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Do Physicians Respond to the Costs and Cost-Sensitivity of Their Patients?[†]

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We use individual level data on purchases of cholesterol-lowering drugs to study the responses of physicians and patients to variation in the cost of drugs. In a sample of first-time statin prescriptions to employees from 12 Fortune 500 firms, we find that co-pay variation across plans has a small effect on the choice of drug, and this effect does not vary with patient income. After the highly publicized patent expiration of Zocor, however, prescriptions for this drug increased substantially, especially for lower income patients. Our analysis suggests that physicians can perceive the price sensitivity of their patients and adjust their initial prescriptions accordingly, but only in response to a large and universal price change. (*JEL* D14, G22, I11, I13, L65)

Over the past two decades, insurers have sought to rein in rising drug costs by increasing patient cost-sharing and adopting incentive-based benefit structures. Tiered formularies, which use multiple co-pay levels ("tiers") to encourage choice of generic or certain brand drugs, have become nearly ubiquitous in both employer-sponsored and Medicare Part D plans.[1] Relative to simpler benefit structures with a fixed co-pay (out-of-pocket cost) for all covered drugs, tiered formularies have been found to reduce overall drug expenditures while shifting costs heavily towards patients. Studies have cautioned, however, that higher cost-sharing hurts utilization rates of important chronic medications, causing savings on pharmaceuticals to be

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[1] In 2014, benefit designs with three or more tiers applied to 80 percent of privately insured workers and over 85 percent of Medicare Part D beneficiaries. In 2000, only 29 percent of privately insured workers faced these benefit designs (Kaiser Family Foundation 2010; Hargrave et al. 2010).

partially offset by increased medical costs (Chandra, Gruber, and McKnight 2010; Gaynor, Li, and Vogt 2007).

Little attention has been paid to the role of physicians, who can, in theory, mitigate the harmful effects of cost-sharing through cost-sensitive prescribing. Tiered formularies operate on the assumption that cost-sensitive patients can choose low-tier drugs, but prescription drugs cannot, by definition, be purchased at will. Instead, patients rely on physicians to write a prescription, wherein three interacting problems emerge. First, the physician may not know the price sensitivity of a given patient. Second, physicians may put too little weight on a patient's costs, relative to her level of price sensitivity.[2] Third, with a variety of multi-tiered formularies operating in any given geographic market, most physicians don't observe a specific patient's array of co-payments (Shrank et al. 2005; Khan et al. 2008). In the prescribing of chronic, preventative drugs, these asymmetric information problems can have both health and welfare consequences.[3]

In this paper, we study how initial prescriptions respond to co-pay changes in plan formularies, and how these responses vary with patient income. We focus on one of the most prescribed classes of drugs in the United States, HMG-CoA reductase inhibitors (statins). Statins reduce blood levels of low-density lipoprotein cholesterol (LDL), and are proven to reduce the risk of coronary heart disease and heart attacks.[4] Beyond its economic importance as the largest class in US sales until 2007, with 255 million dispensed prescriptions in 2012,[5] the statin drug class is arguably the one where we are most likely to find sizeable co-pay effects on prescribing. It contains six drugs that are highly substitutable for the majority of users, in terms of their efficacy and side effects.[6] Furthermore, statins are expensive and meant to be used indefinitely, so a reasonable agent for a patient ought to consider her costs. In our sample, the average yearly out-of-pocket cost for an adherent statin user is $297, but only 45 percent of starting patients are adherent over the first year.

The first goal of this paper is to estimate how co-pay variation across plans affects drug choice for employer-insured non-elderly patients receiving first-time statin prescriptions. In the first half of our study period, 2005 to mid-2006, there were five comparable patented statins that varied in their tier levels across plans, and we find that the effect of this type of co-pay variation is modest, with an elasticity of -0.31. If the most prescribed statin, Lipitor, faced a $10 increase in its monthly co-pay in all plans, its prescribing share would only be reduced from 47.4 percent to 43.1 percent.

Our second goal is to determine whether the price responsiveness of prescribing is constrained by the difficulty of observing patients' plan formularies. To do so, we study a co-pay shock that was highly publicized and highly correlated across

[2] For clarity, we use "he" for the physician and "she" for the patient throughout the paper.

[3] Physicians can only prescribe one drug out of a given choice set, and switching costs are large. Thus, prescribing a more expensive drug than necessary could raise the risk of poor adherence, with negative consequences on health.

[4] Grundy et al. (2004) review recent long-term trials and their implications for recommended treatment guidelines.

[5] Source: IMS Health press release: "Top Therapeutic Classes by U.S. Spending."

[6] In our sample, 84 percent of new statin patients receive a drug that is expected to reduce their LDL cholesterol by 34 percent to 52 percent, and 5 of the 6 drugs in the choice set are able to achieve such reductions, with minimal therapeutic differences (Rosenson 2012). The sixth is an older statin, available as a generic, and somewhat less potent than the others.

plans: the patent expiration of Zocor in mid-2006. Since generic drugs are always assigned the lowest co-pay tier in incentive-based formularies, Zocor's patent expiration brought about a $12.50 drop in its average monthly co-pay among employer-insured patients (Kaiser Family Foundation 2010). The resulting shift in its initial prescriptions was far larger than would be predicted based on the estimated co-pay effects described above.[7] We argue that this indicates physicians respond more strongly to *expected* co-pays than to actual co-pays. With a range of robustness checks, we test and reject alternate explanations for this divergence. Our estimates suggest that the prescribing response to idiosyncratic co-pay variation is approximately one-third as large as the response to a drug's average co-pay changes, with an estimated elasticity of -0.76 corresponding to the latter.

The third goal of this paper is to test for different price responses by patient income. The extent to which physicians are able to identify lower income patients, and choose a low-cost drug for them, reduces the scope of adverse consequences of high cost-sharing for other drugs. Since patient costs are typically unobserved by physicians, however, their ability to prescribe cost-effectively may depend on how well a patient knows her formulary and communicates with her physician. We find that lower income patients do not receive more cost-sensitive prescriptions when there is no prominent generic drug available. They do, however, experience a greater increase in the prescribing of a statin when it "goes generic." This suggests that despite being generally unaware of their patients' co-pays, physicians know that generic drugs are cheaper, and use this knowledge to provide lower income patients with more affordable drugs.

Exploring counterfactual scenarios, we estimate that providing physicians with perfect information on patient co-pays would reduce patients' out-of-pocket costs significantly, particularly for those with lower incomes. Patients with annual incomes below $50,000 would be prescribed drugs costing them $1.68 to $2.88 less per month, on average, while the predicted change for those with incomes above $80,000 would be only $0.09 to $0.97 per month. An auxiliary analysis of patient adherence supports the hypothesis that lower income patients are more cost-sensitive in their decision to continue taking a statin, a possible reason why physicians write more cost-sensitive prescriptions for them. The results of this analysis, however, do not suggest that giving physicians full information about co-pays would significantly improve adherence rates.

Other studies, which we review in Section 1A, have examined how doctors take into account the costs faced by their patients.[8] Our work departs from this literature in two ways. First, we differentiate between two types of cost variation, one of which is much easier for physicians to observe. While others have suggested that the difficulty of observing prices limits doctors' ability to act as agents for their patients (Shrank et al. 2005; Iizuka 2012), we are the first to estimate the magnitude of this information problem. Second, our ability to observe employee salaries, within a

[7] The model described in the previous paragraph would imply that, ceteris paribus, a $12.50 co-pay drop would increase Zocor's prescribing share from 19.1 percent to 22.8 percent. Once changes in Zocor's advertising are taken into account, however, the predicted change in its prescribing is actually negative.

[8] Iizuka (2012), Lundin (2000), Dickstein (2014), and Limbrock (2011) are some of the most relevant works.

subset of firms in our sample, allows us to examine heterogeneity by income. Most previous studies of cost-sharing focus either on employer-sponsored plans without income data or on low-income populations with government-subsidized insurance (e.g., Chandra, Gruber, and McKnight 2012 and Tamblyn et al. 2001). In a review of this literature, Baicker and Goldman (2011) state that the evidence that the lower income patients are more price-sensitive is "suggestive, but seems less than fully reliable." Our setting allows us to hold plan costs and policies constant in estimating the relationship between income and price sensitivity of prescribing.

This paper proceeds as follows. Section I describes the institutional setting and the statin drug class. Section II describes the data. Section III presents our conceptual framework. Section IV contains our empirical framework and results. Section V discusses robustness. Section VI presents estimated changes under counterfactual scenarios, and Section VII concludes.

I. Background

The key tool used by insurers to influence beneficiaries' drug choices is a tiered or "incentive-based" drug formulary, which assigns competing drugs different rates of coverage. From 2000 to 2014, the share of privately insured workers facing a formulary with three or more tiers grew from 29 percent to 80 percent, while plans with either two tiers or the same payment for all drugs became much less prevalent (71 percent to 15 percent) (Kaiser Family Foundation 2010). This shift has drawn substantial attention to the effects of patient cost-sharing, with most studies finding that cost-sharing in general, and tiered formularies in particular, reduce drug utilization and expenditures.[9] However, it is not clear how much of this reduction results from cost-sensitive prescribing as opposed to worse adherence to high-tier drugs.

A. *Physician Agency*

Traditionally, the duty of physicians has been viewed as selecting a treatment for a patient based on clinical evidence, irrespective of cost. In today's era of cost sharing, however, the medical community has discussed several reasons why physicians ought to consider patients' costs.[10] One reason is to improve patient adherence, a prerequisite of clinical benefit. A second reason is to minimize the economic burden of illness on patients.[11] In surveys, the vast majority of physicians express a desire to choose the least expensive drug for a patient when choosing between "equally effective and safe medications" (Shrank et al. 2005), and physicians treating patients

[9] A 10 percent increase in the price faced by the patient reduces drug spending by 2 percent to 6 percent, depending on drug class and patient health conditions, and the utilization change is largely driven by adherence rather than starting and stopping rates (Goldman, Joyce, and Zheng 2007).

[10] See, for example, Ginsburg (2009).

[11] A physician who is a perfect agent for a patient would consider not only the patient's health but also how the cost of treatment would impact her budget for non-health goods. In theory, this could make the optimal drug different from the "best" drug based on health impact alone, but many physicians would view this as an unethical choice. While the vast majority of physicians agree that it is important to minimize patients' out-of-pocket costs "when choosing between equally effective and safe medications" (Shrank et al. 2005; Khan et al. 2008), we are not aware of any studies that have asked physicians whether they would prescribe a slightly inferior medication that would greatly reduce a patient's costs.

from more distinct health plans prescribe a wider range of competing drugs within a class (Joyce et al. 2011).

Studies of physician agency in the choice of prescription drugs are primarily focused on non-US countries where there is greater variation in physicians' financial incentives to prescribe drugs, but less variation in cost sharing across patients. Studies find that physicians respond to financial motives to prescribe more expensive drugs (Iizuka 2007), but more so when treating insured versus uninsured patients (Lu 2014; Lundin 2000).

In contrast, physicians in the United States generally do not face direct financial incentives to prescribe specific drugs. Pharmaceutical promotion, however, has been found to significantly affect prescribing decisions (Gönül, Virabhak, and Shinogle 2005; Venkataraman and Stremersch 2007; Gonzalez et al. 2008; Ching and Ishihara 2010). This is relevant for our study since the advertising of a drug typically ceases at the time of its patent expiration. Due to their large market, statin manufacturers have historically done a significant amount of promotion, both direct to physicians (detailing, free samples) and direct to consumers (e.g., television advertisements). Looking at 26 patent expirations, Huckfeldt and Knittel (2011) find that total prescriptions for the patent-losing drug molecules actually decrease, by around 20 percent on average, due to the reduction in advertising after their patent expirations. However, as noted by Aitken, Berndt, and Cutler (2009) and Scott Morton and Kyle (2011), the case of Zocor typifies a "special class of exceptions" in which the potential price savings dominates the effect of advertising cessation: "the entry of a first generic in a large therapeutic class with close substitutes." (Scott Morton and Kyle 2011).

Iizuka (2012) examines the choice to prescribe a brand versus generic version of a drug in Japan, where some physicians not only prescribe but also sell drugs. He finds that, consistent with their private financial incentives, these physicians are more likely to prescribe the drugs with higher markups. Interestingly, however, he also finds that these physicians are more responsive to the brand/generic price difference faced by patients, suggesting that this information is not easily accessible to physicians who don't sell drugs themselves. In the United States, surveys find that despite a widespread reported desire to take patient costs into account, 60–70 percent of physicians "never or rarely" know a patient's pharmacy benefit structure or co-payments for different drugs (Shrank et al. 2005; Khan et al. 2008).

B. *Other Influences on Drug Choice*

Since our data consist of *filled* (purchased) rather than *written* prescriptions, what we call the "physician prescribing decision" is the final output of a series of actions that begin and end with the physician. Since the physician must approve any prescription switch suggested by any other party, we think of pharmacist and patient requests as mechanisms through which the physician learns about the co-pays, co-pay sensitivity, and drug preferences of a given patient.

Most individuals in our sample (81 percent) fill their first statin prescription at a retail pharmacy, while the rest purchase by mail. Surveys reveal that it is usually at the pharmacy that a patient first learns her co-pay for the drug prescribed (Shrank et

al. 2006). In some cases, this results in a pharmacist calling the physician to request a switch to a drug with more generous coverage.[12] This is referred to as *therapeutic interchange*: replacing a prescription for a similar, but not molecularly identical, drug, and requires physician approval.

In contrast, *generic substitution* (supplying a generic version of a prescribed drug molecule) does not require contacting the prescribing physician. In all 50 states, pharmacists are either mandated or allowed to offer patients generic versions of a multisource molecule (one that is sold by generic manufacturers), as long as the prescriber has not explicitly prohibited it (Pharmacist's Letter 2006). Partly due to these policies, generic substitution is now extremely common once a generic version of a drug is available, regardless of whether the physician has written the brand or generic name of a molecule.[13] Thus, in this study, we do not focus on whether prescriptions for a multisource drug result in a generic fill, but rather, on the prescriber's choice of drug molecule. We use "generic prescription" to refer to the prescription of a multisource drug, which, among statins, results in a generic fill more than 95 percent of the time.

Finally, apart from drug formularies, insurers and pharmaceutical benefit managers have other ways of influencing prescribing: they can implement various restrictive policies termed "utilization management strategies." For example, *step therapy* requires a patient to have tried a low-cost (Tier 1 or Tier 2) drug prior to purchasing other more costly drugs. *Prior authorization* requires the prescribing physician to document a patient's need for a specific medication prior to its approval for coverage. Limbrock (2011) estimates the average effect of these unobserved insurer strategies through the additional increase in prescribing probability of each plan's "preferred" (lowest tier) drugs beyond the effect explained by the co-pay difference. He finds that these effects are stronger in HMO plans (equivalent to a $8.57 co-pay discount) than in other plans ($4.85 co-pay discount). In an experiment of hypothetical prescriptions to vignette patients, Epstein and Ketcham (2014) find that prior authorization policies greatly reduce a drug's prescribing, but only when physicians are able to observe these policies.

C. *The Statin Drug Class*

Statins are the first-line recommended drug treatment for high cholesterol, and long-term studies have demonstrated their efficacy in preventing cardiac events and the emergence of heart disease (Grundy et al. 2004). All statins are available in several strength (dosage) levels, which reduce blood levels of low-density lipoprotein (LDL) cholesterol by different amounts. Higher strength formulations achieve

[12] Only 25 percent of physicians believe that it is their responsibility to prescribe preferred drugs, while 68 percent believe it is the pharmacists' responsibility to check a drug's formulary status. The same physicians report that about 20 percent of their prescriptions result in a pharmacist's call about nonformulary status, and that in 53 percent of these cases, they approve prescription changes (Shrank et al. 2005).

[13] Most plan formularies now require patients to pay the highest levels of cost-sharing for brand versions of multi-source molecules, and sometimes the full retail price difference between the brand and generic versions, which also contributes to this trend.

TABLE 1—STATINS COMMERCIALLY AVAILABLE IN 2005–2007

Brand (generic)	Share of initial Rx (2005)	LDL reductions expected at available dosage levels	Patent status (2005–2007)
Lescol (fluvastatin)	0.00	17–35 percent	On-patent
Mevacor (lovastatin)	0.05	19–31 percent	Off-patent since 2001
Pravachol (pravastatin)	0.04	22–40 percent	Expired April 20, 2006
Zocor (simvastatin)	0.16	26–50 percent	Expired June 23, 2006
Lipitor (atorvastatin)	0.51	39–57 percent	On-patent
Crestor (rosuvastatin)	0.09	45–63 percent	On-patent
Vytorin (simva., ezetimbe)	0.14	47–65 percent	On-patent

Notes: Each statin is available in a range of dosage levels, typically 10mg, 20mg, 40mg, and 80mg, and each drug-dosage combination is associated with an expected percentage reduction in LDL cholesterol. The ranges shown above are determined from the expected LDL reductions at the lowest and highest commercially available dosage levels of each statin. Shares of initial prescriptions are determined from our data, described in the following section.

Source: Grudy et al. (2004)

greater LDL reductions, but also pose a higher risk of side effects.[14] For this reason, high doses of less potent statins are prescribed less often than low doses of more potent statins.[15]

Table 1 shows the range of expected LDL reductions associated with each statin available in 2005, shown in ascending order of potency. We define these statins as the choice set for our analysis, excluding Lescol, which received virtually no initial prescription. In our main analysis, we leave aside the choice of dose, but we show in a robustness check that our results are not sensitive to this.

As Table 1 shows, the only statin available as a generic in 2005, Mevacor, was less potent than the statins commonly prescribed at that time. During our study period, the patents of two more statins expired. One of these, Zocor (simvastatin), was the second most prescribed statin at the time of its patent expiration, and has potency comparable to Lipitor, the most commonly prescribed statin. Slightly less potent Pravachol (pravastatin) also lost its patent, but was much less commonly prescribed beforehand. As Figure C1 shows, for both of these drugs, generic versions rapidly overtook the full share of initial prescriptions for their respective molecules. The two newest drugs, Crestor and Vytorin, are substantially more potent than Zocor.[16]

There is typically some media attention preceding the patent expiration of a major drug. Being Merck's highest grossing drug at the time, and the top competitor to Lipitor, the highest grossing drug in the United States at the time, Zocor's patent expiration was the topic of 289 news articles in 2006, bolstering our assumption that physicians who prescribe statins were aware of this event.[17]

[14] Statins are generally well tolerated. Muscle symptoms including soreness, stiffness, tenderness, and weakness, are estimated to affect 5 to 10 percent of statin users, while more serious adverse effects (liver damage and rhabdomyolysis) are exceedingly rare (Rosenson 2012, Baker and Rosenson 2012, Joy and Hegele 2009).

[15] In Table A1, we show prescribing probabilities by dose, by statin.

[16] Vytorin is a combination of simvastatin with ezetimbe. We include it in our choice set since it is used as a first-line treatment for high cholesterol.

[17] Author's Lexis-Nexis search for articles with "Zocor" or "simvastatin" in the headline, and "generic" in the body, from six months prior to the patent expiration to six months after.

II. Data

The data used in this paper come from the full medical and pharmaceutical claims for over 150 distinct employee and retiree plans offered by 29 Fortune 500 firms from 2004–2007, with full-year coverage of 1,440,020 primary beneficiaries and 3.0 million lives in 2006. We limit our study to non-retired workers and their dependents between the ages of 30–64.[18]

The drug claims include detailed information on each drug fill, including NDC (National Drug Code), days supplied, place of fill (mail or retail, in/out of network), and all amounts paid (co-pay or coinsurance, amount paid by plan, deductibles and other non-covered amounts paid by patient). Drug fills were matched by NDC to Thompson Redbook data, to obtain drug name, strength, and generic status. Through the corresponding medical claims, rich medical information is available for the length of each patient's tenure within the claims data. We use diagnosed chronic conditions and other drugs purchased, as well as age, sex, and three-digit zip code of residence. In addition, in 12 of the firms, employee salaries are reported in $10,000 bins ranging from *under $50,000 including missing* to *above 250,000*. In online Appendix C, we describe a few simple corrections we made in cleaning the salary variable and converting it to a continuous measure.

We define an initial prescription as a patient's first fill in the statin class after at least one year, using the 2004 data solely to identify which 2005 statin prescriptions fit this definition.[19] Of those who are observed for 2 years prior to an initial prescription, 15 percent had at least 1 statin fill between 730 and 365 days before the "initial" fill used in the analysis. We control for this occurrence, and for the specific statin most recently purchased in the analysis.[20]

Individual prescribers can be tracked through masked identifiers. However, a large number of prescribers appear in the data (15,775 in our final sample) with few prescriptions across all drug classes (median = 6, ninty-nineth percentile = 317). In our sample of initial prescriptions, 40 percent have unique prescribers, and only 17 percent come from 1 of 476 prescribers with 7+ initial fills. Lacking information on physician areas of specialty, we calculate each prescriber's share of prescriptions for cardiovascular drugs (the therapeutic group containing statins, antihypertensives, and other drugs frequently prescribed by cardiologists), and impute a "cardiac specialist" dummy equal to 1 if more than 60 percent of a physician's observed prescriptions are for cardiovascular drugs.[21]

[18] Medicare Part D, which offers pharmaceutical benefit plans to Medicare beneficiaries, came into effect in 2006, during the period we study. While this reform did not directly affect retirees who already received pharmacy benefits from their employer, it is difficult to rule out indirect effects on retiree plan co-pays or on prescribing toward the elderly. To avoid these complications, we exclude retirees and elderly employees from our sample.

[19] In looking back at the previous year's prescriptions, we require that patients were covered by the same employer (though not necessarily in the same specific plan, because some plans change codes from one year to the next) over the entire previous year.

[20] Our results do not change, however, if we exclude all individuals for whom we have seen any prior statin use (see online Appendix Table A11).

[21] The distribution is bimodal (see online Appendix Figure C2), suggesting 0.6 as a natural breakpoint.

A. *Advertising Data*

We use data from IMS Health on national advertising expenditures by drug, by quarter, starting in 2004 to allow us to estimate immediate and lagged effects over the entire sample period. We use quarterly DTP, the total expenditures by each drug's manufacturer on direct-to-physician promotion. This measure aggregates spending on detailing, medical journal advertisements, and samples.

B. *Defining Key Variables*

In our analysis of prescribing, the key independent variable is plan co-pay. While the claims data report exact out-of-pocket payments for each drug fill, these vary by place of fill, number of days supplied, and, occasionally, for reasons we cannot identify. For the conditional logit analysis done below, we must know the prices faced by each patient for options that were not chosen, and we must use a standard co-pay definition that does not depend on place or size of fill. We define as "standard" the most common type of fill: a 30-day prescription filled at an in-network retail pharmacy.[22]

Using plan identifiers, we empirically identify each plan's standard co-pay for each statin in each quarter within 2005–2007. Specifically, we impute each drug's co-pay at the plan-quarter level as the modal value paid by members of that plan making a "standard" purchase as defined above, with no deductible charged on the same purchase. We consider a plan's co-pays to be accurately defined if its imputed co-pays are within $1 of the patient's observed out of pocket payments in at least 90 percent of all observed initial fills that fill the standard purchase criteria, and limit our main sample to these plans.[23]

After defining co-pays, we define the number of tiers in each plan, by quarter, as the number of distinct co-pay levels (modes separated by $1+ dollars) occupied by the six statins. We exclude from our sample the plans that place all drugs on one tier and the plans that use coinsurance drug payments, since our goal is to study the effectiveness of co-pay incentives in the form of co-pay tiers.[24] Online Appendix C provides more details on the co-pay imputation process and compares average co-pays across our main sample, the remaining sample, and the Kaiser Family Foundation's survey of employer-sponsored plans. Unless otherwise noted, all of our figures and tables pertain to the main sample.

We use a similar method to impute average plan payment (the cost paid by the insurer for each prescription fill) by drug, by quarter.[25] Since insurers can adopt measures outside of co-pays to influence patients' drug utilization, and are more likely to do so when they can save significantly on drug costs, we include the plan

[22] This specification overestimates the long-term co-pay differences between drugs, in dollars, since some patients will begin filling prescriptions in large quantities, by mail, once they are settled on a long-term drug. Co-pays can be 30–40 percent lower when filled by mail in 90-day quantities.

[23] We also exclude 1,168 prescriptions from small plans with missing imputed co-pays at any time, meaning that in an entire year, zero beneficiaries filled a 30-day prescription for one of the six statins.

[24] Of the 1,751 prescriptions from one-tier plans, 89 percent come from one firm with $0 co-pays for all statins. We drop 36 prescriptions from plans that include coinsurance payments.

[25] Instead of the modal value in each plan/quarter, we use the average per day value multiplied by 30.

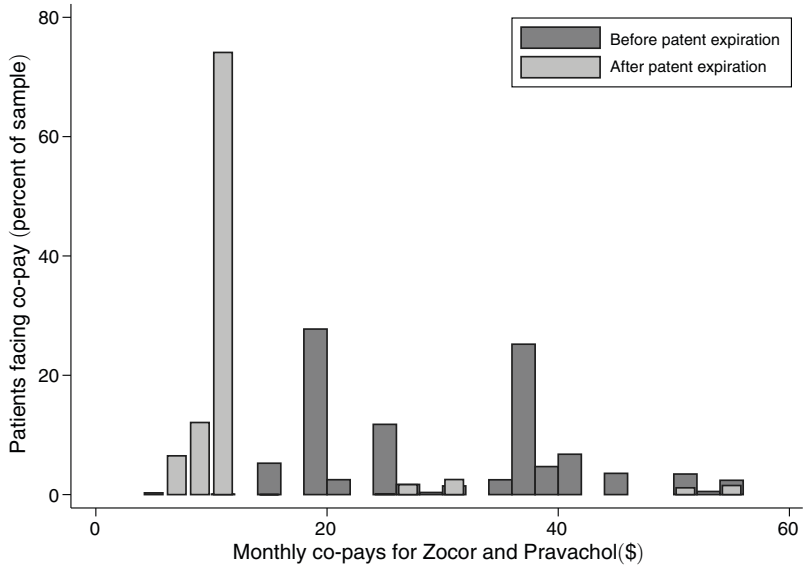

Figure 1. Distribution of Plan Co-pays for Patent-Losing Drugs

Notes: This histogram shows how co-pays varied across plans for two drugs in our sample (Zocor and Pravachol), when they were still on patent (dark gray bars) versus when they became available in generic formulations (light gray bars). The height of each bar represents the share of patients in our sample who faced a given monthly co-pay for Zocor or Pravachol at the time of their initial statin prescription.

cost variable that we observe in our analysis. A caveat is that insurers often receive rebates from drug companies, making their effective price paid lower than the payment we observe. Such rebates are not publicly disclosed and not included in our data. As a result, the plan payment measure we observe fails to capture some of the cross-sectional variation in plan payments for a drug at a given point in time. Nevertheless, including this variable improves the explanatory power of our analysis, suggesting that it is informative despite being imperfect.

Figure 1 illustrates the variation in Zocor and Pravachol's co-pays across plans, as well as the shift in this distribution after their patent expirations. Figures 2 and 3 plot the average co-pay and plan payment, respectively, per 30-day supply of each drug in our main sample over the sample period. The average co-pay of the Zocor molecule has its largest drop between the second and third quarters of 2006, coincident with its patent expiration and the entry of the first generic manufacturer. The cost paid by plans, however, decreased more in the third quarter after Zocor's patent expiration, coincident with the end of the 180-day exclusivity period of the first generic manufacturer, under the Hatch-Waxman Act.

Figure 4 plots the changes in direct-to-physician drug advertising expenditures over the sample period. Both Zocor and Pravachol experienced dramatic reductions at the time of their patent expirations, but Zocor's reduction was larger due to its higher initial level of promotional spending.

Figure 5 plots the initial prescribing shares of each statin in our sample from 2005–2007, demonstrating the sizeable increase in the prescribing of Zocor after

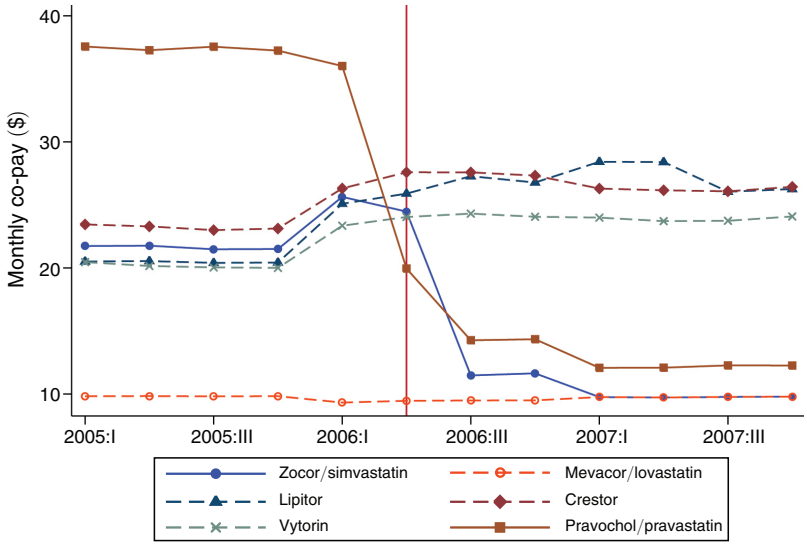

FIGURE 2. AVERAGE CO-PAYS BY MOLECULE, 2005–2007

Notes: The vertical line marks the quarter during which the patents of Zocor (simvastatin) and Pravachol (pravastatin) expired, on June 23 and April 20, respectively. Co-pays are based on the modal value within a plan-quarter for a retail purchase of a 30-day supply at an in-network pharmacy and then averaged over the sample.

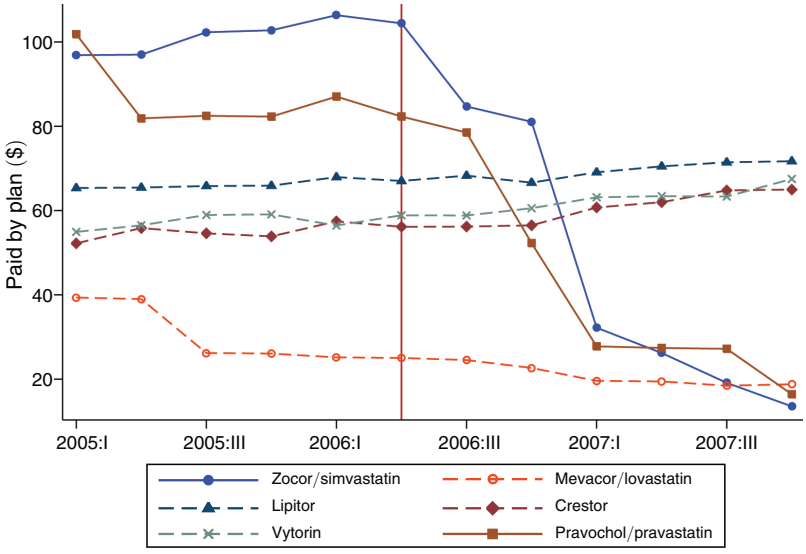

FIGURE 3. AVERAGE PLAN PAYMENTS BY MOLECULE, 2005–2007

Notes: Average plan payments are based on the reported payments in our data for all purchases of each statin, adjusted to be equivalent to a 30-day supply of the medication. The vertical line marks the quarter during which the patents of Zocor (simvastatin) and Pravachol (pravastatin) expired, on June 23 and April 20, respectively.

its patent expiration. There was no visible increase in the prescribing of Pravachol (pravastatin) following its patent expiration in April 2006, perhaps because it was already largely dominated by Zocor.

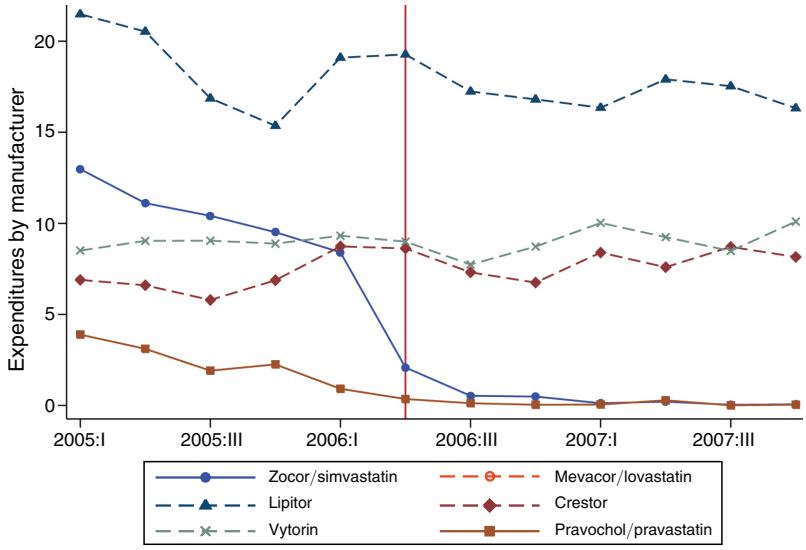

FIGURE 4. QUARTERLY EXPENDITURES ON DIRECT-TO-PHYSICIAN ADVERTISING BY MOLECULE, 2005–2007

Notes: Direct-to-physician advertising expenditures are shown in units of $10 million, and represent the sum of detailing expenditures, print advertisements in medical journals, and drug samples given to physician offices. The vertical line marks the quarter during which the patents of Zocor (simvastatin) and Pravachol (pravastatin) expired, on June 23 and April 20, respectively.

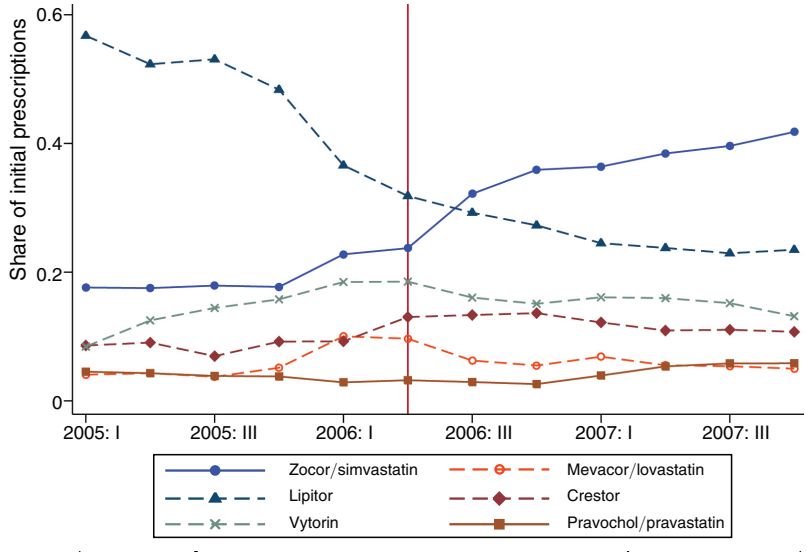

FIGURE 5. INITIAL PRESCRIPTIONS OVER TIME, 2005–2007

Notes: The vertical line marks the quarter during which the patents of Zocor (simvastatin) and Pravachol (pravastatin) expired, on June 23 and April 20, respectively. Initial prescriptions are defined as the first statin purchase observed after at least one year without any statin purchase, among patients observed in the sample continuously for at least the past year.

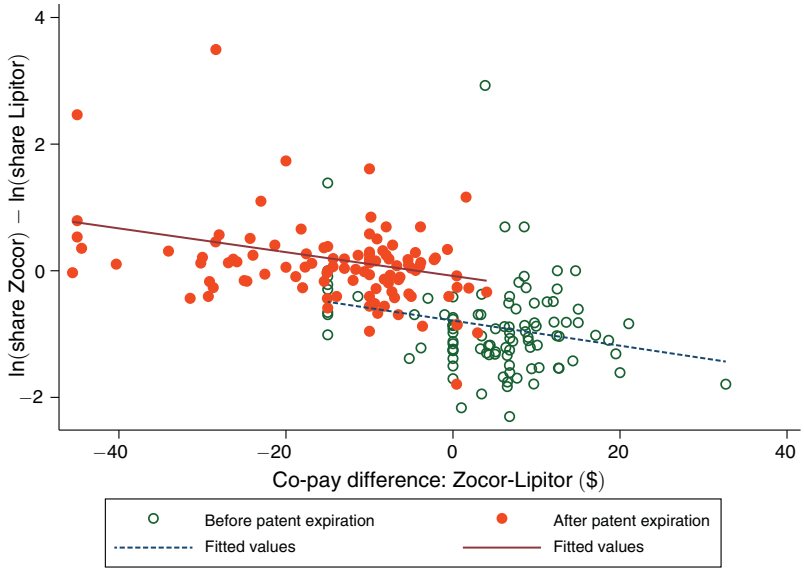

FIGURE 6. PLAN-LEVEL PRESCRIBING OF ZOCOR VERSUS LIPITOR, BY CO-PAY DIFFERENCE

Notes: Each plan in the sample is represented by one point in the period prior to Zocor's patent expiration and another point in the period afterward. The log-odds ratio of Zocor to Lipitor prescriptions $\left(\ln\left(\frac{\Pr(Zocor)}{\Pr(Lipitor)}\right)\right)$ is plotted against the relative difference in their co-pays, averaged within plan over the pre- or post-expiration period. The fitted values show the best linear fit in each time period, with plans weighted by the number of initial prescriptions they represent in the sample.

Interestingly, however, the plan-specific increase in the prescribing of Zocor relative to Lipitor was not strongly tied to the plan-specific changes in their relative co-pays. Figure 6 shows this visually. For each plan and each period, we plot the log-odds ratio of being prescribed Zocor rather than Lipitor $\left(\ln\left(\frac{\Pr(Zocor)}{\Pr(Lipitor)}\right)\right)$ against the relative difference in their co-pays by plan. The logit model posits a linear relationship between this quantity and the within-plan price difference between Zocor and Lipitor. Therefore, the slope of the fitted line for the period prior to Zocor's patent expiration demonstrates the effect of plan formularies on prescribing choice in this period. If this relationship correctly predicted the response to Zocor's patent expiration, we would expect the points representing the post-expiry period to fall along the same fitted line, extending to the left along with Zocor's co-pay drop relative to Lipitor. Instead, we see an upward shift of the entire demand curve, indicating that the increase in Zocor's prescribing cannot be explained by the responsiveness of prescribing to cross-sectional variation in co-pays. This is the puzzle that this paper seeks to explain.

III. Conceptual Framework

Our first objective is to estimate how the prescribing decision responds to cross-plan variation in co-pays. Physicians might consider co-pays either to improve the

chances of patient adherence or simply to decrease the economic burden of treatment. We do not attempt to distinguish between these motivations, but simply to measure the net effects of patients' co-pays on the drug prescribed.[26]

Suppose the physician's utility from prescribing drug j to patient i is a function of the patient's expected therapeutic benefit from the drug (w_{ij}) as well as her income and the co-pay she would pay for this drug, $U_{ij}(w_{ij}, Copay_{ij}, Salary_i)$. Using a conditional logit model and cross-plan variation in the relative co-pays of different drugs, we will test the null hypothesis that $dU/dCopay = 0$. The therapeutic benefit of drug j for patient i is captured by drug-specific constants interacted with each of the observable patient characteristics that enter the Framingham heart risk calculations (age, gender, diagnosed health conditions, previous heart attack) along with an EV1 error term ϵ_{ij}. Our identification of $dU/dCopay$ relies on the following assumption:

ASSUMPTION 1: *Conditional on observed patient characteristics, the relative therapeutic benefit of two drugs is not correlated with their relative co-pays.*

This assumption would be violated if patients sorted themselves into plans that preferentially priced the statin that they use. Since we focus on first-time prescriptions, this is not a major concern, but we conduct related robustness checks in Section VB.

Our second objective is to determine whether the response of prescriptions to actual co-pays is constrained by the difficulty of observing them. Suppose a physician's perceived co-pay of drug j for patient i is characterized as $\tilde{p}_{ij} = \lambda p_{ij} + (1 - \lambda)\bar{p}_j$ where p_{ij} is the patient's actual co-pay and $\bar{p}_j$ is the average co-pay of brand (generic) drugs, which we assume physicians use as their co-pay prior for brand (generic) drugs when treating a patient with private insurance coverage. The parameter λ can be readily interpreted as the probability with which a physician observes the true co-pays of a given patient, or, more broadly, the share of plans' idiosyncratic co-pay variations that are perceived by the average physician.

Estimating $dU_{ij}/dCopay_{ij}$, described above as our first objective in this paper, can now be seen as recovering an estimate of $\alpha_i \lambda_i$, where α_i captures the physician's response to the *perceived* co-pay of patient i, and $0 \leq \lambda_i \leq 1$ dampens this response, due to the imperfect observation of p_{ij}. Therefore, the simple model of prescribing as a function of patient co-pay might severely underestimate how physicians would respond to more easily observed co-pay changes.

To estimate an average value of α_i, we take advantage of the large and highly publicized shock in co-pays that occurs when a drug loses its patent. For each observed prescription, we decompose each drug's co-pay into $\bar{p}_{jt}$ and $p_{ijt} - \bar{p}_{jt}$, where $\bar{p}_{jt}$ represents the national average co-pay of brand or generic drugs (depending on the patent status of drug j at time t) among employer-insured plans. Thus, $dU_{ij}/d\bar{p}_{jt}$ is primarily identified by the overall shift in prescribing of Zocor and Pravachol after their patent status changed in mid-2006, and can be interpreted as the predicted

[26] As noted in Section IC, the choice of drug purchased is a joint decision between the physician who prescribes the drug, the pharmacist who fills the prescription, and the patient who takes the drug. Therefore, an empirical response to patient co-pays might also reflect patients' information and specific drug requests.

effect on prescribing if all plans were to change their co-pays for the same drug in unison, by the same amount. In contrast, $dU_{ij}/d(p_{ijt} - \bar{p}_{jt})$ is identified both by within-period variation across plans in how often different statins are prescribed, relative to their co-pays, and also, by the size of the plan-specific shift toward Zocor prescribing after its patent expiration, relative to the plan-specific co-pay change. Our measure of this partial effect can be interpreted as the predicted change in prescribing when only one small plan changes its co-pay, while all other plans hold theirs constant.[27]

Under the following assumptions, we can estimate α, the parameter that captures how physicians respond to the perceived co-pays of their patients, as $dU_{ij}/d\bar{p}_{jt}$, using the exogenous co-pay shocks of Zocor and Pravachol caused by their patent expirations for its identification. We can also estimate λ as the ratio between the price responses attributed to idiosyncratic co-pays and to average co-pays:

$$\lambda = \frac{dU/d(p_{ijt} - \bar{p}_{jt})}{dU/d\bar{p}_j t}.$$

We will test the null hypothesis that $\lambda = 1$, which would mean physicians perfectly observe patients' co-pays, and thus, respond similarly to co-pay changes that are correlated across plans and those that occur only in one small plan.[28]

ASSUMPTION 2: *Physicians are fully aware of when Zocor's patent expiration occurred and the corresponding drop in its average co-payment among patients with private insurance.*

ASSUMPTION 3: *The expected therapeutic benefit of each drug is constant over the 2005–2007 period, and does not differ between a drug's brand and generic formulations.*

ASSUMPTION 4: *A plan's co-pay difference between brand and generic drugs is not correlated with unobservable patient characteristics.*

ASSUMPTION 5: *The distribution of unobserved characteristics of patients starting statin prescriptions is similar before and after Zocor's patent expirations.*

ASSUMPTION 6: *Conditional on the observed plan payments and advertising expenditures, variation in plans' non-co-pay strategies to influence prescribing are uncorrelated with patent expiration.*

[27] The interpretation requires assuming that the plan changing its co-pay is too small to change the national average. If the plan undergoing co-pay change Δ covers share s of all privately insured adults, then the effect of the co-pay change on prescribing within the plan will be $\Delta[\beta_1 s + \beta_2(1 - s)]$, i.e., slightly larger than the effect of a small plan's co-pay change because it also operates through changing the national average co-pay.

[28] This is equivalent to measuring $dU_{ij}/dCopay_{ij}$ (without decomposing into an idiosyncratic component) along with $dU_{ij}/d\bar{p}_{jt}$ and testing that the latter equals zero, as it should if physicians respond only to each patient's true co-pay.

If Assumption 2 fails because not all physicians are aware of the change in patent status, then our estimate of α will be biased toward zero. Similarly, if some physicians shifted their prescribing toward the patent-losing drugs in advance of their patent expirations, foreseeing that their patients would save money later, our estimate of α will be biased toward zero. We discuss and test this in Section VC. We also consider the implications of expectational error in $\bar{p}$, i.e., the fact that we do not observe physicians' co-pay expectations, in Section VA.

If Assumption 3 fails, then Zocor and Pravachol may be prescribed less often after their patent expiration because their generic versions are less desirable than their brand versions, and α will be biased toward zero. In online Appendix B, we show that controlling for patient costs, the brand/generic status of a drug has no effect on patients' adherence to it. This suggests that patients are just as satisfied with the generic versions of Zocor and Pravachol as they would be with the brand versions at the price of the generic. In Section VD, we address the possibility that the perceived relative therapeutic benefits of different statins might be changing over time.

Assumptions 4 and 5 are necessary for our approach to correctly identify α and λ, for the same reason that Assumption 1 is needed to estimate the effect of co-pays on prescribing. In Section VB, we show that the variation in brand-generic co-pay differentials across firms is far greater than the variation across plans within firms, and our results are robust to excluding the firms in which endogenous plan choices are most likely to be problematic. This evidence is supportive of Assumption 4.

Assumption 5 could be violated if physicians respond to the patent expiration by prescribing statins more broadly, e.g., to a wider set of patients who might be more price-sensitive, or in less need of a statin, than those receiving statin prescriptions earlier. In Table 2, we show demographics and diagnosed health conditions for the patients in our sample before and after the patent expirations of 2006. We see no statistically significant changes in age, gender, average salary, or imputed heart risk of statin initiators across the two time periods.[29] We do see changes in some diagnoses of statin-related chronic conditions, but these generally match the trends we see across all individuals covered in the claims database who would be considered statin-eligible, as well as those who never fill a statin prescription (Table A2, panel B). Furthermore, the changes in observables are similar between patients above and below the median salary, in our sample (Table A2, panel A). This is consistent with the finding of Dunn (2012) that conditional on insurance coverage, income does not affect the likelihood of taking any statin versus no statin.

We also investigate changes in patients' generic share of all drugs purchased in the past year, a proxy measure of price sensitivity or willingness to try generic drugs. If the patent expiration led to an influx of new patients who are more price sensitive than previous starters, we would expect this variable to increase more within our sample of new patients than within the overall population of statin-eligible patients.

[29] Imputed heart risk is the Framingham heart risk score, which estimates the 10-year risk of a cardiac event based on risk factors such as age, gender, blood pressure, and diabetes. For the risk factors that we do not observe, such as smoking and cholesterol level, we use the average values based on the exact combination of factors that we do observe, taken from the nationally representative NHANES dataset.

Table 2—Descriptive Statistics of Statin Initiators, before and after Zocor's Patent Expiration

	Prior to the patent expiration of Zocor		After the patent expiration of Zocor		Difference	
	N (1)	Mean (2)	N (3)	Mean (4)	Post-pre (5)	*P*-value (6)
Panel A. Demographic characteristics						
Age	11,895	50.18	16,662	50.12	−0.05	0.54
Male	11,895	0.57	16,662	0.56	−0.01	0.19
Salary (thousands of dollars)	4,707	71.88	8,040	71.66	−0.22	0.77
Panel B. Relevant health characteristics						
High cholesterol (0/1)	11,895	0.181	16,662	0.195	**0.01**	0.00
Hypertension (0/1)	11,895	0.205	16,662	0.233	**0.03**	0.00
Diabetes (0/1)	11,895	0.131	16,662	0.144	**0.01**	0.00
Cardiac disease (0/1)	11,895	0.094	16,662	0.086	**−0.01**	0.02
Past heart attack (0/1)	11,895	0.024	16,662	0.026	0.00	0.50
Imputed heart risk	11,895	0.051	16,662	0.050	0.00	0.25
Panel C. Drugs purchased in the past year						
Number of unique drugs	11,895	4.99	16,655	5.09	0.11	0.05
Generic share of unique drugs	10,632	0.60	15,029	0.65	**0.05**	0.00
Panel D. Plan co-pays (*1 month supply*)						
Brand statins	11,895	$25.67	16,662	$25.95	**$0.28**	0.002
Generic statins	11,895	$10.10	16,662	$10.97	**$0.87**	0.000
Panel E. Initial statin prescription						
Prescribed by cardiac specialist	11,895	0.072	16,662	0.066	**−0.01**	0.049
Generic statin	11,895	0.080	16,662	0.475	**0.39**	0.000
Co-pay (1 month supply)	11,895	$22.03	16,662	$18.14	**−3.89**	0.000

Notes: *P*-values of a *t*-test of mean equality are shown. Differences that are significant at the 5 percent level are bolded. Salaries are only available for a subset of the firms in our sample. "Past heart attack" is coded as one if the patient has any medical claim with an ICD9 code representing myocardial infarction during their prior years of coverage in the claims data. "Imputed heart risk" is the imputed ten year risk of a cardiac event (Framingham score) based on observed characteristics. "Number of unique drugs" counts any drugs filled at least once in the 365 days prior to the first statin fill, and "generic share" is the share of these drugs that are generic. "Prescribed by cardiac specialist" is imputed to be 1 if the prescribers observed prescriptions for cardiac drugs exceeds 60 percent.

Tables 2 and A2 show that, much like the other observables, the trends for this variable are roughly equal across new patients and all patients with a risk factor for a statin, and above- and below-median salary patients in our sample.

Lastly, Assumption 6 could be violated by changes, at the time of the patent expiration, in plans' use of non-co-pay strategies to influence prescribing of a particular drug. For example, if some insurers had policies requiring patients to try a generic statin before a brand statin would be covered, then our estimate of $\frac{dU}{d\overline{p_{jt}}}$ would be biased away from zero. While these actions are not observed in our data, an examination of Medicare Part D formularies from 2006–2010 shows that policies such as step therapy and prior authorization were rarely used in the statin drug class, predominantly used in more expensive, specialty drug classes, and not commonly adopted in response to the patent expirations of other major chronic drugs (Hargrave et al. 2010). Nevertheless, in Section VE, we implement several robustness checks to verify that such unobserved plan actions are unlikely to influence our results.

Finally, our third objective is to test whether α and λ vary with patient income. We hypothesize that the weight physicians aim to put on a patient's cost is negatively

correlated with the patient's income ($d|\alpha|/dSalary_i < 0$) because lower income patients are generally less likely to adhere to treatment, likely to be more price sensitive, and physicians might care more about their economic burden of illness.

IV. Empirical Specification and Results

A. *Prescribing Response to Co-pays Prior to the Patent Expirations*

We begin by examining the initial prescribing decision in the period prior to the 2006 patent expirations of Zocor and Pravachol. Table 3 reports results of a conditional logit model in which the choice set includes the six drugs: Crestor, Lipitor, Mevacor (available as generic: lovastatin), Pravachol, Vytorin, and Zocor. The specification estimated is

$$
\begin{aligned}
(1) \qquad U_{idj} = {} & T_j + X_i B_j + \beta_1 Copay_{ij} + \beta_2 PlanCost_{ij} \\
& + \beta_3 DocLastStatin_{jd} + \beta_4 PatLastStatin_{ij} + \gamma_0 DTP_{j,t} \\
& + \gamma_1 DTP_{j,t-1} + \gamma_2 DTP_{j,t-2} + \gamma_3 DTP_{j,t-3} + \epsilon_{ijd},
\end{aligned}
$$

where i indexes patients, d indexes prescribers, and j indexes the six drug alternatives. T_j is a fixed effect for each drug molecule, representing a baseline perceived therapeutic value of drug j. The patient characteristics included in X_i (diagnosed conditions, age, prescribed by specialist, and gender) can affect the perceived value of each drug separately, through B_j. $DocLastStatin_{jd}$ is an indicator for the drug most recently prescribed by doctor d to another patient starting statin therapy, meant to capture habit persistence within the doctors who appear more than once in our sample. $PatLastStatin_{ij}$ indicates whether statin j was the last statin taken by a patient, for those patients who have taken statins in the past despite having a one-year "clean" window.[30]

The coefficient of interest, β_1, captures how the plan-specific co-pay for drug j influences its choice value for a patient. Columns 1–2 of Table 3 estimate equation (1) on our main sample, with and without the aforementioned patient characteristics included.[31] Notably, including these characteristics only shifts the co-pay coefficient from −0.183 to −0.186. The average marginal effect of Zocor's co-pay on its prescribing rate is shown at the bottom of Table 3. With controls, a $10 decrease in Zocor's co-pay, holding those of other drugs constant, increases Zocor's prescribing share by 2.3 percentage points on average (relative to a mean of 20.3 percent). This is a small effect, given that a $10 change is a 43 percent decrease. Across all drugs in the choice set, we estimate the elasticity of prescribing to co-pays to be −0.305. The point estimate of $DocLastStatin_{jd}$ indicates that it takes a $36 co-pay reduction,

[30] We observe that 11.9 percent of the patients in the sample have received a statin previously, and 58 percent of them are restarted on the last statin they took (for which $PatLastStatin = 1$). For all other patients, $PatLastStatin = 0$ for all drugs in the choice set.

[31] The coefficients for patient characteristics interacted with each drug are shown in online Appendix Table A3, panel B.

Table 3—Co-pay Effects on Initial Prescription, Prior to the 2006 Patent Expirations

	All firms		Firms reporting salaries	
	(1)	(2)	(3)	(4)
Co-pay (in $10)	−0.183	−0.186	−0.165	−0.160
	(0.046)	(0.045)	(0.054)	(0.054)
× Salary (in $10,000)				−0.0044
				(0.007)
Plan payment (in $10)	−0.015	−0.017	−0.029	−0.028
	(0.03)	(0.03)	(0.04)	(0.04)
Advertising (in $10 mill.)	0.11	0.11	0.08	0.08
	(0.03)	(0.03)	(0.03)	(0.03)
Doctor's last prescription	0.68	0.68	0.83	0.83
	(0.05)	(0.05)	(0.08)	(0.08)
Patient characteristics	No	Yes	Yes	Yes
Observations	9,278	9,278	3,427	3,427
log likelihood	−13,042.38	−12,959.45	−4,909.968	−4,909.748
AME of $10 co-pay increase	−0.023	−0.023	−0.021	−0.020
	(0.009)	(0.009)	(0.009)	(0.009)
Elasticity	−0.305	−0.310	−0.275	−0.266

Notes: Conditional logit coefficients. Standard errors in parentheses, clustered at the plan-quarter level. These models estimate how the cost of different statin drugs affect their probability of being purchased as an initial prescription in the periods from January 1, 2005 until the end of 2006 quarter 1, the quarter prior to the patent expirations of Zocor (June 23) and Pravachol (April 20). To qualify as an initial prescription, the patient must be observed in the data but not purchase any statin in the prior 365 days. The choice set contains the six most prescribed statin drugs, described in Section I. Co-pay is the imputed monthly co-payment that applies to patient *i* for drug *j* at the time of prescribing, in units of $10. Plan payment is the average cost paid by the plan for a 30-day fill of drug *j* at the time of prescribing, in units of $10. The advertising effect shown is the cumulative effect of the coefficients of quarterly DTP (direct-to-physician expenditures promoting drug *j*) and its first three lags. In column 4, salary represents the employee's salary in $10,000 increments normalized so that a value of 0 corresponds to the median salary ($50,000–$60,000). To capture habit persistence, doctor's last prescription is an indicator for the statin prescribed in the most recently observed initial prescription written by the same prescriber. Also included (not shown) is patient's last prescription, among those who were observed to purchase a statin prior to the one-year clean window. "Patient characteristics" indicates the inclusion of drug-specific intercepts interacted with diagnosed health conditions, age, gender, and "prescribed by a cardiac specialist." The estimates of these interactions are shown in online Appendix Table A3, panel B. Salary is allowed to influence the drug intercepts in other specifications shown in online Appendix Table A3, panel C. "AME" is the average marginal effect, in percentage points, of a $10 co-pay change on Zocor's prescribing share. In columns 3–4, the AME is calculated for the median salary patient. "Elasticity" puts the average marginal effect in elasticity terms, averaged over all drugs in the choice set.

all else equal, to overcome a physician's tendency to prescribe the same statin prescribed to his previous patient, in the period prior to Zocor's patent expiration.

In column 3, we estimate the same specification as in column 2 on the subsample of firms reporting patient salaries. Other than the coefficient for *DocLastStatin* being larger in the salary subsample, all estimates are within the confidence intervals of those of our main sample. In column 4, we include an interaction between salary and co-pay, to test whether physicians make more cost-sensitive prescriptions to lower income patients. The salary variable is measured in $10,000 and centered at the median salary ($55,000) so that the coefficient on co-pay represents the co-pay response for the median salary patient. We find that in the period prior to Zocor's

patent expiration, the relationship between co-pay and prescribing is not significantly influenced by a patient's salary.

We also include $PlanCost_{ij}$, the observed payment made by each insurer for each drug, despite its limitations noted in Section IIB. It appears insignificant in this period, with a point estimate only 9 percent the size of the estimated co-pay effect. This is likely because, as previously noted, this variable fails to capture rebates, which are an important source of cross-plan variation in actual drug costs. Note that drug-specific intercepts absorb the between-drug variation in cost over this period, and that within-drug changes in average cost are primarily limited to drops in the price of the two least commonly prescribed statins, Pravachol and lovastatin (see Figure 3).[32]

Quarterly data on direct-to-physician advertising expenditures are included $(DTP_{j,t})$, as well as three lags of this variable. The table reports the estimated cumulative effect of these variables, to be interpreted as the annual effect of a permanent increase of $10 million in quarterly DTP spending.[33] In the pre-period, this cumulative coefficient is estimated to be 0.11 and statistically significant. Based on the pre-period average of $75 million quarterly spending, this implies that a 13 percent increase in DTP spending has the same effect on prescribing as a $5.78 decrease in all patients' co-pays for a drug.

If this relationship between advertising and prescribing were to continue, we would expect to see a decline in Zocor's prescribing rate after its patent expiration, due to the fact that its advertising ceased (DTP expenditures dropped from $840,560 in 2006:I to $5,294 in 2006:IV) and the predicted impact of this cessation outweighs the predicted effect of its reduced co-pay (from $25.63 on average in 2006:I to $11.64 in 2006:IV). Figure 7 plots the predicted change in the initial prescribing shares of Zocor and Pravachol, based on the specification shown in Table 3, column 2, as well as the actual evolution of their prescribing. The stark difference between the predicted and actual prescribing of Zocor illustrates that its prescribing increase cannot be explained by the pre-period responsiveness of prescribing to co-pays.[34] We now turn to our preferred explanation for this difference, and in Section V we conduct several robustness checks to rule out other possible explanations.

B. *Breakdown into Two Types of Co-pay Responses*

As explained in Section III, we decompose co-pay into its expectation, $\bar{p}_{jt}$, and each patient's co-pay deviation from the expectation $(p_{ij} - \bar{p}_{jt})$, to compare physicians' responses to idiosyncratic plan variation in co-pays versus the large-scale co-pay changes induced by patent expiration. We define $\bar{p}_{jt}$ based on whether drug j was available as a generic in period t. If so, $\bar{p}_{jt}$ equals the national average co-pay

[32] Price endogeneity could also bias our estimate toward zero. The 2005 price reductions of the two least potent statins came after an August 2004 change in NCEP guidelines advocating more intensive statin therapy for higher risk patients; this change in perceived efficacy why the prescribing of less potent statins does not appear to increase when their prices drop. When looking instead at our full sample period, the largest price changes are more plausibly exogenous because they are driven by patent expirations and regulatory restrictions on market entry, and we estimate a larger effect of plan costs.

[33] The coefficients on the advertising terms $(\gamma_0 - \gamma_3)$ are shown in online Appendix Table A3, panel A.

[34] If we instead used the specification that does not include advertising controls, we would still underpredict the increase in Zocor's prescribing by over 50 percent.

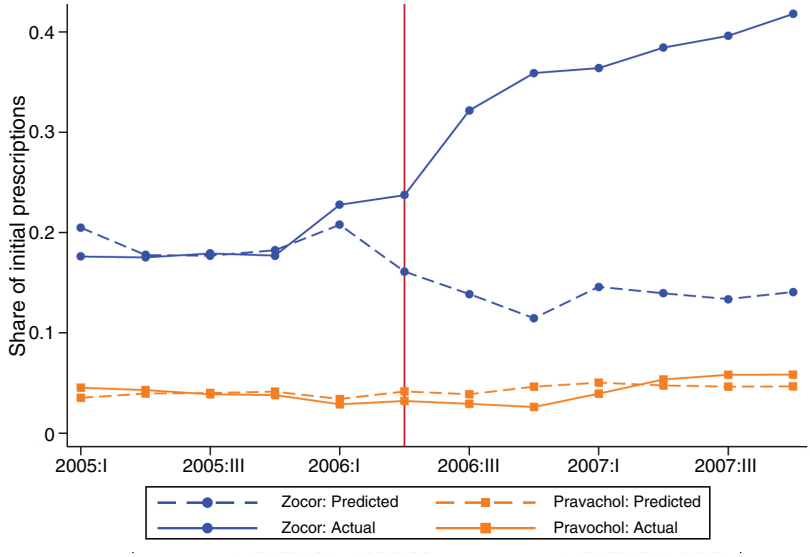

FIGURE 7. PREDICTED PRESCRIBING OF PATENT-LOSING MOLECULES BASED ON PRE-PERIOD MODEL

Notes: The dashed lines show the predicted prescribing shares of Zocor and Pravachol based on the estimated results of equation (1), reported in Table 3, column 2. This specification used patient co-pays, plan payments, and drug advertising to explain the choice of statin over the period 2005:I to 2006:I. The vertical line marks the quarter during which the patents of Zocor (simvastatin) and Pravachol (pravastatin) expired, on June 23 and April 20, respectively. The solid lines are the same prescribing shares shown for Zocor and Pravachol in Figure 5.

of generic drugs for employer-insured patients with a multitiered benefit plan, and if not, it equals the national average co-pay of brand drugs for employer-insured patients facing a multitiered benefit plan, according to Kaiser Family Foundation's annual surveys of employer-sponsored health insurance (Kaiser Family Foundation 2007).[35]

We estimate

$$
\begin{aligned}
(2) \qquad U_{idjt} = {} & T_j + \beta_1 \bar{p}_{jt} + \beta_2 (p_{ijt} - \bar{p}_{jt}) + \beta_3 PlanCost_{ij} \\
& + \beta_4 DocLastStatin_{jd} + \beta_5 PatLastStatin_{ij} + \gamma_0 DTP_{j,t} \\
& + \gamma_1 DTP_{j,t-1} + \gamma_2 DTP_{j,t-2} + \gamma_3 DTP_{j,t-3} + \epsilon_{ijd}.
\end{aligned}
$$

Results are shown in Table 4. If p_{ijt} were perfectly observed, and if patent expiration did not change any factors of the prescribing decision other than drug co-pays, then we would expect $\beta_1 = \beta_2$. Instead, $\hat{\beta}_1$ is significantly larger than $\hat{\beta}_2$, implying that $\lambda = \frac{\hat{\beta}_2}{\hat{\beta}_1}$ (reported at the bottom of the table) is significantly less than one.

Based on the model in Section III, λ can be interpreted as a measure of how accurately plan-specific co-pays are observed by the average physician at the time

[35] In Section VA, we discuss and test other ways of defining this variable, including the possibility that physicians' expectations are inaccurate.

Table 4—Breakdown of Co-pay Effects on Initial Prescription

	Panel A. All firms			*Panel B. Firms reporting salaries*		
	(1)	(2)	(3)	(4)	(5)	(6)
$\bar{p}_{jt}$ (national avg. co-pay, in \$10)	−0.598	−0.808	−0.489	−0.630	−0.806	−0.524
	(0.063)	(0.127)	(0.126)	(0.090)	(0.178)	(0.214)
× Salary (in \$10,000)				0.0374	0.0375	0.0375
				(0.005)	(0.005)	(0.005)
p_{ij}–$\bar{p}_{jt}$ (co-pay difference, in \$10)	−0.111	−0.102	−0.160	−0.154	−0.148	−0.197
	(0.028)	(0.030)	(0.032)	(0.039)	(0.039)	(0.044)
× Salary (in \$10,000)				−0.00338	−0.00340	−0.00302
				(0.006)	(0.006)	(0.006)
Advertising (in \$10 mill.)		0.028	0.047		0.022	0.040
		(0.020)	(0.015)		(0.027)	(0.023)
Plan payment (in \$10)			−0.0864			−0.0742
			(0.016)			(0.022)
Observations	28,557	28,557	28,557	12,747	12,747	12,747
log. likelihood	−41,595.492	−41,572.606	−41,472.414	−18,725.803	−18,718.528	−18,685.682
AME of \$10 change in $\bar{p}_{jt}$	−0.115	−0.156	−0.094	−0.116	−0.149	−0.096
	(0.026)	(0.034)	(0.021)	(0.030)	(0.039)	(0.025)
Elasticity w.r.t $\bar{p}_{jt}$	−0.925	−1.250	−0.757	−0.972	−1.243	−0.808
AME of \$10 change in $p_{ij} - \bar{p}_{jt}$	−0.021	−0.020	−0.031	−0.028	−0.027	−0.036
	(0.005)	(0.004)	(0.007)	(0.007)	(0.007)	(0.009)
Elasticity w.r.t $p_{ij} - \bar{p}_{jt}$	−0.188	−0.172	−0.271	−0.286	−0.274	−0.364
Lambda	0.186	0.126	0.328	0.245	0.183	0.375
	(0.050)	(0.048)	(0.130)	(0.066)	(0.067)	(0.204)

Notes: Conditional logit coefficients. Standard errors are in parentheses, clustered at the plan-quarter level. $\bar{p}_{jt}$ is the national average co-pay for either brand or generic drugs, assigned based on the patent status of each drug in each quarter. The advertising effect shown is the cumulative effect of the coefficients of quarterly DTP (direct-to-physician expenditures promoting drug j) and its first three lags. The AME (average marginal effects) shown are for the Zocor molecule, but the elasicities are averaged across all drugs. The estimated lambda shown at the bottom of the table represents the ratio of the coefficient on $p_{ij} - \bar{p}_{jt}$ to the coefficient on $\bar{p}_{jt}$, and is calculated using the delta method. All estimated lambda values are significantly different from 1 at the 1 percent level.

of the initial prescription. In column 1, when we do not include advertising nor plan costs, we estimate $\lambda = 0.186$. In column 2, we add current and lagged quarterly expenditures on DTP advertising. We would expect the exclusion of advertising from equation (2) to bias the effect of $\bar{p}_{jt}$ toward zero since the reduction of advertising counteracts the effect of a co-pay reduction. Indeed, the coefficient of $\bar{p}_{jt}$ becomes more negative as we move from column 1 to column 2. In column 3, we add *PlanCost*. As expected, given that drugs become cheaper for plans as well as for patients after their patent expirations, we see that adding plan costs to the regression decreases the effect of $\bar{p}_{jt}$. In theory, this could be driven by plans adopting non-co-pay strategies to increase the prescribing of Zocor after its patent expiration, and being more likely to adopt these strategies in 2007 when the cost of generic Zocor dropped significantly (see Figure 3). However, the coefficient on plan payments might also be capturing part of the response to average co-pays if physicians were gradually rather than immediately responding to Zocor's average co-pay drop. We present all remaining estimates and robustness checks based on the specification of column 3, including the plan cost variable that we observe, but note that our estimate of λ is even smaller without it.

Our estimates in column 3 imply that if one small plan raises its co-pay for Zocor by \$10, while all others are held constant, we would expect prescribing of Zocor in that plan to be reduced by 3.1 percentage points. By contrast, if all plans were to raise their Zocor co-pays by \$10, in unison, the reduction in Zocor's prescribing would be three times as large, 9.4 percentage points. In elasticity terms, averaged over all drug choices, the estimates are -0.271 (for an idiosyncratic change in a small plan) and -0.757 (for a uniform change across all plans). While the smaller number is toward the low end of the commonly cited range of estimates of own-price drug elasticity (-0.2 to -0.6), the elasticity we estimate for a change in average co-pay is slightly beyond the upper end of this range (Goldman, Joyce, and Zheng 2007). Figure 8 shows that predictions from the full model match the actual changes in prescribing of Zocor and Pravachol much more accurately than the model shown in Table 3 (and Figure 7).

C. *Heterogeneity by Patient Income*

In columns 4–6 of Table 4, we add interaction terms between each of the co-pay variables and patient salary, as shown in this equation, and use the subsample of firms reporting employee salaries:

$$
\begin{aligned}
(3) \qquad U_{idjt} = {} & T_j + \beta_1 \bar{p}_{jt} + \beta_2 Salary_i \times \bar{p}_{jt} + \beta_3 (p_{ijt} - \bar{p}_{jt}) \\
& + \beta_4 Salary_i \times (p_{ijt} - \bar{p}_{jt}) + X_i B_j + \gamma_1 DocLastStatin_{jd} \\
& + \gamma_2 LastPatRx_{ij} + \epsilon_{ij}.
\end{aligned}
$$

Salary is measured in \$10,000 increments and is centered around the median value (\$55,000), so that the baseline $\hat{\lambda}$, estimated as $\frac{\hat{\beta}_3}{\hat{\beta}_1}$ and shown at the bottom of each column, represents the median-salary patient. These λ values are somewhat larger but within the standard error of the estimates obtained for the full sample, and the progression of their estimates across the three columns is similar. The statistically significant estimates of $\hat{\beta}_2 > 0$ imply that, as hypothesized, physicians are less responsive to average co-pays when prescribing to higher income patients. This estimate is driven by the fact that lower income patients saw larger shifts toward Zocor prescriptions when it became available as a generic. Among patients with salaries at or below the median, the share receiving Zocor prescriptions increased from 0.21 to 0.42, versus an increase from 0.17 to 0.32 in the above-median salary group.

Our estimate of β_4, however, is not significantly different from zero, suggesting that the responsiveness of prescriptions to idiosyncratic co-pays does not vary with income. When combined with the finding that $\beta_2 > 0$, this suggests that λ for higher income patients is closer to one. In Figure 9, we plot the estimated marginal effects of co-pay on Zocor prescribing share for patients of different salary levels, based on the models of columns 5 and 6, respectively. The right-most area of each graph, where the response to average co-pays appears to grow smaller than the response to idiosyncratic co-pays, represents less than 5 percent of our sample.

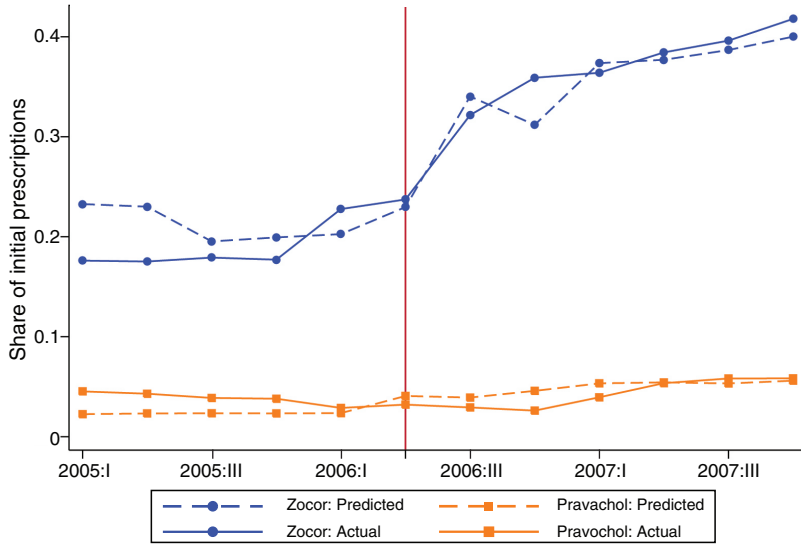

FIGURE 8. PREDICTED PRESCRIBING OF PATENT-LOSING MOLECULES BASED ON FULL MODEL

Notes: The dashed lines show the predicted prescribing shares of Zocor and Pravachol based on the estimated results of equation (2), reported in Table 4, column 3. In this specification, prescribing is allowed to respond differently to changes in a drug's average (expected) co-pay and idiosyncratic variation in plan-specific co-payments.

The left-most two markers in each line (at levels $45,000 and $55,000) represent 58 percent of our sample, and 91 percent of our sample falls below the $135,000 point, where the average marginal effects are equal for the two types of co-pay variation in the right-most panel. Thus, under the assumption that income only affects prescribing through co-pay-sensitivity, we find that physicians aim to prescribe more cost-sensitively to lower income patients, but may have greater difficulty in observing their co-pays. In Section VG, we discuss alternate specifications in which the baseline value of each statin is allowed to vary with income.

D. *Interpretation of Results*

An alternate interpretation of our empirical findings is that all else equal, physicians prefer to prescribe generic drugs; that is, their utility for prescribing the same drug molecule increases when it becomes available as a generic. However, it is difficult to explain why physicians would prefer to prescribe generic drugs for any reason other than cost savings. In fact, the prevailing concern in the public health arena has long been that too many physicians are averse to prescribing generics due to skepticism of their clinical equivalence.[36] However, surveys asking physicians what they do to assist patients who are burdened by the cost of medication find that

[36] A survey of 506 physicians in 2009 found that one-quarter of respondents reported that they strongly (6.5 percent) or somewhat (17 percent) disagree with the statement "I believe that generic medications are as effective as branded medications," while 67 percent somewhat or strongly agreed. Larger shares strongly (17 percent) and somewhat (33 percent) agreed with the statement "I am concerned about the quality of generic medications."

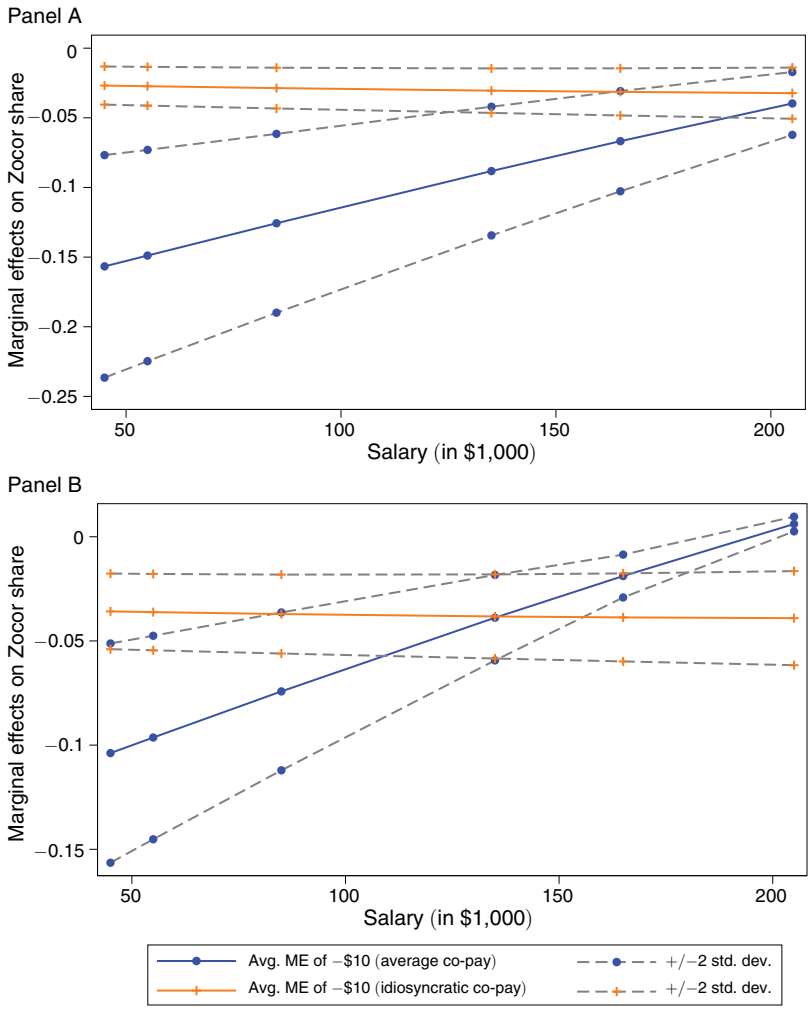

FIGURE 9. MARGINAL EFFECTS OF CO-PAY BY SALARY

Notes: Each point plots the average marginal effect of average co-pays and idiosyncratic co-pays for a different salary bin, based on the estimates of Table 4, columns 5 (panel A) and 6 (panel B). The left-most points shown represent the salary bin "below $50,000 or missing," which we assume to have an average annual salary of $45,000. Other points plotted represent the midpoint of a salary bin with a $10,000 range. Although the sample includes bins up to $250,000, the vast majority of our sample (91 percent) falls at or below the $135,000 point, shown as the third-rightmost point in each figure.

"Switch from a brand-name drug to a generic drug" is the most frequent response.[37] Therefore, we posit that any empirically observed preference for prescribing generic drugs results from a preference for prescribing drugs of lower cost.

A question that follows is whether physicians prefer to prescribe lower cost drugs because of concern for the patient's co-pay or simply to conserve healthcare spending, internalizing the amount spent by other payers in addition to patients' out of

[37] Alexander, Casalino, and Meltzer (2005); Beran et al. (2007).

pocket costs. Two of our secondary results speak to this question. First, we find that all else equal, lower income patients are more likely to be prescribed generics than higher income patients. This supports the view that physicians care about how drug costs impact patient utility, rather than drug costs alone. Second, Zocor's increase in prescribing began strongly and sharply at the time that its average co-pay dropped, rather than 180 days later, when the entry of multiple generic manufacturers caused the largest drop in its total price. Thus, our findings are consistent with other research reporting that physicians believe managing patients' out-of-pocket costs is more important than managing total medication costs.[38]

V. Robustness

In this section, we consider possible bias in the estimation of co-pay responses and λ due to measurement error, endogenous plan selection by employees, forward-looking prescribing, and the fact that we cannot observe unfilled first prescriptions. In all of our checks using the main sample (results shown in Table 5 and Table 6, panel A), the estimated λ continues to remain statistically significantly smaller than 1, with point estimates far below 0.5. In fact, to the extent that any results differ from our main specification, they tend toward smaller estimates of λ. We discuss the robustness and interpretation of our secondary result, that the cost-sensitivity of prescribing is negatively correlated with income, in Section VG.

A. *Measurement Error*

To the extent that our imputed co-pays are inaccurate, measurement error could bias our results toward finding a larger difference between the response to average co-pays and the response to idiosyncratic co-pays (i.e., biasing λ towards zero). In Table 5, we show how the results of equation (2) shift as we adjust the required level of accuracy of imputed co-pays. In column 1, we don't exclude any plans, other than those with insufficient observations to define a modal co-pay for every drug in every observed quarter. In columns 2–5, we impose increasingly stringent restrictions on the share of observed co-pays that fall within \$0.99 of the imputed co-pay among 30-day fills with no deductible applied. Column 3, with minimum share of 90 percent, is our main sample. Moving from left to right across the first three columns, the correlation between actual and imputed co-pays (shown at the bottom of the table) increases from 0.75 to 0.89. We see only moderate, and not monotonic, variation in the estimated responses to both idiosyncratic and expected co-pay variation. In the bottom panel of the table, we show results for the subset of prescriptions for 30-day supplies. This restriction raises the correlation between actual and imputed co-pays, and also appears to reduce the estimate λ values, perhaps because patients starting

[38] Reichert, Simon, and Halm (2000) found that 93 percent of physicians in an urban hospital-based primary care center agreed with the statement "The cost of medications is more of a concern to me when my patient's insurance status is 'self-pay'" while only 30 percent agreed when status was "HMO with prescription plan," consistent with empirical evidence found by Lundin (2000) and Lu (2014). Shrank et al. (2006b) found that 59 percent of physicians surveyed in California agreed that managing patients' out-of-pocket costs was more important than managing the total medication costs, and only 16 percent disagreed.

Table 5—Sensitivity to Measurement Error in Co-pay

	All	> 75 percent	> 90 percent	> 95 percent	> 97.5 percent
Panel A. All initial prescriptions					
$\bar{p}_{jt}$ (national avg. co-pay)	−0.50	−0.51	−0.49	−0.56	−0.46
	(0.07)	(0.10)	(0.13)	(0.11)	(0.14)
$p_{ij} - \bar{p}_{jt}$ (co-pay diff.)	−0.12	−0.13	−0.16	−0.12	−0.17
	(0.01)	(0.02)	(0.03)	(0.03)	(0.04)
Observations	66,145	40,487	28,566	22,328	7,763
Number of plans	111	47	28	22	15
Number of firms	23	18	13	11	8
Lambda	0.24	0.27	0.33	0.22	0.37
	(0.05)	(0.09)	(0.13)	(0.08)	(0.16)
Elasticity w.r.t $\bar{p}_{jt}$	−0.77	−0.78	−0.76	−0.86	−0.70
Elasticity w.r.t $p_{ij} - \bar{p}_{jt}$	−0.21	−0.23	−0.27	−0.20	−0.29
$\hat{\beta}_{p_{ij}} - \hat{\beta}_{\bar{p}_{jt}}$	−0.38	−0.37	−0.33	−0.44	−0.29
	(0.08)	(0.12)	(0.14)	(0.12)	(0.16)
Correlation	0.75	0.84	0.87	0.88	0.89
Panel B. Only 30-day prescriptions					
$\bar{p}_{jt}$ (national avg. co-pay)	−0.51	−0.52	−0.52	−0.59	−0.52
	(0.08)	(0.11)	(0.14)	(0.11)	(0.15)
$p_{ij} - \bar{p}_{jt}$ (co-pay diff.)	−0.11	−0.11	−0.14	−0.11	−0.14
	(0.01)	(0.03)	(0.03)	(0.03)	(0.05)
Observations	48,091	29,803	20,232	15,435	5,915
Lambda	0.21	0.21	0.26	0.18	0.26
	(0.05)	(0.08)	(0.11)	(0.08)	(0.13)
Elasticity w.r.t $\bar{p}_{jt}$	−0.79	−0.81	−0.81	−0.90	−0.80
Elasticity w.r.t $p_{ij} - \bar{p}_{jt}$	−0.19	−0.19	−0.24	−0.18	−0.23
$\hat{\beta}_{p_{ij}} - \hat{\beta}_{\bar{p}_{jt}}$	−0.38	−0.37	−0.33	−0.44	−0.29
	(0.08)	(0.12)	(0.14)	(0.12)	(0.16)
Correlation	0.79	0.87	0.93	0.95	0.96

Notes: The sample used in each column is defined by the accuracy of modal co-pays, which is measured as the percentage of observed co-payments for 30-day fills at retail pharmacies with no deductible applied, in our sample, that fall within a $0.99 bound of the modal co-pay for that plan/quarter/drug based on all statin fills for 30-day fills at retail pharmacies during that quarter. Column 3 uses the sample we use in other tables and analyses. Panel B is limited to initial prescriptions filled as 30-day scripts. At the bottom of each panel, the correlation between observed co-pays (per day supplied) and imputed co-pays within each sample is shown.

with large prescription supplies differ from those starting with a 30-day script. Since even at a correlation of 0.96 (among 30-day prescriptions in the set of plans with accuracy above 97.5 percent), the coefficient for imputed co-pay is one-fourth of the size of the coefficient for expected co-pay, we reject the possibility that our results are driven by measurement error in imputed co-pays.

One might also be concerned about measurement error in $\bar{p}$. Our model assumes that physicians all use, as their co-pay priors, the national average co-pays of brand and generic drugs among privately insured patients. Since we do not actually observe physicians' co-pay priors, expectational error could impact our results.

We explore the robustness of our estimates to a normally distributed doctor-specific expectational error component in $\bar{p}$ using Monte Carlo simulations, and find that this type of error, if it is mean zero (i.e., rational expectations), has virtually no effect on the accuracy of the coefficient estimates. This procedure is described in online Appendix Section A5 and results are shown in online Appendix Table A2.

Table 6—Robustness Checks

	Endogenous plan selection[a]	Forward looking prescribing[b]	Excluding high-risk patients[c]	Excluding possible step therapy[d]	Weighted by primary adherence[e]
	(1)	(2)	(3)	(4)	(5)
Panel A. Full sample					
$\bar{p}_{jt}$ (national avg. co-pay)	−0.50	−0.50	−0.50	−0.60	−0.45
	(0.14)	(0.14)	(0.13)	(0.11)	(0.14)
$p_{ij} - \bar{p}_{jt}$ (co-pay diff.)	−0.16	−0.13	−0.16	−0.11	−0.18
	(0.04)	(0.04)	(0.03)	(0.03)	(0.03)
Plan payment (in $10)	−0.086	−0.086	−0.086	−0.071	−0.087
	(0.02)	(0.02)	(0.02)	(0.01)	(0.02)
Advertising (in $10 mill.)	0.048	0.050	0.043	0.047	0.045
	(0.016)	(0.016)	(0.016)	(0.015)	(0.016)
Observations	25,189	27,198	25,944	25,596	28,557
Lambda	0.33	0.26	0.32	0.18	0.39
	(0.14)	(0.10)	(0.12)	(0.06)	(0.17)
$\hat{\beta}_{p_{ij}} - \hat{\beta}_{\bar{p}_{jt}}$	−0.34	−0.23	−0.34	−0.49	−0.27
	(0.16)	(0.13)	(0.15)	(0.12)	(0.16)
	(6)	(7)	(8)	(9)	(10)
Panel B. Firms reporting salary					
$\bar{p}_{jt}$ (national avg. co-pay)	−0.54	−0.51	−0.50	−0.77	−0.47
	(0.24)	(0.23)	(0.21)	(0.14)	(0.25)
× Salary (in $10,000)	0.038	0.05	0.037	0.028	0.033
	(0.00)	(0.01)	(0.00)	(0.01)	(0.00)
$p_{ij} - \bar{p}_{jt}$ (co-pay diff.)	−0.19	−0.13	−0.20	−0.12	−0.22
	(0.04)	(0.04)	(0.04)	(0.03)	(0.05)
× Salary (in $10,000)	−0.0042	0.0072	−0.0038	−0.0064	−0.0014
	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)
Plan payment (in $10)	−0.087	−0.075	−0.077	−0.044	−0.078
	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)
Advertising	0.051	0.048	0.037	0.040	0.042
	(0.027)	(0.023)	(0.024)	(0.014)	(0.026)
Observations	11,514	12,094	11,828	10,041	12,747
Lambda (median salary)	0.36	0.25	0.39	0.15	0.46
	(0.21)	(0.14)	(0.22)	(0.05)	(0.29)
$\hat{\beta}_{p_{ij}} - \hat{\beta}_{\bar{p}_{jt}}$	−0.35	−0.38	−0.30	−0.65	−0.26
	(0.26)	(0.24)	(0.24)	(0.15)	(0.27)

Notes: For panel A (B), the corresponding baseline results appear in Table 4, column 3 (column 6). With the exception of column 10, all estimated lambda values are significantly smaller than one. Also shown is the estimated difference between the coefficient on average co-pay ($\bar{p}_{jt}$) and the coefficient on co-pay difference ($p_{jt} - \bar{p}_{jt}$). All specifications are described in Section V.

[a] In column 1, we drop three firms offering different plans with wide variation in co-pays to mitigate concerns about endogenous plan selection.

[b] In column 2, we show the sum of the coefficients for each co-pay term of the current period co-pay and the co-pay at the time of first refill.

[c] Column 3 excludes patients with past heart attack or cardiac disease because clinical trial results concerning these populations were released in 2005–2007.

[d] Column 4 excludes plans with smaller than 5 percent initial prescribing rates of Lipitor, Crestor, or Vytorin.

[e] In column 5, each prescription is weighted by its imputed probability of being filled, based on the Liberman et al. (2010) logit model.

Our estimates of lambda would be biased, however, if physicians did not have rational expectations and made systematic errors in predicting the average co-pay difference between brand and generic drugs. For example, if physicians tended to underestimate this co-pay difference, then we would underestimate their responsiveness to perceived average co-pays and overestimate λ, the ratio of co-pay responses.[39] Biases in the reverse direction would occur if physicians overestimated the average co-pay difference between brand and generic drugs. However, it is straightforward to show the range of elasticities and λ estimates that correspond to a range of reasonable expectations of the co-pay difference between brand and generic drugs. The estimate for the elasticity of prescribing with respect to perceived co-pays ranges from -0.557 if we assume physicians to perceive a brand-generic co-pay difference twice the actual average ($26 perceived difference) to -0.796 if we assume physicians underestimate it by 22.5 percent ($10 perceived difference). Since the estimated elasticity of prescribing with respect to the idiosyncratic portion of co-pays does not change, our estimated λ varies from 0.493 to 0.272 across these scenarios (see online Appendix Table A7).

B. *Endogenous Plan Selection*

Our analysis assumes that from the perspective of the individual patient, the co-pays of the six statins are exogenous. The typical concern with this approach is that employees might choose a plan that preferentially prices the drugs that they already use; this is of little concern in our analysis since we only consider new recipients, rather than existing users, of a statin.[40]

A related concern, however, is that patients who are more price-sensitive, or who use many chronic drugs, may select into plans with lower co-pays overall. If these plans also have smaller *co-pay differences* across the statins, then the fact that these patients may be more likely to receive the lowest cost drug (because they are more price sensitive) or more expensive drugs (because they are more sick) could bias the estimated effect of co-pays on prescribing. In practice, this type of selection is only possible within firms whose assortment of plan offerings differ in the co-pay differences across tiers.[41] If we consider all the plans offered by the firms in our sample (note that some of these plans are excluded from our high-accuracy sample because of the imprecision of their imputed co-pays), and define the mean co-pay difference in a given plan-quarter as the difference between the average imputed co-pays of brand statins and the average imputed co-pays of generic statins, a visual representation of the ranges within each firm shows that the differences across firms are far larger than the differences within firms, in this

[39] This is because the same change in prescribing when Zocor drops from $\bar{p} = 24$ to $\bar{p} = 11$ would instead be attributed to a smaller change in perceived average co-pay, e.g., $\tilde{p} = 22$ to $\tilde{p} = 12$, meaning the coefficient on $\tilde{p}$, if we observed it, would reflect a stronger per-dollar effect on prescribing than the true average co-pay.

[40] We use a one-year window to define new users, and in cases when we observe that a patient had used a statin before the start of the one-year window, we control for the identity of that statin.

[41] The reason we worry about this is because the effect of idiosyncratic plan co-pays is partly identified by the correlation between plan-specific co-pay changes upon Zocor's patent expiration and plan-specific changes in prescribing for Zocor. Empirically, we find that plans with lower co-pays overall also tend to have lower co-pay differences between brand and generic drugs. This could mean that if the most price-sensitive consumers choose those plans, and we see large prescribing shifts toward generic Zocor in these plans, our estimates of the effect of idiosyncratic co-pays on prescribing would be biased toward zero.

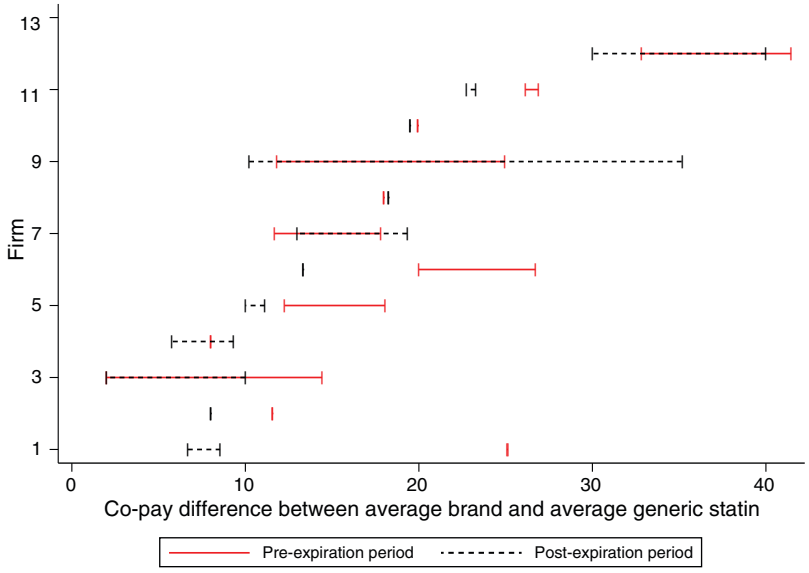

FIGURE 10. RANGE OF BRAND-GENERIC CO-PAY DIFFERENCES ACROSS PLAN OFFERINGS

Notes: This figure shows how the plans offered to employees by each firm differ along the dimension of co-pay incentives to use generic drugs. For the firms appearing in our sample, we used data on all plans appearing in the claims database. For each individual plan, we computed the average monthly co-pay for brand statins ($\bar{p}_{brand}$) and generic statins ($\bar{p}_{generic}$) in the periods prior to and following the patent expirations of Pravachol and Zocor. We plot, for each firm, the range from the smallest to the largest value of $p_{\text{diff}} = \bar{p}_{brand} - \bar{p}_{generic}$ found among the firm's plan offerings in the pre-expiration (solid lines) and post-expiration (dashed lines) periods. If a firm only offered one plan, or if all of its plans had the same co-pay difference between brand and generic drugs, then the figure shows only a vertical dash for that firm and time period.

measure (see Figure 10). Furthermore, a regression of the mean co-pay difference faced by each patient (shown in Table A4) finds that 76 percent of the variation in this variable is explained by firm-quarterly fixed effects, and neither income nor health conditions explain a significant amount of the remaining variation. While this suggests that endogenous choice of plan is not a large concern in our sample, we can go further by excluding the firms offering the largest scope for problematic selection. When we exclude the firms labeled as 3, 9, and 12 in Figure 10, firm quarterly fixed effects explain 96 percent of the variation in co-pay difference (see Table A4, column 4). Table 6, column 1 shows that when we exclude these three firms from our main analysis, our estimated co-pay coefficients hardly change. Furthermore, if we exclude even more firms (those labeled 3, 5, 6, 7, 9, 12), leaving only firms with either one plan or very similar plans, our results remain consistent (shown in the online Appendix Table A11, column 7).

C. *Forward-Looking Prescribing*

Another possible source of bias is forward-looking behavior by prescribing physicians. Since statins are prescribed for long-term use, physicians might have begun prescribing Zocor more frequently in the months prior to its patent expiration. This would bias our estimate of the expected co-pay effect on prescribing toward zero.

To address this, we estimate a specification that includes each patient's co-pay at the time of their hypothetical second fill (typically one month but sometimes three months in the future, depending on the days supplied by the prescription), broken down into average and idiosyncratic components. We find that the average co-pay of the second fill has an effect on prescribing that is 43 percent as large as the effect of the first fill's co-pay, with a p-value of 0.06, while the idiosyncratic co-pay at first refill has no significant effect (point estimate of -0.0048). This makes sense if some physicians anticipated that Zocor would be generally cheaper after its patent expiration, but did not observe plan-specific co-pay changes in advance. In Table 6, column 2, we show the sum of the estimated effects of co-pay at first fill and second fill, for the average and idiosyncratic co-pay components.

Our estimate of lambda shifts from 0.33 to 0.26, consistent with the expected direction of bias. Our estimate of lambda is identical if we use the one-quarter lead of co-pay instead of co-pay at the date of first refill (see Table A11).

A second approach to understanding when physicians started changing their prescribing is to test for changes in specific time periods in the coefficient of *DocLastStatin*, which captures how likely physicians are to prescribe the same drug to their subsequent patients initiating treatment in our sample. The results of this analysis, described in online Appendix Section A4, suggest that physicians changed their prescribing habits immediately following, not preceding, the patent expiration of Zocor.

D. *Changes in Perceived Therapeutic Benefit*

We assume (Assumption 3) that the relative perceived therapeutic benefit of the statins is constant over our 2005–2007 time period. Since we control for advertising expenditures, the main threat to this assumption is changes in the clinical evidence about these drugs or in national recommendations. As discussed in greater detail in online Appendix D, the US National Cholesterol Education Program regularly convenes expert panels to review clinical evidence and develop up-to-date, broadly disseminated guidelines on the identification and treatment of high cholesterol. Reviewing the timeline of updates in these guidelines, and the release dates of the clinical trials that they cite, can identify when perceptions of therapeutic efficacy were most likely to be changing.

For example, an important update released in August of 2004 modified the guidelines to recommend more intensive statin treatment (i.e., choosing stronger statins to achieve a 30–40 percent LDL reductions) for high-risk persons, and an "optional" extension of this treatment to moderately high-risk persons.[42] Notably, for people in lower risk categories, the 2004 update made no proposed changes to the treatment goals and cutpoints, and after the 2004 update, the guidelines remained unchanged until 2013.[43]

[42] "High risk" is defined as having coronary heart disease (CHD) or CHD-equivalent risk factors resulting in an estimated risk of heart attack within the next ten years of more than 20 percent. "Moderately high risk" is defined as an estimated risk of 10–20 percent.

[43] The so-called "ATP IV," officially "2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults" was published online on November 12, 2013 and appeared in the supplement to the June 24, 2014, issue of the journal *Circulation* (Stone et al. 2014).

Looking at all the studies cited in the 2013 guideline's Evidence Statements, we see that two important trials were published during our study period: TNT[44] (April 2005, RCT comparing 20mg simvastatin versus 80mg Lipitor) and IDEAL[45] (November 2005, RCT comparing 10mg versus 80mg Lipitor). These two studies were focused on patients already diagnosed with coronary heart disease, and with a history of heart attack, respectively. Since they found some evidence in favor of even more aggressive statin therapy for patients in these high-risk groups, one might worry that the perceived efficacy of stronger relative to weaker statins might be increasing over our time period for patients with a history of heart attack or coronary heart disease. Thus, we conduct a robustness check that excludes the 9 percent of our sample with either heart disease or a previous heart attack (Table 6, column 3). The results are extremely similar to our main specification. We discuss related checks and their results in online Appendix D.

E. *Unobserved Strategies Used by Plans to Influence Prescribing*

If some plans implemented step therapy or prior authorization requirements for other (brand-name) statins, this would augment the shift of first prescriptions toward Zocor or Pravachol once they become generic, but not because of their drop in perceived co-pays. As mentioned earlier, our inclusion of plan payment in the main specification helps to capture the changes in plans' incentives to implement such policies. In addition, our results are robust to three distinct approaches to reduce any possible bias.

First, we use a straightforward approach to drop the plans most likely to be using step therapy or prior authorization policies in the period following Zocor's patent expiration. Given that these policies directly affect new patients' freedom to start on certain brand drugs, we can look for plans in which the rate of initial prescriptions for Lipitor, Crestor, and Vytorin were particularly low relative to their overall popularity. For example, for one plan in our sample ($N = 2{,}006$ initial prescriptions), fewer than 2 percent of new patients received Lipitor and fewer than 2 percent of new patients received Crestor, strongly suggesting that this plan had restrictions on filling prescriptions for these statins as a point of entry to the statin class. Apart from this large plan, there are 955 observations belonging to smaller plans in which either Lipitor, Crestor, or Vytorin had a prescribing share below 5 percent in either the period prior to Zocor's patent expiration or the period afterwards. When we drop all observations in these plans ($N = 2{,}961$), our results do not suggest that these types of policies are driving our results (see Table 6, column 4). In fact, our estimated λ gets smaller, since the plans that are dropped tended to have above average co-pays for Lipitor, Crestor, and Vytorin and below average prescribing for these drugs.

Second, we conduct a supplemental analysis of Zocor prescribing rates before and after its patent expiration in a different dataset, the National Ambulatory Medical Care Survey (NAMCS). NAMCS differs from our dataset in two

[44] LaRosa et al. (2005) "Intensive Lipid Lowering with Atorvastatin in Patients with Stable Coronary Disease."
[45] Pedersen et al. (2005) "High-Dose Atorvastatin vs Usual-Dose Simvastatin for Secondary Prevention after Myocardial Infarction: The IDEAL Study: A Randomized Controlled Trial."

important ways. First, by collecting data from a nationally representative sample of outpatient physician offices, it records the prescriptions written by physicians rather than those purchased by patients. This means that step therapy or prior authorization requirements that were unanticipated by physicians would not affect the prescriptions recorded in NAMCS, even though they could block a patient's ability to fill those prescriptions. Second, NAMCS includes data on whether each physician's office uses a computerized prescribing system. Epstein and Ketcham (2014) find that physicians' written prescriptions do not respond to step therapy or prior authorization at all, in the absence of easy access to such information, which is typically only available through a computerized prescribing system. Thus, we can focus on prescriptions written by physicians with no access to computerized systems, who are very unlikely to be aware of prior authorization or step therapy policies.

As shown in online Appendix Figures A5 and A6, the pattern of prescribing responses to the patent expirations is very similar in our sample and in NAMCS, suggesting that our results are not driven by ex post changes in prescriptions encouraged by pharmacists or insurers, nor by physicians responding to step therapy and prior authorization policies. We provide more detail on our use of the NAMCS data and these results in online Appendix Section A.5.

Third, in an additional check shown in the online Appendix, we create a proxy measure of plans' use of non-pecuniary incentives based on each plan's success in encouraging take-up of its preferred brand drugs in the period before Zocor's patent expiration, after controlling for their co-pays. Again, we find that controlling for this proxy measure does not affect our main results.

F. *Potential Bias Due to Primary Non-adherence*

A limitation of our dataset is that we do not observe written prescriptions that were never filled. Our main analysis implicitly assumes that all patients prescribed a statin by their doctor purchased a first supply. However, Liberman et al. (2010) uses electronic prescribing information to study the determinants of *primary non-adherence*: prescriptions that are sent to pharmacies but never purchased. In the case of first-time statin prescriptions, Liberman et al. (2010) finds higher co-pays are positively correlated with the rate of primary non-adherence, which is 34.1 percent overall.

If prescriptions for drugs with higher co-pays are more likely to be "missing" from our data, our baseline results could overestimate the response of prescribing to co-pays. To address the problem of data that is not missing at random, we weight the observed prescriptions in our data by the inverse of the probability that they are observed, using the estimated results of Liberman et al. (2010) to impute these probabilities as a function of each patient's income, age, gender, number of recently filled prescriptions, and drug co-pay. The results are shown in Table 6, column 5. The coefficient on average co-pay decreased from -0.49 to -0.45, while the coefficient on idiosyncratic co-pay changed from -0.16 to -0.18. The resulting estimate of lambda (0.39) is larger than in the main specification but still significantly smaller than 1.

G. *Robustness of Heterogeneity by Patient Income*

In this section, we discuss the robustness of our secondary result—that co-pay-sensitivity of prescribing is negatively associated with patient income, addressing possible concerns regarding the limitations of the data, the functional form, and the exclusion of salary-drug interaction terms. First, our data on employees' salaries has some limitations; the lowest bin ($50,000 and below) accounts for 45 percent of the salary subsample, and may include patients with unreported salaries. The results we describe in Section IVC remain qualitatively similar, although noisier, when we exclude this entire bin. They remain very similar when we exclude the top 5 percent of earners, which includes the topcoded bin $200,000 and above. These results are shown in online Appendix Table A8.

Interestingly, the interaction between a patient's salary and co-pay remains significant when we control for the average salary of each doctor's patients.[46] The results in column 4 of Table A8 also suggest that doctors who treat a larger share of low-income patients may adopt more cost-sensitive treatment patterns for all their patients. However, the fact that the interaction between average co-pay and the difference between a patient's salary and her doctor's average patient salary is also significant, and 70 percent as large as it is when we don't include doctor's average patient salary, shows that our results cannot be fully explained by heterogeneity in physicians' treatment styles.

Our finding that prescriptions to higher income patients are less responsive to average co-pays is robust to varying the functional form of the salary interaction terms; online Appendix Table A9 shows results using salary squared, above/below median, tertiles, and percentiles of salary. This finding is not robust, however, to the inclusion of salary-drug interaction terms. When we add these, the interactions of salary with the intercepts for Zocor, Mevacor, and Vytorin are negative and significant, while $\hat{\beta}_2$, the coefficient on the interaction between salary and average co-pay, diminishes in magnitude and becomes statistically insignificant (see online Appendix Table A8, column 5). One might worry that this indicates the more expensive statins, e.g., Crestor and Lipitor, are better therapeutic matches for patients with higher incomes. However, to the extent that income might be correlated with unobserved individual characteristics that enter the Framingham Heart Risk calculations, such as smoking or specific cholesterol counts, we would expect lower income patients to have higher predicted risk, and therefore, a higher relative therapeutic value for stronger statins.[47] Instead, our estimates show that income is negatively correlated with preferences for the two commonly prescribed generic drugs (Zocor (simvastatin) and Mevacor (lovastatin)) and for Vytorin, the least costly brand drug in our sample.[48] Therefore, this result can be interpreted as showing that controlling

[46] We use all statin prescriptions (not only initial prescriptions) to compute the average salary of each doctor's patients who are treated with statins. For the observations in our salary subsample, the median number of patients used to calculate the average salary is 4, but for 25 percent of the observations it is larger than 13.

[47] In fact, when we estimate a richer model at the product-dose level, as described in online Appendix Section A.7, we do find that higher salaries are associated with slightly less weight on LDL reduction, but also a greater aversion to taking higher dosages, which can make side effects more likely (see online Appendix Table A12, panel B).

[48] Within our sample of firms with salary information, the average co-pays of brand-name drugs after Zocor's patent expiration were $24.92 (Vytorin), $28.21 (Crestor), and $30.97 (Lipitor).

for actual co-pays, doctors are more likely to prescribe drugs that generally have lower co-pays to lower income patients. In other words, the results of this alternate specification are consistent with the notion that physicians make an effort to prescribe lower-cost drugs to lower-income patients, despite the finding that they do not respond more strongly to their plan-specific co-pays. In online Appendix Figure A7, we show graphically that the salary-drug interaction estimates are highly correlated with the deviations of each drug's average co-pay within our sample from the national average co-pay of brand/generic drugs used as $\bar{p}_{jt}$.

VI. Predicted Outcomes under Counterfactual Scenarios

We have established that much of the variation in prescription drug co-pays is unobserved by physicians at the time of their prescribing decisions. Our findings also suggest that lower income patients are most affected by this information problem. In this section, we predict prescribing outcomes under two counterfactual scenarios. For each scenario, we calculate changes relative to the status quo in the generic prescribing rate, average co-pays, and predicted adherence, for patients at different income levels.

The first scenario we consider is one in which physicians have perfect knowledge of p_{ij}. Following the framework described in Section III, we take the weight placed on $\bar{p}_{jt}$ to indicate how prescribers would weight plan-specific co-pays if they observed them, and predict the choice probability of each statin for each patient if the weight placed on $p_{ij} - \bar{p}_{jt}$ were equal to the weight placed on $\bar{p}_{jt}$ (i.e., $\lambda = 1$) for each income level.

In the second scenario, we assign all patients the drug with the lowest co-pay, according to their formulary, that achieves a similar level of LDL reduction as the drug they were actually prescribed.[49] In practice, this scenario could be achieved if plans required that patients try a low-tier statin prior to receiving coverage for low doses of high-cost statins such as Crestor or Lipitor, but not for high doses of these statins, which achieve steeper levels of LDL reduction than possible with the older statins.

Table 7 reports the predicted changes, relative to the status quo, under both scenarios. For the first scenario, we report results based on the main specifications of Table 4, columns 5 and 6, in panel A. For low-salary patients, these models predict that an additional 3.8–7.3 percent of patients would receive a generic drug if co-pays were perfectly observed. Since average co-pays of generic drugs are on average $15 less than brand drugs, this shift in prescribing would correspond to an approximate $0.57–$1.09 drop in predicted co-pay for the average patient. However, since the counterfactual scenario also leads patients to receive lower cost brand drugs, given their formularies, the total average co-pay reduction would be $1.68–$2.88

[49] We use the dose of a patient's prescribed statin to infer the desired LDL reduction (see Table A1), and rule out the choice of alternative statins that are not available in a dose that achieves a similar reduction. We impose this restriction because it likely explains why Mevacor, the only available generic statin in 2005, was uncommonly prescribed. Without this restriction, this scenario would require that all patients be prescribed Mevacor in the period prior to Zocor's patent expiration, since it has the lowest co-pay.

Table 7—Simulated Changes under Counterfactual Prescribing Regimes

	Change in generic prescribing rate		Change in monthly co-pay (average)		Predicted change in adherence rate	
	(1)	(2)	(3)	(4)	(5)	(6)
Panel A. Perfectly observed co-pays						
Salary of $50,000 or below	0.073	0.038	−$2.88	−$1.68	0.0085	0.0050
Salary of $50,000–$80,000	0.030	0.014	−$2.18	−$1.20	0.0061	0.0033
Salary above $80,000	0.009	0.000	−$0.94	−$0.09	0.0024	0.0004
All	0.043	0.021	−$2.15	−$1.12	0.0062	0.0037

	(7)	(8)	(9)
Panel B. Lowest co-pay drug in the same strength category			
Salary of $50,000 or below	0.244	−$6.21	0.023
Salary of $50,000–$80,000	0.278	−$6.56	0.023
Salary above $80,000	0.352	−$5.85	0.021
All	0.283	−$6.21	0.022

Notes: In panel A, all odd numbered columns are based on the results of Table 4, column 5, while even numbered columns use the results of Table 4, column 6. This table summarizes the results of the simulation exercise described in Section VI. Within the sample of firms reporting salaries, we predict the share of patients who would be prescribed a different statin if the weight placed on idiosyncratic co-pays in the prescribing decision was equivalent to the weight placed on average co-pay, based on the estimates shown in Table 4, columns 5 and 6, in panel A. In panel B, we predict changes in prescribing if all patients started out on the lowest-co-pay drug available in the same strength category as the drug they were actually prescribed (see Table A1 for a listing of strength categories by drug).

per month for low-salary patients. The predicted changes under the scenario of perfectly observed co-pays are much smaller for the higher income groups.

For low-salary patients, the co-pay savings if co-pays were perfectly observed would be at least 27 percent as large as the co-pay reduction that would be achieved under the second scenario, in which generic prescribing is more pervasive, by design, and the average co-pays of low-salary patients drop by $6.22. These changes are sizeable, given that the average co-pay paid by low-salary patients for their first month's supply was $26 prior to the patent expiration and $18 afterward, and statins are prescribed to be used long-term with low rates of switching between drugs.

In a third scenario, shown in online Appendix Table A10, we assume physicians do not observe idiosyncratic co-pays at all ($\lambda = 0$) and prescribe solely based on average co-pays and patient characteristics. As we would expect, results show that patients would pay higher co-pays on average (98 cents more than in the status quo, with the lowest income patients paying $1.09 more).

Providing physicians with perfect knowledge of patient co-pays would likely save plans money, as well, given the fact that incentive-based formularies are designed to incentivize the choice of drugs that cost insurers less. However, as mentioned earlier, our data on plan payments do not include rebates made by drug companies to plans, which are often tied to co-pay tier placement on incentive-based formularies (Scott Morton and Kyle 2011). Therefore, our predicted changes in observed plan payment (available from the authors upon request) are smaller than the predicted changes in patient co-payments, but are almost surely underestimated.

The problem of imperfectly observed co-pays could also have health costs, since patients are less likely to continue taking more costly drugs, and thus, less likely to

accrue their therapeutic benefits. Relying on the assumption that the variation across plans in individual statins' co-pays is exogenous to patient unobservables, we use this variation to estimate the effects of co-pays on patient adherence, in order to make predictions of adherence rates under these two alternate scenarios.[50] In online Appendix B, we describe our estimation of the co-pay sensitivity of patient adherence and the required assumptions. In our preferred specification, a $10 co-pay increase reduces the adherence of low-salary patients by 3.4 percentage points, or 7 percent. Relative to low salary patients, high salary patients are much more likely to adhere (59 percent versus 46 percent), and their adherence is less sensitive to co-pay.

We use these results to make out-of-sample predictions of each patient's adherence to each statin, in order to roughly estimate how the prescribing changes of these two scenarios would impact adherence rates.

As shown in columns 5 and 6 of Table 7, the predicted changes in adherence for low-salary patients are between one-half and 1 percentage point (0.0055 and 0.0093) in our two models for the perfectly observed co-pays scenario.[51] A back-of-the-envelope calculation predicts that this adherence increase would prevent 1–1.4 cardiac events per 10,000 low-salary statin prescribees, in the year following their first prescriptions.[52] This represents 20–40 percent of the adherence increase (and associated reduction in cardiac events) that we predict in scenario 2. Nevertheless, this is a small predicted change in adherence, and for patients with higher salaries, the changes are smaller.

VII. Conclusion

Our study is the first to attempt to estimate the consequences of the difficulty of observing drug co-pays in the fragmented US healthcare system. We examine a highly publicized patent expiration and find that the resulting prescribing change was far larger than would be predicted by a simple model of prescribing estimated in the period prior to the patent expiration. To explain this, we propose and estimate a model of prescribing in which physicians respond to their expectations of a patient's co-pay, which change with generic entry. Our results suggest that a co-pay change that is implemented nationally, across all plans, has three times the effect of a single plan's idiosyncratic co-pay change on a patient's likelihood of being prescribed a drug. Our results also suggest that physicians attempt to prescribe more cost-sensitively to their lower income patients, but are constrained by the difficulty of observing co-pays. We estimate that employer-insured patients with an annual salary below $50,000 would pay, on average, $1.68–$2.88 less on their first monthly

[50] We define *class-based full adherence over six months* (henceforth *adherence*) as refilling enough statin prescriptions to maintain a supply of medication during at least 80 percent of the days in the 6 months following the initial fill. We allow patients to switch to a different statin and still be classified as adherent because we aim to measure the costs of suboptimal prescribing on adherence to statin therapy; if switching costs were low, then the initial prescribing decision would matter less.

[51] While our estimated adherence effects are small, the fact that we don't observe unfilled prescriptions, as discussed in Section VF, biases our estimates of the co-pay effect on adherence toward zero.

[52] We used observed rates of cardiac-related ER visits within the sample, in the calendar year following statin initiation, as baseline. We used 0.62 as the odds ratio effect of statin treatment, as reported for the below age 65 subgroup in a meta-analysis of RCTs focused on populations with no prior history of cardiac events (Brugts et al. 2009).

prescription if physicians could observe cross-plan variations in co-pays as easily as they can gauge the average difference between brand and generic drugs' co-pays.

There are several policy implications of these findings. Mechanisms making co-pays easier to observe, such as mobile apps linked to plan formularies, could help reduce patients' medication costs. The heavy-handed policy of requiring all patients to start with a low cost drug would reduce monetary costs more drastically, but not without imposing costly hurdles on patients who need stronger statins.

Our results also speak to the value of generic drugs, suggesting that the first major patent expiration in a class of chronic drugs has important welfare consequences for the chronically ill.

Furthermore, caution is warranted as insurers begin dividing generic drugs into two distinct co-pay tiers, a trending strategy in response to recent price hikes of generic drugs (Dickson 2014). Unless it is easy for physicians to determine which generics are the least costly, prescribing might not respond fully and lower income patients may bear the burden of this change.

Our study has a few limitations. First, like virtually all related work, we cannot observe unfilled first prescriptions. We use a novel approach to adjust our results for this. A second limitation shared with related work is that we cannot observe plan policies, such as step therapy or prior authorization, but our results hold under several approaches to address this problem. Third, because we focus on statins, a relatively homogenous drug class, it is unclear whether our conclusions apply to other chronic drug classes. In this regard, we view our results as cautionary; co-pays might have even less of an effect on prescribing in classes with less substitutable products, calling into question the widespread use of tiered formularies seen in the US today.

This study provides new evidence of a costly consequence of the US health care system's fragmentation. Until the patient financial incentives set by plans are more easily observed at the time of treatment decisions, they will continue to have a muted effect, even when physicians and consumers are truly price-sensitive.

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