Impact of Treatment Effectiveness and Side-effects on Prescription Decisions: The Role of Patient Heterogeneity and Learning

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Abstract

The goal of a standard clinical study is to assess the mean or median effectiveness and side effects of drugs through randomized clinical trial experiment. In this paper we argue that, it is important to understand how physicians and patients evaluate the effectiveness and side effects. Second, it is also important to understand the extent of heterogeneity in these outcomes across patients, especially when physicians and patients are risk averse in choosing treatments. Finally, using data from a market environment has advantages over clinical trials since in the former patients and physicians are faced with alternative drugs they can choose from while exposed to marketing efforts from pharmaceutical companies.

In this study we use a physician panel data in the Erectyle Desfunction (ED) category to examine how the mean effectiveness and side effects as well as the heterogeneity in these treatment outcomes affect prescription decisions. To separately identify the patient evaluation of effectiveness and side effects, we augment the observed prescription choices with a unique data on self-reported reasons for switching in our estimation. Two sources of uncertainty in the evaluation of the effectivness and side effects of drugs are accounted for in our model. First, effectiveness and side effect of a drug can vary across patients and second even the mean effectiveness and side effects may be unknown to physicians and patients, especially for those drugs that are new to the market. We allow physicians to learn about the effectiveness and side effects of new drugs based on patient feedbacks and detailing visits from pharmaceutical companies. Results show that though the two new drugs, Levitra and Cialis, have higher mean effectiveness and lower mean side effects than the exiting drug, Viagra, their competitive weakness is the larger heterogeneity in effectiveness and side effects, respectively. Detailing visit is effective in reducing the uncertainty of effectiveness but much less effective in reducing the uncertainty of side effects. We also find that for both new drugs the informative role of detailing visit is more important than its persuasive role in influencing the prescription utility.

Key Words: Effectiveness and side effects, prescription choices, patient heterogeneity, Bayesian learning and uncertainty

1. Introduction

Drugs can be effective in curing an illness or relieving a symptom but can have harmful side effects. The value of a drug, among others, depends on the trade-off of patients between its treatment effectiveness and side effects. Recognizing this, firms routinely conduct clinical trials to compare effectivenss and severity of side effect of their drungs in comparison to other drugs in the market place. For example, in 2004 Bristol-Myers Squibb carried out a clinical trial to compare the effectiveness of its cholesterol lowering drug Pravachol against Pfizer's Lipitor. After four and half years the median cholesterol level was 95 mg per deciliter among those who took Pravachol compared to 62 mg per deciliter in the Lipitor group. Another measurement showed that 26.3% of patients in the Pravachol group either died, suffered a heart attack or other complications, compared to 22.4% of those in the Lipitor group (see Cannon et al 2004). Based on these findings, the researchers concluded that Lipitor provides greater protection against death or major cardiovascular events than does Pravachol. Bresalier et al (2005) found from their study that patients who used Merck & Co.'s blockbuster painkiller Vioxx had a significantly higher risk of heart attacks and strokes compared with patients in the placebo group (1.50 vs. 0.78 thrombotic events per 100 patient-year). Safety concerns were so high that in September 2004 Vioxx was pulled out from the market. However, comparison along single dimension does not reveal the full picture. Though less effective in lowering cholesterol, Pravachol may have fewer side effects. For example, only 1.1% of patients in the Pravachol group had a higher level of enzymes that could lead to liver problems, compared with 3.3% in the Lipitor group. With the side effect of higher cardiovascular risk, Vioxx was more effective in treating rheumatoid arthritis – Rombardier et al (2000) reported in their study that patients in the Vioxx group had significantly lower grastrointestinal and other complicated events than patients in the group who used another existing treatment. At a three-day hearing held by the Food & Drug Administration in late February, 2005, even though the 32 outside experts agreed that Vioxx did pose serious risks, they also recommended that Vioxx was useful enough that it shouldn't be banned (Carey and Capell, 2005).

Based on our readings of past clinical trials, we make three arguments in this paper. It is important (i) to assess the effectiveness and side effects of a drug and understand how

physicians and patients evaluate these treatment outcomes; (ii) to measure the mean (or median) effectiveness and side effects and the extent of heterogeneity in these outcomes across patients, especially when physicians and patients are risk averse in choosing treatments; (iii) to use data from clinical trials and prescription choices after introduction. We summarize the justification for these.

While the goal of a clinical trial is to assess effectiveness and side effects, it is important for researchers to also understand how prospective patients and physicians evaluate these. Without understanding such evaluations it is impossible for policy makers to determine the value of a medical treatment. The reason is obvious. Often patients and physicians are forced to make trade offs between effectiveness and side effects based on host of factors. For example, how should patients evaluate the difference between 1.50 and 0.78 thrombotic events per 100 patient-year in the Vioxx study? Would most patients rather take a more effective drug in relieving pain but with higher cardiovascular risk instead of a less effective but safer drug? If the answer is yes, it may benefit the society that Vioxx remain in the market as long as patients are well informed of the risk. From a managerial perspective, to effectively market their products phamarceutical companies have to convey the benefits of their drugs that most physicians and patients consider as important.

Second, though the comparison of mean or median effectiveness and side effects across drugs is important, we argue that the heterogeneity of treatments outcomes across the population should not be ignored because of two reasons. First, different drugs work for different patients[1]. A drug that lags behind the others in mean or median treatment outcomes may still work best for a significant number of patients. When considering the value of a drug, policy makers should not just look at the mean or median measurement but also the number and characteristics of patients for whom the drug works better than the others. Heterogeneity in consumer preference has been widely studied in the economics and marketing literature but in clinical studies importance of heterogeneity in treatment outcomes has not received enough attention. Second, patients may be very risk averse especially when a bad outcome is life threatening, such as a heart attack or stroke in the Vioxx examples we discussed above. If the

[1] We use ‘treatment’ and ‘drug’ interchangeably.

effectiveness or side effects of a drug vary greatly across patients it is unlikely that physicians will prescribe the drug especially to new patients since larger risk is involved. Therefore, understanding the extent of the heterogeneity in treatment outcomes among patients is important to the firm. For example, if Pravachol is able to lower cholestral more consistently among all patients than Lipitor, Bristol-Myers Squibb can promote this to risk averse physicians and patients.

In summary, we believe that it is important to measure how patients and physicians evaluate effectivenees and side effects of drugs and how large the heterogeneity in effectivenees and side effects is among patients. Consistent with the economics and marketing literature, this paper uses the observed choice made by patients and physicians to identify such evaluations. To our knowledge, Chan and Hamilton (2006) is the paper closest to our research objective. They found from a clinical trial involving the treatment of AIDS that not only treatment effectiveness but also side effects had a significant impact on patients' evaluation of the treatement they received. Clinical trials are the typical data source for most medical studies, during which patients can choose their compliance effort (whether to continue or drop out from the assigned treatment arm in Chan and Hamilton) but not switching to other drugs. In contrast, we use data where physicians and patients jointly decide whether to continue the drug previously prescribed or to switch to a new drug. Using data from a market environment over clinical trials has several advantages. First, a larger number of observations can be collected from the market data to identify the existence of rare side effects such as liver failure or aplastic anemia (Okie 2005). Second, in market environments patients and physicians are faced with alternative drugs they can choose from while exposed to marketing efforts such as detailing from phamarceutical companies. Managers are interested in understanding the impacts marketing activities on treatment choices that cannot be studied from clinical trials where patients are assigned to single treatment condition. Finally, observed switching among drugs

helps us identify correlations of effectiveness and side effects across drugs.[2] We will further amplify this point in the model section.

To estimate the impacts of treatment effectiveness and side effects of different drugs on treatment choice as well as the heterogeneity of such impacts, we rely on (1) the observed treatment choice for each physician-patient pair and, (2) self-reported reasons for switching drugs. While the former allows us to infer the overall evaluation of treatments by physicians and patients, the latter helps to separately identify the effectiveness and side effects across drugs as well as the heterogeneity of their impacts. A drug that accounts for greater proportion of those switching out due to treatment ineffectiveness (side effects) implies that, compared with other drugs, more patients find this drug less effective (with severe side effects) than expected. Since the data also reports to which other drugs these patients switch, we can further infer that, that drug switched into is more effective (with less severe side effects) for that particular patient. Hence the potential correlations of both treatment effectiveness and side effects across drugs can be estimated from the data. Self-reported consumer survey data was proposed by Manski (2004) to help understand the extent of consumer uncertainty. Berry et al (2004) used the data of consumers' self-reported secondary choice in the automobile market to identify the correlation of consumer preferences for product attributes. Our approach in this paper is similar to theirs.

Unlike other product categories such as CPG where consumers have more knowledge of the product quality and their own preferences, large uncertainty exists among physicians and patients in the pharmaceutical market. This uncertainty comes from two sources: First, as discussed above, treatment outcomes may be heterogeneous across patients – a drug that works effectively for some patients may turns out to be ineffective for the others. Though the impacts may be quickly learnt once a patient has taken the drug, it is still uncertain about the treatment impacts if he were to switch to another drug. If patients are risk averse, physicians are less likely to prescribe them drugs for which treatment outcomes vary greatly across other patients. Second, the mean treatment effectiveness and side effects may be unknown to physicians and

[2] We acknowledge that tested drugs in clinical trials are usually not yet in the market hence market data is unavailable for evaluating these drugs. After a drug has been approved and introduced, however, market data will

patients, especially for those drugs new in the market. Many questions are likely to be asked by physicians when a new drug is introduced: Is the drug more effective or with fewer side effects compared other existing drugs? Does the drug work better for patients with severe or mild conditions? Public domain information such as clinical trial reports may not be sufficient to address all these concerns. Physicians also rely on a variety of other information sources including marketing communication such as detailing, learning from the feedback from their patients, and/or recommendations from other physicians either formally or informally. In order to correctly infer how physicians and patients evaluate the trade-offs between treatment effectiveness and side effects, we have to first understand how treatment decisions are made under uncertainty. Uncertainty may vary across physicians due to their past treatment experiences, exposure to marketing efforts from pharmaceutical companies and other information sources.

A number of studies in marketing and economics have investigated how physicians and patients learn about the quality of drug in the market. The study by Ching (2005) considers a model where physician learn of the overall attribute of a generic drug through patients' feedback in the presence of heterogeneity. Using a dataset of anti-ulcer drug prescriptions, Crawford and Shum (2005) estimated a dynamic demand model under uncertainty in which patients learn from usage experience about the effectiveness of alternative drugs. In Narayanan et al (2005) and Narayanan and Manchanda (2006), the authors focus on physicians' learning about the quality of new drugs through the marketing communication as well as past prescription experience. Unlike these previous studies which assume an overall "attribute" or "quality" of drug, our study examine the separate impact of effectiveness and side effects on physician's choice of treatment. The learning process of physicians in our model involve both effectiveness and side effects. Given that all clinical studies try to measure effectiveness and side effects, we believe that it is important when studying the patient and physician evaluation of drugs we should also distinguish between these two attributes.

Similar to Narayanan et al (2005) and Narayanan and Manchanda (2006) we allow detailing to have an informative and persuasive role. However in our model we allow for the

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be useful to supplement its further evaluation.

detailing informational content to be different for effectiveness and side effects. Our data provides information on two different types of detailing, i.e., detailing visit with and without a meal. By estimating and comparing the informative and persuasive function of both types of detailing visits in the model, we are able to shed light on some much debated topics in the medical field: Does detailing help to provide physicians information of effectiveness and side effects, or only bias their prescription decisions? Compared with normal detailing, does "dash-and-dine" perform better in either of the functions? Further, how does the informative role of detailing, with or without meal, change overtime as physicians have learnt more about the effectiveness and side effects through own experiences? Answering the above questions is important from both policy and managerial perspectives.

We develop a structural model where physicians make prescription decisions under uncertainty to maximize a joint utility function with their patients. An advantage of a structural model is that we can directly infer the preference weights for effectiveness and side effects. Further, factors such as treatment heterogeneity, uncertainty about outcomes and risk aversion as well as their changes over time, can be explicitly modeled and estimated and hence their impacts on prescription choices can be better understood. Finally, it is well known that the behavioral parameters in the structural model are invariant to changes in marketing policies such as detailing and other communication strategies. Hence, one can conduct counter-factual policy experiments useful for managerial decisions. We apply our model to a unique dataset from the Erectile Dysfunction (ED) category. We choose the ED category because this is one of the few categories with significant new drugs launched in the recent years and therefore provides an appropriate context to study physician learning associated with new drugs. We have the prescription and promotion data from a physician panel. Moreover, the dataset contains the self-reported reasons for switching when a patient switches from one drug to another. We are able to separately identify the impact of treatment effectiveness and side effects on prescription choices.

The estimation results show that the two new drugs, Levitra and Cialis, have higher mean evaluation in both effectiveness and side effects than the existing drug, Viagra. Specifically, Cialis is the most effective drug with the least side effects among the three.

However, Cialis also has the largest variance in its side effects. It would gain higher market share among new patients if the variance of its side effects could be reduced, whereas Levitra would gain more if the variance of its effectiveness could be reduced. Because of the small heterogeneity in treatment outcomes with the lowest mean effectiveness and side effects Viagra still has a significant market share in the long run. An interesting comparison is that the main reason for choosing Viagra is lower side effects, while the main reason for choosing Cialis is its effectiveness. In another scenario, for those patients who are on Viagra, if they switch to Cialis it is due to greater perceived effectiveness, while if they switch to Levitra it is due to less severe side effects.

Our results also show that there exists significant amount of prior uncertainty among physicians for new drugs. This implies that it is critical for the new drugs to reduce such uncertainty to gain market share. We find that detailing with or without meal is much more effective in reducing the uncertainty of effectiveness among physicians compared with learning from patient feedbacks; however, detailing is less effective in reducing the uncertainty of side effects. Roughly speaking, the informative role for side effects of one detailing with or without meal is comparable to that of one patient feedback. We also find that for both new drugs the informative role of detailing visit is more important than its persuasive role in influencing the prescription utility. Finally, differences in the informative and persuasive role between detailing with meal and detailing without meal are not very significant.

The rest of the paper is organized as follows. In Section 2, we describe the model. In Section 3 and Section 4 we describe the data and details of estimation. In section 5 we discusses the results and conlude our paper in section 6 pointing out future directions in this stream.

2. The Model

Let E_h^j and S_h^j be the clinical measurements of the effectiveness and side effects,[3] respectively, of drug j on patient h. The main objective of clinical studies is to compare the

[3] E and S can be continuous or discrete such as the number of incidents.

mean or median $\bar{E}^j$ and $\bar{S}^j$ across patients with other drugs or with placebo. As we argued in the introduction, such measurements do not have a meaning unless we know the preference weights ω_h^E and ω_h^S that the patient associates with E_h^j and S_h^j. Consistent with the revealed preference theory that is the basis for the choice literature, we use the observed patient and physician choice to infer such preferences.

Our model is conditional on patients seeking treatment from physicians who make prescription decisions among the available drugs in the market. Due to data constraints that we will discuss later, our model excludes those patients who seek treatment but are not prescribed any of the three drugs. When a patient seeks treatment from a physician, we assume that the physician makes the final decision on which drug should be prescribed. A physician's prescription decision depends among others on (a) patient's evaluation of the effectiveness and side effects of alternative drugs, (b) out-of-pocket cost for the patient and (c) marketing activities of the phamarceutical companies. We assume that the physician maximizes a joint-utility function that captures the effects (a)-(c) when making prescription decision. If the patient has a diminished role in the prescription decision we should find the weights of the patient effects including his evaluation of the effectiveness and side effects lower than the weights of the physician effects.

Our model differs from extant economics and marketing literature in the phamarceutical industry as we estimate the impacts of effectiveness and side effects separately in prescription decisions. The identifiability comes from the fact that we also use the additional data of self-reported switching reasons. In this section we will discuss the assumptions we make in our model related to the reported switching reasons. Finally we will discuss how physicians learn about the effectiveness and side effects of new drugs from two information sources – patient feedbacks and the detailing visits from sales representatives of phamarceutical companies.

2.1 Model Specifications

Unlike clinical studies we do not directly observe clinical measurements E_h^j and S_h^j from data. We infer, from observed treatment choices, the patient's evaluation of effectiveness

and side effects, e_h^j and s_h^j, which can be treated as the product of E_h^j and S_h^j and his corresponding preference weights ω_h^E and ω_h^S. For physician *i* who treats a patient *h* at occasion *t*, we specify a joint-utility function of prescribing drug *j* as follows:

$$U_{ih,t}^j = f(e_h^j, s_h^j) + X_{ih,t}^j \beta + \varepsilon_{ih,t}^j \quad (1)$$

where e_h^j is the patient's evaluation of the effectiveness, and s_h^j is the patient's evaluation of the side effects, of drug *j*. The function $f(\cdot)$ represents patient *h*'s overall utility obtained from the treatment. The vector $X_{ih,t}^j$ contains patient characteristics such as age and race, an interaction between insurance and drug identity which captures the out-of-pocket cost for the patient, marketing activities such as detailing by phamarceutical companies, that could shift the physician-patient preference. Finally $\varepsilon_{ih,t}^j$ is a random shock *i.i.d.* across physician, patient, drug and time which will affect the prescription decision but is unobserved to researchers.

When seeking treatment, the patient reveals his own information on his own evaluation of the effectiveness e_h^j and side effects s_h^j if drug *j* was previously used. We assume that the physician has complete information about $X_{ih,t}^j$ and the random shock $\varepsilon_{ih,t}^j$. Therefore the physician can evaluate $U_{ih,t}^j$ in (1) without uncertainty. For other drugs that the patient has not used before, the physician has to form expectation on the patient's utility. Let Ω_{it} be the physician's information set at time *t* that includes his knowledge of the treatment effectiveness and side effects of all available drugs.[4] For an existing patient the physician Ω_{it} also consists of the patient's evaluation of the previously used drug e_h^j and s_h^j. The expected utility of physician *i* in prescribing another drug *j'* is represented as follows:

$$E[U_{ih,t}^{j'} \mid \Omega_{it}] = E[f(e_h^{j'}, s_h^{j'}) \mid \Omega_{it}] + X_{ih,t}^{j'} \beta + \varepsilon_{ih,t}^{j'} \quad (1')$$

This implies that for patient *h* the expected utility function for drug *j'* is conditional on his evaluations of the previous drug *j*, e_h^j and s_h^j.

[4] We will provide the details of the physician knowledge in later section.

For a new patient, the physician will form expectation for the patient's utility $f(\cdot)$ with the same representation as (1'). However, no evaluation of effectiveness and side effects of any drugs for this particular patient is included in the physician's information set Ω_{it}. For this patient, the physician prescribes drug *j* if the following condition is satisfied:

$$E[U^{j}_{ih,t} \mid \Omega_{it}] \geq E[U^{j'}_{ih,t} \mid \Omega_{it}], \quad \forall j' \neq j \tag{2}$$

For an exisitng patient, we assume that there is a switching cost related to changing prescription. The switching cost may exist due to the psychological impact (e.g., patient's perceived risk of the new drug) as well as the time and effort associated with filling the prescription for the new drug. We assume this cost is same for all possible pairs of drugs. The physician prescribes the same drug to the patient if the following condition is satisfied:

$$E[U^{j}_{ih,t} \mid \Omega_{it}] \geq E[U^{j'}_{ih,t} \mid \Omega_{it}] - SC, \quad \forall j' \neq j \tag{3}$$

where *j* is the drug previously prescribed, and SC is the switching cost. Otherwise the physician will switch to a new drug that provides the highest expected utility.

We assume that patients are risk averse. In this case uncertainty about treatment effectiveness and side effects will reduce their expected utility. As a new drug may have more uncertainty, such specification helps to explain why new drugs take time to gain market share. We capture the risk aversion in the utility function by the following specification:

$$f(e^{j}_{h}, s^{j}_{h}) = -exp[-(e^{j}_{h} + s^{j}_{h})] \tag{4}$$

Let $x^{j}_{h} = e^{j}_{h} + s^{j}_{h}$. Equation (4) implies the property of constant absolute risk aversion (CARA), where the Arrow-Pratt coefficient of absolute risk aversion $r_A(x^{j}_{h}) = -f''(x^{j}_{h}) / f'(x^{j}_{h})$ is constant. Similar specification has been used in Chan and Hamilton (2006).

As discussed above patient evaluations, e^{j}_{h} and s^{j}_{h}, represent the combination of clinical measurements and the patient preference weights for effectiveness and side effects. Heterogeneity in e^{j}_{h} and s^{j}_{h} represents differences in either treatment outcomes across patients or the patient preferences of treatment outcomes, or the combination of both. The difference in the mean of *e* and *s* between drugs, therefore, represents the mean difference in effectiveness or

side effects outcomes weighted by patient preferences. Such difference between drugs have an implication on the patient utility or prescription choice.

Let J be the total number of drugs in the market. We denote $\bar{E}$ as a $J\times 1$ vector of average effectiveness evaluation across patients of all drugs, and $\bar{S}$ as a $J\times 1$ vector of average side effects evaluation. We specify that

$$e_h = \bar{E} + \xi_h^E \tag{5}$$

where e_h is a $J\times 1$ vector of effectiveness evaluation from patient h, and

$$s_h = \bar{S} + \xi_h^S \tag{6}$$

is similary defined for side effects evaluation.[5] Our model allows e_h and s_h to be correlated across drugs – a patient experiencing more side effects with a drug j may also experience more side effects with another drug k, a patient who has higher valuation for effectiveness than other patients will have a higher value of e_h for all drugs etc. We assume that $\xi_h^E \sim N(0,\Sigma_\xi^E)$, and $\xi_h^S \sim N(0,\Sigma_\xi^S)$, where Σ_ξ^E and Σ_ξ^S are $J\times J$ variance-covariance matrices representing the extent of heterogeneity in effectiveness and side effects, respectively, across patients. The larger the value of the diagonal element (variance) the larger is the heterogeneity. Further, the off-diagonal elements represent covariances of effectiveness and side effects between drugs. We estimate the full variance-covariance matrices in model estimation.

2.2 Modeling Reasons to Switch

Under the distribution assumption of ε^j in equation (1), the observed prescription data can only help identify the sum of e^j and s^j, i.e., the overall quality of each drug as perceived by patients or physicians. However, we cannot infer whether the choice of drug j is due to higher effectiveness or lower side effect, i.e., e^j and s^j cannot be separately identified. Their identification comes from an additional information source: our data reports for every existing patient the previously and newly prescribed drugs. The reason for switching drugs is also

[5] For simplicity of notation we will refer the effectiveness evaluation and side effects evaluation of patients as "effectiveness" and "side effects" hereon in paper as long as there is no confusion.

reported if the previously and newly prescribed drugs are different. We model these switching reasons together with the prescription choice in our model to help us separately identify the impact of effectiveness vs. side effects on prescription decisions.

Suppose the prescription for patient h is switched from drug j to drug k. We assume that, first of all, the expected utility associated with drug k, $E[U^k_{ih,t} \mid \Omega_{it}] - SC$, is the highest among all alternatives including drug j (equation (3)). Moreover, if from data "side effects" was stated as the switching reason, we assume that the following two conditions have to be satisfied:

(i) $s^j_h < E[s^k_h \mid \Omega_{it}]$; and

(ii) $s^j_h < e^j_h$

Condition (i) is based on a reasonable assumption that if switching is due to side effects the physician will not prescribe another drug with higher expected side effects than the current prescription. Condition (ii) is based on the assumption that otherwise ineffectiveness of drug j will be indicated as the switching reason. In (i) and (ii) we use true values of effectiveness and side effects for drug j instead of their expectations because of the assumption that s^j_h and e^j_h are fully revealed after the drug was used. Further, the information set Ω_{it} in (i) also consists of s^j_h and e^j_h.

If "ineffetiveness" was stated as the switching reason, we have two similar conditions:

(iii) $e^j_h < E[e^k_h \mid \Omega_{it}]$; and

(ii) $e^j_h < s^j_h$

In our data a considerable number of switchings are either without reasons provided or due to other reasons such as "patients request". We group them into "other reasons". We believe that there are several reasons why physicians do not report ineffectiveness or side effects as switching reasons. First, switching may be due to reasons other than effectiveness and side effects concerns. For example, patients may be affected by direct-to-consumer promotions hence have very strong preferences for a particular drug. The underlying reasons of their brand preferences of course may still be effectiveness or side effects concerns. Another

reason is that the conditions listed above are not satisfied for some switchings. For example, the physician may expect drug *k* to be more effective than drug *j* (condition (iii) satisfied) but the patient evaluates the effectiveness of *j* higher than its side effects (condition (iv) violated). Since we do not want to impose any restrictions on switching reasons for these cases, we assume that s_h^j and e_h^j of the previously prescribed drug are generated from the estimated distribution of effectiveness and side effects of drug *j*, conditional on the restriction that the realized utility of using *j* (equation (1)) is lower than the expected utility of using *k* (equation (1')) plus the switching cost, i.e., $U_{ih,t}^j < E[U_{ih,t}^k \mid \Omega_{it}] - SC$.

2.3 Uncertainty and Learning

Physicians may be uncertain about the true distribution of effectiveness and side effects across patients especially when a drug is newly introduced. Our modeling approach is consistent with the previous literature on learning (for examples see Erdem and Keane (1996), Ching (2005), Crawford and Shum (2005) etc.) with the key difference that we explicitly model the learning of effectiveness and side effects separately. We assume that there are prior beliefs among physicians. To simplify analysis we further assume the means of effectiveness and side effects in physicians' prior beliefs are consistent with the true values $\bar{E}$ and $\bar{S}$ (equations (5) and (6)). That is, physicians have rational expectations. We also assume that physicians know the heterogeneity matrices Σ_ξ^E and Σ_ξ^S. However, physicians are uncertain of the true means of effectiveness and side effects. Such prior uncertainty is consistent with the Bayesian framework and is specified as follows:

$$E^0 \sim N(\bar{E}, \Sigma_{\upsilon,0}^E), \text{ and } S^0 \sim N(\bar{S}, \Sigma_{\upsilon,0}^S), \tag{7}$$

where the superscript "0" in (7) denotes physicians' prior beliefs of the mean values in period 0. We assume that the variance-covaraince matrices $\Sigma_{\upsilon,0}^E$ and $\Sigma_{\upsilon,0}^S$ are diagonal matrices of which the *j*-th diagonal element is $\sigma_{E,j}^{\upsilon,2}$ and $\sigma_{S,j}^{\upsilon,2}$, respectively. If a drug has existed in market for long time before our sample period starts (such as Viagra in our empirical application), the prior uncertainty is likely to be low; hence, its corresponding variances in $\sigma_{E,j}^{\upsilon,2}$ and $\sigma_{S,j}^{\upsilon,2}$ are

negligible. However, $\sigma_{E,j}^{\upsilon,2}$ and $\sigma_{S,j}^{\upsilon,2}$ can be high for new drugs in the market.[6] We assume that there is no correlation in the prior uncertainties, i.e., the off-diagonal elements in $\Sigma_{\upsilon,0}^{E}$ and $\Sigma_{\upsilon,0}^{S}$ are all zero. For model identification (details will be provided in the estimation section) we assume that there is no uncertainty about the heterogeneity of effectiveness and side effects as well as the correlations of effectiveness and side effects among drugs.

We assume that physicians use two sources to update their prior beliefs and reduce uncertainty: (i) detailing from phamarceutical companies and, (ii) patient feedbacks. Let's first discuss the functions of detailing in affecting physicians' prescription choice. Consistent with the literature on advertising and promotion, our model allows for two functions – persuasive and informative – from detailing. Persuasive function refers to the activity of detailing that changes the preference of physicians when prescribing drugs that is unrelated to the consideration of effectiveness and side effects. In our model detailing visits for drug *j* is a component of the explanatory variables $X_{ih,t}^{j}$ (see equation (1)). That is, the persuasive function of detailing is modeled as simply shifting the utility function $U_{ih,t}^{j}$.

The informative function of detailing is modeled as providing information about the true effectiveness and side effects for a drug when uncertainty exists among physicians, i.e., when $\Sigma_{\upsilon,0}^{E}$ and $\Sigma_{\upsilon,0}^{S}$ (see equation (7)) are non-zero. Following Erdem and Keane (1996), we allow for the case that detailing may not provide perfect information; instead, there may be noise regarding effectiveness and side effects associated each detailing message. For simplicity we assume that detailing for a drug only provides information for that particular drug, and no credible information can be provided for other drugs. In each period *t*, the physician receives detailing message regarding effectiveness and side effects as follows

$$D_{it}^{E} = 1_{it}^{D} \cdot (\overline{E} + \zeta_{it}^{E}), \text{ and } D_{it}^{S} = 1_{it}^{D} \cdot (\overline{S} + \zeta_{it}^{S}), \tag{8}$$

[6] Alternatively, one can assume that the physician's prior beliefs for *Z*, $Z = \{E, S\}$, on a patient *h*, are

$$Z_{h}^{0} = \overline{Z} + \chi_{h}^{Z}$$

and $\chi_{h}^{Z} \sim N(0, \Sigma_{\xi}^{Z} + \Sigma_{\upsilon,0}^{Z})$. That is, the perceived variances in effectiveness or side effects for new drugs are larger than what they truly are.

where 1_{it}^{D} is a $J\times 1$ indicator of which the *j-th* element is equal to one if detailing for drug *j* happened at *t* and zero otherwise, and the operator "·" is an element-by-element multiplication. The variables ζ_{it}^{E} and ζ_{it}^{S} are $J\times 1$ vectors of noises associated with detailing messages. For simplicity we assume that ζ_{it}^{E} and ζ_{it}^{S} are normally distributed with means zero and variances $\sigma_{E,\zeta}^{2}$ and $\sigma_{S,\zeta}^{2}$, respectively. That is,

$$\zeta_{it}^{E} \sim N(0, \sigma_{E,\zeta}^{2} \cdot I_J);\ \zeta_{it}^{S} \sim N(0, \sigma_{S,\zeta}^{2} \cdot I_J)$$

where I_J is a $J\times J$ identity matrix. This implies that the noise of detailing message is *i.i.d.* over time and across drugs. Further, detailing for a drug does not reveal information about the effectiveness and side effects of other drugs.

We separately examine the persuasive and informative roles of detailing visits. Public opinion and policy makers are concerned that the persuasive effect of detailing biases the physician's prescription decision and hurt the patient welfare. Specifically, there are deep concerns that phamarceutical companies provide physicians non-monetary benefits such as vacation trips and banquests through inviting physicians to the medical conferences organized by the companies (Weintraub, 2007, Periera, 2007). However, industry insiders argue that, instead of biasing their decisions, these practices help physicians to learn the true effectiveness and side effects of drugs leading to lower uncertainty and hence will enhance patient welfare. As discussed in the introduction, we differentiate the impacts of detailing visits with and without meal provided. Given the controversy on the practice of providing benefits (such as meal provision) to physicians, we believe that it is important to identify the persuasive and informative role of these two types of detailings on prescription decisions.

The second source of information through which physicians may learn the true effectiveness and side effects of drugs is patient feedbacks. As discussed above, once patient *h* used drug *j* before his revisits, we assume that the physician will fully observe the effectiveness and side effects of drug *j* on that particular patient. The physician still has uncertainty regarding the effectiveness and side effects of drug *j* on other patients and, if he switches patient *h* to other drugs, the uncertainty regarding the effectiveness and side effects of other drugs on that patient. The physician will use the observed e_h^j and s_h^j to form his expectations for the effectiveness

and side effects of other drugs on this patient (given that effectiveness and side effects across drugs are correlated if off-diagonal elements in Σ_{ξ}^{E} and Σ_{ξ}^{S} (equations (5) and (6)) are non-zero). Further, when there is uncertainty regarding the true treatment impacts, i.e., when $\Sigma_{\upsilon,0}^{E}$ and $\Sigma_{\upsilon,0}^{S}$ (see equation (7)) are non-zero, the observed experience of patient *h* using drug *j* provides valuable information for the physician to update his beliefs regarding the true means of effectiveness and side effects of the drug on other patients.

We model the learning of physicians through detailing and patient feedbacks using a Bayesian learning framework. Let $\Omega_{i,t}$ be the information set of physician *i* regarding the treatment effectiveness and side effects of all available drugs. In period 0, the period before our sample period starts, all physicians are assumed to have the same prior beliefs E^0 and S^0 as in equation (7). For $Z = \{E, S\}$, i.e., effectiveness and side effects, suppose that at time *t* physician *i* has patient *h* who is an existing patient visited, or that the physician receives a detailing message from sales representatives of phamarceutical companies. Physicians will update their beliefs according to the Bayesian rule (DeGroot 1970) as follows:

$$E[Z \mid \Omega_{i,t}] = E[Z \mid \Omega_{i,t-1}] + I_{iht}^{P}\Gamma_{1,it}(Z_{iht} - E[Z \mid \Omega_{i,t-1}]) + I_{it}^{D}\Gamma_{2,it}(D_{it}^{Z} - E[Z \mid \Omega_{i,t-1}]) \qquad (9)$$

where I_{iht}^{P} is a $J \times J$ matrix of which the *j*-th diagonal element is equal to one if at time *t* patient *h* who used drug *j* in the previous period re-visits and zero otherwise, and its off-diagonal elements are all zero. Likewise I_{it}^{D} is a $J \times J$ matrix of which the *j*-th diagonal element is equal to one if at time *t* the physician was detailed by sales representative of drug *j* and zero otherwise, and off-diagonal elements are all zero. The terms $Z_{iht} - E[Z \mid \Omega_{i,t-1}]$ and $D_{it}^{Z} - E[Z \mid \Omega_{i,t-1}]$ represent the deviations of the values of realized treatment outcomes and detailing message, respectively, from the expected value of *Z* conditional on the information set $\Omega_{i,t-1}$.

The Kalman gain coefficients Γ's (see Erdem and Keane 1996) are defined as

$$\Gamma_{1,it} = \Sigma_{\upsilon,t}^{Z} \cdot (\Sigma_{\upsilon,t}^{Z} + \Sigma_{\xi}^{Z})^{-1}, \text{ and } \Gamma_{2,it} = \Sigma_{\upsilon,t}^{Z} \cdot (\Sigma_{\upsilon,t}^{Z} + \sigma_{Z,\zeta}^{2} \cdot I_{J})^{-1}, \qquad (10)$$

where $\Sigma^Z_{\upsilon,t}$ is the updated variance of the physician's beliefs of mean effectiveness or side effects at time *t*, and Σ^Z_{ξ} is the variance-covariance matrix for effectiveness or side effects defined above. $\sigma^2_{Z,\zeta}$ is the variance for effectiveness or side effects associated with detailing noise, and I_J is a $J \times J$ identity matrix. According to the Bayesian rule we have the variance $\Sigma^Z_{\upsilon,t}$ updated as

$$\Sigma^Z_{\upsilon,t} = [(\Sigma^Z_{\upsilon,0})^{-1} + (\Sigma^Z_{\xi})^{-1} \cdot \sum_{s=0}^{t} I^P_{iht} + (\sigma^2_{Z,\zeta} \cdot I_J)^{-1} \cdot \sum_{s=0}^{t} I^D_{it}]^{-1} \quad (11)$$

where $\Sigma^Z_{\upsilon,0}$ is the period 0 prior beliefs defined in equation (7).

3. Data Description

Our data is from the ED category made available to us by ImpactRX, a pharmaceutical consulting firm based in New Jersey. There are three drugs in the category: Viagra launched in March 199, followed by Levitra in August 2003, and finally Cialis in November 2003. To estimate our choice model we use the sample period from August 2003 to October 2004. Thus, during the first three months of our observations only Viagra and Levitra existed and for the remainder all three drugs were in the market.

Our data consists of individual physician level prescription data and detailing activities of phamarceutical companies. We have 828 physicians in the panel with a total of 13,619 patient visits during the sample period. About 54% of the patient visits were for exisiting patients (i.e., patients who had visited physician for the same illness before and had been prescribed a drug in the ED category), and the rest were new patients. For each of the patient visits, we observe which of the three ED drugs were prescribed to the patient. We also observe the switching behavior of the existing patients. Among the 7,324 visits by these, 5,672 visits (77.4%) resulted in a prescription for the same drug as the previous visit, and the remaining 1,652 visits resulted in switching to a different drug. In addition, we observe the self-reported switching reasons if drug switching happened. Table 1 summarizes the major types of switching reasons as reported by the physician. "Other Reasons" in the table include patient request and more often no reason reported. As mentioned in the model section, in these cases

we do not impose restrictions on switching reasons except that the drug switched to has the highest expected utility, and assume that the unobserved effectiveness and side effects for the previously prescribed drug are generated from the corresponding estimated distributions of different drugs.

Switching Reasons	Count	Percentage
Ineffectiveness	929	56.2%
Severe Side Effects	161	9.7%
Other Reasons	563	34.1%
Total	1,652	100%

Table 1: Switching Reasons for Existing Patients

One of the limitations of the data is that there is no patient panel data. We do not observe the past treatment history of existing patients other than the drugs prescribed during their previous visits and if switching occurs the reason that they switch. Further, for a new patient we do not know if the patient has sought treatment in the past but chosen an option that is out of the three drugs in our data. All these may introduce a potential bias in model estimation as we will discuss in the later section.

The prescription trends of the three ED drugs for the data period are plotted in Figure 1. The data period starts from August 2003 when the first prescription of Levitra was observed in the data, labled as Day 1 in Figure 1. The first prescription of Cialis was observed in the data on Day 110. As we can see from the Figure, the market share of the newest drug Cialis has grown steadily in the first six months after its introduction and then stablized. In terms of the total market share, Viagra still has an edge over the two newer drugs; in terms of the market share for new patients alone, Cialis has almost the same market share as Viagra at the end of the sample period. These product penetration processes might be driven by two reasons: (1)

physicians have large uncertainty associated with new drugs and they have to learn (from either detailing messages or patient feedbacks) over time; (2) there exists switching cost from one drug to another among existing patients hence existing drugs such as Viagra have an sustainable advantage over new drugs for existing patients even after long periods.

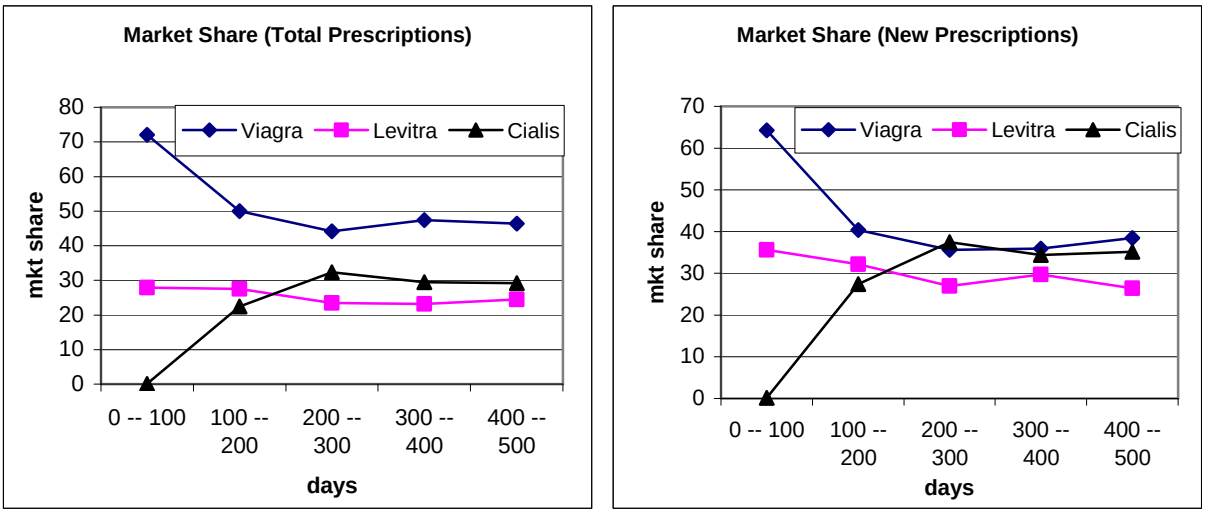

Figure 1. Prescription Trends of the ED Drugs in Sample Period

Other than prescription records, we also have the detailing data for the physician panel. There are altogether 26,509 detailing visits in our sample period. The majority of the detailing visits (82.5%) are visits without meals, and the remaining visits are detailing visits accompanied by meals. In Figure 2, we plotted the total number of detailing visits of the three ED drugs in the sample period. The two new drugs, Levitra and Cialis, were both promoted heavily immediately following their market entry. As a response Viagra also increased detailing efforts after Levitra entered the market. Then the detailing efforts dropped considerably for all three drugs in later periods. The trend of detailing visits with meals provided also demonstrate a similar pattern. This poses an interesting question: Can this declining trend of detailing be explained by the declining marginal impact of detailing over time in a standard cost-benefit

analysis framework? If the answer is yes, why would the marginal impact of detailing decline over time?

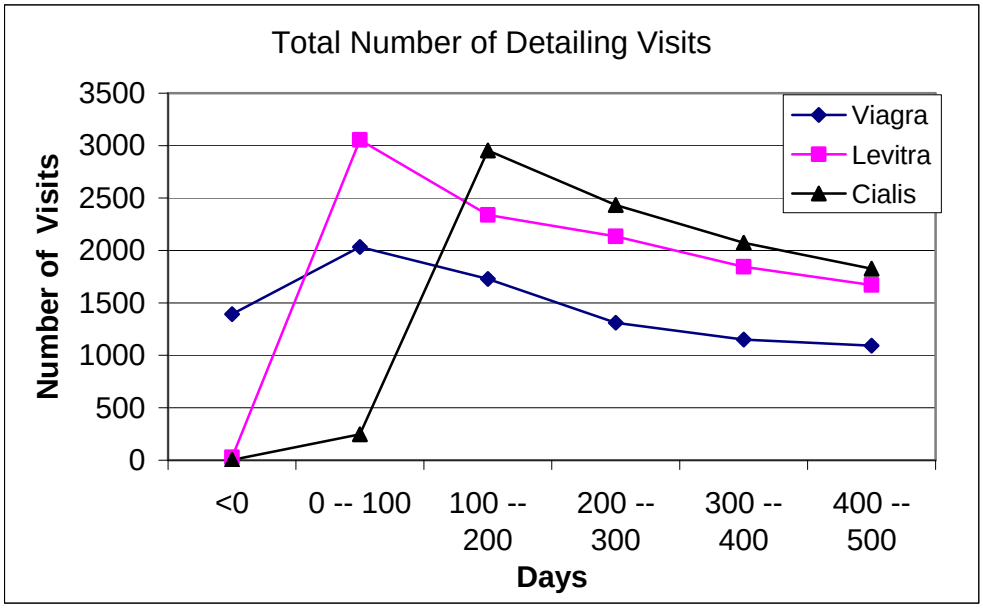

Figure 2. Detailing Trends of the ED Drugs in Sample Period

Patient characteristics, such as age, ethnicity, insurance coverage, and severity status of disease are also provided in the data. These characteristics may shift the patient preferences for various drugs. For example, if an insurance covers the cost of prescribing one drug but not the others, we may observe more patients covered by the insurance choose the drug due to lower out-of-packet cost. Some descriptive statistics of the patient characteristics are provided in Table 2. We can see that most of the patients are Caucasians in the age range of 51-60. HMO/PPO/PPS is the main insurance coverage followed by Medicare. Most of the patients in data are moderate disease status (73%) while very few are severe. For our model estimation purpose, we group patients of moderate and severe status together as "moderate" patients vs. "mild" patients in data.

	Count	Percentage
Patient Age		
<= 40	918	6.7%
41-50	3,118	22.9%
51-60	4,769	35.0%
61-70	3,387	24.9%
>=71	1,427	10.5%
Patient Ethnicity		
African American	2,320	17.0%
Asian	229	1.7%
Caucasian	10,013	73.5%
Hispanic	995	7.3%
Native American	22	0.2%
Other	40	0.3%
Insurance Coverage		
HMO/PPO/POS	8,745	64.2%
Indemnity	1,270	9.3%
Medicaid	374	2.7%
Medicare	2,769	20.3%
No Coverage	461	3..4%
Disease Severity Status		
Mild	3,309	24.3%
Moderate	9,964	73.2%
Severe	346	2.5%

Table 2. Some Summary Statistics of Patient Characteristics

4. Model Estimation

The major problem in estimating our model is that, unlike Chan and Hamilton (2006), we do not observe the clinical measurements of effectiveness and side effects from our data. Instead, their evaluations are inferred from the observed prescription choices of physicians and reported reasons for switching drugs. There is also an econometrician's uncertainty that we have to account for in our model:[7] after observing the treatment outcomes for a patient and/or detailing messages from sales representatives, physicians update their expectations of the true effectivness and side effects of drugs that are unobserved by researchers. To estimate the model we have to account for these unobserved variables in our specification that include the stochastic terms ξ_h^E (equation (5)), ξ_h^S (equation (6)), and the physician's uncertainties (equation (7)) on the likelihood of the observed prescription decisions and switching reasons. Finally, when physicians are uncertain of the true mean effectiveness and side effects of drugs and learning is involved, their expectations may be different from the true values. In other words, for $Z=\{E, S\}$, $Z_{iht} - E[Z \mid \Omega_{i,t-1}]$ and $D_{it}^Z - E[Z \mid \Omega_{i,t-1}]$ (equation (9)) may or may not be the same as the true values of ξ_h^Z (the true treatment outcome shocks for specific patients) and ζ_{it}^Z (the true detailing noise), respectively.

For the purpose of exposition we denote the information set for physician *i* at time *t*, $\Omega_{i,t}$, as $\Omega(\xi_{i,-t}^E, \xi_{i,-t}^S, \zeta_{i,-t}^E, \zeta_{i,-t}^S)$, where each variable inside the bracket is a vector of the stochastic outcomes from either the patient feedbacks of past treatments or past detailing messages, and subscript "-*t*" denotes the physician's information before time *t*. These variables represent the asymmetric information between researchers and physicians. As we will discuss later, we rely heavily on the simulation method to evaluate the likelihoods of the observed data.

[7] The econometrician's uncertainty stems from researchers not observing from data some important variables that affect the objective function of decision makers, but decision makers observe these variables and account for them in their optimization behavior. See Reiss and Wolak (2005).

4.1 Likelihood Functions

Suppose at time t physician i prescribes a drug j, $j = V$ (Viagra), L (Levitra) and C (Cialis), for a new patient h. Given that, conditional on the observed characteristics of the new patient, the effectiveness and side effects of any drug on the patient are unknown, the physician has to form expectations based on his information set $\Omega_{i,t}$. We assume type I extreme value distribution for the stochastic term ε in equations (1) and (1'). Based on this distribution assumption the probability of prescribing drug j is

$$P^1_{i,h,j,t} = prob(i \text{ prescribing } j \text{ for new patient } h \mid \Omega_{it}(\xi^E_{i,-t}, \xi^S_{i,-t}, \zeta^E_{i,-t}, \zeta^S_{i,-t}))$$
$$= \frac{\exp(E[f(e^j_h, s^j_h) \mid \Omega_{it}(\xi^E_{i,-t}, \xi^S_{i,-t}, \zeta^E_{i,-t}, \zeta^S_{i,-t})] + X^j_{ih,t}\beta)}{\sum_{k=1}^{J} \exp(E[f(e^k_h, s^k_h) \mid \Omega_{it}(\xi^E_{i,-t}, \xi^S_{i,-t}, \zeta^E_{i,-t}, \zeta^S_{i,-t})] + X^k_{ih,t}\beta)} \quad (12)$$

In the second case, suppose patient h is an existing patient who used drug j before. Compared with the new patient case, the physician has the additional information of true $e^j_h = \bar{E}_j + \xi^E_{h,j}$ and $s^j_h = \bar{S}_j + \xi^S_{h,j}$ now. They have become part of the information set for the physician at time t, which is useful in forming expectations for the treatment outcomes if the patient is switched to other drugs. To differentiate from the new patient case, we specify the new information set as $\Omega_{it}(\xi^E_{i,-t}, \xi^S_{i,-t}, \zeta^E_{i,-t}, \zeta^S_{i,-t}, \xi^E_{h,j}, \xi^S_{h,j})$ when the the treatment outcomes $\xi^E_{h,j}$ and $\xi^S_{h,j}$ are revealed. Suppose in the data the same drug j is prescribed again. Based on the distribution assumption for ε and the prescription choice rule in equation (3), the probability of prescribing the same drug j is the following:

$$P^2_{i,h,j,t} = prob(i \text{ prescribing same } j \text{ for on-going } h \mid \Omega_{it}(\xi^E_{i,-t}, \xi^S_{i,-t}, \zeta^E_{i,-t}, \zeta^S_{i,-t}, \xi^E_{h,j}, \xi^S_{h,j}))$$
$$= \frac{\exp(f(e^j_h, s^j_h) + X^j_{ih,t}\beta)}{\exp(f(e^j_h, s^j_h) + X^j_{ih,t}\beta) + \sum_{k \neq j} \exp(E[f(e^k_h, s^k_h) \mid \Omega_{it}(\xi^E_{i,-t}, \xi^S_{i,-t}, \zeta^E_{i,-t}, \zeta^S_{i,-t}, \xi^E_{h,j}, \xi^S_{h,j})] + X^k_{ih,t}\beta - SC)} \quad (13)$$

Note that switching cost *SC* enters the choice probability function for existing patients. Further, there is no uncertainty of e_h^j and s_h^j hence for *j* there is no need to form expectation.

Finally, suppose patient *h* is an existing patient who used drug *j* before and is switched to another drug *k* at time *t*. The reason of switching will be reported in this case. Suppose "side effects" was stated as the reason. Based on our discussion in the model section conditions (i) and (ii) have to be satisfied. In order to identify the distribution of e_h^j and s_h^j, we estimate the joint likelihood of these two conditions together with the prescription choice probability. That is, we estimate the joint probability

$$P_{i,h,j,t}^3 = prob(s_h^j < E[s_h^k \mid \Omega_{it}],\ s_h^j < e_h^j, \text{ and } E[U_{iht}^k \mid \Omega_{it}] - SC \geq \max\{U_{iht}^j,\ E[U_{iht}^l \mid \Omega_{it}] - SC\}),^8$$

where the superscript "*l*" denotes the identity of the other drug different from *j* and *k*.

The joint probability can be expressed as the following conditional probability

$$\begin{aligned} P_{i,h,j,t}^3 &= prob(s_h^j < E[s_h^k \mid \Omega_{it}]) \times prob(s_h^j < e_h^j | s_h^j < E[s_h^k \mid \Omega_{it}]) \\ &\quad \times prob(E[U_{iht}^k \mid \Omega_{it}] - SC \geq \max\{U_{iht}^j,\ E[U_{iht}^l \mid \Omega_{it}] - SC\} \mid s_h^j < E[s_h^k \mid \Omega_{it}] \text{ and } s_h^j < e_h^j) \\ &\equiv P_{i,h,j,t}^{3,1} \times P_{i,h,j,t}^{3,2} \times P_{i,h,j,t}^{3,3} \end{aligned} \tag{14}$$

We will provide details about the calculation of the conditional probabilities later. The third probability function $P_{i,h,j,t}^{3,3}$ in (14) is the prescription choice probability. It is similar to the logit function in (13) except that $P_{i,h,j,t}^{3,3}$ is conditional on $s_h^j < E[s_h^k \mid \Omega_{it}]$ and $s_h^j < e_h^j$. That is,

$$\begin{aligned} P_{i,h,j,t}^{3,3} &= prob(i \text{ prescribing } k \text{ for on-going } h \mid s_h^j < E[s_h^k \mid \Omega_{it}] \text{ and } s_h^j < e_h^j) \\ &= \frac{\exp(E[f(e_h^k, s_h^k) \mid \Omega_{it},\ s_h^j < E[s_h^k \mid \Omega_{it}] \text{ and } s_h^j < e_h^j] + X_{ih,t}^k \beta - SC)}{\left(\begin{array}{l} \exp(f(e_h^j, s_h^j) + X_{ih,t}^j \beta \mid s_h^j < E[s_h^k \mid \Omega_{it}] \text{ and } s_h^j < e_h^j) \\ \\ + \sum_{j' \neq j} \exp(E[f(e_h^{j'}, s_h^{j'}) \mid \Omega_{it},\ s_h^j < E[s_h^k \mid \Omega_{it}] \text{ and } s_h^j < e_h^j] + X_{ih,t}^{j'} \beta - SC) \end{array} \right)} \end{aligned} \tag{15}$$

The likelihood function when "ineffetiveness" was stated as the switching reason is similar to equations (14) and (15) above, except that conditions (iii) and (iv) have to be satisfied (see our discussion in the model section).

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[8] For notation simplicity we use $\Omega_{it} \equiv \Omega_{it}(\xi_{i,-t}^E, \xi_{i,-t}^S, \zeta_{i,-t}^E, \zeta_{i,-t}^S, \xi_{h,j}^E, \xi_{h,j}^S)$ here.

Finally, there is a closed-form expression for $E[f(e_h^k, s_h^k) | \Omega_{it}]$ in equations (13) and (15). The utiltity function is specified as $f(e_h^k, s_h^k) = -exp[-(e_h^k + s_h^k)]$ in equation (4). If *k* is different from drug *j* which is previously prescribed, the conditional expectation can be written as

$$
\begin{aligned}
&E[f(e_h^k, s_h^k) | \Omega_{it}(\cdot, \xi_{h,j}^E, \xi_{h,j}^S)] \\
&= -\exp(-E[e_h^k | \Omega_{it}(\cdot, \xi_{h,j}^E, \xi_{h,j}^S)] - E[s_h^k | \Omega_{it}(\cdot, \xi_{h,j}^E, \xi_{h,j}^S)] \\
&\quad + \frac{\text{var}[e_h^k | \Omega_{it}(\cdot, \xi_{h,j}^E, \xi_{h,j}^S)] + \text{var}[s_h^k | \Omega_{it}(\cdot, \xi_{h,j}^E, \xi_{h,j}^S)] + \Sigma_{\upsilon,t}^E[k,k] + \Sigma_{\upsilon,t}^S[k,k]}{2})
\end{aligned}
$$

where $\Omega_{it}(\cdot, \xi_{h,j}^E, \xi_{h,j}^S)$ is to highlight the fact that treatment outcomes of *j* are revealed via $(\xi_{h,j}^E, \xi_{h,j}^S)$, and in the second line of the equation $\text{var}[e_h^k | \Omega_{it}(\cdot, \xi_{h,j}^E, \xi_{h,j}^S)]$ and $\text{var}[s_h^k | \Omega_{it}(\cdot, \xi_{h,j}^E, \xi_{h,j}^S)]$ are the conditional variances of effectiveness and side effects, respectively. Variances $\Sigma_{\upsilon,t}^E[k,k]$ and $\Sigma_{\upsilon,t}^S[k,k]$ represent the uncertainty of the physician regarding the mean effectiveness and side effects of drug *k* (the *k*-th diagonal element in equation (11)) updated by all previous patient feed-backs and detailing efforts from sales representatives. From the above expression it is clear that the higher the uncertainties the lower the expected utility for the risk-averse physician.

4.2 Simulated Likelihoods

The major problem in evaluating the above likelihoods is that we, as modelers, do not observe $\{\xi_{i,-t}^E, \xi_{i,-t}^S, \zeta_{i,-t}^E, \zeta_{i,-t}^S, \xi_{h,j}^E, \xi_{h,j}^S\}$ which are used by physicians to update beliefs and make prescription decisions. Hence, we have to integrate out these stochastic variables in our likelihood functions. For example, let *F* be the joint distribution function of $\{\xi_{i,-t}^E, \xi_{i,-t}^S, \zeta_{i,-t}^E, \zeta_{i,-t}^S\}$, we will need to evaluate the prescription probability for a new patient as follows;

$$P^{1}_{i,h,j,t} = \int prob(i \text{ prescribing } j \text{ for new patient } h \mid \Omega_{it}(\xi^{E}_{i,-t}, \xi^{S}_{i,-t}, \zeta^{E}_{i,-t}, \zeta^{S}_{i,-t}))dF(\xi^{E}_{i,-t}, \xi^{S}_{i,-t}, \zeta^{E}_{i,-t}, \zeta^{S}_{i,-t})$$

$$= \int \frac{\exp(E[f(e^{j}_{h}, s^{j}_{h}) \mid \Omega_{it}(\xi^{E}_{i,-t}, \xi^{S}_{i,-t}, \zeta^{E}_{i,-t}, \zeta^{S}_{i,-t})] + X^{j}_{ih,t}\beta)}{\sum_{k=1}^{J} \exp(E[f(e^{k}_{h}, s^{k}_{h}) \mid \Omega_{it}(\xi^{E}_{i,-t}, \xi^{S}_{i,-t}, \zeta^{E}_{i,-t}, \zeta^{S}_{i,-t})] + X^{k}_{ih,t}\beta)} dF(\xi^{E}_{i,-t}, \xi^{S}_{i,-t}, \zeta^{E}_{i,-t}, \zeta^{S}_{i,-t}) \qquad (16)$$

The likelihood functions $P^{2}_{i,h,j,t}$ in (13) and $P^{3,3}_{i,h,j,t}$ in (15) are similarly evaluated.

Given that there is no closed-form expression for the likelihoods above, we use simulations based on the distributional assumptions for $\{\xi^{E}_{i,-t}, \xi^{S}_{i,-t}, \zeta^{E}_{i,-t}, \zeta^{S}_{i,-t}, \xi^{E}_{h,j}, \xi^{S}_{h,j}\}$ (see our discussion of distribution assumptions for ξ and ζ in the model section) to numerically compute the likelihoods. To do so we follow several steps. First, for each physician we order by time his treatment and detailing events in data. Each period "*t*" in our model represents either a treatment or a detailing occurs within the sample period. Let "*Y*" represents a treatment event and "*D*" a detailing event. For each physician *i* we generate a sequence of events starting from period $t=1$ to end period $t=T_i$, e.g., $\{D_i(1), D_i(2), Y_i(3), \ldots, D_i(T\text{-}1), Y_i(T_i)\}$. If in period *t* detailing for drug *j* occurs, we simulate the stochastic noise in detailing message regarding effectiveness and side effects of *j*, $\{\zeta^{E,ns}_{it,j}, \zeta^{S,ns}_{it,j}\}$, $ns = 1, \ldots, NS$, where *NS* is the total number of simulation draws,[9] based on our normal distribution assumption for ζ's.

If in period *t* treatment for a new patient occurs, no simulation is needed for that period; however, if prescription for an existing patient occurs, we simulate the stochastic variables of treatment outcomes of the patient's previously used drug *j*, $\{\xi^{E,ns}_{h,j}, \xi^{S,ns}_{h,j}\}$, $ns = 1, \ldots, NS$. If no switching reasons are given due to either non-switching or other stated switching reasons, there is no constraint for the range of simulated ξ's. They are drawn from the whole range $(-\infty, +\infty)$ based on our normal distribution assumption. However, if, say, "side effect" is stated as the reason of switching from *j* to *k*, we first simulate $\xi^{S,ns}_{h,j}$ conditional on $\overline{S}_{j} + \xi^{S,ns}_{h,j} < E[s^{k}_{h} \mid \Omega_{it}(\cdot, \xi^{S,ns}_{h,j})]$ (i.e., condition (i)). The right hand side of the inequality implies that the expected side effects of drug *k* has been updated by a simulated $\xi^{S,ns}_{h,j}$. Next, we simulate $\xi^{E,ns}_{h,j}$ conditional on the simulated $\xi^{S,ns}_{h,j}$ which satisfies the constraint

$\bar{S}_j + \xi_{h,j}^{S,ns} < \bar{E}_j + \xi_{h,j}^{E,ns}$ (i.e., condition (ii)). Similar exercise is performed to simulate $\xi_{h,j}^{E,ns}$ and then $\xi_{h,j}^{S,ns}$ if "ineffectiveness" is stated as the switching reason from *j* to *k*: we first draw $\xi_{h,j}^{E,ns}$ based on condition (iii), then draw $\xi_{h,j}^{S,ns}$ conditional on the simulated $\xi_{h,j}^{E,ns}$ and condition (iv).

Using the above procedure in each period *t* for each physician *i* we have the simulated history of $\{\xi_{i,-t}^{E,ns}, \xi_{i,-t}^{S,ns}, \zeta_{i,-t}^{E,ns}, \zeta_{i,-t}^{S,ns}\}$, where the superscript "*ns*" indicates a sequence of simulation draws. Based on this simulated history we compute, for *Z* = *E* and *S*, and *j* = *V, L* and *C*, (i) $E[Z_h^j \mid \Omega_{it}(\xi_{i,-t}^{E,ns}, \xi_{i,-t}^{S,ns}, \zeta_{i,-t}^{E,ns}, \zeta_{i,-t}^{S,ns})]$ (see equation (9)); (ii) $\Sigma_{\upsilon,t}^{Z}(\Omega_{it}(\xi_{i,-t}^{E,ns}, \xi_{i,-t}^{S,ns}, \zeta_{i,-t}^{E,ns}, \zeta_{i,-t}^{S,ns}))$ (see equation (11)). These are the beliefs of mean effectiveness and side effects of drug *j* updated through Bayesian learning. If in period *t* detailing for *j* occurs, we draw $\{\zeta_{it,j}^{E,ns}, \zeta_{it,j}^{S,ns}\}$ as discussed above and updated $E[Z_h^j \mid \Omega_{it}]$ and $\Sigma_{\upsilon,t}^{Z}(\Omega_{it})$ again. If prescription for a new patient occurs, we evaluate $P_{i,h,j,t}^{1}$ (equation (12)) based on $E[Z_{iht}^j \mid \Omega_{it}]$ and $\Sigma_{\upsilon,t}^{Z}(\Omega_{it})$. If prescription for an existing patient who was previously prescribed drug *j* occurs, we simulate $\{\xi_{h,j}^{E,ns}, \xi_{h,j}^{S,ns}\}$ as discussed above. Based on that we evaluate

(i) $f(e_h^j(\xi_{h,j}^{E,ns}), s_h^j(\xi_{h,j}^{S,ns}))$;

(ii) $E[Z_{iht} \mid \Omega_{it}(\xi_{i,-t}^{E,ns}, \xi_{i,-t}^{S,ns}, \zeta_{i,-t}^{E,ns}, \zeta_{i,-t}^{S,ns}, \xi_{h,j}^{E,ns}, \xi_{h,j}^{S,ns})]$ (see equation (9));

(iii) $\Sigma_{\upsilon,t}^{Z}(\Omega_{it}(\xi_{i,-t}^{E,ns}, \xi_{i,-t}^{S,ns}, \zeta_{i,-t}^{E,ns}, \zeta_{i,-t}^{S,ns}, \xi_{h,j}^{E,ns}, \xi_{h,j}^{S,ns}))$ (see equation (11)); and

(iv) $E[f(e_h^k, s_h^k) \mid \Omega_{it}(\xi_{i,-t}^{E,ns}, \xi_{i,-t}^{S,ns}, \zeta_{i,-t}^{E,ns}, \zeta_{i,-t}^{S,ns}, \xi_{h,j}^{E,ns}, \xi_{h,j}^{S,ns})]$, $k \neq j$.

Then we use these to evaluate $P_{i,h,j,t}^{2}$ (equation (13)) and $P_{i,h,j,t}^{3,3}$ (equation (15)). We also evaluate $P_{i,h,j,t}^{3,1}$ and then based on $\xi_{h,j}^{S,ns}$ or $\xi_{h,j}^{E,ns}$, depending on the reported switching reason, evaluate $P_{i,h,j,t}^{3,2}$ in equation (14). Such procedure is done iteratively for any physician *i* from period *t=1* to end period *t=T_i*.

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[9] In our model estimation *NS* is fixed at 1,000.

We evaluate the simulated likelihood for every physician *i*. For every simulation *ns* we evaluate the the likelihood

$$L_i^{ns} = \sum_{t=1}^{T_i} \left[\begin{pmatrix} \ln(P^1_{i,h,j,t}) \cdot \{h \text{ is new patient with } j \text{ prescribed at } t\} \\ +\ln(P^2_{i,h,j,t}) \cdot \{h \text{ is revisiting patient with same } j \text{ prescribed at } t\} \\ +[\ln(P^{3,1}_{i,h,j,t}) + \ln(P^{3,2}_{i,h,j,t}) + \ln(P^{3,3}_{i,h,k,t})] \\ \quad \cdot \{h \text{ is revisiting patient switching from } j \text{ to } k \text{ at } t\} \end{pmatrix} \begin{pmatrix} \xi^{E,ns}_{i,-t}, \xi^{S,ns}_{i,-t}, \zeta^{E,ns}_{i,-t}, \\ \zeta^{S,ns}_{i,-t}, \xi^{E,ns}_{h,j}, \xi^{S,ns}_{h,j} \end{pmatrix} \right] \tag{17}$$

where $\{\cdot\}$ in the bracket is an indicator function that equals 1 if the logical expression inside is true, and 0 otherwise. Our simulated likelihood estimator Θ is obtained by maximizing the following simulated likelihood of all physicians

$$L = \sum_{i=1}^{N} \left(\frac{1}{NS} \sum_{ns=1}^{NS} L_i^{ns} \right) \tag{18}$$

4.3 Model Identification

We only observe the decisions of drug switchings and indicators of switching reasons, not the clinical measurements of effectiveness and side effects. Further, we only have data of those patients who are prescribed one of the three drugs in the market, i.e., there is no outside option in our model. Without proper normalization our model is not identifiable. For illustration purpose let's assume that $\hat{e}_h^j$ and $\hat{s}_h^j$, $j = V, L$ and C, are the effectiveness and side effects for patient *h*. For simplicity let's further assume that the utility function of prescribing *j* is the linear sum of $\hat{e}_h^j$ and $\hat{s}_h^j$. Then

$$prob(j \text{ is prescribed to } h) = \frac{\exp(\hat{e}_h^j + \hat{s}_h^j)}{\sum_k \exp(\hat{e}_h^k + \hat{s}_h^k)} = \frac{\exp\left(\frac{\hat{e}_h^j - \bar{E}^V}{\sigma_{E,V}} + \frac{\hat{s}_h^j - \bar{S}^V}{\sigma_{E,V}}\right)}{\sum_k \exp\left(\frac{\hat{e}_h^k - \bar{E}^V}{\sigma_{E,V}} + \frac{\hat{s}_h^k - \bar{S}^V}{\sigma_{E,V}}\right)}$$

The second equality above is obtained by subtracting $\bar{E}^V$, the mean effectiveness of Viagra, from $\hat{e}_h^j$ and $\bar{S}^V$, the mean side effect of Viagra, from $\hat{s}_h^j$, and then dividing both by $\sigma_{E,V}$, the standard deviation of effectiveness of Viagra. The probability of prescription does not change under such normalization. For model identification we normalize $e_h^j = \frac{\hat{e}_h^j - \bar{E}^V}{\sigma_{E,V}}$ and $s_h^j = \frac{\hat{s}_h^j - \bar{S}^V}{\sigma_{E,V}}$, implying that the mean effectiveness and side effects of Viagra are both zero, and the standard deviation in the distribution of effectiveness of Viagra is one, under such normalization. Interpretation of the mean effectiveness and side effects of Levitra and Cialis in our model should always be relative to that of Viagra.

Given that $\sigma_{E,V}^2 = 1$ and $\bar{E}^V$ and $\bar{S}^V$ are all zero, the proportion of switchers from Viagra who reported "ineffectiveness" as the switching reason, relative to the proportion who reported "side effects" as the switching reason, in data will help to identify the standard deviation of side effects of Viagra, $\sigma_{S,V}$. Further, the proportion of switchers from Viagra to drug *j* who reported "ineffectiveness" or "side effects" will help to identify the mean effectiveness and side effects of *j*, $\bar{E}^j$ and $\bar{S}^j$ (given the normalization for Viagra). Given $\bar{E}^j$ and $\bar{S}^j$, the proportion of switchers from *j* who reported "ineffectiveness" as the switching reason, relative to the proportion who reported "side effects" as the switching reason, in data will help to identify the standard deviations of effectiveness and side effects of *j*, $\sigma_{E,j}$ and $\sigma_{S,j}$, respectively. Under our risk-aversion assumption in the specification $f(e_h^j, s_h^j) = -exp[-(e_h^j + s_h^j)]$, market share of *j* is an additional identifying instrument for us to estimate the magnitudes of $\sigma_{E,j}$ and $\sigma_{S,j}$.

Switching patterns and stated reasons from drug *j* to *k* in data also help to identify the covariance parameters $\sigma_{E,jk}$ and $\sigma_{S,jk}$ (see the discussion after equations (5) and (6)). For instance, suppose patients who reported "ineffectiveness" as switching reason choose to switch from Viagra to Cialis instead of to Levitra. Given that these are the patients who experienced

negative ξ_V^E, the fact that most of them switch to Cialis implies that $\sigma_{E,VC}$ is lower than $\sigma_{E,VL}$, conditional on the mean effectiveness and side effects.

Furthermore, the time-varying tendency of prescribing a new drug *j* helps to identify physicians' prior uncertainty of mean effectiveness and side effects, $\sigma_{E,j}^{\upsilon,2}$ and $\sigma_{S,j}^{\upsilon,2}$ (equation (7)). If the prior uncertainty is large, physicians will be less likely to prescribe *j* to their patients in the initial periods when the drug was introduced, relative to later periods when they have more information of the treatment outcomes. As Viagra has existed in the market for more than five years when our sample period starts the prior uncertainties for Viagra in period 0 should be very low. Difference in the probability of prescribing *j* to those patients who want to switch from Viagra due to "ineffectiveness" and due to "side effects" in the early periods when *j* was newly introduced also help to identify the difference in magnitude between $\sigma_{E,j}^{\upsilon,2}$ and $\sigma_{S,j}^{\upsilon,2}$.

Finally, the difference in prescription behavior across physicians who are exposed to different detailing efforts helps to identify the magnitude of noise in detailing message, $\sigma_{E,\zeta}^2$ and $\sigma_{S,\zeta}^2$ (see the discussion after equation (8)). If the noise is small (i.e., $\sigma_{E,\zeta}^2$ and $\sigma_{S,\zeta}^2$ are small), physicians who receive only one detailing message from *j* are more likely to prescribe *j* afterward, in comparison with those who have not been detailed. Further, after physicians receiving detailing message, the difference between the probability of switching patients from other drugs to *j* who report "ineffectiveness" as reason and that who report "side effects" as reason helps to identify the difference between $\sigma_{E,\zeta}^2$ and $\sigma_{S,\zeta}^2$.

4.4 Model Details

As discussed above we normalize the mean effectiveness and side effects of Viagra to zero and the standard deviation of effectiveness of Viagra to 1. Since Viagra has existed in the market for five years when our sample period starts, we assume that there are no prior uncertainties of effectiveness and side effects for Viagra among physicians, i.e, the variances for Viagra in $\Sigma_{\upsilon,0}^E$ and $\Sigma_{\upsilon,0}^S$ (equation (7)) are zero. We use several demographic variables in data for $X_{ih,t}^j$ (equation (1)). These include age ("ln(age)"), race indicators ("Black" and

"White" with other races as the normalized variable), type of insurance ("HMO", "Indenmity", "Medicaid", "Medicare", with no coverage as the normalized variable), all interacting with drug identities. Parameters of these variables for Viagra are normalized to zero. By interacting with drug identities we allow the effect of patient characteristics on prescription decisions for Levitra and Cialis to be different.

To allow for the persuasive function of detailing we include detailing visits in $X_{ih,t}^{j}$ also. To capture both long-run and short-run persuasive effect of detailing and to distinguish the differential impact of detailing with and without meal, we break down this variable into (i) ln(number of detailings with or without meals in the past 30 days); (ii) ln(number of detailings with or without meals more than 30 days ago); (iii) ln(number of detailings with meals in the past 30 days); (iv) ln(number of detailings with meals more than 30 days ago). Parameters for (i) and (iii) measure the persuasive role of recent detailing as compared with detailing far in the past. Parameters for (iii) and (iv) measure the additional impacts of detailing when meals are offered over the total detailing impact in (i) and (ii).

Finally, we estimate $\overline{E}^{j}$, j = Levitra or Cialis, separately for the groups of patients with "mild" and "moderate" status of illness. Such differentiation implies that different drugs may have different efficacies in treatment depending on the severity of the condition. Alternatively, it may imply that different patients have different valuations regarding the effectiveness of drugs depending on the severity of their conditions. For simplicity of analysis we do not differentiate the side effects $\overline{S}^{j}$ for the mild and moderate group. This implies that the impact of side effects on utility is independent from severity of illness, which seems to be a reasonable assumption.[10]

In summary, our parameter set Θ in the model includes the following:

$$\Theta = [\overline{E}^{mild},\ \overline{E}^{\text{mod}},\ \overline{S},\ \Sigma_{\xi}^{E},\ \Sigma_{\xi}^{S},\ SC,\ \Sigma_{v,0}^{E},\ \Sigma_{v,0}^{S},\ \sigma_{E,\varsigma},\ \sigma_{S,\varsigma},\ \beta]$$

[10] This does not imply that the treatment choices of patients with different severity are the same. If, for example, compared with the mild group, patients with moderate condition have a higher value for effectiveness than side effects in their utility function, they will be more likely to choose more effective drugs.

where $\overline{E}^{mild}$ is a 2×1 vector of mean effectiveness of Levitra and Cialis for patients with mild condition, and $\overline{E}^{\text{mod}}$ is that for patients with moderate condition. Other parameters are defined as before.

4.5 Limitations

One of the major limitations in our model is that we do not observe the clinical measurements of effectiveness and side effects. Because of this, we can only estimate the patient's drug-specific evaluations e_h^j and s_h^j but not the patient preference weights for effectiveness and side effects ω_h^E and ω_h^S that are same across drugs (see our discussion in the model section). The difference in *e* and *s* across patients may reflect either the heterogeneity in treatment outcomes or the heterogeneity in patient preferences. In contrast, typically clinical studies have data on clinical measurements but not prescription choice. Chan and Hamilton (2006) is the only study we are aware of that uses subjects' drop-out decisions from experiment to evaluate their preferences for effectiveness and side effects.

Our study is conditional on patients seeking treatment from physicians who then make prescription decisions out of the available drugs in the market. We do not observe those patients who seek treatment but finally decide not to use any of the drugs. Further, for a new patient we do not know whether he has sought treatment in the past but chosen the option out of the drugs in data. If these "non-prescription" outcomes do exist, by ignoring them in the model our study is subjected to the standard selection bias problem and estimation results may be biased. Though we do not observe any systematic time-varying changes in the number of total patient visits or new patient visits,[11] we acknowledge this issue as a limitation in our analysis.

Finally, due to data unavailability, we make several restrictive assumptions in the model. For example, we assume that an existing patient has no knowledge about the other drugs that

[11] The number of total visits in the first 100 days of our sample period when there were only Viagra and Levitra in the maket is 3,231, and that in the last 100 days when all three drugs existed in market is 2,722. The number of new patient visits in the first 100 days is 1,490, and that in the last 100 days is 1,231. The number of visits fluctuated over periods. If the selection bias comes from that patients choose no treatment because existing drugs do not work for them, we should expect to see an increasing number of patients after the new Cialis entered the market. This is not the case in our data.

are not previously used. However, we do not know if he has tried any of the other drugs before, otherwise the patient's knowledge of other drugs would have been different. In our data Levitra and Cialis have not existed for long so multiple swtichings between drugs may be rare; hence, we believe this problem may not be critical. The last issue also relates to drug switching – there are many observations which physicians do not report ineffective or side effects reasons. Our method of estimating the likelihoods for these observations may not be proper. For example, if most of those who report "patient request" are indeed due to the "ineffectiveness" concern, our results will be biased.

5. Results

We report the estimation results in Table 3, 4 and 5. In Table 3 we provide estimates of the mean effectiveness and side effects and their correlation coefficients among the three drugs, as well as the switching cost ($\overline{E}^{mild}, \overline{E}^{\text{mod}}, \overline{S}, \Sigma_{\xi}^{E}, \Sigma_{\xi}^{S}, SC$ in the parameter set). From table 3, we can see that in terms of mean effectiveness and side effects, Cialis ranks best and Levitra is second.[12] The two newer drugs are significantly better than the existing drug, Viagra (for which the mean effectiveness and side effects are both normalized to be zero). Turning to the estimate of heterogeneity in treatment effectiveness, we find the standard deviation of Levitra's effectiveness is significantly larger than that of Viagra (for which the standard deviation is normalized to one), and the standard deviation of Cialis' effectiveness is significantly smaller than that of Viagra. There are significant correlations among the three drugs in terms of effectiveness.[13] While Viagra is positively correlated with Levitra as well as with Cialis, the correlation coefficient is negative between Levitra and Cialis. The implication is that, if Levitra is ineffective for one patient, everything else being equal, Cialis is more likely to be effective for that patient than Viagra. The estimated standard deviations in side effects of the three drugs

[12] A high estimate of side effects in the table imply less severe or fewer side effects experienced by patients.
[13] We choose to report the correlation coefficients in the table since they are normalized by standard deviations of drugs hence the magnitude of the correlation coefficients across different pairs of drugs can be directly compared.

suggest that the heterogenenity in side effects of Levitra and especially Cialis is much larger than that of Viagra. The correlations between three drugs are significantly positive. However, Viagra and Cialis are less correlated with each other than between Viagra and Levitra or Cialis and Levitra. Finally, we find a rather large swithing cost for existing patients, which implies that these patients are unlikely to switch drugs unless the previously prescribed drugs are very ineffective or with severe side effects.

	Estimate	**Standard Error**
Mean Effectiveness and Side Effects		
Mean Effectiveness of Levitra (Mild)	0.693	0.015
Mean Effectiveness of Levitra (Moderate)	0.722	0.009
Mean Side Effects of Levitra	0.003	0.001
Mean Effectiveness of Cialis (Mild)	1.900	0.017
Mean Effectiveness of Cialis (Moderate)	1.947	0.010
Mean Side Effects of Cialis	0.071	0.009
Correlation Coefficients of Effectiveness		
Corr(Viagra, Levitra)	0.395	0.000
Std Dev(Levitra)	1.744	0.000
Corr(Viagra, Cialis)	0.745	0.000
Corr(Levitra, Cialis)	-0.319	0.000
Std Dev(Cialis)	0.745	0.000
Correlation Coefficients of Side Effects		
Std Dev(Viagra)	0.126	0.000
Corr(Viagra, Levitra)	0.151	0.000
Std Dev(Levitra)	0.837	0.009
Corr(Viagra, Cialis)	0.053	0.002
Corr(Levitra, Cialis)	0.166	0.088

Std Dev(Cialis)	2.394	0.004
Switching Cost	1.658	0.033

Table 3. Estimates of Mean Effectiveness and Side Effects, Their Correlation Coefficients, and Switching Cost

In table 4 we provide estimates of the prior uncertainty associated with the two newer drugs in effectiveness and side effects, and the extent of noise in the detailing signal for effectiveness and side effects ($\Sigma_{v,0}^{E}, \Sigma_{v,0}^{S}, \sigma_{E,\varsigma}, \sigma_{S,\varsigma}$ in the parameter set).

	Estimate	**Standard Error**
Prior Uncertainty		
Std Dev for Effectiveness of Levitra	0.866	0.018
Std Dev for Effectiveness of Cialis	0.526	0.075
Std Dev for Side Effects of Levitra	0.524	0.016
Std Dev for Side Effects of Cialis	0.945	0.013
Detailing Noise		
Std Dev for Effectiveness (without meal)	0.171	0.054
Std Dev for Side Effects (without meal)	1.096	0.034
Std Dev for Effectiveness (with meal)	0.015	0.711
Std Dev for Side Effects (with meal)	0.805	0.020

Table 4. Estimates of Prior Uncertainties and Detailing Noises

Results show that physicians were very uncertain of the effectiveness of Levitra when it was introduced. In contrast, when Cialis was introduced they were less uncertain of its effectiveness but the uncertainty of side effects was significantly higher. For risk averse patients such uncertainties contribute to lower market share of new drugs; hence, it is important for Levitra to reduce the prior uncertainty related to effectiveness, and for Cialis to reduce the uncertainty

related to side effects. Detailing visit is one of the mechanism to reduce these uncertainties. Our results show that detailing is efficient in informing physicians about the effectiveness of a drug, as the estimate of the magnitude of noise in detailing message regarding effectiveness is very small. Specifically, the standard deviation of the noise of detailing with meals is close to zero implying that perfect information regarding effectiveness is provided to physicians. However, the estimated noise of detailing message regarding side effects is significantly much larger in magnitude, implying that physicians may still be very uncertain of the side effects of new drugs after multiple detailing visits. A detailing with meal is more informative than a detailing without a meal for both effectiveness and side effects, as the associated noise of the former is significantly smaller than that of the latter, perhaps because during dinners phamarceutical companies usually invite experts in the medical field to provide credible information that helps to reduce physicians' uncertainty.

In table 5 we provide estimates of the effect of demographic variables and the persuasive detailing effect (β's).

	Estimate	**Standard Error**
Demographic Variables		
*ln(age+1)*Levitra*	0.269	0.006
*Black*Levitra*	-0.009	0.059
*White*Levitra*	0.070	0.028
*HMO*Levitra*	0.108	0.029
*Indemnity*Levitra*	0.201	0.076
*Medicaid*Levitra*	-0.152	0.152
*Medicare*Levitra*	0.154	0.052
*ln(age+1)*Cialis*	0.379	0.007
*Black*Cialis*	-0.103	-0.074
*White*Cialis*	0.071	0.032
*HMO*Cialis*	0.094	0.034
*Indemnity*Cialis*	0.252	0.088
*Medicaid*Cialis*	-0.521	0.216

*Medicare*Cialis*	-0.155	0.065
Persuasive Detailing Effects		
ln(total detailing>30days)	0.19311	0.02249
ln(total detailing<30days)	0.40177	0.02925
ln(detailing with meal >30days)	-0.07023	0.03269
ln(detailing with meal <30days)	0.08650	0.04944

Table 5. Estimates of the Effects of Demographic Variables and Persuasive Detailing Effects

Results show that the two newer drugs are more likely to be prescribed to old and Caucasian patients. Patients with HMO and indemnity insurance are also more likely to receive the new drugs; however, those covered by Medicaid or Medicare are less likely to choose Cialis. These results probably indicate the average difference in out-of pocket cost of these drugs for patients under different insurance coverages. Finally, we find a positive and significant persuasive effect from detailing in both short-term (fewer than 30 days) and long-term (more than 30 days), and the short term effect is stronger than the long term effect. Further, detailing visits with meal have an additional short term persuasive effect, though that additional effect does not exist in the long term.

The Importance of Effectiveness and Side Effects: One of our major research objectives is to understand the weights of treatment effectiveness vs. side effects in the prescription decision. Because of the normalization we use in model estimation all comparisons are relative to Viagra. Further, due to the difference in knowledge about the treatment outcomes of drugs (e.g., new vs. existing patients) the impacts may vary across patients. To illustrate the relative importance of effectiveness and side effects in the prescription decision, we conduct a series of "what-if" experiments. We simulate the prescription decisions for two sets of patients:[14]

[14] For the following "what-if" experiments, we assume that there is no prior physician uncertainty in effectivenss and side effects. Our results can be treated as the long-run equilibrium outcomes after three drugs entered the market.

(1) New patients who only know the distribution of effectivenss and side effects of the three drugs, but do not know how well these drugs would actually work on them;

(2) Existing patients who used one drug previously and know exactly how this particular drug worked for them in both effectiveness and side effects and, conditional on the effectiveness and side effects of the the drug, they form expectations of the effectiveness and side effects of the other two drugs.

In Figure 3, the first "original" bars show the steady-state market share of Levitra and Cialis among new patients based on our estimation results (25% for Levitra and 40% for Cialis). Then we simulate the choice of these new patients under the following "what-if" scenarios: (i) when the mean effectiveness of Levitra or Cialis is equal to the mean effectiveness of Viagra; (ii) when the mean side effects of Levitra or Cialis is equal to the mean side effects of Viagra; (iii) when the variance of effectiveness of Levitra or Cialis is equal to the variance of effectiveness of Viagra; and (iv) when the variance of side effects of Levitra or Cialis is equal to the variance of side effects of Viagra. This experiment illustrates the relative importance of mean and variance of treatment outcomes in prescription decision.

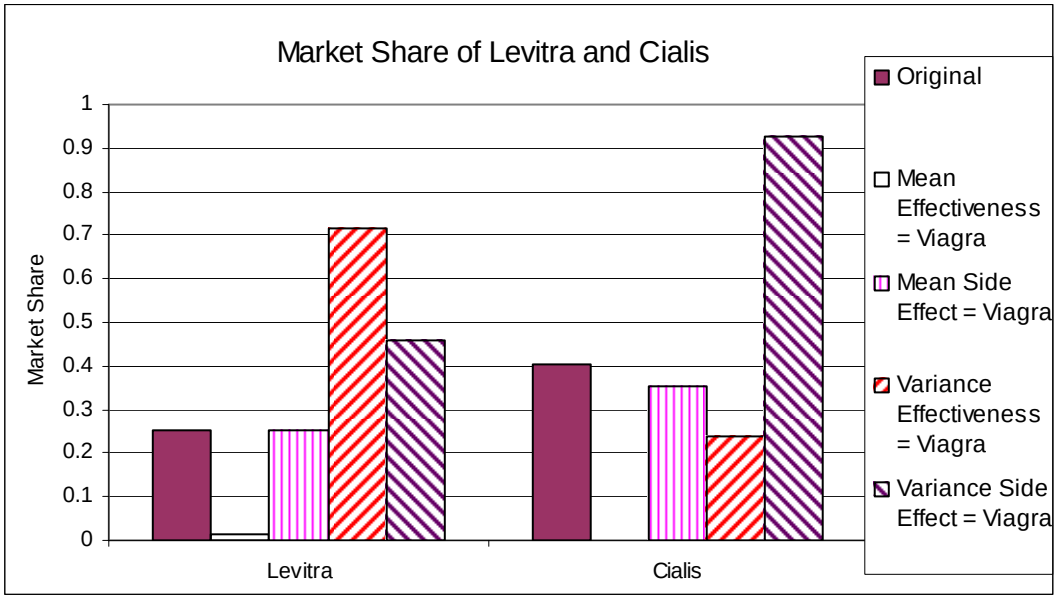
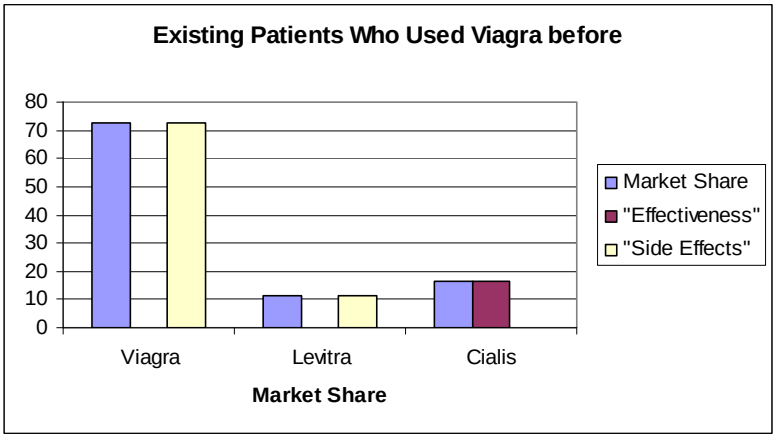
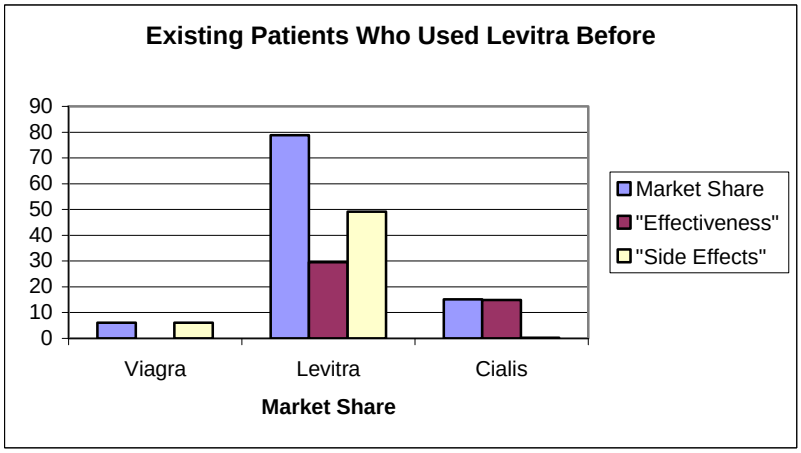


Figure 3. "What-if" Experiment 1: Treatment Choices of New Patients

Since Levitra and Cialis both dominate Viagra in mean effectiveness and side effects, their market share will decline under scenarios (i) and (ii). While the market share are not much changed when their mean side effects are equal to that of Viagra, they virtually drop to zero when their mean effectiveness is equal to that of Viagra (normalized to 0). Patients would rather choose Viagra in the latter case though side effects of Viagra are worse than the other two because both Levitra and Cialis have a much larger heterogeneity hence uncertainty in either effectiveness or side effects. To illustrate, the market share of Levitra would increase from 25% to 72% if it could reduce its variance in effectivenss to match with Viagra in scenario (iii). In fact, among the three ED drugs, Levitra is the one with the largest heterogeneity in treatment effectiveness. If we reduce the variance in side effects for Cilais to match with Viagra in scenario (iv), the market share of Cialis would increase from 40% to 92%. The explanation is that Cialis has higher mean evalution in both effectiveness and side effects than Viagra, but its variance in side effects is the largest among the three drugs, and this acts as a competitive weakness. Our results imply that it is critical for the two new drugs to reduce the uncertainty instead of improving the mean effectiveness or side effects as perceived by physicians and patients. This supports our early argument that it may be more important for firms to understand the extent of heterogeneity of treatment outcomes, instead of the overall means which most clinical studies attempt to measure.

Figure 4 plots the simulated market share for those exisiting patients who (1) used Viagra before; (2) used Levitra before, and (3) used Cialis before. A general pattern we can immediately identify from all three graphs in the figure is that the drug that patients start with has a significant “first-mover” advantage, as between 70 and 80 percent of patients would stay with their previous drug treatment. This is because of three reasons: the switching cost associated with changing the drug treatment; the asymmetric information that existing patients have regarding the treatment outcomes; and the risk aversion of patient-physician pair.





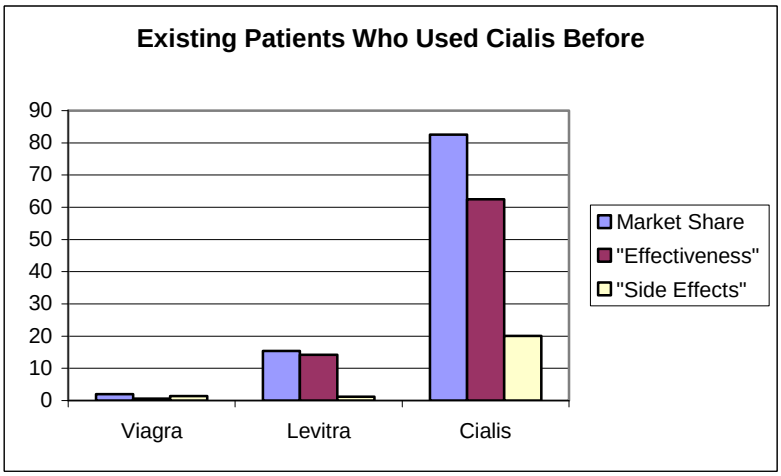


Figure 4. "What-if" Experiment 2: Treatment Choices of Existing Patients

To better understand the decisions of exisiting patients we also examine the reasons why a patient chooses either to stay with the previous drug or to switch to another drug. We assume that the reason for choosing (either staying with or switching to) a drug is "effectiveness" if the difference in effectivess between the chosen drug with the highest utility and the drug with the second highest utility is greater than the difference in side effects between these two drugs, otherwise the reason of the choice is "side effects". Results in Figure 4 show some interesting substitution patterns among drugs that are driven by either effectiveness or side effects: for patients who used Viagra before (see the first panel), if they decide to stay with Viagra or switch to Levitra, it is because of fewer side effects; if they decide to switch to Cialis, it is all due to higher expected effectiveness. For patients who used Levitra before (see the second panel), all will switch to Cialis if they find Levitra ineffective, but will switch to Viagra if Levitra has strong side effects. Finally, for patients who used Cialis before (see the last panel), most of them will stay due to its effectiveness, while a few will switch to either Viagra because of expected side effects or Levitra due to the expected effectiveness. In summary, switching to Cialis from Viagra or Levitra is due to expected effectiveness, while switching to Viagra from the other two drugs is due to the expected side effects.

The Informative Role of Detailing vs. Patient Feedback: To illustrate how physicians learn about effectiveness and side effects through patient feedbacks and detailing, panels in Figure 5 show the total physician uncertainty, which is the sum of the treatment heterogeneities across patients (i.e., square of the standard deviations in Table 3) and prior uncertainties (square of the standard deviations in Table 4), in effectiveness and side effects of Levitra and Cialis when they were introduced. We examine the change in the total uncertainty of a physician, under the Bayesian updating rule in equation (11), when his patient feedback increases from 1 to 10, compared with when his exposure to detailing visits (with meal and without meal) increases from 1 to 10. Note that the treatment heterogeneity is inhererent to the physician's prescription problem when he treats new patients and this will not change over time; hence, the treatment heterogeneity is the lower bound for the total uncertainty. In terms of effectiveness, Levitra has a much larger hetergoneity than Cialis (the variance of effectiveness is 3.04 and 0.55 for

Levitra and Cialis, respectively), while in terms of side effects it is the opposite (the variance of side effects is 0.70 and 5.73 for Levitra and Cialis respectively).

From the upper two panels in Figure 5, we find that detailing visit is very efficient in reducing the uncertainty in effectiveness, especially detailing visit with a meal: with one detailing visit with a meal, the total uncertainty in effectiveness is reduced from 3.79 to 3.04 for Levitra and from 0.83 to 0.55 for Cials, which are the lowest uncertainty levels that can be achieved. In contrast, patient feedbacks are much less informative. For example, with feedback from 1 revisiting patient, the total uncertainty in effecitiveness for Levitra is reduced from 3.79 to 3.64, and even with feedback from 10 revisiting patients, there still exists considerable amount of prior uncertainty in effecitveness. We observe similar patterns for Cialis.

The lower two panels in Figure 5 show that detailing visits are less efficient in helping physicians to lower their uncertainty of side effects. Though detailing visit with meal is the most efficient way in reducing the prior uncertainty for both Levitra and Cialis, it is far less efficient when compared to the reduction of uncertainty in effectiveness. With one detailing visit with meal, the total uncertainty in side effects is reduced from 0.97 to 0.89 for Levitra, and from 6.62 to 6.11 for Cialis, way above the possible lowest levels that one can achieve. Patient feedbacks are comparable to detailing visits in terms of reducing the uncertainty of side effects. Indeed for Levitra, patient feedbacks are more informative than detailing visit without meal.

How important is it for phamarceutical companies to reduce the prior uncertainty for physicians? Suppose a physician treats a new patient with the following characteristics: Caucasian, age 40, with moderate severity and covered by HMO. Assume that there is no prior uncertainty related to Viagra which is a reasonable assumption since the drug has existed in the market for long. If the total uncertainty of both effectiveness and side effects for Levitra and Cialis is at the level of period 0 (i.e., variances at 4.8 and 7.5 for Levitra and Cialis, respectively), one Levitra detailing without meal will increase the probability of prescribing Levitra from 7 to 31 percent,[15] and one Cialis detailing will increase the probability of prescribing Cialis from 8 to 30 percent. If there is no prior uncertainty for Levitra (and for

[15] As comparison, five patient feedbacks from Levitra will increase the probability of prescribing the drug to 22 percent.

Viagra), one Cialis detailing will increase the probability of prescribing Cialis from 5 to 22 percent. This exercise illustrates the importance of detailing visits to phamarceutical companies when a drug was newly introduced.

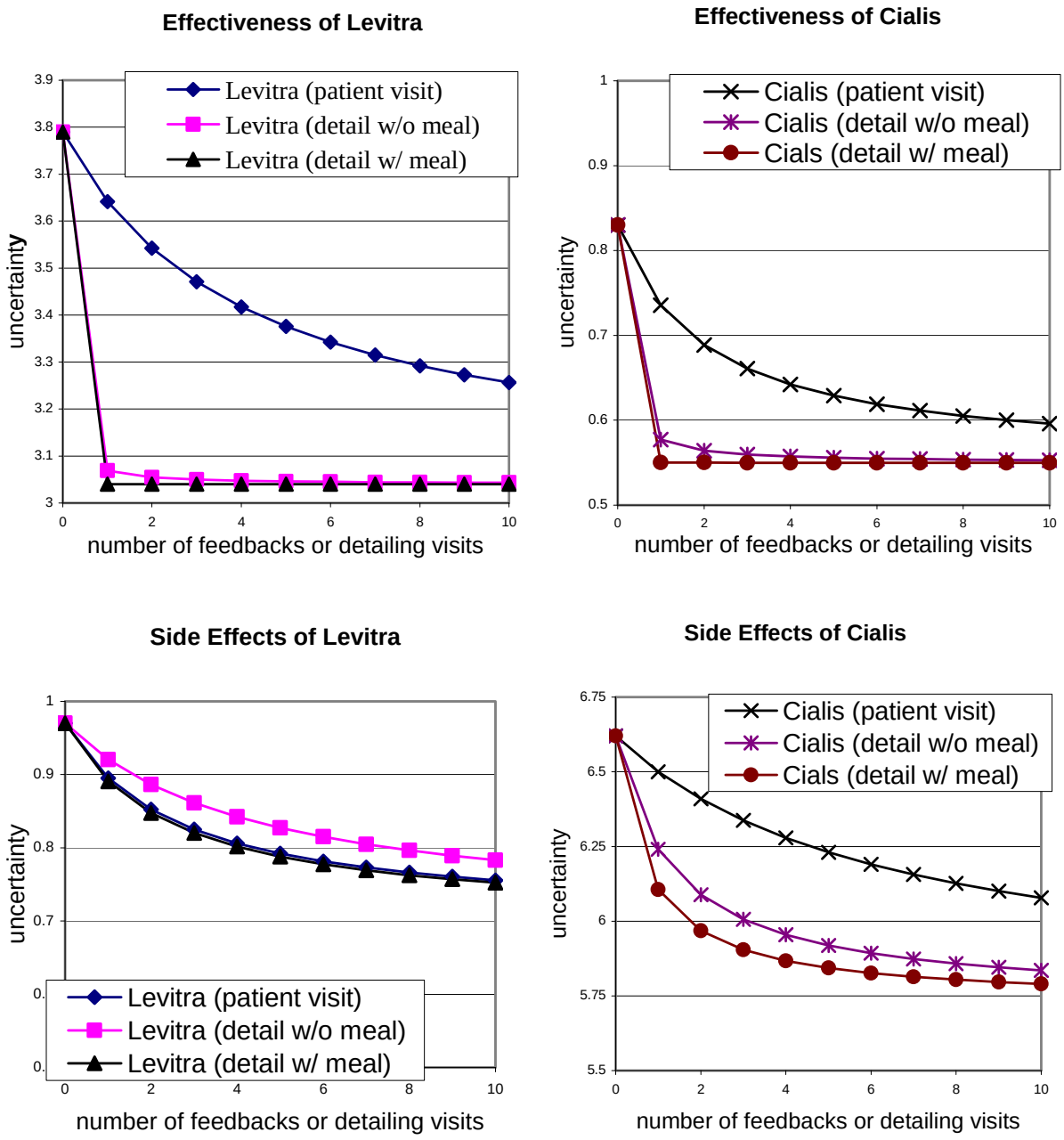


Figure 5. Uncertainty Reduction Through Patient Feedback vs. Detailing Visits

The Informative vs. Persuasive Role of Detailing: Our model explicitly incorporates two functions for detailing: the persuasive effect that directly impacts the prescription utility, and an informative effect that indirectly influences the prescription utility through the reduction of the physician uncertainty on effectiveness and side effects. The persuasive function of detailing only affects the utility for a physician and not patients since it is not directly related to patient's welfare. In Figure 6, we demonstrate these effects on drug prescription for a patient.[16] We plot the two effects in changing the total prescription utility, relative to the utility level when the physician's uncertainty for Levitra and Cialis is at the level of period 0, as the number of detailing visits for each drug increases from 1 to 10. A general pattern we can easily identify from the figure is that for both Levitra and Cialis, the informative role of detailing is more important than the persuasive role in influencing the utility, but the marginal impact of the informative role of detailing visit declines rapidly. One detailing visit with meal can reduce the prior uncertainty considerably, then such informative role becomes quite small for subsequent visits. In contrast, the persuasive effect of the detailing visits is more persistent.

A few observations we can make from these results: first, detailing visits are important even from the patient welfare perspective. The informative effect of detailing helps to reduce patient uncertainty and hence increases the utility. Without detailing they may not be prescribed new drugs such as Cialis that is more effective and with fewer side effects than existing drugs. Second, we do not find evidence that detailing with meal creates serious bias in the physician prescription decisions. Indeed this type of detailing is the most informative method to reduce the physician uncertainty, but its persuasive role is not too different from that of normal detailing (by comparing the two effects from Figure 6). Finally, if the cost of providing meals (e.g., cost of food and inviting expert speakers etc.) is high, a couple normal detailing visits by sales representatives is sufficient to compensate for the effect of a detailing visit with meal. Of course detailing without meal is not costless to firms. Indeed it can be very difficult to get busy physicians to talk to sales representatives which may be the major reason why phamarceutical companies provide non-monetary benefits such as meals to physicians.

[16] The calculation of the utility is based on the following assumptions on the patient's demographics: forty-year old, Caucasian, with moderate severity and covered by HMO.

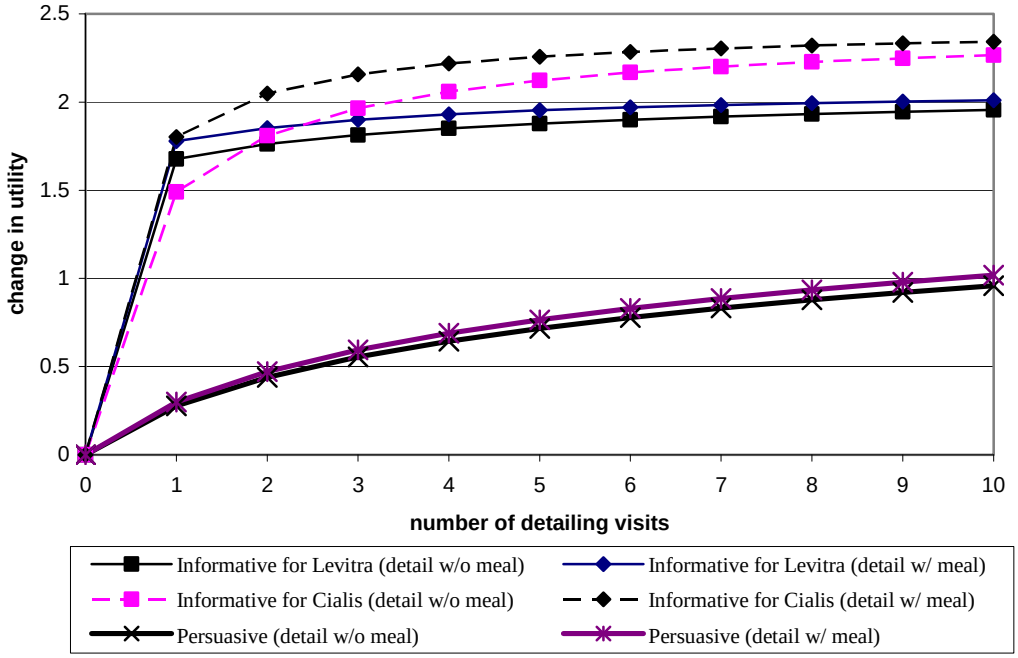


Figure 6. The Informative vs. Persuasive Role of Detailing

6. Conclusion and Future Research

A standard clinical study assesses the mean or median effectiveness and side effects of drugs through randomized clinical trial experiments. In this paper we argue that it is important (i) to assess the effectiveness and side effects of a drug and understand how physicians and patients evaluate these treatment outcomes (ii) to measure the mean or median effectiveness and side effects of a drug and evaluate the heterogeneity of their impacts across patients, especially when physicians and patients are risk averse in choosing treatments. Finally we believe that to better understand patient-physician choices data from a market environment has advantages over clinical trials since in the former patients and physicians are faced with alternative drugs they can choose from while exposed to marketing efforts such as detailing from pharmaceutical companies.

In this paper we study how patients and physicians evalutate effectiveness and sideeffects of drugs in their joint prescription choice decision using data from the ED market.

We use a physician panel dataset that contains prescription choices made in real market environment to examine how the mean effectiveness and side effects as well as the heterogeneity in treatment outcomes across patients affect prescription choices. We combine the observed prescription choices with a unique dataset of self-reported reasons for switching treatment in our estimation to separately identify the patient evaluation of effectiveness and side effects. We find that the two new drugs, Levitra and Cialis, have higher mean effectiveness and lower mean side effects than the exiting drug Viagra. However, the heterogeneity in effectiveness for Levitra and the heterogeneity in side effects for Cialis are larger. Because patients and physicians are risk averse uncertainty about the mean effectiveness and the effect on a particular patient is important for the two new drugs.

Large amount of uncertainty in the effectivness and side effects exists among physicians in the pharmaceutical market. This uncertainty comes from two sources: first, treatment outcomes can be heterogeneous across patients; and second, even the mean effectiveness and side effects may be unknown to physicians and patients, especially for those drugs that are new to the market. We allow physicians to learn from their own experience based on patient feedbacks, as well as from the pharmaceutical company's one-to-one marketing communication efforts such as the detailing. Estimation results show that it is much more effective for the physicians to learn from the detailing visit than from the patient feedback; however, detailing visit is much less effective in reducing the prior uncertainty on side effects. We also find that the informative role of detailing visit is more important than its persuasive role in influencing the prescription choice for both new drugs, and the differences in the persuasive role between detailing with meal and detailing without meal is not very significant.

There are several directions for the future research. First, we applied our model to life-style drugs. It would be interesting to see how the results would be different in life-saving drugs such as cancer or AIDS drugs. Conceptually in these categories the evaluation of treatment effectiveness vs. that of side effects can be vastly different from the ED category that we studied. Second, as we mentioned earlier, we do not observe the clinical measurements of effectiveness and side effects in the current dataset. As a result, we can not identify the patient preference weights for effectiveness and side effects from the heterogeneity in these outcomes.

This may be an interesting question to study if the clinical measurement data becomes available. Third, we assumed in our model that physicians maximize the joint utility for the current occasion. In reality, the physicians can well be forward-looking dynamic optimizers, who might strategically experiment the new drugs to maximize his long-run utility. This assumption may be worth testing in the future research. Finally, patients may learn about the new drugs through the direct-to-consumer (DTC) advertising by the pharmaceutical companies, which might induce patients to request for a particular drug. Future research can investigate how much these patient-oriented advertising effort, together with detailing efforts that target physicians, would influence patient and physician's evaluation of the treatment effectiveness and side effects of the new drugs.

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