

Is Advertising Informative? Evidence from Contraindicated Drug Prescriptions*

Guofang Huang
Yale University

Matthew Shum
Caltech

Wei Tan
SUNY-Stony Brook

January 23, 2012

Abstract

Crestor, an important but controversial cholesterol-lowering drug, is contraindicated for use by senior and Asian patients. In this paper, we exploit this fact and a unique doctor-level prescription and advertising exposure data for statin drugs to examine the hypothesis of informative advertising. Our tests are based on the intuition that, if advertising is informative, it should lead to fewer contraindicated matches: Doctors should prescribe the drug less frequently to patients with characteristics for which the drug is contraindicated. We find strong evidence for the informative-advertising hypothesis: The match quality signaled by doctor-level advertising for contraindicated patients is significantly inferior to that signaled for the other patients. Our results are robust to the potential endogeneity in doctor-level advertising.

1 Introduction

Pharmaceutical companies spend tremendous resources to promote their drugs. Schweitzer (1997, pg. 46) states that, throughout the 1980s and early 1990s, promotional expenditures (advertising and marketing) in the pharmaceuticals industry exceeded \$5 billion annually, which translates to roughly \$8000 per physician in the United States. This rate of spending also outstrips research expenditures, by about \$1 billion annually.

*We thank Michelle Goeree, Daniel Sgroi, and Juanjuan Zhang for extensive remarks on previous drafts.

One reason that drug companies have such large promotional budgets is because the largest proportion of promotional activity takes the form of “detailing”: drug-company representatives’ expensive visits to doctors’ offices and hospitals, with the representatives often asking for attention in exchange for free meals or medical textbooks. The huge promotional expenditures in pharmaceutical markets is a cause of concern, especially given the asymmetric information characterizing the drug prescription relationship between doctors and patients, and the potential for drug companies to sway doctors to prescribe drugs that may not be in patients’ best interests.

In this paper, we explore the nature of these promotional office visits. In particular, we focus on advertising related to a particular cholesterol-lowering drug, Astra-Zeneca’s Crestor (active ingredient *rosuvastatin*), during a period closely following its introduction to the market. Crestor’s launch in late 2003 was accompanied by a huge marketing campaign. While this is typical for many new drugs, Crestor’s case is noteworthy because, apparently, its marketing push was deemed sufficiently excessive, relative to Crestor’s perceived therapeutic benefits, as to warrant a highly critical editorial in *The Lancet*, the flagship British medical journal:

AstraZeneca’s tactics in marketing its cholesterol-lowering drug, *rosuvastatin*, raise disturbing questions about how drugs enter clinical practice and what measures exist to protect patients from inadequately investigated medicines.¹

Given the controversy surrounding the role of advertising for Crestor, and the policy concerns arising from the potential agency conflicts between doctors and patients, it is interesting to look for evidence of advertising’s benefits vis-a-vis this drug. Our investigation exploits a unique dataset containing records of detailing visits and subsequent prescriptions of cholesterol-lowering statin drugs at the individual doctor level. This dataset, as well as medical features of the pharmaceutical prescription process, allow us to assess whether Crestor’s advertising plays a beneficial role of providing information to doctors.

Our analysis is based on the contraindications indicated for Crestor. The general intuition underlying the analysis is quite straightforward. Suppose that detailing provides doctors with the contraindication information. Then detailing should lead to fewer contraindicated matches, meaning that doctors should prescribe the drug less frequently to patients with characteristics that are contraindicated for the drug. For Crestor, senior patients and

¹From *The Lancet* (2003).

patients of Asian descent are specifically contraindicated. So, under the above assumption, an intuitive test is to see if doctors who are detailed prescribe Crestor less often to these two types of patients. Such tests are relatively easy to conduct.

We find strong evidence for the informativeness of detailing. Our tests strongly reject the null hypothesis of detailing being uninformative or purely persuasive. Our results are robust against the possibility of detailing being endogenous. Finally, as validity checks of our test strategy, we perform “placebo tests” on some non-contraindicated patient groups, including male patients for Crestor and senior and Asian patients for Pravachol and Lipitor (other drugs in the statin category). For these cases, we do not find similar patterns in our analysis, confirming the soundness of the basic idea underlying our tests.

The rest of the paper is organized as follows. Section 2 surveys the literature on testing the informativeness of advertising. Section 3 presents our empirical model and our tests. Section 4 is a short description of the market for the statin class of cholesterol-lowering drugs and the patient types contraindicated for Crestor according to the Food and Drug Administration’s recommendations. It also introduces the data used in our analysis. Section 5 presents the estimation and test results. Section 6 concludes.

2 Literature

The advertising literature has drawn a distinction between the *informative* and *persuasive* effects of advertising. Informative advertising informs consumers about the prices and characteristics of the available products, while persuasive advertising is modeled as advertising that simply raises their willingness-to-pay for the advertised product. Well-known theoretical treatments of persuasive advertising include Dixit and Norman’s (1978) provocative paper on the welfare effects of advertising, while Butters (1977) and Grossman and Shapiro (1984) provide models of purely informative advertising. See Bagwell (2007) for a thorough survey of the literature.

However, the signaling models of advertising (cf. Nelson (1974), Kihlstrom and Riordan (1984), Milgrom and Roberts (1986)) point out that, in *vertically-differentiated* (i.e., quality-differentiated) product markets where consumers are ill-informed regarding the relative qualities of the competing products, the effects of persuasive and informative advertising can be observationally equivalent. This is because in separating equilibria of these models, only high-quality firms undertake advertising, so that advertising is strictly informative

regarding quality differences between competing products. Therefore, if product quality enters consumers' utility functions, advertising for a product informs consumers that it is high-quality, and thus raises their willingness-to-pay, just as in the case of persuasive advertising.

This potential observational equivalence between persuasive and informative advertising makes it difficult to empirically test between them. The existing empirical work has addressed this question in both reduced-form and structural fashion. One important example of the reduced-form approach is Akerberg (2001), who overcomes the observational equivalence problem by focusing on a market for a new good (a new brand of yogurt). By investigating whether advertising has a larger effect on consumers who have tried the new brand or on those who have not, he is able to distinguish between persuasive and informative advertising.

Examples of the structural approach to this question include Erdem and Keane (1996), Akerberg (2003) and Anand and Shachar (2011). Both of these papers model the effect of advertising within a Bayesian-learning model, where consumers who are uninformed about the quality of a product learn about it through advertising. In this structural approach, the distinction between persuasive and informative advertising is modeled parametrically: Persuasive advertising enters consumers' utility functions directly, while informative advertising provides a signal that allows consumers to update their beliefs regarding product quality.

While our approach is more reduced-form, the starting point of our analysis is closest to Anand and Shachar's (2011) paper. Particularly, like them, and unlike Akerberg (and the signaling literature), we focus on advertising's role in *horizontally-differentiated* product markets, where the relative qualities of the competing products vary across consumers. In horizontally-differentiated markets, persuasive and informative advertising are no longer observationally equivalent: While persuasive advertising would still encourage higher usage across all consumers, informative advertising would encourage higher usage only for those consumers for which the advertised product is a good match. For consumers who are ill-matched to the product, strictly informative advertising should actually *discourage* use. Anand and Shachar (2011) use this insight to examine the role of advertising on television viewers' choice of programs to watch, in the context of a structural model of TV program choice. Here, we use a similar intuition to assess whether advertising has informative effects, by examining whether advertising increases or decreases doctors' probabilities of prescribing Crestor to contraindicated patients relative to the other patients.

This paper also utilizes a unique dataset containing information of prescription and exposure to detailing at the individual doctor level. Particularly, the availability of doctor-level advertising exposure information distinguishes it from most other papers focusing on the pharmaceutical prescription process (Stern (1996), Ellison, Cockburn, Griliches, and Hausman (1997), Ching (2010), Coscelli and Shum (2004), Crawford and Shum (2005)). Narayanan and Manchanda (2009) utilize data from the same source, but on a different drug market. Their focus is on estimating a Bayesian learning model with physician specific learning parameters to accommodate physicians’ heterogeneous learning rates. Chintagunta, Jiang, and Jin (2009) incorporate adverse news events into their learning model of prescriptions in the Cox-2 Inhibitors market, but the role of advertising is not the main focus of their paper.

3 Empirical Model and Tests

Our tests of the informativeness of advertising will be based on the relationship between advertising and contraindicated drug prescriptions. Although promotional activities take a variety of forms in the pharmaceutical industry (journal advertising, television commercials, company-sponsored conferences, etc.), we will, for convenience, use the generic term “advertising” in this paper in reference to the largest component of these promotional expenditures – those devoted to detailing, or visits of representatives from pharmaceutical firms to doctors’ offices.

We start by setting up a model to illustrate how informative advertising would be reflected in drug prescriptions. We consider the effects of advertising within a simple Gaussian Bayesian learning model, based on Coscelli and Shum (2004). Suppose that Crestor is prescribed for M types of patients, indexed by $i = 1, \dots, M$. Type i patients obtain true utility of δ_i ($i = 1, \dots, M$) from Crestor. Doctors do not observe $\delta_1, \dots, \delta_M$ and only learn about it via detailing visits. On each detailing visit, a doctor receives a set of signals x_1, \dots, x_M , specific to each patient type. We assume that doctors’ prior beliefs on $\delta_1, \dots, \delta_M$ are normal distributions, and that advertising signals are random draws also from normal distributions. Let \mathcal{A}_1 and \mathcal{A}_0 respectively be the set of *contraindicated* and *non-contraindicated* patient types. Then it is reasonable to assume that $\delta_i \ll \delta_j$ for all $i \in \mathcal{A}_1$ and $j \in \mathcal{A}_0$. While doctors can observe the types of their patients, they may not know, in the absence of advertising, which patient types are contraindicated.

We allow advertising signals to be either *informative* or *persuasive*: An informative advertising signal for patient type m is drawn from $N(\delta_m, \sigma_s^2)$, while a persuasive advertising

signal is drawn from $N(\bar{\delta}, \sigma_s^2)$, with $\bar{\delta}$ being a large positive number, and $\bar{\delta} \gg \delta_m$, for all $m = 1, \dots, M$, and σ_s^2 being the variance. That is, an informative signal is centered around the true utility δ_m , while the persuasive signal is centered around a mean that far exceeds the true utility – that is, persuasive advertising leads to advertising signals which *exaggerate* the true utilities.

Given these assumptions, in each period t , a doctor's belief about δ_m will also be summarized by a normal distribution with a posterior mean $\mu_{m,t}$ and posterior variance $\sigma_{m,t}^2$, which vary over time. In particular, the sequence of posterior means regarding δ_m is characterized by

$$\mu_{m,t} = \mu_{m,t-1} + d_t \gamma_t (x_{m,t} - \mu_{m,t-1}) \quad (1)$$

where the gain coefficient $\gamma_t = \frac{\sigma_{m,t}^2}{\sigma_{m,t}^2 + \sigma_s^2}$, and d_t is a binary variable that indicates whether the doctor is being detailed in period t . That is, the doctor's expected value for δ_m in period t is equal to last period's expected value, plus an updating term that depends on the deviation of this period's advertising signal (if the doctor is detailed this period) from last period's expected value.

For the purpose of testing the hypothesis of informative detailing, we assume that there are only two patient types, $M = 2$, and that these are the contraindicated types and non-contraindicated types. Let subscript a denote the contraindicated patient type, na denote the non-contraindicated type, and A_t be an indicator variable for the period t patient being the contraindicated type. Let μ_t denote the period t posterior mean for a patient. For the simplicity of notation, we omit the subscript for doctor for now. Then we have

$$\begin{aligned} \mu_t &= A_t \mu_{a,t} + (1 - A_t) \mu_{na,t} \\ &= \mu_{na,t-1} + d_{jt} \gamma_t (x_{na,t} - \mu_{na,t-1}) + A_t (\mu_{a,t-1} - \mu_{na,t-1}) + \\ &\quad A_t d_{jt} \gamma_t (x_{a,t} - x_{na,t} - (\mu_{a,t-1} - \mu_{na,t-1})) \end{aligned} \quad (2)$$

where the second equality follows by substituting the expression in (1) for $\mu_{a,t}$ and $\mu_{na,t}$. Note that $x_{a,t}$ and $x_{na,t}$ are the two signals sent during the same detailing visit about the Crestor's match quality for the two types. We say that detailing is informative if $x_{a,t} < x_{na,t}$.² That is, the Crestor detailing is regarded as *informative* if the match signal for the contraindicated type is inferior to that for the noncontraindicated type. Therefore, we can test whether detailing is informative by testing the null hypothesis of

$$H_0 : x_{a,t} - x_{na,t} \geq 0 \quad (3)$$

²This definition of informativeness allows advertising to be persuasive, in the sense that both $E[x_{at}] > \delta_a$ and $E[x_{na,t}] > \delta_{na}$. But as long as $x_{at} < x_{na,t}$, we consider detailing to be informative. In this framework, then, the informative and persuasive hypotheses are not mutually exclusive.

Now, suppose that the utility of prescribing Crestor to the period t patient can be measured by the following indirect utility function:

$$U^* = h(X_t, \mu_t) + \varepsilon_t$$

where X_t is a vector of patient characteristics, and ε_t is a scalar random shock that captures other unobserved factors affecting the prescription behavior. The utility of not prescribing Crestor is normalized to zero. Then the physician will prescribe Crestor if and only if U^* exceeds zero. If we further assume that ε_t is a standard normal random variable, we would get the following probit model for the Crestor prescription probability:

$$\Pr(y_t = 1) = \Phi(h(X_t, \mu_t))$$

Notice that the null hypothesis (3) is equivalent to

$$\gamma_t(x_{a,t} - x_{na,t} - (\mu_{a,t-1} - \mu_{na,t-1})) + \gamma_t(\mu_{a,t-1} - \mu_{na,t-1}) \geq 0$$

Then, after substituting in the expression in (2) for μ_t in the $h(X_t, \mu_t)$, we get the following prescription probability model:

$$\Pr(y_t = 1) = \Phi(h(X_t, \beta_0 + \beta_1 d_t + \beta_2 A_t + \beta_3 A_t d_t)) \quad (4)$$

where $\beta_2 \equiv \mu_{a,t-1} - \mu_{na,t-1}$, and $\beta_3 \equiv \gamma_t(x_{a,t} - x_{na,t} - (\mu_{a,t-1} - \mu_{na,t-1}))$. In the estimation, we will assume that physicians are risk-neutral and that $h(X_t, \mu_t)$ is a linear function of its arguments. After estimating model (4), we can test the informative detailing hypothesis by testing the null hypothesis of

$$H_0 : \beta_3 + \gamma_t \beta_2 \geq 0 \quad (5)$$

One problem with the test is that we do not know γ_t , and we do not have an estimate of it within the model. However, we know that γ_t lies between 0 and 1, so that by fixing γ_t at each of its extreme values, we can consider *least* and *most conservative* tests of the null hypothesis (5). Specifically, given that physicians are either ignorant about the contraindication facts or they have some prior knowledge about the contraindication facts before a detailing visit, we would have $\mu_{a,t-1} - \mu_{na,t-1} \leq 0$ and β_2 estimated to be negative. In this case, the least conservative test for informative advertising, implying the largest type I error for any given value of γ_t , would be to test the null hypothesis of $H_0 : \beta_3 + \beta_2 \geq 0$.³ And the most

³As our data cover a period soon after Crestor became available on the market, some medium values for γ_t may be reasonable.

conservative test for informative advertising would be to test against the null hypothesis of $H_0 : \beta_3 \geq 0$. Given the possibility of prior knowledge, the least conservative test is a reasonable first step for our analysis. If we fail to reject such a least conservative test and $\beta_3 + \beta_2$ turns out to be significantly positive, it amounts to strong evidence for the persuasion hypothesis.⁴

4 Crestor and the Statin Drug Market

In order to implement our test of persuasive vs. informative advertising using data on Crestor detailing and prescriptions, we need to identify contraindicated patient types for the drug. In this section, we first briefly describe the market for the *statin* class of cholesterol-lowering drugs (of which Crestor is a member), and then proceed to a more detailed discussion of the United States Food and Drug Administration’s (FDA) recommendations for Crestor, which we use to pin down patient types who are contraindicated for Crestor.

Worldwide, the statin-class of cholesterol-lowering drugs constitutes the largest drug market, in terms of both sales and prescriptions. Statin drugs were introduced in the mid-1990s, and gained popularity quickly because they led to rapid and dramatic reductions of blood cholesterol levels in patients. Statins work mainly in the liver by inhibiting the enzyme *HMG-CoA reductase*, which triggers increased absorption of low-density lipoprotein (LDL, also known as “bad cholesterol”) from the bloodstream and eventual clearance through the kidneys.

Besides Astra-Zeneca’s Crestor, which was introduced in September 2003, the two other major statin drugs during our sample period were: Pfizer’s Lipitor (*atorvastatin*), introduced in 1996, and Merck’s Zocor (*simvastatin*), introduced in 1991.⁵ Because all statin drugs impose some strain on the liver and kidneys, they are contraindicated for patients who have liver or kidney damage.

However, because Crestor was the most powerful statin drug when it entered the market (and still is), there were some extra precautions for Crestor. In particular, the FDA label for Crestor, which appeared in its first form on August 12, 2003, contained a warning regarding patients of Asian descent, who appeared in clinical studies to retain much higher levels of

⁴We focus on the case that $\beta_2 = \mu_{a,t-1} - \mu_{na,t-1} \leq 0$, which is the relevant case for our results. However, if $\beta_2 \geq 0$, the above least and most conservative tests would be reversed.

⁵Zocor lost patent protection in 2006, and its active ingredient simvastatin is now available in generic versions.

drug concentration in their blood, relative to Caucasian users:

Pharmacokinetic studies show an approximate 2-fold elevation in median exposure in Japanese subjects residing in Japan and in Chinese subjects residing in Singapore when compared with Caucasians residing in North America and Europe. No studies directly examining Asian ethnic population residing in the U.S. are available, so the contribution of environmental and genetic factors to the observed increase in *rosuvastatin* drug levels have not been determined.

In the March 2, 2005 version of the FDA label, this precaution was strengthened, on the basis of studies on U.S. subjects:

Pharmacokinetic studies, including one conducted in the US, have demonstrated an approximate 2-fold elevation in median exposure in Asian subjects when compared with the Caucasian control group.

Furthermore, there is a another warning regarding prescribing Crestor to senior patients (over age 65), as these patients are more likely to develop myopathy (muscle pain and weakness), severe cases of which have resulted in death in patients taking Crestor:

Rovustatin should be prescribed with caution in patients with disposing factors for myopathy, such as renal impairment, advanced age, and hypothyroidism.

Based on the FDA labels, we define senior patients and patients of Asian descent as the contraindicated patient types for Crestor in this paper. (For convenience, we will refer to patients of Asian descent as simply “Asian patients.”) The warning regarding these patients is specific to Crestor and is not present for the other statin drugs. Though patients with myopathy are also warned about some other statin drugs, senior (“advanced-age”) patients are specifically warned only about Crestor. This is an important detail given that we observe only the prescription of statin drugs (and not non-statin cardiovascular drugs) in our data. If other statin drugs were also contraindicated for senior patients, how informative advertising would be reflected in Crestor prescription probabilities would be ambiguous.

4.1 Data

We use a panel dataset comprising prescriptions of statin drugs from a representative sample of U.S. physicians.⁶ The dataset is unique in that, for each physician, we observe a sample of prescriptions written between January 1 2004 and December 31 2004, as well as some characteristics of the patients. The observed patient characteristics allow us to identify the contraindicated patients. In addition, we also have a record of all the detailing visits made by pharmaceutical sales representatives during the same period. We construct our data by combining the prescription data and detailing data. Thus, each observation in our sample is a prescription for which we observe the patient’s characteristics, the prescription made by the physician and measures of detailing activity at the physician’s office.

Table 1 shows the summary statistics of the variables included in the analysis. The first set of variables used in the regression analysis includes a measure of detailing activities at the physician’s office. We use a dummy variable (*detail_id*) to indicate whether a physician is detailed by Crestor in the week immediately preceding the prescription to measure Crestor’s advertising activity. From Table 2 we can see that about 94 percent of the cases have either 0 or 1 detail visit in the previous week, which seems a good balance for our application. A longer time-window would lead to more cases of multiple detailing visits within the time-window, whereas a shorter time-window would miss more very-recent detailing visits. All of our analysis results are qualitatively robust to small changes in the definition of this dummy variable. We also measure the competitors’ advertising activities by using the total number of detailing visits by Crestor’s competitors in the same period. The average number of detailing visits are respectively 0.35 and 1.12, respectively for Crestor and its eight competitors in the previous week.

The second set of variables we control for are a number of patient characteristics, including gender, diagnosis types, prescription types, payment methods (cash, indemnity and medicaid), and a dummy variable for the contraindicated patients (senior patients and Asian patients). About 53 percent of visits are made by male patients, and 44 percent are made by senior patients who are 65 and older. Asian patients account for 2.5 percent all the patient visits. 78 percent are considered to have moderate conditions, six percent severe conditions, and the rest mild conditions. 91 percent of the cases are from ongoing diagnosis. Patients differ in their payment method as well: 51 percent are covered by HMO/PPO/POS; six

⁶ These data are obtained from a pharmaceutical consulting firm, which also provided a similar dataset to a marketing study by Narayanan and Manchanda (2009).

percent patients' payment type is indemnity; while two percent and 39 percent of patients are covered by Medicaid and Medicare respectively.⁷

5 Empirical Results

Before discussing the estimation and test results, let us first look at some patterns from the raw data. Table 3 shows the prescriptions by drug and patient type. As expected, senior and Asian patients are less likely to be prescribed Crestor; senior patients are prescribed Crestor about 4.6-percent less frequently than other patients; Asian patients are prescribed Crestor 4.8-percent less frequently than non-Asian patients. These numbers indicate that, on average, doctors have to some extent become aware of the contraindication of Crestor for senior and Asian patients. The question, then, is whether detailing constitutes a source of such information.

Furthermore, Table 4 shows the Crestor prescription probability by patient types and whether or not a doctor was detailed in the previous week. It shows that, overall, the prescription probability increases after detailing for all three groups of patients. This is consistent with the fact that detailing is, first of all, a marketing tool. But, it also shows that the increase for senior and Asian patients is less than that for the other patients, which suggests that detailers might have revealed that Crestor is not as appropriate for these patients. Obviously these are raw figures, but the message seems clear. We next use a more formal apparatus to test the hypothesis of informative advertising, as described earlier.

5.1 Baseline Empirical Results

Table 5 shows the estimation results of the prescription probit model (4). The dependent variable is the indicator of Crestor prescription, *conditional* on one of the statin drugs being prescribed. The control variables omitted from the table to save space include gender, payment methods, indicator of new or ongoing diagnoses, indicator of new prescription or refill and dummies of prescription month. The difference in the specifications of the two Probit models is that month dummies are included in the second specification. The estimates of the two specifications are very close, indicating that our estimates are robust to adding additional controls of time. Our estimates are strikingly clear. First, the coefficient

⁷ The dummy for Medicare is not included as a control variable because it is highly collinear with the senior patient indicator.

of the detailing indicator is significantly positive, showing that detailing significantly increases the prescription probability for patients for whom Crestor is not contraindicated. In addition, the overall effect of detailing is significantly positive for all patients, including the contraindicated patients. This is consistent with findings in the literature using similar data, and suggests that detailing is above all an effective marketing tool. However, we are unable to conclude whether detailing has a persuasive nature, because we cannot infer whether the detailing signals *exaggerate* the true match qualities of Crestor – that is, whether $E[x_{at}] > \delta_a$ and $E[x_{na,t}] > \delta_{na}$ – because we observe neither δ_a nor δ_{na} .

Furthermore, the coefficient of contraindication indicator (CtrInd.) is significantly negative, meaning that the contraindicated patients are indeed less likely to be prescribed Crestor. It suggests that, on average, physicians have some prior knowledge about the contraindication facts before being detailed. More interestingly, the coefficient of the interaction term of “CtrInd*detail” is also significantly negative, meaning that the prescription probability of Crestor for the contraindicated patients is decreasing relative to the other patients. This suggests that detailing does inform physicians that Crestor does not suit the contraindicated patients as well as it suits the other patients. Lastly, patients with moderate and severe symptoms are more likely to be prescribed Crestor, which is consistent with Crestor being stronger than its competitors.

Given our empirical model, these point estimates imply that $x_{a,t} - x_{na,t} < 0$, which means that the detailing does signal that Crestor is an inferior match for the contraindicated patients. Formal statistical test results are presented in Table 6.⁸ Both tests, including the most conservative test, significantly reject the null, with the most conservative test rejecting the null at slightly higher than 1% significance level. This preliminary evidence suggests that detailing is, indeed, informative about the contraindication facts, as opposed to being a completely indiscriminate marketing tool. In what follows, we first check the robustness of our results against the possibility of detailing being endogenous, and we then demonstrate the validity of our test by applying similar tests to other irrelevant patient types and drugs.

5.2 Endogenous Detailing

Detailing might be endogenous, for example, due to targeted marketing and omitted control variables. To further check the robustness of our results, we estimate again the prescription

⁸We denote, for example, the null hypothesis of the sum of the coefficients of *CtrInd* and *CtrInd * Detail* being greater than 0 by $H_0 : CtrInd + CtrInd * Detail \geq 0$.

probability models for Crestor by using an instrumental variable method (“IV probit”). The instrumental variables (IV) we use are based on the total number of detailing visits to the same physicians by the representatives of the other statin drugs in the same week during the previous year 2003 (mostly before the introduction of Crestor). The instruments are motivated by cost-side considerations. The cost of detailing a physician is determined mainly by such factors as the physician’s geographical location and how hard it is to schedule detailing office visits with the physicians. The IV essentially works as a proxy variable for the physician-specific detailing cost at specific times. It could be correlated with Crestor detailing in 2004 as the cost of visiting a physician is correlated across brands and serially correlated across time. Meanwhile, after controlling for the variables in our data, factors affecting the total detailing of the other brands in 2003 are unlikely to be correlated with the unobserved factors determining the prescription of Crestor in our 2004 model. This is especially true given that we are focusing on the prescription of Crestor, *conditional* on one of the statin drugs being prescribed.⁹

The first-stage results for detailing, presented in the first two columns of Table 7, shows that the first stage is strong enough. The IV estimation results for the prescription probit model are presented in the last two columns of Table 7. The difference between the two specifications is whether the dummies for prescription month are controlled for. The sample is relatively smaller than the original sample because the detailing data for some physicians are not available for 2003. The IV estimation results are very similar to the estimation results without using IV. All the coefficients here have the same signs as the simple probit estimates. The main difference is that the estimated coefficients of “CtrInd” and “CtrInd*detail” have somewhat larger absolute value than the previous estimates, and the estimates with month dummies controlled for are statistically less significant.

The formal test results based on the IV estimation results in the last column of Table 7 are presented in Table 8. Both tests reject the null hypothesis again at the 5% significance level. Therefore, our test results provide strong and robust evidence for the hypothesis that detailing has played a role in informing physicians.

⁹One might argue that the competitors’ lagged total detailing should also be affected by physicians’ prescription volumes, which are normally quite persistent. However, it is not clear why physicians’ prescription volumes would be related to such conditional choice decisions, controlling for the information we have in our data.

5.3 Validity Checks: Evidence from “Placebo Tests”

The above tests of the informativeness of detailing are based on observable contraindicated groups of patients. The underlying argument is that if detailing were informative, we should be able to find that it signals the inferior match quality of Crestor for the contraindicated patients. In this subsection, we use placebo tests to confirm the validity of our basic test idea. In these placebo tests, we show that the observed pattern of the coefficients in our baseline specifications disappears if we conduct the same tests on Crestor with patient groups that are not specifically contraindicated, or on other statin drugs that are not contraindicated for senior and Asian patients.

First, we look at the prescription of Crestor to male patients, who, as a group are not specifically contraindicated for Crestor. The estimates of models, including dummy variables and interaction terms for male patients, are shown in Table 9. The first and second columns are the estimates of the prescription probit model without and with instruments, respectively.

The coefficient of the male indicator is slightly negative in the simple probit model, but it is not significant at any standard significance level in the probit model estimated with instruments. More importantly, the interaction term of “Male*detail” is not significant in either statistical or economic terms. These results are consistent with the fact that male patients are not contraindicated as a group.

The formal results of the replicated tests based on the model estimated with and without instruments are shown in Table 10, where the first two tests are based on the probit model estimated without using instruments. Though the first least conservative test (test #1) rejects the null hypothesis at 5% level, the most conservative test cannot reject the null at any standard significance level. None of the remaining tests based on probit model estimated with instruments can reject the null at any standard significance level. Thus, overall, the test results show no evidence that detailing is signaling a different match quality of Crestor for male and female patients.

We further replicate our tests using the same prescription probability model for two other statin drugs: Pravachol and Lipitor. Pravachol was introduced in the U.S. market in late 1991, and Lipitor was launched in January 1997. As senior and Asian patients are specifically contraindicated only for Crestor among the statin drugs, we should not see the same pattern of prescription of other statin drugs. More specifically, we should not see that detailing lowers the probability of prescribing Pravachol and Lipitor to elderly and Asian patients relative to other patients.

Table 11 presents the estimation results for the prescription probit model for Pravachol and Lipitor. Columns (2) and (4) are the prescription models estimated with instruments. First of all, in the prescription models estimated with instruments, the coefficients of the interaction term “CtrInd*detail” are close to zero and statistically insignificant for the case of Pravachol, and positive but statistically insignificant for the case of Lipitor. These estimates are quite different from what we have seen for Crestor, consistent with our expectations.

Second, the estimates show that patients for whom Crestor is contraindicated are more likely to be prescribed Pravachol but less likely to be prescribed Lipitor, which suggests that these other statin drugs do not match senior and Asian patients equally well. Furthermore, it is worth noting that, in the probit model of Lipitor (column (3)), the coefficient of “CtrInd*detail” is significantly negative, in contrast to being positive but insignificant when the model is estimated with instruments. As we pointed out above, the estimates of simple prescription Probit models can be biased, because detailing is often endogenous as a result of targeted marketing. Our estimates for Lipitor suggest that the detailing of Lipitor was targeted more at physicians who are less inclined to prescribe Lipitor to senior and Asian patients. Such targeted marketing seems quite reasonable, given that our estimates show that physicians are significantly less likely to prescribe Lipitor to senior and Asian patients relative to other patients.

Formal test results based on the IV Probit estimates are shown in Table 12. None of the test results is similar to our previous test results for Crestor.

To summarize this section, first, our test results presented strong evidence indicating that detailing actually is informative; second, the results are robust to the possibility of detailing being endogenous; last, the validity of our tests is supported by the results we found by conducting similar tests for other irrelevant cases.

6 Conclusion

In this paper, we examined the potential beneficial role of pharmaceutical detailing in informing the prescription process. As profit-driven as detailing is, we find some strong evidence showing that it is also informative of the negative features of the drug being promoted. This evidence is important for the debate over potential regulations on the pharmaceutical industry’s advertising activities.

In the meantime, our findings also raise the question of why self-interested pharmaceutical

companies and sales representatives should actively reveal such negative information about their own drugs. Understanding the mechanism underlying such "self-discipline" would further inform the controversy surrounding pharmaceutical advertising. However, answers to such questions are beyond the scope of the current paper, and we leave it for our future research.

Appendix: Tables

Table 1: Summary Statistics

Variable	Description	Mean	Std. Dev.	Min	Max
Crestor	Indicator variable	0.111	0.314	0	1
Detail_id	Indicator of Crestor detailing visits	0.296	0.456	0	1
Detail	Number of Crestor detailing visits	0.348	0.624	0	5
Detailcomp	Total # of competitors' detailing visits	1.123	1.481	0	15
Male	Indicator variable	0.532	0.499	0	1
Age65	Indicator of senior patients	0.442	0.497	0	1
Asian	Indicator of Asian patients	0.025	0.157	0	1
CtrInd.	Indicator of contraindicated patients	0.457	0.498	0	1
Severe	Severe symptoms	0.060	0.238	0	1
Moderate	Moderate symptoms	0.784	0.412	0	1
New prescription	Indicator variable	0.164	0.371	0	1
Ongoing diagnosis	Indicator variable	0.910	0.285	0	1
Hmoppopso	Indicator of being covered by HMO/PPO/PSO	0.509	0.500	0	1
Indemnity	Indicator of paying through indemnity	0.056	0.229	0	1
Medicare	Indicator of being covered by Medicare	0.394	0.489	0	1
Medicaid	Indicator of being covered by Medicaid	0.024	0.154	0	1

Table 2: Number of Detailings

detail	Freq.	Percent
0	102,052	72.05
1	31,401	22.17
2	6,814	4.81
3	1,194	0.84
4	167	0.12
5	8	0.01
Total	141,636	100

Table 3: Prescription to Contraindicated Patients and Other Patients

Drugs	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
	Senior Patients		Asian Patients		Other Patients	
Crestor	5,383	8.60	307	8.36	10,377	13.20
Other Drugs	52,217	91.40	3,365	91.64	68,213	86.80

Table 4: The Prescription of Crestor at Detailed and Non-detailed Doctors

	Senior Patients	Asian Patients	Other Patients
Non-Detailed	0.0788 (0.0013)	0.0731 (0.0051)	0.1194 (0.0014)
Detailed	0.1033 (0.0022)	0.1083 (0.0094)	0.1620 (0.0024)
Difference	0.0245	0.0352	0.0426

Note: The standard errors of the prescription likelihoods are in the parenthesis.

Table 5: Probit Models of Crestor Prescriptions

	Probit1		Probit2	
	Coef.	Marginal Effect	Coef.	Marginal Effect
Detail	.187 (.012)***	.033 (.002)***	.199 (.013)***	.035 (.002)***
CtrInd	-.185 (.012)***	-.031 (.002)***	-.185 (.012)***	-.031 (.002)***
CtrInd*detail	-.042 (.02)**	-.007 (.003)**	-.043 (.02)**	-.007 (.003)**
Moderate	.234 (.014)***	.036 (.002)***	.232 (.014)***	.036 (.002)***
Severe	.661 (.02)***	.157 (.006)***	.661 (.02)***	.156 (.006)***
Indemnity	.106 (.019)***	.019 (.004)***	.108 (.019)***	.019 (.004)***
Medicaid	-.109 (.031)***	-.017 (.004)***	-.109 (.031)***	-.017 (.004)***
Cash	.012 (.041)	.002 (.007)	.012 (.041)	.002 (.007)
Male	-.051 (.009)***	-.009 (.002)***	-.05 (.009)***	-.008 (.002)***
Constant	-.736 (.024)***		-.900 (.030)***	
Month Dummies	No	No	Yes	Yes
Obs.	144862	144862	144862	144862

Notes: 1. Standard errors in parentheses; * significant at 10%; ** significant at 5%; *** significant at 1%; 2. Extra Controls: prescription types and the dummy of new diagnosis.

Table 6: One-Sided Normal Tests Based on Probit Estimates

	Null Hypothesis	Test-Stat	p-value
#1	H0: CtrInd.+CtrInd.*detail ≥ 0	-13.773	1.85e-43
#2	H0: CtrInd.*detail ≥ 0	-2.16	.015

Table 7: Crestor Prescriptions to Contraindicated Patients: IV-Probit Estimates

	Detail	CtrInddetail	IV-Probit1	IV-Probit2
CtrInd	-.001 (.004)	.249 (.002)***	-.132 (.034)***	-.135 (.039)***
Detail			.5 (.055)***	.417 (.07)***
CtrInd*detail			-.229 (.099)**	-.223 (.119)*
IvDetail	.057 (.001)***	.003 (.0008)***		
CtrInd*IvDetail	-.001 (.002)	.051 (.001)***		
Moderate	.007 (.004)*	.006 (.003)**	.212 (.016)***	.212 (.017)***
Severe	-.003 (.007)	.003 (.004)	.649 (.023)***	.651 (.023)***
Indemnity	.015 (.006)**	-.002 (.004)	.107 (.021)***	.11 (.021)***
Medicaid	-.008 (.009)	.002 (.006)	-.113 (.036)***	-.114 (.036)***
Cash	.0008 (.015)	.001 (.01)	.033 (.048)	.034 (.05)
Male	-.002 (.003)	-.002 (.002)	-.06 (.011)***	-.059 (.011)***
Constant	.500 (.010)***	.103 (.006)***	-.806 (.032)***	-.966 (.044)***
Month Dummies	Yes	Yes	No	Yes
R-Squared	0.06	0.2		
Obs.	105501	105501	105501	105501

Notes: 1. Standard errors in parentheses; * significant at 10%; ** significant at 5%; *** significant at 1%; The same marks for significance levels also apply to the other tables in the following. 2. Extra Controls: prescription types and the dummy of new diagnosis.

Table 8: One-Sided Normal Tests Based on IV Probit Estimates

	Null Hypothesis	Test-Stat	p-value
#1	H0: CtrInd.+CtrInd.*detail ≥ 0	-4.375	6.07e-06
#2	H0: CtrInd.*detail ≥ 0	-1.882	.030

Table 9: The Prescription of Crestor to Male Patients: Placebo tests

	Probit		IV Probit	
	Coef.	Marginal Effect	Coef.	Marginal Effect
Detail	.187 (.014)***	.033 (.002)***	.347 (.085)***	.064 (.014)***
Male	-.021 (.011)*	-.004 (.002)*	-.019 (.041)	-.003 (.006)
Male*detail	-.008 (.019)	-.001 (.003)	-.038 (.124)	-.006 (.016)
Moderate	.235 (.014)***	.037 (.002)***	.216 (.017)***	.034 (.002)***
Severe	.674 (.02)***	.161 (.006)***	.665 (.023)***	.157 (.007)***
Indemnity	.186 (.018)***	.035 (.018)***	.192 (.021)***	.036 (.004)***
Medicaid	-.043 (.03)	-.007 (.005)	-.045 (.037)	-.007 (.006)
Cash	.085 (.041)**	.015 (.008)**	.108 (.05)**	.019 (.010)**
Constant	-0.990 (.030)***		-1.040 (.042)***	
Obs.	144862	144862	105501	105501

Notes: Extra Controls: prescription types and the dummies of new diagnosis and month.

Table 10: One-Sided Normal Test Based on IV-Probit Estimates: Placebo tests

	Null Hypothesis	Test-Stat	p-value
#1	H0: male+male*detail ≥ 0	-1.821	0.034
#2	H0: male*detail ≥ 0	-0.429	0.334
#3	H0: male+male*detail ≥ 0	-0.654	0.257
#4	H0: male*detail ≥ 0	-0.302	0.381

Table 11: The Prescription of Pravachol and Lipitor to Patients Contraindicated for Crestor: Placebo tests

	Pravachol(Probit)	Pravachol(IV-Probit)	Lipitor(Probit)	Lipitor(IV-Probit)
Detail	.21 (.017)***	.743 (.128)***	.047 (.011)***	-1.231 (.096)***
CtrInd	.063 (.01)***	.058 (.034)*	-.105 (.008)***	-.176 (.033)***
CtrInd*detail	-.021 (.025)	-.036 (.209)	-.061 (.017)***	.217 (.15)
Moderate	-.08 (.012)***	-.083 (.014)***	-.012 (.009)	.0003 (.012)
Severe	-.314 (.024)***	-.306 (.028)***	-.081 (.016)***	-.073 (.02)***
Idemnity	.016 (.02)	.034 (.023)	.015 (.015)	-.0003 (.018)
Medicaid	.074 (.029)**	.041 (.035)	-.064 (.022)***	-.039 (.028)
Cash	-.226 (.056)***	-.301 (.071)***	.071 (.034)**	.098 (.044)**
Male	-.074 (.009)***	-.075 (.011)***	.016 (.007)**	.019 (.008)**
Constant	-1.494 (.036)***	-1.721 (.056)***	-.123 (.024)**	.464 (.044)**
Obs.	144848	105494	144843	105488

Notes: Extra Controls: prescription types and the dummies of new diagnosis and month.

Table 12: One-Sided Normal Test Based on IV-Probit Estimates: Placebo Tests

	Null Hypothesis	Test-Stat	p-value
#1	$H_0: \text{CtrInd} + \text{CtrInd} * \text{detail} \geq 0$	0.130	0.550
#2	$H_0: \text{CtrInd} * \text{detail} \geq 0$	-0.172	0.431
#3	$H_0: \text{CtrInd} + \text{CtrInd} * \text{detail} \geq 0$	-0.344	0.635
#4	$H_0: \text{CtrInd} * \text{detail} \geq 0$	1.446	0.926

References

- ACKERBERG, D. (2001): “Empirically Distinguishing Informative and Prestige Effects of Advertising,” *RAND Journal of Economics*, 32, 316–333.
- (2003): “Advertising, Learning, and Consumer Choice in Experience Good Markets: A Structural Examination,” *International Economic Review*, 44, 1007–1040.
- ANAND, B., AND R. SHACHAR (2011): “Advertising, the matchmaker,” *The RAND Journal of Economics*, 42(2), 205–245.
- BAGWELL, K. (2007): “The Economic Analysis of Advertising,” in *Handbook of Industrial Organization*, Vol. 3, ed. by M. Armstrong, and R. Porter. North-Holland.
- BUTTERS, G. (1977): “Equilibrium Distributions of Sales and Advertising Prices,” *Review of Economic Studies*, 44, 465–491.
- CHING, A. (2010): “A Dynamic Oligopoly Structural Model for the Prescription Drug Market After Patent Expiration,” *International Economic Review*, 51, 1175–1207.
- CHINTAGUNTA, P., R. JIANG, AND G. JIN (2009): “Information, learning, and drug diffusion: The case of Cox-2 inhibitors,” *Quantitative Marketing and Economics*, 7(4), 399–443.
- COSCELLI, A., AND M. SHUM (2004): “An Empirical Model of Learning and Patient Spillovers in New Drug Entry,” *Journal of Econometrics*, 122, 213–246.
- CRAWFORD, G., AND M. SHUM (2005): “Uncertainty and Learning in Pharmaceutical Demand,” *Econometrica*, 73, 1137–1174.
- DIXIT, A., AND V. NORMAN (1978): “Advertising and Welfare,” *Bell Journal of Economics*, pp. 1–19.
- ELLISON, S., I. COCKBURN, Z. GRILICHES, AND J. HAUSMAN (1997): “Characteristics of Demand for Pharmaceutical Products: An Examination of four Cephalosporins,” *RAND Journal of Economics*, 28, 426–446.
- ERDEM, T., AND M. KEANE (1996): “Decision-making Under Uncertainty: Capturing Dynamic Brand Choice Processes in Turbulent Consumer Goods Markets,” *Marketing Science*, 15, 1–20.

- FOOD AND DRUG ADMINISTRATION (2003, 2005): “Labels for *Crestor*,” Available at http://www.fda.gov/cdei/foi/label/2003/21366_crestor_lbl.pdf.
- GROSSMAN, G., AND C. SHAPIRO (1984): “Informative Advertising with Differentiated Products,” *Review of Economic Studies*, 51, 63–81.
- KIHLSTROM, R., AND M. RIORDAN (1984): “Advertising as a Signal,” *Journal of Political Economy*, 92, 427–450.
- MILGROM, P., AND J. ROBERTS (1986): “Price and Advertising Signals of Product Quality,” *Journal of Political Economy*, 94, 796–821.
- NARAYANAN, S., AND P. MANCHANDA (2009): “Heterogeneous Learning and the Targeting of Marketing Communication for New Products,” *Marketing Science*, 28, 424–441.
- NELSON, P. (1974): “Advertising as Information,” *Journal of Political Economy*, 82, 729–755.
- SCHWEITZER, S. (1997): *Pharmaceutical Economics and Policy*. Oxford University Press.
- STERN, S. (1996): “The Demand for Pharmaceuticals,” Kellogg School, Manuscript.
- The Lancet* (2003): “The statin wars: why AstraZeneca must retreat,” Vol. 362, October 25.