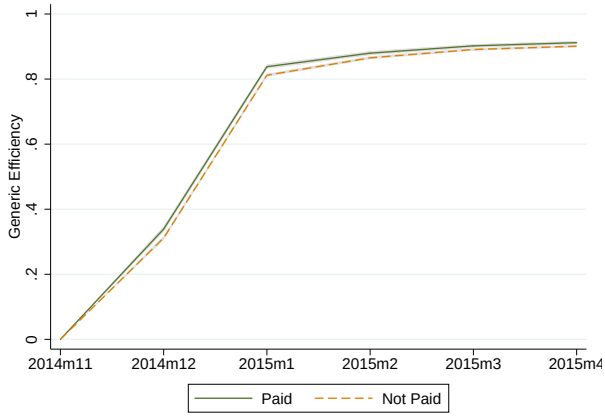
Figure 5: Generic Efficiency in the First Six Months After Patent Expiry



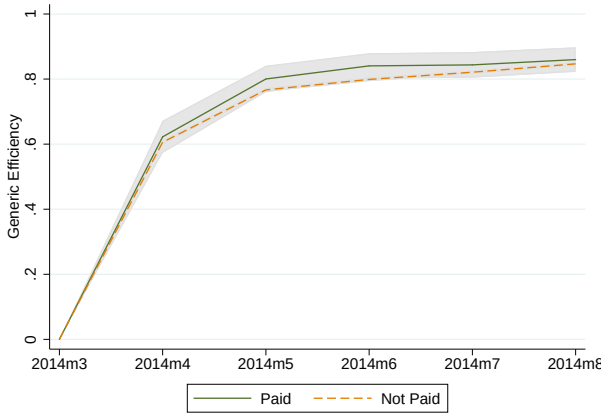
(a) Abilify



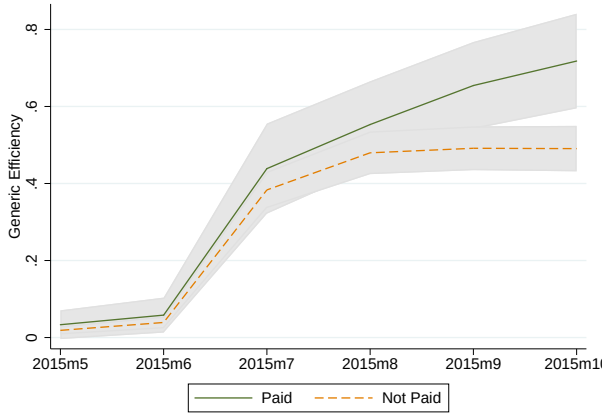
(b) Namenda



(c) Celebrex



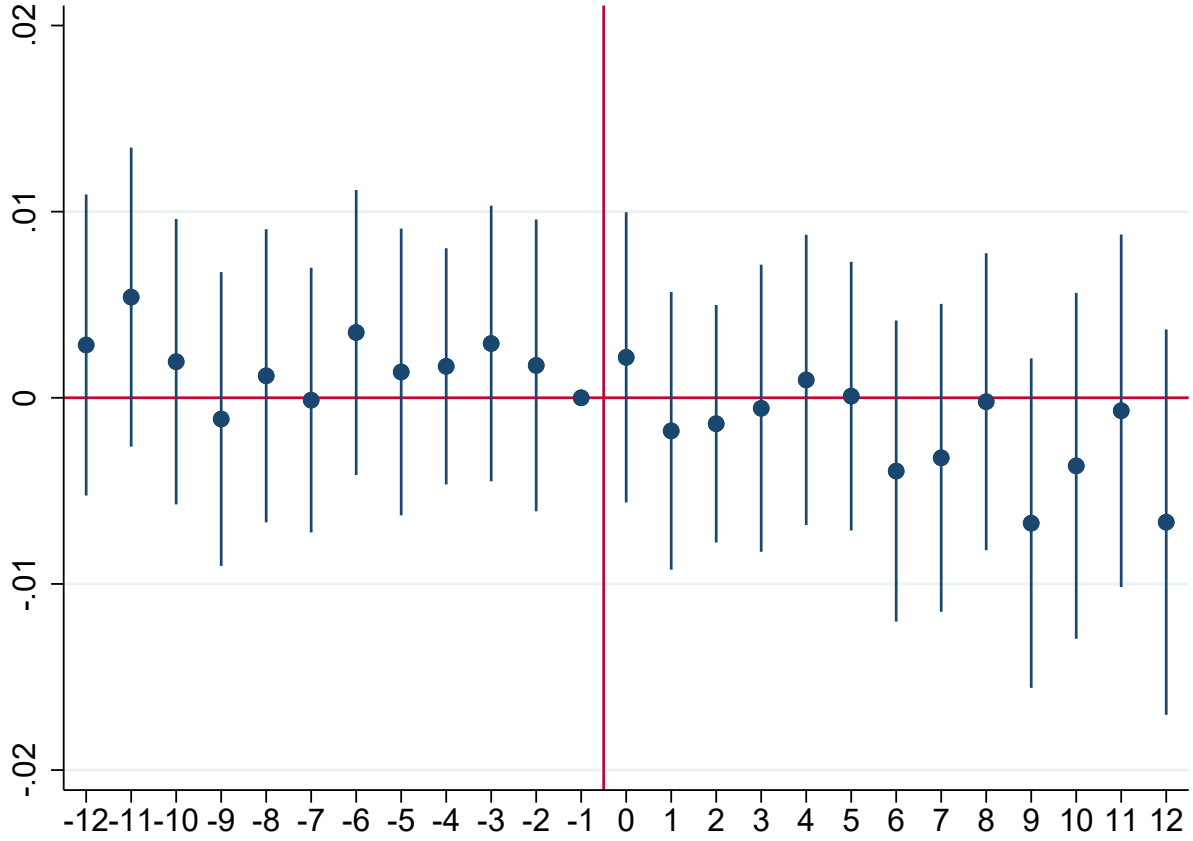
(d) Evista



(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.

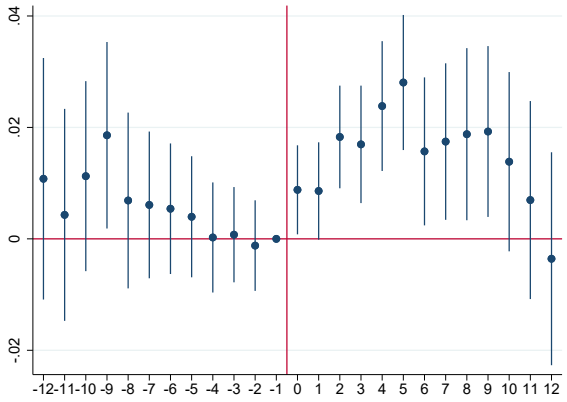
Figure 6: Impact of Payments on Average Efficacy



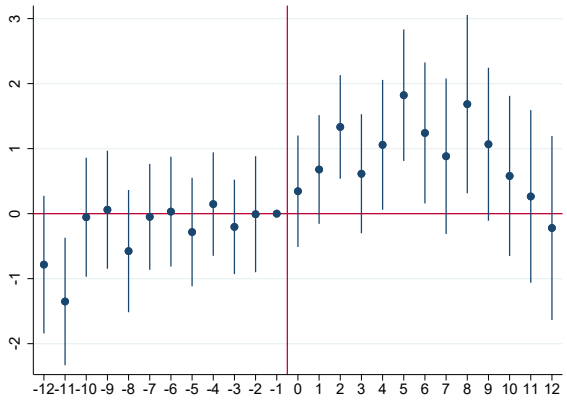
Estimated coefficients and 95% confidence intervals from the estimation of Equation 2 are presented. The dependent variable is the standardized efficacy measure for a physician in a given therapeutic class and month. The month prior to the payment is the reference group. Physician-class and class-month fixed effects are always included. Standard errors are clustered by physician.

Appendices

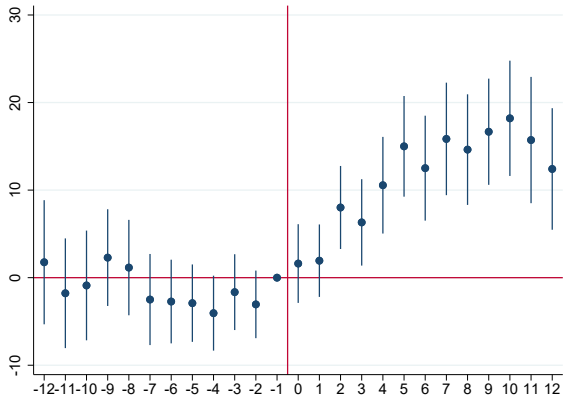
Figure A.1: Impact of Payments on Quantity and Expenditure: Including Physicians Paid Prior to August 2014



(a) Number of Patients



(b) Days Supply



(c) Expenditure

Coefficients and 95% confidence intervals from the estimation of Equation 1 are presented. The data including physicians who were paid in 2013, who are dropped from our main specification (Figure 3). The omitted time period is the month prior to the payment.

Table A.1: Impact of Payments on Quantity and Expenditure: Including Physicians Paid Prior to August 2014

	Number of Patients	Total Days	Expenditure
Months 0 - 5	0.017**	0.975***	7.24***
	(0.004)	(0.359)	(1.99)
Months 6 - 12	0.015**	0.953*	15.59***
	(0.007)	(0.4904)	(2.73)
No. physicians	494,923	494,923	494,923
Observations	194,344,524	194,344,524	194,344,524

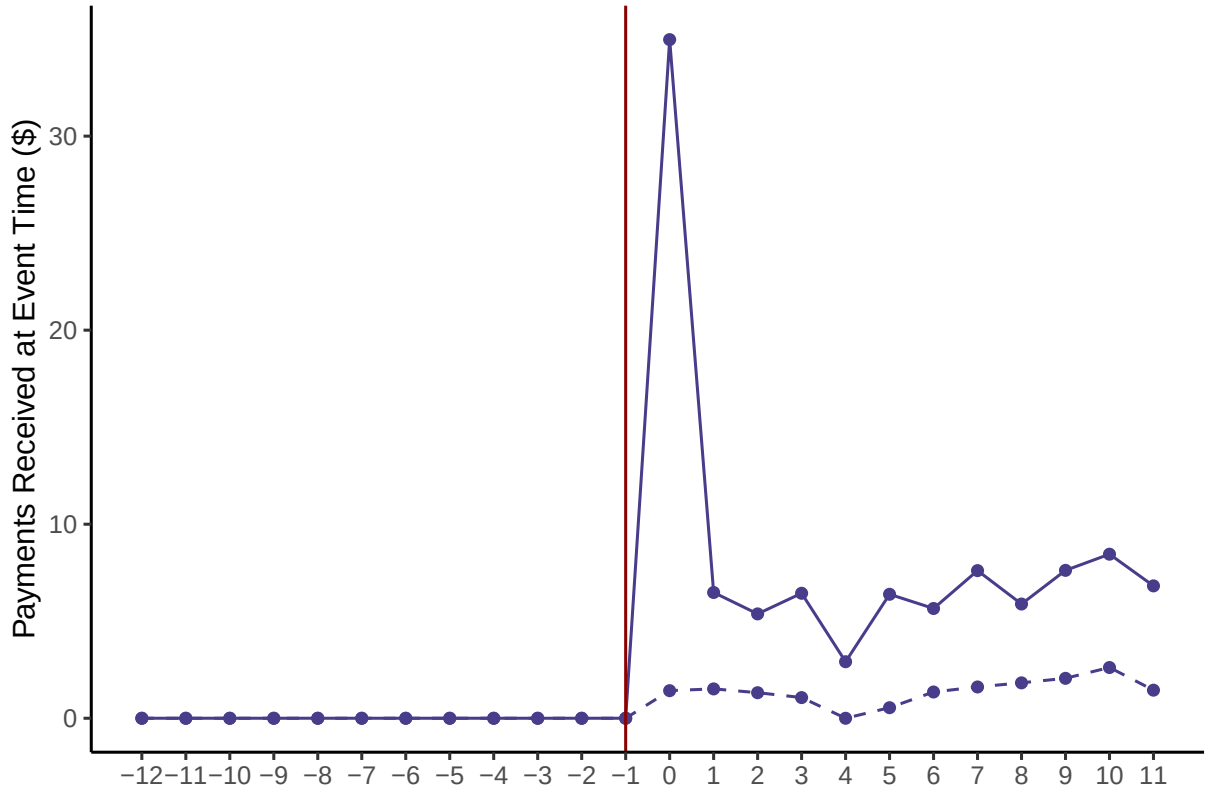
Dependent variable is listed in the first row. Estimates are linear combinations of event study estimates presented in Figure A.1. The month prior to the payment is the reference group. Standard errors are clustered by physician.

Table A.2: 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

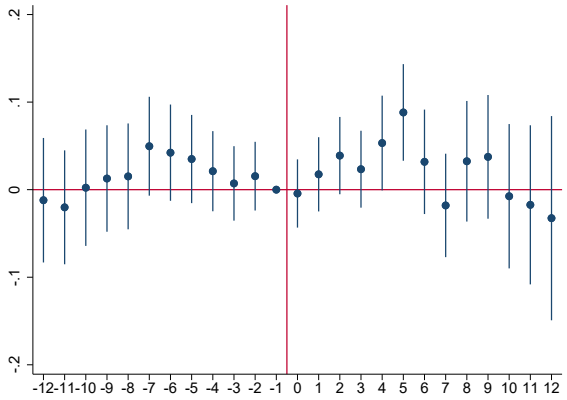
This table provides details for the five case studies of generic entry evaluated in Section 5.

Figure A.2: Average Payment Amount Received In Each Event Time for First Firm Paying in Therapeutic Class (Solid) and All Other Firms Paying in Therapeutic Class (Dashed)

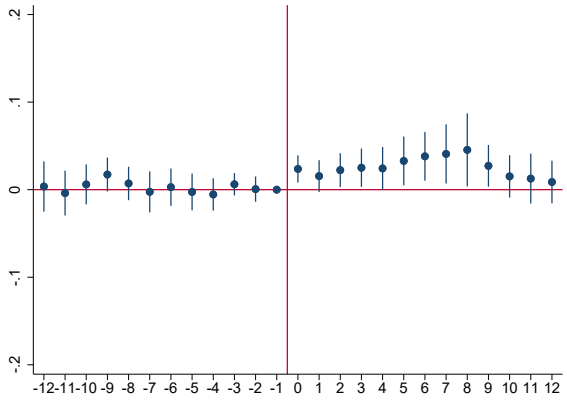


Average amount received from first paying drug firm in class (solid) and all other drug firms in class (dashed) by paid physicians up until event time denoted on X-axis. Event times are defined relative to first observed payment from drug firm.

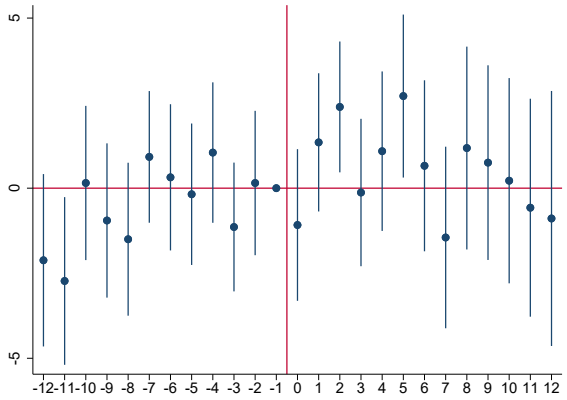
Figure A.3: Impact of Payments on Quantity and Expenditure: Splitting Sample by Median Monthly Expenditure Per Patient



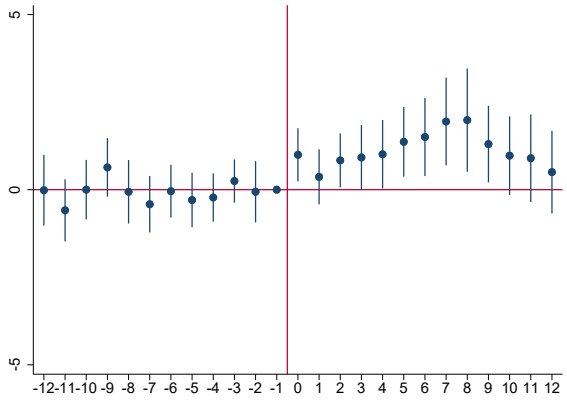
(a) Number of Patients, Less expensive



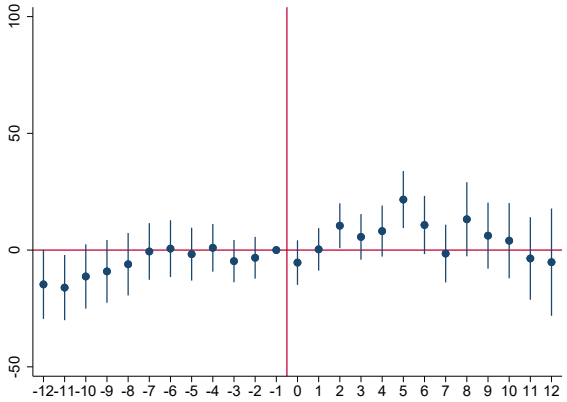
(b) Number of Patients, More expensive



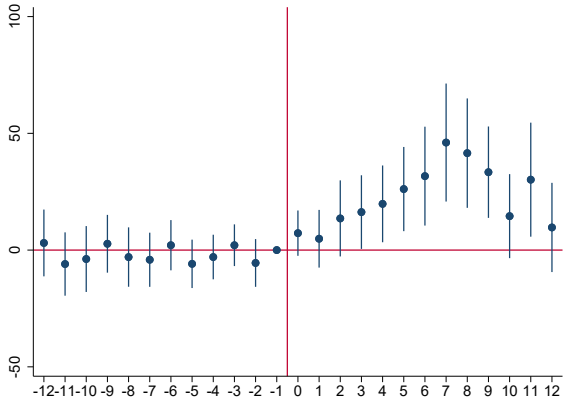
(c) Days Supply, Less expensive



(d) Days Supply, More expensive



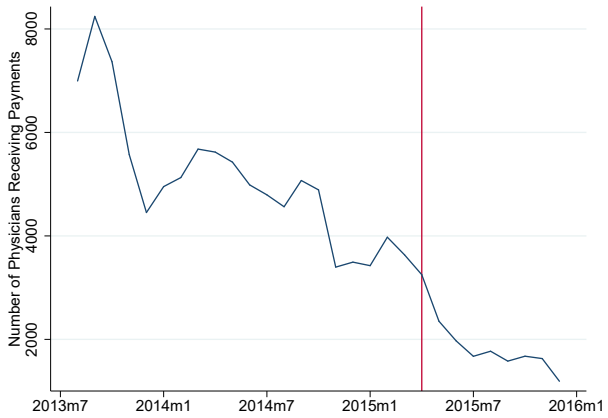
(e) Expenditure, Less expensive



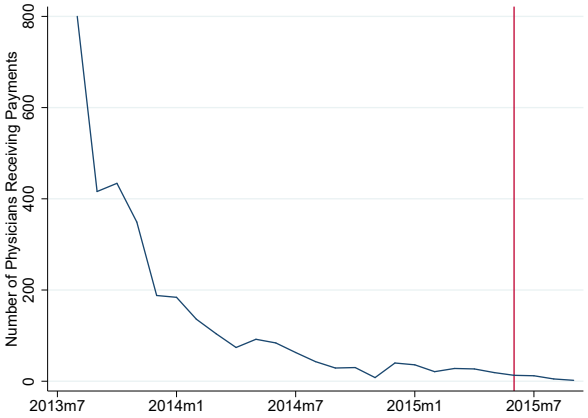
(f) Expenditure, More expensive

Coefficients and 95% confidence intervals from the estimation of Equation 1 are presented. Panels (a), (c), and (e) use drugs with an average monthly expenditure below the median of $225, while (b), (d) and (f) use drugs with an above-median average monthly expenditure. The omitted time period is the month prior to the payment.

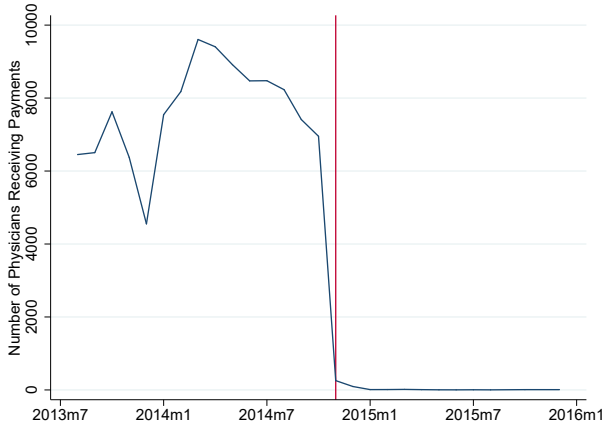
Figure A.4: Number of Payments Around Patent Expiries



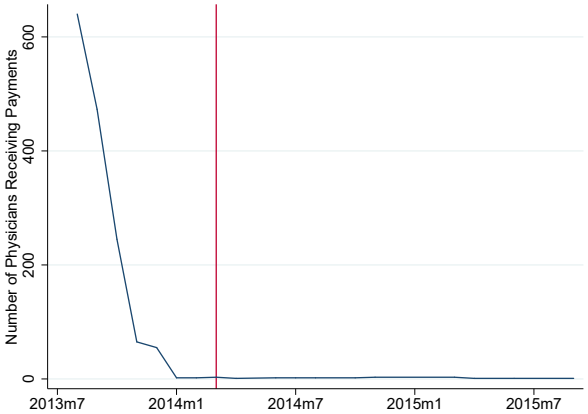
(a) Abilify



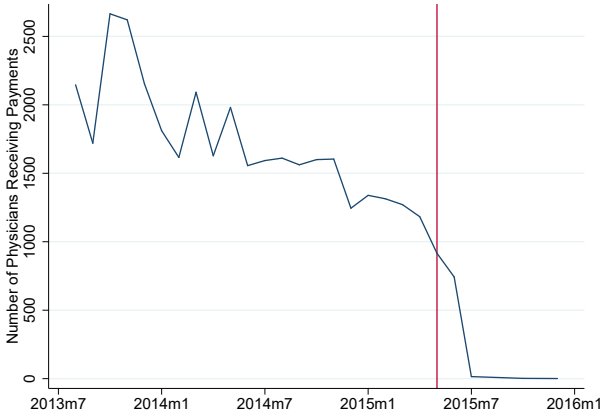
(b) Namenda



(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 line denotes the month of patent expiry.

Table A.3: Drug Efficacy for Atypical Antipsychotics, Measured by Improvement in Positive and Negative Syndrome Scale

Ingredient	Efficacy	Source	Measurement Details
Quetiapine	13	Mullen et al. (2001)	253.9 mg/day (mean), measured at 4 months
Risperidone	11.8	Mullen et al. (2001)	4.4 mg/day (mean), measured at 4 months
Olanzapine	14	Lindenmayer et al. (2007)	15-20 mg/day, measured at 12 weeks
Aripiprazole	15.5	Kane et al. (2002)	15 mg/day, measured at 4 weeks
Ziprasidone	25.8	Addington et al. (2004)	114.18 mg/day (mean), measured at 8 weeks
Paliperidone	19.9	Davidson et al. (2007)	15 mg/day, measured at 6 weeks
Clozapine	19.94	Howanitz et al. (1999)	Up to 300 mg/day, measured at 12 weeks
Lurasidone	25.7	Meltzer et al. (2011)	40 mg/day, measured at 6 weeks
Iloperidone	12	Crabtree et al. (2011)	24 mg/day, measured at 4 weeks
Asenapine	21.3	Kane et al. (2010)	10 mg/day, measured at 6 weeks

Sources:

Mullen, J., Jibson, M.D., Sweitzer D. A Comparison of the relative safety, efficacy, and tolerability of Quetiapine and Risperidone in outpatients with schizophrenia and other psychotic disorders: The Quetiapine experience with safety and tolerability (QUEST) study. *Clinical Therapeutics*, 2001; 23(11): 1839-1854.

Lindenmayer, J.P., Khan, A., Iskander, A., Abad, M.T., Parker, B. A randomized controlled trial of Olanzapine vs. Haloperidol in the treatment of primary negative symptoms and neurocognitive deficits in schizophrenia. *J Clin Psychiatry*, 2007; 68: 368-379.

Kane, J., Carson, W.H., Saha, A.R., et al. Efficacy and safety of Aripiprazole and Haloperidol versus placebo in patients with schizophrenia and schizoaffective disorder. *J Clin Psychiatry*, 2002; 63:763-771.

Addington, D.E.N., Pantelis, C., Dineen, M., Benattia, I., Romano, S.J. Efficacy and tolerability of Ziprasidone versus Risperidone in patients with acute exacerbation of schizophrenia or schizoaffective disorder: An 8-week, double-blind, multicenter trial. *J Clin Psychiatry*, 2004; 65: 1624-1633.

Davidson, M., Emsley, R., Kramer, M., et al. Efficacy, safety and early response of paliperidone extended-release tablets (paliperidone ER): Results of a 6-week, randomized, placebo-controlled study. *Schizophrenia Research*, 2007; 93: 117-130.

Howanitz, E., Pardo, M., Smelson, D.A., et al. The efficacy and safety of Clozapine versus Chlorpromazine in geriatric schizophrenia. *J Clin Psychiatry*, 1999; 60:41-44.

Meltzer, H.Y., Cucchiaro, J., Silva, R., et al. Lursaidone in the treatment of schizophrenia: a randomized, double-blind, placebo- and Olanzapine controlled study. *Am J Psychiatry*, 2011; 168:957-967.

Crabtree, B.L., Montgomer, J. Iloperidone for the management of adults with schizophrenia. *Clinical Therapeutics*, 2011; 33(3): 330-345.

Kane, J., Cohen, M., Zhao, J., et al. Efficacy and safety of asenapine in a placebo- and haloperidol-controlled trial in patients with acute exacerbation of schizophrenia. *J Clin Psychopharmacol*, 2010; 30: 106-115.

Table A.4: Drug Efficacy for ARBs, Measured by Reduction in Systolic Blood Pressure

Ingredient	Efficacy	Source	Measurement Details
Losartan	9	Oparil et al. (2001)	50 mg, measured at 8 weeks
Irbesartan	11.3	Oparil et al. (2001)	150 mg, measured at 8 weeks
Olmesartan	12.5	Oparil et al. (2001)	20 mg, measured at 8 weeks
Candesartan	13.3	Bakris et al. (2001)	16 mg, measured at 8 weeks
Telmisartan	13.2	Williams et al. (2009)	80 mg, measured at 8 weeks
Eprosartan	5.8	Sachse et al. (2002)	600 mg, measured at 8 weeks
Valsartan	8.1	Oparil et al. (2001)	80 mg, measured at 8 weeks
Valsartan + Aliskiren	17.2	Oparil et al. (2007)	160 + 150 mg, measured at 8 weeks
Hydrochlorothiazide	6.35	Messeli et al. (2011)	12.25-25 mg , measured at 17 weeks

Sources:

Oparil, S., Williams, D., Chrysant S.G., et al. Comparative efficacy of Olmesartan, Losartan, Valsartan, and Irbesartan in the control of essential hypertension. *J Clin Hypertens*, 2001;3:283-291.

Bakris, G., Gradman, A., Reif, M., et al. Antihypertensive efficacy of Candesartan in comparison to Losartan: the CLAIM study. *J Clin Hypertens*, 2001; 3: 16-21.

Williams, B., Lacourciere, Y., Schumacher, H., et al. Antihypertensive efficacy of telmisartan vs ramipril over the 24-h dosing period, including the critical early morning hours: a pooled analysis of the PRISMA I and II randomized trials. *J Human Hypertension*, 2009. 23: 610-619.

Sachse, A., Verboom, C.N., and Jager, B. Efficacy of eprosartan in combination with HCTZ in patients with essential hypertension. *J Human Hypertension*, 2002. 16:169-176.

Oparil, S., Yarows, S.A., Patel, S., et al. Efficacy and safety of combined use of aliskiren and valsartan in patients with hypertension: a randomised, double-blind trial. *Lancet*, 2007. 370:221-229.

Messeli, F.H, Makani, H., Benjo, A., et al. Antihypertensive efficacy of Hydrochlorothiazide as evaluated by ambulatory blood pressure monitoring; A meta-analysis of randomized trials. *J Am Coll Cardiol*, 2011. 57:590-600.

Table A.5: Drug Efficacy for Statins, Measured by Reduction in LDL

Ingredient	Efficacy	Source	Measurement Details
Lovastatin	24.0%	Bradford et al. (1991)	20 mg/daily, measured at 48 weeks
Pravastatin	29.7%	Jones et al. (2003)	40 mg/daily, measured at 6 weeks
Simvastatin	35.0%	Jones et al. (2003)	20 mg/daily, measured at 6 weeks
Atorvastatin	42.6%	Jones et al. (2003)	20 mg/daily, measured at 6 weeks
Fluvastatin	17.0%	Jones et al. (1998)	20 mg/daily, measured at 8 weeks
Rosuvastatin	52.4%	Jones et al. (2003)	20 mg/daily, measured at 6 weeks
Pitavastatin	37.6%	Saito et al. (2002)	2 mg/daily, measured at 12 weeks

Sources:

Bradford, R.H., Shear, C.L., Chremos, A.N., et al. Expanded clinical evaluation of lovastatin (EXCEL) study results. *Archives of Internal Medicine*, 1991; 151:43-49.

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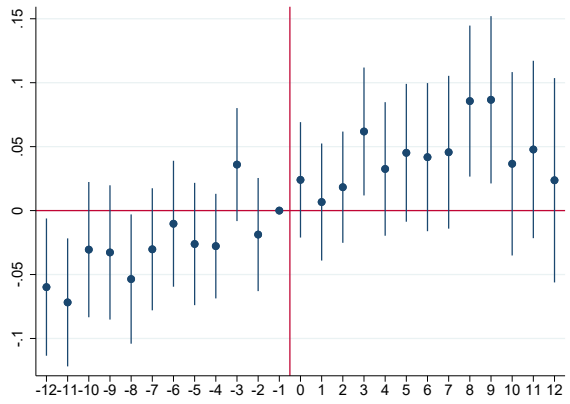
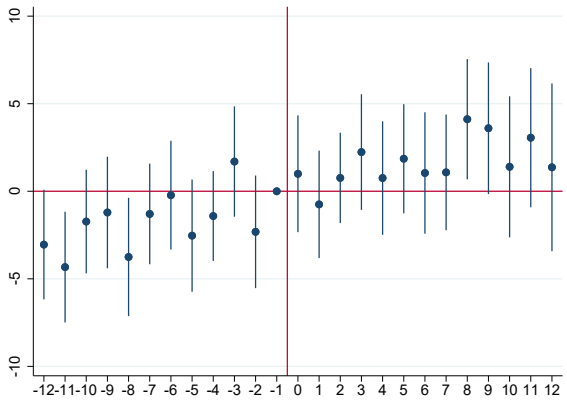
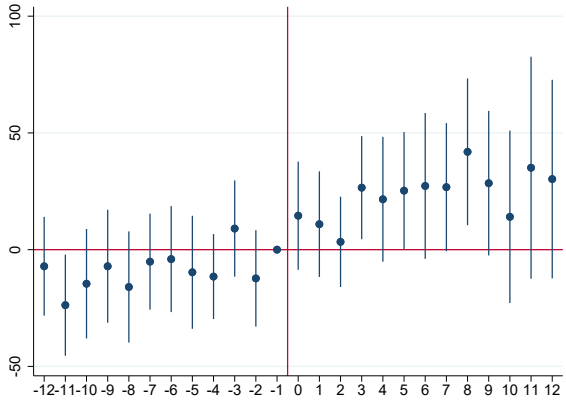
Figure A.5: Impacts of Payments on Expenditure and Patients: Therapeutic Classes for Efficacy Analysis



(a) Number of Patients



(b) Days Supply



(c) Expenditure

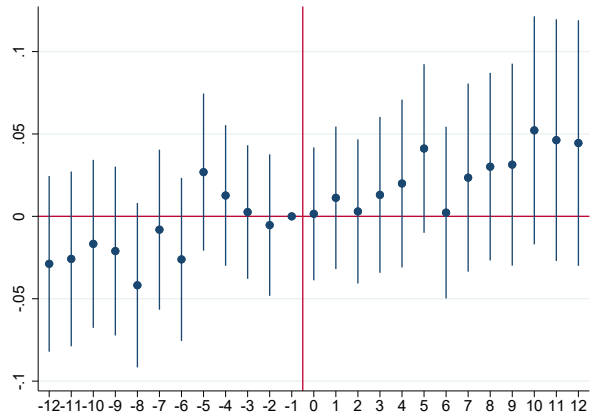
Coefficients and 95% confidence intervals from the estimation of Equation 1 are presented for the three therapeutic classes used in the efficacy analysis in Section 6. The dependent variable is (a) the number of patients, (b) the total days supply, or (c) total expenditure for a physician-drug-month. The month prior to the payment is the reference group. Controls for other payments in the therapeutic class as well as physician-drug and drug-month fixed effects are always included. Standard errors are clustered by physician.

Table A.6: Impact of Payments on Quantity and Expenditure: Therapeutic Classes for Efficacy Analysis

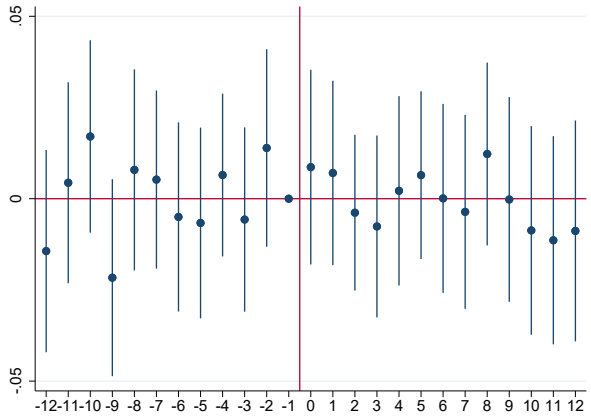
	Number of Patients	Total Days Supply	Expenditure
	(1)	(2)	
Months 0 - 5	0.031*	0.978	17.04*
	(0.019)	(1.158)	(8.95)
Months 6 - 12	0.0573**	2.382*	28.93**
	(0.026)	(1.412)	(14.53)
Mean dep. var.	1.98	100.35	$231.54
No. physicians	224,988	224,988	224,988
Observations	19,909,188	19,909,188	19,909,188

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.

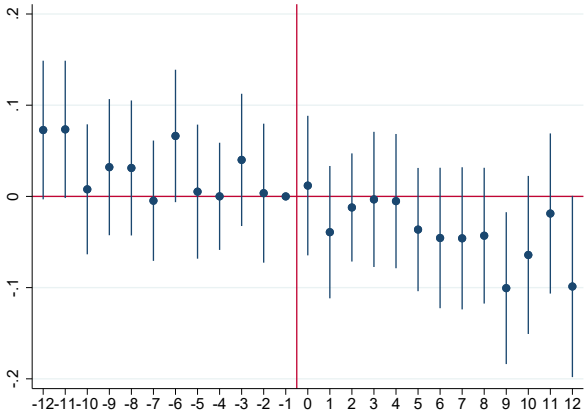
Figure A.6: Impact of a Payment on Average Efficacy by Individual Therapeutic Class



(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.7: 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	-0.0000841	0.0150	-0.014	0.0022
	(0.0028)	(0.018)	(0.027)	(0.0094)
Months 6 - 12	-0.003	0.031	-0.053*	-0.0019
	(0.0033)	(0.024)	(0.030)	(0.0106)
Mean dep. var.		13.87	37.43	9.21
No. physicians	490,382	198,627	409,445	307,047
Observations	17,113,017	2,885,172	8,251,720	5,976,25

Dependent variable is given in column heading. Estimates are linear combinations of event study estimates presented in Figures 6 and A.6. The month prior to the payment is the reference group. Standard errors are clustered by physician.