Drug Diffusion through Peer Networks: The Influence of Industry Payments

Leila Agha* Dan Zeltzer†

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PRELIMINARY

Abstract

Medical drug and device companies invest over $8 billion annually in payments to physicians and hospitals; many of these payments are targeted at encouraging use of new drugs. Drug detailing efforts of pharmaceutical companies leverage peer influence within existing provider networks to broaden their reach beyond the directly targeted physicians. Using matched physician data from Medicare Part D and Open Payments, we investigate the influence of pharmaceutical payments on the prescription of new anticoagulant drugs. First, we show that pharmaceutical payments target physicians who share patients with many different providers and thus may influence a broader network of peers. Within a difference in differences framework, we find a physician's own prescription of new anticoagulant drugs increases following a pharmaceutical payment, relative to the physician-specific baseline prescribing rate for that drug. The effect scales with the size of the payment, with large payments such as speaking and consulting fees spurring larger increases in prescribing than small payments for food. Peers of targeted physicians also increase their prescribing of the new drug after the targeted physician receives a large payment, introducing entirely new patients to the drug class. We find no evidence that drug detailing leads to curtailed prescription volume for patients at high risk of dangerous side effects or low potential benefit of anticoagulation.

Keywords: health care, innovation diffusion, peer effects, networks, pharmaceutical detailing

*Department of Economics, Dartmouth College, leila.agha@dartmouth.edu
†School of Economics, Tel Aviv University, dzeltzer@tauex.tau.ac.il

1 Introduction

Drug and medical device companies invest over $8 billion annually in payments to physicians and hospitals; many of these payments support advertising efforts encouraging providers to adopt new clinical products. Recent evidence suggests these efforts impact prescription behavior, and an ongoing public debate centers on the influence of drug manufacturers' promotional efforts (Sinkinson and Starc, 2015), and particularly payments to physicians (e.g., Campbell et al., 2007; Navathe and David, 2009; David et al., 2010; DeJong et al., 2016; Grennan et al., 2018). While pharmaceutical companies' engagements with physicians may educate doctors about new drugs, such engagement may also increase the volume of higher cost, brand name products marketed by industry, not necessarily in the best interest of patients.[1]

Large detailing payments reportedly target thought leaders, i.e. physicians who may be highly influential on the practice of their peer providers. Supported by a burgeoning commercial intelligence industry that identifies, profiles, and tracks Key Opinion Leaders in different locations and therapy areas, pharmaceutical marketing increasingly leverages indirect influence. In this paper, we consider the impact of pharmaceutical detailing efforts on local prescription patterns by studying how payments impact drug diffusion through the peer network of targeted doctors.

Peer influence in technology adoption has been documented in other contexts (e.g., Bandiera and Rasul, 2006; Tucker, 2008; Duflo et al., 2008; Conley and Udry, 2010; Oster and Thornton, 2012). However, absent experimental variation, research into peer influence faces a significant hurdle, which is that local clustering may be the result of common shocks or correlated preferences, and not the direct result of peer effects. To isolate peer effects from these competing explanations, we exploit quasi-experimental variation in promotional payments and in-kind transfers physicians receive from pharmaceutical companies. This study's contribution is twofold: it provides both a lens for understanding the role of information diffusion through local physician networks and a more complete accounting of the impact of pharmaceutical companies' promotional efforts through spillovers.

To study prescription behavior and the influence of pharmaceutical payments, we use Medicare Part D administrative claims data. We focus on prescriptions of anticoagulants (commonly referred to as "blood thinners"), a widely utilized therapeutic class to which several new drugs were introduced during or shortly before our sample period. Branded Novel Oral Anticoagulants (NOACs) cost roughly 20 times more than a common off-patent

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

incumbent anticoagulant. The new drugs improved upon the incumbent product (Warfarin) by not requiring routine coagulation monitoring for dose adjustment.[2] On the other hand, for much of the study period, specific antidotes needed to reverse the NOACs effect in the event of a major bleed were not yet FDA approved, whereas the incumbent drug was reversible. The net benefit of NOACs compared to the older therapy were ambiguous, and likely varied across patients.

We match prescription data with two other data sources: (i) the universe of payments and value transfers to US physicians by drug manufacturers and distributors, and (ii) data on physician networks, where physicians are considered connected if they share patients. Combined, these data provide a unique opportunity to study spillovers in prescription behavior and the effects of industry payments for two reasons. First, shared-patient relationships are not transitive. Namely, the peer groups of physicians who share patients with each other do not generally overlap. Thus, we observe physician-level variation in the exposure to peers who received pharmaceutical payments. Second, the longitudinal nature of the data allows us to study how doctor's prescription volume changes after they are exposed to pharmaceutical payments.

Analyzing this novel matched database, we confirm earlier findings showing payments and prescriptions are positively correlated. Furthermore, we show that while a large fraction of practicing physicians receive small payments associated with detailing visits by marketing salespersons, relatively few, more specialized physicians, receive large payments that are associated with speaking, consulting, and other services. Nonetheless, large payments account for two thirds of the total dollar volume transferred. Consistent with influencer marketing tactics, large payments are disproportionately made to physicians with a large number of peers, even controlling for other observed characteristics.

To identify peer effects separately from unobserved factors that may be correlated across referring physicians, such as correlated physician tastes or patient demand, we exploit variation in both the timing of payments to physicians and their peer group composition. Using a difference-in-differences framework, we estimate the impact of payments on the physician receiving the payments as well as the paid physician's peers.

Directly receiving a payment is associated with increases in prescription volume, with larger effect sizes tracking larger payment sizes. Small payments for food lead to 0.06 additional prescribed beneficiaries per quarter in our sample, an 8 percent increase over the average prescription volume. Payments for consulting and compensation for services lead to

[2]Price data for Eliquis, Xarelto, Pradaxa and warfarin from goodrx.com. NOACs Eliquis, Xarelto, Pradaxa are currently priced at $400 to $600 for a one month supply; incumbent Warfarin is priced around $18 and is available at Walmart for $4.

0.37 additional prescribed beneficiaries per quarter, a 50 percent increase over the average prescription volume.

Consulting or compensation payments are also associated with a significant increase in prescription volume of the paid physician's peers. Following a payment, each peer of the direct recipient increases prescription volume on average by 0.02 additional beneficiaries per quarter. This effect on each peer is roughly 1/3 the estimated effect size of directly receiving a food payment, and 1/20 the size of an own payment of the same magnitude. But while spillover effects are smaller than the direct effect of payments, given that the physicians targeted with these large payments have more than 60 peers on average, the overall estimated impact of a large payment on all first-degree peers eclipses the estimated impact of a large payment on the paid physician's own patient volume.

We find that the estimated peer effects are not solely the result of refilling prescriptions originally written by other doctors. Both direct recipients of large payments and their peers initiate more NOAC prescriptions in patients with no prior prescription for anticoagulants—of any kind, by any physician—in the previous year.

To quantify the direct and indirect effects of payments on overall prescription volumes, we use the estimated model and the existing network structure, and compare actual and counterfactual prescription volumes given alternative payment scenarios. Relative to a counterfactual with no payments, we estimate that in 2014–2016, pharmaceutical payments have increased NOAC prescription volumes by 16 percent. About a quarter of this increase is due to spillovers to peers of recipients, mainly spillovers of large compensation payments. 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 amplified through peer effects and that drug manufacturers and distributors ability to influence medical practice is greater than one would have estimated neglecting peer spillovers.

These patterns of payment influence on prescriptions further suggest that pharmaceutical detailing payments may contribute to regional variation in the adoption of new health technologies. Prior research has documented significant local clustering of treatment patterns (Agha and Molitor, 2018; Cutler et al., 2013; Skinner and Staiger, 2015; Moen et al., 2016; MacLeod and Currie, 2018). We show that pharmaceutical companies' drug detailing efforts not only increase the mean adoption but also its variance. Because payments are not evenly distributed across space, but rather are concentrated in areas where initial adoption is already high, they contribute to the divergence of practice across locations, 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 prescrip-

tion safety and value. Because NOACs are relatively new and guidelines for their use are still evolving, it is difficult to assess the appropriateness of individual use in many cases. Nonetheless, for the subset of patients with atrial fibrillation, a common condition treated with anticoagulants, evidence-based risk scores exist that identify patients facing a high risk of dangerous bleeding side-effects if anticoagulated (Gage et al., 2001; Pisters et al., 2010; Lip et al., 2011). And while in each specific case physicians may have reasons to conclude that benefits outweigh the potential risks, by calculating these risk scores for our entire cohort, we can test how payments increase prescriptions among low and high benefit patients *on average*. We find that the increases in prescription volume associated with payments accrue similarly across all subgroups, including in cases where evidence-based guidelines suggest anticoagulant prescriptions have high expected risk. This finding suggests that detailing efforts did not improve anticoagulant prescription safety and appropriateness. While not conclusive, it calls into question the welfare gains from detailing.

Taken together, our results suggest that peer effects may amplify the influence of manufacturers and reinforce geographic variation in practice patterns. Therefore, spillover effects should be acknowledged when considering the nature of competition in the markets for new medical technologies and in the marketing strategies associated with promoting such products. Our paper contributes to several literatures. Most directly, it is related to the literatures studying the effects of pharmaceutical marketing and detailing (David et al., 2010; DeJong et al., 2016; Larkin et al., 2017; Shapiro, 2018; Sinkinson and Starc, 2018; Grennan et al., 2018), physician networks (Barnett et al., 2012; Agha et al., 2018), the adoption of new technologies in medicine, and the study of peer effects, learning, and geographic variation therein (Skinner, 2011; Oster and Thornton, 2012; Cutler et al., 2019; Chan, 2018). More broadly, this paper is also related to the extensive literature that studies the impact of targeted intervention, diffusion, and learning in networks (Banerjee et al., 2013; Golub and Sadler, 2017; Galeotti et al., 2017).

Understanding the scope of marketing efforts and their relationship to peer influence in medicine is of particular importance for policy. While influencer marketing, viral marketing, and celebrity endorsement are common marketing strategies in consumer good markets (Iyengar et al., 2011), information asymmetries characteristic of health care markets leave large scope for over and under adoption of new technologies, with substantial consequences for consumers. In principle, the same forces that may cause over-adoption of certain technologies can lead others to be under-adopted. Interactions between physicians could be exploited to target interventions in order to beneficially expedite the diffusion of new clinical practices. Although, the strength of spillovers may vary by context: Donohue et al. (2018) estimated peer effects in prescription of first-in-class drugs among physicians in Pennsylva-

nia, while Sacarny et al. (2019) found no peer effects on for CMS warning letters sent to physicians discouraging overuse of antipsychotic drugs. These results underscore then need for more empirical work in this area.

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

2 Data and context

Our analysis focuses on anticoagulants (commonly referred to as "blood thinners"), studying the diffusion of three new oral anticoagulant drugs (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 1). These three NOACs were introduced between 2010 and 2012, shortly before our sample period begins 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 cause 250,000 deaths per year in the United States. The NOAC global market was $23 billion in 2013, and is projected to double by 2025.[4]

NOACs are considered non-inferior 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, priced at more than USD 500 per month, multiple times the price of off-patent Warfarin.[5]

[3]The FDA first approved Pradaxa on Oct 19, 2010; Xarelto on Jul 1, 2011; Eliquis on Dec 28, 2012. This slight variation in the introduction of drugs means that we have a chance to observe slightly different stages in the lifecycle of product introduction.

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

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

2.1 Data Sources

To estimate peer effects in the diffusion of new drugs, we combine multiple databases on prescription, payments, and connections as follows. Physician prescription volumes are derived from Medicare Part D administrative claims. Associated payments and in kind transfers to physicians made by drug manufacturers are identified in the Open Payments database. Physician shared-patients relationships are merged in from the Referral Patterns database. Additional physician characteristics, including practice location and group-practice affiliations are from Physician Compare.[6]

Prescriptions We analyze a 40% sample of Research Identifiable Medicare Part D claims in 2014–2016 (CMS, 2013–2015). To track the adoption and use of new anticoagulant drugs, we restrict attention to physicians of medical specialties that together include the majority of NOAC prescribers: primary care and cardiology.[7]

For each physician from these specialties 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.[8] 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 total anticoagulant prescriptions. This relative share variable is defined only in quarters with at least one anticoagulant prescription.[9]

Peers To study peer effects in prescription decisions, we combine prescription information with physician referral data from 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

[6]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.

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

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

[9]Because this measure is only available for physician-quarters with any AC prescriptions (the denominator of the fraction), it corresponds to a smaller sample size (See Table 2).

to the same Medicare patient within a 30 days period 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. 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.

Survey analysis has validated that physicians with multiple shared patients are typically familiar with each other (Barnett et al., 2011), suggesting peers thus defined may also influence each other's practice. One channel for such influence is via observing peer prescription behavior for shared patients.

Table A2 presents summary statistics on the distribution of the number of peers. The mean physician in our sample share 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, 2014–2015). 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 (ACA). Beginning in 2013, manufacturers are required to submit data about all payments and other transfers of value made to physicians (which we henceforth refer to as *payments*). The reports include the amount paid (or value of non-monetary transfer, such as food or travel expenses), the associated drug(s), and the nature of the transfer. 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 1 show 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 2 shows the average cumulative payments associated with each drug that were received by physicians of different specialties.

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. 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 18,00 travel transactions, accounting for only 5% 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. 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 by physicians who share at least one group practice. We use these to supplement our baseline measure of peer linkages defined by shared patients.

2.2 Patterns of Pharmaceutical Payments, Prescriptions, and Number of Peers

Doctors who share patients with many peer providers are more likely to receive compensation payments. Figure 3 sorts doctors by decile of peer linkages ("degree") within each hospital referral region (HRR) and specialty type. 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 providers. By contrast, highly connected physicians in the top deciles of the degree distribution 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 providers. Table A2 regression results show that higher degree is associated with higher payments even after accounting for other observed physician characteristics.[10] This data is consistent with the possibility that pharmaceutical companies target large payments to highly connected doctors, who may be

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

better positioned to amplify the payment's impact.

Table 2 shows summary statistics by physician own and peer payment status. This table restricts to our analysis sample for consistency with the subsequent regression results. Specifically, we 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 well as peer compensation payments. This restriction ensures that we have a balanced panel for at least 5 quarters around the first payment event, which is important to accurately comparing doctor's prescription volume before and after the payment.

The table reports that 73% of doctors in our sample receive no payments directly. On average, 27% of doctors receive food payments for each drug, and these doctors average $148 in payments for the targeted drug over the 12 quarters of our sample. This total transfer is typically spread across several transactions: physicians receiving food payments are paid in 4 out of 12 quarters on average. By contrast, the 0.3% of physicians who receive compensation payments for each drug are drawing much larger transfers from pharmaceutical companies, averaging $38,167 per doctor cumulatively over 12 quarters. Physicians receiving compensation payments average 6 quarters (out of 12) with compensation payments. Cardiac specialists constitute the majority (81%) of recipients of compensation payments.

Even though only 0.3% of doctors in our sample receive compensation payments for a given drug, these paid doctors are highly connected, so we find that 14.3% 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 targeted 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% sample of Medicare Part D enrollees. The Kaiser Family Foundation reports that 70% of Medicare beneficiaries were enrolled in Part D, suggesting our sample covers roughly 28% of Medicare beneficiaries. Further, in the 2014 Medical Expenditure Panel Survey, 66% 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.

3 Identification and Estimation

The focus of our analysis is estimating spillover effects of pharmaceutical payments on 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 use a difference-in-differences approach exploiting variation in the timing of payments and the peer group of targeted physicians.

3.1 Regression models of payment impact

We model prescription decisions as a function of payments, including both payments directly made to the physician and payments to the index doctor's peer. Let $i = 1, \ldots, N$ index physician providers, $t = 1, \ldots, T$ index time in quarters, and $d \in D$ index drugs. Let Y_{itd} denote the volume prescriptions of drug d made by i at period t, and . Let G denote the network of relationships among providers based on having common patients (see Section 2 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.[11] Because peer relationships are non-transitive, $j \in G_i$ does not imply $G_j = G_i$, i.e. peer groups vary even among connected peers.

Our first approach is to graphically analyze prescription patterns before and after the first payment. In each of our specifications, we separately model six types of payment exposure: own food, own travel, own compensation, peer food, peer travel, peer compensation. We compare prescription volume before and after the first payment made to each physician and/or to this physician's peers. We estimate the model:

$$Y_{itd} = \alpha_{id} + \beta_{dts} + X'_{idt}\gamma + Z_{id}\delta_{r(i,t)} + Z_{Gi,d}\eta_{r(i,t)} + \varepsilon_{idt}, \tag{1}$$

where i index doctors, t index time, s index medical specialties (PCP or specialist), and d index drugs. 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

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

Z_{id} defines indicator variables for whether doctor i ever receives each of the three types of payments (food, travel, compensation) 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. 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.

The model pools all drugs together in the analysis, estimating a homogeneous effect of payment for each drug. To flexibly capture the differential effect of various payment types (e.g. small food and beverage payments vs. large speaking and consulting fees), we estimate separate treatment effects for each type of own and peer payments.

For doctors who receive payments in quarters 3 or 4 of 2013, before the beginning of our Part D sample, we include a separate time trend by payment type for each of these early payment recipients. In addition, we show specifications both with and without differential pre-trends by payment type for doctors who receive payments during our sample period. To estimate specifications that allow for pre-trends, we first run 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, as well as a full vector of indicator variables for post-treatment quarters. As a second step, we residualize the outcome variable by the estimated pre-trend, and estimate the full 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 non-linear trends in the pre-treatment period.

These regression models allow us to make a series of plots of the estimated impact of pharmaceutical company payments on prescription volume. The graphical analysis displays what happens in the quarters before and after the **first** payment. As described in the summary statistics reported in Table 2, 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.[12]

To estimate the impact of each individual payment, we turn to a regression specification

[12]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 4 observable quarters before that first payment. Our estimates of the effects of payments may be biased toward zero, as we cannot identify the first payment over the doctor's complete history, because our payment data set begins in Quarter 3 of 2013, after some payments have presumably been made.

that uses the running sum of paid quarters as the key independent variable. 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.

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

The control variables in this new equation parallel those in equation 1, including the same set of doctor×drug and drug×quarter×specialty fixed-effects. We continue to include differential time trends for paid doctors: one set of time trends by payment type for doctors whose first observed payment occurs before our Part D sample begins, and a second set of time trends by payment type for doctors whose first observed payment occurs during our sample period. The key independent variables of interest include the P_{idt} vector, which contains three separate variables capturing the count of quarters to date with food payments, travel payments, and consulting and compensation for services payments, respectively. In addition, the $P_{Gi,d,t}$ vector includes three separate variables capturing the count of peer-quarter pairs that received food payments, travel payments, and consulting/compensation payments to date. Both the P_{idt} and $P_{Gi,d,t}$ variables are set to 0 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.

We continue to include differential time trends by (own or peer) payment type for doctors who receive payments in quarters 3 or 4 of 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 will allow for differential pre-trends for doctors paid during our sample.

Recall from the discussion in Section 2.2 that we also drop doctor-drug pairs from the sample when we do not have at least 2 pre-payment quarters and 2 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 data to contribute to pre/post comparison 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 on non-zero variables of the cumulative payment counts) were unpaid for at least four quarters prior to the first payment.

We estimate several variants of equation 2. First, we consider three outcome measures related to physician prescription volume for the targeted 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.

We then 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 shared patient ties and are in the same group practice. We use this model to explore how the impact of peer payment varies by the type of the tie.

Additional models test for whether there is a differential impact of the first payment of a given type relative to subsequent payments, and whether the impact of pharmaceutical payments varies with whether the drug prescription is guideline concordant.

3.2 Instrumental variable model of peer influence

As a supplement to the main specifications, we also estimate an instrumental variable (IV) model to explore the possible mechanisms of peer effects. There are two key channels for peer influence: indirect influence when a physician observes her peer's prescription choice by monitoring medications on a shared patient; and direct influence when a physician directly communicates about a new drug with a peer physician. Our instrumental variable strategy will attribute peer influence to the indirect mechanism, and allow us to estimate an upper bound on the possible magnitude of indirect influence.

As a doctor observes greater peer adoption of a new drug, she may become more likely to prescribe the drug herself. Our instrumental variable approach uses detailing payments to a physician's peers as an instrumental variable for peers' average prescription volume. The reduced form of this IV 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 for identifying variation. The key endogenous variable of interest is the doctor's peers' average prescription volume for the targeted drug in the previous quarter.[13] We use peer's lagged payments of each type at $t-1$ and $t-2$ as instrumental variables for average peer prescription volume at $t-1$. The first and second stage equations are as follows:

$$Y_{Gi,d,t-1} = \tilde{\eta}_1 P_{Gi,d,t-1} + \tilde{\eta}_2 P_{Gi,d,t-2} + \tilde{\delta}_0 P_{i,d,t-0} + \tilde{\delta}_1 P_{i,d,t-1} + X'_{idt}\tilde{\gamma} + \tilde{\alpha}_{id} + \tilde{\beta}_{dts} + u_{it} \quad (3a)$$

$$Y_{idt} = \theta \widehat{Y}_{Gi,d,t-1} + \delta_0 P_{i,d,t-0} + \delta_1 P_{i,d,t-1} + X'_{idt}\gamma + \alpha_{id} + \beta_{dts} v_{idt} \quad (3b)$$

Where $Y_{Gi,d,t}$ is the mean prescriptions of each drug d by i's peers at t, and $P_{Gi,d,t}$ is a vector

[13] We use this lag structure because learning about a peer's prescription choice is not likely to happen instantaneously, but will presumably require time for patients to seek care from a second doctor.

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 targeted 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 focal doctor's own prescriptions ($E[v_{idt}P_{Gi,d,t-2}] = 0$). This imposes the 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 targeted 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.

Because the IV exogeneity assumption could plausibly be violated, we consider this an upper bound estimate 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.

3.3 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, and therefore there is little variation in the reference groups of similar agents.[14] In contrast, physician shared-patient networks are intransitive (the global clustering coefficient is 0.37, meaning only a third of connected triples are fully connected), and so even similar physician often interact with different sets of peers.

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

[14]Unless groups partially overlap, see De Giorgi et al. (2010).

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 identification could arise with this approach if payments coincide with changes in prescription volume for the targeted 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.

4 Results

4.1 Event study graphs

We begin by estimating equation 1 to explore the relationship between peer payment and prescription volume. Figure 4 graphs explore the stability of pre-trends prior to first payment. These graphs plot the event-time coefficients from a regression where 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 4 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 pattern holds up 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 4 Panel (b) displays the same results in a more flexible specification that allows for differential pre-trends, as described in Section 3.1. The quarters prior to the doctor's first payment now show a flat pattern of prescription volume, implying that there is no *acceleration* in targeted 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 rising by approximately 0.4 following the doctor's first compensation payment. Prescriptions also rise after the first food payment, reaching roughly 0.03 additional prescribed patients per quarter in the first quarter following the food transfer. Finally, after a peer physician receives a compensation payment, the targeted doctor's peers increase their prescription of the new drug by 0.01 to 0.02 additional prescribed patients per quarter.

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 could represent either a gradual adjustment of prescriptions to the payment received in quarter 0, or it could simply reflect the accumulating impact of subsequent payments.

4.2 Baseline regression results

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 this regression 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. Smaller transfers have smaller estimated effects; each quarter with a compensation payment increases a doctor's own prescribing by 0.06 additional prescribed beneficiaries per quarter. Having a peer doctor receive a compensation payment associated with a modest increase in own prescription volume of 0.02 additional beneficiaries per month.

Recall that our baseline definition of peer affiliation is based on patient-sharing patterns. In the regression specification reported in column 2, we consider group practice peer relationships as well. 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 0.020 per quarter, 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.[15] 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 targeted 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 doctors who share a group practice.

Part of the peer effects we estimate may be driven by prescription refills, for example 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

[15] 0.014 is the sum of the "Shared patients" and the "Group practice and shared patient" coefficients reported in Table 3 column 2.

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 sample to patients who have no prior prescription for anticoagulants (by any physician) in the previous year (Table 3, column 3). Between 8–10% 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 targeted drug to new patients.

Next, we turn to a third outcome measure: the fraction of anticoagulant prescriptions that were written for the targeted 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 towards the targeted drug. This outcome is only defined for the 68% of doctor-drug-quarters from our full sample that have non-zero 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 targeted 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.

4.3 Instrumental variable estimation of peer effects

There are two mechanisms by which having a peer targeted with a pharmaceutical payment may raise a doctor's prescribing, holding constant any own payments received. First, the physician network we study is linked through shared patients. When a patient sees two different physicians within a short time window, each physician has an opportunity to learn about the other physician's practice patterns. 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.

The second mechanism by which a paid physician may influence his peers is through direct "proselytizing" about the new drug. Based on our conversations with physicians and consultants with expertise in drug detailing, we hypothesize that this mechanism is less important, 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, holding fixed the volume of shared patients between two doctors.

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. In this specification, the pharmaceutical detailing payment to a physician's peers is an instrumental variable for peer prescribing volume. As discussed in Section 3, we instrument for the average prescription volume across each physician's direct peers in period $t-1$, using as instruments average peer payments in periods $t-1$ and $t-2$. We then trace out the influence of peer prescriptions on own prescribing.

If we assume there is no proselytizing, then these instrumental variable estimates of peer effects may generalize to settings where peer prescription decisions are not driven by pharmaceutical payments. Since we cannot rule out the proselytizing channel, we will interpret our instrumental variable estimates as an upper bound on the magnitude of peer effects we would expect in settings where an increase in peer prescription volume for a new drug is not accompanied by proselytizing that may be specifically inspired or motivated by the pharmaceutical payment.

Using peer payments as an instrumental variable for peer prescription volume helps us isolate the impact of payment from correlations between each physician's prescriptions and his peers' prescriptions that may be driven by common shocks. The instrumental variable analysis continues to exploit the panel structure of our data to isolate deviations from a doctor's baseline use of a new drug that occur shortly after a new peer payment shock. As before, we control for differential trends in prescription volume for physicians that may differ depending on whether the physician had a paid peer, and whether the physician himself received a food, travel, or compensation payment. We also continue to control for physician-drug fixed effects, and quarter-drug-specialty fixed effects.

First-stage estimates suggest that an additional compensation payment to a doctor's peers two or more quarters ago raises the average quarterly peer prescription volume by 0.024 beneficiaries per quarter and an additional payment to a doctor's peers one quarter ago raises quarterly peer prescription volume by 0.04 beneficiaries per quarter (both statistically significant at the 1% level; Table 4). 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.

Our second-stage regression estimates show that if a doctor's peers' prescription volume for a new anticoagulant drug increases by 1 beneficiary per quarter on average, the doctor's own prescription volume will increase by 0.33 prescriptions per quarter. This result suggests

that physician peer effects driven by indirect observation of peer practice patterns may play an important role in the diffusion of new drugs. Should this finding be driven by indirect observation of peer prescription choice (rather than proselytizing), it suggests that the prescription increases may ripple out beyond first-degree peer connections.

4.4 Robustness and heterogeneity analysis

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 the period 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 targeted 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 (i.e. not the target or the match) 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 paid peers. These peers may themselves be recipients of compensation payments.

Descriptive statistics for the matched sample are shown in Table A6. Results from the matching estimation are reported in Table 5. Columns 1, 3, and 5 do not re-weight the matched sample in the case that a single paid physician matches to multiple unpaid physicians. Columns 2, 4, and 6 reweight the sample so that the group of all peers of a target physician and the group of all peers of its matches each have an equal weight. Reweighting increases the standard errors, but does not substantively change our estimated effect of peer compensation payments. As in our baseline results, we continue to find that the focal doctor increases his prescription volume of the targeted drug by 0.02 patients per quarter for each additional compensation payment targeted at the focal doctor's peers.

In Appendix Table A4, we test whether the first observed payment has a differential impact relative to subsequent payments. 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.

Point estimates suggest that a doctor's first compensation payment and first food payment have slightly smaller estimated impact 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 A7. Own and 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 so have more scope to increase their use of targeted drugs.

We also test the influence of payments on each drug separately. 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.

5 Welfare Implications

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

To address this question in our context, we analyzed how the increase in NOAC prescriptions following associated pharmaceutical payments varies by clinical appropriateness. Because guidelines are not available to cover all patient indications for anticoagulation, we narrow our focus to patients with atrial fibrillation, which is a common reason for anticoagulation. There are two popular risk scores to assess the risks and benefits of anticoagulation for patients with atrial fibrillation: the HAS-BLED and CHADS scores.[16] Note that current

[16]For 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 July, 2019.

guidelines provide little guidance on selecting among the various anticoagulant drugs; rather, they focus on determining whether the patient is appropriate for anticoagulation at all.[17]

Studying these clinical risk scores for atrial fibrillation introduces two further challenges. First, insurance claims data do not cover all of the clinical information required to reconstruct the guideline precisely, such as lab measurements (e.g. INR). Second, the guidelines themselves do not provide sharp recommendations on whether or not to prescribe anticoagulation.[18] Given these hurdles, our analysis of clinical appropriateness should be interpreted as suggestive.

The HAS-BLED score (Pisters et al., 2010; Lip et al., 2011) estimates risk of bleeding for patients on anticoagulation, the major safety concern that should be weighed against the stroke reduction benefits of the drug. While this score does not fully determine prescription value for each individual case, it does contain validated information about risk, and we use it to assess the prescription decisions in the aggregate.

For this analysis, we use the CMS Chronic Condition Warehouse data file to identify patients with diagnosed atrial fibrillation. As before, we count up the number of unique beneficiaries prescribed anticoagulation 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 for each prescribed patient, so that we can designate the patient as being at low or high risk of bleeding. We can 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.[19] The guideline is scored simply: one point per risk factor. Patients scoring 0 to 1 are considered low risk; 2 points corresponds to moderate risk; 3 or more points corresponds to high risk.

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. We call the rest of our sample "low risk"; it is important to note that our "low risk" sample will

[17]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 July, 2019.

[18]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].

[19]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: liver disease, prior major bleeding or predisposition to bleeding, labile INR, medication use predisposing to bleeding (including aspirin and NSAIDS which are not prescription drugs), and alcohol use (at least 8 drinks per week).

include some high risk patients for whom we do not observe their risk factors. 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 guideline, we would expect fewer prescriptions written to patients at high risk of bleeding.

Results are reported in Table A5. In panel A, we pool patients together regardless of which anticoagulant they receive (Xarelto, Pradaxa, Eliquis, Savaysa, 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 by quarter fixed effects to accommodate the new sample structure (which is no longer drug-specific).

Point estimates suggest that own food, own compensation, and peer compensation payments are all estimated to increase prescription volume for both high and low risk patients, although the estimates are generally noisy. The only category of payment that is 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% increase from the mean prescription volume.

In Table A5 panel B, we disaggregate the data by drug to test whether drug detailing efforts increase guideline-concordant prescribing for the targeted 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 A5, we perform another analysis of guideline concordance that incorporates compliance with the CHADS2 guideline (Gage et al., 2001, 2004). Unlike the HAS-BLED score that assesses patient risk for serious bleeding side effects, the CHADS2 score assesses the patient's potential benefits from anticoagulation due to reduced stroke risk. In this case, we can approximate each of the five factors of the guideline in claims records: congestive heart failure, hypertension history, age, diabetes mellitus history, and stroke or transient ischemic attack symptoms.[20] We dichotomize the CHADS2 score, following a threshold used in the clinical guideline. 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 not as strong.

We use the CHADS2 score in combination with our approximated HAS BLED score to divide patients into three categories: low value (low CHADS2 benefit and high HAS BLED

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

risk), medium value (low CHADS2 benefit and low HAS-BLED risk, or high CHADS2 benefit and high HAS-BLED risk), or high value (high CHADS2 benefit and low HAS-BLED 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.

We acknowledge that the scores we use do not determine the optimal treatment choice for each case, because they miss potentially relevant clinical information. But 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.

6 The Overall Impact of Payments on Prescription Volume and Spatial Distribution

To evaluate the impact of pharmaceutical payments on prescription volumes, we use the estimated model as a quantification framework to perform several counterfactual analyses. We consider two questions. First, what is overall contribution of payments to prescription volumes? Second, what part of this impact occurs directly, through payment effects on recipient, versus indirectly, through payment effects on peers? To address these questions, we combine the estimated unit-effects of payments of different types with information on the number of payments, their timing, and the network position of recipients. Considering all these factors is important: for example we estimate that on average, each compensation payment results not only in 0.37 additional prescriptions by the direct recipient, but also in 0.02 additional prescriptions by each of the dozens of peers recipients of such payments have. Therefore, summing these indirect effects of payments leads to substantially higher estimates of the overall effects of compensation payments on prescription volumes.

For this analysis we use estimates from equation (2). 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) the actual payments, (2) only direct payment effect (zeroing out any peer-payment effects) and (3) no payments. In all cases, we keep 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.

Figures 5–7 show the result of this analysis. The contribution of payments accumulates over time (Figure 5). We estimate that by the end of our sample period, payments increased average prescription volume by 0.11 beneficiaries over a baseline of 0.70, a 16 percent increase. The effect is slightly greater for more recently patented drugs, which have more payments associated with them. About a quarter of the total effect of payments is due to their indirect effect, through recipient peers (Figure 6).

Further decomposing this effect by payment types (Table 7) reveals that food payments, by far the most common (see Table 1), have the greatest overall effect on prescribing levels. Among the three types of peer effects studied (from compensation, food, and travel payments), spillovers from compensation payments have the largest effect on aggregate prescribing, despite the fact that they are relatively infrequent.

The second question we consider is whether changes in prescription behavior induced by pharmaceutical payments contribute to geographic variation in the adoption of NOACs. To the extent that payments are autocorrelated and focus on already high adoption areas, payments may augment geographic disparity in technology adoption. On the other hand, payments may reduce variation if they raise adoption in lower-adoption areas.

Figure 8 shows that payments are in fact higher in areas with higher initial adoption, as documented at the beginning of our sample. 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: Figure 9, which is based on our model estimates, shows that HRR-level estimated increase in prescription during 2014–2016 is positively associated with baseline prescription levels. Appendix figure A2 shows that for each of the studied drugs, payment effect 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.

7 Conclusion

This study estimated the spillover effects of pharmaceutical payments on prescriptions of new anticoagulant drugs. We used rich administrative data on physician prescriptions, the universe of payments to physicians from pharmaceutical companies, and networks of patient sharing. The research design exploits variation in both the timing of payments and differences between physician in the reference group of peers. We use difference in differences to evaluate

the response of prescription behavior to both own and peer payments.

Event study results show a significant and persistent increase in prescription of new drugs following the receipt of payments associated with these drugs, with larger payments for consulting and compensation for services having a greater effect on prescriptions than small payments for food and beverages. Payments not only affect prescriptions made by their direct recipients, but also have spillover effects—they lead to increased prescriptions by recipients' peers. Such effects reflect not only renewing prescriptions of patients with previous anticoagulant prescriptions, but also new prescriptions to patients with no prior anticoagulant prescriptions in the previous year.

This work leaves several open questions. We do not test whether these peer effects arise when prescription patterns change for reasons other than pharmaceutical payments. We also do not explore how peer effects vary depending on which physician is initially targeted. Finally, we also provided only preliminary evidence regarding the nature of competition among pharmaceutical companies, and the potential interactions between multiple different payments. These remain important avenues for future research.

Summed over all peers, spillover effects on the peers of directly targeted doctors account for about a quarter of the overall estimated impact of payments on prescription volumes. Our results suggest that learning from peers is an important channel through which pharmaceutical payments impact clinical practice, and perhaps also an important channel for adoption of new technologies in medicine more generally.

References

Agha, Leila, Keith M. Ericson, Kimberley H. Geissler, and James B. Rebitzer (2018), "Team formation and performance: Evidence from healthcare referral networks." *NBER Working Paper No. 24338*.

Agha, Leila and David Molitor (2018), "The local influence of pioneer investigators on technology adoption: Evidence from new cancer drugs." *The Review of Economics and Statistics*, 100, 29–44, URL `https://doi.org/10.1162/REST_a_00670`.

Bandiera, Oriana and Imran Rasul (2006), "Social networks and technology adoption in northern mozambique." *The Economic Journal*, 116, 869–902.

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

Barnett, Michael L, Nicholas A Christakis, A James OMalley, Jukka-Pekka Onnela, Nancy L Keating, and Bruce E Landon (2012), "Physician patient-sharing networks and the cost and intensity of care in us hospitals." *Medical care*, 50, 152.

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

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

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

Chan, David C. (2018), "Influence and information in team decisions: Evidence from medical residency." *Working Paper*.

CMS (2013), "Physician shared patient patterns." Data retrieved from `http://downloads.cms.gov/foia/physician-shared-patient-patterns-2013-days30.zip`.

CMS (2013–2015), "40% Research Identifiable Medicare Part D Database." Data dictionaries are available at `https://www.resdac.org/cms-data/files/pde`.

CMS (2014–2015), "Open Payments Databases." `https://openpaymentsdata.cms.gov/`.

Conley, Timothy G. and Christopher R. Udry (2010), "Learning about a new technology: Pineapple in ghana." *American Economic Review*, 100, 35–69.

Cutler, David, Jonathan Skinner, Ariel Dora Stern, and David Wennberg (2013), "Physician beliefs and patient preferences: A new look at regional variation in health care spending." *NBER Working Paper*.

Cutler, David, Jonathan S. Skinner, Ariel D. Stern, and David Wennberg (2019), "Physician beliefs and patient preferences: A new look at regional variation in health care spending." *American Economic Journal: Economic Policy*, 11, 192–221.

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

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

DeJong, Colette, Thomas Aguilar, Chien-Wen Tseng, Grace A Lin, W John Boscardin, and R Adams Dudley (2016), "Pharmaceutical industry–sponsored meals and physician prescribing patterns for medicare beneficiaries." *JAMA internal medicine*, 176, 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 (2018), "Influence of peer networks on physician adoption of new drugs." *PloS one*, 13, e0204826.

Duflo, Esther, Michael Kremer, and Jonathan Robinson (2008), "How high are rates of return to fertilizer? evidence from field experiments in kenya." *American Economic Review*, 98, 482–88.

Gage, Brian F, Carl van Walraven, Lesly Pearce, Robert G Hart, Peter J Koudstaal, BSP Boode, and Palle Petersen (2004), "Selecting patients with atrial fibrillation for anticoagulation: stroke risk stratification in patients taking aspirin." *Circulation*, 110, 2287–2292.

Gage, Brian F, Amy D Waterman, William Shannon, Michael Boechler, Michael W Rich, and Martha J Radford (2001), "Validation of clinical classification schemes for predicting stroke: results from the national registry of atrial fibrillation." *Jama*, 285, 2864–2870.

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

Golub, Benjamin and Evan Sadler (2017), "Learning in social networks." *Working Paper*.

Grennan, Matthew, Kyle Myers, Ashley Swanson, and Aaron Chatterji (2018), "Physician-industry interactions: Persuasion and welfare." *NBER Working Paper No. 24864*.

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

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

Lip, Gregory YH, Lars Frison, Jonathan L Halperin, and Deirdre A Lane (2011), "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*, 57, 173–180.

MacLeod, Bentley W and Janet Currie (2018), "Small area variations and physician decision making: The case of depression." *Working Paper*.

Manski, Charles F (1993), "Identification of endogenous social effects: The reflection problem." *The review of economic studies*, 60, 531–542.

Mekaj, Ymer H, Agon Y Mekaj, Shkelzen B Duci, and Ermira I Miftari (2015), "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*, 11, 967.

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

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

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

Pisters, Ron, Deirdre A Lane, Robby Nieuwlaat, Cees B De Vos, Harry JGM Crijns, and Gregory YH Lip (2010), "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*, 138, 1093–1100.

Sacarny, Adam, Andrew R Olenski, and Michael L Barnett (2019), "Association of quetiapine overuse letters with prescribing by physician peers of targeted recipients: A secondary analysis of a randomized clinical trial." *JAMA Psychiatry*.

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

Sinkinson, Michael and Amanda Starc (2015), "Ask your doctor? direct-to-consumer advertising of pharmaceuticals." *NBER Working Paper*.

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

Skinner, Jonathan (2011), "Causes and consequences of regional variations in health care." In *Handbook of health economics*, volume 2, 45–93, Elsevier.

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

Tucker, Catherine (2008), "Identifying formal and informal influence in technology adoption with network externalities." *Management Science*, 54, 2024–2038.

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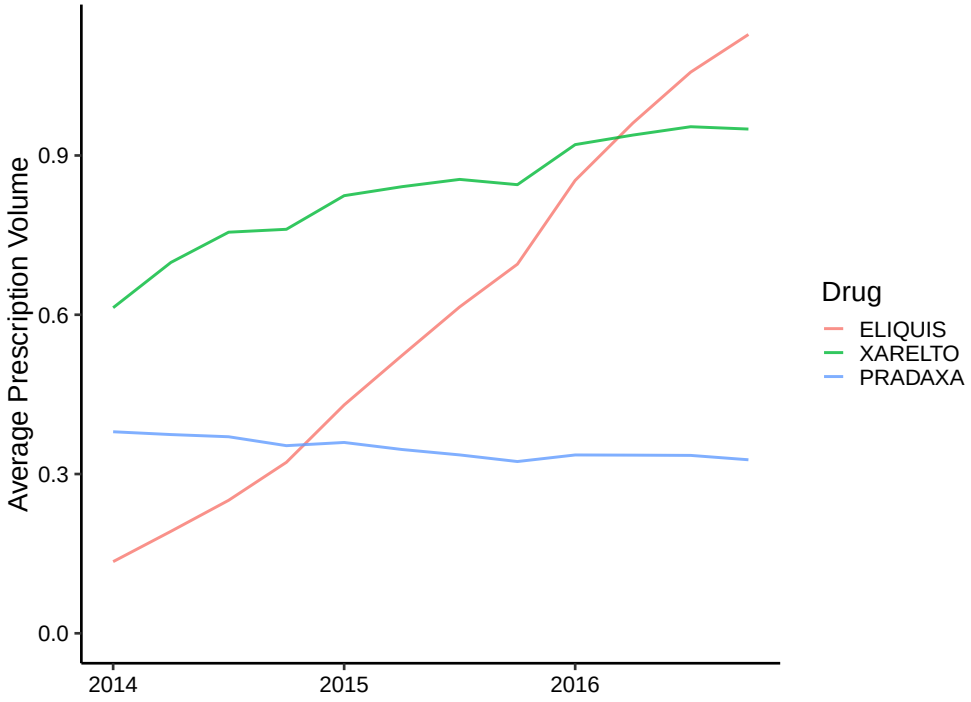
Figure 1: NOAC Prescription Volume over Time



Notes: For the three NOACs we study, the figure shows the prescribed beneficiaries per quarter in our sample. The FDA first approved Pradaxa in 2010; Xarelto in 2011; Eliquis in 2012.

Source: authors' calculations based on 2014–2016 Medicare Part D data

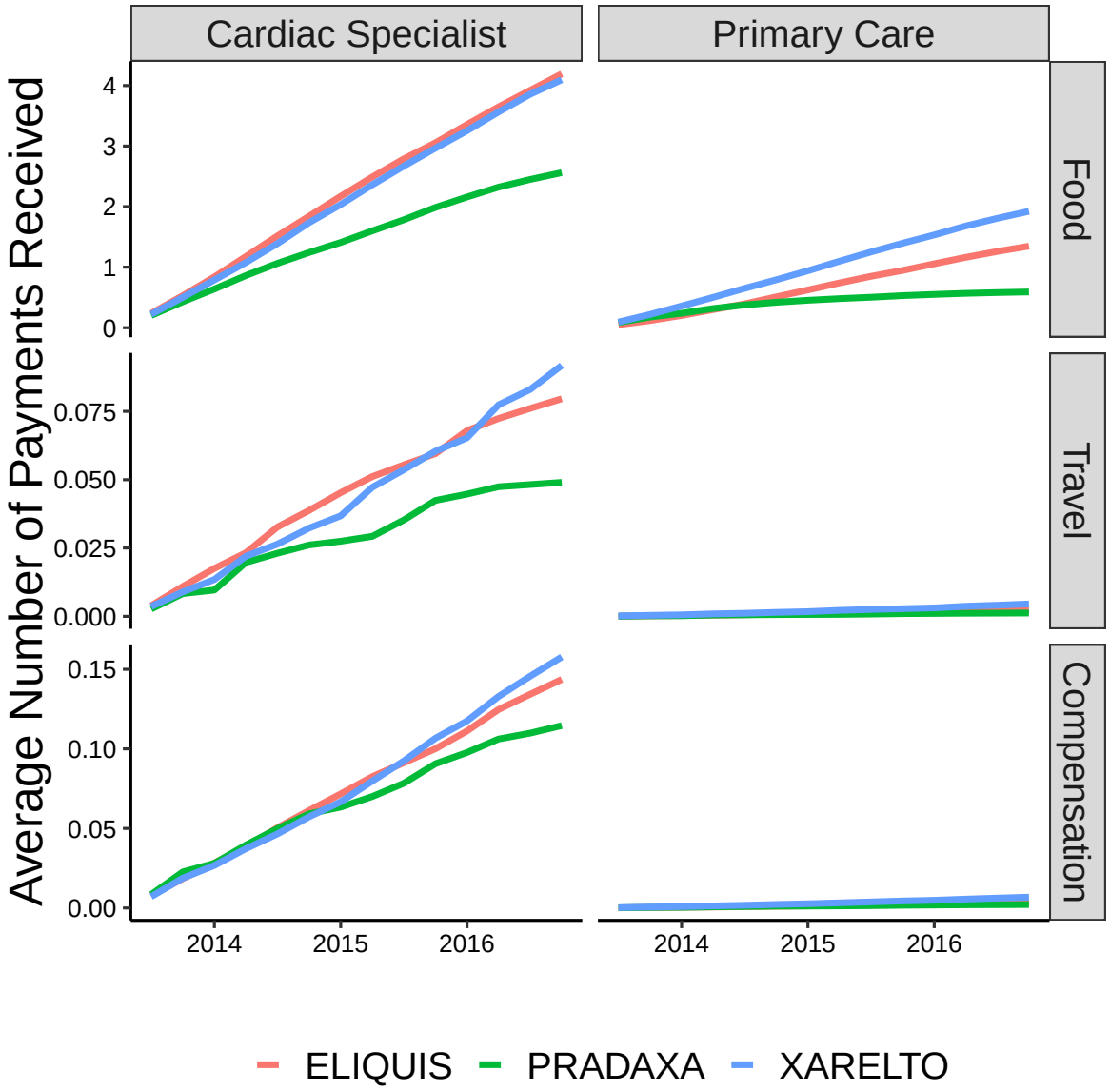
Table 1: Summary Statistics for Different Types of Pharmaceutical Payment

Payment Type	Assigned Category	Total Number of Payments	Mean Payment Size	Median Payment Size	Payment Total Amount (USD)
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: NOAC-Related Payments to sampled physicians, 2014–2016. Rows are shown in descending order of mean payment size, which guided the grouping into the three categories, which are labeled in short: Compensation, Travel, and Food.

Source: authors' calculations based on 2014–2016 Open Payments data

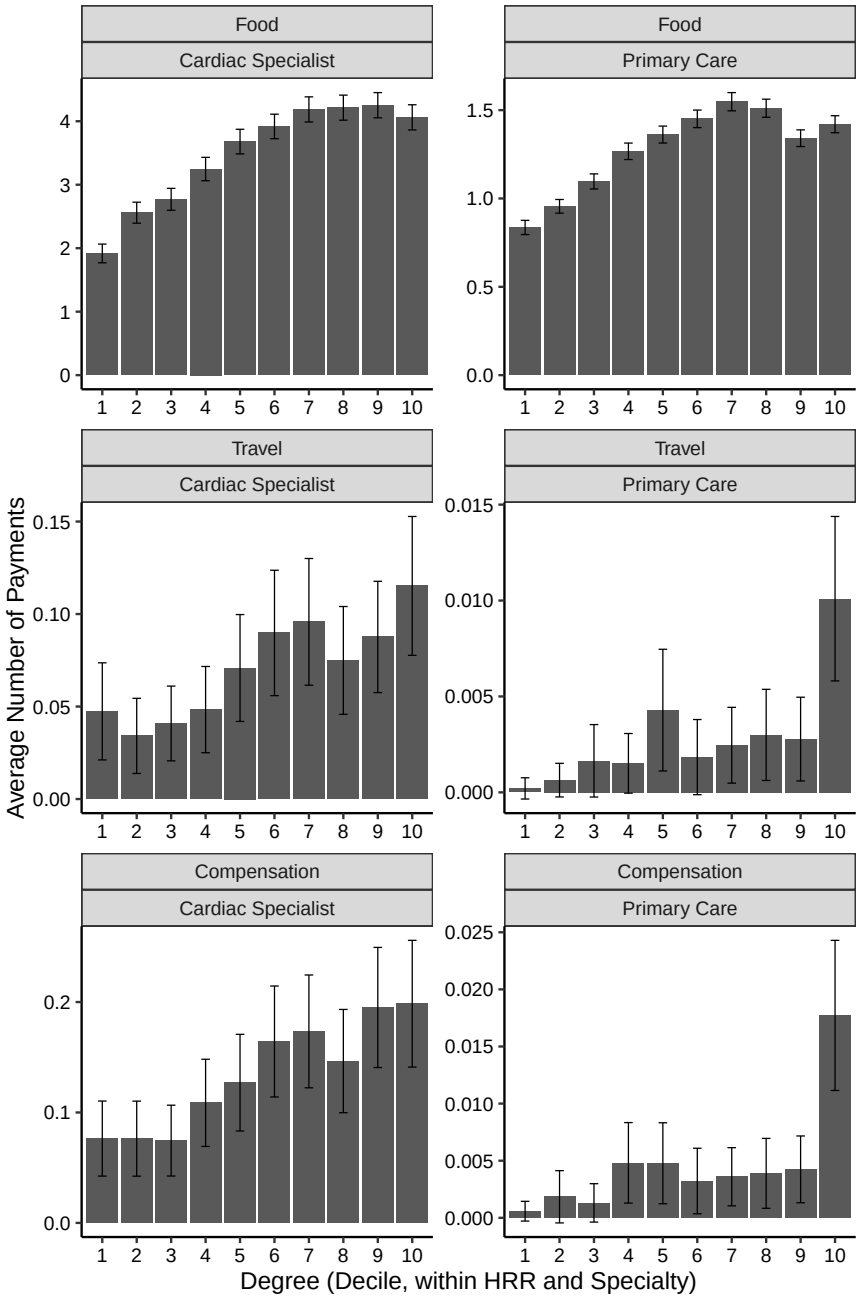
Figure 2: Average Number of Payments per Physician, by Type of Payment and Medical Specialty



Notes: Average cumulative number of payments associated with each drug that were made to sampled primary care physicians and cardiac specialists.

Source: authors' calculations based on Open Payments and Physician Compare data.

Figure 3: Average Number of Payments by Recipient Degree



Notes: For each specialty and type of payment, the figure shows the average number of payments by deciles of the recipient's number of peers. Deciles are calculated separately for each HRR and specialty. Vertical axes scales vary across plots.

Source: author's calculations based on Open Payments Physician Compare and Referral Patterns data

Table 2: Summary Statistics by Payment Status

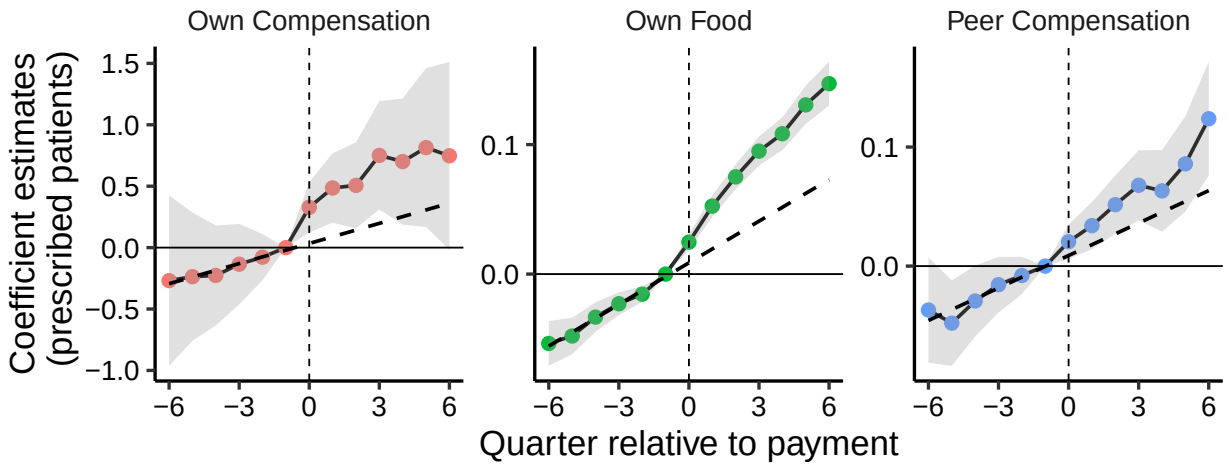
	Own Payments			Peer Payments		
	None	Food or Travel	Compensation	None, Food, or Travel	Compensation	All Physicians
Prescribed patients (per qtr)	.320	1.117	5.945	0.452	1.124	0.548
Newly prescribed patients (per qtr)	0.024	0.081	0.388	0.033	0.085	0.040
Target NOAC/all AC (%)	13.7	20.2	35.6	15.2	19.7	15.8
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: Summary statistics are based on our sample of 5,467,536 physician-drug-quarter observations, 166,422 physicians, 12% are cardiologists. A subset of 3,725,260 observations with anticoagulant prescriptions is used for calculating the Target drug/all Anticuagulant volume measure.

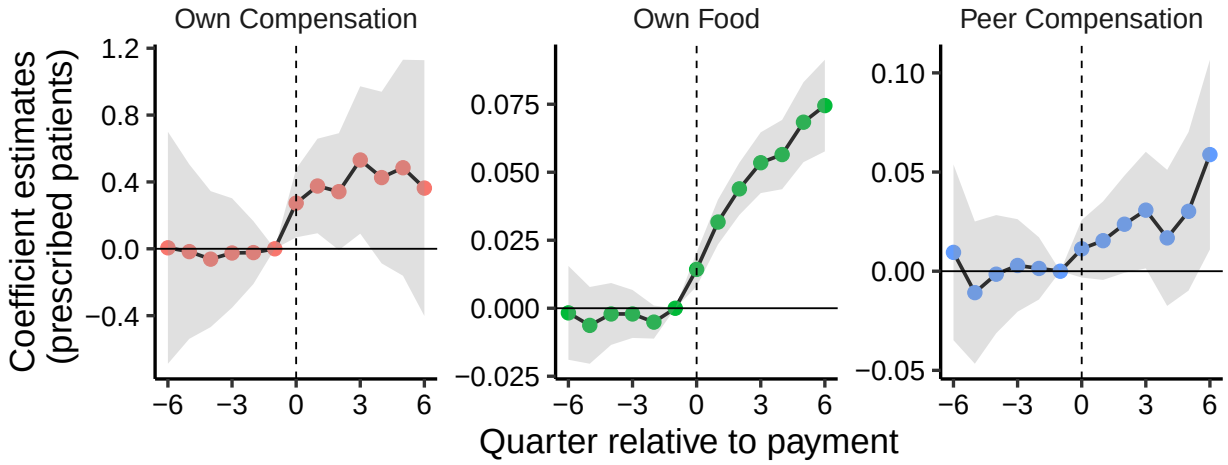
Source: authors' calculations based on Medicare Part D, Open Payments, Physician Compare, and Referral Patterns data.

Figure 4: Event Study: The Impact of Payments on Prescription Volume

(a) Before Detrending



(b) After Detrending



Notes: 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) shows estimates without detrending, with a dashed line fitted to the pretrend. Panel (b) shows estimates after detrending. Quarter 0 indicates the quarter of the first payment of each type. Shaded areas show 95 percent confidence intervals. Note that facets vertical axes have different scales.
Source: authors' calculations

Table 3: The Influence of Own and Peer Payments on Prescription Volumes

	Dependent Variable:					
	Number of Prescribed Patients		Newly Prescribed Patients		Fraction of Anticoagulant Prescriptions	
	(1)	(2)	(3)	(4)	(5)	(6)
Own Compensation Payment	0.3704	0.3701	0.0283	0.0283	0.0095	0.0094
	(0.1158)	(0.1159)	(0.0160)	(0.0160)	(0.0058)	(0.0058)
Own Food Payment	0.0589	0.0587	0.0049	0.0048	0.004	0.0038
	(0.0037)	(0.0038)	(0.0006)	(0.0006)	(0.0007)	(0.0007)
Peer Compensation, by Type of Affiliation:						
Shared Patients	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 Patients		-0.0057		0.0003		-0.0011
		(0.0145)		(0.0020)		(0.0017)
Group Practice without Shared Patients		0.0137		0.0022		0.0001
		(0.0045)		(0.0006)		(0.0012)
Mean dep. var.	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 (1) for all drugs combined. Physician-drug and specialty-drug-quarter fixed-effects, controls for all other types of payments, and payment-type-specific linear time trends were included in all specifications. The dependent variables capture different (own) prescription volume measures: Number of Prescribed Patients is the number of unique Medicare beneficiaries the physicians prescribed the drug to in each quarter. Newly Prescribed Patients restricts to patient with no anticoagulant prescriptions (in Part D, by any physician) in the previous year. Fraction of anticoagulant prescription is the fraction of the count of the drug prescriptions out of the count of all anticoagulant prescriptions by the physician, in quarters with any such prescriptions (thus the smaller sample size). Food and Compensation payments are the cumulative number of payments for food and beverages and for speaking and consulting. Own denotes payments to the prescribing physician. Shared Patients denotes payments made to physicians who share patients with the prescribing physician. Group Practice denotes payments made to physicians who are affiliated with the same group practice as the prescribing physician. See Section 2 for exact definitions and data sources.

Source: authors' calculations

Table 4: Peer Effects in Prescription Behavior: Fixed-Effects IV Estimates

A. 1st Stage:

	Dependent Variable:	
	Peer Prescription [t-1]	
	(1)	(2)
Peer Compensation Payment [t-1]	0.0427	0.0405
	(0.0032)	(0.0037)
Peer Food Payment [t-1]	-0.0025	-0.0016
	(0.0015)	(0.0019)
Peer Compensation Payment [t-2]	-0.0185	-0.0164
	(0.0033)	(0.0039)
Peer Food Payment [t-2]	0.0188	0.0161
	(0.0016)	(0.0020)
N (Doctor×Drug×Quarter)	4,556,280	3,102,501

B. 2nd Stage:

	Dependent Variable:		
	Number of Prescribed Patients [t]	Newly Prescribed Patients [t]	Fraction of Anticoagulant Prescriptions [t]
	(3)	(4)	(5)
Peer Prescription [t-1]	0.3260	0.0068	0.0429
	(0.0345)	(0.0106)	(0.0114)
Own Compensation Payment	0.6777	0.1043	0.0227
	(0.0303)	(0.0093)	(0.0086)
Own Food Payment	0.0494	0.0076	0.0036
	(0.0026)	(0.0008)	(0.0008)
Own Compensation Payment [t-1]	-0.3734	-0.0886	-0.0175
	(0.0317)	(0.0098)	(0.0089)
Own Food Payment [t-1]	0.0051	-0.0031	-0.0003
	(0.0027)	(0.0008)	(0.0008)
N (Doctor×Drug×Quarter)	4,556,280	4,556,280	3,102,501

Notes: Generalized method of moments estimates of the instrumental variable model in equations 3a and 3b. Column (1) shows the first stage results of the second stage results in Columns (3) and (4). Column (2) shows the first stage results of the second stage results in Column (5). The panel data used for the IV regressions is slightly shorter due to the inclusion of lagged variables.

Source: authors' calculations

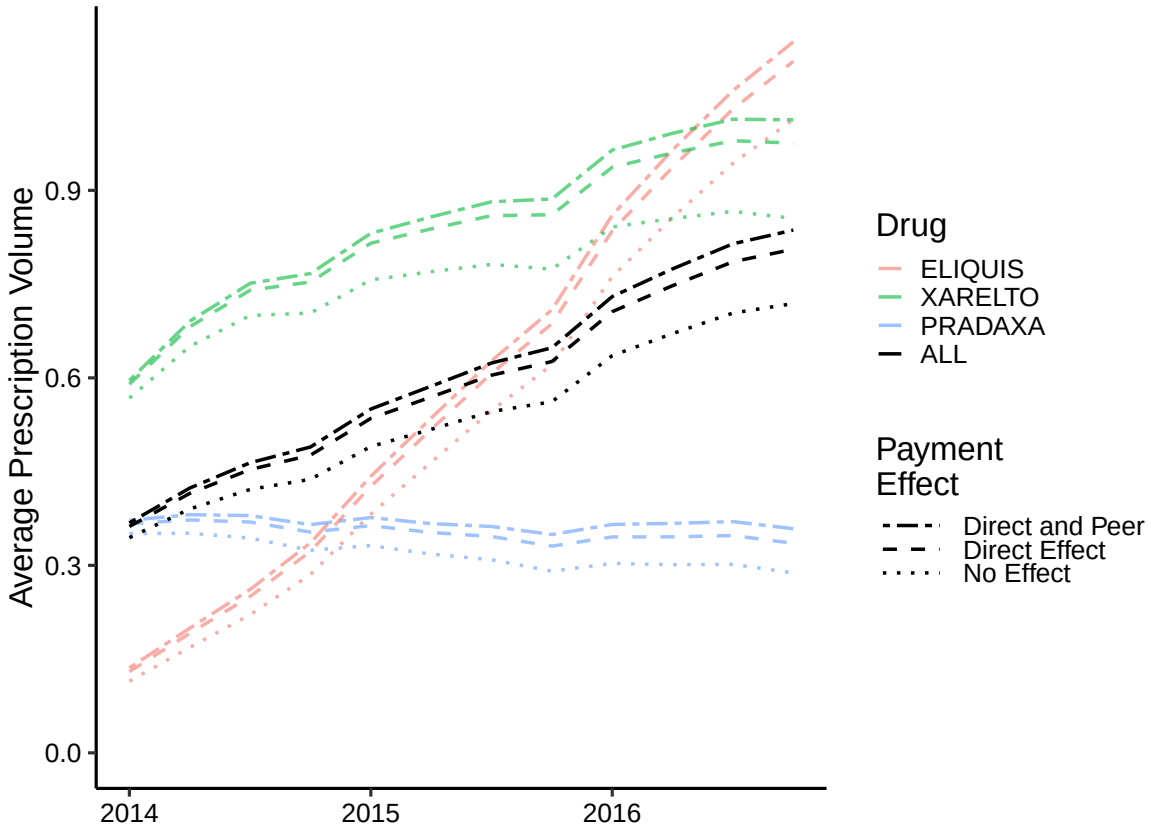
Table 5: Matching Estimates of the Impact of Payments on Prescriptions

	Dependent Variable:					
	Number of Prescribed Patients		Newly Prescribed Patients		Fraction of Anticoagulant Prescriptions	
	(1)	(2)	(3)	(4)	(5)	(6)
Own Compensation	0.3782	0.7201	0.0195	0.0226	0.0035	0.0311
	(0.1337)	(0.2552)	(0.0179)	(0.0244)	(0.0059)	(0.0143)
Own Food	0.0711	0.0709	0.0053	0.0023	0.0040	0.0011
	(0.0062)	(0.0152)	(0.0009)	(0.0023)	(0.0009)	(0.0028)
Peer Compensation	0.0241	0.0223	0.0024	0.0038	0.0019	0.0024
	(0.0068)	(0.0121)	(0.0010)	(0.0017)	(0.0009)	(0.0019)
Weighted	N	Y	N	Y	N	Y
N (Doctor×Drug×Quarter)	2,164,884	2,164,884	2,164,884	2,164,884	1,592,856	1,592,856

Notes: Estimation results using a sample of peers of recipients of compensation payments and matched non-recipients of such payments. Matching was performed exactly on specialty and drug and coarsely on group practice network degree, shared-patient network degree, and years of experience. See text for details and Table A6 for descriptive statistics of the sample. Weighted regressions use probability weights assigning equal weight to peers of recipients and non-recipients. Physician-drug and specialty-drug-quarter fixed-effects, controls for all other types of payments, and payment-type-specific linear time trends were included in all specifications.

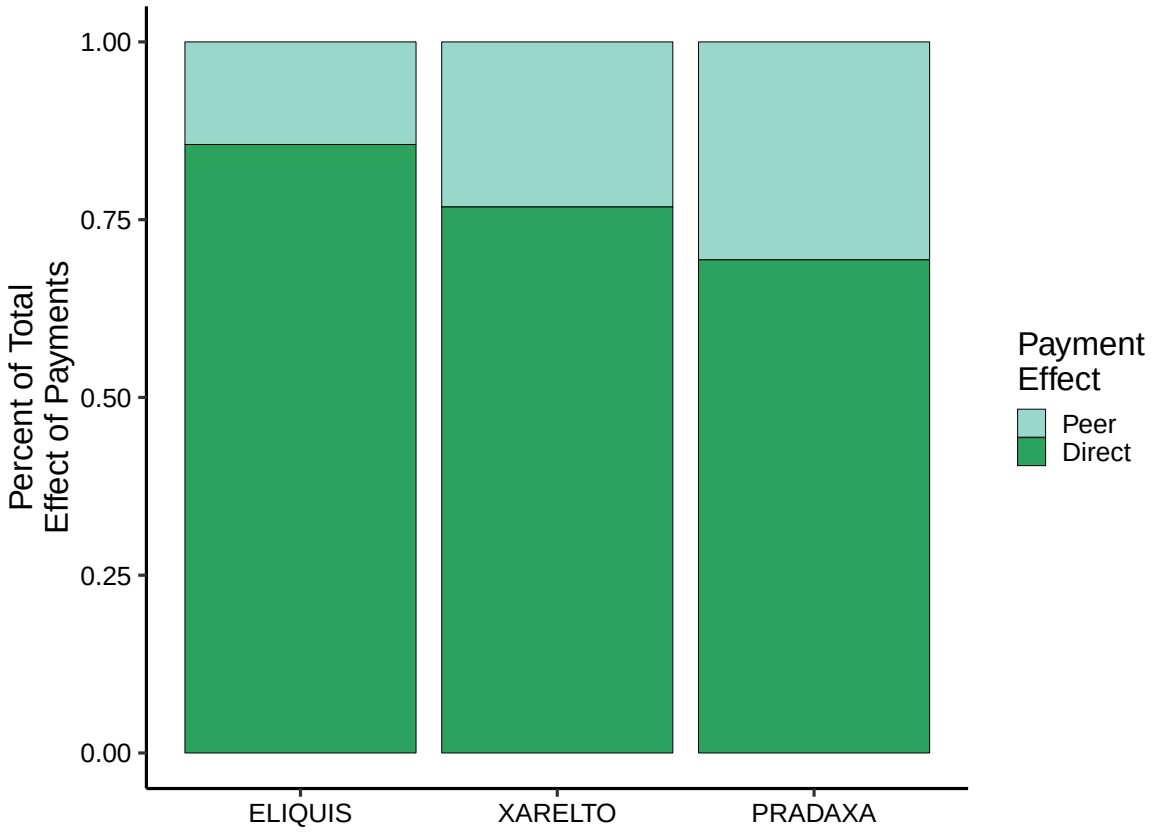
Source: authors' calculations

Figure 5: Counterfactual Prescription Volumes with Different Payment Effects



Source: authors' calculations using Open Payments data and model estimates

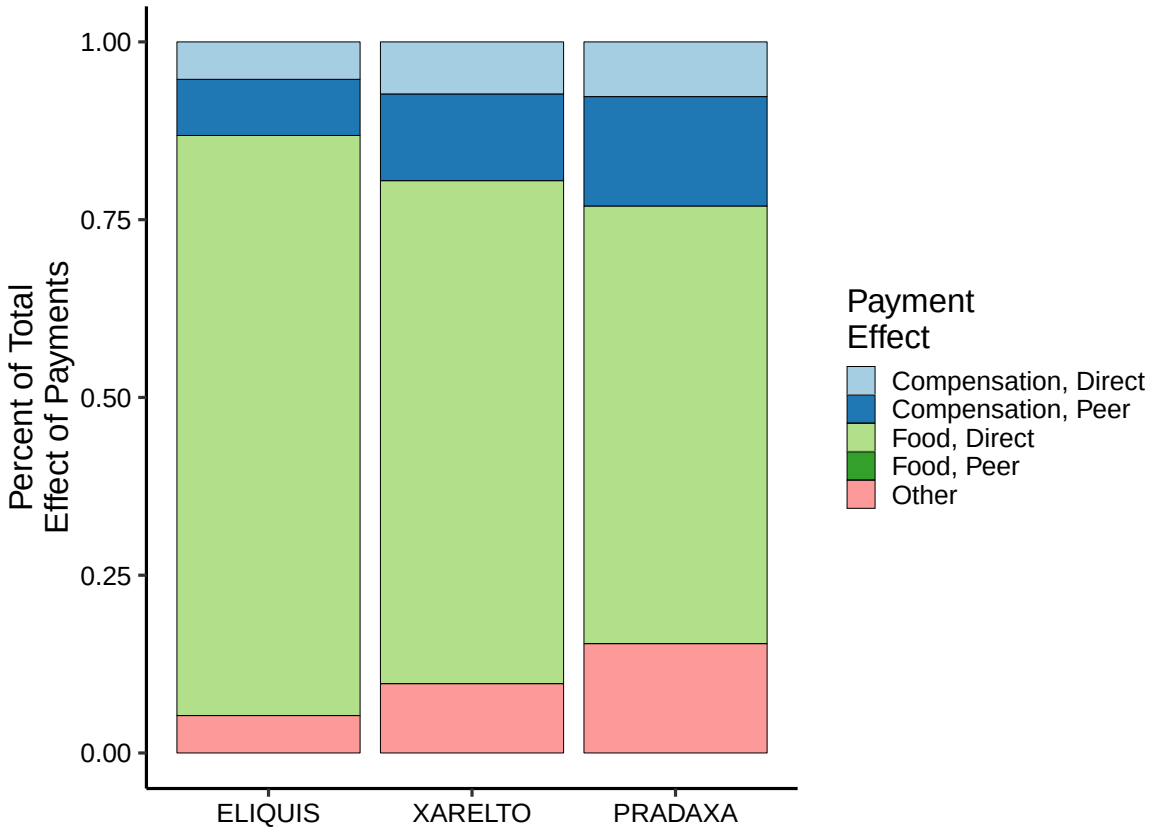
Figure 6: Payment Contribution to Overall Adoption, Direct versus Indirect Effects



Notes: For each drug, the bar shows the break-down of the estimated contribution of direct and indirect effects of payments on total prescription volume in 2014–2016.

Source: authors' calculations using Open Payments data and model estimates

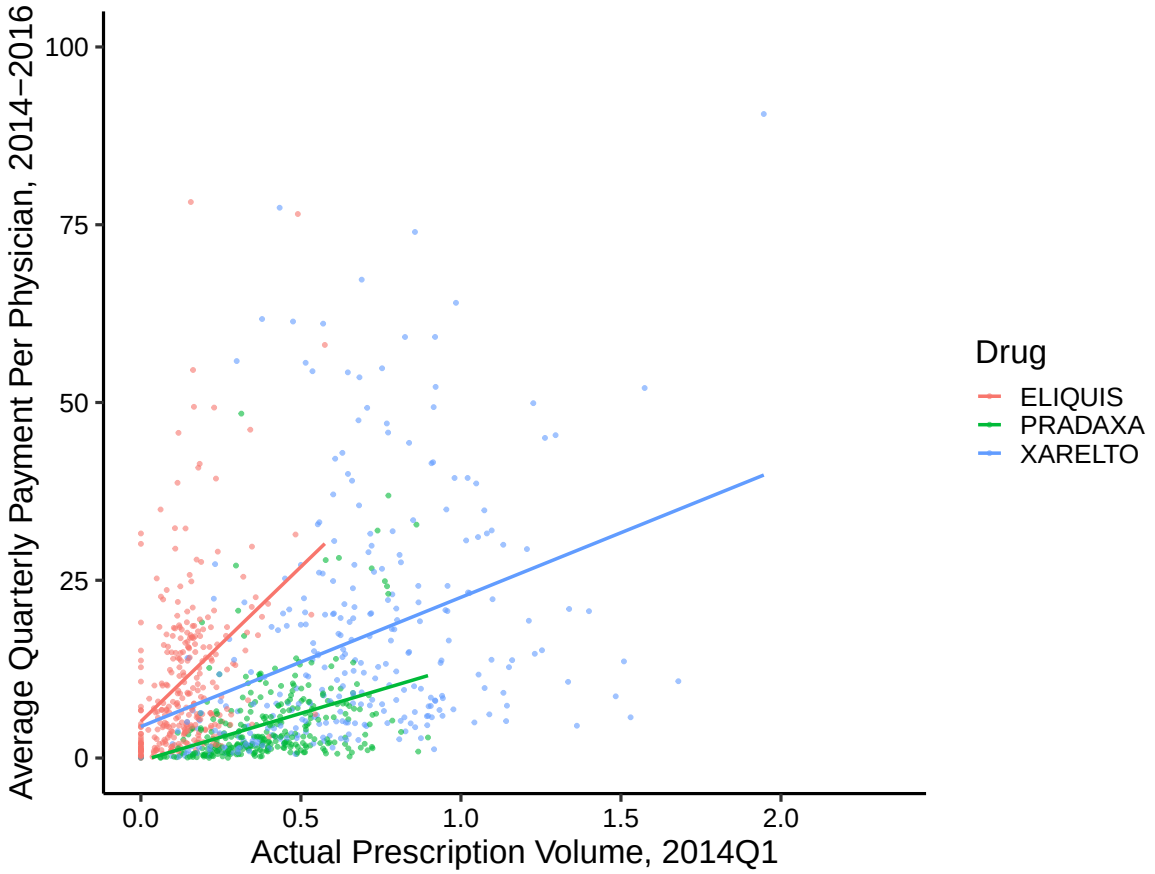
Figure 7: Payment Contribution to Overall Adoption, by Type and Recipient of Payment



Notes: For each drug, the bar shows the break-down of the estimated contribution of direct and indirect effects of payments of different types on total prescription volume in 2014–2016.

Source: authors' calculations using Open Payments data and model estimates

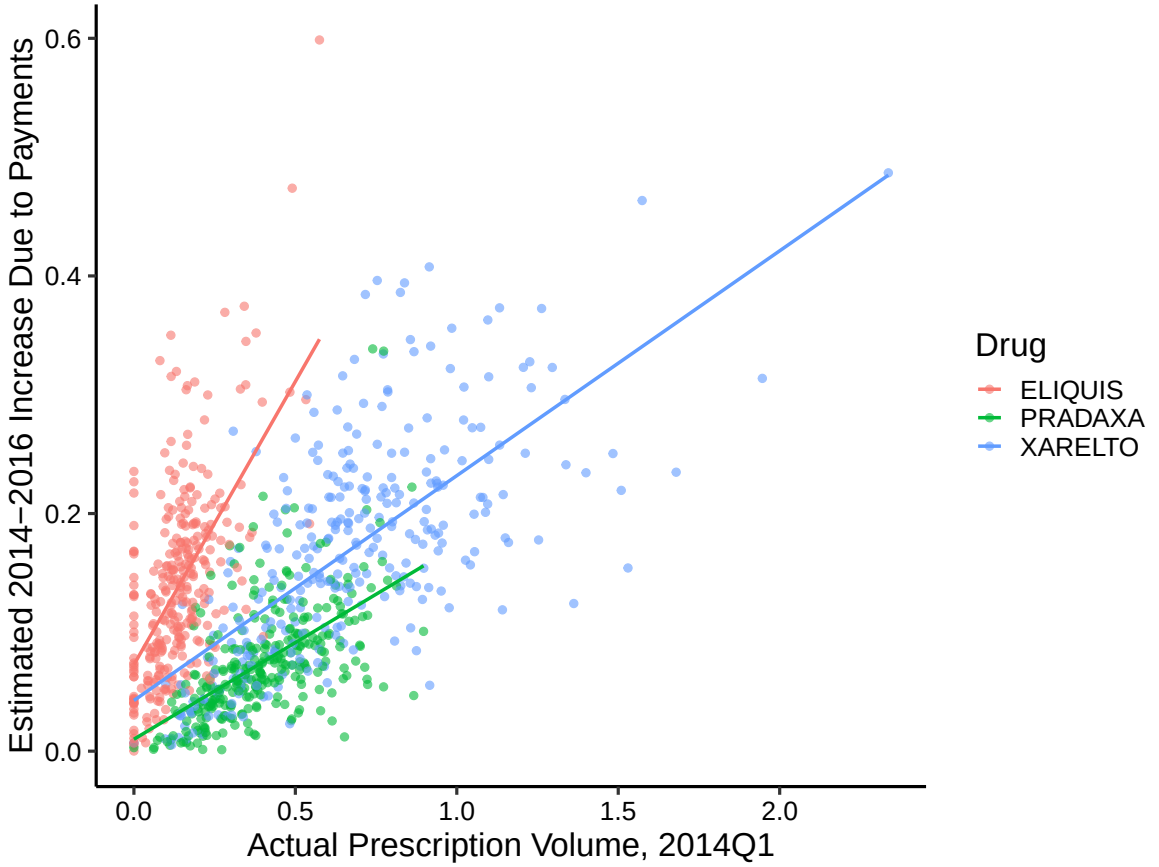
Figure 8: HRR-Level Average Payment over Baseline Prescription Volume



Notes: Each point represents one HRR-drug cell. The scatter plot shows the average payment size over the actual prescription volume in the first quarter of the sample. The lines are linear regression fit, separately for each drug.

Source: authors' calculations using Open Payments data and model estimates

Figure 9: HRR-Level Estimated Payment Impact over Baseline Prescription Volume

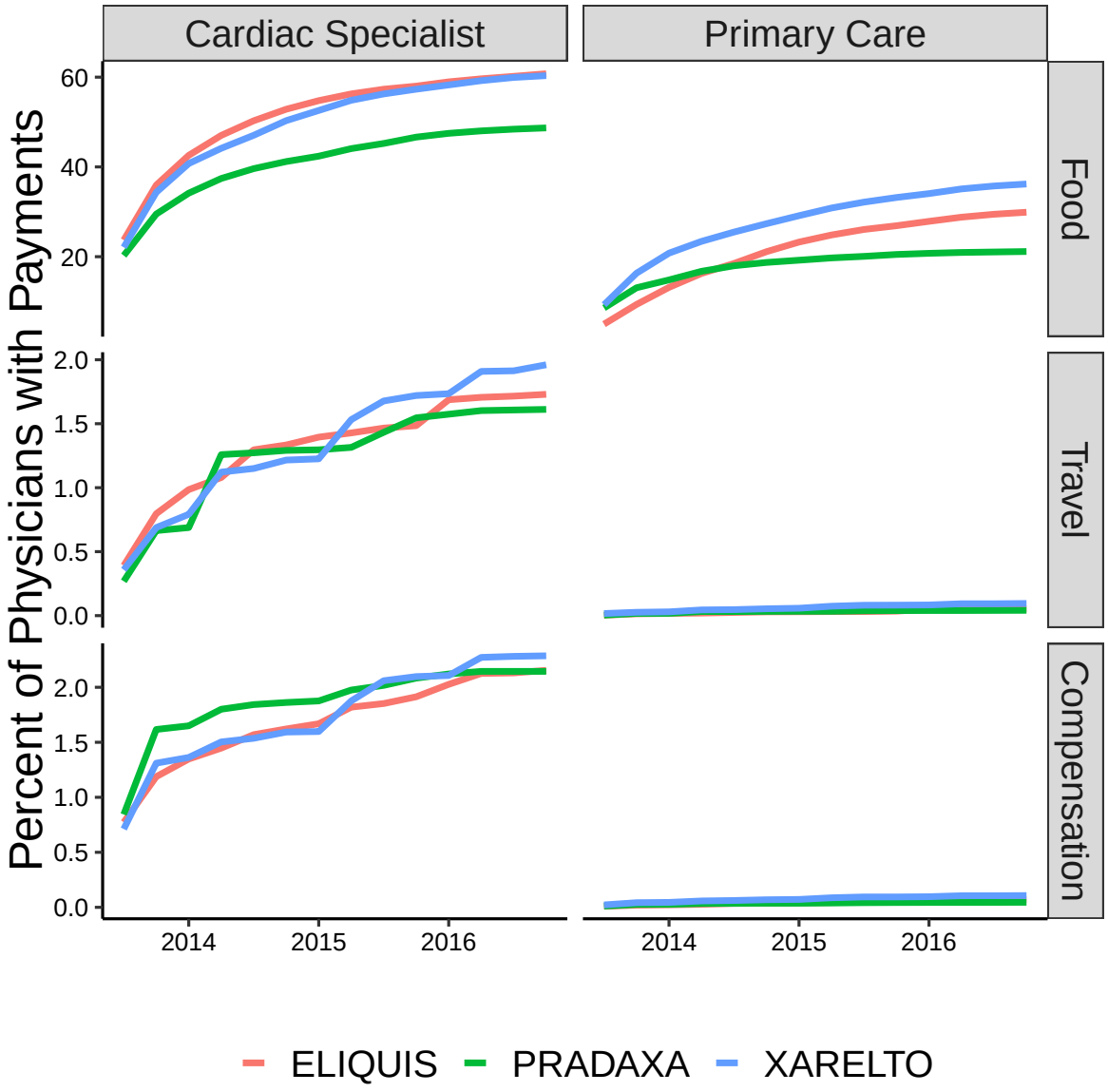


Notes: Each point represents one HRR-drug. The scatter plot shows the estimated overall increase in prescription volumes over the actual prescription volume in the first quarter of the sample. The lines are linear regression fit, separately for each drug.

Source: authors' calculations using Open Payments data and model estimates

A Online Appendix

Figure A1: Cumulative Fraction of Paid Physicians, by Type of Payment and Medical Specialty



Notes: The average cumulative number of payments associated with each drug that were made to primary care physicians and cardiac specialists during the study sample period.

Source: authors' calculations based on Open Payments and Physician Compare data

Table A1: Payment and Recipient's Number of Peers

	Dependent variable:			
	Payment Type			
	Food	Travel	Compensation	Total Value
	(1)	(2)	(3)	(4)
Number of Peers	0.0999***	0.0279***	0.0372***	0.0222***
	(0.0017)	(0.0019)	(0.0019)	(0.0018)
N (Physician×Drug)	484,815	484,815	484,815	484,815
R Sqr.	0.1060	0.0073	0.0114	0.0063

Notes: Number of peers refers to shared-patient peers. Variables were scaled to have mean zero and s.d. of 1. All regressions included controls for drug, physician gender, experience (10-year bins, top coded at 40+), and specialty. *p<0.1; **p<0.05; ***p<0.01.

Source: authors' calculations based on Referral Patterns and Open Payments data

Table A2: Descriptive Statistics: Number of Shared-Patient Peers

	Category	Mean	Se	10%	25%	50% (median)	75%	90%
Primary Specialty								
	Primary Care	17.100	0.049	1	4	11	24	42
	Cardiac Specialist	60.200	0.288	12	28	53	84	116
Gender								
	Female	15.700	0.087	1	3	8	21	40
	Male	26.000	0.088	2	6	15	35	64
Graduation Year								
	(1942,1983]	22.800	0.139	2	5	12	28	59
	(1983,1994]	24.000	0.133	2	5	13	31	61
	(1994,2003]	23.800	0.125	2	5	14	34	57
	(2003,2015]	18.800	0.126	1	4	11	28	46
Total		22.800	0.067	2	5	13	31	57

Notes: Number of shared-patient peers in 2013, for all physicians of at least one peer.
Source: authors' calculations using Referral Patterns and Physician Compare data.

Table A3: The Impact of Payments of Different Types on Prescription Volumes

	Dependent Variable:		
	Number of Prescribed Patients (1)	Newly Prescribed Patients (2)	Fraction of Anticoagulant Prescriptions (3)
Own Compensation	0.3704	0.0283	0.0095
	(0.1158)	(0.0160)	(0.0058)
Own Travel	-0.0277	-0.0158	0.0132
	(0.1559)	(0.0205)	(0.0067)
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 Travel	0.0115	-0.0012	0.0007
	(0.0063)	(0.0010)	(0.0009)
Peer Food	-0.0004	0.0002	0.0005
	(0.0013)	(0.0002)	(0.0004)
N (Doctor×Drug×Quarter)	5,467,536	5,467,536	3,725,260

Source: authors' calculations

Table A4: The Influence of Own and Peer Payments on Prescription Volumes, First versus Later Payments

		Dependent Variable:		
		Number of Prescribed Patients	Newly Prescribed Patients	Fraction of Anticoagulant Prescriptions
Own Payment				
Compensation	Count	0.3722	0.0202	0.0082
		(0.1218)	(0.0167)	(0.0060)
Travel	Count	-0.0475	-0.0198	0.0126
		(0.1675)	(0.0211)	(0.0072)
Food	Count	0.0612	0.0047	0.0037
		(0.0040)	(0.0006)	(0.0007)
Compensation	First	-0.0414	0.1061	0.0171
		(0.2049)	(0.0449)	(0.0151)
Travel	First	0.1615	0.0305	0.0041
		(0.2178)	(0.0491)	(0.0134)
Food	First	-0.0278	0.0019	0.0045
		(0.0061)	(0.0014)	(0.0015)
Peer Payment				
Compensation	Count	0.0199	0.0015	0.0018
		(0.0063)	(0.0010)	(0.0009)
Travel	Count	0.0123	-0.0010	0.0006
		(0.0066)	(0.0010)	(0.0009)
Food	Count	-0.0004	0.0002	0.0005
		(0.0014)	(0.0002)	(0.0004)
Compensation	First	-0.0222	0.0091	0.0004
		(0.0130)	(0.0033)	(0.0026)
Travel	First	-0.0108	-0.0039	0.0026
		(0.0111)	(0.0024)	(0.0020)
Food	First	0.0023	-0.0003	-0.0020
		(0.0035)	(0.0008)	(0.0016)
N (Doctor×Drug×Quarter)		5,467,536	5,467,536	3,725,260

Notes: Physician-drug and specialty-drug-quarter fixed-effects, controls for all other types of payments, and payment-type-specific linear time trends were included in all specifications.

Source: author's calculations

Table A5: The Effect of Payments, by Prescription Value

A. The effect of payments on total AC use (NOAC and Warfarin)

	Dependent variable: Patients prescribed a specific anticoagulant					
	Prescription Value				Bleeding Risk	
	Low	Medium	High	Total	Low	High
	(1)	(2)	(3)	(4)	(5)	(6)
Own Compensation	-0.0142	0.3738	-0.0014	0.3582	0.1058	0.2524
	(0.0472)	(0.1776)	(0.0843)	(0.2309)	(0.1275)	(0.1584)
Own Travel	0.0290	-0.3061	-0.1335	-0.4105	-0.2074	-0.2032
	(0.0622)	(0.1881)	(0.1217)	(0.2592)	(0.1696)	(0.1680)
Own Food	0.0074	0.0624	0.0120	0.0819	0.0336	0.0483
	(0.0022)	(0.0096)	(0.0039)	(0.0116)	(0.0061)	(0.0085)
Peer Compensation	0.0028	0.0230	0.0035	0.0293	0.0125	0.0168
	(0.0031)	(0.0147)	(0.0063)	(0.0175)	(0.0086)	(0.0136)
Peer Travel	0.0031	-0.0203	-0.0082	-0.0253	-0.0180	-0.0073
	(0.0045)	(0.0196)	(0.0093)	(0.0234)	(0.0121)	(0.0185)
Peer Food	-0.0010	-0.0029	0.0025	-0.0014	0.0026	-0.0040
	(0.0009)	(0.0056)	(0.0017)	(0.0062)	(0.0025)	(0.0053)
Adj. R Sqr.	0.7628	0.7609	0.5403	0.7843	0.6400	0.8188
Mean Dep. Var.	0.3115	3.5161	0.9358	4.7635	1.9591	2.804
N	1,554,864	1,554,864	1,554,864	1,554,864	1,554,864	1,554,864

B. The effect of payments on specific NOAC use

	Dependent variable: Patients prescribed a specific NOAC					
	Prescription Value				Bleeding Risk	
	Low	Medium	High	Total	Low	High
	(1)	(2)	(3)	(4)	(5)	(6)
Own Compensation	0.0593	0.3228	0.1380	0.5201	0.2083	0.3117
	(0.0373)	(0.1336)	(0.0551)	(0.1688)	(0.0966)	(0.1129)
Own Travel	-0.0087	0.0190	-0.1504	-0.1401	-0.0197	-0.1204
	(0.0490)	(0.1921)	(0.0709)	(0.2339)	(0.1311)	(0.1527)
Own Food	0.0057	0.0525	0.0084	0.0666	0.0250	0.0415
	(0.0015)	(0.0062)	(0.0024)	(0.0074)	(0.0039)	(0.0054)
Peer Compensation	0.0000	0.0092	0.0090	0.0183	0.0145	0.0037
	(0.0024)	(0.0091)	(0.0039)	(0.0112)	(0.0061)	(0.0080)
Peer Travel	0.0043	0.0118	-0.0014	0.0147	0.0018	0.0129
	(0.0031)	(0.0097)	(0.0041)	(0.0127)	(0.0063)	(0.0092)
Peer Food	0.0010	-0.0012	-0.0005	-0.0008	-0.0016	0.0008
	(0.0010)	(0.0029)	(0.0009)	(0.0034)	(0.0015)	(0.0028)
Adj. R Sqr.	0.4883	0.7013	0.5856	0.7485	0.7011	0.6556
N	3,689,520	3,689,520	3,689,520	3,689,520	3,689,520	3,689,520

Notes: Estimates of the impact of pharmaceutical payments on anticoagulant prescriptions by prescription risk and net value, for the sample of patients diagnosed with atrial fibrillation (AFib) and who received at least one anticoagulant prescription during the study period. Part A shows estimates of the impact of payments on the number of patients per physician per quarter who are prescribed who are prescribed any anticoagulant. Part B shows similar estimates, but where the analysis is done at the specific NOAC, for all NOACs in our study. We partitioned patients into groups based on BLEED score for bleeding risk (a severe side effect of NOAC use) and CHAD score which captures benefits of anticoagulant prescriptions. Columns 1–3 show the results separately by value. High value are patients with low risk and high benefits; medium value are patients with either high risk and high benefits or low risk and low benefits; low value are patients with high risk and low benefits. Columns 4–5 show results separately by risk.

Source: authors' calculations

Table A6: Matching Sample Descriptive Statistics

	Paid Physician	Unpaid Match
Experience (years)	25.2	25.9
Shared-Patient Peers (count)	53.2	48.1
Group-Practice Peers (count)	93.5	94.0
Male (fraction)	0.93	0.79
Physicians	1,127	10,964
Peers without additional paid peers	1,505	18,940

Notes: Paid Physician is a recipients of compensation payments during the sample period. Unpaid Matched are non-compensated physicians, matched exactly on drug, specialty and HRR and coarsely on experience and number of peers. Peers without additional paid peers are all peers of Paid Physicians and Unpaid Matches that have no additional peer who received compensation payments.

Source: authors' calculations

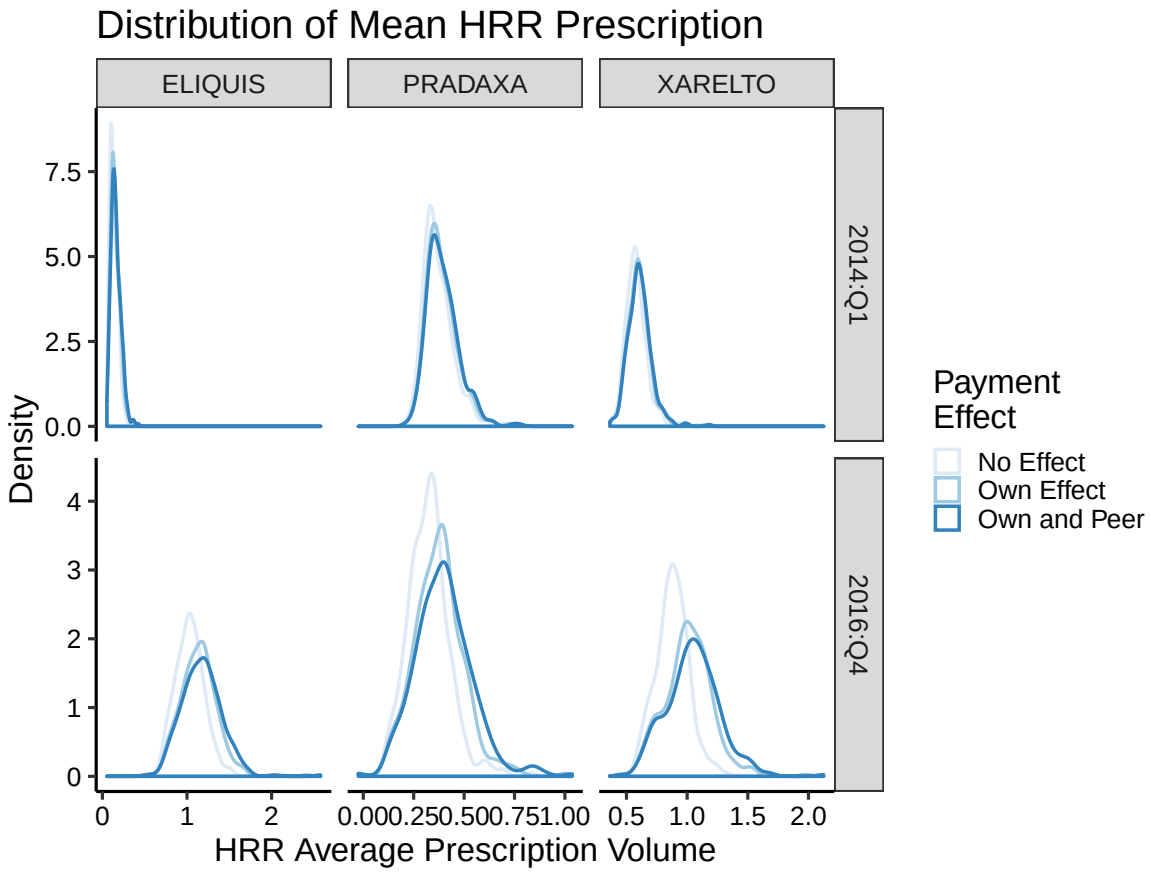
Table A7: Robustness: The Impact of Payments on Prescriptions

Specification	*Independent Variables:*			N
	Own food, count	Own compensation, count	Peer compensation, count	
Baseline	0.059	0.371	0.022	5,467,536
	(0.004)	(0.116)	(0.005)	
Cardiologists only	0.119	0.393	0.049	653,580
	(0.0153)	(0.1417)	(0.1590)	
Primary care only	0.047	0.175	0.010	4,813,956
	(0.003)	(0.141)	(0.004)	
Xarelto only	0.033	0.438	0.025	1,797,300
	(0.005)	(0.167)	(0.007)	
Eliquis only	0.086	0.565	0.023	1,789,008
	(0.006)	(0.242)	(0.011)	
Pradaxa only	0.037	0.026	0.009	1,881,228
	(0.008)	(0.074)	(0.006)	

Notes: Estimates of (1), different sub-samples.

Source: authors' calculations

Figure A2: Payment Contribution to Geographic Variation



Notes: The plots show the distribution of counterfactual (model-predicted) HRR average prescription volume, for different payment scenarios: own and peer effect of payments, own effect only (with zero peer effects), and no effect of payments. Each facet shows results for a different combination of drug (columns); The top and bottom rows show results for the first and last quarter in the sample.

Source: authors' calculations

Table A8: The Impact of Payments of Different Types on Prescription Volumes: Restricted Sample

	Dependent Variable:		
	Number of Prescribed Patients (1)	Newly Prescribed Patients (2)	Fraction of Anticoagulant Prescriptions (3)
Own Compensation	0.1553	0.0328	-0.0171
	(0.1393)	(0.0182)	(0.0138)
Own Travel	0.1037	-0.0380	0.0295
	(0.1963)	(0.0211)	(0.0194)
Own Food	0.0602	0.0050	0.0037
	(0.0037)	(0.0005)	(0.0006)
Peer Compensation	0.0148	0.0008	0.0005
	(0.0043)	(0.0009)	(0.0012)
Peer Travel	-0.0101	-0.0042	-0.0013
	(0.0043)	(0.0014)	(0.0018)
Peer Food	0.0004	0.0004	0.0008
	(0.0009)	(0.0001)	(0.0003)
N (Doctor×Drug×Quarter)	4,189,392	4,189,392	2,685,826

Notes: Estimates of (1), on a sample including only physicians with no own or peer payments of any type in the first three quarters.

Source: authors' calculations

Table A9: The Impact of Payments of Different Types on Prescription Volumes: Restricted Sample

	Dependent Variable:					
	Number of Prescribed Patients		Newly Prescribed Patients		Fraction of Anticoagulant Prescriptions	
	(1)	(2)	(3)	(4)	(5)	(6)
Own Compensation Payment	0.1553	0.1556	0.0291	0.0289	-0.0090	-0.0085
	(0.1393)	(0.1391)	(0.0181)	(0.0181)	(0.0160)	(0.0160)
Own Food Payment	0.0593	0.0588	0.0050	0.0050	0.0043	0.0038
	(0.0037)	(0.0037)	(0.0005)	(0.0005)	(0.0007)	(0.0007)
Peer Compensation, by Type of Affiliation:						
Shared Patients	0.0202	0.0054	0.0019	0.0010	0.0031	0.0027
	(0.0060)	(0.0063)	(0.0011)	(0.0013)	(0.0013)	(0.0016)
Group Practice and Shared Patients		0.0481		0.0035		0.0015
		(0.0145)		(0.0024)		(0.0029)
Group Practice without Shared Patients		0.0059		0.0013		0.0002
		(0.0038)		(0.0006)		(0.0014)
N (Doctor×Drug×Quarter)	4,189,392	4,189,392	4,189,392	4,189,392	2,685,826	2,685,826

Notes: Estimates of (1), on a sample including only physicians with no own or peer payments of any type in the first three quarters.

Source: authors' calculations