Persistence in Prescriptions of Branded Drugs.

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Abstract

The American Medical Association and the Pharmaceutical Research and Manufacturers of America have developed new standards to curb the influence sales representatives may have on physicians' drug choices. Yet the literature fails to clarify the extent to which shares of prescriptions for branded drugs are driven by advertising to physicians or by usage persistence in choices. Using unique aggregate data on major Therapeutic Classes (i.e. Statins, SSRIs, COX2s), we show that a majority of prescriptions are best characterized as automatic renewals for current users. Choice probabilities across all other prescriptions seem driven by brand attributes rather than promotion to physicians.

Keywords: Market structure; Advertising; Monte Carlo estimation; Pharmaceutical drugs

JEL Classifications: L11, I11, C15

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1. Introduction

In response to increased government scrutiny and to rising drug prices, the American Medical Association and the Pharmaceutical Research and Manufacturers of America have issued new guidelines to modulate the interaction between physicians and industry sales representatives. Underlying this evolution in policy are growing concerns that advertising to physicians by sales representatives (hereafter detailing) may exert considerable influence on choice among branded drugs within a Therapeutic Class.[1] Yet, Wazana (2000) remarks that the effectiveness of detailing is hard to assess from the literature, and lack of data has limited economic analyses to a few Therapeutic Classes, such as the Anti-Ulcer drugs.[2] In Berndt et al. (1995, 1997) and King (2000), detailing generates long-lived goodwill effects that significantly affect, in the aggregate, prescription choices. In Coscelli (2000), it is physician and patient habits in usage that may yield trends in aggregate prescription shares. We know from Givon and Horsky (1991), however, that controlling for usage persistence may moderate the ability of advertising to influence choices among substitute brands. In this paper, using unique data on major Therapeutic Classes, we examine how detailing affects shares of prescriptions for branded drugs within a Class, once we account for usage persistence.

We expand on the findings of the existing literature as we propose a model with two types of prescriptions. The first type identifies prescriptions that are best described as *automatic* in that a single drug is considered and consequently prescribed, irrespective of contemporaneous detailing or available substitutes. This type of prescription best applies to a current user of a drug for whom the process of obtaining a prescription to extend treatment is akin to an *automatic renewal* of the usage of that drug. The second type includes all non-automatic

prescriptions. Following Berndt et al. (1995, 1997), these prescriptions are characterized as outcomes of a multinomial logit that include all drugs, their detailing expenses and attributes. The probability distribution over these types is unobserved in aggregate prescription data, and we specify a dynamic probability distribution over the prescription types.

We analyze prescriptions within three major Therapeutic Classes that treat chronic illnesses; i.e. the Statins (hyperlidimia), the SSRIs (anxiety), and the COX2s (osteoarthritis). The Classes are identified using IMS Health's 5-digit Uniform Standard Classification (USC) codes, and the data consist of monthly aggregates for the US market on prescriptions and advertising dollars from 1995 to 2001. All of the drugs were under patent protection during this time. The likelihood specification of the model involves high-dimensional integrals that are analytically intractable, and its evaluation requires non-trivial Monte Carlo simulation techniques. We use the technique of Efficient Importance Samplers (see Richard and Zhang 1998, Liesenfeld and Richard 2001, 2003a, 2003b), and we estimate the parameters of the model with the method of Simulated Maximum Likelihood.

We find that detailing influences only a fraction of contemporaneous prescription choices, as the estimated proportion of automatic renewals averages 53% per month in the COX2s, 76% in the Statins, and 93% in the SSRIs. Even then, the marginal effect of detailing on a drug's prescription probability is small, in absolute terms, compared to the estimated differences in brand attributes across drugs. Detailing effects are also of brief duration; i.e. from 5 to 7 months. This finding is consistent with Leone (1995)'s study of advertising, and it contrasts with results in Berndt et al. (1995, 1997, 2000) and King (2000). Hence, to the extent incumbent drugs in a Class benefit from persistence in prescription choices over later entrants,

we suggest that this advantage is linked to their larger installed base of patients, rather than to acquired stocks of advertising goodwill.

In other words, our results indicate that if detailing influences choice among branded drugs within a Class, its influence is limited to a small fraction of prescriptions, and its effect is not as pervasive as suggested in some of the literature.

The paper is structured as follows. We present the model in Section 2, the data in Section 3, and the estimation methodology in Section 4. In Section 5, we discuss the results, and we explore their implications for firm conduct in the conclusion in Section 6.

2. A Model

A Therapeutic Class is a group of drugs that are close therapeutic substitutes for the treatment of a medical condition. In this paper, the Classes are for chronic conditions requiring extended care, and a single drug within a Class is prescribed for treatment at any given time. To explain differences in the number of prescriptions across branded drugs within a Class, we propose a simple model with detailing that controls for usage persistence in prescription choices.

A prescription for a drug is written by a physician during an office visit, typically for a period of one month.[3] This prescription may then be refilled afterwards with a pharmacist, but a physician must ultimately provide another prescription to extend treatment. As we focus on advertising to physicians, we consider only the prescriptions written by the physician, not the periodic refills with the pharmacist. Prescriptions may be written to new patients and to current users of a drug who extend treatment.

Coscelli (2000) documents that physicians and patients are creatures of habit, exhibiting

persistence in usage and prescription patterns over time (see, as well, Bond and Lean (1977), Scherer (1993), Hellerstein (1998)). For instance, in Claims data for 1999-2000 from a large managed care organization (covering 500,000+ patients), over 95% of patients in our sample Therapeutic Classes persistently used the same drug. To account for this phenomenon in a simple yet realistic way, we assume that there are two mutually exclusive types of prescriptions.

The first type are automatic prescriptions, and this type best applies to current users of a drug who, to extend treatment, automatically renew their usage of that drug. In particular, if J_t is the number of drugs in the Class in month t, then the conditional probability that drug k is prescribed in month t given the prescription is an 'automatic prescription of drug j' is equal to 1 when $k = j$, and 0 when $k \neq j$, $\forall j = 1, ..., J_t$. Hence, in month t, each of the drugs in the market may be automatically prescribed, and there are, thus, J_t different sub-types of automatic prescriptions (hereafter *automatic renewals*).[4]

The second type of prescriptions includes all non-automatic prescriptions, and it may apply to new patients and to current users who are ambivalent in their use of a specific drug. Following Berndt et al. (1995, 1997, 2000) and King (2000), we model these prescriptions as outcomes of a multinomial logit that include all drugs, their detailing and attributes. The conditional probability that a prescription in month t is written for drug j, rather than for another available drug in the Class, is given by a ratio of indices:[5]

$$\frac{v_{t,j}}{\sum_{k=1}^{J_t} v_{t,k}} \quad with \quad v_{t,j} = \exp(\beta \sum_{l=1}^{t} \delta^{t-l} A_{l,j} + \alpha_j) \qquad \forall j,\ j = 1, ..., J_t, \tag{2.1}$$

where β is a parameter; $A_{l,j}$ are the detailing expenses of drug j's manufacturer in month l; δ is the monthly carry-over rate in detailing effects; and α_j is a dummy variable for drug j with,

for identification purposes, $\alpha_2 = 0$ (i.e. the dummy variable for the second drug in the market is normalized to zero).

The dummy variables in (2.1) proxy, in part, for fixed differences across drugs based on order-of-entry (see Berndt et al. (1995)), and for relative differences in the therapeutic attributes of the drugs. These attributes are determined by the drugs' chemical compounds, which are invariant over time.[6] The inclusion of detailing in (2.1) recognizes that advertising may enhance the likelihood that a drug is prescribed not only by making the drug appear more prestigious and desirable, but also by providing information on how to use the drug more effectively, in the sense of an instruction manual on usage (see Becker and Murphy (1993), Pepall et al. (2001)).[7] Finally, we do not include price in (2.1), as its role as a factor of choice among branded prescription drugs within a Class is not established in the literature (see Scherer (1993), Gonul et al. (2001)).[8]

We then complete the model by specifying a probability distribution over the types. With probability $(1 - q_t)$, the prescription is an outcome of the multinomial logit process in (2.1) (i.e. a non-automatic prescription). With probability $q_t s_{t-1,j}$, the prescription in month t is an automatic prescription of drug j, $\forall j = 1, ..., J_t$, where $s_{t-1,j}$ is drug j's share of all prescriptions and pharmacy refills in the Class in prior months. Namely, the probabilities of automatic prescriptions across drugs within a Class are proportional to the drugs' market shares of all prescriptions and refills in the Class in the prior months.[9] This hypothesis is reasonable since prescriptions are written for a similar number of months across drugs within our Therapeutic Classes. We may then consider the monthly fraction of users of a drug with automatic renewals to be similar across drugs within a Class. In that context, the probability

q_t represents the proportion of all prescriptions that are best described as automatic renewals.

The probability q_t is specified based on a first-order autoregressive process:

$$q_t = \frac{1}{1+\exp(q_t^*)} \quad with \quad q_t^* = \psi + \rho q_{t-1}^* + \varepsilon_t \quad and \quad \varepsilon_t \sim N\left(0, \sigma^2\right) \tag{2.2}$$

where ψ and ρ are parameters, and ε is a Gaussian white noise process that accounts for unobserved factors, such as press releases or medical reports, which may affect the proportion of automatic renewals. The autoregressive formulation allows for persistence in these effects over time. For instance, a press release may prompt patients to visit a physician, but scheduling constraints at physician offices may postpone some visits until the following month.

In the model, we have these probability distributions on prescription types:

- With probability $q_t s_{t-1,j}$, the type is an 'automatic prescription of drug j',

  in which case $\Pr\left(\text{prescription of drug } j \mid \text{'automatic prescription of drug } j\text{'}\right) = 1$ and

  $\Pr\left(\text{prescription of drug } k \mid \text{'automatic prescription of drug } j\text{'}\right) = 0 \ \ \forall k \neq j,\ k = 1, ..., J_t$;

- With probability $1 - q_t$, the type is a 'non-automatic prescription', in which case

  $\Pr\left(\text{prescription of drug } j \mid \text{'non-automatic prescription'}\right) = v_{t,j} / \sum_{k=1}^{J_t} v_{t,k} \quad \forall j = 1, ..., J_t.$

Hence, the probability distribution for a prescription choice in month t is a multinomial, where the (unconditional) probability that drug j, $j = 1, ..., J_t$, is prescribed is:

$$\begin{aligned} p_{t,j} &= \sum_{i=1}^{J_t+1} \Pr\left(\text{prescription of drug } j \mid type_i\right) \Pr\left(type_i\right) \\ &= \left(q_t s_{t-1,j}\right) 1 + \left(1 - q_t\right) \frac{v_{t,j}}{\sum_{k=1}^{J_t} v_{t,k}} \quad , \end{aligned} \tag{2.3}$$

since $\Pr$ (prescription of drug j | 'automatic prescription of drug k') $= 0$, $\forall k \neq j$, $k = 1, ..., J_t$.

The likelihood for the model is given by:

$$L = \int \prod_{t=1}^{T} \prod_{i=1}^{N_t} \prod_{j=1}^{J_t} (p_{t,j})^{x_{t,i,j}} \, f(\varepsilon) \, d\varepsilon \quad , \tag{2.4}$$

where N_t is the total number of prescriptions in month t, $p_{t,j}$ is given in (2.3), and $x_{t,i,j} = 1$ if prescription i is for drug j in month t, 0 otherwise. In (2.4), we examine the effectiveness of detailing in a model where prescriptions are, in essence, characterized either as automatic prescriptions based on prior usage or as outcomes of a probability process that include all drugs and their detailing. This dual sourcing of prescriptions bears some similarities to repeat-purchase diffusion models, using aggregate data, in the marketing literature (see Lillien et al. (1981), Mahajan et al. (1983), Hahn et al. (1994) for pharmaceutical applications). These models explain the growth in adoption (diffusion) rates of a new drug or Class with regard to outside alternatives. In this paper, we focus instead on differences in the number of prescriptions across drugs within a Class.

3. The Data

The data are on branded pharmaceutical drugs within three Therapeutic Classes, identified using IMS Health's 5-digit USC codes.[10] The Classes are the Statins which treat hyperlidimia (high cholesterol; e.g., a popular drug is Lipitor), the SSRIs which treat anxiety and depression (e.g. Prozac), and the COX2s which help alleviate osteoarthritis (e.g. Celebrex, Vioxx). These Classes apply to chronic medical conditions requiring extended treatment, albeit the typical treatment length for the COX2s is only about 6 months. We note that the Statins ranked

second in worldwide sales in 2000, the SSRIs ranked third, and the COX2s are one of the fastest growing Classes. Tables 1 and 2 provide summary statistics on the Classes and their drugs.

[Tables 1 and 2 roughly here]

The data are monthly aggregates for detailing dollars, prescriptions, and refills for wholesalers to pharmacies and drugstores for the U.S. market. The detailing data are adjusted for inflation using the Consumer Price Index (1982-84=100), and all data are scaled to 30-day months. We note that pharmaceutical companies observe, in practice, their prescription data with a 5-6 week lag from sources such as IMS Health. In that context, we consider, reasonably, that aggregate detailing expenses in month t are pre-determined with regards to prescription choices in month t.[11]

The prescription data span from July 1995 to June 2001 (see graphs 1-3), while the refill and advertising data extend from April 1993 to June 2001 (see appendix).[12] During that time, all of the drugs within the Classes are under patent protection and no generic substitutes are available. The number of drugs within a Class evolves over time as new drugs are released, and our Classes contain from two to seven drugs by June 2001.[13] As explained in Berndt et al. (1997, 2000), manufacturers need approval from the Food and Drug Administration for the release of a drug, and the lengthy public proceedings of this agency determine and inform of a drug's release date and therapeutic classification.

[graphs 1-3 roughly here]

4. Estimation Methodology

Given that the monthly number of prescriptions (N_t) is in the millions (see table 1), we first marginalize the multinomial distribution at time t in (2.3) as a multinormal distribution with mean vector μ_t and variance-covariance matrix Ω_t, with

$$\mu_t = N_t p_t \quad \text{and} \quad \Omega_t = N_t \left(p_t' I_{J_t} - p_t p_t' \right) \quad \text{where } I_{J_t} \text{ is a } J_t \times J_t \text{ identity matrix.}$$
$$\text{and } p_t = \left(\begin{array}{cccc} p_{t,1} & ... & p_{t,j} & ... & p_{t,J_t} \end{array} \right)' \text{ is a } J_t \times 1 \text{ vector.} \tag{4.1}$$

For given parameter values, the evaluation of the likelihood in (2.4) demands the computation of high-dimensional integrals that are analytically intractable. We use the method of Efficient Importance Samplers to obtain a highly efficient Monte Carlo estimate of the likelihood function (see Richard and Zhang 1998, Liesenfeld and Richard 2001, 2003a, 2003b).[14] This Monte Carlo method constructs importance samplers for the (initial) sampling density in (2.2), and it identifies the parameters indexing the importance samplers using a set of low-dimensional auxiliary regressions.

The parameters of the model are then estimated with the method of Simulated Maximum Likelihood, using the Common Random Number technique and a 'downhill simplex' optimization algorithm. We obtain statistical root mean square errors for the estimators from fifty replications using simulated market share data.[15] To simulate the share data, we need a Cholesky decomposition of the variance-covariance matrix Ω_t in (4.1), which is singular. This decomposition is given by the following theorem (where time subscripts are dropped for parsimony).

Theorem: Let the matrix $\Omega = N\left(p'I_J - pp'\right)$ where $N > 0$, I_J is a $J \times J$ identity matrix, and $p = \begin{pmatrix} p_1 \ldots & p_j \ldots & p_J \end{pmatrix}'$ is a $J \times 1$ vector with $0 \leq p_j \leq 1 \; \forall j = 1, .., J$, and $\sum_{j=1}^{J} p_j = 1$. The Cholesky decomposition of Ω is given by:

$$\Omega = N(LL'),\; L = \begin{pmatrix} l_{11} & 0 & \ldots & 0 \\ l_{21} & l_{22} & \ldots & 0 \\ \ldots & \ldots & \ldots & 0 \\ l_{J1} & l_{J2} & \ldots & l_{JJ} \end{pmatrix}, \quad \begin{array}{ll} l_{jk} = -p_j \sqrt{\frac{p_k}{q_{k-1} q_k}} & j{:}1 \to J-1, \\ & k{:}1 \to j, \\ l_{jj}^2 = p_j \frac{q_j}{q_{j-1}} & j{:}1 \to J-1, \\ q_j = 1 - (p_1 + \ldots + p_j) & j{:}1 \to J-1, \\ q_0 = 1, \quad q_J = 0. & \blacksquare \end{array} \tag{4.2}$$

[proof by recursive algebra]

Then the (simulated) number of prescriptions of drug j in month t is equal to $\mu_{t,j} + \sqrt{N_t} L_t z_t$ where $\mu_{t,j} = N_t p_{t,j}$; L_t is given in (4.2); and z_t is a vector of J_t identically and independently distributed standard normal random values. Estimation results and root mean square errors are listed in Table 3.

[Table 3 roughly here]

Finally, in the SSRIs, the coefficient on the dummy variable for the drug Prozac in the logit model in (2.1) is estimated as a highly negative number, and the probability that a non-automatic prescription is written for Prozac is negligible. Hence, between 1995 and 2001, prescriptions of Prozac, one of the most recognized brand-name drugs, seem best described in terms of automatic prescriptions based on usage and habit. To facilitate computations, we drop this drug from the logit model in (2.1). In the Statins, the drug Baycol was withdrawn by its manufacturer (Bayer) in August 2001 following reports of patient deaths. Although

the data provide no indications of an impending withdrawal, the drug diffuses slowly in the market following its release, and we find that the model fit the data better if we control for this variation by adding a time trend to the specification for Baycol in (2.1).[16]

5. Results

Predicted values match closely with the sample data, and correlations between observed and mean predicted shares of prescriptions average around 0.97 across drugs and Classes (see Table 3). This attests to the goodness of fit of the model and provides support for the specifications.

The random auto-regressive specification for the proportion q_t in (2.2) is also supported by the data. The variance on the noise variable ε is significant at the 5% level across all Classes. The autocorrelation coefficient ρ is positive and significant in the Statins and SSRIs, indicating some persistence in unobserved shocks over time. For instance, a press release or medical report may prompt a decrease in the proportion q_t of automatic renewals, due perhaps to an influx of new users, and this effect will carry across a few months.

The estimation results indicate that most prescriptions are best characterized as automatic renewals. The monthly mean proportion of automatic renewals is 53% for the COX2s, 76% for the Statins, and 93% for the SSRIs. This finding reinforces the approach of this paper. The nature of the Classes may explain the cross-sectional differences. Treatment length in the COX2s is at most a few months, suggesting a higher turn-over rate in patients and fewer automatic renewals. Physicians also tend to be more conservative in treating anxiety and depression (i.e. in the SSRIs Class), if only due to the delicate nature of the medical condition.

Among non-automatic prescriptions (i.e. among outcomes of the logit model in (2.1)), we

find that choice probabilities are mostly driven, in absolute terms, by the brand dummies; a result that generalizes findings in Rizzo (1999).[17] Indeed, estimated differences in brand dummies are worth millions of detailing dollars, given the estimated detailing coefficients. For instance, at equal stocks of detailing, the SSRI drug Zoloft would have to spend about $7.28 million more on detailing than the SSRI drug Paxil for the two drugs to be equally likely to be chosen in a given month.[18] Results in that regard are consistent across the three Classes.

Our results also suggest that incumbent drugs (i.e. drugs that are first in the market) may not benefit from order-of-entry advantages with regard to prescriptions that are not automatic renewals. Estimation results for the logit model in (2.1) do not display any trends, based on order-of-entry, in brand dummies across drugs and Classes. Monthly carry-over rates in detailing, ranging from 65% to 72% across Classes, are also well below the 92.5%+ figures in Berndt et al. (1995, 1997, 2000) and King (2000). Our figures are consistent with Leone (1995), as we estimate a duration interval of 5.3 months for detailing in the COX2s, 6.1 months in the Statins, and 7.1 months in the SSRIs.[19] In other words, accounting for usage persistence lowers estimated carry-over rates in advertising, as in Givon and Horsky (1991). Any stock of advertising goodwill accumulated by an incumbent drug is short-lived, in contrast to findings in Berndt et al. (1995, 1997, 2000) and King (2000).

Hence, to the extent that incumbent drugs have a long-lasting advantage in prescription shares in (2.3), our results suggest that it is directly linked to their larger installed based of patients (i.e. higher market share of prescriptions and refills) and to persistence in prescription choices (i.e. high estimated rate of automatic renewals). We find, in particular, that detailing has only a limited influence on choice among branded drugs within a Therapeutic Class.

6. Concluding Remarks

Our objective in this study was to expand the existing literature by analyzing how detailing may affect differences in the number of prescriptions for branded drugs within a Therapeutic Class, once we control for usage persistence in choices. We proposed a simple model with two types of prescriptions and a dynamic probability distribution over these types. The estimation of the model then relied on recent Monte Carlo simulation techniques to evaluate the sample likelihood function. We find that the majority of prescriptions are best described in terms of automatic renewals based on usage, and choice probabilities across all other prescriptions seem primarily driven by brand attributes rather than detailing.

Our results indicate that there is substantial segmentation in prescription probabilities across drugs within a Therapeutic Class and, in contrast to some of the literature, they downplay detailing's influence on drug substitution within a Class.[20] This does not suggest, however, that guidelines on ethical promotion behavior are unwarranted, since it is possible that, in some cases, detailing may exert undue influence on drug choice at the level of an individual physician or sales representative. Nor does our paper explore how detailing affects patient welfare. As Hellerstein (1998) and Coscelli (2000) highlight, an answer to this question depends very delicately on the non-trivial specification of the patient-physician relationship, and it requires patient and physician data.

Our paper does emphasize that pharmaceutical firms should consider instruments other than detailing to steal market share away from substitute brands. The industry's current focus on implementing *three-tiered* pharmacy benefit plans is consistent with that perspective (see *US News and World Report* 08/12/02, *Wall Street Journal* 08/14/02). If most branded drugs

within a Class have historically had the same effective price (copay) for patients in managed care, a three-tiered plan designates a particular drug as the preferred drug and gives it a lower copay in a drug formulary. An objective of these plans is, therefore, to try to generate price sensitivity and then use price to counteract persistence in usage. This strategy fits within the comprehensive scope of our results, although its effectiveness remains, of course, to be seen.

7. TABLES

TABLE 1: Summary Information on the Sample Therapeutic Classes

Therapeutic Class	*Major Indication*	*Inception date*	*# of drugs in Jun-01*	*# of prescriptions and refills in Jun-01*	*# of prescriptions in Jun-01*
COX2	Osteoarthritis	Jan-99	2	4,461,000	2,143,000
Statin	Hyperlidimia, cholesterol	Sep-87	6	9,055,000	2,789,000
SSRI	Anxiety, depression	Feb-88	7	8,727,000	3,731,000

Note: SSRI stands for Selective Serotonin Reuptake Inhibitors.

TABLE 2: Summary Information on the Drugs within the Sample Therapeutic Classes

Drugs by order of entry:	1st drug	2nd drug	3rd drug	4th drug	5th drug	6th drug	7th drug
COX2 Class	Celebrex	Vioxx					
Date of release in market	*Jan-99*	*May-99*					
Share of prescriptions in Jun-01	0.492	0.508					
Share of prescriptions and refills in Jun-01	0.510	0.490					
Monthly detailing expenses ($): mean *	7,575,576	6,115,578					
standard deviation	(710,950)	(859,810)					
Statin Class	Mevacor	Pravachol	Zocor	Lescol	Lipitor	Baycol	
Date of release in market	*Sep-87*	*Nov-91*	*Jan-92*	*Apr-94*	*Jan-97*	*Dec-97*	
Share of prescriptions in Jun-01	0.015	0.128	0.231	0.034	0.510	0.082	
Share of prescriptions and refills in Jun-01	0.017	0.128	0.225	0.038	0.518	0.074	
Monthly detailing expenses ($): mean *	400,827	3,023,589	3,186,008	1,836,597	5,382,180	2,778,273	
standard deviation	(470,624)	(899,510)	(774,419)	(821,410)	(910,108)	(752,201)	
SSRI Class	Prozac	Zoloft	Paxil	Effexor	Luvox	Effexor XR	Celexa
Date of release in market	*Jan-88*	*Feb-92*	*Jan-93*	*Mar-94*	*Dec-94*	*Oct-97*	*Jul-98*
Share of prescriptions in Jun-01	0.210	0.254	0.238	0.018	0.005	0.113	0.162
Share of prescriptions and refills in Jun-01	0.222	0.259	0.241	0.017	0.005	0.104	0.152
Monthly detailing expenses ($): mean *	2,600,500	2,433,677	2,548,577	845,365	646,000	1,345,783	2,988,744
standard deviation	(521,713)	(400,338)	(506,713)	(377,893)	(295,450)	(266,704)	(621,903)

Note: * Detailing figures are detailing expenses from July 1995 (or release date if ex-post July 1995) to June 2001, and they are adjusted for inflation using the Consumer Price Index (1982-84=100).

TABLE 3: Estimation and Prediction Results

Estimation results	***Variables***	***Parameters***	***SSRI***	***STATIN***	***COX2***
Equation (2.1)			72 months	72 months	25 months
Dummy variables:[1]	1st drug:[1] *Prozac, Mevacor, Celebrex*	α_1	---	**-1.9860**	**-0.1653**
				(0.0168)*	(0.0414)*
	2nd drug:[1] *Zoloft, Pravachol, Vioxx*	α_2	**0**	**0**	**0**
	3rd drug:[1] *Paxil, Zocor*	α_3	**0.7292**	**0.4993**	---
			(0.0049)*	(0.0015)*	
	4th drug:[1] *Effexor, Lescol*	α_4	**-0.0849**	**-0.8717**	---
			(0.0071)*	(0.0031)*	
	5th drug:[1] *Luvox, Lipitor*	α_5	**-0.3960**	**0.9664**	---
			(0.0092)*	(0.0029)*	
	6th drug:[1] *Effexor XR, Baycol*	α_6	**1.2418**	**-2.2076**	---
			(0.0067)*	(0.0095)*	
	7th drug:[1] *Celexa*	α_7	**1.2095**	---	---
			(0.0069)*		
	Months since release (for *Baycol*) [4]	γ	---	**0.3148**	---
				(0.0027)*	
Detailing: [2]	Coefficient on detailing	β	**1.0016**	**0.7079**	**0.1291**
			(0.0214)*	(0.0255)*	(0.0806)**
	Monthly carry-over rate	δ	**0.7242**	**0. 6867**	**0.6454**
			(0.0055)*	(0.0109)*	(0.2529)*
Equation (2.2)	Constant term	ψ	**-1.9273**	**-0.8303**	**-0.0793**
			(0.3412)*	(0.1449)*	(0.1059)
	Autocorrelation	ρ	**0.2854**	**0.2805**	**0.2428**
			(0.1224)*	(0.1026)*	(0.2451)
	White noise variance	σ^2	**0.7454**	**0.7921**	**0.5917**
			(0.2505)*	(0.1111)*	(0.1926)*
Prediction results: [3]	Correlation: observed & predicted		0.9669	0.9780	0.9625
	Percentage deviations	Mean	-1.49%	-1.14%	-0.62%
	Proportion of automatic renewals	Mean	0.9347	0.7567	0.5264

Notes: Root mean square errors for estimates are listed in parentheses below the estimates.

[1] Drugs are listed by order of entry in each Class; e.g. Prozac, Mevacor, Celebrex are the first drugs in, respectively, the SSRI, Statin, and COX2. Figures for the second drugs are equal to 0 by hypothesis (α_2=0 for identification purposes). For comments on Prozac, see Section 4 in the text.

[2] Units for detailing are $10,000,000.

[3] Correlations between observed and mean predicted monthly shares. Percentage deviations = (observed-predicted numbers of prescriptions)/ (observed number of prescriptions). All figures are averages across 100 random draws.

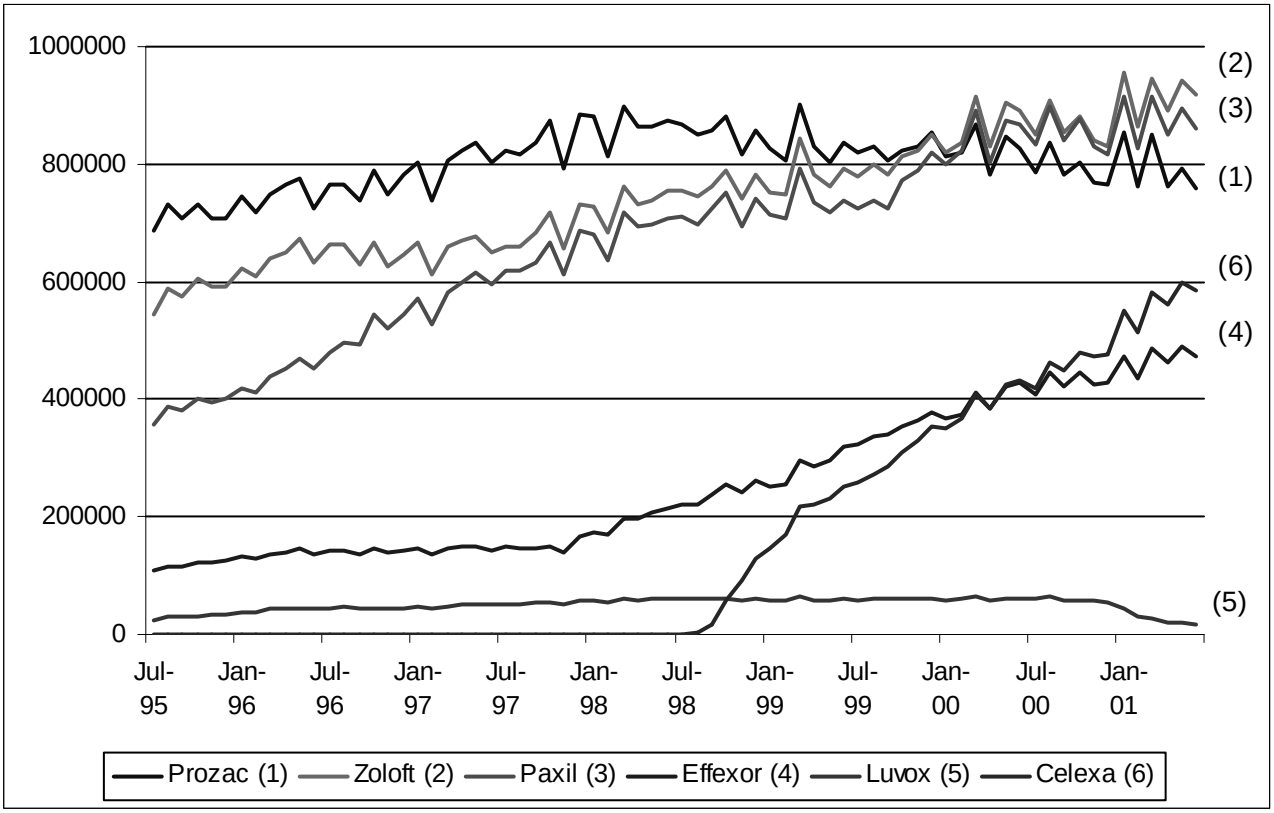
[4] See Section 4 and endnote 16.

[*] The estimate is significantly different from 0 at a 5% level.

[**] If ψ is not significantly different from 0 at a 5% level, the proportion of automatic renewals differs from 0 (see equation (2.2) in the text).

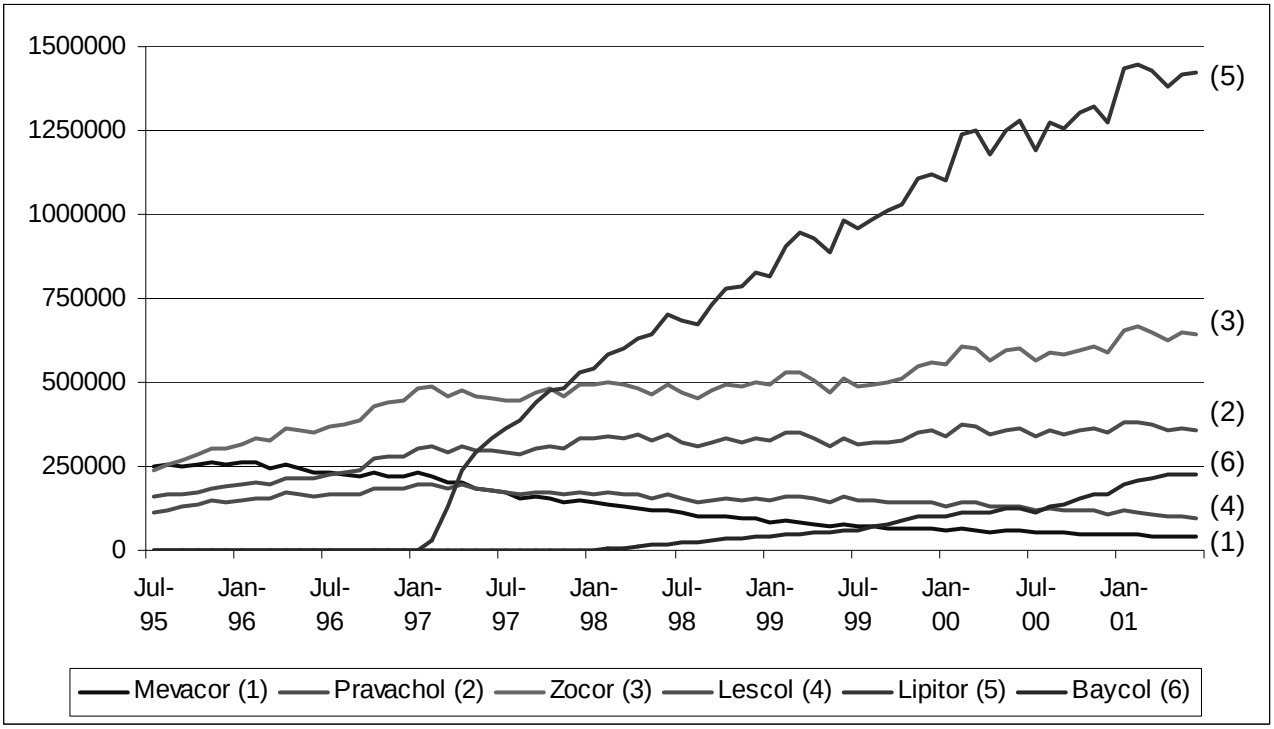
8. GRAPHS

Graph 1: Prescription Data for the SSRI Therapeutic Class



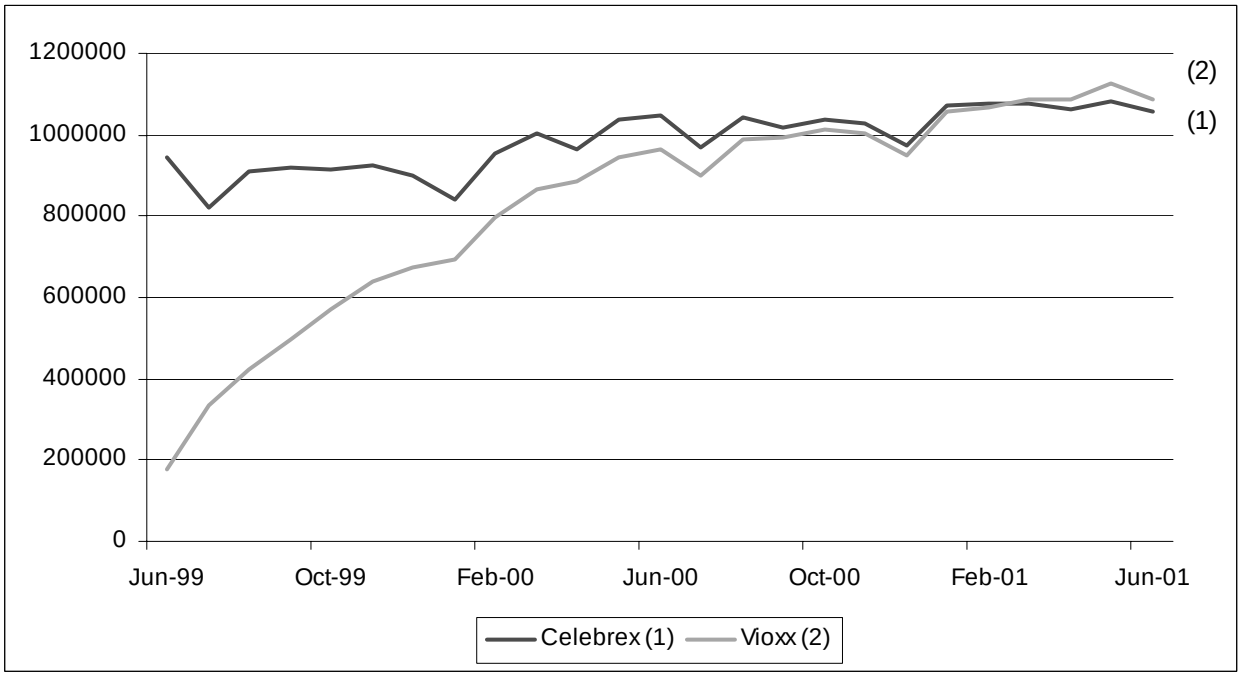
Notes: Numbers after the names of the drugs in the legend correspond to numbers on the right of the graph, and they identify the series for each drug. The series for Effexor is combined with the series for Effexor XR, once Effexor XR is released in Oct-97 (see endnote 13 in the text for details).

Graph 2: Prescription Data for the Statin Therapeutic Class



Note: Numbers after the names of the drugs in the legend correspond to numbers on the right of the graph, and they identify the series for each drug.

Graph 3: Prescription Data for the COX2 Therapeutic Class



Note: Numbers after the names of the drugs in the legend correspond to numbers on the right of the graph, and they identify the series for each drug.

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10. Endnotes

1. IMS Health's 5-digit Uniform Standard Classification code identifies a Therapeutic Class in this paper. Branded drugs refer to prescription drugs under patent, as these are typically known by their brand name. Pharmaceutical firms spend $5 billion a year on detailing, generating about 60 million visits by sales representatives to physicians. The American Medical Association's web site (www.ama-assn.org) discusses the 2001-2002 guidelines. Compliance with the guidelines is, at this time, voluntary. See the Activism and Medicine web site at Case Western Reserve University (home.cwru.edu/activism/buydrug.html) for ample references to articles in the academic medical literature (1995-2002) and in the popular press (e.g. Wall Street Journal, 1999-2002).

2. Wazana (2000) surveys the medical academic literature. In the economic literature on branded drugs alone (our focus), see Bond and Lean (1977) on the Oral Effective Diuretic drugs and the Antianginals, and Berndt et al. (1995, 1997, 2000), King (2000), Coscelli (2000) on the Anti-Ulcer drugs. See, as well, Rizzo (1999) on the Antihypertensive drugs and Gonul et al. (2001). Coscelli and Gonul et al. have physician-level data, while the other authors have aggregate data for the US market.

3. The physician may provide the patient with drug samples. We assume that the prescription data for month t refer to prescriptions written in month t.

4. The characterization of automatic prescriptions as automatic renewals is made to facilitate discussion. Automatic prescriptions may, eventually, apply to new patients who are automatically prescribed a given drug, irrespective of any substitutes or detailing, following either a request for it or a physician's usage of that drug.

5. While the probabilities could potentially be derived from an analysis of utility maximization, we make no such attempt, if only due to the difficulty in identifying the particulars of the physician-patient relationship (see, e.g., Hellerstein (1998)), and the potential market size (see, e.g., Berndt et al. (2000)). From a behavioral perspective, our model is a simplification in that the prescription types include, in their effective choice set, either 1 drug (i.e. automatic prescriptions) or J_t drugs (i.e. non-automatic prescriptions). As explained in the text, the evidence from Claims data suggest that fewer than 5% of current users in our sample Classes switch drugs. Even then, the drugs within a Class are close therapeutic substitutes, and we cannot assert from the data that a switch is not eventually reversible. A richer model would require both physician and patient data, and it is beyond the scope of the paper.

6. Sometimes a new therapeutic indication for the drugs in a Class is found ex post the Class's inception (see, e.g., the GERD indication for Anti-Ulcer drugs in Berndt et al. (1997)). In this paper, we are not aware of major asymmetric changes in our drugs' therapeutic attributes ex post their release on the market (for 1995-2001).

7. Manufacturers also advertise in Pharmaceutical and Medical Journals at the time of the release of their drug. Journal expenditures are minimal compared to detailing and, following Rizzo (1999), King (2000), and Berndt et al. (2000), we do not include this form of advertising in (2.1). To be thorough, we note that we also found that this advertising was either insignificant or wrongly signed in our estimations. Finally, pharmaceutical firms also advertise in print and broadcast media (direct-to-consumer advertising). Data on this advertising are sparse and incomplete. Wosińska (2002) suggests that the influ-

ence of this advertising on drug substitution within a Class (our focus) is negligible and dwarfed by the effect of detailing.

8. To be thorough, we did test for the inclusion of price in (2.1) using two series from IMS Health: (a) price per extended (i.e. most common) unit of usage; (b) sales dollars per prescription. In both cases, price was either insignificant or wrongly signed. Following Berndt et al. (1995, 1997, 2000), Rizzo (1999), and King (2000), and as to maintain consistency with our treatment of price, we also do not single out the availability of free drug samples, which are provided to physicians as part of detailing activities.

9. Prescriptions may be refilled with a pharmacist for periods of 1 to 3 months, and we define $s_{t-1,j}$ as drug j's share of a 3-month moving average in prescriptions and pharmacy refills.

10. The USC-5 codes are 32111 for the Statins, 64360 for the SSRIs, and 09150 for the COX2s. See the appendix in Berndt et al. (1997) for details on the IMS data and for a listing of data adjustments.

11. Given the joint presence of lagged detailing in (2.1) and an autoregressive error term in (2.2), we also estimated the model while instrumenting for monthly detailing expenses with power functions of the number of months elapsed since a drug's release. Differences in parameter values, relative to the estimates reported in the present paper, are inconsequential for our results.

12. Results in this paper are robust to extrapolations of the missing detailing data, as in Rizzo (1999).

13. In the SSRIs, the drug Effexor XR is an extended release version of the drug Effexor. In

the logit model in (2.1), we do not distinguish between the two drugs, and Effexor XR assumes Effexor's prescriptions and stocks of detailing upon its release. Effexor is then dropped from the model. In the Statins, Mevacor and Zocor have the same manufacturer (Merck). The model fits the data better if both drugs are kept separate in (2.1).

14. Liesenfeld and Richard (2001) is a very accessible discussion of Efficient Importance Sampling (EIS). Liesenfeld and Richard (2003a) provides comprehensive technical details on EIS, and Liesenfeld and Richard (2003b) applies EIS to a Gaussian AR(1) process.

15. This number of replications provides a good compromise between computation time and numerical accuracy.

16. For drug j = Baycol, we specify in (2.1):

$$v_{t,\text{baycol}} = \exp(\beta \sum_{l=1}^{t} \delta^{t-l} A_{l,\text{baycol}} + \alpha_{\text{baycol}} + \gamma\sqrt{m_{t,\text{baycol}}})$$

where γ is a parameter and $m_{t,\text{baycol}}$ is the number of months in period t since Baycol's release in the market.

17. In an analysis of sales, Rizzo (1999) sets yearly carry-over rates in detailing effects at 0.7 (about a 0.9 or 90% monthly carry-over rate) and finds that detailing does not have a large effect on brand substitution.

18. In Table 2, divide the dummy coefficient for Paxil (0.7292) by the detailing coefficient (1.0016), where units for detailing are $10,000,000.

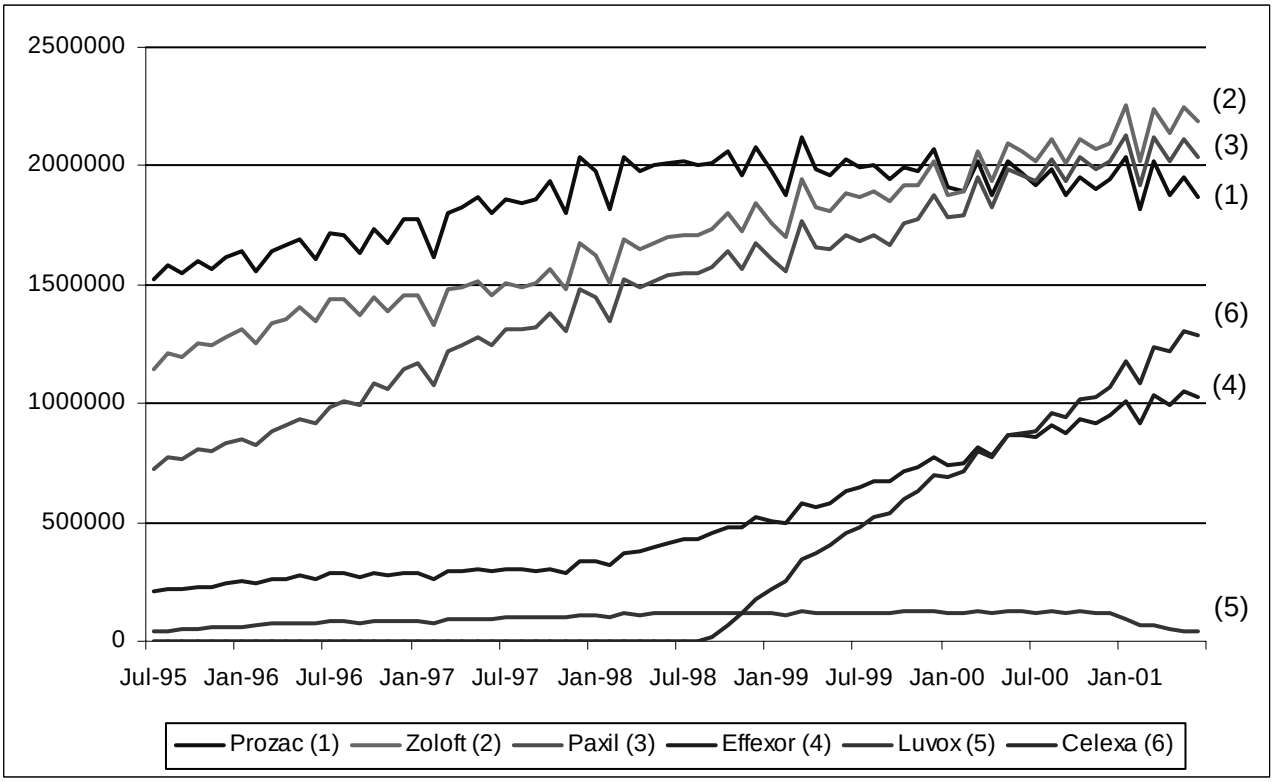
19. The duration interval we report is the number of months after which $1 spent today is worth only $0.1. Note that a 65% carry-over rate means that $1 of detailing in month t

is still worth $\$(0.65)^k$ in month $t + k$.

20. Detailing may not particularly costly to the industry. For instance, the ratio of total monthly detailing dollars to the estimated number of non-automatic renewals (e.g. new prescriptions) averages only to \$14-\$69 across Classes over time. Nowadays, these amounts hardly buy a month's supply of our sample drugs, and we are not accounting in this computation for the persistence in usage documented in the paper.

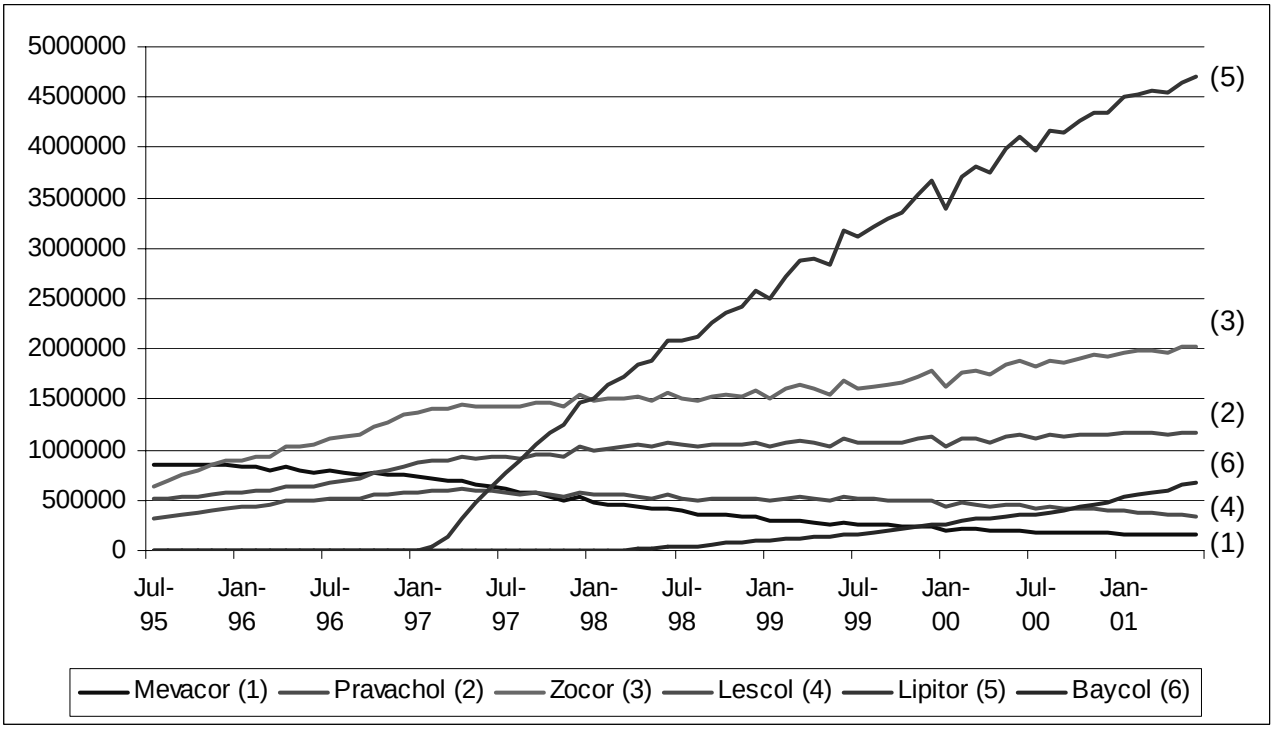
10. APPENDIX

Graph A1: Prescription and Refill Data for the SSRI Therapeutic Class



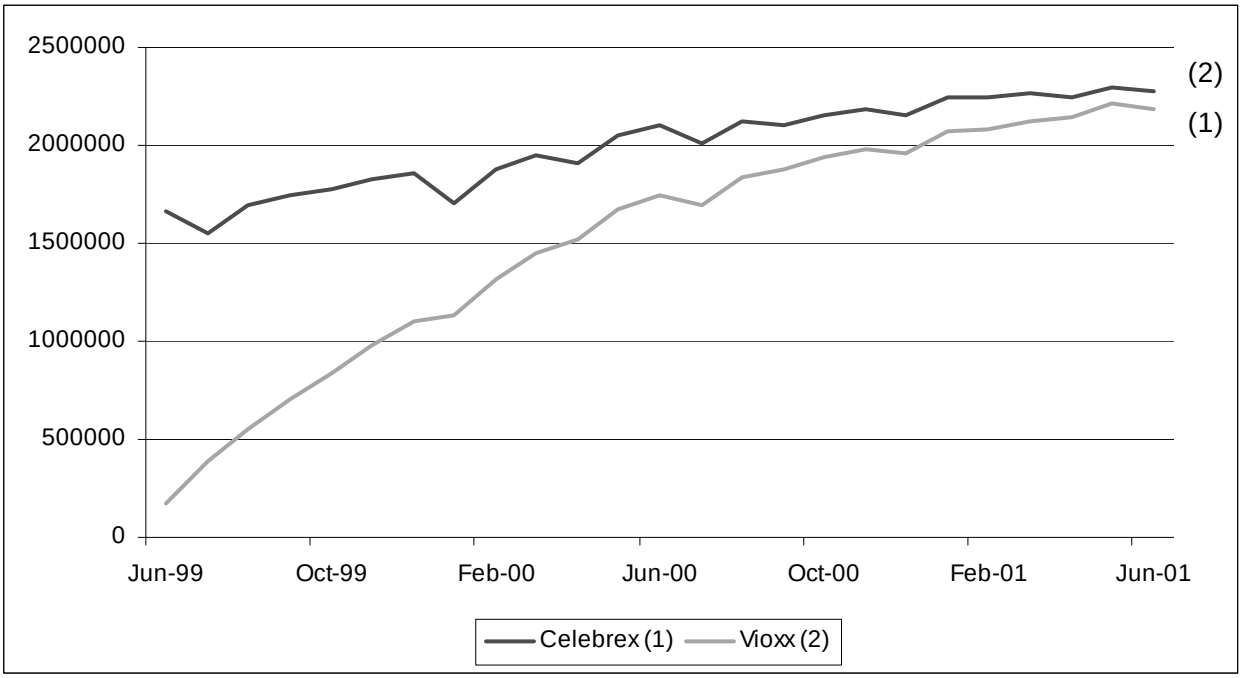
Notes: Numbers after the names of the drugs in the legend correspond to numbers on the right of the graph, and they identify the series for each drug. The series for Effexor is combined with the series for Effexor XR, once Effexor XR is released in Oct-97 (see endnote 16 in the text for details).

Graph A2: Prescription and Refill Data for the Statin Therapeutic Class



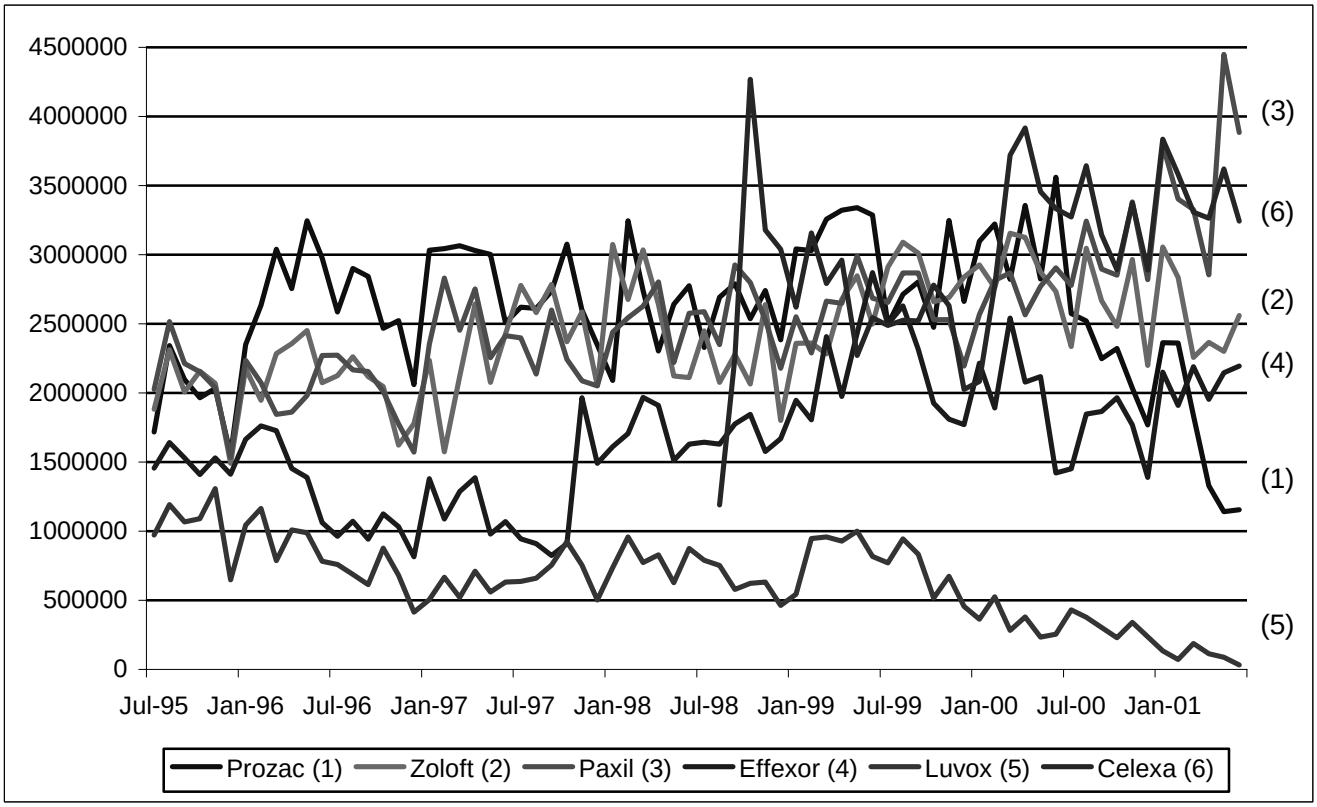
Note: Numbers after the names of the drugs in the legend correspond to numbers on the right of the graph, and they identify the series for each drug.

Graph A3: Prescription and Refill Data for the COX2 Therapeutic Class



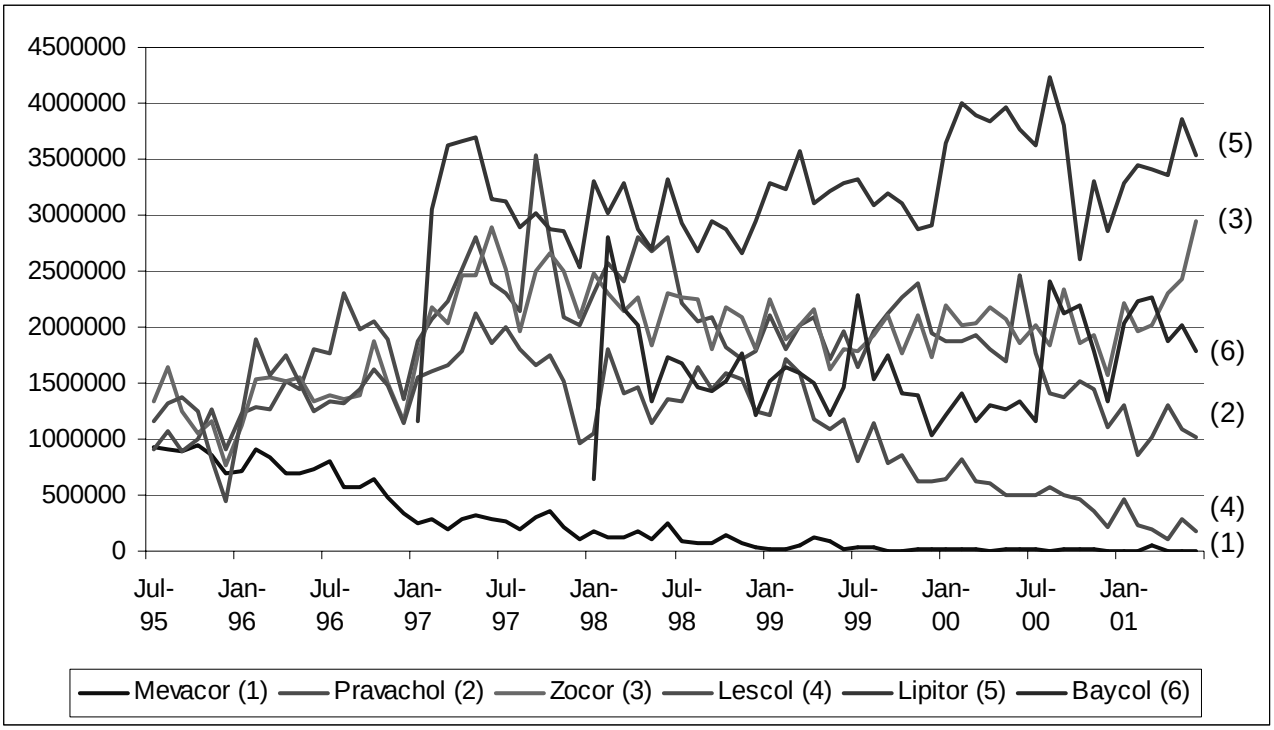
Note: Numbers after the names of the drugs in the legend correspond to numbers on the right of the graph, and they identify the series for each drug.

Graph A4: Detailing Data for the SSRI Therapeutic Class



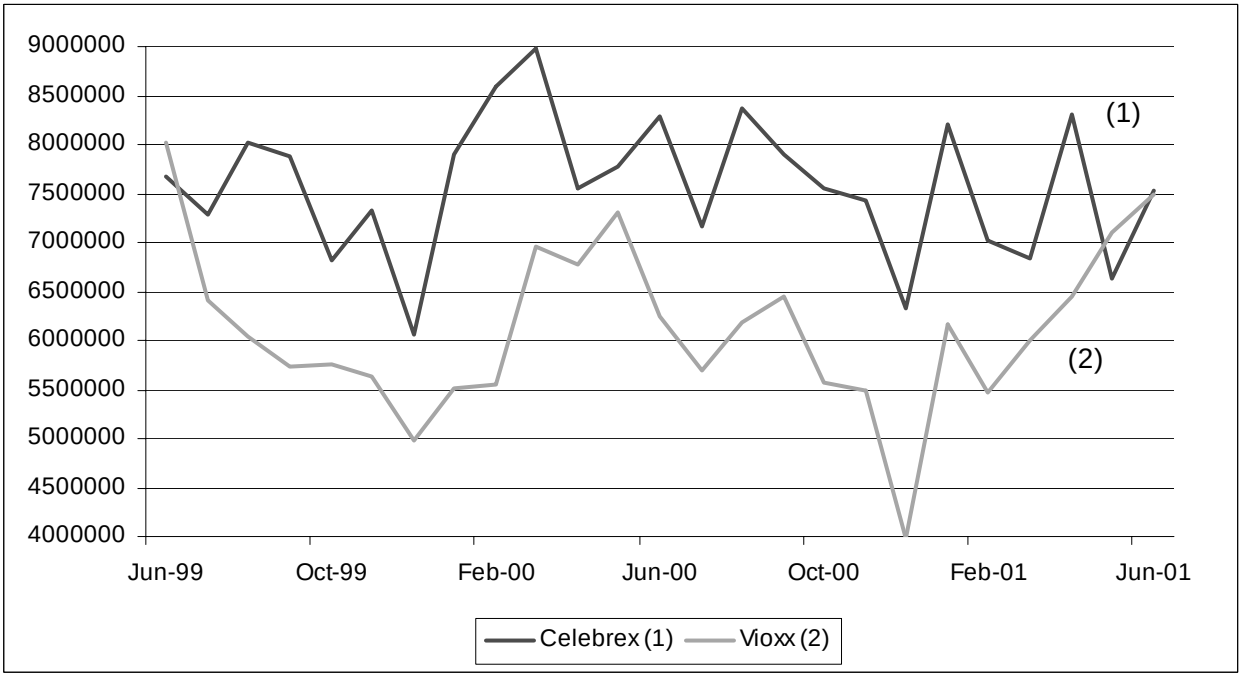
Notes: Numbers after the names of the drugs in the legend correspond to numbers on the right of the graph, and they identify the series for each drug. The series for Effexor is combined with the series for Effexor XR, once Effexor XR is released in Oct-97 (see endnote 16 in the text for details). Units on the vertical axis are in dollars (i.e. range is $0 to $4,500,000) that are adjusted for inflation using the Consumer Price Index (1982-84=100).

Graph A5: Detailing Data for the Statin Therapeutic Class



Note: Numbers after the names of the drugs in the legend correspond to numbers on the right of the graph, and they identify the series for each drug. Units on the vertical axis are in dollars (i.e. range is $0 to $4,500,000) that are adjusted for inflation using the Consumer Price Index (1982-84=100).

Graph A6: Detailing Data for the COX2 Therapeutic Class



Note: Numbers after the names of the drugs in the legend correspond to numbers on the right of the graph, and they identify the series for each drug. Units on the vertical axis are in dollars (i.e. range is $0 to $9,000,000) that are adjusted for inflation using the Consumer Price Index (1982-84=100).