Drug Diffusion Through Peer Networks: The Influence of Industry Payments

Leila Agha and Dan Zeltzer

December 11, 2020

A Online Appendix

A.1 Instrumental Variable Approach to Estimating Peer Effects in Prescriptions

In this section, we develop an alternative empirical strategy for identifying social interaction effects in prescriptions. Following De Giorgi et al. (2010), we use characteristics of peers-of-peers as an instrument for endogenous behaviors of direct peers. Because shared-patient relationships are non-transitive, a physician typically has peers of peers that are not also her direct peers. The presence of such "excluded peers" overcomes the reflection problem highlighted by Manski (1993), as this set varies even among connected physicians. Furthermore, to the extent that payments to a physician's excluded peers affect her direct peers' prescriptions, such payments can serve an instrument for identification of the effect of direct-peer prescriptions on the physician's own prescriptions.

We use the same notation as in Section 2. That is, physician's i set of peers is denoted G_i. We further denote by E_i the group of *excluded peers* of physician i, defined as all physicians who share peers with i but are not linked to i directly. Namely, $E_i = \{k | \exists j \in G_i \cap G_k \text{ and } k \notin G_i\}$. We estimate the following two-stage least-square model:

$$\begin{aligned} \overline{Y}_{G_i,d} &= P'_{E_i,d}\kappa + P'_{G_i,d}\gamma_1 + P'_{i,d}\delta_1 + \nu_{id}, \\ Y_{id} &= \beta\widehat{\overline{Y}}_{G_i,d} + P'_{G_i,d}\gamma_2 + P'_{i,d}\delta_2 + \epsilon_{id}. \end{aligned} \tag{A3}$$

Where i denotes physicians, d denotes drugs, and $P_{z,d}$ denotes the vector of the number of cumulative payments of different types made to physician or group z in association with drug d. The term $\overline{Y}_{G_i,d}$ is a shorthand for the average prescription volume among peers of i. The parameter of interest is β, which captures the impact of an increase in the average drug prescription volume among a physician's peers on her own prescription volume of the same drug. The identification assumption is that payments to a physician's excluded (indirect) peers affect the physician's prescription volume only through the prescription volume of direct peers.

We implement this strategy using data on excluded shared-patient peers of physicians in our sample. Panel C of Table 2 shows the average number of excluded peers in our sample, by the target physician's payment status. On average, physicians in our sample have 205 excluded peers. Compensated physicians have more excluded peers than non-compensated ones, but the disparity between physicians with different payment status in

the number of excluded peers is lower than the disparity in their number of direct peers. In our implementation of this strategy, we use cross-sectional data on cumulative payments and prescriptions over our entire study period.[19]

Table A2 shows estimates of equation (A3). Panel A shows the first stage. Controlling for own and peer payments of different types, we find a strong and positive relationship between the average number of quarters with compensation payments among excluded peers and the average cumulative prescription volume of direct peers. Panel B shows the second stage, with different columns showing estimates for different prescription volume measures. An increase of one prescribed patient per quarter among a physician's direct shared-patient peers is associated with the physician prescribing to 0.27 additional patients. Of them, 0.029 (about ten percent), are entirely new patients, not previously prescribed anticoagulants. The same one patient increase in peer prescription volume among peers also leads a physician to increase the fraction of the prescribed drug, out of all anticoagulants prescribed, by 0.4 percentage points (from a baseline of 16 percentage points). To the extent that payments to excluded peers do not directly effect the physician's prescription behavior (other than through their impact on connected peers), these results imply that there are strong and significant peer effects in prescription behavior.

Finally, it is worth clarifying that the magnitude of the coefficients on the control variables for direct and peer compensation exposure are not directly comparable to those reported in our main regression specification. Recall that the unit of observation in this IV regression is doctor×drug aggregating over all quarters. Thus to compare prescription volume reported here to the main regression specification would require dividing by 12, because our sample covers 12 quarters. After making this adjustment, we find similar effect sizes, with each direct compensation payment increasing prescription volume of the targeted doctor by $4.7/12 = 0.39$ beneficiaries per quarter, similar to our baseline estimate of 0.37 (see Table 3). This is particularly notable given the different sources of identifying variation in each specification; this regression is identified using cross sectional variation in payment exposure, whereas the baseline regression accounts for doctor×drug fixed effects and uses time-variation in payment exposure within doctor.

[19]This approach departs from our baseline approach reported in the rest of the paper that exploits time variation in payment exposure to trace the effects on prescription volume. In this context, we are relying on rippling influence from excluded peers to direct peers and then to the index doctor, which may occur with an unknown lag. In addition, exploiting identifying variation from excluded peer payment exposure reduces our concern about endogenous payment targeting. For these reasons, we follow the set-up in De Giorgi et al. (2010) and Bramoullé et al. (2009) and use a cross-sectional data structure.

A.2 Construction of the sample of matched compensated and uncompensated physicians

To construct the sample of matched physicians used in our robustness specification, we first sample all physicians who received compensation payments at any point during 2014–2016 (henceforth, *targets*). We match each target with similar physicians who did not receive compensation payments. We match exactly on specialty, the target drug, and hospital referral region. We perform coarsened exact matching (by quartiles) on experience, number of shared-patient peers, and number of group practice peers. We also drop a small number of matches who share a group practice with the target, so all our matches are from the same area as the target but not from the same practice. We then sample all shared-patient peers of targets and their matches. We exclude peers of targets or matches who have an additional peer (beyond the target) who received compensation payments. Therefore, the resulting sample has two disjoint sets of physicians who are peers of either a paid physician or a matched unpaid one, and who have no other compensation-paid peers. Descriptive statistics for the matched sample are shown in Appendix Table A8 below. Results of the matching estimation are reported in Table 5.

A.3 Constructing clinical risk scores

HAS-BLED score We observe four of the nine clinical characteristics included in the HAS-BLED score to construct our estimate: patient age > 65, hypertension history, renal disease, and stroke history.[20] The guideline is scored simply: one point per risk factor. Patients scoring zero to one are considered low risk; two points correspond to moderate risk; three or more points correspond to high risk.[21]

CHADS2 score To construct the CHADS2 score, we can approximate each of the five factors underlying the guidelines from claims records: congestive heart failure, hypertension, age, diabetes mellitus, and history of stroke or transient ischemic attack symptoms.

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

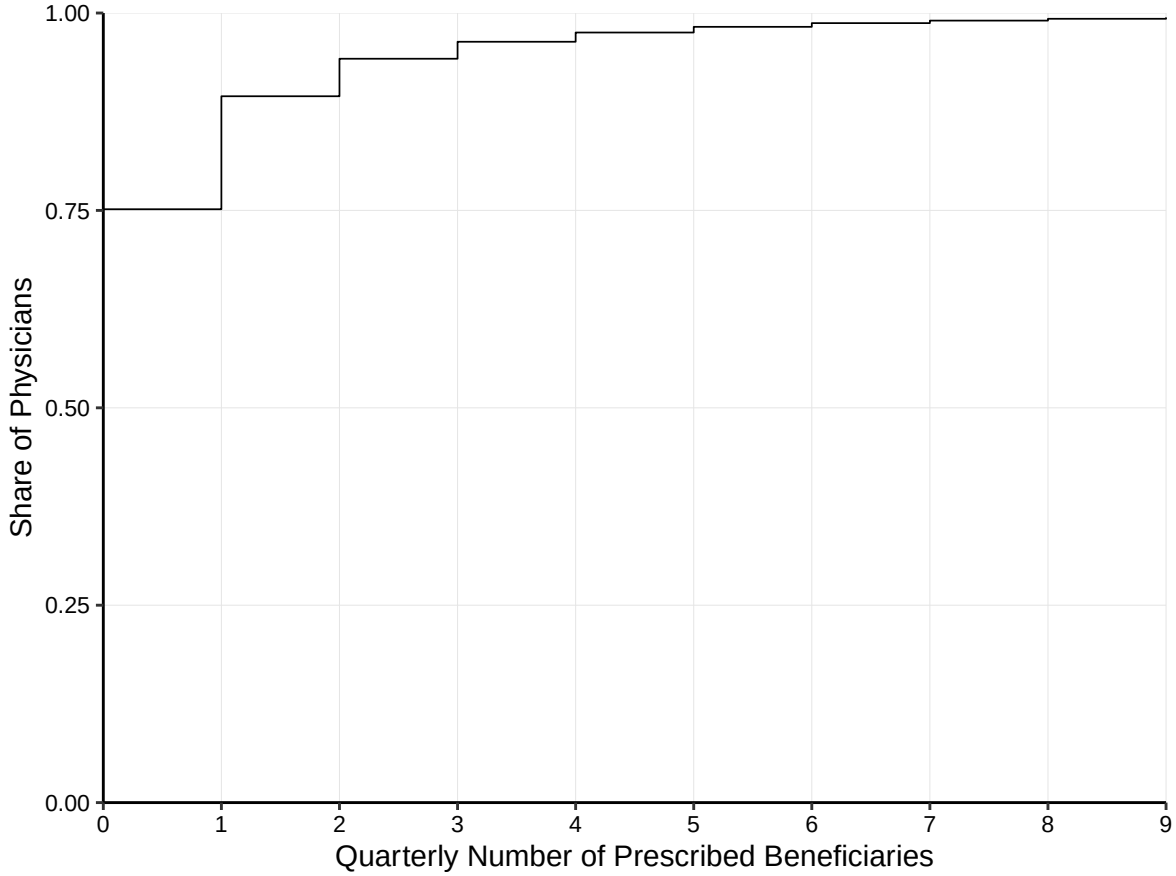
[21] Note that the guidelines themselves do not provide sharp recommendations on whether or not to prescribe anticoagulation drugs. For example, the HAS-BLED score recommendations provided on MDCalc.com are worded as "anticoagulation should be considered" [strongest recommendation], "anticoagulation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

We dichotomize the CHADS2 score, following a threshold used in the clinical guidelines. Patients with three or more risk factors are at high risk of stroke and anticoagulation is recommended; patients with fewer risk factors may still benefit from anticoagulation, but the recommendation is weaker.

Results by risk score value Section 5 and Table 7 describes the results by value of the HAS-BLED score. In Appendix Table A6, we report additional results that use the CHADS2 score in combination with our approximated HAS-BLED score to divide patients into three categories by their estimated stroke-reduction benefit and bleeding risk: low value (low benefit and high risk), medium value (low benefit and low risk, or high benefit and high risk), or high value (high benefit and low risk). If pharmaceutical detailing led doctors to more guideline-concordant practice patterns, we might expect declining use in the low-value population and increasing use in the high-value population.

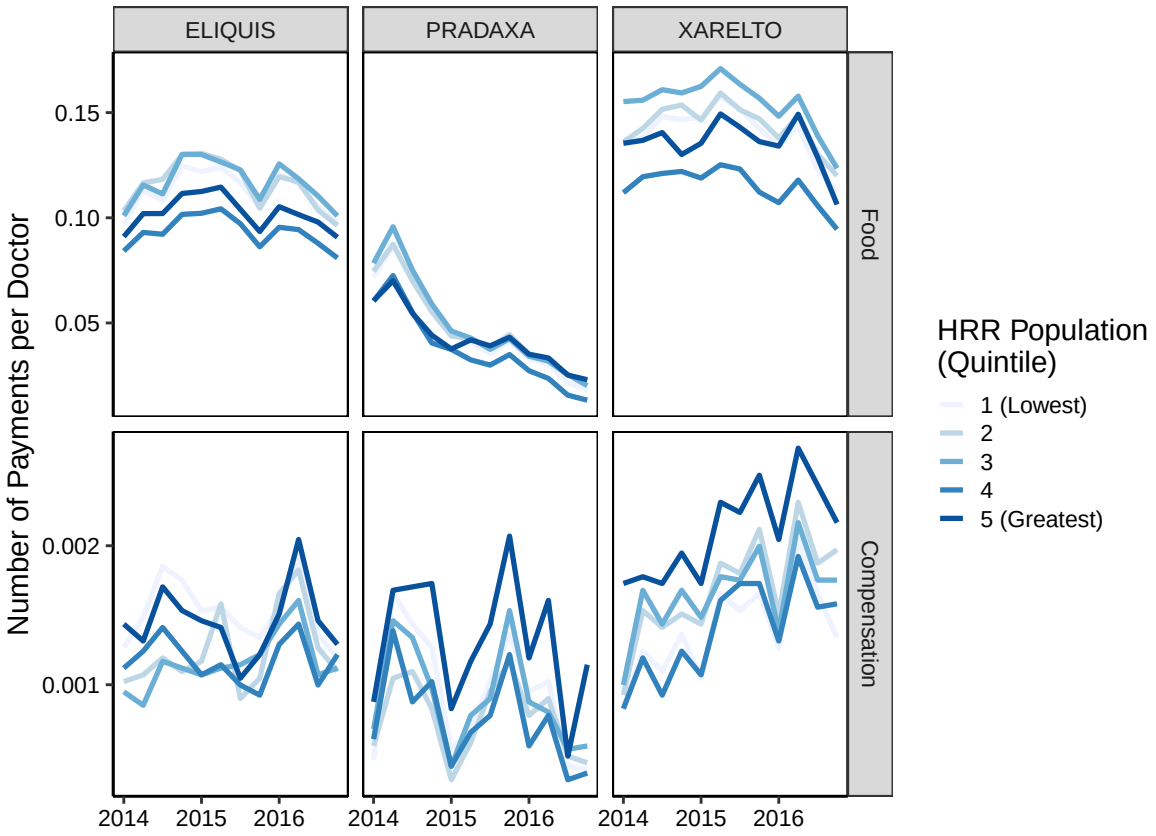
A.4 Additional Tables and Figures

Figure A1: Cumulative Distribution of Prescription Volume



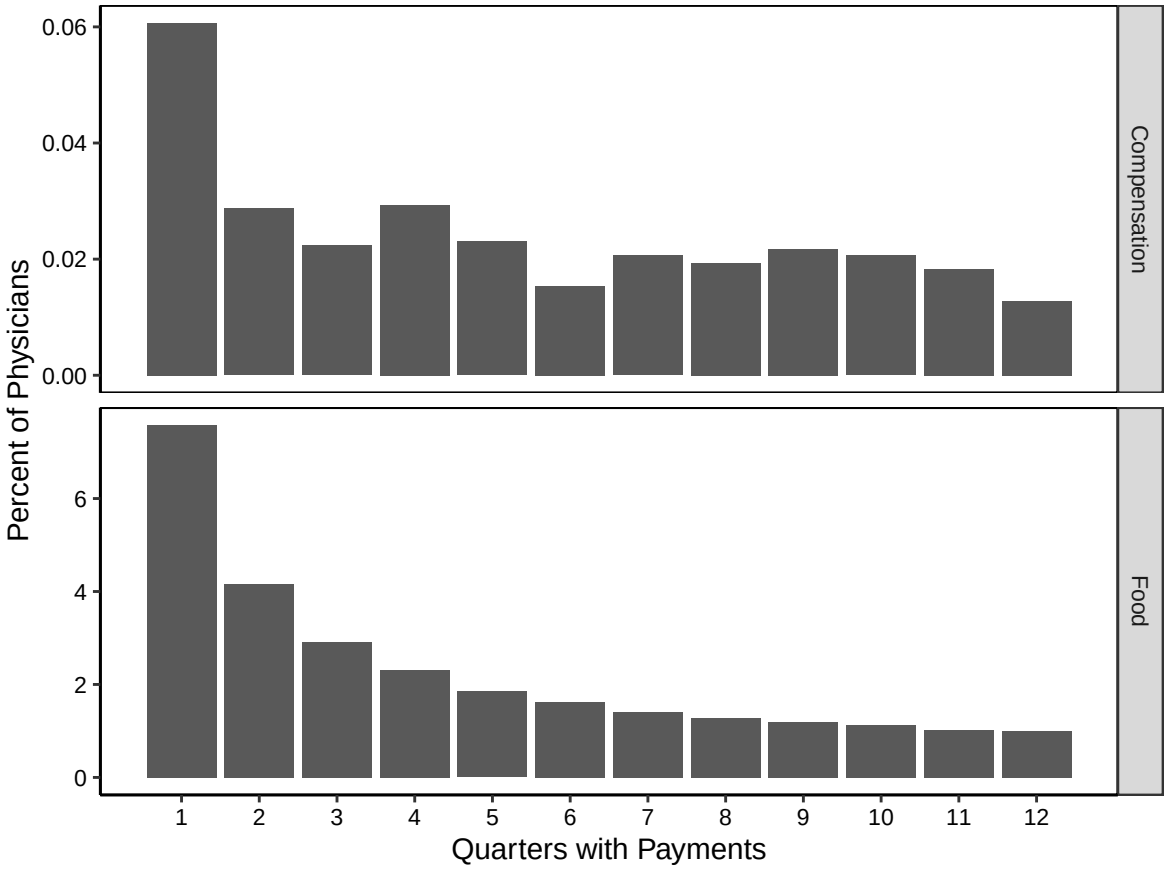
Notes: Figure shows the (right-continuous) cumulative distribution function for the main prescription volume measure: the quarterly number of beneficiaries to which the physician prescribed the targeted drug. The y-axis shows the share of physicians whose prescription volume is equal to or smaller than the value on the x-axis. The results average over the three targeted drugs during the study period.

Figure A2: Number of Physician Payments by HRR Population



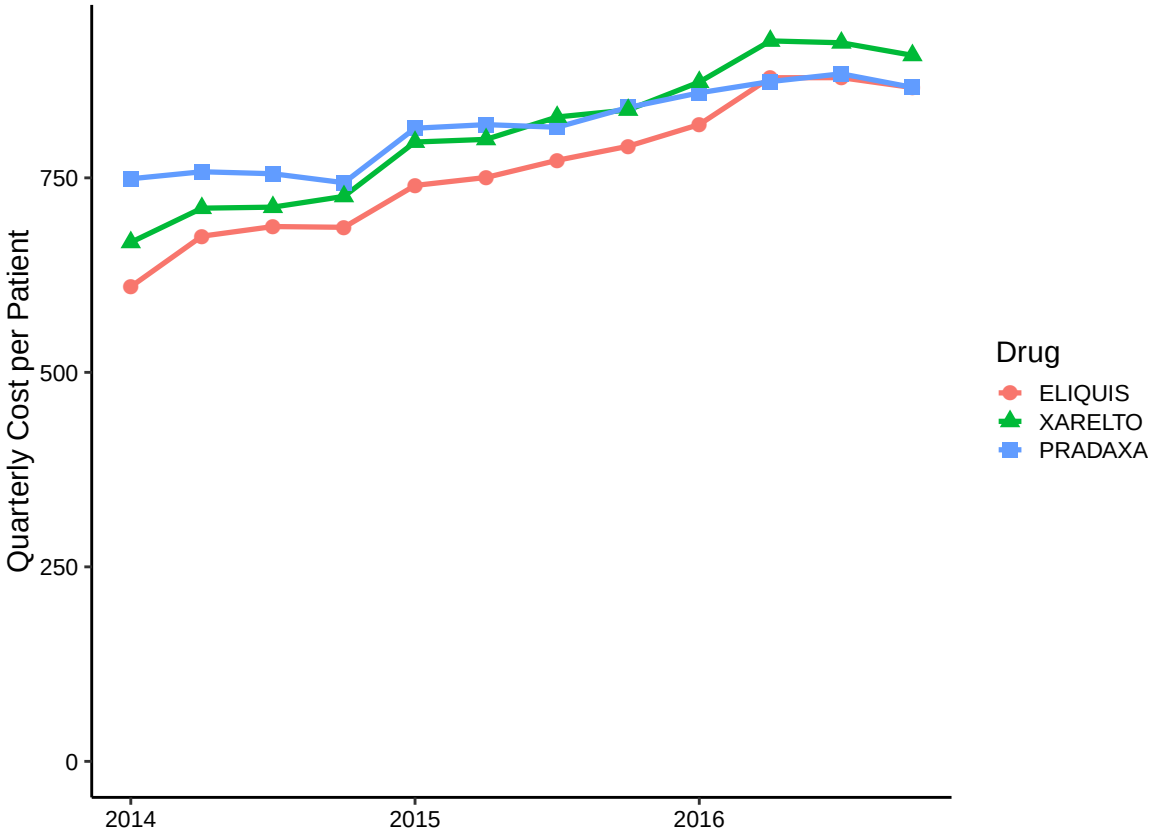
Notes: Table shows the average number of quarterly payments per doctor by HRR population size. Column facets show data separately for the different drugs we study; row facets show data for different types of payments. Within each facet, darker lines show data for more populated HRRs, based on population size reported in the 2010 Census.

Figure A3: Distribution of Number of Quarters with Payments



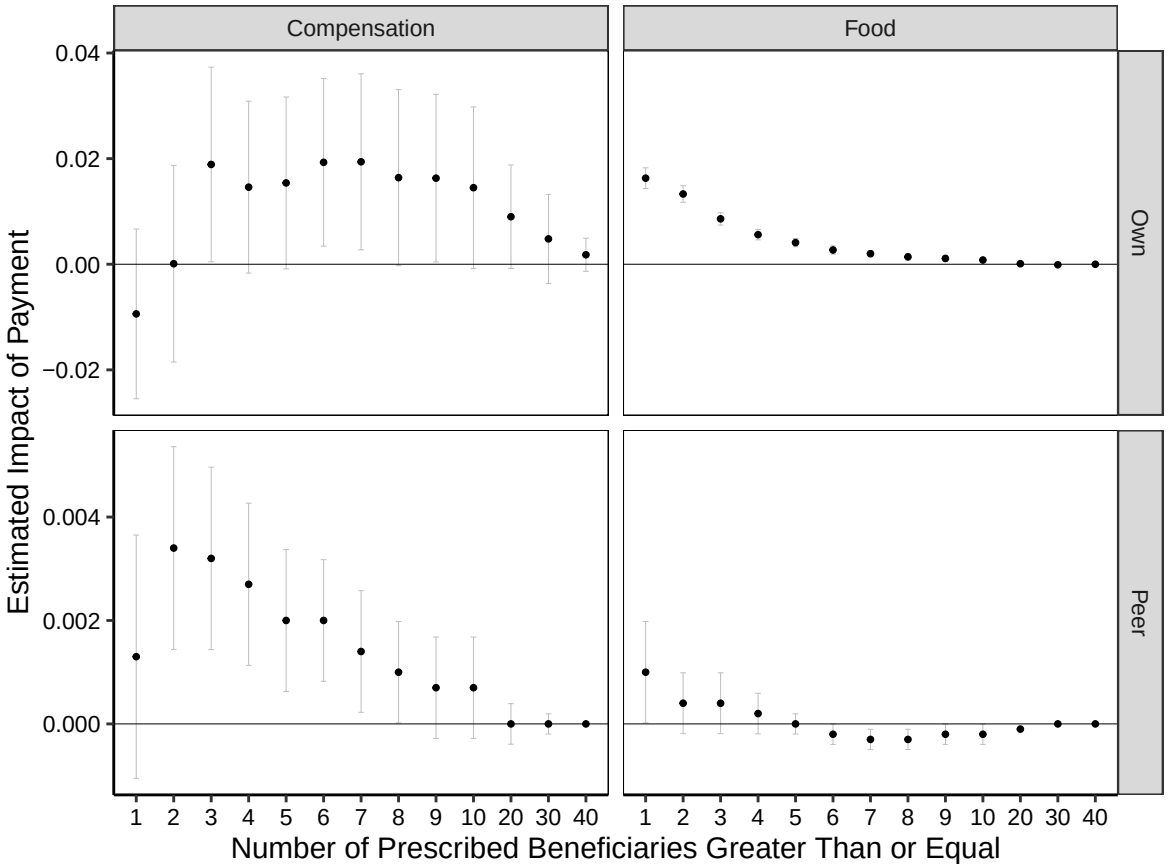
Notes: Figure shows the share of physicians in our sample with different numbers of quarters with payments. A quarter with a payment is defined as a quarter during which the physician received at least one payment of the specific type: compensation in the top panel, and food in the bottom panel. Scales differ between panels and total shares do not add to 100, because data for (the majority of) physicians who received no payments during our study period are not shown. See Section 1 for detailed definitions.

Figure A4: Average Quarterly Prescription Cost per Patient



Notes: Figure shows the average quarterly cost of prescriptions per patient (by all payers), by drug, for all prescribed patients in our Medicare Part D sample.

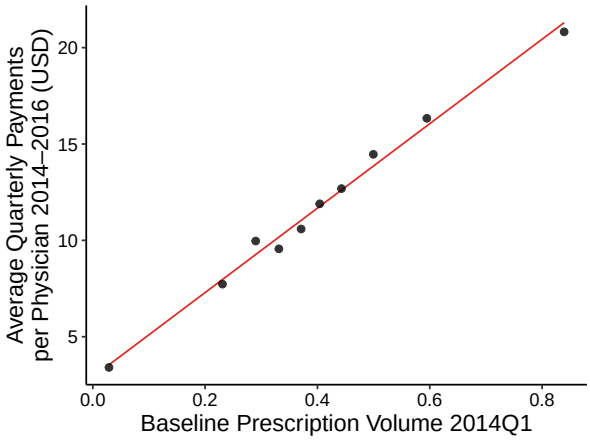
Figure A5: Heterogeneity in Influence of Payments on Target Drug Prescription, by Volume



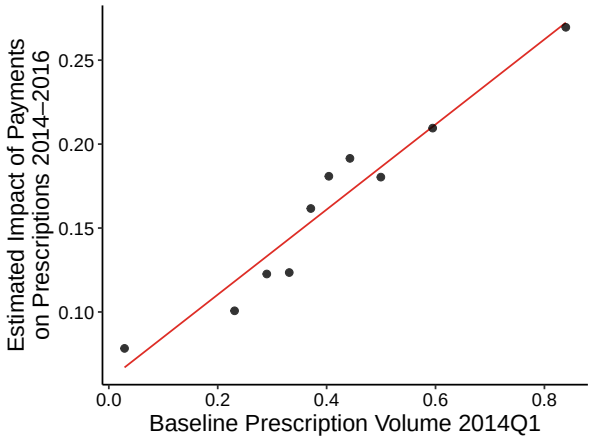
Notes: Figure shows estimates of equation (2) where the dependent variable is a dummy for prescribing the target drug to at least Q beneficiaries. Each panel shows coefficient estimates and 95 percent confidence intervals, for different levels of Q. The different panels show results for different types of payments made to the prescribing physicians ("Own") or to others with whom the prescribing physicians shared patients ("Peers"), jointly estimated. Food includes payments for food and beverages, and educational items. Compensation includes payments for consulting, speaking, and other services. Note that facet vertical axes have different scales. See Section 1 for detailed definitions. Physician-drug, specialty-drug-quarter fixed effects, controls for all other types of payments, and payment-type-specific linear time trends included in all specifications. Standard errors are clustered within doctor.

Figure A6: Regional Differences in Baseline Prescription Volumes, Subsequent Payments, and Payments' Impact

(A) Average Payment Per Physician



(B) Estimated Cumulative Impact on Prescriptions



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

Table A1: Correlation Between Different Types of Payments

	Shared-Patient Peer Compensation	Group-Practice Peer Compensation	Own Compensation	Own Food
Shared-Patient Peer Compensation	—			
Group-Practice Peer Compensation	0.2365	—		
Own-Compensation	0.0255	0.0207	—	
Own-Food	0.0905	0.0114	0.1053	—

Notes: Table shows the correlation in physicians' quarterly payment exposure (measured as number of payments). See Section 1 for detailed definitions.

Table A2: Peer Effects in Prescription Behavior

A. First Stage:

	Dependent Variable: Number of Prescribed Patients, Average Across Peers
	(1)
Payment Count, by Type	
Excluded Peer Compensation	0.1300
	(0.0124)
Own Compensation	0.2324
	(0.2251)
Peer Compensation	0.2304
	(0.0385)
Mean dependent variable	14.0985
N (Doctor × Drug)	455,535

B. Second Stage:

	Dependent Variable: Own Prescription		
	Number of Prescribed Patients	Newly Prescribed Patients	Fraction of Anticoagulant Prescriptions
	(2)	(3)	(4)
Mean Peer Prescription	0.2735	0.0295	0.0039
	(0.0197)	(0.0017)	(0.0002)
Payment Count, by Type			
Own Compensation	4.7010	0.4160	0.0118
	(1.2308)	(0.0970)	(0.0037)
Peer Compensation	0.0681	0.0301	0.0017
	(0.0565)	(0.0043)	(0.0004)
Mean dependent variable	6.5835	0.4914	0.1596
N (Doctor × Drug)	455,535	455,535	455,535

Notes: Generalized method of moments estimates of the instrumental variable model specified in equation (A3). The endogenous variable is the average number of prescribed patients across the index doctor's shared-patient peers. Compensation payments for "excluded" shared-patient peers—peers of peers of the target physician who are not themselves peers of the target physicians—act as an instrumental variable for the (direct) peer prescription volume. Panel A shows the first-stage results and Panel B shows the second-stage results for alternative measures of prescription volume. All specifications include parallel variables for food and travel payment exposure, as well as specialty-drug fixed effects. Standard errors are clustered within doctor.

Table A3: Robustness: The Impact of Payments on Prescriptions for Different Subsamples and Specifications

	Independent Variables:					
	Own Compensation, Count	Own Food, Count	Peer Compensation, Count	Peer Food, Count	Mean Dep. Var.	N
Specification	(1)	(2)	(3)	(4)	(6)	(6)
Baseline						
	0.3684	0.0584	0.0196	-0.0005	0.5486	5,466,420
	(0.1155)	(0.0037)	(0.0060)	(0.0013)		
Primary Care Only						
	0.1811	0.0463	0.0078	0.0019	0.3245	4,812,780
	(0.1392)	(0.0030)	(0.0040)	(0.0011)		
Cardiologist Only						
	0.3929	0.1154	0.0431	-0.0112	2.1989	653,640
	(0.1419)	(0.0152)	(0.0174)	(0.0082)		
Xarelto Only						
	0.4377	0.0326	0.0233	0.0001	0.7809	1,796,832
	(0.1659)	(0.0048)	(0.0082)	(0.0016)		
Eliquis Only						
	0.5583	0.0825	0.0089	0.0031	0.5474	1,788,900
	(0.2418)	(0.0063)	(0.0131)	(0.0023)		
Pradaxa Only						
	0.0255	0.0363	0.0123	-0.0034	0.3279	1,880,688
	(0.0741)	(0.0074)	(0.0062)	(0.0016)		
Low Experience Only						
	0.4145	0.0570	0.0133	-0.0002	0.4058	2,714,124
	(0.1786)	(0.0052)	(0.0070)	(0.0019)		
High Experience Only						
	0.3502	0.0584	0.0255	-0.0005	0.6895	2,752,296
	(0.1567)	(0.0052)	(0.0095)	(0.0019)		

Notes: Key coefficients from estimating equation (2) on different subsamples. The dependent variable is the number of prescribed patients. The row label indicates the alternative subsamples. "Baseline" repeats the results using our full sample, shown in Table 3. The remaining rows show estimates of our main specification on separate subsamples defined by the focal doctor's specialty, by drug. and by the focal doctor's experience (above or below median).

Table A4: The Impact of Payments on Prescription Volumes: Alternative Specifications

	Dependent Variable: Number of Prescribed Beneficiaries		
	Specification:		
	Baseline	Random-Effects	Restricted Sample
	(1)	(2)	(3)
Payment count, by type:			
Own Compensation	0.3684	0.4308	0.1687
	(0.1156)	(0.1129)	(0.1436)
Own Food	0.0584	0.0643	0.0604
	(0.0037)	(0.0036)	(0.0038)
Peer Compensation	0.0197	0.0213	0.0202
	(0.0061)	(0.0059)	(0.0061)
Peer Food	-0.0006	-0.0001	0.0022
	(0.0014)	(0.0013)	(0.0013)
Mean dependent variable	0.5486	0.5486	0.3416
N (Doctor × Drug × Quarter)	5,466,420	5,466,420	4,142,652

Notes: Table compares estimates obtained from different variants of equation (1). Column 1 shows our fixed effects estimates of the effects of payments of different types on the quarterly number of prescribed beneficiaries, using the baseline sample; these results are already shown in Table 3. Column 2 shows random effects estimates of the same coefficients, using the baseline sample. For the random effects specification, we include additional controls for whether the doctor ever has any exposure to each type of own and peer payment; these controls account for possible differences in baseline enthusiasm for the new drug across paid and unpaid physicians. (These controls are not necessary in the main fixed effect specification because they would be colinear with the included doctor-by-drug fixed effects.) The random effects model is used in the counterfactual analysis. Column 3 shows fixed effects estimates of equation (1) on a restricted sample including only physicians with neither own payments of any type in the first three quarters, nor exposure to compensated peers in the first three quarters.

Table A5: The Influence of Own and Peer Payments on Prescription Volumes, First versus Later Payments

		Dependent Variable:		
		Number of Prescribed Patients (1)	Newly Prescribed Patients (2)	Fraction of Anticoagulant Prescriptions (3)
Own Payments				
Compensation	Count	0.3712	0.0205	0.0080
		(0.1215)	(0.0167)	(0.0060)
Food	Count	0.0607	0.0046	0.0036
		(0.0040)	(0.0006)	(0.0007)
Compensation	First	-0.0574	0.1069	0.0178
		(0.2039)	(0.0448)	(0.0150)
Food	First	-0.0274	0.0020	0.0044
		(0.0061)	(0.0014)	(0.0015)
Peer Payments				
Compensation	Count	0.0213	0.0015	0.0018
		(0.0064)	(0.0010)	(0.0009)
Food	Count	-0.0006	0.0002	0.0004
		(0.0014)	(0.0002)	(0.0004)
Compensation	First	-0.0251	0.0094	0.0002
		(0.0130)	(0.0033)	(0.0026)
Food	First	0.0019	-0.0003	-0.0020
		(0.0035)	(0.0008)	(0.0016)
Mean dependent variable		0.5486	0.0409	0.1588
N (Doctor × Drug × Quarter)		5,466,420	5,466,420	3,724,720

Notes: Each column reports results from a separate regression. We estimate an augmented version of equation (2) that includes an additional dummy variable that equals 1 after the first observed payment of each type has been made. The coefficients on the "first" variable can be used directly to test whether the impact of the first payment differs from the impact of subsequent payment; in addition, the coefficient on the "first" variable may be summed with the coefficient on the corresponding "count" variable to find the total impact of the first payment. Physician-drug, specialty-drug-quarter fixed effects, controls for all other types of payments, and payment-type-specific linear time trends included in all specifications. Standard errors are clustered within doctor.

Table A6: The Effect of Payments, by Prescription Clinical Value

	Dependent variable:					
	Patients Prescribed any Anticoagulant			Patients Prescribed the Target NOAC		
	Low Value	Medium Value	High Value	Low Value	Medium Value	High Value
	(1)	(2)	(3)	(4)	(5)	(6)
Payment Count, by Type						
Own Compensation	-0.0139	0.3746	-0.0018	0.0592	0.3173	0.1384
	(0.0471)	(0.1774)	(0.0842)	(0.0372)	(0.1332)	(0.0550)
Own Food	0.0074	0.0613	0.0121	0.0055	0.0515	0.0083
	(0.0022)	(0.0095)	(0.0039)	(0.0015)	(0.0062)	(0.0024)
Peer Compensation	0.0030	0.0227	0.0031	0.0003	0.0100	0.0095
	(0.0031)	(0.0147)	(0.0063)	(0.0024)	(0.0091)	(0.0039)
Peer Food	-0.0009	-0.0029	0.0025	0.0010	-0.0016	-0.0007
	(0.0010)	(0.0057)	(0.0017)	(0.0010)	(0.0029)	(0.0009)
Adj. R Sqr.	0.5403	0.7843	0.6400	0.4883	0.7013	0.5856
Mean dependent variable	0.3116	3.5169	0.9358	0.0767	0.7424	0.1961
N (Doctor × Drug × Quarter)	1,554,036	1,554,036	1,554,036	3,688,884	3,688,884	3,688,884

Notes: Table shows estimates of the impact of pharmaceutical payments on anticoagulant prescriptions for patients with atrial fibrillation. We partition patients into high or low risk of bleeding side effects using the HAS-BLED risk score and, separately, to high or low stroke-reduction benefits of anticoagulation using the CHADS2 score. High value are patients with low risk and high benefits; medium value are either high risk and high benefits or low risk and low benefits; low value are high risk and low benefits. See Section 5 and Appendix Section A.3for details. Columns 1–3 show estimates of the impact of payments (pooled across all three NOAC drugs) on the total number of anticoagulants prescribed per quarter (pooled across all anticoagulants). Columns 4–6 show similar estimates, but where both payments and the prescription volume outcomes are measured separately for each NOAC in our sample. Physician-drug, specialty-drug-quarter fixed effects, controls for all other types of payments, and payment-type-specific linear time trends included in all specifications. Standard errors are clustered within doctor.

Table A7: Estimated Total NOAC Market Size with and Without Pharmaceutical Payments

Drug	Estimated Annual Prescription Volume (USD million)			Contributed Volume (USD million)	
	Actual	Counterfactual Without Peer Pay	Counterfactual Without Any Pay	All Payments	Peer Payments
	(1)	(2)	(3)	(4)	(5)
ELIQUIS	3,524.0	3,395.0	3,019.0	505.2	128.6
XARELTO	3,109.0	2,948.0	2,444.0	665.8	160.9
PRADAXA	1,021.0	923.5	729.8	291.6	97.9
All	7,654.0	7,267.0	6,192.0	1,463.0	387.4

Notes: Table shows the estimated annual dollar volume of prescriptions for each of our three sampled NOACs and for all three combined. Units are millions of current USD. The calculations are based on the most recent quarter in our sample, Q4 of 2016. All numbers are in annual terms and are scaled up by a factor of 5.4 to obtain an estimate of total US market size, including non-Medicare and non-elderly patients. This scaling factor is discussed in Section 1. Column 1 shows the actual prescription volume, based on prescriptions observed in our Medicare sample. Column 2 shows the estimated counterfactual prescription volume when only direct influence but not peer effects of payments are considered. Column 3 shows the estimated counterfactual prescription volume without any payments. Column 4 shows the relative contribution of payments' direct effects on recipients, defined as the differences between columns 1 and 3. Column 5 shows the relative contribution of peer payment spillovers, defined as the differences between columns 1 and 2.

Table A8: Matching Sample Descriptive Statistics

	Paid Physician (1)	Unpaid Match (2)
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
Number of Physicians	1,127	10,964
Peers without additional paid peers	1,505	18,940

Notes: A "Paid Physician" is a recipient of compensation payments during the sample period. "Unpaid Match" 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 who have no additional peer directly receiving compensation payments.