

A Structural Analysis of Detailing, Publicity and Correlated Learning:  
The Case of Statins

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### Abstract

When Lipitor, an anti-cholesterol drug (statin) of Pfizer, hit the market in 1997, Pfizer did not establish any direct evidence on its ability in reducing heart disease risks. Despite its lack of direct evidence, Lipitor became very successful. We define a variable, “efficiency ratio”, which measures how efficiently a drug can translate *reduction in cholesterol levels* into *reduction in heart disease risks* and allow the physicians’ initial prior perceptions on the efficiency ratio to be correlated across drugs. We assume that the physicians learn about the efficiency ratios from landmark clinical trials. Because of the correlated prior perceptions, new information on one drug can update physicians’ belief on other statins. The correlated learning may potentially allows late entrants to free-ride on the scientific evidence and informative marketing activities of the incumbents.

In addition to using product level market share data, we supplement them with switching rates. The demand estimation literature using product level data usually ignore the possibility that patients may face switching costs. This could potentially lead to bias in parameter estimates. Unlike the previous literature, we take the presence of switching costs into consideration when we estimate our demand model by using switching rate data.

Our estimation results suggest that there is information spill-over of landmark clinical trial results across drugs. Hence, Lipitor may gain late mover advantage by free-riding on the information provided by its rivals’ clinical trials. However, it is not the only driving force for its success. The fact that Lipitor is very effective in lowering cholesterol levels and its intensive detailing efforts also contribute to its success. Our counterfactual experiments also suggest that take-off of a new drug would be very fast in the absence of switching costs. For example, Lipitor would have become the best selling drug in the category right after its entry (Q2 1997) without switching cost.

**Keywords:** Correlated Learning, Late Mover Advantage, Switching Costs, Statins, Publicity

# 1 Introduction

Even a few years after a drug is introduced to the market, uncertainty for the drug can remain and deter physicians from prescribing it (Lasser et al., 2002). To reduce this uncertainty, it is quite common for pharmaceutical firms to invest in post-marketing clinical studies. Since pharmaceutical firms are only allowed to make claims which are supported by scientific evidence,<sup>1</sup> these post-marketing clinical trial results can be very important to the design of firms' marketing strategies. For example, statin is the most popular class of anti-cholesterol drugs and most patients take a statin to lower their cholesterol levels (short-term efficacy), hoping that it will reduce their heart disease risks (long-term efficacy) by lowering cholesterol levels. However, before a clinical study on reducing heart disease risks becomes available, a drug company can make a direct claim only on the efficacy in lowering cholesterol levels. Although a positive correlation between high cholesterol levels and coronary heart disease risks has been found in medical research, a drug that can lower cholesterol levels effectively does not necessarily reduce heart disease risks.<sup>2</sup> This is because the drug might have some unknown side-effects that raise the heart disease risks and counter the benefits of lowering cholesterol levels. To make a claim that their drugs are effective in reducing heart disease risks, statin manufacturers have invested in post-marketing clinical trials to provide such direct evidence. Very often, however, getting post-marketing clinical trial results on reducing heart disease risks usually takes several years and requires large financial costs.

When Lipitor (atorvastatin), the best-selling statin synthesized by Warner-Lambert and co-promoted by Pfizer, hit the market in 1997, Warner-Lambert did not establish any direct evidence on whether Lipitor can reduce heart disease risks. Instead, the companies focused on communicating with physicians its superior efficacy in lowering cholesterol levels. Interestingly, even though Lipitor did not have a clinical trial result which provides direct evidence that it can reduce heart disease risks, it had expanded

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<sup>1</sup>FDA Code of Federal Regulations Title 21 (<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=203&showFR=1&subpartNode=21:4.0.1.1.4.1>, accessed on Aug 31, 2012).

<sup>2</sup>For instance, a recent clinical trial shows that a new anti-cholesterol combination drug, Vytorin, does not reduce heart disease risks even though it is very effective in lowering the cholesterol levels (Park, 2008).

the market volume steadily and rapidly since its entry. Before the entry of Lipitor, three incumbent statins had already established scientific evidence on their ability in reducing heart disease risks. If physicians prioritize the long-term benefits of their patients and want to reduce the patients' heart disease risks, these prescription patterns are not easy to understand.

In this paper, we propose the following explanation to rationalize this puzzle. Since statins use the same chemical mechanism to lower cholesterol levels (Zhou et al., 2006), it is plausible that physicians believe that statins share similar efficacies and side effects. Therefore, when physicians encounter clinical evidence describing the efficacy in reducing heart disease risks of older statins, they may infer that Lipitor, the more potent statin (in lowering cholesterol levels), can reduce heart disease risks more effectively than its competitors even though it does not yet have direct scientific evidence to prove this.

To capture this information spill-over story, we develop a structural demand model of correlated learning. First, we define a variable, "efficiency ratio," which measures how efficiently a drug can translate *reduction in cholesterol levels* into *reduction in heart disease risks*. Then, we allow physicians to learn about the efficiency ratio for each drug from landmark clinical trials. Most physicians and patients might not actively search for clinical trial results and indirectly learn about scientific information through certain types of media. In this research, we allow detailing<sup>3</sup> and publicity to play a role in delivering information embedded in clinical trials to physicians and patients. A pharmaceutical representative may inform or remind a physician of the drug's efficacies. Alternatively, a patient exposed to publicity on a drug could ask his physician about the drug, and such an inquiry could motivate his physician to look up clinical evidence for that drug.

In addition to using product level market share data, we supplement them with data on switching rates (the percentage of patients who switch from one statin to another statin, by drug) and discontinuing rates (the percentage of drug  $j$ 's patients who decide to discontinue statin treatment). Although

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<sup>3</sup>Detailing refers an marketing activity that a pharmaceutical representative visits a physician and explains efficacies and side-effects of a drug.

patients face switching costs when they decide to switch to competing prescription drugs, the switching costs are usually ignored in the literature using product level market share data (e.g. Azoulay, 2002; Berndt et al., 1997; Ching, 2010a,b; Ching and Ishihara, 2010, 2012; Narayanan et al., 2005). Ignoring these switching costs could lead to biased estimation results. Even though we do not explicitly estimate switching costs due to data limitations, we take their presence into consideration when we estimate our demand model by using switching rate data.

The estimated results show physicians' initial prior belief on the efficiency ratio is relatively low and they learn about the true efficiency ratio from clinical trials. The initial prior correlation on efficiency ratio across statins is positive and significant (0.66), which suggests that there is correlated learning across statins. This implies that after reading the results of a clinical trial, physicians learn about not only the drug studied in the clinical trial, but also other drugs not mentioned in it, although the information spill-over is not perfect. We also find that detailing plays both persuasive and informative roles in physicians' prescription choices. Moreover, we find that publicity in reducing the heart disease risks dimension increases physicians' chance to learn about clinical trial results.

Our estimation results suggest that there is information spill-over of landmark clinical trial results across drugs. Hence, Lipitor may gain late mover advantage by free-riding on the information provided in its rivals' clinical trials. How large was the late mover advantage? How much did the incumbent drugs benefit from first movers' clinical trials and marketing efforts? To address these questions, we conduct a counterfactual experiment to measure how important the correlated learning is for Lipitor's sales. The counterfactual experiment shows that Lipitor benefits 4% to 7% of its quarterly sales from the information spill-over from incumbent drugs.

Since our model incorporates consumers' learning about clinical trials, the results can also be used to forecast the returns of landmark clinical trials (measured by how much demand they can generate) which are usually sponsored by pharmaceutical firms. Such results are important for managers who

need to decide which clinical trials to fund. Note that Lipitor obtained its own landmark clinical trial results six years after its entry in 1997. How much of the impact did these landmark clinical trials have on Lipitor’s sales? Were the landmark clinical trials worth the investment for Pfizer given that Lipitor were able to free-ride the clinical trials conducted by its rivals? Results of our counterfactual experiment suggest that annual global sales of Lipitor would have decreased by at least \$500 million in 2003 and 2004 if Pfizer had not invested in the landmark clinical trials. This suggests that it probably makes sense for Pfizer to invest in post-marketing clinical trials for Lipitor.

In another counterfactual experiment, we test how fast Lipitor can take off in the absence of switching costs. The result shows that Lipitor would become the best selling drug in the category right after its entry (Q2 1997) and all the incumbent drugs would lose market shares very quickly in the absence of switching costs. However, the experiment also shows that the absence of switching costs would help the take-off of a newer drug, Crestor, and that could hurt the sales of Lipitor in the longer term.

The rest of this paper is organized as follows. Section 2 reviews previous literature. Section 3 describes background information including the market for statins. Section 4 summarizes how we collect advertising and publicity data. Section 5 describes the structural model. Section 6 presents the estimation results. Section 7 is the conclusion.

## 2 Literature Review

Although some papers have developed learning models to study the pharmaceutical market, most of them (e.g. Chan et al., 2010; Ching, 2010a,b; Ching and Ishihara, 2012; Chintagunta et al., 2009; Crawford and Shum, 2005; Narayanan et al., 2005) do not model clinical evidence as a source of quality signals at all. An exception is the study by Ching and Ishihara (2010). But they only use qualitative information of comparison clinical studies. In this study, we treat clinical trial results more seriously than previous research. More specifically, we treat the information reported in landmark clinical trials as “observable” signals to researchers. This greatly simplifies the estimation procedure by avoiding the

integration of unobserved signals when forming the likelihood, which is typically the case in previous literature. In addition, the clinical trial data also help identify the parameters of the model, as we will discuss later.

Among the existing papers, Chan et al. (2010) is the most related to ours. They propose a learning model incorporating multi-dimensional attributes. They investigate physicians' learning on the effectiveness and side effects of drugs separately through patients' reported reasons of switching in the erectile dysfunction (ED) category. Their research is closely related to ours because both models employ a multi-dimensional model. Yet, the sources of identification are very different. They rely on physician level survey data, while we rely on the content of clinical trials and the variation of the number of prescriptions at the product level. Their model also incorporates switching costs since their data indicates that the market share of a new drug among returning patients is significantly lower than that among new patients. Their estimation results show that a large switching cost exists in the ED market.

Our study is also closely related to Janakiraman et al. (2009), who extend the umbrella branding framework of Erdem (1998) and Erdem and Sun (2002) to investigate correlated learning (information spill-over) across competing brands in the antidepressant market. However, like most of the previous studies, they do not consider the possibility that the release of post-marketing clinical trials may provide more information for the sales representatives to detail. Instead, they follow Erdem and Keane (1996) and assume that detailing activities always provide physicians with noisy and unbiased signals on product quality. This assumption implies that drug manufacturers are always fully informed of their drugs' true quality and they can make physicians learn about the true quality of their products after paying the physicians many detailing visits. This implication is inconsistent with the findings of other empirical analysis (e.g. Azoulay, 2002; Venkataraman and Stremersch, 2007; Ching and Ishihara, 2012), which show evidence that clinical trial results can affect the effectiveness of detailing. Unlike

Janakiraman et al. (2009), our model is able to study the interactions between post-marketing clinical trials and informative marketing activities across drugs.

Our modeling framework significantly extends the study of Ching and Ishihara (2010), which provides a structural modeling framework that allows the effectiveness of informative detailing to vary with clinical trial evidence. Unlike our study, Ching and Ishihara (2010) do not consider correlated learning. Moreover, we use quantitative information of clinical studies, instead of just the qualitative clinical evidence outcomes of comparison studies (which say whether drug A is better than B). It should also be highlighted that most of the studies mentioned above do not take switching costs into consideration, except Chan et al. (2010), who use physician level data.

### 3 Background

There are two main types of cholesterol: LDL (“bad” cholesterol) and HDL (“good” cholesterol).<sup>4</sup> The medical literature has shown that high cholesterol is a risk factor for heart diseases. Although the main purpose of statins is to reduce heart disease risks, a drug company cannot make the direct claim that its statin can reduce heart disease risks until it obtains direct evidence from a clinical trial to support the claim. This is because the public health agency is worried that some unknown side-effects of the drug could counter its benefits of lowering cholesterol levels. The information on the effectiveness of a statin in reducing heart disease risks, however, is usually unavailable when the statin is marketed because it takes a few years to obtain direct evidence of it. To obtain the direct scientific evidence, pharmaceutical firms invest in very expensive post-marketing clinical trials, which are called landmark clinical trials. More specifically, the clinical endpoint (the target outcomes) of landmark clinical trials for statins is the drugs’ efficacy in reducing heart disease risks.<sup>5</sup> Landmark clinical trials also report how much each statin lowers cholesterol levels in patients’ blood. By looking at these two efficacies,

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<sup>4</sup>Usually, when people simply use the word *cholesterol*, they refer it to LDL. We will follow this tradition in this study.

<sup>5</sup>We should note that the definition of landmark trial is not universally agreed for statins although most medical sources will give a similar set of landmark clinical trials. Our definition is relatively broad. Some sources will further classify our list of landmark trials to:(i) very influential trials; (ii) enrichment trials.



the effectiveness in lowering cholesterol levels and in reducing heart disease risks, physicians can learn about the efficiency ratio of a statin. In this research, we assume that landmark clinical trials are the only source of information for the effectiveness in reducing heart disease risks of statins. One might argue that physicians could learn from their patients' feedbacks. However, a heart attack is a very rare event and it is very hard for a physician to learn from his/her own patients' feedbacks. Therefore, we model the efficiency ratios reported in clinical trials as the only quality signals in physicians' learning process.

On the other hand, it is much easier and quicker for physicians to learn about a drug's effectiveness in lowering cholesterol levels. The manufacturer of each statin is required to prove the statin's ability in lowering cholesterol levels through clinical trials before the drug's entry to the market. In addition to clinical trials, physicians also learn about the effectiveness in reducing cholesterol levels from his/her own patients' feedbacks. Once physicians prescribe statins to their patients, they can observe their patients' cholesterol levels in a relatively short period. Therefore, in this research, as the first approximation, we assume that physicians always know the effectiveness of reducing cholesterol levels for all statins.

Table 1 contains a brief synthesis of the main descriptive statistics for the five major statins, Mevacor, Pravachol, Zocor, Liptior and Crestor. Although there are seven statins available in our dataset, our analysis focuses on these five major statins because their combined market shares exceed more than 95% of the total statin market across the whole sample period. We treat the other two statins as part of the outside good.

In general, statins do not relieve any acute symptoms from patients and the real benefits of statins are not easily observable to patients. Because patients do not feel any direct discomfort from the discontinuation of statin treatment, a significant proportion of patients discontinues statin treatment in each period (Neslin et al., 2009). Unlike the high discontinuation rate, switching rates between statins are very low, which suggests that large switching costs exist in this market. Chan et al. (2010)

incorporate switching costs when they model prescription drug choice and find that large switching costs exist in the erectile dysfunction (ED) drug market. While Chan et al. (2010) use physician level data, we only observe product level data. Hence, we do not estimate the switching costs. But we take their presence into consideration by supplementing product level data with switching rate data. More details about the switching rate data will be provided in subsection 4.2.

## 4 Data

The analysis in this research integrates four different data sources: (i) product level quarterly prescription volume and detailing data for the Canadian statin market from IMS Canada; (ii) product level quarterly prescription switching rates between statins and discontinuing rates from statins from Ontario Health Insurance Program (OHIP); (iii) landmark clinical trials obtained from published medical journals and a meta-analysis which summarizes statins' efficacy in lowering cholesterol levels; (iv) news articles covering statins collected from Factiva.

### 4.1 Prescription Volume and Detailing – Evidence for Correlated Learning

The product-level data obtained from the market-research firm, IMS Canada, consist of quarterly observations of prescription volumes and detailing costs for each statin across Canada from Q2 1993 ( $t = 1$ ) to Q4 2004 ( $t = 47$ ). The market is defined as the national market for quarter  $t$ . The observation is defined as a molecule-quarter combination.

We now present some preliminary evidence to support our correlated learning hypothesis. In figure 1, we plot the quarterly prescription volumes for the five statins in Canada. The prescription volume for Lipitor reached almost three million by 2001 while the earlier arrivals, Zocor and Pravachol, had 900,000 and 500,000 quarterly prescriptions, respectively. In 2002, Lipitor achieved estimated annual global sales of \$7.4 billion and became the best-selling product in the prescription drug market. When Lipitor hit the market in 1997, Warner-Lambert, the manufacturer of Lipitor, released a head-to-head

study supporting superior efficacy of Lipitor in lowering cholesterol levels over existing statins but did not establish any direct scientific evidence that Lipitor is effective in reducing heart disease risks. ASCOT-LLA, the first landmark clinical trial to support Lipitor's efficacy in reducing heart disease risks, was released in 2003, six years after Lipitor's entry. On the other hand, the existing statins had well established direct evidence that they are effective in reducing heart disease risks. Figure 1 indicates that Lipitor became very successful before the direct evidence supporting its efficacy in reducing heart disease risks became available. If we believe that physicians want to reduce their patients' chance of getting heart disease, their behavior of prescribing a new drug without direct clinical evidence over drugs with direct evidence, is not easy to apprehend.

One possible explanation for Lipitor's success without direct evidence is correlated learning, which will be modeled in section 5. The other possible explanation is that Lipitor is the most effective statin in lowering cholesterol levels and physicians might still infer that Lipitor is the most effective in reducing heart disease risks in the absence of information spill-over even if physicians may believe that Lipitor's efficiency ratio is low. Our structural model and the clinical data will yield the results to allow us to take both of these factors into account. Our estimates will be useful to measure their relative importance.

Previous research has documented that marketing activities have an influence on physicians' learning. Since detailing is considered a major activity of the pharmaceutical industry, we incorporate information on detailing expenditures for each drug. To convert from nominal to real dollars for detailing, we use the Consumer Price Index from Statistics Canada. Figure 2 graphs the evolution of the quarterly detailing spending for five statins. The market entries of Lipitor (Q2 1997) and Crestor (Q1 2003) coincide with their large detailing efforts. Mevacor (Q2 1997), Pravachol (Q3 2000), and Zocor (Q1 2003) stopped detailing when the generic substitutes for their own products were introduced in the market. While on average Pravachol spent more detailing than Lipitor between Q1 1997 and Q4 1998, Lipitor became the best selling statin in Q1 1999. This figure shows that although detailing may

partially account for the sales, the success of Lipitor cannot be fully explained by detailing spending only. By estimating our structural model, we can quantify the relative importance of each factor in contributing to the success of Lipitor.

## 4.2 Switching and Discontinuing Rate Data

The product-level data obtained from OHIP (Ontario Health Insurance Program) consist of quarterly number of patients who continue using the same statin ( $a_{jt}$ ), number of patients who switch to other statins ( $b_{jt}$ ), and number of patients who discontinue statin medication ( $c_{jt}$ ) at time  $t$  among the patients who use statin  $j = 1, \dots, 5$  at time  $t - 1$  in the province of Ontario from Q2 1993 ( $t = 1$ ) to Q4 2004 ( $t = 47$ ). From this dataset, we obtain the switching rate  $S_{jt} = \frac{b_{jt}}{a_{jt} + b_{jt} + c_{jt}}$  and the discontinuing rate  $D_{jt} = \frac{c_{jt}}{a_{jt} + b_{jt} + c_{jt}}$ . We will use the switching rates and the discontinuing rates for the analysis. Figures 3 and 4 present the switching and discontinuing rates, respectively. Figure 3 shows that the switching rates between statins are less than 5% for almost all quarters for all drugs. These low switching rates indicate the existence of switching costs in the statin market. In other words, if a patient is currently taking a certain statin treatment, the patient is unlikely to switch to a different statin in the next period. Figure 3 also shows that switching rates became higher when new drugs, Lipitor in 1997 and Crestor in 2003, were introduced. These high switching rates coinciding with new drugs' entry seem to implicate that there is heterogeneity in switching costs across patients, i.e., patients with low switching costs switch to new statins first. This implication is beyond the scope of this research and we leave it for future research. Figure 4 presents that discontinuing rates are almost 15% on average, which are much higher than switching rates.

Note that prescription volume and detailing data described in the previous subsection are nation-wide (Canada) and switching and discontinuing data described in this subsection are province-wide (Ontario). However, we assume that nation-wide switching and discontinuing rates would be the same as province-wide switching and discontinuing rates from the province of Ontario for the following

reasons:

1. This assumption could be reasonable if switching and discontinuing rates are not very sensitive to physicians' beliefs about statins' efficacy in reducing heart disease risks. This could happen if switching rates and discontinuing rates are more closely related to each patient's idiosyncratic match with statins than physicians' learning process.
2. The population in Ontario is more than one third of the population in Canada. Therefore, the sample size should be large enough to represent the population distribution of Canada.

Therefore we will use switching rates and discontinuing rates as if they are nation-wide data.

### 4.3 Clinical Trials

Azoulay (2002), Ching and Ishihara (2010), and Cockburn and Anis (2001) find evidence that clinical trials have significant impacts on physicians' prescribing decisions. We believe that clinical trial outcomes affect physicians' decisions by providing them with information on efficiency ratios of statins, i.e., how efficiently a statin can translate reduction in cholesterol levels into reduction in heart disease risks. This is because patients with high cholesterol levels take statins to mainly reduce their heart disease risks.

Each landmark clinical trial has slightly different clinical endpoints and follows patients with different conditions for different follow-up periods. For example, some clinical trials measure relatively healthy patients' chances of the first heart attack for a relatively long period and others investigate a statin's second heart attack prevention effects on patients with high risks for a relatively short term. To collect the landmark clinical trial data and create a consistent and reliable measure across different types of landmark clinical trials, we follow a similar method adopted by a meta-analysis (Delahoy et al., 2009). We use placebo- or usual care- controlled randomized trials that report statins' clinical endpoint (efficacy in reducing heart disease risks) and follow more than 1,000 patients for more than 1 year. Even

though clinical endpoints are slightly different across landmark clinical trials, all the landmark clinical trials report mean LDL reduction and relative risk reduction in a major coronary event. A major coronary event is defined as a nonfatal myocardial infarction or coronary heart disease-related death. Since medical literature has claimed that there is an overall positive and linear relationship between reduction in LDL and reduction in the risk for major coronary events across landmark clinical trials, we adopt the efficiency ratio as a measure on how efficiently a drug can translate absolute LDL reduction into the reduction in the risks for major coronary events (see figure 1 in Delahoy et al. (2009)). Table 2 lists the 12 landmark clinical trials we include in this research.

Every statin is approved as a cholesterol lowering drug because the manufacturer is required to prove its statin's ability in lowering cholesterol levels through clinical trials to market the drug. This type of information is considered relatively easy for physicians to obtain since there are abundant numbers of clinical trial results before the drug's entry. Moreover, physicians can directly observe the cholesterol levels of their patients within a short period of time after prescribing a statin. In this research, therefore, we assume that physicians immediately learn about the true efficacy in lowering cholesterol levels of each stain when the statin is marketed.

For our analysis, we take the information on each drug's cholesterol lowering ability from the study of Law et al. (2003) who conducted a meta-analysis summarizing the results of clinical trials which investigate effectiveness of statins on reducing LDL. Law et al. (2003) include all double blind clinical trials reporting mean absolute LDL reductions (mmol/L) in the statin treated group and in the placebo group from Medline, Cochrane Collaboration, and Web of Science databases. They define drug efficacy as the difference between the LDL reductions in the treated and placebo groups, and calculate the drug efficacy for each clinical trial. From the drug efficacy data across clinical trials, they report the mean absolute reduction in LDL of statins including Mevacor, Pravachol, Zocor, Lipitor, and Crestor by dosage (5mg, 10mg, 20mg, 40mg and 80mg) across clinical trials. Since this meta-analysis does not

report the effectiveness in LDL reduction of Mevacor with 5mg dose, we exclude data for all other statins with 5mg dose. Table 3 shows the mean LDL reduction of each statin by strength.<sup>6</sup> The numbers are taken from table 2 of Law et al. (2003). By taking the average of the reported mean LDL reductions across strengthes of each drug, we create a drug specific variable denoting LDL reduction efficacy. The values of this variable is 1.59 for Mevacor, 1.28 for Pravachol, 1.66 for Zocor, 2.22 for Lipitor, and 2.44 for Crestor.<sup>7</sup> The data from the study of Law et al. (2003) is very important for our research because it allows us to pin down the effectiveness of lowering cholesterol levels for each statin without the need of estimating them. If we had to estimate the effectiveness of lowering cholesterol levels, it would be very hard for us to identify the learning parameters. The identification strategy will be discussed in subsection 5.8.

#### 4.4 Publicity

To investigate the impact of media coverage on physicians' learning, we use the similar publicity dataset from chapter 1.

Recall that collect news article data covering statins that contain the word “statin” or words related to statin, such as the chemical names or brand names from Factiva from 1986 to 2004. Then, we restrict the sample to news articles from sources to which Canadian patients may have access. For each article, we extract its headline, source, content and publication date. We first map the information of each article into two multidimensional variables: (a) *general* publicity variable ( $publicity_t^g$ ) – if it has sentences that discuss statins in general without referring to any particular statin by brand or chemical name; (b) *drug specific* publicity variable ( $publicity_{jt}$ ) – if it has sentences that refer to one or more statins by either brand or chemical name. Note that an article may contain information that can be mapped onto both variables – it can provide information about statins in general at the beginning, and

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<sup>6</sup>While table 3 uses mmol/L as unit of LDL reduction, the unit in table 2 is mg/dL. Because molar mass of cholesterol is 386.65g, 1 mmol/L of LDL can be converted to 38.6mg/dL.

<sup>7</sup>We have also collected data from CURVES study, with which Pfizer provided the FDA to get an approval for Lipitor. The results on the LDL reduction abilities are consistent with those of Law et al. (2003). However, CURVES study does not report the efficacy of Crestor. Therefore, we do not use the results from CURVES study.

then later mention which particular statin is the most effective. Our intuition is that general publicity is more likely to affect the overall demand for statins, while drug specific publicity could influence both total demand for statins and which particular statin to use. For *drug specific* publicity, we sometimes encounter articles that compare drugs. Therefore, we further classify drug specific publicity into *comparison* (*c*) or *non-comparison* (*nc*). The results of chapter 1 indicate that comparison publicity does not have much variation. Therefore, we only use non-comparison drug specific publicity.

We classify both *general* and *drug specific* publicity into three dimensions: lowering cholesterol levels, reducing heart disease risks and side-effects. Hereafter, we use  $(lc_t^s, rh_t^s, se_t^s)$  to represent the three dimensions of the general publicity variable, where the superscript *s* means that they are for the whole statin class; *t* indexes time. For the drug specific publicity variable, we use  $(lc_{jt}, rh_{jt}, se_{jt})$ , to represent its three dimensions, where *j* is an index for drug. For each dimension of both *drug specific* and *general* publicity, we use a two-step Likert scale (+1, -1) to assess its tone. We assign “+1” (“-1”) if the article contains sentences which favor (do not favor) the focal drug.

In our empirical analysis, the length of a period is a quarter. Since there are usually more than one news story published/broadcasted in each quarter, we need to aggregate the outcomes of the news appeared in the same quarter to obtain a quarterly observation. We use the following procedure to do the aggregation. Let  $(publicity_{t,l}^s, publicity_{jt,l})$  denote the publicity variables associated with article *l* that is published in quarter *t*. Also, let  $L_t$  be the total number of news stories appeared in quarter *t*. Then the values of  $(publicity_t^s, publicity_{jt})$  are obtained by simply summing  $(publicity_{t,l}^s, publicity_{jt,l})$  across the news stories appeared in quarter *t*. For example,  $publicity_t^s = \sum_{l=1}^{L_t} publicity_{t,l}^s$ .

Figure 5 shows the general publicity flow variables. While there are some bad news articles about statins’ side-effects, especially in 2001 when Baycol was removed from market, most news articles report that statins are effective in lowering cholesterol levels and reducing heart disease risks. Table 4 presents a descriptive summary of drug specific publicity variables. In general, *lc*-type articles are more common



than *rh*-type articles, while *se*-type articles are the least common.

## 5 Model and Estimation

In this section, we propose a structural demand model incorporating physicians' correlated learning about clinical trial outcomes. We also discuss how to construct the likelihood function, and the identification issues.

### 5.1 Bayesian Learning Model

To investigate correlated learning across drugs, this study employs a dataset which comprises of five different drugs. Without the loss of generality, we assume there are only two drugs here. We provide the generalized version of our learning model with  $J$  drugs in appendix B. Consider a situation where physician  $k$  prescribes anti-cholesterol drug  $j = 1$  or  $2$  to patient  $i$ .

The utility of patient  $i$  who consumes drug  $j$  at time  $t$  is given by

$$U_{ijt} = \omega \cdot q_j^h + b_j + \epsilon_{ijt}, \quad (1)$$

where  $q_j^h$  denotes drug  $j$ 's efficacy in reducing heart disease risks and  $b_j$  captures time-invariant brand specific preference, e.g., price difference across brands.<sup>8</sup>  $\epsilon_{ijt}$  is an i.i.d. random shock and is extreme value distributed.

We assume that the physician chooses a drug to maximize the sum of her patient's utility conditional on her information set and her utility from marketing spending of pharmaceutical firms such as persuasive detailing.<sup>9</sup> The demand system is obtained by aggregating this discrete choice model of an individual physician's behavior. Note that physicians/patients are uncertain about  $q_j^h$ . We therefore assume that physicians make their prescribing decisions based on her expected utility. Let  $I^k(t)$  denote physician  $k$ 's information set at time  $t$ . Physician  $k$ 's expected utility of prescribing drug  $j$  to patient

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<sup>8</sup>Due to the strict regulations on prescription drug prices in Canada, prices for statins hardly changed over our sample period.

<sup>9</sup>We will discuss how to model persuasive detailing in subsection 5.3.

$i$  at time  $t$  will be:

$$E[U_{ijt}^k | I^k(t)] = \omega \cdot E[q_j^h | I^k(t)] + b_j + \epsilon_{ijt}, \quad (2)$$

where  $E[\cdot | I^k(t)]$  denotes the expected value given physician  $k$ 's information set at time  $t$ . We assume that physicians make their prescribing decisions based on their current expected utility. One might argue that physicians can be forward-looking and experiment different drugs to learn about  $q_j^h$ . However, since a heart attack is a very rare event, it is unlikely that physicians can use patients' experiences to update their prior about  $q_j^h$ . Consequently, we do not consider that physicians have an incentive to experiment different drugs on their patients.

Let  $q_j^c$  be the efficacy in lowering cholesterol levels of drug  $j$ , and  $\beta_j$  be the efficiency ratio. We define the "efficiency ratio" as a measure on how efficiently a drug can translate a reduction in cholesterol levels into a reduction in heart disease risks. Then,  $q_j^h$  can be expressed as follows:

$$q_j^h = q_j^c \cdot \beta_j. \quad (3)$$

Because we assume that physicians have complete information about the efficacy in lowering cholesterol levels of each drug ( $q_j^c$ ) but are uncertain about the efficiency ratio of each drug ( $\beta_j$ ),<sup>10</sup> physician  $k$ 's expectation about  $q_j^h$  can be expressed as follows.

$$E[q_j^h | I^k(t)] = q_j^c \cdot E[\beta_j | I^k(t)]. \quad (4)$$

Now we turn to explain how physicians learn about the efficiency ratios. We model physicians' learning process by adopting the Bayesian learning framework (DeGroot, 1970). Physicians construct their initial prior belief before they learn about the results of landmark clinical trials. As discussed earlier, because all statins use a similar mechanism to lower cholesterol levels, the efficiency ratios across statins in their initial prior belief may be correlated. In other words, one statin's revealed information

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<sup>10</sup>Physicians can easily learn about the efficacy in lowering cholesterol levels of each drug from abundant non-landmark clinical trials or from patients' consumption experience. On the other hand, physicians can learn about the efficiency ratio only from landmark clinical trials.

on the efficiency ratio can be a good indicator to the levels of other statins' efficiency ratios. Due to these intrinsic quality correlations, physicians may infer the quality of statin  $j$  in reducing heart disease risks indirectly from the clinical trial evidence of other drugs in the statin class. Our model captures this information spill-over effect by allowing physicians' initial priors on efficiency ratio to be correlated across drugs. Therefore, we allow the off-diagonal elements in the variance-covariance matrix for the initial prior beliefs to be non-zero. The initial prior on the efficiency ratio can be expressed as follows:

$$\begin{pmatrix} \beta_1 \\ \beta_2 \end{pmatrix}_{t=0} \sim N \left( \begin{pmatrix} \beta \\ \beta \end{pmatrix}, \sigma_\beta^2 \begin{pmatrix} 1 & \rho_0 \\ \rho_0 & 1 \end{pmatrix} \right). \quad (5)$$

Note that we use five drugs in our empirical analysis. In principle, we can let the correlation parameter values differ across pairs of drugs. However, estimating the heterogeneous correlation parameter would probably require much richer dataset than what we currently have. Therefore, we restrict  $\rho_0$  to be the same across all pairs of drugs when implementing our model.

Since it is unlikely for physicians to learn about the efficacy in heart disease risks of statins from their patients' experiences, landmark clinical trials, which are specifically designed to prove the efficacy of drugs in heart disease risks, become the main sources of information about this efficacy. Physicians are assumed to update their beliefs on the efficiency ratio of each drug when they are exposed to landmark clinical trial results. A landmark clinical trial provides a noisy but unbiased signal for the efficiency ratio. A signal from clinical trial  $l$  for drug  $j$ ,  $\tilde{\beta}_{jl}$ , can be expressed as:

$$\tilde{\beta}_{jl} = \beta_j + \zeta_l, \quad (6)$$

where  $\beta_j$  is the true mean level of the efficiency ratio for drug  $j$  and  $\zeta_l$  is a signal noise and i.i.d. normally distributed with zero mean and variance  $\sigma_\zeta^2$  for landmark clinical trial  $l$ . Let  $\sigma_\zeta^2$  be signal variance for one patient, and  $N_l$  be the number of patients who participate in landmark clinical trial  $l$ . As long as the individual signals are i.i.d. across patients, it can be shown that  $\sigma_{\zeta_l}^2 = \sigma_\zeta^2/N_l$ . This implies that the more participants a clinical trial has, the more physicians will trust its results. Note

that, unlike previous literature, we are able to treat quality signals as *observables* to researchers by using the information from the landmark clinical trials.

To explain how physicians update their beliefs through learning about clinical trials, let us provide a simplified example which can be easily generalized. The general model is provided in the appendix. In this example, we assume that there is only one landmark clinical trial, which investigates drug 1's efficacy in reducing heart disease risks. Let  $\beta_{jt}$  be the expected perceived efficiency ratio, and  $\sigma_{\beta_{jt}}^2$  be the perceived variance of drug  $j$ , conditional on the physician  $k$ 's information set at time  $t$ . The variance-covariance matrix for prior beliefs of physician  $k$  at time  $t$  becomes,

$$V[\beta_j|I^k(t)] = \begin{pmatrix} \sigma_{\beta_{1t}}^2 & \pi_t \\ \pi_t & \sigma_{\beta_{2t}}^2 \end{pmatrix}. \quad (7)$$

If the physician learns about clinical trial  $l$  for drug 1, she will update her beliefs on the efficiency ratio of drug 1 as follows:

$$\beta_{1t+1} = \beta_{1t} + \frac{\sigma_{\beta_{1t}}^2}{\sigma_{\beta_{1t}}^2 + \sigma_{\zeta_{1l}}^2} \cdot (\tilde{\beta}_{1l} - \beta_{1t}). \quad (8)$$

She also updates her prior variance on the efficiency ratio of drug 1 at time  $t$  as follows:

$$\sigma_{\beta_{1t+1}}^2 = \frac{\sigma_{\beta_{1t}}^2 \sigma_{\zeta_{1l}}^2}{\sigma_{\beta_{1t}}^2 + \sigma_{\zeta_{1l}}^2}. \quad (9)$$

With correlated prior beliefs on the efficiency ratio, signals for drug 1 are used to update beliefs on drug 2 as well. Posterior beliefs for drug 2 are given as

$$\beta_{2t+1} = \beta_{2t} + \frac{\pi_t}{\sigma_{\beta_{2t}}^2 + \sigma_{\zeta_{1l}}^2} (\tilde{\beta}_{1l} - \beta_{1t}), \quad (10)$$

where  $\pi_t$  denotes the off-diagonal element in the variance-covariance matrix of the perceived quality on the efficiency ratio at time  $t$ .

The variance of her posteriors on the efficiency ratio of drug 2 at time  $t$  becomes

$$\sigma_{\beta_{2t+1}}^2 = \sigma_{\beta_{2t}}^2 - \frac{\pi_t^2}{\sigma_{\beta_{2t}}^2 + \sigma_{\zeta_{1l}}^2}. \quad (11)$$

The off-diagonal element of variance-covariance matrix for posterior beliefs becomes

$$\pi_{t+1} = \frac{\pi_t \sigma_{\zeta 1l}^2}{\sigma_{\beta 1t}^2 + \sigma_{\zeta 1l}^2}. \quad (12)$$

As a result, the variance-covariance matrix for posterior beliefs becomes

$$V[\beta_j | I^k(t+1)] = \begin{pmatrix} \frac{\sigma_{\beta 1t}^2 \sigma_{\zeta 1l}^2}{\sigma_{\beta 1t}^2 + \sigma_{\zeta 1l}^2} & \frac{\pi_t \sigma_{\zeta 1l}^2}{\sigma_{\beta 1t}^2 + \sigma_{\zeta 1l}^2} \\ \frac{\pi_t \sigma_{\zeta 1l}^2}{\sigma_{\beta 1t}^2 + \sigma_{\zeta 1l}^2} & \sigma_{\beta 2t}^2 - \frac{\pi_t^2}{\sigma_{\beta 2t}^2 + \sigma_{\zeta 1l}^2} \end{pmatrix}. \quad (13)$$

## 5.2 Roles of Detailing

In this subsection, we explain how detailing influences demand. The economics and marketing literature studying the pharmaceutical industry find evidence that detailing can play both informative and persuasive roles (Chan et al., 2010; Ching and Ishihara, 2012; Leffler, 1981; Narayanan et al., 2005). To encourage physicians to prescribe their drugs, detailers might inform physicians of their drug’s efficacies and side effects (informative role). However, they can also persuade physicians to prescribe their drugs regardless of the clinical information about their drugs (persuasive role). For example, detailers provide physicians with free gifts, which can affect physician’s prescribing decisions. We will model both roles and discuss how to separately identify them.

## 5.3 How Does Persuasive Detailing Work?

We first describe how we model the persuasive role. Here, we adopt the standard approach by modeling a detailing goodwill stock entering physicians’ utility function directly. Therefore, we modify eq(2) as follows:

$$E[U_{ijt}^k | I^k(t)] = \omega \cdot E[q_j^h | I^k(t)] + \kappa_d \cdot STK\_detail_{jt} + b_j + \epsilon_{ijt}, \quad (14)$$

where  $STK\_detail_{jt}$  is a persuasive detailing goodwill stock for drug  $j$  at time  $t$ . The persuasive detailing stock is defined as:

$$STK\_detail_{jt} = \delta_p \cdot STK\_detail_{jt-1} + detail_{jt}, \quad (15)$$

where  $\delta_p$  is the monthly carryover rate for detailing;  $detail_{jt}$  denotes the flow of detailing spending for drug  $j$  at time  $t$ .

#### 5.4 How Does Informative Detailing Work?

We now explain how to model the informative role of detailing. Then we describe physicians' learning through detailing and forgetting behaviors. Generally speaking, most physicians are busy with their own practices. We assume that physicians may not learn about the efficiency ratio directly from clinical trial results. Following Ching and Ishihara (2010), we assume that some of the physicians learn about the efficiency ratios through visits of pharmaceutical representatives (detailers). Since detailers are not able to reach all the physicians at the same time, only some of physicians will be detailed and learn about the most updated clinical trial results in each period. We assume the probability that each physician learns about the latest landmark clinical trial result for drug  $j$  at time  $t$  is a function of detailing at time  $t$  and the probability is expressed as follows:

$$P_{info}(detail_{jt}) = \frac{\exp(\alpha_0 + \alpha_d \cdot detail_{jt})}{1 + \exp(\alpha_0 + \alpha_d \cdot detail_{jt})}, \quad (16)$$

where  $detail_{jt}$  denotes detailing spending for drug  $j$  at time  $t$ . It should be highlighted that this probability does not depend on a physicians' current information set (i.e., independence assumption).

Similar to Ching and Ishihara (2010), we also model the physicians' forgetting behavior about the clinical trial results. We assume that the probability that a physician remembers the information in the next period is  $\delta_i$  given that the physician is informed of clinical trial information for drug  $j$ .  $\delta_i$  can be interpreted as the carryover rate of informative detailing (or information). For instance, if there are one half of physicians who are informed of a new clinical trial and the other half are totally uninformed at time  $t$ , only  $\frac{1}{2}\delta_i$  of physicians will retain the clinical trial information and  $1 - \frac{1}{2}\delta_i$  will be the proportion of uninformed physicians at the beginning of time  $t + 1$  before they are exposed to  $detail_{jt+1}$ .

Since we allow physicians to be heterogenous with respect to their information sets, the number of physician types (characterized by their information sets) increases exponentially as the number of

published clinical trials increases. If there are total  $n$  clinical trials up to time  $t$ , theoretically there will be  $2^n$  types of physicians at time  $t$ . To make the estimation of our model feasible, we make the following additional assumptions:

1. If a physician learns about a clinical trial for drug  $j$  at time  $t$ , she will learn about all the published clinical trials for drug  $j$  prior to time  $t$ .
2. If a physician forgets information about drug  $j$ , her information set on drug  $j$  becomes the same as the initial priors. Suppose that there are two clinical trials for drug  $j$ . If a physician is informed of both clinical trials 1 and 2 at time  $t$  and she happens to forget the information on drug  $j$  at the end of time  $t$ , she will forget both the clinical trials and will become totally uninformed of clinical trials for drug  $j$  at the beginning of time  $t + 1$ .

The above assumptions significantly reduce the computational burden of estimating the model. More specifically, if there are  $n_j$  clinical trials up to time  $t$  for drug  $j \in \{1, \dots, J\}$ , then the number of physician types reduces from  $2^{n_1+n_2+\dots+n_J}$  to  $(n_1 + 1) \cdot (n_2 + 1) \cdots (n_J + 1)$ .

The following example should help understand how the learning and forgetting processes work. Suppose that there is only one drug, and that there are two clinical trials available for this drug. One of them is published at the beginning of period 1 and the other one at the beginning of period 3. Let  $P_t^l$  denote proportion of physicians who are informed of clinical trial  $l$ .  $P_t^0$  denotes proportion of physicians who are totally uninformed at time  $t$ . Also, let  $detail_t$  denotes detailing spending for the drug at time  $t$ .

1. At time  $t = 0$ , every physician has the same initial prior belief and is totally uninformed, i.e.,  $P_{t=0}^0 = 1$ .
2. At time  $t = 1$ , clinical trial 1 is available and the firm spends  $detail_{t=1}$ . As a result,  $P_{t=1}^1 = P_{info}(detail_1)$ , and  $P_{t=1}^0 = 1 - P_{info}(detail_1)$ .

3. At the beginning of period 2, the proportion of physicians remained being informed of clinical trial 1 becomes  $\delta_i P_{t=1}^1$ . Moreover, at the beginning of period 2, the proportion of physicians who are uninformed about clinical trial one becomes  $P_{t=1}^0 + (1 - \delta_i)P_{t=1}^1 = 1 - \delta_i P_{t=1}^1$ . At time  $t = 2$ , the firm spends  $detail_{t=2}$  (and recall that only clinical trial one is available). Therefore, at the end of period  $t = 2$ ,  $P_{t=2}^1 = \delta_i P_{t=1}^1 + (1 - \delta_i P_{t=1}^1)P_{info}(detail_2)$ , and  $P_{t=2}^0 = (1 - \delta_i P_{t=1}^1)(1 - P_{info}(detail_2))$ .
4. At time  $t = 3$ , now clinical trial 2 is available and the firm spends  $detail_{t=3}$ . Following the similar calculation in step 3,  $P_{t=3}^0 = (1 - \delta_i P_{t=2}^1)(1 - P_{info}(detail_3))$ , and  $P_{t=3}^1 = \delta_i P_{t=2}^1(1 - P_{info}(detail_3))$ . Moreover, by the independence assumption, The proportion of physicians who are informed of both clinical trials at time  $t = 3$ ,  $P_{t=3}^2 = P_{info}(detail_3)$ .

It should be highlighted that the way we model heterogeneity in information sets is more flexible than Ching and Ishihara (2010), who simply assume that a physician either knows the most updated information or uninformed about drug  $j$  at time  $t$ . In other words, they assume that at time  $t$ , a physician either knows all the clinical trials for drug  $j$  published up to time  $t$ , or they do not know any clinical trials about drug  $j$  at all.

## 5.5 How Does Informative Publicity Work?

In this subsection, we explain how we can extend the informative role of detailing to publicity. Since statins are a very popular class of anti-cholesterol drugs, they have received extensive media coverage. We are interested in whether this media coverage has any impact on physicians' learning. While physicians might not rely on TV news or newspaper articles as a source of information about drugs' efficacies or side-effects, it is plausible that their patients who were exposed to media coverage about a statin would ask or motivate physicians to read the most updated clinical trial results. Therefore, publicity might work as informative detailing works. Chapter 1 empirically investigates the impact of publicity and the results suggest that non-comparison brand specific publicity has impact on brand choice. Therefore, we include non-comparison publicity in the dimensions of lowering cholesterol levels,



reducing heart disease risks and side effects. To capture the above mentioned physicians' behaviors we can extend equation (16) and model the "informative" publicity as follows:

$$P_{info}(detail_{jt}, PUB_{jt}) = \frac{\exp(\alpha_0 + \alpha_d \cdot detail_{jt} + \alpha_p \cdot PUB_{jt})}{1 + \exp(\alpha_0 + \alpha_d \cdot detail_{jt} + \alpha_p \cdot PUB_{jt})}, \quad (17)$$

where  $PUB_{jt}$  denotes a vector of three dimensional ( $lc$ ,  $rh$  and  $se$ ) brand specific publicity variables for drug  $j$  at time  $t$ .

## 5.6 Prescribing Decisions

Based on patients' choices at the previous period ( $t - 1$ ), we classify patients at time  $t$  into two groups, "potential patients" and "existing patients." First, we will explain the decision making process of "potential patients." As figure 6 depicts, our model assumes that their decision making process consists of two stages. The first stage (adoption decision stage) determines whether a potential patient will use statins. The decision in this stage could be jointly made by the patient and his physician. For example, news articles reporting the problem of high cholesterol levels or the benefits of taking statins could entice the patient to see a physician. Alternatively, a physician detailed by pharmaceutical representatives might recommend her patient to get a blood test. Therefore, we model that sum of publicity and sum of detailing spending affect the decision making process in this stage. The probability that a physician prescribes one of the statins to her potential patients at time  $t$ ,  $P_t(statin)$ , is expressed as the follows:

$$P_t(statin) = \frac{\exp((\alpha_d^s + \alpha_c^s \cdot Clinical_t^s) \cdot STK\_detail_t^s + \alpha_p^s \cdot STK\_PUB_t^s + \alpha_0^s)}{1 + \exp((\alpha_d^s + \alpha_c^s \cdot Clinical_t^s) \cdot STK\_detail_t^s + \alpha_p^s \cdot STK\_PUB_t^s + \alpha_0^s)}, \quad (18)$$

where  $STK\_detail_t^s$  denotes a stock of detailing for the whole statin class and  $Clinical_t^s$  denotes the accumulated number of participants in landmark clinical trials for statins up to time  $t$ . We introduce the variable  $Clinical_t^s$  to investigate whether clinical trial results increase the impact of detailing on category demand. Lastly,  $STK\_PUB_t^s$  denotes a vector of three types of general publicity ( $rh_t^s$ ,  $lc_t^s$ ,  $se_t^s$ ) stocks for the class of statin.

If a potential patient decides to use statins, then we move to the second stage (statin choice stage),

which determines which statin to be prescribed. The physician evaluates all the statins available given her information set and chooses the most appropriate statin for her patient. The probability that physician  $k$ , who is type  $g$  at time  $t$ , prescribes  $j$  to new patient  $i$  conditional on prescribing one of the statins,  $P_{it}^k(j|statin, k_{type})$ , is expressed as follows:

$$P_{it}^k(j|statin, k_{type}) = \frac{\exp(E[U_{ijt}^k|I^k(t)])}{\sum_{r=1}^J \exp(E[U_{irt}^k|I^k(t)])}. \quad (19)$$

Note that the information set of physician  $k$ ,  $I^k(t)$  is a function of physicians' type  $g$  at time  $t$ . Section 5.4 describes how we separate physicians into  $(n_1 + 1) \cdot (n_2 + 1) \cdots (n_J + 1)$  types according to their information set. Let  $N_d$  denotes the number of physicians' types and  $P_t(k_{type} = g)$  denotes the probability of physician  $k$  being a type  $g$  physician. The expected "new patients demand" (group 1) for drug  $j$  at time  $t$ ,  $\hat{d}_{jt}^1$ , can be expressed as :

$$\hat{d}_{jt}^1 = (m_t - \sum_{r=1}^J d_{rt-1}) \cdot P_t(statin) \cdot \sum_{g=1}^{N_d} P_t(k_{type} = g) \cdot \frac{\exp(E[U_{ijt}^k|I^k(t)])}{\sum_{r=1}^J \exp(E[U_{irt}^k|I^k(t)])}. \quad (20)$$

Note that  $(m_t - \sum_{r=1}^J d_{rt-1})$  can be considered a potential patient pool for statins at time  $t$ .

For "existing patients," their decisions are more complicated than "potential patients". Figure 7 depicts the decision tree of existing patients. In the first stage, they decide either to quit taking statins or to keep taking statins. Once they decide to keep taking statin, they will decide either to stay with the same statin or switch to other statins. Once they decide to switch to other statins, they will decide which statin to switch. If a patient is already on a statin treatment, the patient might keep taking the same statin even though there are alternatives to give him a better expected consumption utility. One of the reasons for this could be that because many patients with high cholesterol problems might already take several drugs, it will be very troublesome for patients to learn how to take the new medication and to understand its potential side-effects. If the existing patient decides to stay with the current statin, we classify the patient as a "retainer." If he decides to switch to one of other statins, we classify him as a "switcher."

The expected demand for retainers (group 2) can be expressed as :

$$\hat{d}_{jt}^2 = d_{jt-1} \cdot (1 - S_{jt} - D_{jt}), \quad (21)$$

where  $S_{jt}$  and  $D_{jt}$  denote switching and discontinuing rates of drug  $j$  at time  $t$  which is from our data set. It should be highlighted that the whole sequence of  $\{\hat{d}_{jt}^2\}$  will be determined by the equation above because we observe  $S_{jt}$ ,  $D_{jt}$  and  $d_{jt}$ .

The “switchers” (group 3) are patients who took a statin other than drug  $j$  in the previous period but take statin  $j$  at period  $t$ . Switchers do not consider the same drug which they chose in the previous period. The estimated demand for switchers can be expressed as :

$$\hat{d}_{jt}^3 = \sum_{m=1, \neq j}^J d_{mt-1} \cdot S_{mt} \cdot \sum_{g=1}^{N_d} P_t(k_{type} = g) \cdot \frac{\exp(E[U_{ijt}^k | I^k(t)])}{\sum_{r=1, \neq m}^J \exp(E[U_{irt}^k | I^k(t)])}. \quad (22)$$

Note that once a patient leaves from taking statin treatment, he will be back to the potential patient pool in the next period.

We should also highlight that we do not use nested logit framework for the switchers’ decision making process. Because we do not model  $S_{jt}$  as a function of physicians’ expected utilities in prescribing each statin, the decision on whether to switch is independent of the decision on which drug to prescribe. We do not model  $S_{jt}$  as a function of physicians’ expected utilities for the following reasons:

1. It is very hard for a patient or a physician to directly observe the efficacy in reducing heart disease risks from patient’s experience. Therefore, the patient’s or physician’s switching decision could mainly rely on factors other than heart disease risks.
2. If we model the switching rate as a function of physicians’ expected utilities, the model will become too complex to estimate. If the switching rate is a function of physicians’ expected utilities, the patients of physicians who evaluate drug  $j$  the least will switch from drug  $j$  to other statins first. Then, the physicians of remaining patients with drug  $j$  will have a different distribution of utilities on prescribing  $j$  from the physicians of switching patients from drug  $j$ . To model these switching

or staying behaviors, we have to simulate a very large number of physicians and patients and then follow their decisions at each period. Such a simulation procedure will significantly increase the computational burden of estimating the model.

Because we do not endogenize  $S_{jt}$ , we do not estimate switching costs.

## 5.7 Estimation

### Likelihood

The quantity demand  $d_{jt}$  at time  $t$  for drug  $j$  can be expressed as:

$$d_{jt} = \hat{d}_{jt}^1 + \hat{d}_{jt}^2 + \hat{d}_{jt}^3 + e_{jt}, \quad (23)$$

where  $e_{jt}$  represents a measurement error.  $\hat{d}_{jt}^1$ ,  $\hat{d}_{jt}^2$  and  $\hat{d}_{jt}^3$  denote the estimated demand for group 1, 2 and 3, respectively. Note that subsection 5.6 describes how we model estimated demand for each group.

Assuming that the measurement error,  $e_{jt}$  in equation (23) is normally distributed, we can obtain the likelihood function:

$$l(\{d_{jt}\}_{j=1}^J | \{\{detail_{jp}\}_{j=1}^J\}_{p=1}^t, \{\tilde{\beta}_{jl}\}_{l=1}^{l_t}, \{N_l\}_{l=1}^{l_t}, \{PUB_p^s\}_{p=1}^t, \{PUB_{jt}\}_{j=1}^J; \theta_d), \quad (24)$$

where  $\theta_d$  is the vector of parameters;  $detail_{jt}$  is detailing spending for drug  $j$  at time  $t$ ;  $l_t$  denotes the number of landmark clinical trials up to time  $t$ ;  $\tilde{\beta}_{jl}$  is a level of quality signal from landmark clinical trial  $l$ ;  $N_l$  is the number of patients which clinical trial  $l$  follows;  $PUB_t^s$  and  $PUB_{jt}$  are vectors of general publicity and brand specific publicity, respectively. The likelihood of observing  $d = \{\{d_{jt}\}_{j=1}^J\}_{t=1}^T$  is

$$\begin{aligned} & L(d | \{\{detail_{jt}\}_{j=1}^J\}_{t=1}^T, \{\tilde{\beta}_{jl}\}_{l=1}^{l_t}, \{N_l\}_{l=1}^{l_t}, \{PUB_t^s\}_{t=1}^T, \{\{PUB_{jt}\}_{j=1}^J\}_{t=1}^T; \theta_d) \\ &= \prod_{t=1}^T l(\{d_{jt}\}_{j=1}^J | \{\{detail_{jp}\}_{j=1}^J\}_{p=1}^t, \{\tilde{\beta}_{jl}\}_{l=1}^{l_t}, \{N_l\}_{l=1}^{l_t}, \{PUB_p^s\}_{p=1}^t, \{PUB_{jt}\}_{j=1}^J; \theta_d). \end{aligned} \quad (25)$$

We estimate parameters by maximizing the log-likelihood function. Unlike the previous literature on learning models, all the quality signals are “observable” in our model. Therefore, we can simply construct the likelihood function without adopting any simulation method.

## Initial condition problem

Note that our detailing data starts from Q2 1993. Therefore, the data do not include the period when Mevacor, Pravachol, or Zocor were introduced. By Q2 1993, these three drugs might have accumulated goodwill stocks of persuasive detailing efforts. To control for the initial condition problem, we follow Ching and Ishihara (2010) and assume that before Q2 1993, the manufacturers of these three drugs would have devoted the same detailing efforts as they did on average between Q2 1993 and Q1 1994.<sup>11</sup> However, the initial condition problem does not apply to informative detailing because the first landmark clinical trial is published in Q4 1994, which is within our sample period.

## 5.8 Identification

In this subsection, we provide some intuitions about how the parameters of our model can be identified. The parameters in the adoption decision stage ( $\alpha_0^s, \alpha_c^s, \alpha_d^s, \alpha_{ic}^s, \alpha_{rh}^s, \alpha_{se}^s, \delta_d^s, \delta_p^s$ ) can be identified by the variation of market share of statins as a whole and the variation of the explanatory marketing variables, such as, sum of detailing, sum of clinical trial outcomes and sum of publicity across statins.

Correlation in the initial prior beliefs ( $\rho_0$ ) can be identified from the observed (to researcher) quality signals on efficiency ratios from clinical trial outcomes and the timing of each clinical trial release as well as the changes in relative market shares of statins before and after the release of each clinical trial. In identifying the correlation parameter, the observed quality signals play a pivotal role because the change in market shares before and after the release of a clinical trial can be moderated by both the realized quality signal from the clinical trial and the extent of correlated learning. For example, if a drug does not gain relative market share after the release of its own clinical trial, there are two possible explanations: (i) The realized quality signal from the clinical trial is the same as physicians' current perceived quality for the drug, and there is no correlated learning (i.e.,  $\rho_0 = 0$ ). Or, (ii) the realized quality signal is higher than physicians' current perceived quality, but the extent of correlated learning

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<sup>11</sup>For the publicity variables, we use the pre-sample period data from Q1 1986 to Q1 1993 to create  $STK\_publicity_{t=1}$ . It is unlikely that there are much news about statins available prior to Q1 1986 because the first statin was launched in Q3 1987.

is extremely high (i.e.,  $\rho_0 \simeq 1$ ); consequently, physicians update their prior beliefs about the qualities of both drugs by the same amount. By explicitly using the information reported in a clinical trial, we can observe the realized quality signals. This is how we can tell which explanation plays a bigger role, and hence identify the correlation parameter.

The parameters that determine the persuasive ( $\kappa_d, \delta_p$ ) and informative detailing ( $\alpha_0, \alpha_d, \delta_i$ ) can be separately identified because (i) they enter the model in two very different structural ways, and (ii) we assume that clinical trial outcomes only affect the informative detailing and we explicitly use the information from clinical trials. As a result, clinical trials provide exclusion restrictions needed to disentangle the persuasive and the informative effects of detailing. It is worth emphasizing that clinical trials differ in terms of (a) which drugs they study; (b) number of subjects (patients); (c) reported mean efficiency ratio; (d) release time. All of these would only change the way informative detailing affects physicians' expected utility associated with different drugs. For example, the observed clinical trial results and their release timings help identify the informative detailing parameter by determining the number of physician types and physicians' perceived quality by type in each period. Therefore, the variation of the market shares, the variation of physician types over time, and the corresponding variation of detailing help identify the proportion of each physician type and informative detailing parameters.

Note that the change in physicians' information sets would also shift the impact of persuasive detailing on physician's choice in our random utility modeling framework, but in a very specific way determined by the model. Therefore, the persuasive detailing parameters are essentially acting as "free" parameters to help fit the variation of market shares that cannot be fully explained by informative detailing and learning.

## 6 Results

### 6.1 Parameter Estimates

We now discuss the parameter estimates. The total number of structural demand parameters is 26. Recall that we treat Mevacor, Pravachol, Zocor, Lipitor and Crestor as inside goods because they compose more than 95% of the demand for statins for the whole sample period. We treat two other statins, Lescol and Baycol, as part of the outside good.

Table 5 shows the parameter estimates. The first section in the table describes learning parameters. Physicians' initial prior belief ( $\underline{\beta}$ ) on efficiency ratio is 0.113. As in table 2, most signals on the efficiency ratios from landmark clinical trials are larger than 0.5. Therefore, physicians have relatively low initial prior beliefs on statins' efficiency ratios and later learn about true efficiency ratios. Due to our model structure, we are only able to estimate the ratio of signal variance on efficiency ratio ( $\sigma_{\zeta}^2$ ) to initial prior variance on efficiency ratio ( $\sigma_{\beta}^2$ ). We normalize  $\sigma_{\beta}^2$  to 1. We report the signal variance from 10,000 patients instead of the signal variance from 1 patient by rescaling the parameter ( $\sigma_{\zeta}^2$ ). The rescaled  $\sigma_{\zeta}^2$  is estimated to be 6.035. The initial prior correlation on efficiency ratio across drug ( $\rho_0$ ) is 0.658, which suggests that there is a partial information spill-over effect across statins. This implies that if one statin receives a new clinical trial result, physicians update their beliefs about the efficiency ratio of not only the focal statin in the clinical trial, but also other statins.

To demonstrate the rate of learning, in figure 8 we graph how the most updated physician learn about the efficiency ratios (i.e.,  $E[\beta_{jt}]$ ) over time based on our parameter estimates. "The most updated physician" refers to a physician who has learned about all the clinical trial results available up to time  $t$ . The figure shows that the physician updates her beliefs about all the drugs whenever the clinical trial is released. Because of correlated learning (information spill-over), she learns about the efficacies of not only a drug studied in the clinical trial, but also other statins. Before Q4 1994, there has been no landmark clinical trial to support statins' efficacy in reducing heart disease risks. The physician

has exactly the same prior belief about Mevacor, Pravahol, and Zocor before Q4 1994. In Q4 1994, Zocor received a new clinical trial (4S study) supporting its efficacy in reducing heart disease risks. Now the physician updates her beliefs about all three drugs not just about Zocor due to correlated learning. However, because the information spill-over is not 100%, the physician's belief on Zocor is higher than those on other drugs. Lipitor's first landmark clinical trial was released in Q2 2003. Before Q2 2003, the physician has the lowest belief on Lipitor among all statins. However, after the clinical trial results, her  $E[\beta_{Lipitor,t}]$  became the highest among all statins. The graph seems to suggest that Lipitor benefits much from other statins' investment in landmark clinical trials but there is still room for its own investment. In one of our counterfactual experiments, we will investigate this further.

We find that both informative ( $\alpha_d$ ) and persuasive ( $\kappa_d$ ) detailing parameters are positive and significant. The results indicate that detailing has both persuasive and informative roles in physicians' prescription choices. Among brand specific publicity, only publicity in reducing heart disease risks ( $\alpha_{rh}$ ) has a significant impact on statin choice stage. The results seem to indicate that patients who are exposed to heart disease publicity encourage their physicians to read clinical trial results. We also find that the coefficient for the perceived quality ( $\omega$ ) to be marginally significant.

We normalize the Mevacor's brand dummy to be zero. All the brand dummies are positive and significant except for Crestor. Crestor's brand dummy is positive but insignificant. It is possible that we do not have enough observations for Crestor to pin down its brand dummy. Carryover rate for information ( $\delta_i$ ), i.e., 1 - forgetting rate, is estimated to be 0.70. The interpretation is that about 30% of physicians forget about the clinical trial results and become totally uninformed at each quarter. One might argue that the forgetting rate is too high. Because physicians prescribe many other drugs in addition to statins, they might not remember the details of clinical trials well. We believe that this is also one reason why pharmaceutical firms keep detailing until its drug's patent expires.

Next, we discuss parameters in the adoption decision stage. The coefficient of sum of detailing stock



$(\alpha_d^s)$  is 0.008. This positive and significant coefficient implies that the aggregate detailing stocks increase the total demand for the whole statin class. We are also interested in whether the impact of aggregate detailing increases with the accumulated scientific evidence for the statins category. The coefficient of the interaction term of aggregate clinical trial results and aggregate detailing ( $\alpha_c^s$ ) is positive but insignificant, which indicates that accumulated clinical trial information does not significantly increase the effectiveness of detailing in converting potential patients to statin users.

We should also point out that the publicity stocks for reducing heart disease risks and side-effects are not significant in the adoption decision stage, although lowering cholesterol levels is marginally significant. This finding appears to be different from the market expansion stage results in chapter 1. But we should emphasize that the adoption decision stage here only focuses on potential patients, but the market expansion stage in chapter 1 applies to both potential patients and current statin users. The difference between the results of these two studies suggests that general publicity stocks have a significant impact on keeping existing statins users from quitting statins.

## 6.2 Counterfactual Experiments

Now we turn to counterfactual experiments.

### Experiment 1

Since the qualities on most pharmaceutical products are uncertain, to reduce this uncertainty, pharmaceutical firms sponsor clinical trials even after marketing the drug. By sponsoring a post-marketing clinical trial, firms want to achieve clinical trial results related to the effectiveness in reducing heart disease risks. However, a clinical trial to prove efficacy in reducing heart disease risks requires medical researchers to follow up on thousands of patients for a few years. Therefore, sponsoring a post-marketing clinical trial is a big investment for the firm. If physicians can indirectly learn about the ability of a new statin in reducing heart disease risks through incumbent statins' clinical trials for heart disease risks, additional landmark clinical trial results for its own may not be necessary to

convince physicians to prescribe it. This could be the case for Lipitor. Prior to its entry in 1997, several incumbent firms had already obtained landmark clinical results for reducing heart disease risks. Lipitor obtained its own landmark clinical trial results several years after its introduction in 1997. How much of the impact did these landmark clinical trials have on Lipitor's sales? Were the landmark clinical trials for its own drug, Lipitor, worth the investment of the drug company?

To address these questions, we use our model to forecast the demand for Lipitor in a counterfactual situation where Lipitor does not receive any clinical results supporting that it reduces heart disease risks by shutting down Lipitor's landmark clinical trials. Figure 10 graphs the benchmark and counterfactual demand for statins. The dotted lines denote the counterfactual demands. The counterfactual demand is almost 100,000 prescription per quarter lower than the benchmark demand by the end of 2004. Although we shut down all three landmark clinical trials for Lipitor, the counterfactual demand for Lipitor is slightly lower (around 4%) than the benchmark demand. Lipitor's global annual sales is almost \$13 billion in 2003. Therefore, the 4% loss would cost more than \$500 million per year. In a post-marketing clinical trial, following one patient would cost roughly tens of thousand dollars for a few years. Even with rough calculation, we can tell the 4% sales difference per year is big enough for Lipitor to invest in its own post-marketing clinical trials.

## **Experiment 2**

Our estimation results suggest that (i) there is information spill-over of landmark clinical trial results across drugs, and (ii) Lipitor may gain late mover advantage by free-riding on the information provided by its rivals' clinical trials. Therefore, we are interested in quantifying how important this correlated learning is. How big is the effect of correlated learning? How much did Lipitor benefit from the clinical trials which other drug companies conducted? To answer the above questions, we forecast the demand for each statin in a counterfactual situation where there is no correlated learning. Under this counterfactual condition, we set the correlated learning parameter ( $\rho_0$ ) to be zero. Figure 11

presents the benchmark and counterfactual demand for statins. The counterfactual demand is almost 4% to 7% per quarter lower than the benchmark demand for most quarters. As we argue in the previous counterfactual experiment, this amount of sales decrease is still substantial considering the global sales volume of Lipitor.

Nevertheless this experiment also shows that correlated learning cannot be the only driving force for the early success of Lipitor. So what else can contribute to its success? One possibility is its superior efficacy in lowering cholesterol levels. Because Lipitor has the highest  $q^c$  (except Crestor), Lipitor may have the highest  $E[q^h]$  although it has a relatively low  $E[\beta]$ . To investigate this possibility, we graph the most updated physician's  $E[q^h]$  over time under the condition that no correlated learning exists in figure 13. The figures confirms that Lipitor has the highest  $E[q^h]$  even in the absence of correlated learning. Therefore, we can conclude that Lipitor's early success is also driven by its superior efficacy in lowering cholesterol levels.

### **Experiment 3**

While correlated learning generates late mover advantage, switching cost is a source of first mover advantage. Our next question relates to the benefits incumbent drugs receive due to the switching costs. Although we do not estimate switching costs, we can still conduct a counterfactual experiment to shed light on its importance by assuming that all patients make a decision as if they are part of the "potential patients group." In other words, we do not use switching rates or discontinuing rates in the counterfactual experiment. Figure 12 depicts the counterfactual experiment result. The figure shows that a new drug, Lipitor, would become the best selling drug in the category right after its entry (Q2 1997) and all the incumbent drugs would lose market shares very quickly under the counterfactual condition. This implies that a policy which reduces switching costs would help a new drug penetrate into the market quicker. The figure, however, also shows that the counterfactual demand would eventually be similar to the benchmark demand. Therefore, it seems that switching costs do not have a long-

lasting impact. Interestingly enough, the figure also shows that the absence of switching costs helps the take-off of a newer drug, Crestor. Recall that Crestor was introduced in 2002. Lipitor would have lost market share to Crestor much faster if there was no switching cost.

## 7 Conclusion and Future Research

We develop a new structural model of physicians' prescribing decisions under the environment where qualities are uncertain and physicians can learn about the quality of drugs through correlated learning. We define a variable, "efficiency ratio," which measures how efficiently a drug can translate reduction in cholesterol levels into reduction in heart disease risks. We assume that physicians learn about the efficiency ratio for each drug from landmark clinical trials and allow physicians' initial prior perceptions of the efficiency ratio to be correlated across drugs. We find that the initial prior perceptions on the efficiency ratio are positively correlated. This information spill-over allows a late mover such as Lipitor to significantly benefit from incumbents in the absence of its direct evidence for the efficacy in reducing heart disease risks.

Unlike the previous literature which assumes that quality signals from clinical trials are unobservable to researchers, we treat quality signals from clinical trial results as observable by taking a careful look at clinical trial results and extracting detailed information from the clinical trials. By treating clinical trials in this manner, we are able to clearly identify the correlated learning parameters.

In addition to using product level market share data, we supplement them with switching rates and discontinuing rates. The switching rate data are particularly useful for taking the presence of switching costs into consideration. Our counterfactual experiment shows that in the absence of switching costs, Lipitor would become a top-selling statin within three months of its entry. Interestingly enough, the absence of switching costs would also help the take-off of the newer statin, Crestor, and hurt the sales of Lipitor. The results indicate that switching costs have two counteracting effects on Lipitor.

Our model also allows detailing to have both persuasive and informative roles in physicians' pre-

scribing decisions. Our detailed clinical trial data and the sales and detailing variations help separately identify these two different roles of detailing. The estimation results find both persuasive and informative roles to be significant in this market. The results could be used to help marketing managers understand how to allocate their detailing budgets optimally according to the information levels of physicians.

We should point out that switching rates or discontinuing rates can differ under some counterfactual conditions. However, because we do not explicitly model switching rates or discontinuing rates, we assume that switching rates or discontinuing rates will be the same as the benchmark condition in the counterfactual experiments. In the future, we plan to model switching rates and discontinuing rates as a function of switching costs, continuing costs, and physicians' information set.

Also we plan to relax the assumption on detailer's visiting decision. In our simplified model, the model assumes that a detailer visits a physician randomly. In other words, the probability of a detailer's visit to any given physician is independent of whether the physician is informed in that period. In reality, however, pharmaceutical firms may prefer to detail uninformed physicians. If this is the case, the more informed physicians there are, the higher is the chance that uninformed physicians receive a detailing visit for any given detailing spending. Then the return of detailing should increase with the portion of informed physicians. To capture this selective detailing behavior, we will interact detailing with the portion of informed physicians. A positive coefficient of the interaction term would imply that pharmaceutical firms selectively details physicians.

We can also re-estimate the model by assuming that every patient makes a prescription decision as if he/she is a potential patient. We do this re-estimation by ignoring the switching rates and discontinuing rates. By comparing the new results and our current results, we can measure the potential biases of the estimates when ignoring the choice difference between existing and potential patients.

## References

- Azoulay, Pierre. 2002. Do Pharmaceutical Sales Respond to Scientific Evidence? *Journal of Economics & Management Strategy* **11**(4) 551–594.
- Berndt, Ernst R., Linda T. Bui, David H. Reiley, Glen L. Urban. 1997. The Roles of Marketing, Product Quality and Price Competition in the Growth and Composition of the U.S. Anti-Ulcer Drug Industry. *The Economics of New Goods, NBER Studies in Income and Wealth* **58** 551–594.
- Chan, Tat, Charkravarthi Narasimhan, Ying Xie. 2010. An Empirical Model of Physician Learning on Treatment Effectiveness and Side-effects. Working Paper, Washington University in Saint Louis.
- Ching, Andrew T. 2010a. A Dynamic Oligopoly Structural Model for the Prescription Drug Market after Patent Expiration. *International Economic Review* **51**(4) 1175–1207.
- Ching, Andrew T. 2010b. Consumer Learning and Heterogeneity: Dynamics of Demand for Prescription Drugs after Patent Expiration. *International Journal of Industrial Organization* **28**(6) 619–638.
- Ching, Andrew T., Masakazu Ishihara. 2010. The Effects of Detailing on Prescribing Decisions under Quality Uncertainty. *Quantitative Marketing and Economics* **8**(2) 123–165.
- Ching, Andrew T., Masakazu Ishihara. 2012. Measuring the Informative and Persuasive Roles of Detailing on Prescribing Decisions. *Management Science* **58**(7) 1374 – 1387.
- Chintagunta, Pradeep K., Renna Jiang, Ginger Z. Jin. 2009. Information, Learning, and Drug Diffusion: the Case of Cox-2 Inhibitors. *Quantitative Marketing and Economics* **7**(4) 399–443.
- Cockburn, Iain M., Aslam H. Anis. 2001. Hedonic Analysis of Arthritis Drugs. *Medical Care Output and Productivity*. National Bureau of Economic Research, Inc, 439–462.
- Crawford, Gregory S., Matthew Shum. 2005. Uncertainty and Learning in Pharmaceutical Demand. *Econometrica* **73**(4) 1137–1173.
- DeGroot, Morris. 1970. *Optimal Statistical Decisions* New York: McGraw-Hill.
- Delahoy, Philippa J., Dianna J. Magliano, Kate Webb, Mendel Grobler, Danny Liew. 2009. The relationship between reduction in low-density lipoprotein cholesterol by statins and reduction in risk of cardiovascular outcomes: An updated meta-analysis. *Clinical Therapeutics* **31**(2) 236 – 244.
- Erdem, Tulin. 1998. An Empirical Analysis of Umbrella Branding. *Journal of Marketing Research* **35**(3) 339–351.
- Erdem, Tulin, Michael P. Keane. 1996. Decision-Making Under Uncertainty: Capturing Dynamic Brand Choice Processes in Turbulent Consumer Goods Markets. *Marketing Science* **15**(1) 1–20.
- Erdem, Tulin, Baohong Sun. 2002. An Empirical Investigation of Spillover Effects of Marketing Mix Strategy in Umbrella Branding. *Journal of Marketing Research* **39**(4) 408–420.
- Janakiraman, Ramkumar, Catarina Sismeiro, Shantanu Dutta. 2009. Perception Spillovers Across Competing Brands: A Disaggregate Model of How and When. *Journal of Marketing Research* **46**(4) 467 – 481.
- Lasser, Karen E., Paul D. Allen, Steffie J. Woolhandler, David U. Himmelstein, Sidney M. Wolfe, David H. Bor. 2002. Timing of new black box warnings and withdrawals for prescription medications. *Journal of American Medical Association* **287**(17) 2215–2220.

- Law, M R, N J Wald, A R Rudnicka. 2003. Quantifying Effect of Statins on Low Density Lipoprotein Cholesterol, Ischaemic Heart Disease, and Stroke: Systematic Review and Meta-analysis. *BMJ* **326**(7404) 1423.
- Leffler, Keith B. 1981. Persuasion or Information? The Economics of Prescription Drug Advertising. *Journal of Law and Economics* **24**(1) 45–74.
- Narayanan, Sridhar, Puneet Manchanda, Pradeep K. Chintagunta. 2005. Temporal Differences in the Role of Marketing Communication in New Product Categories. *Journal of Marketing Research* **42**(3) 278–290.
- Neslin, Scott A., Edward E. Rhoads, Paul Wolfson. 2009. A Model and Empirical Analysis of Patient Compliance and Persistence in Pharmaceuticals. Dartmouth College.
- Park, Alice. 2008. Is Vytarin a Failure? *Time* <http://www.time.com/time/health/article/0,8599,1703827,00.html> accessed Aug 2, 2012.
- Venkataraman, Sriram, Stefan Stremersch. 2007. The Debate on Influencing Doctors' Decisions: Are Drug Characteristics the Missing Link? *Management Science* **53**(11) 1688–1701.
- Zhou, Zheng, Elham Rahme, Louise Pilote. 2006. Are statins created equal? evidence from randomized trials of pravastatin, simvastatin, and atorvastatin for cardiovascular disease prevention. *American Heart Journal* **151**(2) 273 – 281.

Table 1: Summary of Statins

| Brand     | Molecule     | Entry Date | Generic Entry     | Manufacturer         |
|-----------|--------------|------------|-------------------|----------------------|
| Mevacor   | lovastatin   | Sep-1987   | Apr-1997          | Merck & Co.          |
| Pravachol | pravastatin  | Nov-1991   | Aug-2000          | Bristol-Myers Squibb |
| Zocor     | simvastatin  | Feb-1992   | Mar-2003          | Merck & Co.          |
| Lipitor   | atorvastatin | Apr-1997   | N.A. <sup>1</sup> | Pfizer               |
| Crestor   | rosuvastatin | Mar-2003   | N.A. <sup>1</sup> | AstraZeneca          |

1 - The patent expiration date is beyond our sample period.

Table 2: Landmark Clinical Trials for Statins

| Title                 | Publication date | Drugs Studied | # of Subjects | Follow-up period | Sponsors             | LDL Reduction (mg/dL) | Heart-Disease Risk Reduction | Efficiency Ratio (HRRR / LDL) |
|-----------------------|------------------|---------------|---------------|------------------|----------------------|-----------------------|------------------------------|-------------------------------|
| <b>4S</b>             | Dec,1994         | Zocor         | 4,444         | 5.4 years        | Merck & Co.          | 68.45                 | 34.30%                       | 0.50                          |
| <b>WOSCOPS</b>        | Nov,1995         | Pravachol     | 6,595         | 4.9 years        | Bristol-Myers Squibb | 41.38                 | 31.50%                       | 0.76                          |
| <b>CARE</b>           | Oct,1996         | Pravachol     | 4,159         | 5 years          | Bristol-Myers Squibb | 39.83                 | 22.70%                       | 0.57                          |
| <b>AFCAPS/TexCAPS</b> | May,1998         | Mevacor       | 5,705         | 5.2 years        |                      | 36.35                 | 37.10%                       | 1.02                          |
| <b>LIPID</b>          | Nov,1998         | Pravachol     | 9,014         | 6.1 years        | Bristol-Myers Squibb | 39.83                 | 22.20%                       | 0.56                          |
| <b>HPS</b>            | Jul,2002         | Zocor         | 20,536        | 5 years          | Merck & Co.          | 49.88                 | 26.00%                       | 0.52                          |
| <b>PROSPER</b>        | Nov,2002         | Pravachol     | 5,804         | 3.2 years        | Bristol-Myers Squibb | 40.22                 | 17.40%                       | 0.43                          |
| <b>ALLHAT-LLT</b>     | Dec,2002         | Pravachol     | 10,355        | 4.8 years        | Pfizer               | 20.88                 | 9.50%                        | 0.45                          |
| <b>ASCOT-LLA</b>      | May, 2003        | Lipitor       | 10,305        | 3.3 years        | Pfizer               | 41.38                 | 35.40%                       | 0.86                          |
| <b>ALLIANCE</b>       | Jul, 2004        | Lipitor       | 2,422         | 4.3 years        | Pfizer               | 15.47                 | 38.30%                       | 2.48                          |
| <b>CARDS</b>          | Aug, 2004        | Lipitor       | 2,838         | 3.9 years        | Pfizer               | 44.08                 | 31.30%                       | 0.71                          |
| <b>A to Z</b>         | Sep, 2004        | Zocor         | 4,498         | 2 years          | Merck & Co.          | 14.31                 | 13.80%                       | 0.96                          |



Table 3: Statins' Mean Cholesterol Reduction by Strength (mmol/L)

|           | Daily Dose (mg) |      |      |      |      | Mean |
|-----------|-----------------|------|------|------|------|------|
|           | 5               | 10   | 20   | 40   | 80   |      |
| Mevacor   | N/A             | 1.02 | 1.40 | 1.77 | 2.15 | 1.59 |
| Pravachol | 0.73            | 0.95 | 1.17 | 1.38 | 1.60 | 1.28 |
| Zocor     | 1.08            | 1.31 | 1.54 | 1.78 | 2.01 | 1.66 |
| Lipitor   | 1.51            | 1.79 | 2.07 | 2.36 | 2.64 | 2.22 |
| Crestor   | 1.84            | 2.08 | 2.32 | 2.56 | 2.80 | 2.44 |

Table 4: Summary of Publicity Variables

| Lowering Cholesterol Levels     | # of Quarters | # of Articles | Values |           |       |       |
|---------------------------------|---------------|---------------|--------|-----------|-------|-------|
|                                 |               |               | Mean   | Std. Dev. | Min.  | Max.  |
| Mevacor                         | 47            | 255           | 6.54   | 4.54      | 0.00  | 20.19 |
| Pravachol                       | 47            | 262           | 6.30   | 4.25      | 0.00  | 17.42 |
| Zocor                           | 47            | 470           | 10.74  | 7.90      | 0.00  | 34.00 |
| Lipitor                         | 32            | 707           | 22.40  | 15.99     | 1.19  | 51.30 |
| Crestor                         | 8             | 120           | 14.92  | 14.18     | 0.95  | 41.00 |
| Reducing Risks of Heart Disease | # of Quarters | # of Articles | Values |           |       |       |
|                                 |               |               | Mean   | Std. Dev. | Min.  | Max.  |
| Mevacor                         | 47            | 41            | 0.86   | 1.79      | -1.58 | 7.13  |
| Pravachol                       | 47            | 81            | 2.01   | 2.69      | 0.00  | 12.67 |
| Zocor                           | 47            | 94            | 2.05   | 3.17      | -3.00 | 14.25 |
| Lipitor                         | 32            | 92            | 2.88   | 4.24      | 0.00  | 16.15 |
| Crestor                         | 8             | 7             | 0.84   | 1.07      | 0.00  | 2.85  |
| Side-Effects                    | # of Quarters | # of Articles | Values |           |       |       |
|                                 |               |               | Mean   | Std. Dev. | Min.  | Max.  |
| Mevacor                         | 47            | 5             | 0.13   | 0.57      | 0.00  | 3.56  |
| Pravachol                       | 47            | 14            | 0.30   | 0.87      | -1.19 | 4.75  |
| Zocor                           | 47            | 15            | 0.33   | 0.98      | -1.19 | 4.75  |
| Lipitor                         | 32            | 18            | 0.15   | 0.72      | -1.19 | 2.00  |
| Crestor                         | 8             | 72            | -0.99  | 1.77      | -5.00 | 0.00  |

Table 5: Parameter Estimates

|   | Estimates      | S.E.   |
|---|----------------|--------|
| <b>Learning Parameters</b>  |                |        |
| $\beta$ (Initial Prior Belief on Efficiency Raito)                        | 0.1132         | 0.0596 |
| $\sigma_{\beta}^2$ (Initial Prior Variance on Efficiency Raito)           | 1.0000         |        |
| $\sigma_{\zeta}^2$ (Signal Variance from 1,000 Patients)                  | <b>6.0353</b>  | 0.9996 |
| $\rho_0$ (Correlation Term in Initial Prior)                              | <b>0.6578</b>  | 0.2634 |
| <b>Statin Choice Stage, Utility Parameters</b>                            |                |        |
| $\alpha_0$ (Constant)   | <b>-8.0521</b> | 0.9993 |
| $\alpha_d$ (Informative Detailing)  | <b>3.4070</b>  | 1.0096 |
| $\alpha_{lc}$ (Brand Specific Publicity in Lowering Cholesterol Levels)   | 0.3661         | 0.2702 |
| $\alpha_{rh}$ (Brand Specific Publicity in Reducing Heart Disease Risks)  | <b>0.3514</b>  | 1.0335 |
| $\alpha_{se}$ (Brand Specific Publicity in Side Effects)                  | -0.0184        | 1.0018 |
| $\omega$ (Coefficient of Perceived Quality)                               | 1.1112         | 0.6330 |
| $\kappa_d$ (Persuasive Detailing)   | <b>0.0120</b>  | 0.0042 |
| <b>Brand Dummies</b>  |                |        |
| Pravachol   | <b>0.8696</b>  | 0.3887 |
| Zocor   | <b>0.9702</b>  | 0.3859 |
| Lipitor   | <b>1.0990</b>  | 0.5409 |
| Crestor   | 0.2380         | 0.7339 |
| <b>Adoption Decision Stage Parameters</b>                                 |                |        |
| $\alpha_0^s$ (Market Expansion Stage Constant)                            | <b>-5.2073</b> | 0.2441 |
| $\alpha_c^s$ (Clinical Trial * Aggregate Detailing Stock)                 | 0.0111         | 0.0085 |
| $\alpha_d^s$ (Aggregate Detailing Stock)                                  | <b>0.0082</b>  | 0.0011 |
| $\alpha_{lc}^s$ (General Publicity Stock in Lowering Cholesterol Levels)  | 0.3661         | 0.2702 |
| $\alpha_{rh}^s$ (General Publicity Stock in Reducing Heart Disease Risks) | 0.3514         | 1.0335 |
| $\alpha_{se}^s$ (General Publicity Stock in Side Effects)                 | -0.0184        | 1.0018 |
| <b>Additional Parameters</b>  |                |        |
| $\delta_d^s$ (Carryover Rate of Detailing in Adoption Decision)           | <b>0.9720</b>  | 0.0060 |
| $\delta_p^s$ (Carryover Rate of Publicity in Adoption Decision)           | <b>0.7375</b>  | 0.0432 |
| $\delta_i$ (Carryover Rate of Information in Statin Choice)               | <b>0.7028</b>  | 0.2102 |
| $\delta_p$ (Carryover Rate of Persuasive Detailing in Statin Choice)      | <b>0.8878</b>  | 0.0466 |
| Standard Deviation of $e_{jt}$ (in Hundred Thousand)                      | <b>0.3213</b>  | 0.0207 |
| Log Likelihood  | -2064.56       |        |

Estimates shown in bold are significant at 5% level.

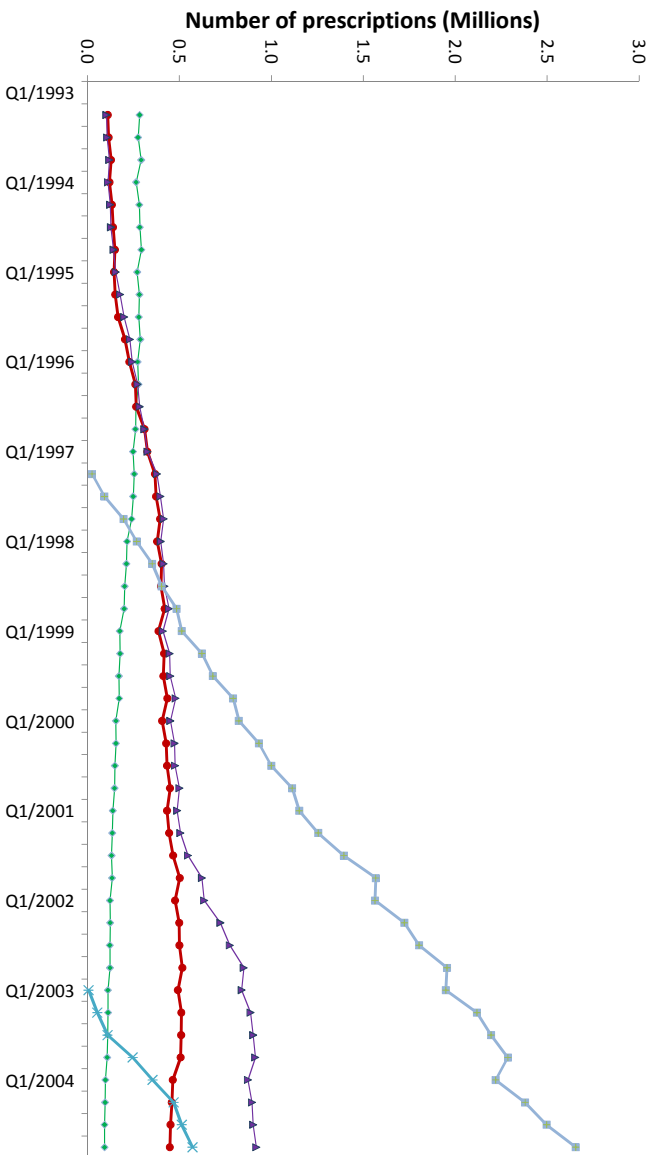


Figure 1: Quarterly Number of Total Prescriptions for Statins

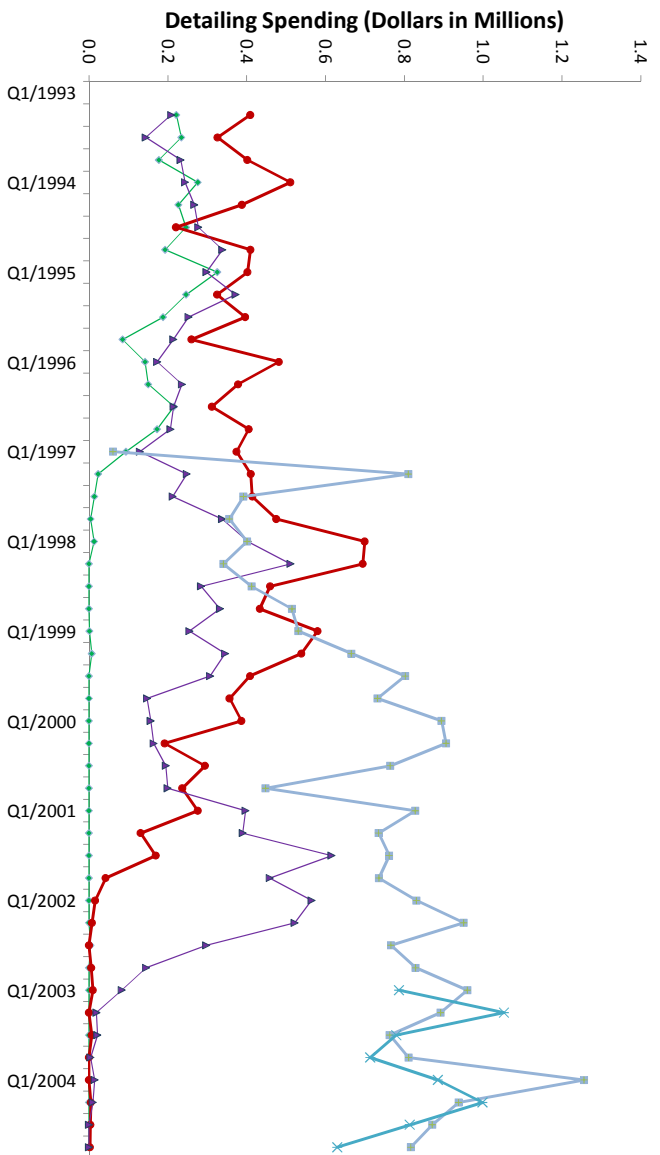


Figure 2: Quarterly Detailing Spending for Statins

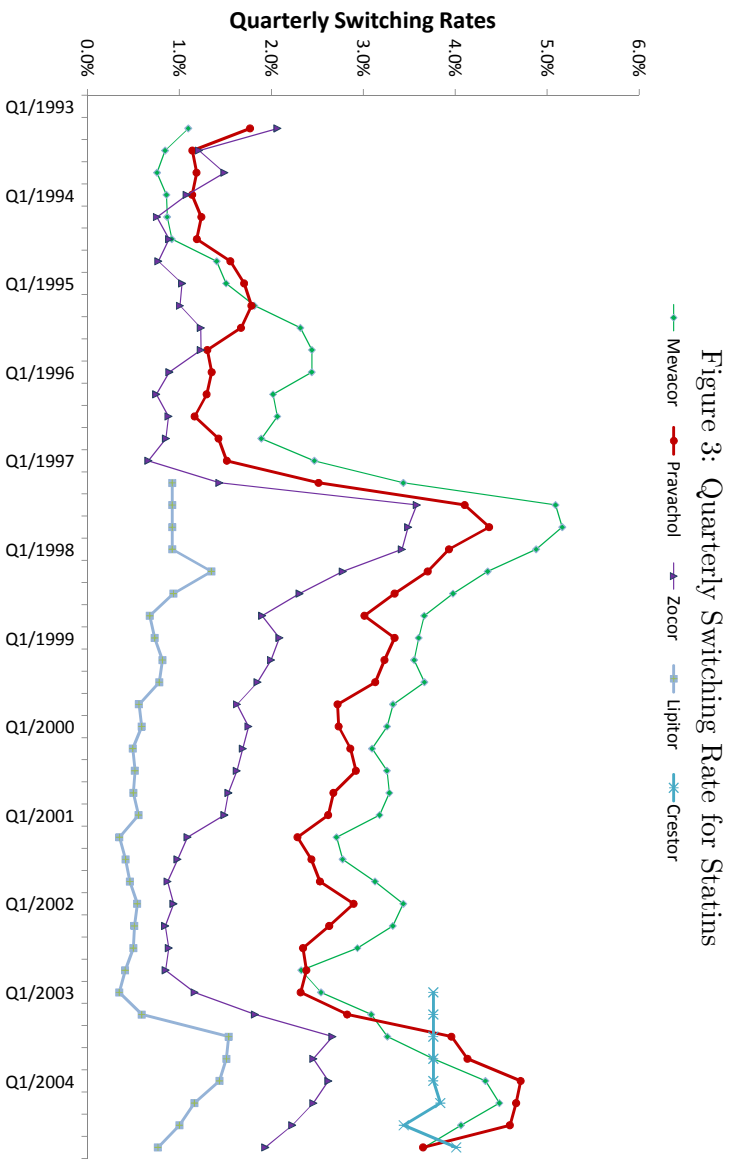


Figure 3: Quarterly Switching Rate for Statins

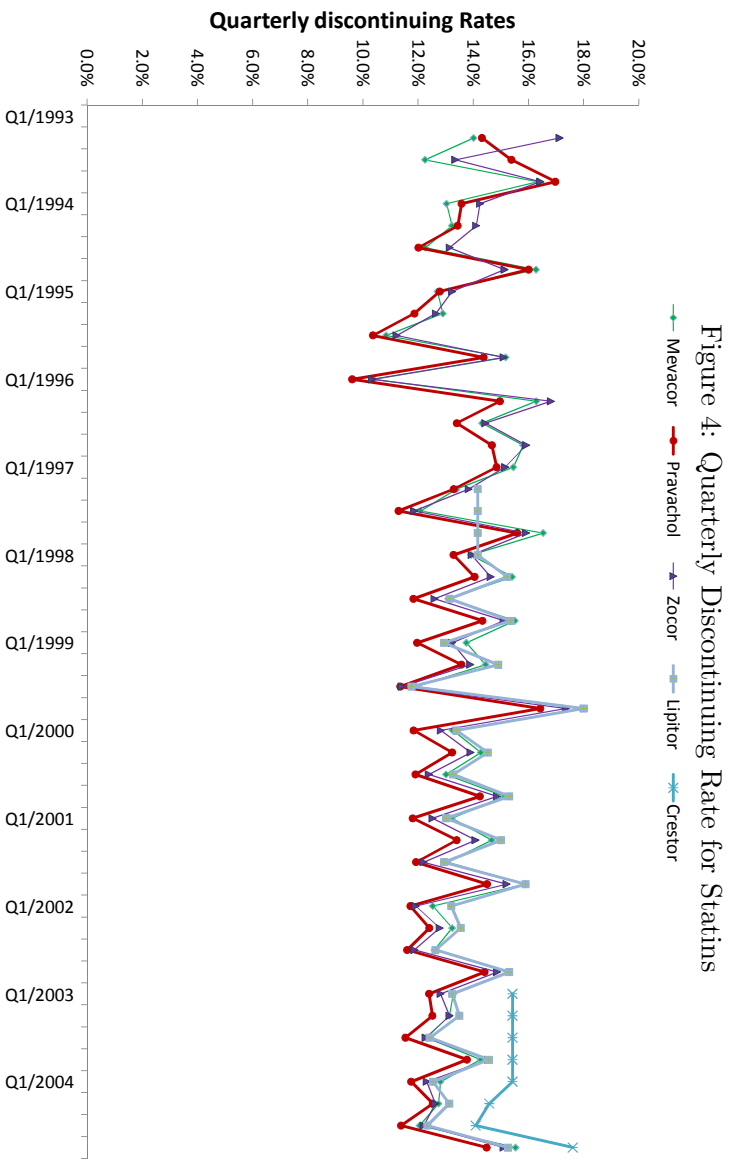


Figure 4: Quarterly Discontinuing Rate for Statins

Figure 5: Quarterly Flow of General Publicity

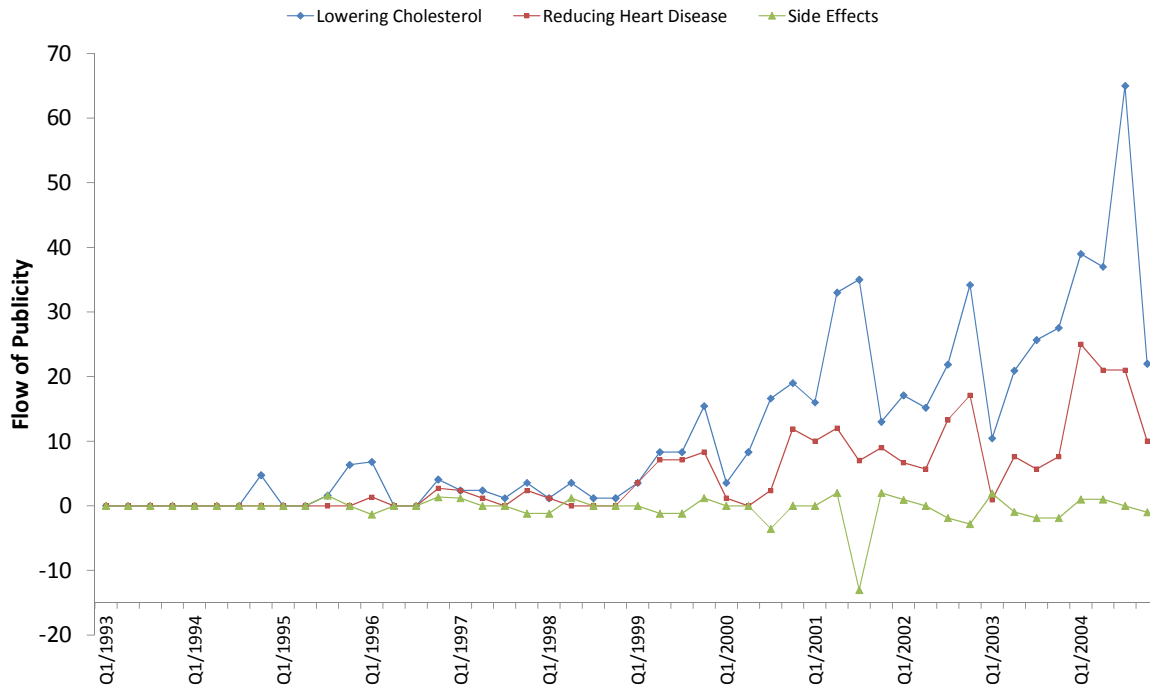


Figure 6: Decision Process of Potential Patient

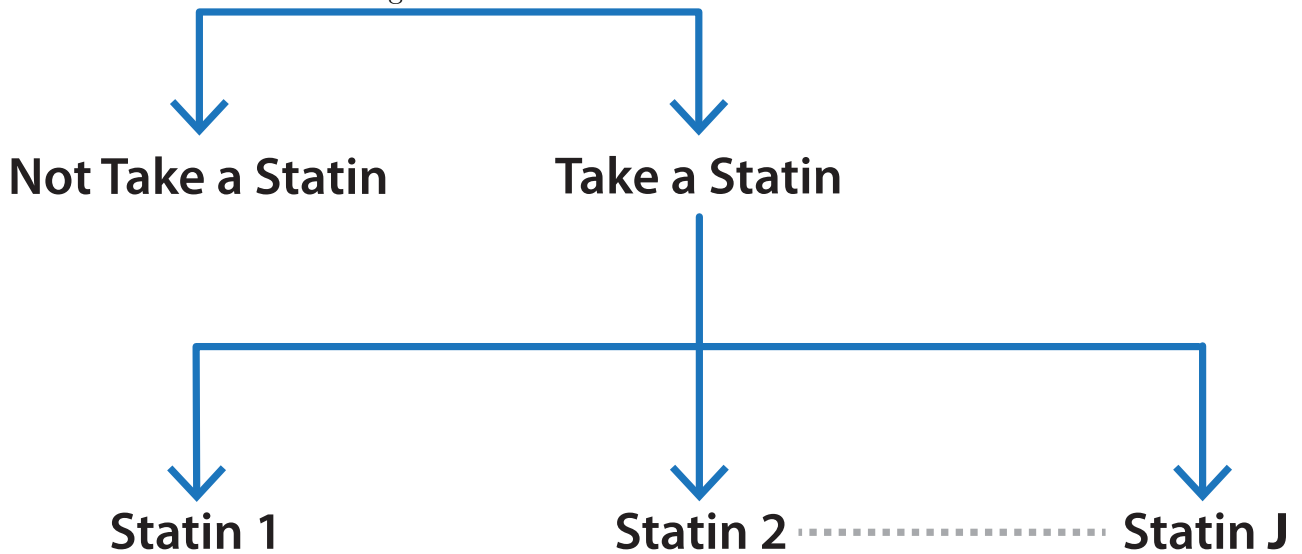


Figure 7: Decision Process of Existing Patient

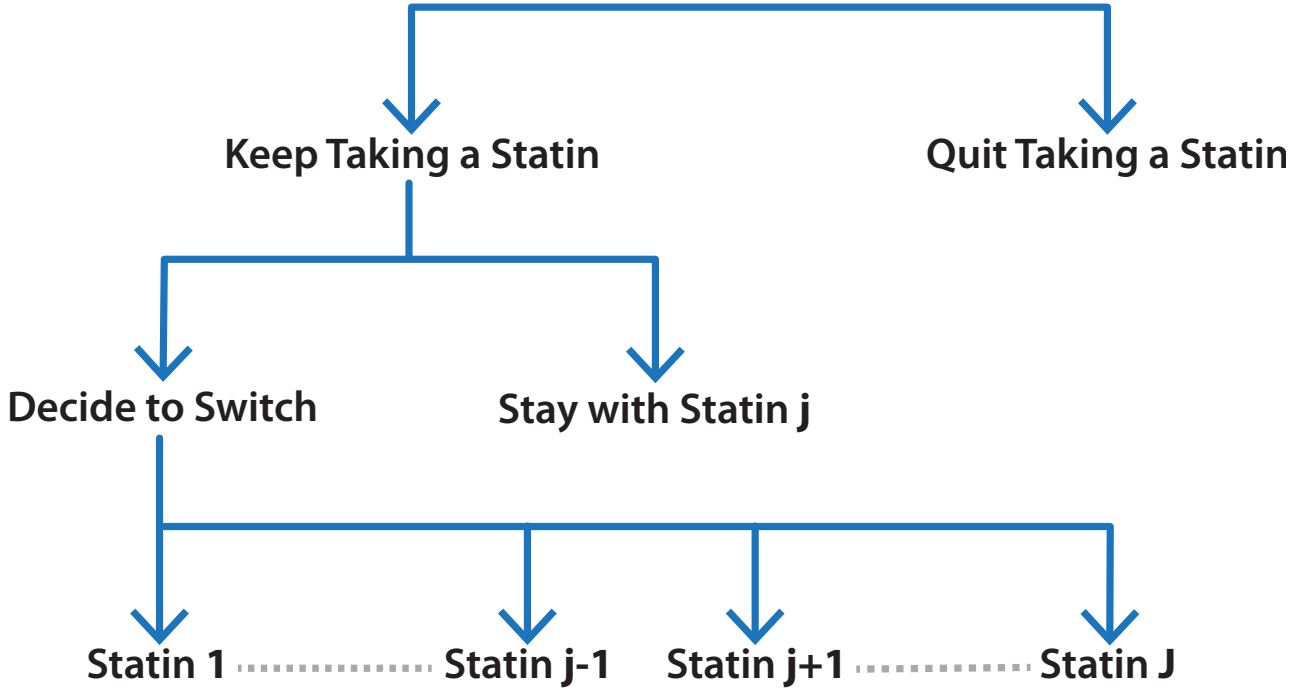


Figure 8: The Most Updated Physician's Learning over Time

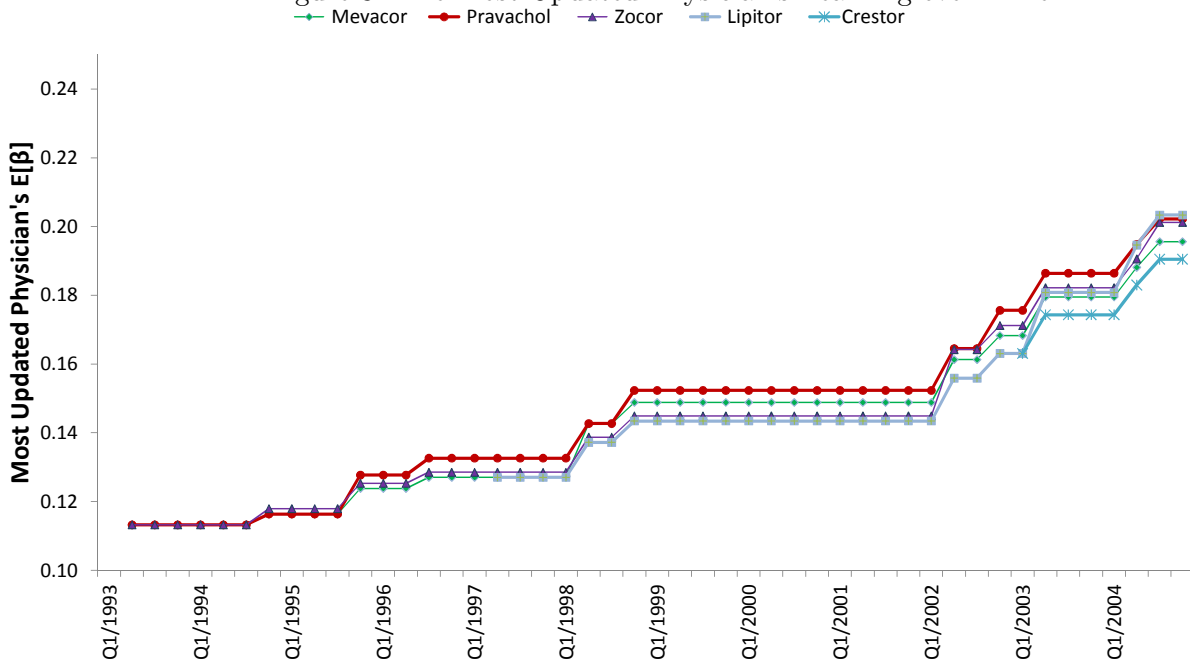


Figure 9: Fit: Actual and Simulated Prescription Volume

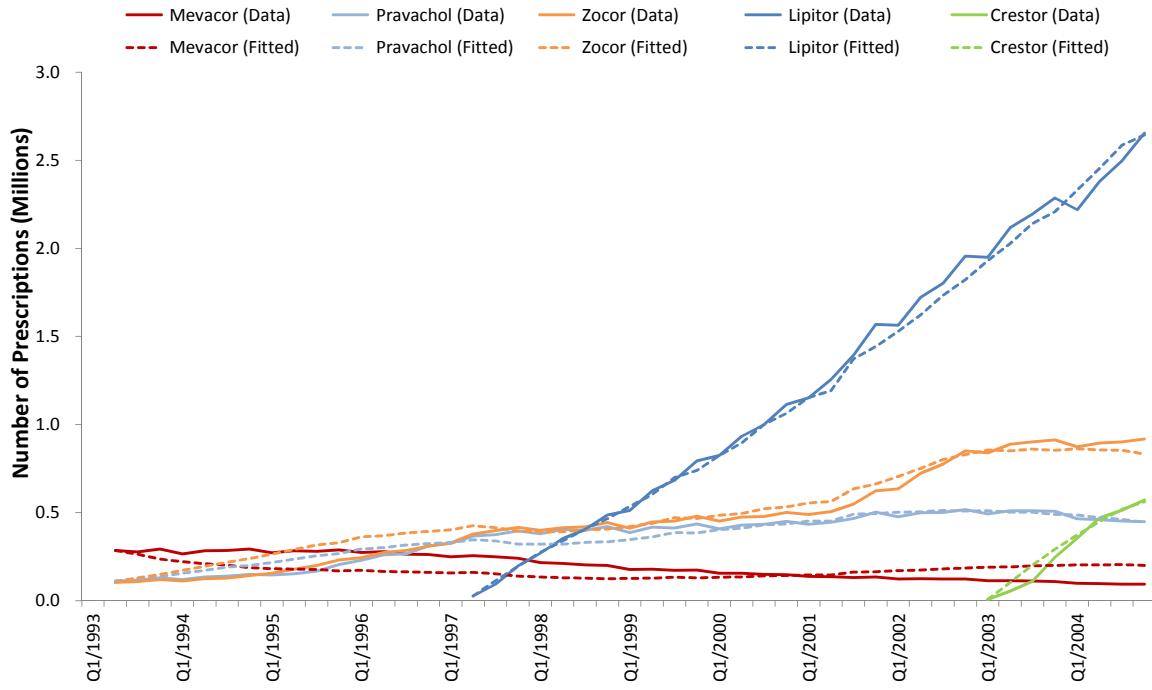
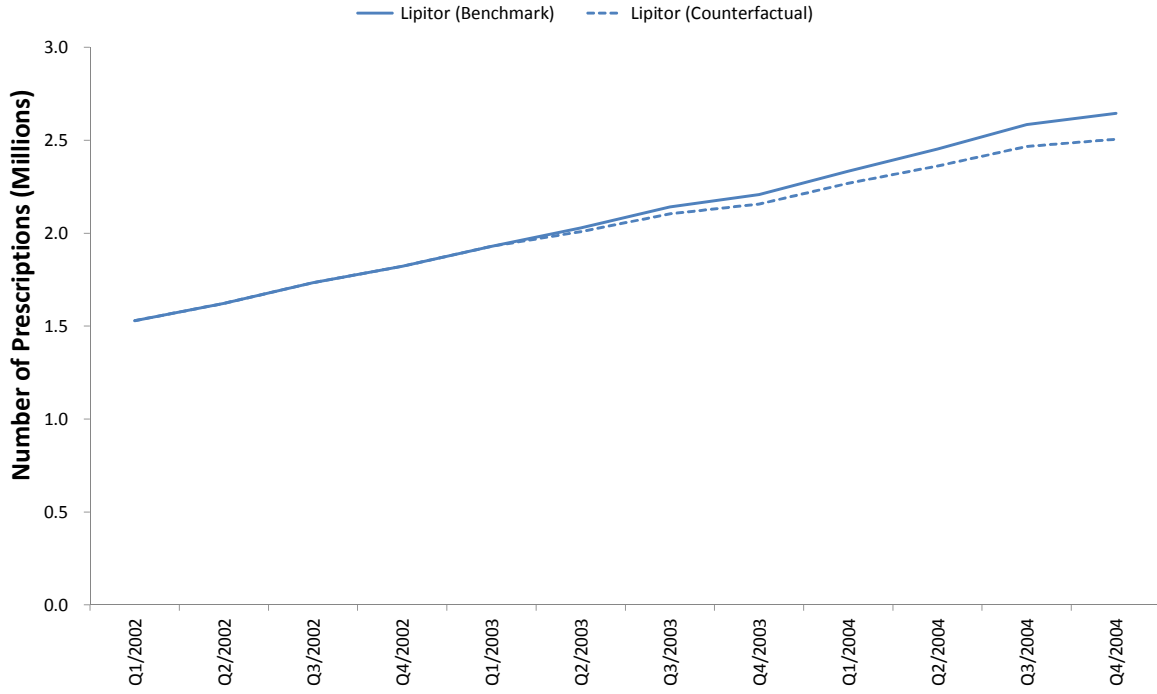
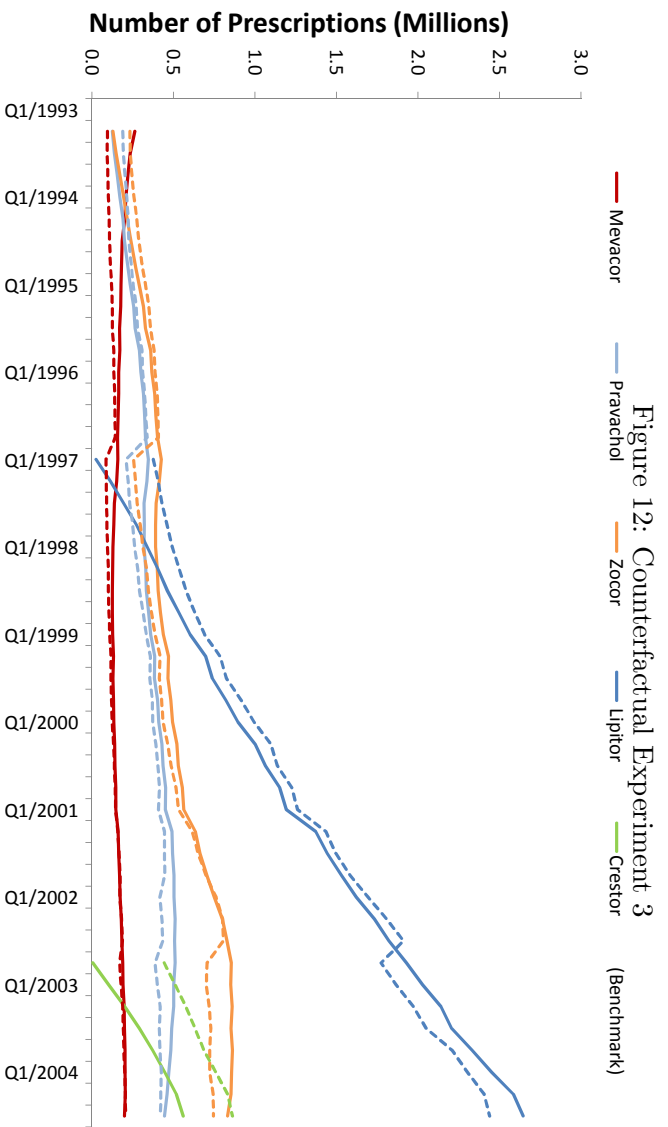
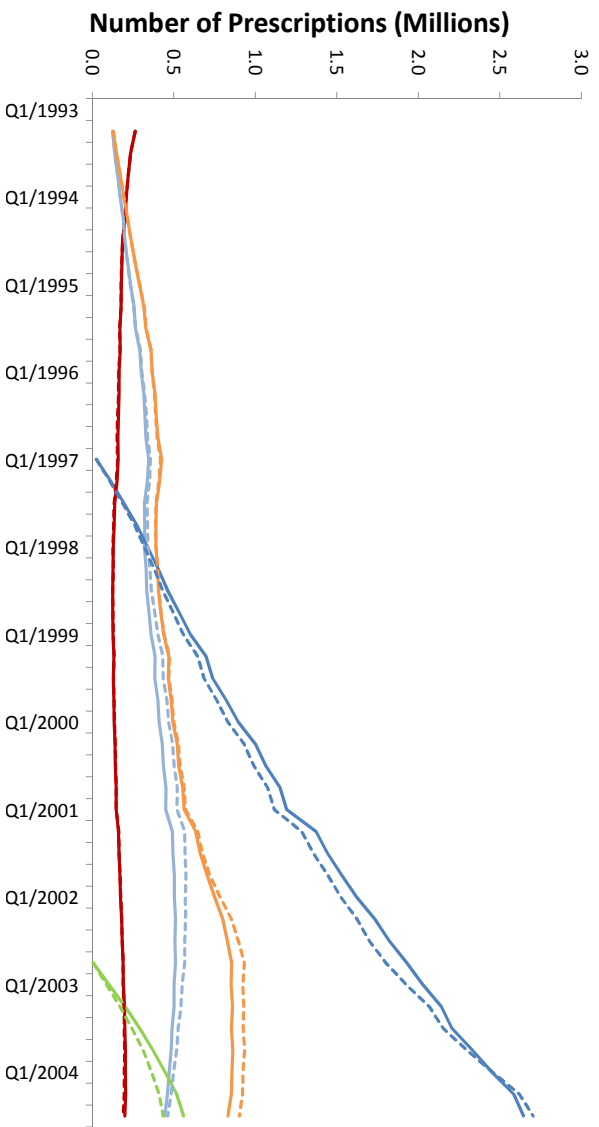
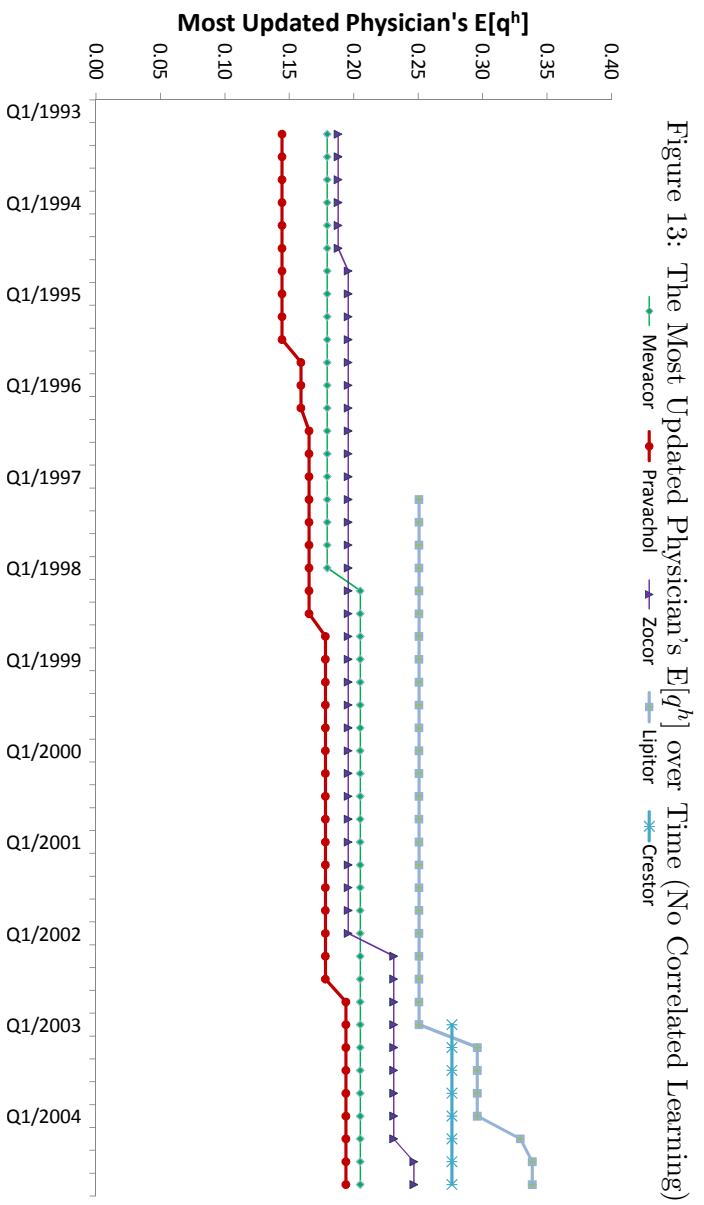


Figure 10: Counterfactual Experiment 1









## A Full Learning Model

In this appendix, we explain our full learning model. In the full model, we formulate the learning with matrix notations. Following the simple learning model, we can define physician  $k$ 's expected conditional utility to prescribe drug  $j$  to patient  $i$  at time  $t$  as follows:

$$E[U_{ijkt}|I^k(t)] = \omega \cdot E[\beta_j|I^k(t)] + \kappa_d \cdot STK\_detail_{jt} + b_j + \epsilon_{ijt}, \quad (26)$$

where  $E[\cdot|I^k(t)]$  denotes the expected value given physician  $k$ 's information set at time  $t$ .

Physician  $k$ 's initial prior on the efficiency ratio at time  $t = 0$  can be expressed as follows:

$$B_{k0} \sim N(\underline{B}, \Sigma_0), \quad (27)$$

where  $\underline{B}$  is a  $J \times 1$  matrix whose elements are  $\underline{\beta}$ ;  $\Sigma_0$  is a  $J \times J$  matrix whose diagonal elements are  $\sigma_\beta^2$  and off-diagonal elements are  $\sigma_\beta^2 \cdot \rho_0$ .

Landmark clinical trials are the main sources of information about this efficacy. Physicians are assumed to update their beliefs on the efficiency ratio of each drug when they are exposed to landmark clinical trial results. A signal from clinical trial  $l$  for drug  $j$ ,  $\tilde{\beta}_{jl}$ , is :

$$\tilde{\beta}_{jl} = \beta_j + \zeta_l, \quad (28)$$

where  $\beta_j$  is the true mean level of the efficiency ratio for drug  $j$  and  $\zeta_l$  is a signal noise and i.i.d. normally distributed with zero mean and variance  $\sigma_\zeta^2 = \sigma_\zeta^2 \cdot 1,000/N_l$  for landmark clinical trial  $l$ .  $\sigma_\zeta^2$  is signal variance from 1,000 patients.  $N_l$  denotes the number of patients who participate in landmark clinical trial  $l$ .

Let  $B_{kt}$  and  $\Sigma_{kt}$  denote physician  $k$ 's prior belief and prior variance on the efficiency ratio at time  $t$ , respectively.<sup>12</sup> If the physician does not learn about any clinical trial at time  $t$ , prior belief and prior variance on the efficiency ratio at time  $t + 1$  will be the same as prior belief and variance at time  $t$ , i.e.,

$$B_{kt+1} = B_{kt} \text{ and } \Sigma_{kt+1} = \Sigma_{kt}.$$

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<sup>12</sup>Note that  $B_{k0} = \underline{B}$  and  $\Sigma_{k0} = \Sigma_0$

If she learns about the clinical trial  $l$  for drug  $j$  at time  $t$ , she will update her belief as follows:

$$B_{kt+1} = B_{kt} + K_{kt}^{\beta} \cdot (\tilde{B}_{kt} - B_{kt}), \quad (29)$$

where  $K_{kt}^{\beta} = (\Sigma_{kt}^{-1} + \Sigma_{lt})^{-1} \cdot \Sigma_{lt}$  denotes the Kalman coefficient;  $\Sigma_{lt}$ 's  $j$ th diagonal element is  $\frac{1}{\sigma_{\zeta l}^2}$  and all other elements are zero. The physician updates her prior variance and her posterior variance becomes:

$$\Sigma_{kt+1} = (\Sigma_{kt}^{-1} + \Sigma_{lt})^{-1}. \quad (30)$$

If the physician learns about more than one landmark clinical trial result, she will update the her belief again in a similar way when she learns about clinical trial  $l$ .