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NOTHING FOR SOMETHING: MARKETING CANCER DRUGS TO PHYSICIANS INCREASES PRESCRIBING WITHOUT IMPROVING MORTALITY

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ABSTRACT

Physicians commonly receive marketing-related transfers from drug firms. We examine the impact of these relationships on the prescribing of physician-administered cancer drugs in Medicare. We find that prescribing of the associated drug increases 4% in the twelve months after a payment is received, with the increase beginning sharply in the month of payment and fading out within a year. A marketing payment also leads physicians to begin treating cancer patients with lower expected mortality. While payments result in greater expenditure on cancer drugs, there are no associated improvements in patient mortality.

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1 Introduction

Innovations in biomedical science have resulted in nearly 500 cancer drug approvals over the past decade.¹ The novelty of these therapies create a special role for direct-to-physician marketing in this setting. Cancer regimens are complex and the evidence base for optimal management is fast-changing. Drug firms use face-to-face visits with firm representatives, usually involving a meal, to educate physicians about the clinical evidence for new therapies or new indications and answer questions about side effects or drug interactions. These marketing activities have long been viewed as a policy concern due to their potential influence on physician prescribing decisions (Angell, 2005; Chao and Larkin, 2022). They can be especially problematic in light of the high prices for certain cancer drugs with small survival benefits, such that distortions to physicians' prescribing decisions could have large impacts on healthcare spending with limited impacts on patient health (MedPAC, 2023).

In this paper, we provide novel evidence on the impact of marketing payments between drug firms and physicians on the prescribing of physician-administered cancer drugs and subsequent patient mortality. We combine large-scale prescribing and mortality records from Medicare with mandatorily-reported marketing payments from the federal Open Payments dataset.

Using our novel linkage of Open Payments to cancer prescribing records, we find that physicians prescribing cancer drugs have frequent marketing encounters, with 67% of our sample of cancer-treating physicians receiving at least one cancer-drug marketing payment between 2014 and 2018. Major drugs such as Opdivo and Keytruda reach more than half of prescribers with marketing payments.

We find that physicians increase prescribing of cancer drugs for which they have received payments precisely in the month in which the payment occurs. Expenditure on the relevant drug stays elevated for about ten months. The magnitude of the effect constitutes a 4% increase in drug expenditure. Our analysis uses a within-physician design that compares a physician's prescribing after a payment to her prescribing just before to overcome potential bias from drug firms' selective targeting of high-prescribing physicians. The fact that the increase in prescribing occurs right after the marketing payment lends credibility to a causal interpretation of our difference-in-differences research design.

Following the first payment, we also see aggregate increases at the physician level in total expenditure on cancer drugs and the number of patients receiving cancer drugs. To characterize the marginal cancer patients whom physicians begin treating with drugs after

 $^{^1\}mathrm{Authors'}$ calculations from Oncology Approval Notifications (FDA, n.d.), including both first approvals and additional indications.

a payment, we develop a model of predicted mortality estimated with our cancer patient sample. We find that after a payment, physicians expand treatment to patients with lower predicted mortality.

If the marketing payments educate physicians, the increased expenditures after a payment could result in patients getting higher-efficacy drugs. If so, the payments should result in improvements in overall survival, the "gold standard" endpoint in clinical trials of cancer drugs (Delgado and Guddati, 2021). However, we find no changes in patient survival among physicians who receive payments, ruling out any reduction in one-year mortality larger than about 0.74 percentage point (p.p.), or 4.2% of the mean. Our result is all the more striking given that a payment induces physicians to prescribe cancer drugs to patients with low predicted mortality, meaning that compositional changes alone should have reduced mortality.

We conclude that direct-to-physician marketing payments, considered as an intervention, result in no mortality improvements despite the extra spending they induce (i.e., "nothing for something"). Our confidence interval rules out estimates of the survival benefits of novel cancer therapies as measured in clinical trials. We also evaluate the cost effectiveness of marketing payments, showing that even at our confidence interval's lower bound, marketing payments induce too little mortality improvement to justify the increased spending.

Our study is distinguished from previous literature by its inclusion of a well-measured and clinically-relevant outcome: patient mortality. In principle, marketing activities could play a useful role in disseminating new drugs to ensure the potential benefits of these innovations reach patients. However, we find that while marketing payments increase expenditure, the increased outlays do not result in mortality improvements.

Our core finding implies that the incremental cancer drug spending induced by marketing payments has no survival benefits. Marketing payments may have led physicians to shift patients to cancer drugs with limited survival benefit (MedPAC, 2023). This could be because of a divergence between clinical trial efficacy and real-world effectiveness of prescription drugs; alternatively, the marketed drugs may have small-to-no survival advantage over the drugs they replace (Berger et al., 2016; Sumarsono et al., 2020). It is also possible that after a marketing payment, physicians are deploying the drugs outside of cancer settings/indications where survival benefit was shown. Consistent with that hypothesis, Mitchell et al. (2023) find that direct-to-physician marketing reduces guideline concordance in cancer care, while Agha and Zeltzer (2022) show that marketing of anticoagulants increases their prescription to contraindicated patients.

We find that a marketing payment induces physicians to begin treating patients with low predicted mortality. To our knowledge, our paper is the first to show that marketing payments induce physicians to expand treatment to healthier patients. This finding supports the hypothesized mechanisms above about why the induced prescribing has no mortality benefit; perhaps these drugs are being used on slower-growing cancers or cancers commonly treated successfully with surgery and radiation. In addition, it's possible that these incremental patients will experience survival benefits from these drugs beyond the 12- or 24-month windows that we use in our five-year panel.

Our paper brings a state-of-the-art research design to the question of the effect of physician-directed marketing on cancer drug prescribing.² The recent review of Mitchell et al. (2021) found that more than half of 36 studies examining the association of financial incentives and physician prescribing did not account for drug firms' targeting of payments to high-prescribing physicians (Fugh-Berman and Ahari, 2007). Our design compares prescribing within physicians in the months surrounding a payment to isolate the effect of the payment from the selection into marketing payments.

Finally, our study focuses on the effect of marketing activities for cancer drugs. Cancer drug spending doubled over our sample period (2014 to 2018), leading policymakers to consider reforms to sharpen price competition and dampen the payment-based physician incentive to prescribe higher-priced drugs (IQVIA, 2019; Nguyen and Sheingold, 2020; Howard et al., 2015). The tools that limit the use of high-priced drugs in Medicare Part D – formulary exclusion or tiered copays – are not used for Part B physician-administered drugs. Given the incentives physicians face to prescribe high-priced cancer drugs and the lack of limitations on such prescribing, it is noteworthy that we find that payments have a similar effect for cancer drugs as Carey, Lieber and Miller (2021) found for Part D drugs with no such physician incentives and substantial limitations on prescribing.

2 Background

2.1 Direct-to-Physician Marketing

Pharmaceutical firms focus most of their marketing expenditures on physicians, due to physicians' key role in deciding whether to prescribe a drug and choosing among competitors. In 2012, pharmaceutical firms directed \$23 billion in marketing expenditures towards physicians, in the form of detailing, samples, or sponsorship of educational meetings (Pew Charitable Trusts, 2013). These marketing activities have long been viewed with suspicion, with influential physician Marcia Angell describing them as "bribery from the drug companies" (PBS Frontline, 2002). However, defenders note that these financial relationships can facili-

²Mitchell, Winn and Dusetzina (2018) complements our prescribing results using a dataset covering a subset of Part D prescriptions of oral cancer therapies.

tate education on pharmaceutical advances or correct underprescribing (Campbell, 2007).

Both health care organizations and governments have taken action to regulate directto-physician marketing activities. In recent years, many academic medical centers or large health systems prohibited or restricted direct-to-physician marketing (Larkin et al., 2017). At the federal level, the 2010 Physician Payments Sunshine Act required pharmaceutical firms to track financial interactions with physicians and mandated their public disclosure. The resulting database, *Open Payments*, was intended to increase transparency around physicianindustry relationships (Richardson et al., 2014).

2.2 Provision and Reimbursement of Cancer Drugs in Medicare

We study prescribing of cancer drugs in Medicare which provides coverage for more than half of new cancer cases (Stockdale and Guillory, 2013). Drug therapy is the most expensive component of cancer care, with about 70% of cancer expenditures going to drugs (Newcomer, 2020).

Medicare coverage for cancer drugs depends on whether they are administered by a physician or self-administered by the patient at home. Cancer drugs that are infused or injected, or with a potential for adverse reactions, are administered by a physician and covered by Medicare Part B. This category represents two-thirds of cancer drugs spending in Medicare (Abt Associates, 2021). Over our sample period, Medicare reimbursed physician-administered drugs at 104.3% of the drug's average sales price, regardless of the actual costs the physician incurred in obtaining the drug (Nguyen and Sheingold, 2020). Self-administered cancer drugs are covered under Medicare Part D.

3 Data and Empirical Strategy

3.1 Data Sources

Medicare Claims Our prescribing and mortality outcomes are measured for a 20% random sample of Medicare fee-for-service (FFS) beneficiaries 2014–2018. We observe the use of physician-administered cancer drugs in office settings (Carrier file) and hospital outpatient departments (Outpatient file). Each claim contains the Healthcare Common Procedural Coding System (HCPCS) codes used to identify specific cancer drugs, the service date, the expenditure, and the physician's National Provider Identifier (NPI). **Open Payments** The Open Payments dataset contains nearly the universe³ of all payments and in-kind "transfers of value" from pharmaceutical companies to physicians beginning in August 2013. Each Open Payments entry records the physician's name and address (which we link to NPIs via the National Plan and Provider Enumeration System database), the marketed drug, and a description (such as meals, travel, research, consulting, and speaking fees). We follow the database administrators in referring to the Open Payments transfers as "payments". Payments in the dataset - particularly meals - primarily occur as part of "detailing" visits in which a marketing representative describes the drug's benefits. Among the cancer-drug payments we link to physicians treating cancer in Medicare, 97% are for meals and 90% are below \$35.

3.2 Sample Construction

Physician-Administered Cancer Drugs We develop a sample of 99 physician-administered cancer drugs from the intersection of cancer drugs collected by the National Cancer Institute (National Cancer Institute, 2021) and physician-administered drugs covered by Medicare (CMS, 2020). We exclude drugs that are commonly used for non-cancer indications.⁴

Fourteen of these cancer drugs were launched (first FDA approval) between 2014 and 2018. We can measure prescribing of these new drugs once they obtain their unique HCPCS code in the following January (Dranove et al., 2021).

We characterize the "price" of each cancer drug by taking the average monthly expenditure on that drug for all patient-months with any claims. This time-invariant concept abstracts away from differences in drug regimens as well as changes in price that could co-occur with marketing.

Cancer-Treating Physicians We measure each physician's prescribing via cancer drug administrations where they are listed as the "performing" physician (Carrier claims) or "attending" physician (Outpatient claims). A physician could administer a treatment regimen that was prescribed by another physician – i.e., a partner in the practice. If so, any single physician would account for only a small share of a patient's administrations. Instead, we find that 65% of cancer patients receive all drugs from a single physician, and on average

³Exemptions apply if a payment is below a threshold (\sim \$10) or if total payments in a year are below a threshold (\sim \$100). However, we observe many payments that meet the exemption criteria, suggesting that pharmaceutical firms may report all encounters.

⁴We include drugs if at least 25% of the claims are from medical oncologists, or at least 10% are from medical oncologists and 25% are from a broader set of specialties that commonly treat cancer: internal medicine, urology, obstetrics/gynecology, radiation oncology, surgical oncology, and hematology. This process rules out drugs that are frequently used for non-cancer purposes, the most common category of which is hormone therapy. We additionally exclude all hormone therapies.

cancer patients receive drugs from only 1.7 physicians. This suggests that the physician administering the drugs is also the physician choosing among cancer therapies. We reassign cancer drug administrations by mid-level providers (< 2% of administrations) to physicians treating the same patient, because we expect they are implementing a physician's treatment plan. Finally, we require physicians prescribe at least one cancer drug per year; this excludes early-career physicians, for whom we would inaccurately impute zero prescribing prior to entry. Our final physician sample consists of more than 20,000 physicians; 30% report a specialty in medical oncology, while the remainder are in specialties that treat specific cancers (e.g., urologists treat prostate cancer).

Outcomes We examine outcomes at two levels of aggregation. The first is the physiciandrug-month level. We aggregate expenditure (i.e., the sum of spending by the patient and all payers) for administrations by a particular physician of a particular drug⁵ in each month. We also consider the number of patients receiving the drug from this physician in a month. For both outcomes, we form a balanced panel of physician-drug-month outcomes (imputing zeroes when no claims are observed) for the years 2014–2018.

We also consider outcomes at the physician-quarter level. To characterize total prescribing, we measure expenditure on all cancer drugs, as well as the number of patients receiving cancer drugs. The majority of sampled physicians prescribe cancer drugs in every quarter, and we impute zero for physicians that have any quarters without prescribing. At the physician-quarter level, we expect a payment to have multiplicative effects, and so we normalize these outcomes by their levels prior to any payment, as recommended by (Chen and Roth, 2023). Thus, we are predicting the prescribing (expenditure or number of patients) of cancer drugs in a quarter relative to the physician's average quarterly prescribing of cancer drugs in 2014. These normalized outcomes, however, exhibit massive right skew, particularly for expenditure. Appendix Table A.1 reports percentiles of the distribution of the physician-quarter outcomes. In our analysis sample (described below), the median physician-quarter expenditure is \$13,132 and the median normalized expenditure, 1.19, represents a 19% growth in prescribing relative to 2014. The first two columns show that the upper percentiles of the normalized outcome are much further from the median than for the outcome in levels; for some physicians, expenditure grows more than 4000-fold from its 2014 levels. Due to the leverage of these outlier observations, we winsorize the normalized outcomes at the 97th percentile, essentially topcoding a physician's growth in cancer drug

⁵Note that we count only expenditure on the drug itself, not the service of drug administration. This outcome represents drug firm revenues, which is what marketing encounters are designed to influence, and is comparable between the Carrier and Outpatient files (Moran Company, 2013).

expenditure at a fourteen-fold increase from their 2014 average.^{6,7}

To further characterize a physician's prescribing, we calculate the average price of cancer drugs prescribed using our time-invariant price concept (i.e., we assign each patient taking the drug its average monthly expenditure and take the mean price across patient-months). This outcome is observed in any quarter with positive prescribing.

Finally, we measure mortality among a physician's patients. We construct a 12-month mortality rate where the denominator is the number of a physician's cancer drug patients in a quarter and the numerator is the number of those individuals who die in that quarter or the following three. An alternative 24-month measure reflects mortality in that quarter or the following seven.⁸

Our two levels of aggregation – physician-drug-month and physician-quarter – are complementary. The more granular physician-drug-month outcome allows us to isolate the outcomes most likely to respond to drug-specific marketing activities. In addition, examining the outcome at monthly frequency lets us describe the time pattern of prescribing changes precisely. However, mortality is not well-measured at the physician-drug-month level because it is undefined in any cell in which the number of patients is zero. Measuring mortality among a physician's full panel of patients avoids double-counting patients taking multiple drugs, while aggregating to the quarter level smooths the series and reduces missingness.

3.3 Summary Statistics

We begin by constructing and summarizing our dataset linking cancer drug prescribing and marketing payments. To form this "descriptive" dataset, we combine three categories of physician-drug pairs. The first are physicians prescribing one of our 99 cancer drugs for which they receive no marketing payments. The second are physicians who both prescribe a drug and receive a payment for it at some point. The third are sampled physicians who receive a payment for a drug but never prescribe it. Combining the three types together amounts to 372,940 physician × drug pairs; the proportion of each type in the "descriptive" dataset is described in Panel A of Table 1. Physicians who ever prescribe the drug receive more than half of marketing payments (=0.18/(0.18+0.16)), so cancer drug marketing is successful at reaching its target market.

The next set of rows refer to the intensity of marketing. Among physician-drugs with any payment, about a third have only one payment over the time period, while 38% have

⁶No data edits are required at the left tail, where the 3rd percentile is the minimum value of 0 for both normalized expenditure and normalized patients.

⁷We explore robustness to functional form and winsorization in Section 4.5.

⁸Because our data end in 2018Q4, a physician's 12-month mortality rate is observed in any quarter with positive prescribing prior to 2018Q1 and a 24-month mortality rate prior to 2017Q1.

2-5 payments for the same drug over the time period, and 29% have 6+ payments. The final two rows in Panel A report the average outcomes (applying analysis weights described in Section 3.4) at the physician \times drug \times month level.

Panel B of Table 1 provides detail on our physician-quarter aggregates, where we aggregate payments and prescribing across all cancer drugs. We find that 67% of cancer-treating physicians received at least one payment for a cancer drug between 2014 and 2018.

Marketing payments are especially common among high-priced and commercially successful cancer drugs. Figure 1 characterizes drugs by their monthly price (x-axis) and the share of the drug's prescribers with a marketing payment for that drug (y-axis). The size of the marker represents the drug's total expenditure in 2018 in Medicare, with the top six drugs labeled. Marketing payments for the highest-expenditure drugs are commonly reaching a substantial share of the drug's prescribers, as many as 53.5% (Keytruda).

To estimate the event study we describe in the next Section, we form an "analytical" subsample for both levels of aggregation and describe it in the second column of Table 1. We first exclude 40 drugs⁹ that do not make payments over the sample period. In addition, we restrict the sample to physician-drug pairs (physician×drug×month dataset) or physicians (physician×quarter dataset) where the first payment occurred in or after January 2015, ensuring twelve months of "clean" pre-period prior to "treatment" (i.e.,payment).¹⁰ Finally, we require that physicians have positive cancer-drug prescribing in the pre-treatment period (2014), so that we can normalize expenditure and number of patients by the 2014 averages. After these restrictions, Table 1 reports that our analytical sample has a similar distribution of payments among physicians as the descriptive sample.

However, the analytical samples are qualitatively different from the set of physicians ever receiving payments because it excludes physicians who have very frequent interactions with drug firms. Comparing to the descriptive samples, the analytical samples overrepresent physician-drugs (Panel A) or physicians (Panel B) who are paid only once over the sample period while underrepresenting those who are paid six or more times over the sample period. Frequently-paid physicians are excluded by the requirement of a 12-month "clean" preperiod. This difference in sample selection means our results are most applicable to occasional marketing interactions.

⁹Specifically, we exclude 34 drugs with no Open Payments records and 6 drugs with fewer than 10.

¹⁰For the 14 drugs launched during our analysis period we restrict to physicians where the first payment for this drug occurred at least 12 months after the drug's HCPCS issuance allows us to observe its prescribing.

3.4 Econometric Approach

Our core empirical strategy is a difference-in-differences implemented via an event study. Since physicians who receive payments for a specific drug may be more likely to prescribe that drug even in the absence of such payments, the cross-sectional relationship between payments and prescribing is biased upward from the causal impact. Our research design instead isolates changes in the prescribing of paid physicians before and after they receive a payment, using the change over the same time period for unpaid physicians as a control.

First, we consider physician-drug-month outcomes as a function of whether the physician has been paid for that drug. The primary specification is as follows:

$$y_{pdt} = \sum_{r \neq -1} PresPaid_{pd}\beta_r + \delta_{pd} + \delta_{dt} + \epsilon_{pdt}, \qquad (1)$$

where p indexes physicians, d indexes drugs, and t indexes year-months. y_{pdt} is one of the two dependent variables (drug expenditures or number of patients) at the physician-drug-month level. $PresPaid_{pd}$ is an indicator that equals 1 if the physician ever received a payment associated with drug d in our study period; we dichotomize our payment variable because of evidence in Carey, Lieber and Miller (2021) that even small payments are influential in prescribing. The index r counts the month relative to the month when the physician first received a payment (if ever). The coefficients β_r measure the time pattern of prescribing for physician-drug pairs with a payment, net of the average difference between paid and unpaid physician-drugs. We estimate β_r for all periods but report only the subset $-12 \leq r \leq 12$.

Physician × drug fixed effects δ_{pd} account for any time-invariant physician characteristics that lead to both higher likelihood of the physician receiving a payment and of prescribing the drug in the absence of the payment. Drug-month fixed effects δ_{dt} account for secular changes in prescribing a specific drug common to all physicians, such as patent expiration. Observations for both physician-drug pairs with and without an associated payment will contribute to drug × month fixed effects. Standard errors are clustered at the physician level to accommodate correlation within a physician across drugs and time.

In estimating Equation 1, we weight each physician-drug-month observation by the average number of patients that received any cancer drug from that physician across all periods. This weighting choice is analogous to Carey, Lieber and Miller (2021), who weight by the average number of patients in the drug's therapeutic class. There are two advantages to this weighting. First, weighting by the number of patients means our analysis is representative of patients' experiences rather than physicians'. Second, weighting by the average number of patients on any cancer drug means that observations in which a physician is paid for a drug but does not prescribe it still have positive weights. To examine the effect of payments on physician-quarter outcomes, we estimate the following:

$$y_{pq} = \sum_{r \neq -1} PresPaid_p \gamma_r + \delta_p + \delta_q + \epsilon_{pq}, \tag{2}$$

In this equation, $PresPaid_p$ is 1 if the physician is ever paid for any cancer drug, and γ_r captures the change in the outcome r quarters before or after that payment. The fixed effect δ_p nets out the physician's average outcome over the sample period, while δ_q captures quarterly effects common to all sampled physicians.

In both equations 1 and 2, we restrict attention to the *first* reported payment from the drug company to the physician, although there can be further payments within the postperiod. Thus, the event-time coefficients should be interpreted as the effect of the initiation of marketing transfers after at least 12 months without any, rather than the effect of the first payment alone. Appendix Figure A.1 explains the time pattern of payments after the first by estimating event studies for the outcome variable of a contemporaneous payment at the physician-drug-month level (Panel (a)) or physician-quarter level (Panel (b)). By construction, the outcome is zero in the pre-period and one at event-time zero. After the first payment for a specific drug, less than 10% of physicians are paid again for the drug in the next twelve months. At the physician level, the first payment after at least one year without payments is somewhat more likely to be followed by other payments, with about one-quarter of the treated physicians being paid again, whether for the same or a different drug, in the following quarters.

The key identifying assumption for the post-period β_r coefficients in Equation 1 to yield unbiased estimates of the effect of a payment on prescribing of physician-administered cancer drugs is the parallel trends assumption, i.e. that the time pattern of prescribing by unpaid physicians represents the counterfactual time pattern of prescribing by paid physicians (if unpaid). While this assumption cannot be directly tested, the pre-period β_r coefficients allow us to observe any non-parallel trends in prescribing among the paid physicians before the payment occurs.

Even if parallel trends holds, our research design can be biased if there is heterogeneity in treatment effects over time (see de Chaisemartin and D'Haultfœuille (2022) for a survey). de Chaisemartin and D'Haultfœuille (2020) have developed an estimator that can produce unbiased estimates in this setting, which we apply in Section 4.5.

4 Results

4.1 Impact of drug-specific payments on drug-specific prescribing

We begin with Equation 1 relating payment for a drug with the physician's prescribing of that drug. In Figure 3(a) we find that physicians who will be paid (at time 0) are not altering prescribing relative to never-paid physicians prior to the payment. Beginning sharply at the month of payment, expenditure on the associated drug jumps. The flat pre-trends and the sharp jump in prescribing lend credence to a causal interpretation. The magnitude of the response is nontrivial. A linear combination of the post-period coefficients, reported in Appendix Table A.2, is \$40.82 (se 17.48), or a 4.1% increase relative to the mean of \$1002. This is comparable to the percent response in Carey, Lieber and Miller (2021), who report a 5.2% increase in expenditures. The effect of a payment on the number of patients (Figure 3(b)) is small and imprecise. The linear combination of the post-period coefficients for number of patients is not statistically different from zero (0.001, se 0.005).

Our results reveal a statistically significant increase in expenditure without corresponding increases in the number of patients taking the drugs. Examining heterogeneity by drug price can reconcile these findings. We separately estimate the model for drugs with prices above and below the median (approximately \$3000 in average monthly expenditure) and report the results in Appendix Figure A.2. For expensive drugs, we find a statistically significant increase in the number of patients taking the drug, with the 12-month post-period coefficients averaging 0.0049 (se 0.0030, 3.0% of the mean). There is no increase in the number of patients for cheaper drugs. For the expenditure outcome, we find increases among expensive drugs – an average increase of \$43.59 (se \$25.12) over the 12-month post period, with a smaller (\$27.58, se \$12.46) increase in expenditure for cheaper drugs. Thus, we infer that the overall treatment effect is driven by expensive drugs. Because of skew in the expenditure distribution, the treatment effect among expensive drugs pulls up the average treatment effect on all drugs. But there is no skew in the distribution of number of patients outcome, thus leaving the average treatment effect unaffected for that outcome.

4.2 Impact of any payment on prescribing and mortality

We next estimate the impact of receiving any payment on overall prescribing using Equation 2. Figure 4(a) shows that, following the physician's first payment from a drug company, quarterly expenditure on cancer drugs prescribed by that physician increases conspicuously and remains elevated for the year after the first payment. A linear combination of the post-period coefficients finds an increase of 8.9% (se 4.2%) in the physician's expenditure

on cancer drugs over the quarters after payment. Physicians who will be paid (at time 0) were trending very similarly to never-paid physicians during the four quarters prior to first payment, suggesting that the post-payment response is plausibly causal. Figure 4(b) demonstrates that the increase in expenditure is driven by an increase averaging 6.3% (se 2.4%) in the number of patients to whom the physician is prescribing cancer drugs. Figure 4(c) shows results for the average price of cancer drugs, and suggests that physicians do not appear to prescribe more expensive drugs after payment.

The extra expenditure on cancer drugs could mean that patients are getting higherefficacy drugs, which should be observable in reduced mortality. Figure 5(a) estimates Equation 2 for the physician's 12-month mortality rate. The pre-period coefficients suggest a statistically-insignificant pre-trend, suggesting that payments were not selectively targeting physicians with changing levels of patient mortality, and after a payment coefficients are close to zero for the following three quarters. Our confidence interval for the effect over the first five quarters rules out reductions beyond about 0.74 p.p., or 4.3% of the mean. Figure 5(b) repeats this analysis for 24-month mortality. This figure exhibits no pre-period trend among paid physicians, while also suggesting slightly higher mortality after a payment. These results suggest that payments from drug companies lead to higher expenditures without a corresponding improvement in patient mortality.

4.3 Impact of any payment on patient composition

Finally, we examine whether a payment changes the type of patients a physician treats with cancer drugs. Figure 4(b) suggests that physicians give cancer drugs to more patients after a payment; if these marginal patients are particularly likely to die, their addition to the physician's patient pool could be masking a true improvement in mortality among inframarginal patients.

To examine this possibility directly, we predict each cancer patient's expected 12-month mortality. Following Zeltzer et al. (2023) we form a prediction using cancer type, comorbidities, markers of complications (hospitalizations), and demographics (see Appendix for full details and model fit). We aggregate to the physician-quarter to measure predicted 12-month mortality for the patients the physician is treating in that quarter.

We find that payments alter patient composition towards individuals with ex ante lower mortality. Figure 5(c) uses the physician-quarter expected mortality measure as a dependent variable; by the third quarter after the payment, predicted mortality is about 5% lower than it was in the three quarters preceding the payment. Figure 5(d) uses realized 12month mortality as the dependent variable with expected mortality as a control. Since we find that after a payment physicians begin treating healthier patients, including this control suggests that payments may actually increase mortality, although the result is not statistically significant (0.0064, se 0.0043).

4.4 Interpretation of mortality results

To contextualize our mortality results, we draw from the literature about expected effects of recent cancer therapies. As an input to their model of life insurance, Koijen and Van Nieuwerburgh (2019) use clinical studies to approximate the improvement in 12-month mortality rates for cancer patients who receive immunotherapies instead of the previous standard of care. They estimate that immunotherapies restore about half of the 12-month mortality increase associated with a cancer diagnosis.

To apply their estimates in our study, we first note that immunotherapies represent 66% of the payments we study. Lam et al. (2018) estimate that in 2014 (before widespread use of immunotherapies), the 12-month mortality rate among Medicare beneficiaries with cancer was 21.9%, 6.2 p.p. higher than the mortality rate for beneficiaries without cancer. If immunotherapies restore half of that mortality gap, and a 2/3rds of the payments induce expenditure on immunotherapies, we would expect a 2.05 p.p. reduction in 12-month mortality, far outside of our confidence interval.

A second way to contextualize our results is to calculate the cost-effectiveness of the extra expenditure induced by a payment, which is commonly measured in terms of the incremental cost effective ratio (ICER):

$$\frac{Cost_{treat} - Cost_{control}}{QALY_{treat} - QALY_{control}},\tag{3}$$

The numerator in Equation 3 is the incremental cost of the treatment relative to the control, or this case, the increase in drug expenditure resulting from payment initiation; the denominator in (3) represents the incremental benefit of the treatment relative to the control in terms of gain in quality adjusted life years (QALY). We calculate incremental expenditure as 8.9% (e.g., the average of post-period coefficients in Figure 4(a)) of the weighted 2014 quarterly mean expenditure (\$30,886) times four quarters, or \$10,995.

To calculate the incremental QALY, we first note that the majority of the confidence interval in Figure 5(a) covers *increases* in mortality, indicating that the incremental expenditure purchases *negative* health. We evaluate the ICER at the lower bound of the linear combination of the post-period coefficients, which is -0.741 pp or 7.41 averted deaths per 1000 cancer patients for Figure 5(a) without controlling for expected mortality, and -0.198 pp in Figure 5(d) controlling for predicted mortality. Next, we require an estimate of the number of incremental QALYs associated with each averted cancer-patient death. Following the assumptions in Briggs et al. (2021) for COVID-19 deaths, we assume that individuals in our sample – individuals taking cancer drugs – who do not die have conditions that, collectively, increase their mortality risk by a factor of 2 and reduce their quality of life to 80%of perfect health. Following Briggs et al. (2021), we collect estimates for discounted incremental QALYs for each averted death for specific age bins, and weight those by the age-bin composition of our sample. This results in an incremental QALY benefit of 4.63 per averted death. Finally, we multiply by the number of patients treated per year by paid physicians (8.56).¹¹ Depending on the mortality results we use, the product (number of averted deaths * 4.63 QALYs per averted death * 8.56 patients) is 0.294 QALYs per payment (for 0.00741 averted death in Figure 5(a)) or 0.0785 QALYs per payment (for 0.00198 averted death in Figure 5(d) controlling for expected mortality), leading to an ICER of \$37,452 in the former case and \$140,072 in the latter case. While the former is within the range of prevailing thresholds for cost-effectiveness in the UK and other countries (\$28,471 - \$42,857) (Cherla et al., 2020), the latter is above even the prevailing threshold in the US (\$100,000). These calculations suggest that payments lead to changes in prescribing that are not cost-effective even at the lower bound of our mortality estimates that account for patient risk.

4.5 Robustness

We assess the robustness of our findings to alternative assumptions and specifications.

Physician-Quarter Outcomes: Appendix Section A.2 explores the normalization and winsorization of the outcomes in the physician-quarter analyses. Since we are interested in a multiplicative effect for that outcome, we also explore the outcomes ln(1 + expenditure) and ln(1 + #patients), despite the unreliability of that transformation noted by Chen and Roth (2023)). We also explore winsorizing the normalized outcomes at higher percentiles. These results broadly confirm that after a payment physicians increase cancer drug prescribing by 5-10%.

Treatment Effect Heterogeneity: Appendix Section A.3 applies the estimator of de Chaisemartin and D'Haultfœuille (2020) to our setting to remove potential bias from treatment effect heterogeneity; our results are similar when using this estimator.

¹¹Note that both the cost differences and this patient count refer only to a 20% sample of Medicare feefor-service beneficiaries, but scaling up would inflate the numerator and denominator by the same amount.

Newly-Launched Drugs: Take-up of newly-launched drugs is poorly accommodated by a physician fixed effect. To avoid overstating the effect of marketing in the physician-quarter analyses, Appendix Section A.4 demonstrates robustness to the exclusion of newly-launched drugs.

5 Conclusion

In this paper, we examined how marketing-related payments affect cancer prescribing patterns and mortality in Medicare. We find that after a payment, physicians increase cancer drug expenditure, specifically on the marketed drug. However, these increased expenditures result in no detectable decrease in mortality among these patients, and our results are precise enough to rule out decreases beyond 4.2%.

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Panel A: Physician-Drug-Month Dataset		
Sample:	Descriptive	Analytical
# of physician \times drug \times months	21,708,660	12,141,216
$\#$ of physician \times drugs	$372,\!940$	$207,\!805$
# physicians	$27,\!271$	19,744
Share of physician \times drugs		
ever paid, ever prescribe	0.18	0.16
ever paid, never prescribe	0.16	0.16
never paid, ever prescribe	0.66	0.68
Among physician \times drugs ever paid, share with		
1 payment 2014–2018	0.33	0.45
2-5 payments 2014–2018	0.38	0.41
6+ payments 2014–2018	0.29	0.15
Expenditure (\$, weighted average)	828	1002
# Patients (weighted average)	0.42	0.47
Panel B: Physician-Quarter Dataset		
Sample:	Descriptive	Analytical
$\#$ of physician \times quarters	545,392	226,336
# of physicians	$27,\!271$	$11,\!319$
Share of physicians ever paid	0.67	0.40
Among physicians ever paid, share with		
1 payment 2014–2018	0.12	0.30
2-5 payments 2014–2018	0.25	0.42
6+ payments 2014–2018	0.63	0.28
Expenditure (\$, weighted average)	69,898	41,186
Normalized Expenditure (weighted, winsorized)	1.93	2.17
# Patients (weighted average)	12.97	7.88
Normalized # Patients (weighted, winsorized)	1.43	1.56
Price (\$, weighted average)	2,045	2,384
12-Month Mortality Rate	0.191	0.176
12-Month Predicted Mortality Rate	0.186	0.175

Table 1: Descriptive Statistics

Notes: This table reports on our sample of cancer drug prescribing in Medicare 2014–2018 joined to Open Payments records 2013–2018. The descriptive sample in the top panel includes physician-drug-months observations covering 99 cancer drugs. The analytical sample further excludes 40 drugs not making payments, physicians with zero prescribing in 2014, and physician-drug pairs whose first payment occurred during the first year of our study period. The lower panel reports on physician-quarter aggregates, with the descriptive sample reporting for all 99 cancer drugs, and the analytical sample reporting for 59 cancer drugs making payments and physicians whose first payment (for any drug) was in the first year of our study period and who had positive prescribing in 2014.

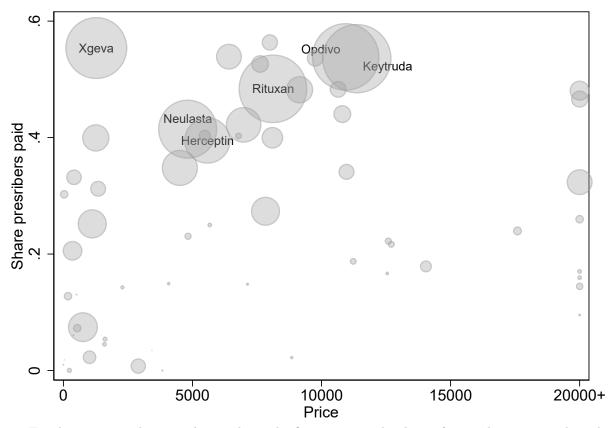
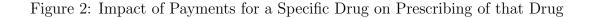
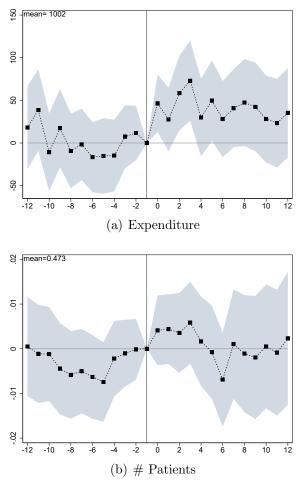


Figure 1: Drug price, share of prescribers paid, and expenditure

Notes: For the 59 cancer drugs used in analysis, the figure reports the share of prescribers ever paid on the y-axis and the price (average monthly expenditure per patient) on the x-axis. The size of the circle represents total drug expenditures in 2018 in Medicare, with the five drugs with the highest expenditure labeled.





Notes: Figure 2 reports the event-time coefficients from estimation of Equation 1 for drug expenditure and number of patients. The x-axis represents months before or after a first payment for the drug (time 0), with event-time -1 omitted as a reference. Analyses are weighted by each physician's average number of cancer patients. The gray area denotes 95% confidence intervals with standard errors clustered on physicians.

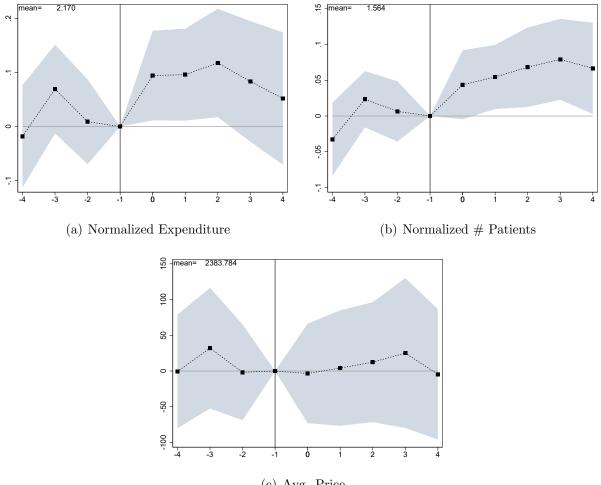


Figure 3: Impact of Any Payment on Physician's Prescribing



Notes: Figure 3 reports the event-time coefficients from estimation of Equation 2. The dependent variables, measured at the physician-quarter level, are cancer drug expenditure, normalized by average quarterly cancer drug expenditure in 2014 (panel (a)), cancer drug patients, normalized by average quarterly cancer drug patients in 2014 (panel (b)), and the average price of prescribed drugs (panel (c)). The x-axis represents quarters before or after a first payment for the drug (time 0), with event-time -1 omitted as a reference. Analyses are weighted by each physician's average number of cancer patients. The gray area denotes 95%confidence intervals with standard errors clustered on physicians.

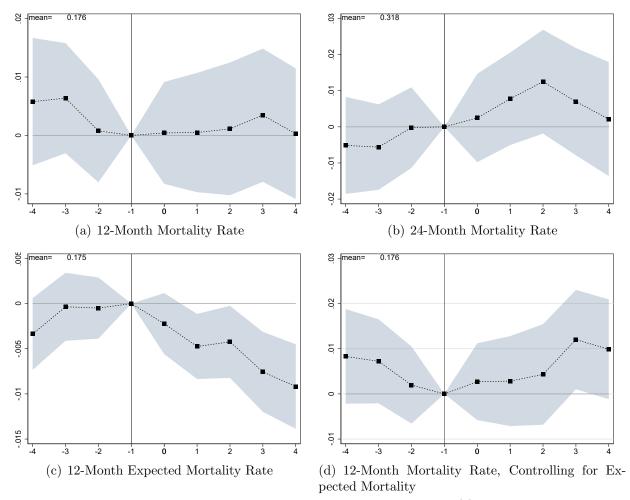


Figure 4: Impact of Any Payment on Actual and Expected Mortality

Notes: Figure 4 reports the event-time coefficients from Equation 2. In Panel (a), the dependent variable is the share of a physician's patients in given quarter that die within the following 12 months, while in Panel (b) it is the share that die within the following 24 months. In Panel (c), the dependent variable is the expected mortality for the physician's patients in the following 12 months (see text for expected mortality model), while Panel (d) uses actual mortality as the dependent variable and expected mortality as a control. The x-axis represents quarters before or after a first payment for the drug (time 0), with event-time -1 omitted as a reference. Analyses are weighted by each physician's average number of cancer patients. The gray area denotes 95% confidence intervals with standard errors clustered on physicians.

Nothing for Something: Marketing Cancer Drugs to Physicians Increases Prescribing Without Improving Mortality Online Appendix

Colleen Carey, Michael Daly, & Jing Li

A.1 Cancer Mortality Prediction

We build a predictive model of mortality among Medicare beneficiaries taking cancer drugs. The unit of analysis is the patient-quarter, to enable aggregation to the physician-quarter level for later analysis. Our sample comprises more than 5.8 million patient-quarters, representing approximately 900,000 individuals taking cancer drugs from 2014Q1 to 2017Q4, of whom 26% die. The outcome variable is one if the patient dies in that quarter or any of the next three.

Our predictors are measures of cancer type, comorbidities, complications, and demographics. Specifically, we apply the Clinical Categorization Software (CCS) to derive indicators for 285 clinically-relevant diagnoses. Thirty-six of these are for specific types of cancer. Our data spans the transition to ICD10 diagnosis codes, and we find evidence of more CCS diagnoses in 2015Q4 onwards. The CCS diagnoses rely on an encounter documenting the diagnosis in each calendar quarter; since these diagnoses are highly chronic, we carry them forward for three quarters following their documentation. We measure complications by the number of hospital admissions in the quarter. Our final model uses a linear probability model to predict mortality using

- Indicators for the 36 cancer CCS diagnoses
- $\bullet\,$ The number of cancer CCS diagnoses, as indicators, interacted with an indicator for 2015Q4 and later
- $\bullet\,$ The number of non-cancer CCS diagnoses, as indicators, interacted with an indicator for 2015Q4 and later
- Indicators for the number of hospital admissions in the quarter
- Indicators for five-year age bin interacted with sex
- Indicators for year-quarter

Appendix Figure A.3 demonstrates the fit of our model. The patient-quarters are first sorted into twenty vingtile bins according to predicted mortality. In the figure, each dot represents one such bin, with the x-axis reporting mean predicted mortality in that bin and the y-axis the mean realized mortality. We note that the use of the linear probability model results in a small number of observations with negative predicted mortality. With more than 5.8m observations and only 205 coefficients, our good model fit is not likely to be due to overfitting.

A.2 Robustness: Physician-Quarter Normalized Outcomes

Our physician-quarter analysis predicted the dependent variables expenditure and number of patients normalized by their 2014 (pre-treatment) levels. In Appendix Figure A.4, we explore the logged outcomes $\ln(Expenditure + 1)$ and $\ln(Patients + 1)$ despite concerns about this functional form described in Chen and Roth (2023). Another potential concern is that, as shown in Appendix Table A.1, the normalized physician-quarter outcomes exhibit extreme skew. For that reason, our baseline analysis winsorizes these outcomes at the 97th percentile. Appendix Figure A.5 reports results that relax this winsorization threshold.

A.3 Robustness: Alternative Estimators

We implement the de Chaisemartin and D'Haultfœuille (2020) estimator to address bias in our estimated induced by treatment effect heterogeneity. Figure A.6 reports the results of the conventional estimator (panels (a) and (c)) as well as the de Chaisemartin and D'Haultfœuille's alternative (panels (b) and (d)). We find a very similar pattern, suggesting that the sources of bias are not large in our setting. Figure A.7 applies the alternative estimator to our analysis of the impact of any payment at the physician-quarter level, finding very similar patterns as are shown in Figures 3 and 4.

A.4 Robustness: Newly-Launched Drugs

In this section, we explore whether the special dynamics of newly-launched drugs could be potentially distorting our results. As a reminder, 14 of 99 cancer drugs were launched in our sample period. The potential distortion arises in the analysis of the impact of marketing payments using the physician-quarter dataset. We demonstrate the bias with an example. Suppose a drug is newly-launched in January 2016 (and is immediately issued a unique HCPCS code to ensure accurate measurement). Suppose the new drug had promising clinical trial results – as was true of a number of the newly-launched drugs in our dataset – and physicians immediately begin prescribing it. Assume that simultaneously, the drug firm makes a large number of marketing payments associated with the new drug, targeting those payments on likely prescribers of the drug. Regardless of the true causal impact of the payment, we would observe increases in expenditure among physicians who receive a payment right after they receive a payment.

The distortion arises because, in the presence of changing drug technology, the physician fixed effect does a poor job capturing the physician's expected counterfactual prescribing in the absence of a payment. To address an upward bias in the effect of a payment arising from the co-occurrence of marketing campaigns and drug launches, we reestimate our analyses, removing newly-launched drugs from our physician-quarter aggregates and also excluding physicians whose first payment for any cancer drug is for a newly-launched drug within its first year of observable utilization (i.e., within the twelve months after its HCPCS code is issued.) Appendix Figure A.8 reports results broadly similar to the findings in Figure 3; if anything, magnitudes are somewhat higher.

Т

	Expenditure	Normalized Expenditure	# Patients	Normalized # Patients
	stat ($\%$ of median)	stat (% of median)	stat ($\%$ of median)	stat ($\%$ of median)
median	13,132 (100%)	1.19 (100%)	5 (100%)	1.11 (100%)
p20	1,076~(8%)	0.46~(39%)	1 (20%)	0.62~(56%)
p40	5,591~(43%)	0.96~(81%)	3~(60%)	0.97~(87%)
p60	27,307~(208%)	1.49~(125%)	7~(140%)	1.33~(120%)
p80	73,100 (557%)	2.68~(225%)	13 (260%)	2 (180%)
p90	118,507 (902%)	4.62 (388%)	9 (180%)	3.33 (300%)
p95	164,957 (1256%)	8.67 (729%)	25 (500%)	5 (450%)
p97	200,845 (1529%)	14.16 (1190%)	30 (600%)	8 (721%)
p98	229,655 (1749%)	21.15(1777%)	34 (680%)	10 (901%)
p99	281,730 (2145%)	44.49 (3739%)	43 (860%)	16 (1441%)
p99.5	330,456 (2516%)	98.27(8258%)	53 (1060%)	22 (1982%)
p99.9	440,803 (3357%)	401.51 (33740%)	70 (1400%)	44 (3964%)
p99.99	670,885 ($5109%$)	3,875.48(325671%)	94(1880%)	152(13694%)
mean	41,186 (314%)	9.17~(771%)	7.88~(158%)	1.83~(165%)

Table A.1: Skewness of Outcomes: Physician-Quarter Analytical Sample

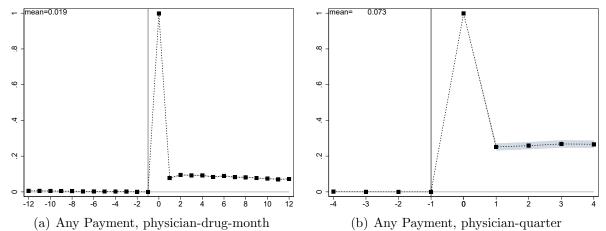
Notes: This table reports weighted percentiles and means from the full distribution of 226,336 physician-quarter prescribing outcomes for the analytical sample. The weights are each physician's average number of cancer patients. All statistics computed prior to 97th percentile winsorization used in analysis.

Panel A: Effect of Dr	ug-Specific Pay	ments (Physici	an-Drug-Month	n Analytical S	ample)			
	All Drugs		Price≥\$3000		Price<\$3000			
	Expenditure	# Patients	Expenditure	# Patients	Expenditure	# Patients		
Lin. Comb. 0m-12m	40.82	0.00091	43.59	0.00485	27.58	-0.00913		
	(17.48)	(0.00465)	(25.12)	(0.00296)	(12.46)	(0.01323)		
Mean Dep. Var.	1002	0.473	1451	0.222	563.43	0.717		
Ν	12,141,216	12,141,216	5,517,000	5,517,000	6,624,216	6,624,216		
Panel B: Effect of Any Payment (Physician-Quarter Analytical Sample)								
	Normalized	Normalized	. .	12-Month	24-Month	12-Month	12-Month	
	Expenditure	# Patients	Price	Mortality	Mortality	Predicted	Mortality Rate	
				Rate	Rate	Mortality Rate	Predicted Mortality	
Lin. Comb. 0q-4q	0.089	0.063	6.78	0.00116	0.00637	-0.00559	0.00635	
	(0.042)	(0.024)	(33.68)	(0.00437)	(0.00577)	(0.00162)	0.00425	
Mean Dep. Var.	2.17	1.564	2384	0.176	0.318	0.175	0.176	
Ν	226,280	226,280	170,365	144,568	109,439	135,833	$135,\!833$	

Table A.2: Effect of Drug-Specific and Any Payment: Linear Combinations of Post-Period Coefficients

Notes: This table reports the linear combination of post-period coefficients reported in Figures 2, A.2, 3, and 4.

Figure A.1: Time Path of Payments After the First Payment



Notes: Figure A.1 plots the time pattern of the number of payments after the first payment at the physiciandrug-month level (Panel (a)) and at the physician-quarter level (Panel(b)). By construction of the analytical sample, the outcome is zero in the pre-period.

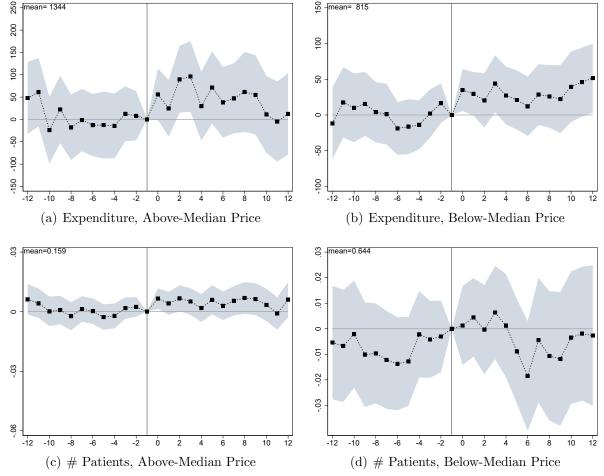


Figure A.2: Impact of Drug-Specific Payments on Drug-Specific Prescribing by Drug Price

Notes: Figure A.2 reports the coefficients from estimation of Equation 1 for expenditure and number of patients separately for drugs with monthly prices above and below the median (approximately \$3000 in average monthly expenditure per patient). The x-axis represents months before or after a first payment for a related drug (time 0). Analyses are weighted by each physician's average number of cancer patients. The gray area denotes 95% confidence intervals with standard errors clustered on physicians.

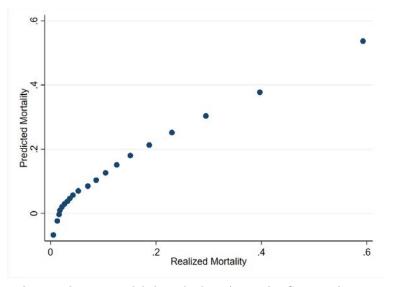
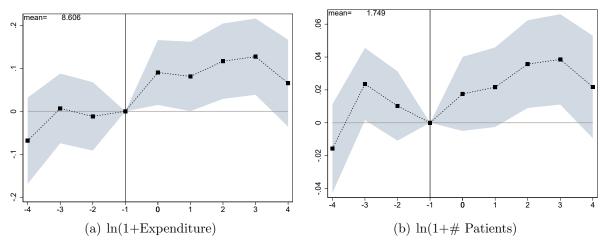


Figure A.3: Mortality Prediction Model Fit

Notes: Using the mortality prediction model described in Appendix Section A.1, we construct 20 equallysized bins of the predicted mortality distrubition. In Figure A.3, the y-axis reports the predicted 12-month mortality for each ventile and the x-axis reports the actual 12-month mortality for the same individuals.

Figure A.4: Impact of Any Payment on Logged Expenditure and Number of Patients



Notes: This figure reports the results of Equation 2 for the physician-quarter analytical sample using a log of each outcome plus 1. The x-axis represents quarters before or after a first payment for any drug (time 0). Event-studies are estimated using all pre- and post-periods but we report only those within our window of interest. We report 95% confidence intervals clustered at the physician-level. We weight by the physician's average number of cancer patients.

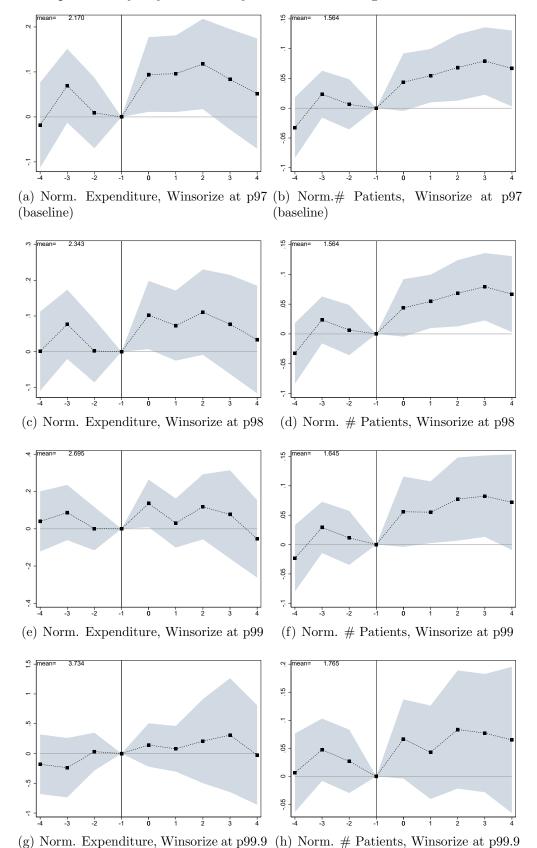
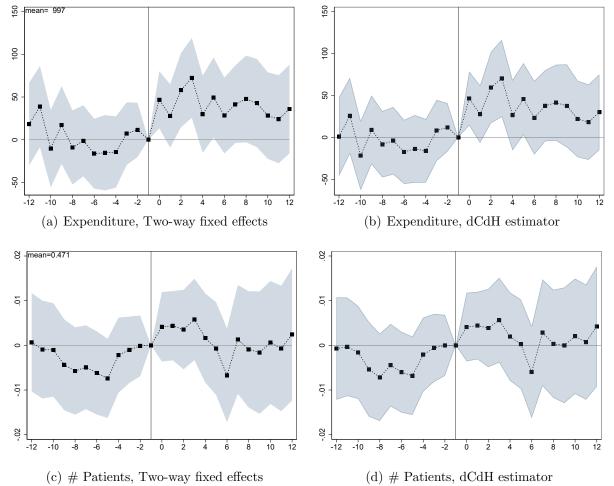


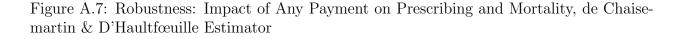
Figure A.5: Impact of Any Payment on Physician's Prescribing: Robustness to Winsorization

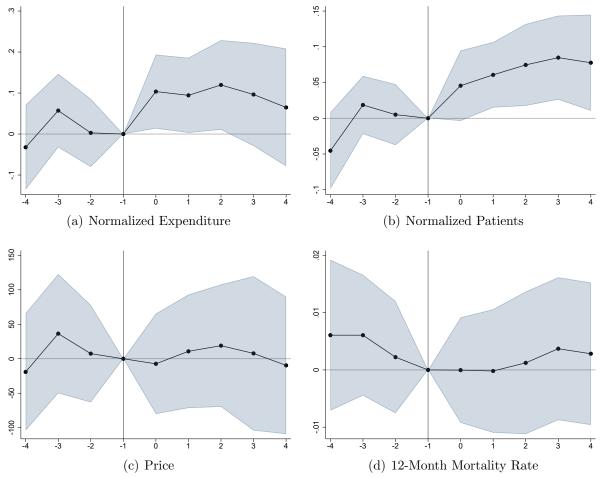
Notes: Panels (a) and (b) repeat Figure 3. Panels (c)-(h) winsorize at successively higher thresholds. The x-axis represents quarters before or after a first payment for any drug (time 0). Analyses are weighted by each physician's average number of cancer patients. The gray area denotes 95% confidence intervals with standard errors clustered on physicians.

Figure A.6: Robustness: Impact of Drug-Specific Payments on Drug-Specific Prescribing, de Chaisemartin & D'Haultfœuille (dCdH) Estimator



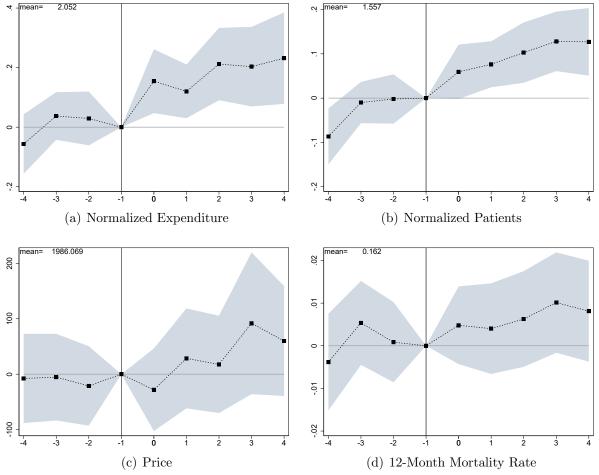
Notes: Panels (a) and (c) report estimation of Equation 1 (repeating Figure 2). Panels (b) and (d) report the coefficients and confidence intervals from the de Chaisemartin and D'Haultfœuille (2020) estimator. The x-axis represents months before or after a first payment for a related drug (time 0). Analyses are weighted by each physician's average number of cancer patients. The gray area denotes 95% confidence intervals with standard errors clustered on physicians.





Notes: Figure A.7 reports the coefficients from the de Chaisemartin & D'Haultfœuille estimator. The x-axis represents quarters before or after a first payment for any drug (time 0). Analyses are weighted by each physician's average number of cancer patients. The gray area denotes 95% confidence intervals with standard errors clustered on physicians.

Figure A.8: Robustness: Impact of Any Payment on Prescribing and Mortality, Excluding Payments from Newly-Launched Drugs



Notes: Figure A.8 reports the coefficients from estimating Equation 2 after excluding drugs launched during 2014 or later. The x-axis represents quarters before or after a first payment for any drug (time 0). Analyses are weighted by each physician's average number of cancer patients. The gray area denotes 95% confidence intervals with standard errors clustered on physicians.