NBER WORKING PAPER SERIES

DRUG DIFFUSION THROUGH PEER NETWORKS: THE INFLUENCE OF INDUSTRY PAYMENTS

Leila Agha
Dan Zeltzer

Working Paper 26338
http://www.nber.org/papers/w26338

NATIONAL BUREAU OF ECONOMIC RESEARCH
1050 Massachusetts Avenue
Cambridge, MA 02138
October 2019

For helpful comments and suggestions we thank Liran Einav, Erzo F.P. Luttmer, Kyle Myers, David Molitor, Jonathan Skinner, Douglas Staiger, and seminar participants at Tel Aviv University, Dartmouth College, ASHEcon, the ASSA Annual Meeting in Atlanta, the Fifth Annual Network Science and Economics Conference at Indiana University, the Barcelona GSE Summer Forum, and the NBER Summer Institute. The authors gratefully acknowledge research support by NIH grants PO1 AG19783 and UO1 AG046840. Dan Zeltzer acknowledges support from The Foerder Institute for Economic Research at Tel Aviv University. We thank Stephanie Tomlin and Weiping Zhou for help obtaining and managing the data. The content is solely the responsibility of the authors. The views expressed herein are those of the authors and do not necessarily reflect the views of the National Bureau of Economic Research.

NBER working papers are circulated for discussion and comment purposes. They have not been peer-reviewed or been subject to the review by the NBER Board of Directors that accompanies official NBER publications.

© 2019 by Leila Agha and Dan Zeltzer. All rights reserved. Short sections of text, not to exceed two paragraphs, may be quoted without explicit permission provided that full credit, including © notice, is given to the source.

Drug Diffusion Through Peer Networks: The Influence of Industry Payments
Leila Agha and Dan Zeltzer
NBER Working Paper No. 26338
October 2019
JEL No. I11,O33

ABSTRACT

Pharmaceutical companies' marketing efforts primarily target physicians, often through individual detailing that entails monetary or in-kind transfers. We study how peer influence broadens these payments' reach beyond the directly paid physicians. Combining Medicare prescriptions and Open Payments data for anticoagulant drugs, we document that pharmaceutical payments target highly connected physicians. We exploit within-physician variation in payment exposure over time to estimate the payments' influence. Unlike the paid doctor, peer physicians are not directly selected by the pharmaceutical company on the basis of their expertise or enthusiasm for the target drug. Yet, following a large payment, prescriptions for the target drug increase both by the paid physician and the paid physician's peers. These peer effects influence doctors who share patients with the paid physician, even when the two doctors are not affiliated with the same group practice. We find no evidence that payments reduce prescriptions among high-risk patients. Over the period 2014--2016, physician payments associated with anticoagulant marketing increased the drugs' prescription volume by 23 percent, with peer spillovers contributing a quarter of the increase.

Leila Agha
Department of Economics
Dartmouth College
6106 Rockefeller Hall
Hanover, NH 03755
and NBER
leila.agha@dartmouth.edu

Dan Zeltzer
The Eitan Berglas School of Economics
Tel Aviv University
P.O.Box 39040
Tel Aviv 6997801
Israel
dzeltzer@tauex.tau.ac.il

A data appendix is available at http://www.nber.org/data-appendix/w26338

Introduction

Drug and medical device companies spend the majority of their promotional budgets, over $20 billion annually, on marketing to health care providers. Much of this spending is on face-to-face detailing efforts to encourage adoption of new clinical products. Recent evidence suggests this marketing impacts prescription behavior, and an ongoing public debate centers on the influence of drug manufacturers' promotional efforts.[1] While pharmaceutical companies' interactions with physicians may educate doctors about new drugs, such engagement may also increase the prescribing volume of higher cost, brand name products marketed by the industry, not necessarily in the best interests of patients or payers.[2]

Large detailing payments reportedly target thought leaders, i.e. physicians who may be highly influential on the practice of their peers. Supported by a burgeoning commercial intelligence industry that identifies Key Opinion Leaders in different locations and therapy areas, pharmaceutical marketing increasingly leverages indirect influence (Campbell 2008). While influencer marketing and viral marketing are common promotional strategies in consumer goods markets (Iyengar et al. 2011), understanding their scope in medicine, where information asymmetries leave a large potential for over- and under-adoption of new technologies, is of particular policy importance. In this paper, we study how pharmaceutical detailing payments impact drug diffusion through the peer networks of targeted doctors.

Absent experimental variation, research into peer influence faces a significant hurdle: local clustering may be the result of common shocks or correlated preferences rather than peer effects. To isolate peer effects from these competing explanations, we exploit within-doctor variation in exposure to promotional payments over time. This study's contribution is twofold: first, it provides a lens for understanding the role of local physician networks in technology diffusion; second, it provides a more complete accounting of the impact of pharmaceutical companies' promotional efforts.

To study the influence of pharmaceutical payments on prescription behavior, we use Medicare Part D administrative claims data. We focus on prescriptions of anticoagulants (commonly referred to as "blood thinners"), a widely used therapeutic class to which several new drugs were introduced during or shortly before our sample period. We match prescription data with two other data sources: (1) the universe of payments and value transfers to US physicians by drug manufacturers and distributors, and (2) data on physician networks, where physicians are considered connected if they share patients.

[1] For a recent overview of drug promotion strategies, spending levels, and impacts, see Schwartz and Woloshin (2019).

[2] E.g., Thomas, Katie et al., "Detailing Financial Links of Doctors and Drug Makers," *New York Times*, September 30, 2014; Elliot, Carl, "The Drug Pushers," *The Atlantic*, April 2016.

Our paper contributes to a growing body of literature investigating the effect of pharmaceutical marketing on prescribing decisions (David et al. 2010; DeJong et al. 2016; Larkin et al. 2017; Shapiro 2018a; Sinkinson and Starc 2018; Grennan et al. 2018). Our empirical approach, which accounts for physician-drug fixed effects, is most similar to Carey et al. (2015). Studying an earlier time period and a different set of drugs, Carey et al. (2015) found that pharmaceutical payments increase the targeted doctor's prescribing volume. Consistent with earlier work, we find that physicians increase their own prescribing of the target drug after a detailing interaction. Furthermore, we present new evidence that large payments increase prescribing by *peers* of targeted physicians. To our knowledge, this is the first paper to investigate the peer effects of pharmaceutical payments.

For each drug in our sample, roughly one-third of practicing physicians receive small in-kind transfers of food and beverages (typically under $20) associated with detailing interactions with marketing salespersons; we refer to these as "food payments". In contrast, fewer than 2 percent of physicians receive large payments associated with speaking, consulting, and other services; we refer to these as "compensation payments". Despite the vastly lower penetration, compensation payments account for two-thirds of the total dollar volume transferred; the median of such payments is above $2,000, and most recipients receive repeated payments for the same drug. We show that compensation payments disproportionately target physicians with many peers.

After a physician receives a compensation payment, *each* of their peers increases use of the target drug by 2 percent on average. This finding is shown graphically in Figure 1 and holds up within an empirical framework that accounts for physician-drug fixed effects and allows for differential pre-trends. The framework allows for physicians who engage with pharmaceutical companies to differ ex ante in both their baseline propensity to prescribe and their speed of new drug adoption. The key identification assumption is that detailing payments to a peer of the focal physician do not coincide with other shocks to the focal physician's demand for the new drug. One advantage of our focus on peer effects is that we are studying payment influence on doctors who were not themselves directly targeted or selected by the pharmaceutical company, which mitigates endogeneity concerns around payment timing.

Peer spillover effects of compensation payments extend to physicians who share patients but are not affiliated with the same group practice. Further, we find that the estimated peer effects are not solely driven by prescription refills; peer influence leads to greater use of the target drug as a first-line therapy for patients without a prior anticoagulant prescription. Increased prescriptions due to payments do not come at the expense of competing drugs, but reflect an expansion of the new anticoagulant drug class as a whole. In contrast to our

findings on large compensation payments, small food payments induce the recipient doctor to prescribe more of the targeted drug but have no economically or statistically significant peer spillover effects.

The indirect effect of compensation payments on each of the recipient's peers' prescription volume is roughly 1/20 the size of the direct effect of the compensation payment on the paid recipient himself and 1/3 the size of directly receiving a food payment. But while spillover effects on each peer are smaller than the direct effect of receiving a payment, given that the physicians targeted with these compensation payments have more than 60 peers on average, the overall estimated impact of a compensation payment on all first-degree peers eclipses the estimated impact of a compensation payment on the paid physician's own patient volume.

Relative to a counterfactual without pharmaceutical payments of any type, pharmaceutical payments have increased New Oral Anticoagulant (NOAC) prescription volume by 23 percent over the 2014–2016 period, increasing their estimated US market size from $6.2 billion to 7.6 billion. While much of this impact is driven by the direct influence of widespread food payments on recipient doctors, about a quarter of the increase is due to peer spillover effects of infrequent (but very large) compensation payments. This estimate of spillovers is conservative because it fails to account for other peer relationships besides measured patient-sharing ties. These results, which take into account the actual network structure and distribution of payments, imply that the impact of pharmaceutical payments on the adoption of new drugs is substantially amplified through peer effects. This amplification helps explain why pharmaceutical companies spend most of their promotional payments on a small number of doctors.

Our counterfactual analysis also suggests that pharmaceutical detailing increases the variance of drug adoption across regions. Prior research has documented significant local clustering of treatment patterns (Cutler et al. 2019; Skinner and Staiger 2015; Moen et al. 2016; MacLeod and Currie 2018). Because payments are concentrated in areas where initial adoption is already high, they contribute to regional divergence in prescription patterns, at least in the intermediate stages of the drug life cycle that we observe.

The welfare implications of pharmaceutical influence are not immediately obvious. If detailing payments propagate useful information to physicians, they could improve prescription safety and value. Studying prescription decisions for patients with atrial fibrillation, we find no evidence that detailing interactions increased concordance with evidence-based clinical guidelines either among directly paid physicians or their peers.

Our findings corroborate prior evidence on the importance of peer influence in health care decisions (Chan 2018; Navathe and David 2009; Oster and Thornton 2012; Silver 2019) as well as in other technology adoption settings (Banerjee et al. 2013; Golub and Sadler

2016; Galeotti et al. 2017). Prior work suggests that peer spillovers may be successful at increasing use of new drugs (Coleman et al. 1957; Donohue et al. 2018; Agha and Molitor 2018), but may not help curb the use of low-value or risky prescribing (Sacarny et al. 2019). Our paper brings a new focus to this area of inquiry, showing that private firms effectively leverage peer influence for marketing purposes.

The rest of this paper proceeds as follows. Section 1 describes the data and contextual information about the class of anticoagulants. Section 2 describes our empirical strategy. Section 3 shows our main estimates of the influence of pharmaceutical payments on prescription volume. Section 4 analyzes whether drug detailing promotes guideline-concordant anticoagulant use for patients with atrial fibrillation. Section 5 quantifies the impact of payments on the aggregate increase and spatial dispersion of prescription volumes. Section 6 shows estimated effects on competitors. Section 7 concludes.

1 Data and Context

Our analysis focuses on anticoagulants, studying the diffusion of three NOACs: apixaban (brand name Eliquis), dabigatran (Pradaxa), and rivaroxaban (Xarelto). These drugs comprise a growing market for alternatives to the older anticoagulant, coumadin (Warfarin), as shown in Figure 2. These three NOACs were introduced between 2010 and 2012, shortly before our sample period began in 2014.[3]

Anticoagulants are primarily used to prevent strokes and other clotting events in patients with atrial fibrillation, deep vein thrombosis, and pulmonary embolism. These conditions are both common and serious, estimated to contribute to 240,000 deaths per year in the United States.[4] The NOAC global market was $23 billion in 2013, and is projected to double by 2025.[5]

NOACs are considered noninferior to existing anticoagulant drugs. Cited advantages of NOACs relative to older anticoagulant drugs include improved safety, convenience of use, fewer interactions with other drugs, a wider therapeutic window, and no need for laboratory monitoring (Mekaj et al. 2015). These benefits come at a cost: NOACs were branded drugs,

[3]The FDA first approved Pradaxa on October 19, 2010, Xarelto on July 1, 2011, and Eliquis on December 28, 2012. This slight variation in the introduction of drugs means that we have a chance to observe slightly different stages in the life cycle of product introduction.

[4]Estimates reported by the Center for Disease Control `https://www.cdc.gov/stroke/facts.htm` and `https://www.cdc.gov/ncbddd/dvt/documents/blood-clots-fact-sheet.pdf`. Accessed August 2019

[5]Global Anticoagulants Market Expected to Reach $43 Billion By 2025. Allied Market Research Report. `https://www.alliedmarketresearch.com/press-release/anticoagulant-drugs-market.html`. Accessed August 2019.

priced at more than $500 per month—multiple times the price of off-patent Warfarin.[6]

1.1 Data Sources

To estimate peer effects in the diffusion of new drugs, we combine multiple databases on prescriptions, payments, and connections as follows. Physician prescription volumes are derived from Medicare Part D administrative claims, from 2014–2016. Associated payments and in-kind transfers to physicians made by drug manufacturers are identified in the Open Payments database, from mid-2013 until the end of 2016. Physician shared-patients relationships are merged from the 2013 Referral Patterns database. Additional physician characteristics, including practice location and group practice affiliations are from Physician Compare.[7]

Prescriptions We analyze a 40 percent sample of Research Identifiable Medicare Part D claims in 2014–2016 (CMS 2013–2016a). To track the adoption and use of new anticoagulant drugs, we restrict attention to physicians of medical specialties that together comprise the majority of NOAC prescribers: primary care and cardiology.[8]

For each physician and each anticoagulant drug, we construct a quarterly panel of the doctor's prescription volume. We use this data to define three outcome variables. Our primary outcome is the number of unique Medicare Part D beneficiaries prescribed the drug in that quarter. Second, we construct a count of newly initiated prescriptions, excluding prescription renewals or drug changes for patients already using anticoagulants. We define newly prescribed patients as those who did not fill any type of anticoagulant prescription for the prior 12 months.[9] Finally, to measure the relative market share of each drug at the physician level, we calculate the fraction of patients prescribed each specific NOAC out of the total anticoagulant prescriptions. This relative share variable is defined only in quarters with at least one anticoagulant prescription and therefore corresponds to a smaller sample size (See Table 1).

[6] Anticoagulants - prices and information, https://www.goodrx.com/anticoagulants. Accessed September, 2019.

[7] With the exception of the Medicare Part D Research Identifiable patient-level data, all data are publicly available. All of these databases are maintained by the Centers of Medicare and Medicaid Services (CMS), a federal agency within the US Department of Health and Human Services.

[8] We define primary care physicians as those whose primary specialty recorded in the Physician Compare database is one of: Family Practice, Internal Medicine, General Practice, or Geriatric Medicine. Cardiologists are defined as physicians whose primary specialty is one of: Cardiology, Interventional Cardiology, or Cardiac Surgery.

[9] For the purposes of this study, when we refer to anticoagulants as a class, we consider all prescriptions for Warfarin, Xarelto, Eliquis, and Pradaxa, which cover all the major prescription anticoagulants over this time period.

Peers To study peer effects in prescription decisions, we combine prescription information with physician referral data from the CMS Referral Patterns data (CMS 2013). In these data, two physicians have a *shared patient* if they both participated in the delivery of health services to the same Medicare patient within 30 days of one another. Two physicians are defined to be *peers* if they have 11 or more shared Medicare Fee For Service patients within a year. The threshold of 11 patients was chosen by CMS to protect patient privacy. But according to survey evidence, it happens to match well the number of shared Medicare patients between two physicians above which the physicians are likely to have a recognized professional relationship.[10] Therefore peers thus defined may also influence each other's practice. Furthermore, a key channel for peer influence is via passively observing peer prescription behavior for shared patients, so this definition of peer ties coincides with a potentially important mechanism for peer effects.

We treat this network as static, undirected, and unweighted. We define peers based on the observed network of shared-patient peers in 2013, the year before our prescription outcome data begins, to reduce concern for endogenous responses of physician work relationships to payments.[11]

Appendix Table A1 presents summary statistics on the distribution of the number of peers. The mean physician in our sample shares patients with 22.8 peers (median 13). Cardiac specialists, whose practice is more specialized, have significantly more peers (mean 60.2, median 53) than generalists (mean 17.1, median 11). More-experienced physicians also tend to have more peers.

Payments We combine data on NOAC drug prescriptions with data on associated payments and value transfers to physicians by drug manufacturers and distributors from the Open Payments database (CMS 2013–2016b). This payment data covers the period from July 1, 2013 through December 31, 2016. This database is maintained by CMS as part of the Physician Financial Transparency Reports (Sunshine Act), a national disclosure program created by the Affordable Care Act. Since 2013, manufacturers have been required to submit data about all payments and other transfers of value made to physicians (which we refer to as *payments*). The reports include the amount paid (or value of nonmonetary transfer, such

[10]Barnett et al. (2011) find that 82 percent of physician pairs with nine patient shared report to have an advice or referral relationship, compared with only 19 percent of physician pairs with one shared patient. Furthermore, using publicly available shared-patient data makes it easier to replicate and reuse all parts of our analysis, except for those that use Medicare Part D confidential data. We are able to reproduce the results using a claims-based definition of referral relationships from confidential data.

[11]However, responses of physician working relationships to payments are likely small. Physician working relationships have been shown to be persistent (Zeltzer forthcoming). Furthermore, shared-patient relationships are measured using all Medicare patients, not just patients with anticolagulant prescriptions.

as food or travel expenses), the associated drug(s), and the nature of the transfer. We match doctors listed in Open Payments to National Provider Identifier codes based on physician name and address.[12] We aggregate payments received to construct a panel of physician payment amounts and payment types in each quarter and for each drug.

From 2014–2016, the reported payments total to $103 million for the three NOAC drugs we study. Table 2 shows the distribution of payment size by payment type. We group payment types into three categories based on average payment size: (1) food, beverage, and education; (2) consulting fees and compensation for services; (3) travel and lodging. Figure 3 shows the average cumulative number of payments associated with each drug that were received by physicians of different specialties. Appendix Figure A1 shows the cumulative fraction of recipients of any payments of each type.

The most common transfers are in the form of food, beverages, and educational materials purchased by salespeople when discussing new drugs with physicians. Our sample includes 1.8 million transfers of this nature, most of them for food and beverages. These small payments, averaging below US$40 per payment, are received by both generalists and specialists.

The largest category of payments by both average size per payment and total dollar expenditure is compensation for services and consulting fees. We observe 30,000 of these large payments, with each transaction averaging over US$2,200. As we later show, these payments are concentrated among a small fraction of physicians, most of whom are cardiac specialists.

Payments for travel and lodging are a third, smaller category. Our sample reports 18,000 travel transactions, accounting for only 5 percent of total detailing expenditures. Transfers in this category are of intermediate value, averaging $260 per transaction. Consistent with their low frequency, we generally do not have sufficient statistical power to estimate the relationship between travel payments and prescription volume. Our results do not change if we omit them altogether. For completeness, we control for travel payments in all regressions.

Physician characteristics Finally, we use the Physician Compare data to identify the physician's primary specialty, experience (measured as years since medical school graduation), and group practice affiliations. The group practice affiliations form the basis of a second measure of physician peer links, defined as physicians who share at least one common group practice. We use these to supplement our baseline measure of peer linkages defined

[12]We use Physician Compare for name and address information. As both Physician Compare and Open Payments are maintained by CMS, more than 97 percent of our matches are exact matches on last name, first name, and state. The remaining matches include slight misspellings; we match these remaining records by blocking on state and first letter of last name, and using fuzzy string matching with the Jaro-Winkler distance.

by shared patients.

1.2 Patterns of Pharmaceutical Payments, Prescriptions, and Peer Connections

Physicians who share patients with many peer physicians are more likely to receive compensation payments. Figure 4 sorts physicians by decile of number of peers (i.e., network degree) within each hospital referral region (HRR) and specialty type; it then plots how the average number of pharmaceutical payments per physician varies across the distribution of peer group size. While physicians with relatively few peers are less likely to receive food from pharmaceutical companies promoting one of our three NOACs, there is little difference in the rate of food payment among the top four deciles of the distribution for either cardiac specialists or primary care physicians. By contrast, highly connected physicians, in the top deciles of the distribution of number of peers, are more likely to be targeted with compensation payments than peers with the median number of connections, a pattern we see for both cardiac specialists and primary care physicians.

Appendix Table A2 regression results show that having a greater number of peers (i.e., a higher network degree centrality) is associated with higher payments even after accounting for other observed physician characteristics.[13] These data are consistent with the possibility that pharmaceutical companies target large payments to highly connected doctors, who may be better positioned to amplify the payment's impact. A caveat to interpreting this relationship is that physicians with more peer connections may also see more patients in their own practice.

Table 1 shows summary statistics by physician own and peer payment status. This table is restricted to our analysis sample for consistency with the subsequent regression results. Specifically, we impose two sample requirements to ensure the physician is actively treating Medicare enrollees: first, the doctor must have at least one peer provider as defined by the CMS Referral Patterns data; second, the physician must write at least one observed anticoagulant prescription (for any of the anticoagulant drugs, including Warfarin) over the three-year study period. These two restrictions together drop 17 percent of the physicians listed in Physician Compare from our sample. We further require that physicians who receive their first observed payment during our sample period (January 1, 2014 through December 31, 2016) have two quarters of pre-payment data and two quarters of post-payment data. We impose this restriction for own compensation, own travel, and own food payments as

[13] We also studied alternative centrality measures, including eigenvector, closeness, and betweenness centrality. Degree centrality appears to be the most robust predictor of payments.

well as peer compensation payments. This restriction ensures that we have a balanced panel for at least four quarters around the first payment event, which is important to accurately compare doctors' prescription volume before and after the payment.

Table 1 reports that 73 percent of doctors in our sample receive no payments directly. On average, 27 percent of doctors receive food or travel payments for each drug, and these doctors average $148 in payments for the target drug over the 12 quarters of our sample. This total transfer is typically spread across several transactions: physicians receiving food payments for a particular drug are paid in four out of 12 quarters on average. By contrast, the 0.3 percent of physicians who receive compensation payments for each drug are drawing much larger transfers from pharmaceutical companies, averaging $38,166 per doctor cumulatively over 12 quarters. Physicians receiving compensation payments average six quarters (out of 12) with compensation payments. Cardiac specialists constitute the majority (81.2 percent) of recipients of compensation payments.

Even though less than one percent of doctors in our sample receive compensation payments for a given drug, these paid doctors are highly connected. Therefore, we find that 14 percent of doctors in our sample are linked to a compensation-paid physician for a given drug. Our econometric approach relies on comparisons of physicians who are and are not linked to compensation-paid peers to identify peer effects.

This table also illustrates that physicians directly and indirectly targeted with payments use the target drug more intensely. Doctors whose peers receive compensation payments prescribe each NOAC to 1.12 patients per quarter, on average, compared to 0.45 patients per quarter for doctors whose peers do not receive compensation payments. We explore this relationship in our regression analysis.

Note that the prescription volumes reported here cover only a modest fraction of doctors' overall patient panel. We observe prescriptions for a 40 percent sample of Medicare Part D enrollees. Hoadley et al. (2015) reports that 72 percent of Medicare beneficiaries were enrolled in Part D as of 2015, suggesting our sample covers roughly 28 percent ($= 0.4 \cdot 0.7$) of Medicare beneficiaries. Further, in the 2014 Medical Expenditure Panel Survey, 66 percent of NOAC prescriptions are written to patients 65 years or older. Thus, roughly scaling our patient counts up to the full population requires multiplying the patient volume by a factor of 5.4. For simplicity and because the scaling requires additional assumptions, e.g. that the impact of pharmaceutical payments on prescribing patterns for non-Part D enrollees is similar, we report unscaled results.

2 Identification and Estimation

Our analysis focuses on estimating pharmaceutical payments' spillover effects on the peers of targeted physicians. The main identification concern is endogeneity of peer prescriptions: peers of paid physicians may have had higher prescription rates even in the absence of their peer's payment. To isolate the impact of peer payment, we begin with an event study approach exploiting variation in the timing of payments and the peer group of targeted physicians.

2.1 Regression models of payment impact

We model prescription decisions as a function of payments, including payments both directly made to the physician and payments to the index doctor's peer. We begin with a graphical event study around the first payment exposure of each type and then move to a specification that studies the accumulating impact of each transfer.

Let i index physicians, t index time in quarters, and d index drugs. Let Y_{itd} denote the prescription volume of drug d by doctor i at period t. Let G denote the network of relationships among physicians based on having common patients (see Section 1 for definitions). That is, for each i, j, let $s_{ij} = 1$ if i and j shared patients and zero otherwise. With slight abuse of notation, let G_i denote the group of direct peers of i in the network G.[14] Because peer relationships are intransitive, $j \in G_i$ does not imply $G_j = G_i$, i.e. peer groups vary even among connected peers, which supports our identification strategy, as discussed in Section 2.3 below. Throughout the analysis, we focus only on the effect of payments on direct first-degree peers of recipients. If payments also influence higher-degree peers, our estimates would be biased toward zero.[15]

Event study. Our first approach is to graphically analyze prescription patterns before and after the first payment event. To flexibly capture the differential effect of various payment types, every specification accounts separately for own and peer exposure to each payment type: food, travel, and compensation. We estimate the model:

$$Y_{itd} = \alpha_{id} + \beta_{dts} + X'_{idt}\gamma + Z_{id}\delta_{r(idt)} + Z_{Gi,d}\eta_{r(idt)} + \varepsilon_{idt}, \tag{1}$$

[14] We model the network as undirected and unweighted. Our model can easily be extended to incorporate weights or directed links.

[15] A third of the physicians in our sample are indirectly connected to a compensated physician, through a common peer; four out of five physicians are connected to a compensated physician through a path of length three or less. Assuming effects decay as they ripple through the network, further indirect effects are likely small.

where $r(idt)$ indexes event time in quarters relative to the physician's first payment (of each type) for the index drug. Our main model pools all drugs together, estimating the average effects of payments associated with each drug on prescriptions of that drug, Y_{itd}. The terms α_{id} and β_{dts} are doctor-drug and drug-quarter-specialty fixed-effects, respectively. X_{idt} includes a vector of differential time trends. The vector Z_{id} defines indicator variables for whether doctor i ever receives each of the three types of payments for drug d; it is multiplied by $\delta_{r(i,d,t)}$, which are the parameters describing how prescription volume changes relative to the quarter of the doctor's first payment of each type. The vector $Z_{Gi,d}$ defines indicator variables for whether doctor i has a peer who ever receives each of the three payment types for drug d; $\eta_{r(i,d,t)}$ are the parameters describing how prescription volume changes relative to the quarter of the doctor's first *peer* payment.

To estimate specifications that allow for pre-trends, we first estimate a model that excludes the pre-treatment quarter parameters from the $\delta_{r(i,d,t)}$ and $\eta_{r(i,d,t)}$ terms; instead, the model includes a differential linear pre-trend for each type of own and peer payment (food, travel, and compensation), as well as the full vector of indicator variables for post-treatment quarters.[16] As a second step, we residualize the outcome variable by the estimated pre-trend and then estimate a version of equation (1) with a full array of pre- and post- treatment quarter parameters. This final specification allows us to directly remove the linear pre-trend from the post-period and graphically assess the presence of nonlinear trends in the pre-treatment period. We report results both with and without implementing this detrending procedure.

The pre-period is uncontaminated by early payments because the graph simply focuses on quarters before and after the first observed payment of each type. All doctors identifying the pre- and post-payment effects were required to have no observed earlier payments over at least four sampled quarters before that first payment. For doctors who received payments in the second half of 2013, for which we only have payment but not prescription data (our Part D sample starts in 2014), we included separate time trends to account for the possibility that early payments targeted different recipients than later ones. Because our payment data set begins in Quarter 3 of 2013, presumably after some payments have been made, our estimates of payment effects may be biased toward zero since we cannot identify the first payment over the drug's complete history.

These regression models allow us to make a series of plots of the estimated impact of pharmaceutical company payments. The graphical analysis displays the evolution of prescription volume in the quarters before and after the *first* payment. As described in the

[16] We pursue this two-step procedure for the graphical analysis to surmount the underidentification problem that would otherwise arise when trying to include both differential time trends and dummy variables for time relative to first payment. For a more detailed discussion of this underidentification problem and possible solutions, see Borusyak and Jaravel (2017).

summary statistics reported in Table 1, most paid doctors receive repeated payments of the same type. As a result, the post-period of these graphs should not be interpreted as the effect of a single payment, but rather the accumulating effect of all payments received over those quarters.

Main specification. The event study graphs illustrate a trend break in prescription volume after the first payment. A key reason for this apparent trend break is that most doctors in our sample receive repeated payments in the post-period. Thus, for the primary regression specification reported in our tables, we use the running sum of paid quarters as the key independent variable to capture the individual impact of each payment. We estimate:

$$Y_{itd} = \alpha_{id} + \beta_{dts} + X'_{idt}\gamma + P_{idt}\delta + P_{Gi,d,t}\eta + \varepsilon_{idt}, \tag{2}$$

where P_{itd} denotes a vector of variables that count the number of quarters up to time t with payments of each type (food, travel, compensation) made to physician i for drug d. $P_{Gi,d,t}$ similarly counts the number of payments (food, travel, compensation) made to doctor d's peers (Gi, d, t) up to time t.[17] The control variables in (2) parallel those in (1), including the same set of fixed-effects. We continue to include differential time trends by own and peer payment type (food, travel, and compensation) for doctors who receive payments in 2013, before the beginning of our Part D sample. In addition, this specification includes additively separable trends by own and peer payment type for any doctor who is paid for the first time during our sample period, which allows for differential pre-trends for doctors paid during our sample.[18]

The key parameters of interest are the δ vector, which captures the effect of each additional quarter with own pharmaceutical payments of each type, and the η vector, which captures the effect of the number of peer-quarter pairs that received each type of payment to date.

[17]Both the P_{idt} and $P_{Gi,d,t}$ variables are set to zero for doctors who are never (own or peer) paid and for doctors who receive their first (own or peer) payment of this type in the two quarters before our Part D sample begins.

[18]Recall from the discussion in Section 1.2, that we also drop doctor-drug pairs from the sample when we do not have at least two pre-payment quarters and two post-payment quarters covered by the Part D sample. This restriction is imposed for all types of own payment (food, travel, compensation) as well as for peer compensation payments. We make this restriction so that we have enough in-sample quarters to contribute to pre/post comparisons within each doctor for our key payment types. This structure ensures that all doctors who contribute directly to identification of payment impact (i.e. take nonzero variables of the cumulative payment counts) were unpaid for at least four quarters prior to the first payment. We check that our results are robust to these sample restrictions by comparing them with an alternative sample that drops all doctors who received a payment of any type or who had a compensation-paid peer for the target drug during the first three quarters in our sample (see Appendix Table A4).

Extensions and robustness checks. We estimate several variants of equation (2). First, we consider three outcome measures related to physician prescription volume for the target drug: the number of distinct beneficiaries prescribed, the number of beneficiaries receiving the target drug as their first anticoagulant prescription, and the fraction of anticoagulant prescriptions written for the target drug. Second, to explore how the impact of peer payment varies by the type of relationship, we test augmented specifications that differentiate three types of physician peer relationships: those defined by shared-patient ties, those defined by shared group practice affiliation, and those that have both. Third, we test whether pharmaceutical payments increase adherence to clinical guidelines (see Section 4). Fourth, we test whether payments affect prescriptions of competing drugs (see Section 6).

Additional models that we use for robustness and heterogeneity analysis test for a differential impact of the first payment of a given type relative to subsequent payments; estimate the model separately for each drug; and estimate the model separately for each physician medical specialty. We also use an alternative regression approach that relies on matching compensation paid physicians to unpaid physicians who have similar observable characteristics. The matching approach is discussed in Section 3.4.

2.2 Scaling payment effects by peer prescription volume

As a supplement to the main specifications, we conduct a scaling exercise to explore possible mechanisms of peer effects. There are two key channels by which having a peer targeted with a pharmaceutical payment may raise a doctor's prescribing, holding constant any directly received payments. First, seeing a colleague prescribe a new drug may provide a positive signal about the value and applications of the new product, increasing the odds that a doctor adopts the new drug and prescribes it himself. Second, paid physicians may directly influence their peers through direct "proselytizing" about the new drug. We apply a two-stage least squares (2SLS) strategy that attributes peer influence to the indirect mechanism and allows us to estimate an upper bound on the possible magnitude of indirect influence.

Our 2SLS approach uses detailing payments to a physician's peers as an instrumental variable (IV) for peers' average prescription volume. We then trace the influence of peer prescriptions on own prescribing. The reduced form of this 2SLS approach is similar to the preceding analysis, which studies the link between peer payments and the doctor's own prescription volume. The IV provides a way to scale this relationship by attributing the effect to increases in the average prescription volume of the doctor's peers.

The IV framework continues to exploit the panel data structure to isolate changes in prescribing patterns that coincide with peer payment shocks.The first- and second-stage

equations are as follows:

$$Y_{Gi,d,t} = \tilde{\eta} P_{Gi,d,t} + \tilde{\delta} P_{idt} + X'_{idt}\tilde{\gamma} + \tilde{\alpha}_{id} + \tilde{\beta}_{dts} + u_{it} \tag{3a}$$

$$Y_{idt} = \theta \widehat{Y}_{Gi,d,t} + \delta P_{idt} + X'_{idt}\gamma + \alpha_{id} + \beta_{dts} + v_{idt}, \tag{3b}$$

where $Y_{Gi,d,t}$ is the mean prescription volume of each drug d by i's peers at t, and $P_{Gi,d,t}$ is a vector of excluded instruments calculating the cumulative sum of the number of peer-quarter pairs with prior payments of each type (food, travel, compensation) for the target drug. We continue to control for the doctor's own payments of each type. X_{idt} echoes the trends included in equation (2): differential time trends for each category of own and peer payment, and differential trends for doctors whose first payment comes before the beginning of our study period. We estimate the model using two stage least squares.

To interpret this model as the causal effect of peers' average prescription volume on the focal doctor requires a strong exogeneity assumption: peer payments are uncorrelated with unobservable variables affecting the focal doctor's own prescriptions ($E[v_{idt}P_{Gi,d,t}] = 0$). Under this assumption, the 2SLS approach will provide an unbiased estimate of peer effects, eliminating both reflection bias and exclusion bias (Caeyers and Fafchamps 2016).

The exclusion restriction imposes the strong assumption that there is no "direct" effect of a peer's payment on a doctor's own prescription volume except through the channel of increases in peer prescriptions. For example, if a paid doctor began proselytizing to his peers about the target drug, and this proselytizing had an independent effect on his peers' prescription decisions, then the instrumental variable specification would overstate the importance of changes in peer prescriptions for doctors' own prescription decisions.

Based on our conversations with physicians and consultants with expertise in drug detailing, we hypothesize that the indirect peer influence mechanism is more likely, particularly given the social and institutional distance between most physicians who share patients. This hypothesis is further bolstered by our finding that estimated peer effects do not exert a stronger influence among physicians who practice at the same location and therefore presumably have more opportunities for "proselytizing," holding fixed the volume of shared patients between two doctors.

Nevertheless, we proceed cautiously. Because the IV exogeneity assumption could plausibly be violated, we interpret the IV result as an upper bound on the magnitude of the indirect learning channel. When interpreting this estimate as an upper bound, we are assuming that any other channels (such as proselytizing) that lead peer payments to change the focal doctor's own prescription patterns would also have the effect of increasing the focal doctor's prescription volume.

2.3 Discussion of econometric approach

These specifications address several threats to identification of peer effects that arise with data on groups (Manski 1993) or with cross-sectional, rather than longitudinal, data on networks (Bramoullé et al. 2009). The problem with group peer relationships (e.g., all physicians affiliated with a hospital) is that being in the same group is mostly a transitive relation; therefore, there is little variation in the reference groups of similar agents.[19] In contrast, physician shared-patient networks are intransitive—even physicians who interact with each other generally interact with different sets of peers (only a third of connected triplets are fully connected). Longitudinal data contribute variation in the timing of payments. Our strategy uses both the across-doctor variation in peer groups *and* the within-doctor variation in the timing of payment to identify treatment effects. Through the inclusion of doctor-drug fixed effects, the framework accounts for the possibility that payments are associated with unobserved time-invariant physician characteristics. For example, if pharmaceutical transfers target doctors who were already high-volume prescribers, this would not bias our findings.

Threats to the identification could arise with this approach if payments coincide with changes in prescription volume for the target drug, which would have occurred even in the absence of payment. One benefit of focusing on the peers of targeted doctors is that these peers have not been directly selected by the pharmaceutical company, making it more plausible that they would otherwise experience parallel trends to other doctors of the same specialty and eventual payment status. We assess the plausibility of the parallel trends assumption through graphical analysis of pre-trends prior to the first payment.

3 Results

3.1 Event study graphs of payment impact

We begin by estimating equation (1) to explore the relationship between peer payment and prescription volume. Figure 1 graphs explore the stability of pre-trends prior to the first payment. These graphs plot the event-time coefficients from a regression in which the outcome is quarterly prescription volume, calculated at the physician level. Quarter 0 indicates the first observed quarter in which the physician receives a payment of the indicated type.

In Figure 1, Panel (A), we show results from a specification that does not account for differential pre-trends by the doctor's eventual payment status. These graphs illustrate that paid doctors are indeed on a trend of increasing use even prior to their first payment; this

[19] The exception is partially overlapping groups (cf. De Giorgi et al. (2010)).

pattern holds for doctors who are targeted with compensation and food payments, as well as for doctors whose peers receive compensation. Accounting for these pre-trends, we see a trend break with accelerating growth in prescription volume after the first payment.

Figure 1, Panel (B) displays the same results in a more flexible specification that allows for differential pre-trends, as described in Section 2.1. The quarters prior to the doctor's first payment now show a flat pattern of prescription volume, implying that there is no *acceleration* in target drug prescribing before the first payment.

Note that the scale of the y-axis varies across each subplot. Own compensation has the largest impact on subsequent prescriptions, with prescription volume to 0.34 additional in-sample patients per quarter within six months of the doctor's first compensation payment; this effect amounts to 62 percent of the average quarterly prescription volume of a physician in our sample.[20] Prescriptions also rise after the first food payment by 0.04 additional patients per quarter, or 7 percent of the average volume, within six months. Finally, after a peer physician receives a compensation payment, the targeted doctor's peers increase their prescription of the new drug by 0.02 additional in-sample patients per quarter, or 3 percent of the average volume. While these in-sample effect sizes appear modest, recall that in-sample patients account for only 18 percent of total NOAC prescription volume, and volume outcomes are reported quarterly (see Section 1.2).

Prescription volume deviates further from the trend as more quarters elapse following the first payment. This pattern is especially salient following the first food and peer compensation payments. Recall that many doctors are exposed to repeated shocks of the same type; the growth in the post-period may reflect the accumulating impact of subsequent payments. For this reason, we avoid simple pre/post comparisons in our main regression results and instead model the prescription volume as a function of cumulative payment exposure.

3.2 Baseline regression estimates of payment influence

To unpack the individual impact of each payment, we turn to regression results reported in Table 3. These results are from direct estimates of equation (2). The key independent variables in these regressions count the number of quarters to date in which the doctor received a payment of each type.

Table 3, column 1 reports that doctors increase the quarterly number of prescribed beneficiaries by 0.37 for each additional quarter with a compensation payment, or 65 percent of the mean quarterly prescription volume in our sample. Smaller transfers have smaller estimated effects; each quarter with a compensation payment increases a doctor's own pre-

[20] Recall that the average quarterly prescription volume across all doctors in our sample is 0.55 beneficiaries.

scribing by 0.06 additional prescribed beneficiaries per quarter, or 10 percent of the average volume. Having a peer doctor receive a compensation payment leads to a modest increase in own prescription volume of 0.02 additional beneficiaries per month, or 3 percent of the average volume. Recall that while every specification also accounts for the impact of own and peer travel payments, we are not reporting these coefficients in our main tables because this payment type is less frequent and we are generally not powered to detect effects; complete results are reported in Appendix Table B1.

Comparing the estimated increases in prescription volume to the pooled average prescription volume in our sample masks heterogeneity in average prescription volumes between recipients of different payment types. Comparing the same estimates to the 2014–2016 average prescription volume of each group of recipients, we see the increase in prescription volume due to compensation payments is 6 percent of the 5.94 prescribed beneficiaries per quarter among large payment recipients, 5 percent of the average 1.11 prescribed beneficiaries per quarter among food recipients, and 1.8 percent of the average 1.12 prescribed beneficiaries per quarter among *peers* of large payment recipients. When interpreting these group averages, note that they are calculated over the entire sample period and partly reflect prescription responses to payments.

One possible mechanism behind the peer effects we estimate are prescription refills, which may happen when a primary care physician orders a refill of a prescription that was initiated by a compensated cardiologist. As the primary care physician becomes more familiar with the new drug, she may also choose to initiate new prescriptions with the drug. To estimate the effects of payments on prescriptions to new patients, we exclude prescription refills by restricting our prescription volume outcome to only include patients without any prior prescription for anticoagulants in the previous year (Table 3, column 3). Between 8 to 10 percent of the effect of payment on total prescription volume is driven by prescriptions written for patients with no prior anticoagulant use. This result includes peers of payment recipients, suggesting the spillover effects of payments on peers also spur prescriptions of the target drug to new patients.

Next, we turn to a third outcome measure: the fraction of anticoagulant prescriptions that were written for the target drug. This outcome measure will allow us to test whether the increases in prescription volume measured in the prior specifications were driven by an increase in the total volume of anticoagulant prescriptions, or alternatively, whether within the set of anticoagulant prescriptions, doctors are shifting patients toward the target drug. This outcome is only defined for the 68 percent of doctor-drug-quarters from our full sample that have nonzero anticoagulant prescriptions during the quarter.

Results from this specification are reported in Table 3, columns 5 and 6. Own food

payments and peer compensation payments are associated with a significant increase in market share of the target drug. Estimates for the effects of own compensation payments on drug market share are not statistically significant, but point estimates are consistent with an increase in market share following direct payments.

A back-of-the-envelope calculation suggests that the estimated returns to payments for the pharmaceutical companies are positive. Assume an average revenue of $800 per prescribed beneficiary per quarter, roughly the average in our sample (see Appendix Figure A2), and consider that spending on food and education payments is approximately $30 per transaction. Food payments are estimated to yield 0.06 new prescriptions each quarter in our 40 percent Medicare sample, which corresponds to an additional quarterly revenue of $260 when both Medicare and non-Medicare patients are considered.[21] In contrast, compensation payments of $3,000 per quarter would appear less profitable if only their direct effect is accounted for, because the 0.37 new beneficiaries it is estimated to add in our sample reflect only $1,600 of additional revenue. However, including the additional 0.02 patients such payments yield in our sample for each of the 60 (on average) peers of the direct recipient, means that their overall return is much greater, as spillovers alone generate an additional $4,800 per payment. These rough estimates suggest that accounting for spillover effects is essential for evaluating the return on pharmaceutical payments, particularly for large payments. We further discuss the aggregate impact of payments in Section 5.

Recall that our baseline definition of peer affiliation is based on patient-sharing patterns. In the regression specification reported in Table 4, we also consider peer relationships based on group practice affiliation. We distinguish three types of peer relationships: doctors who share patients, doctors who share both patients and a group practice affiliation, and doctors who only share a group practice affiliation. The results suggest that doctors who share patients with a compensation-paid peer will increase their prescribing volume by 0.02 per quarter in our sample, while doctors who not only share patients but also a group practice affiliation with a compensation-paid peer will increase their prescribing volume by 0.014 in sample patients.[22] This difference between the two peer types is not statistically significant. Doctors who only share a group practice affiliation (but do not have shared patients) with the compensation-paid peer increase their prescription volume of the target drug by 0.014 patients per quarter. Taken together, these results suggest that compensation payments increase drug prescription volume of both peer types; our results are not driven solely by

[21] The estimated overall value of added prescriptions comes from scaling the regression coefficients from Table 3 upward by a factor of 5.4, which accounts for non-sampled Medicare beneficiaries, as well as non-Medicare patients, as discussed in Section 1. For the food example, this is $0.0589 \cdot 5.4 = 0.324$

[22] As reported in Table 4, column 2, 0.014 is the sum of the "Shared patient" and the "Group practice and shared patient" coefficients.

doctors who share a group practice.

3.3 Assessing the scale of peer effects in prescribing

In this section, we focus on the first learning mechanism and estimate the impact of an increase in peers' prescription volume for a new drug on a doctor's own prescription volume. As discussed in Section 2, we use the number of peer compensation, peer travel and peer food payments to date as instrumental variables for the average prescription volume across each physician's direct peers. We then trace out the influence of peer prescriptions on own prescribing.

If we assume that paid doctors do not directly promote the drugs to their peers (the "proselytizing" mechanism), then these instrumental variable estimates of peer effects may generalize to settings in which peer prescription decisions are not driven by pharmaceutical payments. As we cannot rule out proselytizing behavior, we will interpret our instrumental variable estimates as an upper bound on the magnitude of peer effects we would expect when prescription patterns change for reasons other than a pharmaceutical payment.

First-stage estimates suggest that an additional compensation payment to a doctor's peer raises the quarterly prescription volume averaged across all of the doctor's peers by 0.033 beneficiaries per quarter (statistically significant at the 1 percent level; Table 5). This effect is much smaller than the estimated impact of a large payment on the targeted doctor himself, reflecting the fact that we are averaging prescriptions across all doctors' peers, only one of whom was hit with the payment shock. This averaged impact reflects a combination of the direct impact of a large payment on the targeted physician as well as any ripple effects due to peer linkages between the paid physicians' peers and other peers.

Second-stage regression estimates show that if the average prescription volume across the focal doctor's peers increases by one beneficiary per quarter on average, the focal doctor's own prescription volume will increase by 0.32 prescriptions per quarter. Should this finding be driven by indirect observation of peer prescription choice (rather than proselytizing), it suggests that the prescription increases may ripple (with decay) beyond first-degree peer connections.

3.4 Robustness and treatment effect heterogeneity

In this section we explore alternative specifications and probe whether the estimated effects of physician payments are heterogeneous across the sequence of payments or the type of doctor targeted.

First, we test an alternative regression approach that relies on matching compensation-paid physicians to unpaid physicians who have similar observable characteristics. We construct the matched sample of paid and unpaid physicians as follows. First, we sample all physicians who received compensation payments at any point during 2014–2016. We henceforth refer to these physicians as *targets*. Second, we match each target with similar physicians who did not receive compensation payments, based on the following criteria.

We match exactly on specialty, the target drug, and location (HRR). We match coarsely (by quartiles) on experience, number of shared-patient peers, and number of group practice peers. We also drop a small number of matches who share a group practice with the target, so all our matches are from the same area as the target but not from the same practice. We then sample all shared-patient peers of targets and their matches. We exclude peers of targets or matches who have an additional peer (beyond the target) who received compensation payments. Therefore, the resulting sample has two disjoint sets of physicians who are peers of either a paid physician or a matched unpaid one, and who have no other compensation-paid peers.

Descriptive statistics for the matched sample are shown in Table A3. Results from the matching estimation are reported in Table 6. Columns 1, 3, and 5 replicate the baseline specification included in Table 3 on the matched sample. Columns 2, 4, and 6 show similar results with an alternative specification that excludes differential time trends for doctors paid during our Medicare Part D sample period. Our matched sample yields very similar results to our baseline estimates. In the matched sample, we find that the focal doctor increases his prescription volume of the target drug by 0.025 patients per quarter for each additional compensation payment targeted at the focal doctor's peers (see Table A3, column 1); for comparison, the baseline estimate was 0.018.

In Appendix Table A4, we report additional robustness checks, varying the specification and the estimating sample. Column 1 replicates our baseline estimates (as reported in Table 3) with doctor-drug fixed effects. Column 2 substitutes the fixed effects with random effects at the doctor-drug level, which will yield unbiased estimates of payment impact only if payments are conditionally uncorrelated with doctors' baseline propensity to prescribe the new drug. We find very similar results from the random effects specification; as before, each compensation payment paid to a focal doctor's peer is estimated to increase the focal doctor's prescribing by 0.02 in-sample beneficiaries per quarter. We use this random effects specification as the basis for our counterfactual analysis reported in Section 5. Finally, in column 3, we estimate our baseline fixed effects model on a restricted sample of doctors; this specification drops doctors directly receiving a payment of any type prior to 2014Q3 as well as doctors who have a compensation-paid peer for the target drug prior to 2014Q3.

Estimated peer effects of compensation payments remain similar in this sample; having a compensated peer increases prescribing by 0.015 in-sample beneficiaries per quarter.

In Appendix Table A5, we test whether the first observed payment has a differential impact relative to subsequent payments.[23] The coefficients on the "first payment" variables should be interpreted as the *difference* in the effect of the first payment compared to the effect of subsequent payments; to calculate the total impact of the first payment, the first and count coefficients should be added. Point estimates suggest that a doctor's first compensation payment and first food payment have slightly smaller estimated effects than subsequent payments. The first time a doctor's peer receives a compensation payment it has a nearly zero estimated impact on the doctor's prescription volume, although this estimate is noisy and not statistically distinguishable from the impact of subsequent payments.

Similar results for the effects on payments on prescriptions are obtained when we estimate the effects separately by medical specialty, or by drug, as reported in Appendix Table A6. The first row shows our baseline specification. The second and third rows show results separately by specialty. Peer payments both lead to a larger increase in prescription volume for cardiologists. This pattern is consistent with the fact that cardiologists write more prescriptions for anticoagulants in general, and therefore have more scope to increase their use of target drugs. The remaining rows show estimates of the influence of payments on prescriptions, separately for each drug. Point estimates suggest that own and peer payments increase prescription volume for each of the three NOACs under study. The effect of peer compensation payments on the quarterly number of prescribed patients is similar for Xarelto (0.025) and Eliquis (0.023), and smaller for Pradaxa (0.009), although these comparisons are imprecise.

4 Welfare Implications

A highly contested question is how pharmaceutical detailing payments impact patient welfare. On the one hand, payments may lead physicians to over-prescribe high cost drugs. On the other hand, pharmaceutical companies argue that detailing improves welfare by educating physicians about new drugs and providing up-to-date information to support better practice.

To investigate this question, we analyzed whether pharmaceutical payments lead to increased adherence to evidence-based clinical guidelines on anticoagulant prescriptions. Be-

[23]Recall that because we observe only a censored history of pharmaceutical payments, we cannot definitively identify each doctor's first payment. Instead we tag the earliest payment observed in our sample period as the "first", and we require that doctors identifying our main regression coefficients had no payments for a minimum of four preceding quarters.

cause guidelines are not available to cover all patient indications for anticoagulant drugs, we narrow our focus to patients with atrial fibrillation, which is a common reason for prescribing anticoagulants. There are two popular risk scores to assess the risks and benefits of anticoagulation for patients with atrial fibrillation: the HAS-BLED and CHADS2 scores (Pisters et al. 2010; Lip et al. 2011; Gage et al. 2001, 2004).The HAS-BLED score estimates risk of bleeding for patients on anticoagulation drugs, which is the major safety concern that should be weighed against the stroke reduction benefits of the drug. The CHADS2 score estimates the gains from anticoagulation.[24] Note that current guidelines provide little guidance on selecting among the various anticoagulant drugs; rather, they focus on determining whether the patient is appropriate for anticoagulation drugs at all.[25]

We use the CMS Chronic Condition Warehouse data file to identify patients with diagnosed atrial fibrillation. As before, we count the number of unique beneficiaries prescribed anticoagulants by each doctor in each quarter, but for this analysis we restrict the prescription count to include only patients with diagnosed atrial fibrillation. Within this sample, we construct an estimate of the HAS-BLED risk score and CHADS2 score for each prescribed patient.

We observe four of the nine clinical characteristics included in the HAS-BLED score to construct our estimate: patient age > 65, hypertension history, renal disease, and stroke history.[26] The guideline is scored simply: one point per risk factor. Patients scoring zero to one are considered low risk; two points correspond to moderate risk; three or more points correspond to high risk.[27]

Because we do not observe all the factors that underlie this guideline, we interpret our results as follows. Patients who have three or more risk factors are designated high risk;

[24]For a quick reference guide to clinical scoring for atrial fibrillation, see MDCalc `https://www.mdcalc.com/has-bled-score-major-bleeding-risk` and `https://www.mdcalc.com/chads2-score-atrial-fibrillation-stroke-risk`. Accessed August 2019.

[25]For further discussion, see UpToDate® Nonvalvular atrial fibrillation: Anticoagulant therapy to prevent thromboembolism, `https://www.uptodate.com/contents/nonvalvular-atrial-fibrillation-anticoagulant-therapy-to-prevent-thromboembolism`, Accessed August 2019.

[26]Even among our observed patient characteristics, our definitions do not exactly align with the definitions used in the guideline. For example, hypertension is only considered if it is uncontrolled and the patient has > 60 mmHg systolic pressure. A similarly precise definitions is used for renal disease. Patient characteristics included in the full HAS-BLED score but not observable in our data include: labile INR (a lab blood test value), prior major bleeding or predisposition to bleeding, liver disease, medication use predisposing to bleeding (including aspirin and NSAIDS that are not prescription drugs), and alcohol use (at least eight drinks per week).

[27]Note that the guidelines themselves do not provide sharp recommendations on whether or not to prescribe anticoagulation drugs. For example, the HAS-BLED score recommendations provided on MDCalc.com are worded as "anticoagulation should be considered" [strongest recommendation], "anticoagulation can be considered" [moderate], or "alternatives to anticoagulation should be considered" [weakest].

we label the rest of our sample "low risk." Note that our "low risk" sample will include some high-risk patients for whom we cannot observe all of their risk factors; we have greater confidence that the "high risk" subgroup is identified accurately. On average, doctors in our sample prescribe anticoagulants to 2.8 high-risk patients per quarter and 2.0 low-risk patients per quarter. If doctors were to increase their adherence to the HAS-BLED guidelines, we would expect fewer prescriptions written to patients at high risk of bleeding.

Results for the relationship between payment-induced prescription and bleeding risk are reported in Table 7. In columns 1–3, we pool patients regardless of which oral anticoagulant they receive (Xarelto, Pradaxa, Eliquis, or Warfarin). Recall that the guidelines are not specific to any particular type of anticoagulant, so it is plausible that if detailing efforts educate physicians about appropriate use, these benefits might spill over to all prescribed drugs in the class. We estimate a modified version of equation (2) that includes doctor fixed effects and specialty-quarter fixed effects to accommodate the new sample structure (which is no longer drug-specific). Pharmaceutical payments are pooled across all three drugs for these specifications.

Point estimates suggest that own food, own compensation, and peer compensation payments each increase prescription volume for both low *and* high-risk patients, although the estimates are generally indistinguishable from zero. The only category of payment associated with a statistically significant increase in prescription volume within these subgroups is a doctor's own food payments. Food payments increase the number of high-risk patients prescribed anticoagulants by 0.048 and increase the number of low-risk patients prescribed by 0.034; these both amount to a 1.7 percent increase from the subgroups' mean prescription volume.

The confidence interval around our estimate suggests that compensation payments also did not substantially decrease risky prescribing among peers of the paid physician. Peer compensation is estimated to increase total anticoagulant prescribing among high bleeding risk patients by 0.6 percent, and the 95 percent confidence interval is bounded below by a 0.4 percent decrease in prescribing to high bleeding risk patients.

In columns 4–6 of Table 7, we disaggregate the data by drug to test whether drug detailing efforts increase guideline-concordant prescribing for the target drug, which we would expect if any physician education that occurred with the detailing was drug-specific. Again, we find no significant evidence that doctors are decreasing their prescribing to high-risk patients.

In Appendix Table A7, we perform another analysis of guideline concordance that incorporates compliance with the CHADS2, which assesses the patient's potential benefits from anticoagulation drugs due to reduced stroke risk. In this case, we can approximate each of the five factors of the guidelines in claims records: congestive heart failure, hypertension

history, age, diabetes mellitus history, and stroke or transient ischemic attack symptoms.[28] We dichotomize the CHADS2 score, following a threshold used in the clinical guidelines. Patients with three or more risk factors are at high risk of stroke and anticoagulation is recommended; patients with fewer risk factors may still benefit from anticoagulation, but the recommendation is weaker.

We use the CHADS2 score in combination with our approximated HAS-BLED score to divide patients into three categories by their estimated stroke-reduction benefit and bleeding risk: low value (low benefit and high risk), medium value (low benefit and low risk, or high benefit and high risk), or high value (high benefit and low risk). If pharmaceutical detailing led doctors to more guideline-concordant practice patterns, we might expect declining use in the low-value population and increasing use in the high-value population. Empirically, we see no strong patterns of differential response by category of value.

Our results suggest that payments increase *average* prescription volume for high-risk and for low-value patients. We argue that such findings are hard to reconcile with the idea that payments strictly improve physician's information set; at least in some cases, it appears that payments induce low-value prescribing.

5 Assessing the Aggregate Impact of Payments

So far, we have focused on estimating the average effect of a single detailing payment on prescription volumes of the targeted doctor and her peers. A natural related question is: what is the *aggregate* impact of pharmaceutical payments on diffusion of the marketed products? To explore this topic, we use our estimated model as a quantification framework to perform several counterfactual analyses. We consider three questions. First, what contributions do payments make to total prescription volumes? Second, what part of this impact occurs directly, through payment effects on recipients, versus indirectly, through payment effects on peers? Third, do changes in prescription behavior induced by pharmaceutical payments reduce geographic variation in the adoption of NOACs?

To address these questions, we combine the estimated unit-effects of payments of different types with information on the number and timing of payments and on the network position and physical location of physicians. Considering the number of payments of each type is important for assessing their aggregate impact. For example, as discussed, small payments for food and educational items outnumber any other type of payments by two orders of magnitude. Considering the network centrality of the targets of large payments is important

[28] We cannot observe stroke *symptoms* in claims data, but we do measure patients with history of strokes or transient ischemic attacks.

too: payments to more-connected physicians will induce spillover effects in a larger number of peers.

For this analysis, we use the random-effects version of equation (2). As discussed in Section 3.4 and reported in Table A4 (columns 1 and 2), the random-effects and fixed-effects estimates are very similar. Using the random effects model allows us to relax our sampling restrictions (discussed in Section 1.2) and extend the counterfactual simulations to cover the entire sample.

We keep the observed network structure and physician characteristics as in the data. We then compare the fitted values using three alternative payment schemes: (1) actual payments, (2) only direct payments (zeroing out any peer-payment impact), and (3) no payments. In all cases, we maintain separate time trends for payment recipients, which we think of as capturing unobserved heterogeneity in payment targeting rather than the effects of payments. Excluding these trends would increase the estimated effects of payments. To obtain estimates of total prescription volume in US dollars, we multiply the estimated counterfactual number of beneficiaries per quarter under different scenarios with the quarterly average cost of prescriptions of each drug. These average costs are fairly stable over our sample period, as seen in Appendix Figure A2.

Figures 5 and 6 summarize the results of this analysis. Figure 5 compares the actual NOAC prescription volumes in 2014–2016 to the counterfactual prescription volumes in the absence of any payments, and in the absence of payment spillover effects. Table A8 shows annual prescription rates at the end of our sample period, 2016Q4. By then, prescriptions of new oral anticoagulants in the United States reached an annual volume of $7.6 billion (dollar amounts are scaled by a factor of 5.4 to reflect out-of-sample patients; see Section 1 for a discussion of this scaling factor). Our estimates suggest that absent payments, the market would have only been $6.2 billion. Therefore, by the end of our sample period, payments increased estimated prescription revenue by 23 percent. The effect is slightly greater for more recently patented drugs, which have more payments associated with them.

Figure 6 further decomposes this overall impact by type of payment. Panel (A) shows the estimated average payment impact on the direct recipient and on the recipient's peers. The impact on peers was calculated by multiplying the average effect of the payment on each peer (from Table 1) by the average number of peers per recipient of the relevant payment type (from Appendix Table A4). As discussed in Section 3, compensation payments not only have a much greater impact on the direct recipient than food payments, they also have a much larger cumulative indirect impact on the recipient's peers. The indirect impact of compensation payments is three times greater than the direct effect.

Even though compensation payments are much rarer than food payments (see Panel (B)

of Figure 6), compensation payments make a substantial contribution to the aggregate impact of payments on prescription volume, primarily through their peer effects (see Panel (C) of Figure 6, based on data from Appendix Table A8). About a quarter of the aggregate impact of all payments is due to indirect effects of payments on recipients' peers. In dollar terms, payments' peer spillovers contribute $387 million in prescriptions per year of the total $1.4 billion increase due to payments. We interpret this estimate of total peer effect contribution as a lower bound because it accounts for only one type of peer relationship (physicians with at least 11 shared patients), likely excluding some physician peer relationships.

Finally, we explore whether changes in prescription behavior induced by pharmaceutical payments contribute to geographic variation in the adoption of NOACs. Donohue et al. (2012) reports that variation in the propensity to prescribe brand-name (rather than generic) drugs is a major contributor to total variation in Medicare Part D spending. Differences in pharmaceutical detailing intensity across regions is one potential contributor to these differences in prescription choice. Panel (A) of Figure 7 shows that regions with higher initial adoption are exposed to more subsequent detailing payments. While we cannot rule out that some of the baseline differences reflect earlier payments or other differences in regional demand for new drugs, this evidence suggests that payments increase, rather than decrease, spatial disparity in the adoption of NOACs.

Our counterfactual analysis is also consistent with this pattern. Panel (B) of Figure 7, which is based on our model estimates, shows that the HRR-level estimated increase in prescription during 2014–2016 is positively associated with baseline prescription levels. Appendix Figure A3 shows that for each of the studied drugs, payment effects appear not only to increase overall prescription levels, but also increase the dispersion of prescriptions across areas. This evidence suggests that pharmaceutical payments may play a role in increasing spatial variation in the adoption of new drugs.

6 Payment Effects on Competitor Drugs

In Section 3, we found that pharmaceutical payments to physicians lead them and their peers to prescribe the associated drug to additional beneficiaries. This increase may come at the expense of competitor drugs if payments lead doctors to substitute the advertised drug for its competitor products. Alternatively, the advertising may benefit competitors, if detailing interactions lead payment recipients and their peers to *increase* the prescription of other drugs in the same class.

Prior research has found mixed results on the impact of advertising on the demand for competing drugs. Two recent papers on direct-to-consumer television advertising have found

varying results; Sinkinson and Starc (2018) find business-stealing effects among branded drugs and positive spillovers for non-advertised competitors, while Shapiro (2018b) finds positive spillovers for both generic and branded competitors. There is more limited evidence on how drug detailing efforts targeted at physicians (rather than consumers) affects demand for competing products; early work by Berndt et al. (1994, 1995) finds positive spillovers in the market for anti-ulcer drugs.

To evaluate the possible effects of advertising on rival products, we jointly estimate the impact of payments targeting one drug on the prescription of both the target drug and its competitors. Applying a seemingly unrelated regression framework, we estimate two equations jointly with different outcome variables: the first equation captures prescription volume of the target drug; the second equation captures total prescription volume among all other anticoagulants (excluding the target drug). The regression model echoes the earlier specification laid out in equation (2):

$$\begin{aligned} Y_{i,t,d} &= \alpha_{id} + \beta_{dts} + X'_{idt}\gamma + P_{idt}\delta + P_{Gi,d,t}\eta + \varepsilon_{idt}, \\ \sum_{d' \neq d} Y_{i,t,d'} &= \tilde{\alpha}_{id} + \tilde{\beta}_{dts} + X'_{idt}\tilde{\gamma} + P_{idt}\tilde{\delta} + P_{Gi,d,t}\tilde{\eta} + \nu_{idt} \end{aligned} \tag{4}$$

where, as before, where i indexes doctors, t indexes time, s indexes their medical specialty, and d indexes the target drug. The dependent variable of the first equation, $Y_{i,t,d}$, denotes prescriptions of the target drug. The dependent variable in the second equation, $\sum_{d' \neq d} Y_{i,t,d'}$, denotes prescriptions of all other coagulants, except for d. The rest of the terms are defined exactly as in equation (2). Here, we are interested in comparing the elasticity of prescriptions of the target-drug and the cross-drug elasticity with respect to own payments (δ and $\tilde{\delta}$) and peer payments (η and $\tilde{\eta}$).

We test the null hypothesis that the sum of the additional number of target and competitor prescriptions that is due to payment of each type is zero, using a χ^2 test. If this sum is zero, it implies that on average, the increase in prescription volumes due to payments mainly reflects business stealing. We perform this test for each of the six payment types separately. Namely, we test whether $\delta_j + \tilde{\delta}_j = 0$, where j is each one of food, travel, and compensation. We also perform this test for own payments of all types combined ($\delta + \tilde{\delta} = \vec{0}$), and for peer payments of all types combined ($\eta + \tilde{\eta} = \vec{0}$).

The results of this analysis are summarized in Table 8. The first column shows the SUR estimates of the effects of different types of payments on prescriptions of the target drug. The coefficient estimates are identical to our OLS estimates of equation (2), shown in Table 3, except with updated standard errors that account for the cross-equation error structure. Column 2 shows the effects of payments associated with each target drug on

prescriptions of the competitors. We estimate that receiving compensation or consulting fees or having a peer receive such a payment is not associated with a significant change in prescriptions of competitor drugs. Namely, the increase in prescriptions due to compensation payments is concentrated mostly in the target drug, and reflects neither business stealing nor an expansion of anticoagulant use beyond the target drug. In contrast, we estimate that physicians who receive food payments prescribe both the target *and* the competitor drugs more, suggesting that detailing visits spillover positively to competitors and induce a market expansion.[29] Payments made to peers have small negative effects on competitor drug prescriptions, but these effects are not statistically insignificant. Columns 3 shows the results of the χ^2 tests, rejecting the null that payments increase prescriptions merely through business stealing ($p < 0.001$ for own and $p = 0.029$ for peer payments).

7 Conclusion

Pharmaceutical companies pay physicians large sums of money, in the form of payments for services or in-kind transfers. Survey evidence suggests these payments are widespread, with 94 percent of US doctors reporting some form relationship with pharmaceutical companies and 25 percent receiving a payment from a pharmaceutical company for compensation or consulting services within the past year (Campbell et al. 2007). Using rich administrative data on prescriptions, payments, and physician networks, and exploiting variation in both the timing and targeting of payments, this study has shown that pharmaceutical payments lead to a significant and persistent increase in the prescription of new anticoagulant drugs. Larger payments for consulting and compensation for services have a greater effect on prescriptions than small payments of food and beverages. We find no evidence that payments improved adherence to clinical guidelines.

Furthermore, large payments from pharmaceutical firms, which target a small group of specialized and highly connected physicians, have substantial spillover effects—they lead not only to increased prescriptions by recipients, but also by the recipients' peers. The magnitude of these spillovers is substantial. The indirect influence through spillovers of each large payment is several times greater than its direct effect. Overall, spillover effects of pharmaceutical payments account for about a quarter of their estimated impact on prescription volumes.

Our results suggest that learning from peers is an important channel through which

[29]Note that the counterfactual estimates of the overall effects of payments on prescription volumes, presented in Section 5, only regard the influence of payments on the target drugs. Therefore, the positive effect of food payments on the prescription of competitor products suggests that the contribution of payments to prescription volumes of *all* anticoagulants—including competitors—is even greater.

pharmaceutical payments impact clinical practice. This finding corroborates accounts of marketing strategies that leverage influential individuals for wider impact. More broadly, these results suggest that peer influence may be an important channel for adoption of new technologies in medicine.

This project leaves several open questions. In future work, it would be instructive to extend this framework to study spillover effects of marketing in the diffusion of other technologies. Additionally, it would be interesting to explore whether similar peer effects arise when practice patterns change for reasons other than pharmaceutical payments. Our findings suggest that policy interventions to increase prescribing of recommended drugs may achieve a broader reach by targeting highly connected physicians, but rigorous evaluation should test whether peer spillovers extend to other settings.

References

Agha, Leila and David Molitor, "The Local Influence of Pioneer Investigators on Technology Adoption: Evidence from New Cancer Drugs," *The Review of Economics and Statistics*, 2018, *100* (1), 29–44.

Banerjee, Abhijit, Arun G. Chandrasekhar, Esther Duflo, and Matthew O Jackson, "The diffusion of microfinance," *Science*, 2013, *341* (6144), 1236498.

Barnett, Michael L., Bruce E. Landon, A. James O'Malley, Nancy L. Keating, and Nicholas A. Christakis, "Mapping physician networks with self-reported and administrative data," *Health Services Research*, 2011, *46* (5), 1592–1609.

Berndt, Ernst R., Linda Bui, David R. Reiley, and Glen L. Urban, "Information, marketing, and pricing in the US antiulcer drug market," *The American Economic Review*, 1995, *85* (2), 100–105.

_ , _ , David Reiley, and Glen Urban, "The Roles of Marketing, Product Quality and Price Competition in the Growth and Composition of the U.S. Anti-Ulcer Drug Industry," Working Paper 4904, National Bureau of Economic Research October 1994.

Borusyak, Kirill and Xavier Jaravel, "Revisiting event study designs," *Available at SSRN 2826228*, 2017.

Bramoullé, Yann, Habiba Djebbari, and Bernard Fortin, "Identification of peer effects through social networks," *Journal of Econometrics*, 2009, *150* (1), 41–55.

Caeyers, Bet and Marcel Fafchamps, "Exclusion Bias in the Estimation of Peer Effects," Working Paper 22565, National Bureau of Economic Research August 2016.

Campbell, Eric G., Russell L. Gruen, James Mountford, Lawrence G. Miller, Paul D. Cleary, and David Blumenthal, "A national survey of physician–industry relationships," *New England Journal of Medicine*, 2007, *356* (17), 1742–1750.

Campbell, John J., *Understanding Pharma: The Professional's Guide to how Pharmaceutical and Biotech Companies Really Work*, Pharmaceutical Institute, 2008.

Carey, Colleen Marie, Ethan MJ Lieber, and Sarah Miller, "Drug Firms' Payments and Physicians' Prescribing Behavior in Medicare Part D," *Available at SSRN 2663681*, 2015.

Chan, David C., "Influence and Information in Team Decisions: Evidence from Medical Residency," *Working Paper*, 2018.

CMS, "Physician Shared Patient Patterns," 2013. data retrieved from `http://downloads.cms.gov/foia/physician-shared-patient-patterns-2013-days30.zip`.

_ , "40% Research Identifiable Medicare Part D Database," 2013–2016. data dictionaries are available at `https://www.resdac.org/cms-data/files/pde`.

_ , "Open Payments Databases," 2013–2016. `https://openpaymentsdata.cms.gov/`.

Coleman, James, Elihu Katz, and Herbert Menzel, "The Diffusion of an Innovation Among Physicians," *Sociometry*, 1957, *20* (4), 253–270.

Cutler, David, Jonathan S. Skinner, Ariel D. Stern, and David Wennberg, "Physician Beliefs and Patient Preferences: A New Look at Regional Variation in Health Care Spending," *American Economic Journal: Economic Policy*, 2019, *11* (1), 192–221.

David, Guy, Sara Markowitz, and Seth Richards-Shubik, "The effects of pharmaceutical marketing and promotion on adverse drug events and regulation," *American Economic Journal: Economic Policy*, 2010, *2* (4), 1–25.

DeJong, Colette, Thomas Aguilar, Chien-Wen Tseng, Grace A. Lin, W. John Boscardin, and R. Adams Dudley, "Pharmaceutical industry–sponsored meals and physician prescribing patterns for Medicare beneficiaries," *JAMA Internal Medicine*, 2016, *176* (8), 1114–1122.

Donohue, Julie M., Hasan Guclu, Walid F. Gellad, Chung-Chou H. Chang, Haiden A. Huskamp, Niteesh K. Choudhry, Ruoxin Zhang, Wei-Hsuan Lo-Ciganic, Stefanie P. Junker, Timothy Anderson, and Seth Richars-Shubik, "Influence of peer networks on physician adoption of new drugs," *PLOS One*, 2018, *13* (10), e0204826.

_ **, Nancy E. Morden, Walid F. Gellad, Julie P. Bynum, Weiping Zhou, Joseph T. Hanlon, and Jonathan Skinner**, "Sources of Regional Variation in Medicare Part D Drug Spending," *New England Journal of Medicine*, 2012, *366* (6), 530–538. PMID: 22316446.

Gage, Brian F., Amy D. Waterman, William Shannon, Michael Boechler, Michael W. Rich, and Martha J. Radford, "Validation of clinical classification schemes for predicting stroke: Results from the National Registry of Atrial Fibrillation," *JAMA*, 2001, *285* (22), 2864–2870.

_ , **Carl van Walraven, Lesly Pearce, Robert G. Hart, Peter J. Koudstaal, B.S.P. Boode, and Palle Petersen**, "Selecting patients with atrial fibrillation for anticoagulation: Stroke risk stratification in patients taking aspirin," *Circulation*, 2004, *110* (16), 2287–2292.

Galeotti, Andrea, Benjamin Golub, and Sanjeev Goyal, "Targeting interventions in networks," *arXiv preprint arXiv:1710.06026*, 2017.

Giorgi, Giacomo De, Michele Pellizzari, and Silvia Redaelli, "Identification of social interactions through partially overlapping peer groups," *American Economic Journal: Applied Economics*, 2010, *2* (2), 241–275.

Golub, Ben and Evan Sadler, "Learning in Social Networks," in Yann Bramoullé, Andrea Galeotti, and Brian Rogers, eds., *The Oxford Handbook of the Economics of Networks*, Oxford University Press, 2016.

Grennan, Matthew, Kyle Myers, Ashley Swanson, and Aaron Chatterji, "Physician-Industry Interactions: Persuasion and Welfare," *NBER Working Paper No. 24864*, 2018.

Hoadley, John F, Juliette Cubanski, and Patricia Neuman, "Medicare's Part D drug benefit at 10 years: firmly established but still evolving," *Health Affairs*, 2015, *34* (10), 1682–1687.

Iyengar, Raghuram, Christophe Van den Bulte, and Thomas W. Valente, "Opinion leadership and social contagion in new product diffusion," *Marketing Science*, 2011, *30* (2), 195–212.

Larkin, Ian, Desmond Ang, Jonathan Steinhart, Matthew Chao, Mark Patterson, Sunita Sah, Tina Wu, Michael Schoenbaum, David Hutchins, Troyen Brennan, and George Loewenstein, "Association between academic medical center pharmaceutical detailing policies and physician prescribing," *JAMA*, 2017, *317* (17), 1785–1795.

Lip, Gregory Y.H., Lars Frison, Jonathan L. Halperin, and Deirdre A. Lane, "Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score," *Journal of the American College of Cardiology*, 2011, *57* (2), 173–180.

MacLeod, Bentley W. and Janet Currie, "Small Area Variations and Physician Decision Making: The Case of Depression," *Working Paper*, 2018.

Manski, Charles F., "Identification of endogenous social effects: The reflection problem," *The Review of Economic Studies*, 1993, *60* (3), 531–542.

Mekaj, Ymer H., Agon Y. Mekaj, Shkelzen B. Duci, and Ermira I Miftari, "New oral anticoagulants: Their advantages and disadvantages compared with vitamin K antagonists in the prevention and treatment of patients with thromboembolic events," *Therapeutics and Clinical Risk Management*, 2015, *11*, 967.

Moen, Erika L., Andrea M. Austin, Julie P. Bynum, Jonathan S. Skinner, and A. James O'Malley, "An analysis of patient-sharing physician networks and implantable cardioverter defibrillator therapy," *Health Services and Outcomes Research Methodology*, 2016, *16* (3), 132–153.

Navathe, Amol and Guy David, "The formation of peer reputation among physicians and its effect on technology adoption," *Journal of Human Capital*, 2009, *3* (4), 289–322.

Oster, Emily and Rebecca Thornton, "Determinants of technology adoption: Peer effects in menstrual cup take-up," *Journal of the European Economic Association*, 2012, *10* (6), 1263–1293.

Pisters, Ron, Deirdre A. Lane, Robby Nieuwlaat, Cees B. De Vos, Harry J.G.M. Crijns, and Gregory Y.H. Lip, "A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: The Euro Heart Survey," *Chest*, 2010, *138* (5), 1093–1100.

Sacarny, Adam, Andrew R. Olenski, and Michael L. Barnett, "Association of Quetiapine Overuse Letters With Prescribing by Physician Peers of Targeted Recipients: A Secondary Analysis of a Randomized Clinical Trial," *JAMA Psychiatry*, 2019.

Schwartz, Lisa M. and Steven Woloshin, "Medical Marketing in the United States, 1997-2016," *JAMA*, 01 2019, *321* (1), 80–96.

Shapiro, Bradley T., "Informational shocks, off-label prescribing, and the effects of physician detailing," *Management Science*, 2018, *64* (12), 5925–5945.

_ , "Positive spillovers and free riding in advertising of prescription pharmaceuticals: The case of antidepressants," *Journal of Political Economy*, 2018, *126* (1), 381–437.

Silver, David, "Haste or Waste? Peer Pressure and Productivity in the Emergency Department," *Working Paper*, July 2019. `https://www.dropbox.com/s/ril7ugyvenb0ogk/jmp.pdf?dl=0`.

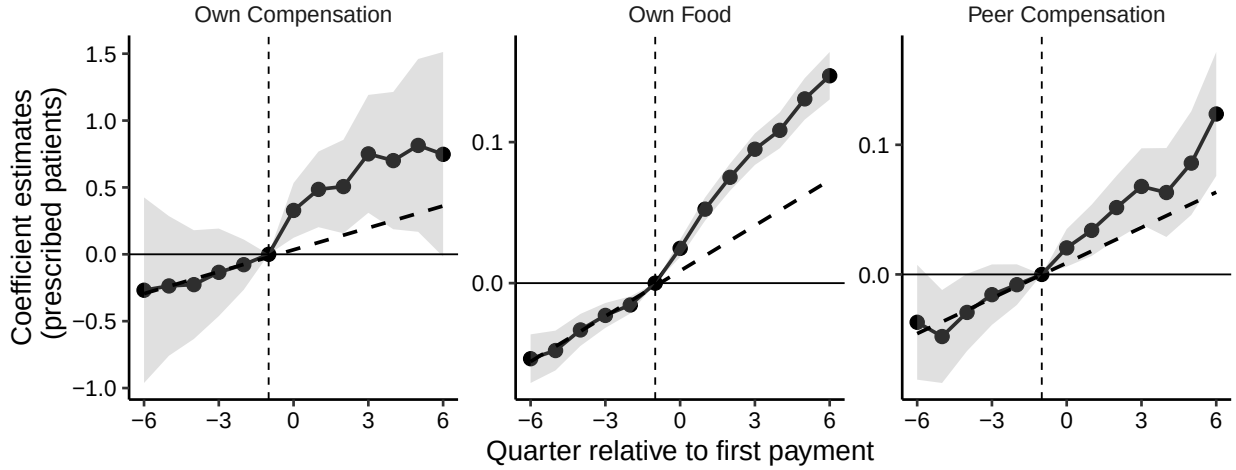
Sinkinson, Michael and Amanda Starc, "Ask your doctor? Direct-to-consumer advertising of pharmaceuticals," *The Review of Economic Studies*, 2018, *86* (2), 836–881.

Skinner, Jonathan and Douglas Staiger, "Technology diffusion and productivity growth in health care," *Review of Economics and Statistics*, 2015, *97* (5), 951–964.

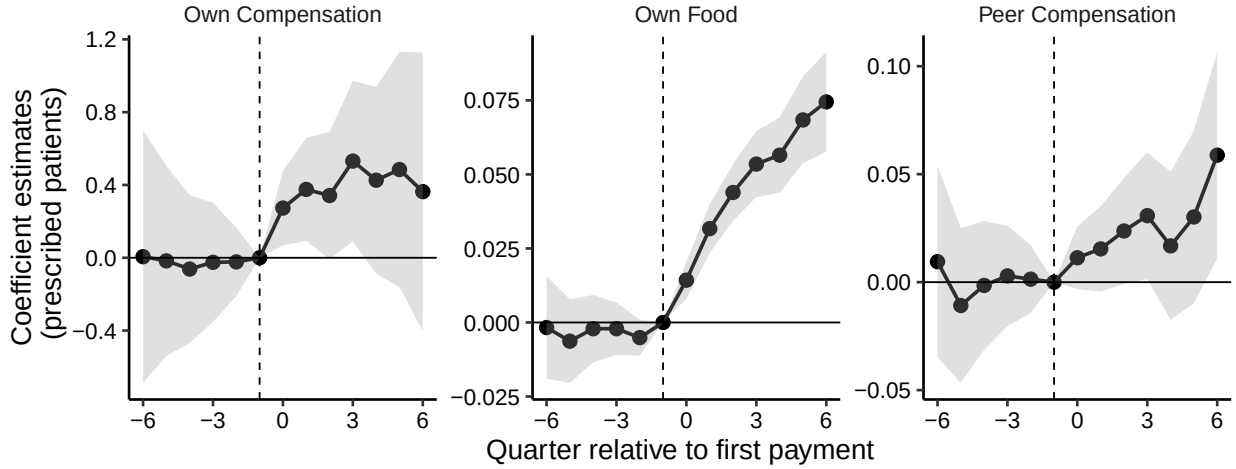
Zeltzer, Dan, "Gender homophily in Referral Networks: Consequences for the Medicare Physician Earnings Gap," *Americal Economic Journal: Applied Economics*, forthcoming.

Figure 1: Event Study: The Impact of Payments on Prescription Volume

(A) Before Detrending

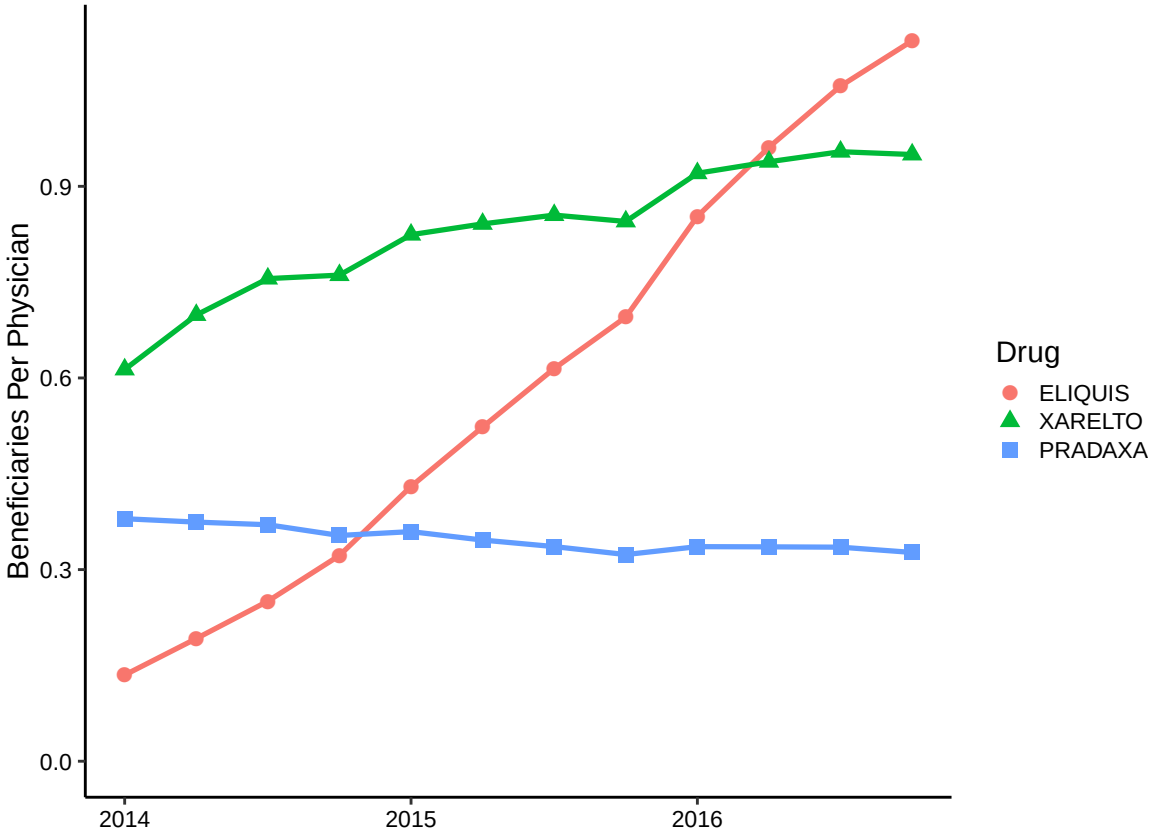


(B) After Detrending



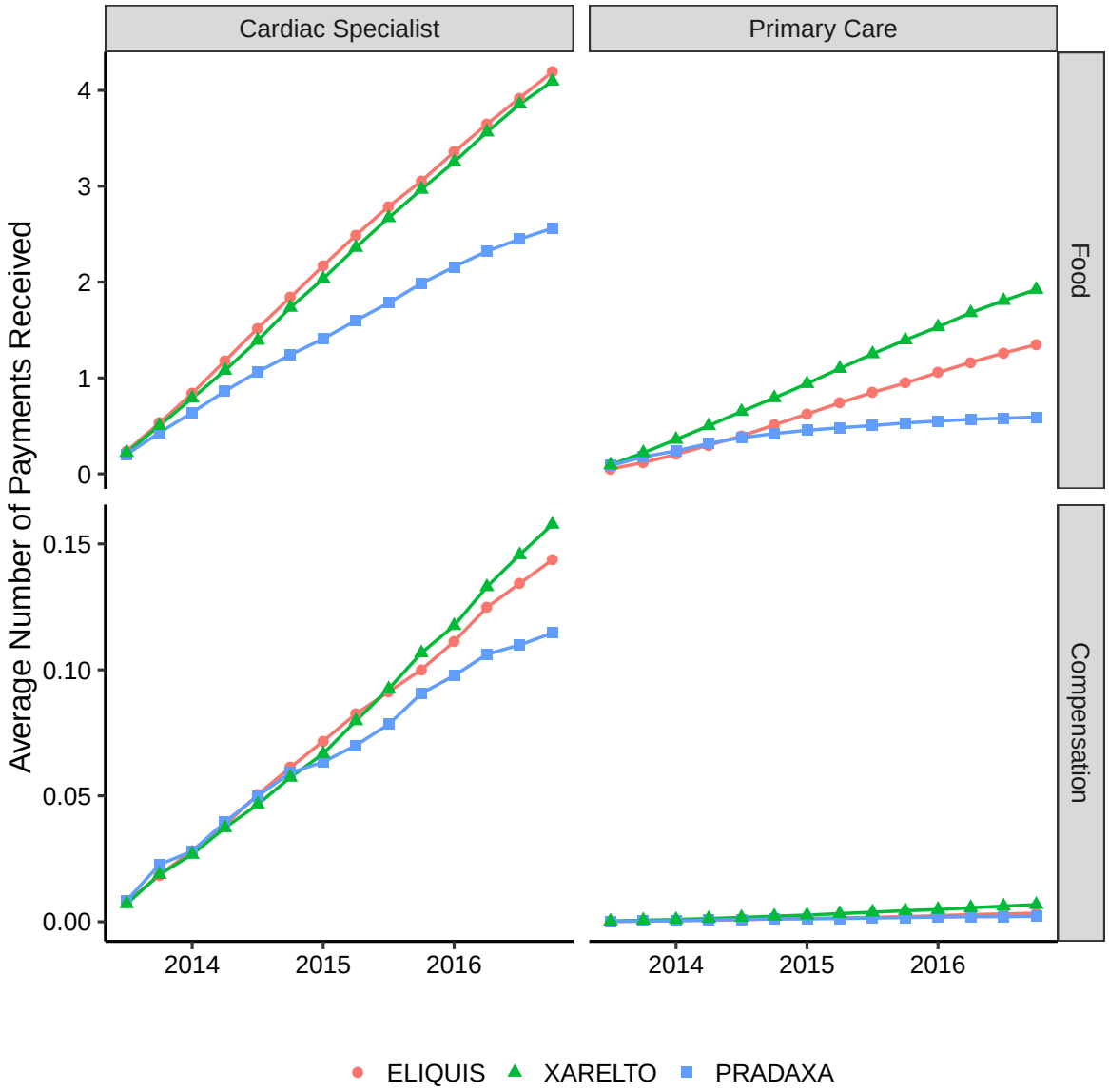
Notes: Figure shows event study coefficients estimated from equation (1), showing the response of physicians to own and peer payments of different types. The facets show coefficients for different payment types—own food, own compensation, and peer compensation—that were all jointly estimated using 5,467,536 doctor-drug-quarter observations. Panel (A) reports coefficients from a single regression that excludes a differential pre-trend for paid physicians; the dashed line fitted to the pre-trend for illustration. Panel (B) reports coefficients from a single regression after detrending, using the two-step procedure described in Section 2. All regressions also include variables for peer food, own travel, and peer travel, alongside fixed effects for doctor-drug and drug-specialty-quarter. Quarter 0 indicates the quarter of the first payment of each type. Shaded areas show 95 percent confidence intervals. Note that facet vertical axes have different scales.

Figure 2: NOAC Prescription Volume over Time



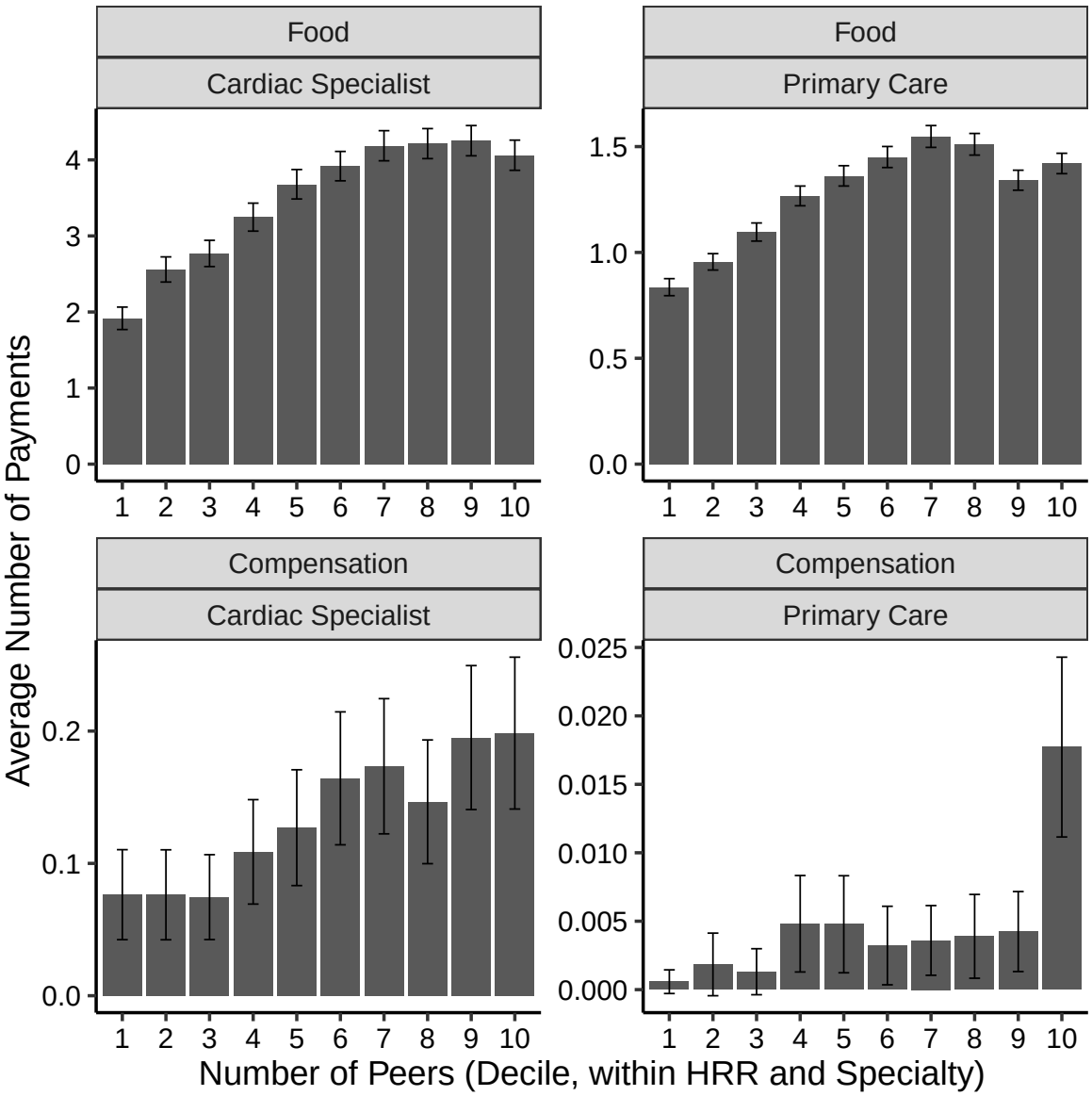
Notes: For the three NOAC drugs we study, figure shows the average number of prescribed beneficiaries per quarter per physician in our sample. Averages are over all physician-quarters in our sample, including those with zero prescriptions. The FDA first approved Pradaxa in 2010, Xarelto in 2011, and Eliquis in 2012. Data are from 40 percent of Medicare Part D claims.

Figure 3: Average Number of Payments per Physician, by Type of Payment and Medical Specialty



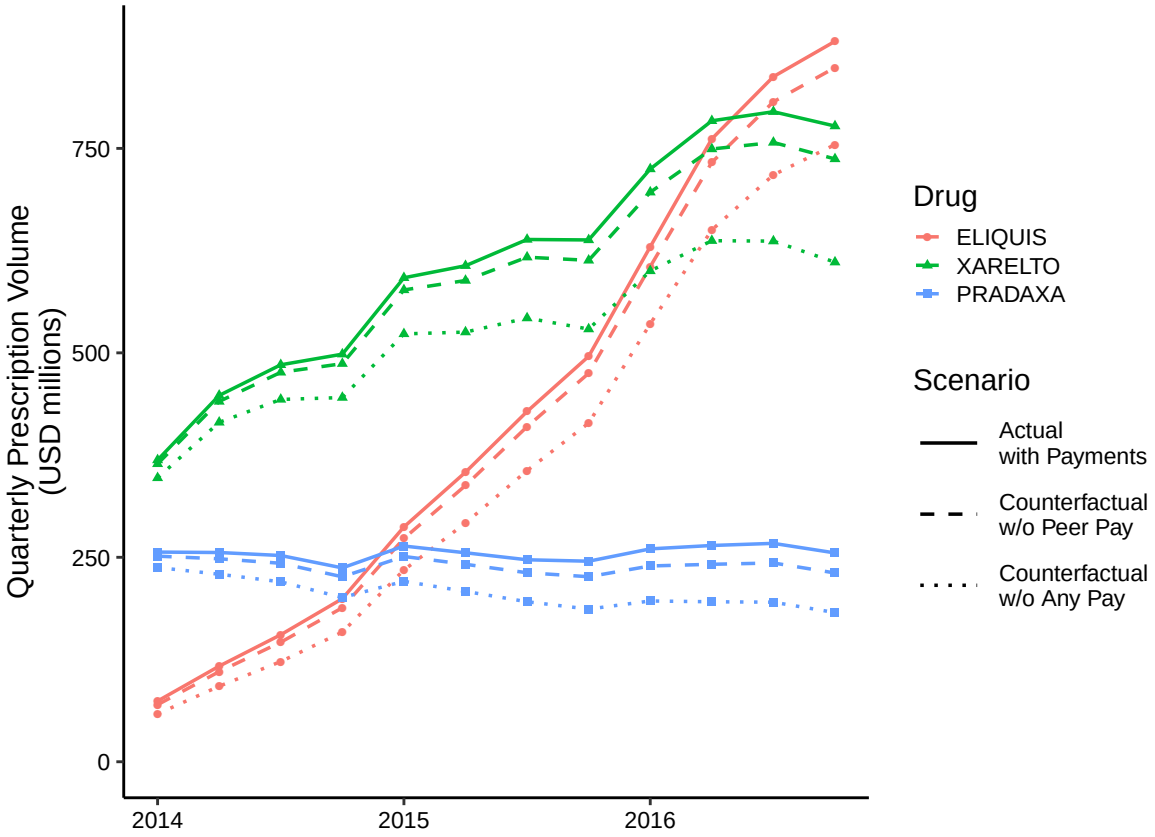
Notes: Figure shows average cumulative number of payments per physician in 2014–2016 associated with each of the three NOACs in our sample. Each column of facets shows data for a different medical specialty: cardiac specialties (left) and primary care (right). Each row of facets shows payments of a different type: Food category includes education, food, and beverage transfers; Compensation includes compensation for services and consulting fees. Section 1 describes the specialty and payment category definitions.

Figure 4: Average Number of Payments by Recipient Number of Peers



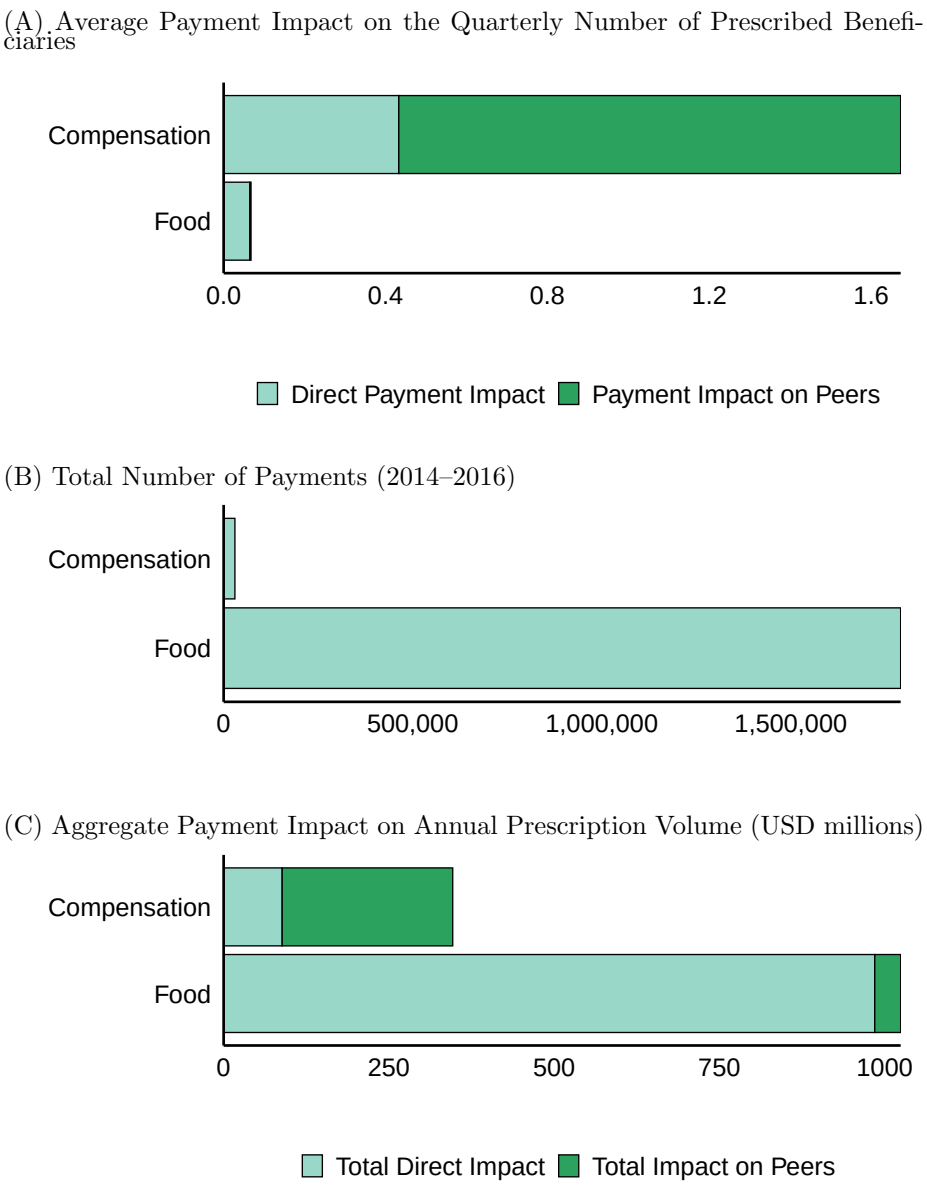
Notes: For each specialty and type of payment, figure shows the average number of payments made to each physician (y-axis), by deciles of the recipient's number of peers (x-axis). Deciles are calculated separately for each HRR and specialty. Error bars show 95 percent confidence interval for the mean. Note that facet vertical axes have different scales. Each row of facets shows payments of a different type: Food category includes education, food, and beverage transfers; Compensation includes compensation for services and consulting fees. Each column shows data for a different medical specialty: cardiac specialties (left) and primary care (righy). For specialty definitions see Section 1.

Figure 5: Actual and Counterfactual US Prescription Volumes



Notes: Figure shows estimated actual and counterfactual total US prescription volume per quarter. Each color represents one drug in our sample. For each drug, the solid line is the actual US quarterly prescription volume. The dashed line labeled "Counterfactual w/o Peer Pay" is the counterfactual volume obtained by shutting off any effects of payments to peers of the directly paid physicians. The dotted line labeled "Counterfactual w/o Any Pay" is the counterfactual volume obtained in the absence of any pharmaceutical payments. Dollar estimates were obtained by summing the estimated number of prescribed beneficiaries over all physicians in our sample and multiplying the sum by the average quarterly prescription cost per patient in our sample (average costs are shown in Figure A2). All estimates are scaled by a factor of 5.4 to reflect the total US market size, including non-Medicare patients; the scaling exercise implicitly assumes that the price per prescription is the same for Medicare Part D patients and other patients prescribed the drug. This scaling factor is discussed in Section 1. Estimates of the average number of beneficiaries per doctor before scaling are shown in Appendix Figure A4.

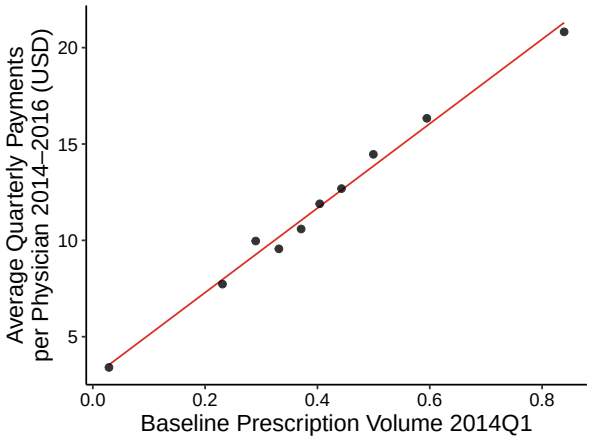
Figure 6: Pharmaceutical Payment Impact on Prescription Volumes



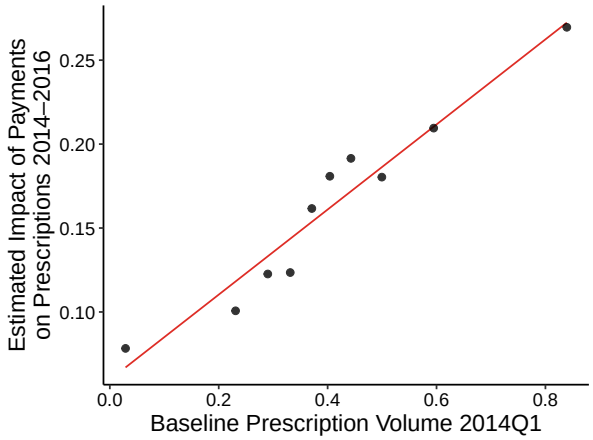
Notes: Figure shows estimates of direct and peer effects of pharmaceutical payments on prescription volume, by type of payment: Compensation are payments for services and consulting fees; Food are payments for or in-kind transfers of food, beverages, and educational items. Panel (A) shows the estimated effect of receiving payments of each type during a quarter on the quarterly number of unique beneficiaries prescribed the target drug by the direct recipient (light shade) and by all of the recipient's peers (dark shade). Panel (B) shows the number of pharmaceutical payments and in-kind transfers associated with NOAC drugs in 2014–2016. Panel (C) shows the estimated overall contribution of payments of each type to annual NOAC prescription volumes by direct recipients (light shade) and their peers (dark shade) in the United States. Panel (A) is based on a 40 percent sample of Medicare Part D beneficiaries; dollar estimates in Panel (C) are rescaled by a factor of 5.4 to extrapolate to all US prescriptions. This scaling factor is discussed in Section 1. Data sources are described in Section 5.

Figure 7: Regional Differences in Baseline Prescription Volumes, Subsequent Payments, and Payments' Impact.

(A) Average Payment Per Physician



(B) Estimated Cumulative Impact on Prescriptions



Notes: Both panels show binned scatterplots in which the x-axis represents HRR-level average prescription volume per physician at the beginning of the sample (2014Q1). Panel (A) shows the relationship between regional baseline prescription volume and the average dollar value of subsequent pharmaceutical payments per physician in the HRR (2014-2016). Panel (B) shows the relationship between regional baseline prescription volume and the estimated contribution of payments to NOAC prescription volume in the HRR. The y-axis of Panel (B) shows the difference between the actual average prescription volume and the model-estimated counterfactual average prescription volume in a scenario without any pharmaceutical payments. Prescription volumes reported here represent unadjusted numbers based on our 40% Part D sample. Both scatterplots show the HRR-level relationship after residualizing drug fixed effects. The data are binned by deciles of the x-axis variable; the coordinates of the points shown are the means of each bin. The solid lines show linear regression fits.

Table 1: Summary Statistics by Payment Status

	Own Payments			Peer Payments		
	None	Food or Travel	Compensation	None, Food, or Travel	Compensation	All Physicians
	(1)	(2)	(3)	(4)	(5)	(6)
Prescribed patients (per qtr)	0.320	1.117	5.945	0.452	1.124	0.548
Newly prescribed patients (per qtr)	0.024	0.081	0.388	0.033	0.085	0.040
Fraction of Anticoagulant Prescriptions (%)	13.7	20.2	35.6	15.2	19.7	15.8
Percent cardiologists	8.0	21.9	81.2	9.3	27.8	12.0
N of shared-patient peers	16.5	28.1	62.0	15.4	46.0	19.7
Total own pharma payments ($)	0	148	38,166	103	344	137.8
N of quarters with food payment	0	4.118	8.368	0.979	2.018	1.127
N of quarters with compensation	0	0	5.074	0.001	0.034	0.013
N of peer-quarters with compensation	0.6856	1.449	2.481	0	6.266	0.895
Percent of observations	72.9	26.8	0.3	85.7	14.3	100
N of doctors	135,425	70,348	973	154,529	41,443	166,422
N of doctor-drug-quarter observations	3,985,728	1,467,756	14,052	4,686,384	781,152	5,467,536
N of observations for fraction outcome*	2,515,420	1,196,775	13,065	3,130,170	595,090	3,725,260

Notes: Table shows summary statistics for the main sample of 5,467,536 physician-drug-quarter observations; this is a balanced panel of 166,422 physicians over 12 quarters and for three NOAC drugs. Columns 1–3 show statistics for subsets of physicians who directly received different types of pharmaceutical payments: no payments, payments for Food or Travel, or payments for Compensation. Columns 4–5 show statistics for the subset of physicians whose peers received compensation payments, and the complement set of those whose peers did not receive such payments. Column 6 shows statistics for the entire sample. Prescribed patients is the number of unique beneficiaries prescribed the drug in the quarter. Newly prescribed patients are prescribed patients without any anticoagulant prescription in the preceding year. Fraction of Anticoagulant Prescriptions is the share of target drug prescriptions out of all anticoagulant prescriptions made by the physician in the quarter. This statistic is based on the subset of 3,725,260 physician-quarters with at least one anticoagulant prescriptions. Definitions of payment types, physician medical specialties, and share-patient peers are discussed in Section 1.

Table 2: Summary Statistics for Different Types of Pharmaceutical Payments

Payment Type	Assigned Category (1)	Total Number of Payments (2)	Mean Payment Size (3)	Median Payment Size (4)	Payment Total Amount (USD) (5)
Consulting Fee	Compensation	2,247	2,370	2,000	5,325,818
Compensation for services	Compensation	27,426	2,275	2,400	62,397,361
Travel and Lodging	Travel	18,076	260	112	4,695,838
Education	Food	30,208	36	9	1,095,886
Food and Beverage	Food	1,759,889	17	13	29,295,620

Notes: Payments for NOAC drugs to sampled physicians, 2014–2016. Rows are shown in descending order of mean payment size. The "Payment Type" column lists the payment category as reported in the Open Payments Database. The "Assigned Category" describes our groupings of these types into three categories based on payment size. We label these categories based on the most common payment type: Compensation, Travel, and Food.

Table 3: The Influence of Payments on Target Drug Prescription Volumes

	Dependent Variable:		
	Number of Prescribed Patients (1)	Newly Prescribed Patients (2)	Fraction of Anticoagulant Prescriptions (3)
Payment count, by type:			
Own Compensation	0.3704	0.0283	0.0095
	(0.1158)	(0.0160)	(0.0058)
Own Food	0.0589	0.0049	0.004
	(0.0037)	(0.0006)	(0.0007)
Peer Compensation	0.0184	0.0020	0.0019
	(0.0060)	(0.0009)	(0.0009)
Peer Food	-0.0004	0.0002	0.0005
	(0.0013)	(0.0002)	(0.0004)
Mean of dependent variable	0.549	0.041	0.159
N (Doctor×Drug×Quarter)	5,467,536	5,467,536	3,725,260

Notes: Estimates of equation (2); each column reports key coefficient estimates from a separate regression. The dependent variables capture different prescription volume measures. The independent variables capture the counts of different types of payments made to the prescribing physicians ("Own") or to others with whom the prescribing physicians shared patients ("Peers"). Food includes payments for food and beverages, and educational items. Compensation includes payments for consulting, speaking, and other services. See Section 1 for detailed definitions. Physician-drug, specialty-drug-quarter fixed-effects, controls for all other types of payments, and payment-type-specific linear time trends included in all specifications. See Table B1 for extended results.

Table 4: The Influence of Payments on Prescription Volume, Different Peer Definitions

	Dependent Variable:					
	Number of Prescribed Patients		Newly Prescribed Patients		Fraction of Anticoagulant Prescriptions	
	(1)	(2)	(3)	(4)	(5)	(6)
Compensation Payment Count, by Recipient Type:						
Own	0.3704	0.3701	0.0283	0.0283	0.0095	0.0094
	(0.1158)	(0.1159)	(0.0160)	(0.0160)	(0.0058)	(0.0058)
Shared-Patient Peer with or without Shared Group Practice	0.0184	0.0199	0.0020	0.0019	0.0019	0.0023
	(0.0060)	(0.0060)	(0.0009)	(0.0010)	(0.0009)	(0.0010)
Group Practice and Shared-Patient Peer		-0.0057		0.0003		-0.0011
		(0.0145)		(0.0020)		(0.0017)
Group Practice Peer and not Shared-Patient Peer		0.0137		0.0022		0.0001
		(0.0045)		(0.0006)		(0.0012)
Mean Dependent Variable	0.548	0.548	0.041	0.041	0.159	0.159
N (Doctor × Drug × Quarter)	5,467,536	5,467,536	5,467,536	5,467,536	3,725,260	3,725,260

Notes: Estimates of equation (2). The dependent variables capture different prescription volume measures. Independent variables capture the counts of exposure to compensation payments. "Own" denotes payments to the prescribing physician. In this specification, the "Shared-Patient Peer with or without Shared Group Practice" coefficients are interpreted as the impact of payments to shared-patient peers who do not also share group practice affiliations. The "Group Practice and Shared Patients Peer" coefficients report the *difference* in payment impact for those with both group practice and shared-patient ties, relative to those with only shared-patient ties. Finally, the "Group Practice Peer and not Shared-Patient Peer" coefficient reports the impact of payments to peers who share a group practice affiliation but do not meet the definition of a shared-patient peer. See Section 1 for exact definitions. Physician-drug, specialty-drug-quarter fixed-effects, controls for all other types of payments, and payment-type-specific linear time trends included in all specifications. See Appendix Table B2 for extended results.

Table 5: Scaling Peer Effects in Prescription Behavior

A. First Stage:

	Dependent Variable:	
	Number of Prescribed Patients, Average Across Peers	
	(1)	(2)
Payment Count, by Type		
Own Compensation	0.0223	0.0113
	(0.0110)	(0.0115)
Own Food	0.0142	0.0114
	(0.0010)	(0.0011)
Peer Compensation	0.0330	0.0331
	(0.0013)	(0.0016)
Peer Food	0.0153	0.0133
	(0.0005)	(0.0006)
N (Doctor × Drug × Quarter)	5,467,536	3,725,260

B. Second Stage:

	Dependent Variable:		
	Number of Prescribed Patients	Newly Prescribed Patients	Fraction of Anticoagulant Prescriptions
	(3)	(4)	(5)
Peer Prescription	0.3194	0.0233	0.0504
	(0.0288)	(0.0084)	(0.0093)
Payment Count, by Type			
Own Compensation	0.3626	0.0276	0.0089
	(0.0136)	(0.0040)	(0.0037)
Own Food	0.0541	0.0045	0.0034
	(0.0013)	(0.0004)	(0.0004)
N (Doctor × Drug × Quarter)	5,467,536	5,467,536	3,725,260

Notes: Generalized method of moments estimates of the instrumental variable model specified in equations (3a) and (3b). The endogenous variable is the average number of prescribed patients across the index doctor's shared-patient peers. Peer payments act as an instrumental variable for peer prescription volume. Column 1 shows the first-stage results that correspond to the second-stage results in columns 3 and 4. Column 2 shows the first stage results that correspond to second stage results in column 5. Physician-drug, specialty-drug-quarter fixed-effects, controls for all other types of payments, and payment-type-specific linear time trends included in all specifications. See Appendix Table B3 for extended results.

Table 6: Estimates of the Impact of Payments on Target Drug Prescriptions Using a Matched Sample of Compensated and Non-Compensated Physicians

	Dependent Variable:					
	Number of Prescribed Patients		Newly Prescribed Patients		Fraction of Anticoagulant Prescriptions	
	(1)	(2)	(3)	(4)	(5)	(6)
Payment Count, by Type						
Own Compensation	0.4475	0.5431	0.0264	0.0452	0.0077	0.0120
	(0.1495)	(0.1230)	(0.0217)	(0.0173)	(0.0068)	(0.0047)
Own Food	0.0666	0.0666	0.0054	0.0049	0.0042	0.0041
	(0.0064)	(0.0047)	(0.0009)	(0.0007)	(0.0009)	(0.0007)
Peer Compensation	0.0250	0.0288	0.0030	0.0031	0.0025	0.0019
	(0.0077)	(0.0055)	(0.0012)	(0.0008)	(0.0012)	(0.0008)
Peer Food	-0.0028	-0.0069	-0.0005	-0.0007	-0.0002	-0.0001
	(0.0027)	(0.0022)	(0.0003)	(0.0002)	(0.0006)	(0.0005)
Differential Pretrends	Y	N	Y	N	Y	N
N (Doctor × Drug × Quarter)	1,914,744	1,914,744	1,914,744	1,914,744	1,404,226	1,404,226

Notes: Table shows alternative estimates of the effects of payments on prescriptions, obtained using a sample of peers of recipients of compensation payments and of matched non-recipients of such payments. Matching was first performed exactly on specialty and drug then coarsely on group practice network degree, shared-patient network degree, and years of experience. Table A3 provides descriptive statistics of the matching sample used for these results. Section 3.4 discusses the details of this analysis. Columns 1–2, 3–4, and 5–6, show our three prescription volume measures discussed in Section 2. Columns 1, 3, and 5 replicate the specification shown in Table 3 on the matched sample. Columns 2, 4, and 6 show models that exclude differential time trends for doctors paid during our Medicare Part D sample period. Own and peer travel payments included but not shown; see Appendix Table B4 for extended results.

Table 7: The Effect of Payments, by Risk of Severe Drug Side Effects

	Dependent variable:					
	Patients Prescribed Any Anticoagulant			Patients Prescribed the Targeted Anticoagulant		
	All Patients	Low Bleeding Risk	High Bleeding Risk	All Patients	Low Bleeding Risk	High Bleeding Risk
	(1)	(2)	(3)	(4)	(5)	(6)
Payment Count, by Type						
Own Compensation	0.3582	0.1058	0.2524	0.5201	0.2083	0.3117
	(0.2309)	(0.1275)	(0.1584)	(0.1688)	(0.0966)	(0.1129)
Own Food	0.0819	0.0336	0.0483	0.0666	0.0250	0.0415
	(0.0116)	(0.0061)	(0.0085)	(0.0074)	(0.0039)	(0.0054)
Peer Compensation	0.0293	0.0125	0.0168	0.0183	0.0145	0.0037
	(0.0175)	(0.0086)	(0.0136)	(0.0112)	(0.0061)	(0.0080)
Peer Food	-0.0014	0.0026	-0.0040	-0.0008	-0.0016	0.0008
	(0.0062)	(0.0025)	(0.0053)	(0.0034)	(0.0015)	(0.0028)
Adj. R Sqr.	0.7843	0.6400	0.8188	0.7485	0.7011	0.6556
Mean Dep. Var.	4.7635	1.9591	2.804	1.0152	0.4488	0.5663
N	1,554,864	1,554,864	1,554,864	3,689,520	3,689,520	3,689,520

Notes: Table shows estimates of the impact of pharmaceutical payments on anticoagulant prescriptions, for the sample of patients diagnosed with atrial fibrillation and who received at least one anticoagulant prescription during the study period. The different columns show results separately by major bleeding risk—a severe side effect of NOAC use—based on the HAS-BLED risk score. The sample is partitioned by bleeding risk based on our calculation of the HAS-BLED score. See Section 4 for details. Columns 1–3 show estimates of the impact of payments (pooled across all three NOAC drugs) on the total number of anticoagulants prescribed per quarter (pooled across all anticoagulants). Columns 4–6 show similar estimates, but where both payments and the prescription volume outcomes are measured separately for each NOAC in our sample. Physician-drug, specialty-drug-quarter fixed-effects, controls for all other types of payments, and payment-type-specific linear time trends included in all specifications. Travel payments included but not shown; see Appendix Table B5 for extended results.

Table 8: The Effects of Payments on Prescription of Target versus Competitor Drugs

	Dependent Variable:		
	Number of Patients Prescribed, by Drug Targeting Status:		
	Targeted Anticoagulant (1)	All Other Anticoagulants (2)	χ^2 test H_0: Col. 1 + Col. 2 = 0 (3)
Payment Count, by Type:			
Own Compensation	0.3704	-0.0204	$p = 0.0492$
	(0.1109)	(0.1202)	
Own Food	0.0589	0.0585	$p < 0.0001$
	(0.0035)	(0.0063)	
Peer Compensation	0.0184	-0.0005	$p = 0.1059$
	(0.0057)	(0.0093)	
Peer Food	-0.0004	-0.0058	$p = 0.0335$
	(0.0012)	(0.0025)	
N (Doctor×Drug×Quarter)	5,467,536	5,467,536	

Notes: Table shows estimates of the effect of payments on targeted versus competitor drugs. The first two columns show the estimated additional number of prescribed beneficiaries per quarter resulting from each payment type, for the target drug (Column 1) and for all other anticoagulants, excluding the target drug (Column 2). The two columns were jointly estimated using a seemingly unrelated regression (SUR) model with the specification detailed in equation (1). Physician-drug, specialty-drug-quarter fixed-effects, controls for all other types of payments, and payment-type-specific linear time trends included in all specifications. Travel payments included but not shown; see Appendix Table B6 for extended results.

Column 3 shows p-values of a χ^2 test, where the null hypothesis is that the sum of the effects of payments of the type specified in each row on the target drug and on all other drugs sum to zero. The p-value of a χ^2 test of the joint null that the sums of the estimated effects of *own* payments for food, travel, and compensation are all zero is $p < 0.0001$; the corresponding p-value for the joint null that the sums of the estimated effects of *peer* payments food, travel, and compensation are all zero is $p = 0.0292$.