Entry of New Drugs and Doctors' Prescriptions

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Abstract

This paper is about entry of new drugs in pharmaceutical markets. More specifically, I analyze the diffusion of new drugs among doctors. My empirical analysis uses non-parametric duration models, which are flexible enough to identify the most important covariates influencing the doctors' adoption decisions. My results speak to issues such as why generic drugs do not have large market shares in post-patent drug markets. When I analyze entry of bio-equivalent products, I find that the doctors' past dispersion across drugs in a therapeutic market is the best predictor of the likelihood of adoption. When a new presentation form is introduced by an incumbent firm, the doctors who extensively prescribed the brand in the other presentation forms are the ones most likely to adopt the new drug. Finally, I find that doctors are not firm-loyal in their prescribing behavior across therapeutic markets.

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1 Introduction

There is an extensive theoretical literature in industrial organization[1] that studies entry in oligopolistic markets. In particular, researchers such as Schmalensee [24] have focused on order of entry effects in oligopolistic markets. That is, they model reasons why we usually observe that later entrants tend to have smaller market shares than earlier ones, even after controlling for price and quality differences among the products. Schmalensee [24] models order of entry effects as due to uncertainty by the consumers about the quality of the new good. In his model, once the consumers find a brand that performs satisfactorily, it becomes harder for later entrants to convince them to learn about the new brand.

The empirical literature on entry in oligopolistic markets is correspondingly large. In particular, many recent contributions have focused on the entry of new drugs in pharmaceutical markets. A recent study by Berndt, Bui et al. [1] analyzes entry and competition among different pioneer drugs, where the price, advertising, and therapeutic value of the product are crucial factors. Most of the other papers (e.g., Caves, Whinston and Hurwitz [4], Grabowki and Vernon [12], Scott Morton [25] and Frank and Salkever [9]) study the entry of generic drugs in post-patent monopoly markets. One of the facts that these researchers try to explain is why the price charged by the pioneer remains substantially higher than the prices charged by the producers of generic goods, even if the Federal and Drug Administration certifies that the products are bio-equivalent. These empirical studies essentially focus on the supply side of the market (e.g., entry, pricing and advertising decisions), without analyzing whether factors on the demand side of the market might be responsible for the price premium paid to the pioneer drug. To date they have adopted this narrow focus because of data limitations. As Pakes [21] pointed out in his comment to Caves, Whinston and Hurwitz [4]: to gain a better understanding of demand in pharmaceutical markets, it is necessary to observe doctors' prescribing behavior over time.

I have doctor prescription data from the Health Department of the Emilia-Romagna Regional Government in Italy. The data includes all the prescriptions filled by doctors in the province of Parma from 1991 to 1994 for two therapeutic classes: A02B (anti-ulcer drugs) and B04A (cholesterol-lowering drugs). For each doctor, I know the total number of units prescribed in each month for every presentation form and the price. Additionally, for each doctor I know their gender, year of birth, year of graduation from medical school, and the monthly total of patients listed with them by the National Health Service.

I use the data to study doctors' adoption of new anti-ulcer and cholesterol-lowering drugs. I address the following questions: do adoption decisions differ across drugs? How

[1] Tirole [27], ch. 8, for example contains a summary of most of the contributions of the 1980's.

long does it take for doctors to start prescribing the new drugs? Are demographics, such as seniority, systematically correlated with adoption? What kind of preferences are consistent with doctors' observed behavior? Additionally, I test whether doctors display brand loyalty by analyzing the proliferation of presentation forms by incumbent vendors. Finally, I test for the existence of firm loyalty at the doctor level, since there are many multi-product firms operating in pharmaceutical markets.

My empirical analysis uses non-parametric duration models, which are flexible enough to identify the most important doctors' covariates influencing their hazard rate of adopting a new drug. The methodology is very similar to the analysis by Meyer [20], who moves from Kaplan-Meier estimates to semiparametric duration models to estimate the effect of unemployment benefits on spells of unemployment.

The main conclusions of the paper are the following. When I analyze entry of identical drugs, I find that doctors' past preference for prescribing across brands is the best predictor of the likelihood of adoption. When a new presentation form is introduced by an incumbent firm, the doctors who extensively prescribed the brand in the other presentation forms are the ones more likely to adopt it. Finally, I find that doctors are not firm-loyal in their prescribing behavior across drug classes. How do my findings relate to the previous literature? First, the observed low level of market penetration of identical drugs is consistent with the order of entry effects found in other studies (such as Berndt, Bui et al. [1], and Gorecki [10] [11]), and with the habit persistence by doctors found by Hellerstein [14]. Second, incumbents behaved as predicted by theories of product proliferation (such as Schmalensee [23]), by covering every possible market niche. This behavior generated the expected reaction by doctors; those who extensively prescribed a particular brand were much faster at adopting a new presentation form for that brand. Third, my finding that doctors are not firm-loyal across drug classes is rather puzzling, since pharmaceutical firms spend large amounts of resources advertising and offering benefits to doctors (such as free samples for their patients, and sponsorship for conferences). A possible explanation for the absence of firm loyalty is that the benefits the doctors receive are non-linear in the quantity prescribed; that is, doctors maximize the benefits they receive by prescribing a certain threshold amount of drugs for as many firms as possible.

In the next two sections I discuss the relationship between this analysis and the literature. Also, I give some details on the structure of the Italian pharmaceutical market. In Section 4, I describe the duration models that I use in the estimations. Section 5 describes the data, and the variables used in the estimations. Sections 6 and 7 present the empirical results. The conclusions and directions for future research make up the final section.

2 Doctors' Demand in Pharmaceutical Markets

Previous literature Most of the recent empirical literature on entry of new drugs studies the supply side of the market. For example, Scott Morton [25] analyzes the decision by the producers of generic drugs whether to enter particular post-patent molecule markets or not, and the pricing and advertising decisions of incumbents and entrants. Frank and Salkever [9] study the price game between the pioneer and the producers of generic goods and find that the price charged by the pioneer actually increases after entry of the generic producers, while the price charged by generic producers declines with entry of additional producers.

There are only a few studies explicitly analyzing the demand side of the market. Stern [26] and Ellison, Griliches, Hausman and Cockburn [7], using different methodologies, analyze both the elasticity of substitution between the pioneer and generic drugs, and the elasticity of substitution among different pioneer drugs in selected therapeutic markets using national level data on quantities and prices. Stern [26] finds the elasticity of substitution to be low between the pioneer and its generic substitutes, while he finds a higher elasticity of substitution between different pioneer drugs whose indications are similar. Gorecki [10] finds that late entrants that were certified to be therapeutically equivalent to existing drugs managed to gain substantial market shares *only* in those Canadian provinces where price competition exists at the pharmacists' level.

The study most closely related to this paper is the analysis by Hellerstein [14]. She studies panel doctors, showing that doctors exhibit "habit persistence" in their choice to prescribe generic or pioneer drugs. In Coscelli [5], I find habit persistence by doctors and brand loyalty by consumers when analyzing repeated prescriptions of the same molecules[2] by a sample of doctors and patients in Rome in the early 1990's. That is, I find that doctors tend to prescribe the same brand to a given patient, but that different patients get different therapeutically equivalent drugs. It is the habit persistence by doctors, and brand-loyalty by patients, that create product differentiation in molecule markets between the incumbent and the new therapeutically equivalent drugs. This product differentiation constitutes a barrier to entry of new drugs. The present study focuses on the doctors' decisions to adopt new drugs, which is a crucial first step in the penetration strategy of an entrant.

Why should we observe entry of equally priced,[3] identical drugs, when the literature (Hellerstein [14], and Coscelli [5]) has shown that both doctors and patients exhibit habit

[2] While in the US market, after patent expiration, the competition is between the pioneer drug and one or more generic substitutes, in the Italian market, licensing is very widespread, therefore, before patent expiration, there is competition between the pioneer drug and one or more licensees.

[3] As I explain in section 3 below, in the Italian market, prices of different brands of the same molecule are regulated to be the same.

persistence in their prescription behavior? While economic theory can easily accommodate entry of new *molecules*, which can be of superior therapeutic value for at least a subset of the patients, it requires either the presence of some important information problem (e.g., an agency problem between doctors and patients) and/or the addition of other heterogeneous dimensions (e.g., unobservable benefits going to doctors, or "perceived" quality differences) to explain the proliferation of identical *products*.[4]

Doctors' and Patients' utilities The agency problem between the doctor and the patient stems from the superior information available to the doctor, together with differences in the utility functions of doctor and patient.

Patient utility The utility the patient receives from being prescribed a particular drug is a function of a vector of patient's characteristics, X, and of the history, H, of the patient's prescriptions up to t. While the doctor knows how similar the drugs are in therapeutic terms, the patient does not have this information. I assume that when the patient starts receiving an anti-ulcer treatment, he is perfectly indifferent among all the S trade-name drugs in the anti-ulcer class. To simplify matters, suppose that there are only two vendors of the molecule: the incumbent vendor, (I), and the entrant, (E). The non-price competition among producers is at the level of the doctor;[5] therefore a new patient is not able to distinguish among different trade-name drugs. If the patient has already been treated for ulcer problems in the past, he incurs a cost in being switched from the brand sold by the incumbent, (I), to the brand sold by the entrant, (E). Since I analyze *only* switches *within* molecules, I can assume that there is a utility loss for the patient, because the benefits associated with switching are zero. The patient will experience *no* therapeutic advantage from receiving a prescription for a different brand of the *same* molecule.

Doctor utility The utility to doctor i of prescribing at time t to patient j either the drug sold by the incumbent, (I), or the drug sold by the entrant, (E), depends on the benefits that the doctor receives from the pharmaceutical firms, the portion of the patient's utility that the doctor internalizes, and the doctor's preferences. Doctors internalize patient utility because their income is increasing in the number of patients listed with them. Therefore doctors prefer to switch patients whose switching costs are lower, everything else equal.

[4] Clearly this is not the case in the US market where generics are priced much lower than the pioneer drug, and where pharmaceutical firms are allowed to compete in prices.

[5] There was no direct-to-consumer advertising inn Italy during the sample period.

What do these utilities predict when a new, equally priced, bio-equivalent drug enters the market? The doctor maximization problem suggests that *without an agency problem* between the doctor and the patient, and with positive switching costs for the patients, none of the doctors should prescribe the new drug to patients who already consumed the drug sold by the incumbent; only new patients, who are perfectly indifferent among all vendors, could receive the new drug. In the *presence of an agency problem*, a necessary condition for the entrant to induce the doctor to start prescribing the new drug would be to give her benefits higher than those she receives from the incumbents. If this condition was not met, we would not observe *any* prescription of bio-equivalent drugs produced by the entrant. Moreover, according to the maximization problem for the doctors, when doctors find it optimal to start prescribing a new brand for an existing molecule, they choose the patients whose switching costs are the lowest (i.e., new patients and patients who have not yet developed brand-loyalty). A fully structural model of doctors' choices over time would require assumptions on the shape of the benefit function for the doctors, and on patients' heterogeneity, that are difficult to make. Therefore, I summarize below the hypotheses that can be tested with my data.

Testable Implications

H1 If I assume that (a) a new vendor offers higher benefits than the incumbents to the doctors, and (b) that the proportion of "new" patients in every period over the total number of listed patients is the same across doctors, then doctors with larger practices are more likely to have "new" patients in every period. Therefore, I expect doctors prescribing more units on average in a therapeutic market to be faster at prescribing a new drug.

H2 Since I cannot observe the ties particular doctors have with some firms, and the identity of the patients, I assume that the past tendency to prescribe various identical brands (rather than remaining loyal to particular vendors) reveals a preference for prescribing across brands. I proxy for the dispersion of doctors' prescriptions both at the level of the *entire* therapeutic market, and *within* the molecule, by constructing herfindahl indexes (HHI) for each doctor before entry of the new drug. I expect doctors who were less brand-loyal in the past to be faster at adopting. This is because the amount of benefits these doctors need to receive to start prescribing a new drug might be lower.

H3 When an incumbent introduces a new presentation form, I expect that the doctors who prescribed that brand in the past would be more likely to adopt the new presentation form. There are two effects working in the same direction: (i) doctors who extensively prescribed the brand in the past have revealed a preference for the brand; therefore, as long as there is persistence in benefits, these doctors should be more likely to prescribe the new presentation form. (ii) If patients have no switching costs in changing presentation forms, as long as the brand does not change, the doctors whose patients are familiar with the brand will not face any switching cost in moving these patients to the new presentation form.

H4 I expect doctors to develop stronger ties to some firms than others, either because benefits are positively correlated over time, or because of personal ties between the physician and the detailer for the particular pharmaceutical company. [6] That is, I test the firm-loyalty that doctors display across markets.

Finally, it should be remembered that these tests study whether some doctors *are more likely than others* to adopt a new drug. They do not say anything about the actual number of doctors adopting.

3 Market Institutions

Market definition I begin by first considering how to define a market. Following most of the recent economic literature on pharmaceuticals (e.g., Stern [26]), I consider therapeutic markets, each containing different molecule markets. I define a therapeutic market as a 4-digit ATC code,[7] and a molecule market as a clearly specified chemical compound. This is a natural definition of demand because a 4-digit ATC code includes all the molecules which can theoretically be prescribed for a certain diagnosis. The molecules themselves differ according to specific indications, prices, side effects, and interactions with other drugs. Furthermore, all the brands within a molecule market are certified to be bio-equivalent by the Italian Health Ministry; therefore, it can comfortably be assumed that they are "homogeneous".[8] Usually, one of the firms is the patent-holder, while the other firms are licensees paying a fixed royalty on every package they sell. Moreover, each producer [9] can sell the drug in different presentation forms: these include pills, tablets,

[6] I interviewed some of the doctors in the sample regarding the benefits they receive from pharmaceutical companies. I was told that there is usually a long-term "arm-lenght"relationship between the "detailers" and the doctors. This is what justifies my assumption of persistence in the benefits over time.

[7] The ATC code is an international classification scheme according to which drugs are divided into different categories by target organ, mechanism of action, and chemical and therapeutic characteristics. ATC is a hierarchical system where each level is divided into sub-levels.

[8] I use "homogeneous" and bio-equivalent interchangeably.

[9] I use producer and vendor interchangeably. In the few cases where they differ, the term vendor would be more appropriate, since it is the vendor who establishes a relationship with the doctor.

and syrup. Each presentation form is further divided by dosage (e.g., 10 pills–300 mg, 20 pills–150 mg). I define a brand as a pair vendor/molecule, and a presentation form as a combination of a particular method of delivery/quantity of the molecule. Figure 1 summarizes both the market structure and the terminology used in the paper.

Institutional Characteristics The Italian National Health Service (*Sistema Sanitario Nazionale*) is administered locally by the Regional Governments; every citizen is entitled to receive services from it. The revenues for the National Health Service come mostly from transfers from the Central Government and increasingly from patients' payments. Every citizen has a general practitioner who issues prescriptions. Patients remain with the same general practitioner for long periods of time, because of high transaction costs in moving from one doctor to another. Moreover, most good doctors have waiting lists. Finally, pharmacists have no role in the prescription process, because no substitution between products is allowed.

Price regulation An authority called *Commissione Unica del farmaco* (Central Commission on Drugs) registers drugs, sets their price, and assigns them to different reimbursement classes. For a new molecule, a file containing the results of all the clinical trials is presented for registration.. A new vendor of an existing molecule must simply prove the therapeutic equivalence of the new drug to the molecule. Since January 1991, prices have been set according to the value of the molecule, thus implying equal prices for homogeneous drugs.[10] Prices do, however, differ across molecules. Patients were required to pay 40% of the listed price of anti-ulcer drugs until December 1993. Afterwards, some of the molecules required a low fixed payment, while the others required a payment equal to 50% of the registered price (Informatore Farmaceutico [19]).[11] Because of such strict price regulation, non-price competition plays a major role in the market. Advertising and benefits to doctors are important strategic variables for pharmaceutical firms. Advertising acts in the direction of "differentiating" brands at the doctors' level. Since the doctors know that the therapeutic value is the same across all producers of the same chemical compound, there is a limit to the amount of product differentiation that can be attained through advertising. Firms give direct benefits to doctors: among them free samples, sponsorship for conferences and

[10] The law required the prices to be equal for new molecules; the prices for vendors of existing molecules were equalized upon revision of the regulated price. Therefore the equalization in some molecule markets took place subsequently.

[11] Price competition is not an issue in the analysis below, because patient payments are the same for groups of similar molecules, therefore changes in patient payments over time are not relevant for the choice among brands within these groups.

new medical devices for offices. I do not focus on the game-theoretic model played by the firms, as I am unable to observe the benefits that the firms give to the doctors.

Entry episodes I analyze entry in two therapeutic markets: anti-ulcer drugs (A02B)[12] and cholesterol-lowering drugs (B04A). I decided to focus on these two markets both because they account for a considerable proportion of the total world expenditure on pharmaceuticals (around 9% in 1994, IMS International [15]), and because they witnessed many episodes of entry during my sample period.

I observe 32 entry episodes during my sample period.[13] I group these episodes into two different categories: (1) new entrants introducing bio-equivalent drugs, and (2) new presentation forms introduced by incumbent firms.

Table 1 and 2 list in a chronological order the entry episodes in the two markets during the four years covered in my sample. All the instances where the firm was already in the molecule market provide examples of proliferation of presentation forms by the incumbent.

4 Empirical Analysis

4.1 Preliminary Descriptive Analysis

Since I do not observe the benefits that doctors receive, I infer something about these benefits by observing doctors' prescriptions *within* molecule markets. The therapeutic value of the competing brands is the same, therefore the heterogeneity in patients' medical conditions does not play a role in doctors' choices.

How dispersed are the doctors in their prescriptions within molecule markets? Doctors prescribe in large measure across brands. For example, figure 2 shows the proportion of doctors who prescribed either one, two or all three brands of *omeprazole* between the beginning of the sample, in January 1991, and the entry of the fourth producer in May 1993. More than 88% of the doctors prescribed all three brands at least once. This indicates that doctors are familiar with all the brands in the market, and that they do not specialize by

[12] This 4-digit number is the ATC code for all anti-ulcer drugs.

[13] Six entry episodes are relative to "me-too" drugs, whose chemical composition differs from the incumbent drugs, but whose indications and side effects are similar. The results for these entry episodes are similar to those I study in the paper. They are not reported, but they are available from the author upon request. The remaining 26 episodes concern therapeutically equivalent drugs. The absence of radically new drugs is is not peculiar to my sample, though; Bozzini et al. [2] analyzed the 29 new molecules that entered the entire Italian pharmaceutical market in the first semester of 1993 finding that only one could be regarded as innovative, while the other ones were either therapeutically similar to molecules already in the market, or dealt with irrelevant pathologies.

Table 1: New Presentation Forms in the Anti-ulcerMarket (1991-1994)

Date of Entry	Molecule	Brand Name	Category	New Producer
5/91	*sucralfate*	SUCRAMAL	2	NO
6/91	*sucralfate*	ANTEPSIN	2	NO
7/91	*sucralfate*	SUCRALFIN	2	NO
6/92	*sucralfate*	CITOGEL	1	YES
7/92	*sucralfate*	GASTROGEL	1	YES
7/92	*sucralfate*	SUCRATE	2	NO
4/93	*famotidine*	FAMODIL	2	NO
4/93	*famotidine*	GASTRIDIN	2	NO
5/93	*omeprazole*	ANTRA	1	YES
7/93	*cimetidene*	NEO-GASTRAUSIL	1	YES
8/93	*niperotidine*	ROTIL	1	YES
10/93	*cimetidene*	NOTUL	2	NO
6/94	*sucralfate*	CRAFILM	1	YES
9/94	*niperotidine*	PERULTID	1	YES

Category: 1-New firm, and bio-equivalent drug; 2-new presentation form by an incumbent. New producer is NO if the firm was already in the molecule market, YES otherwise. Sample period: January, 1991 to December, 1994. Source: Informatore Farmaceutico [19].

Table 2: New Presentation Forms in the Cholesterol-Lowering Market (1991-1994)

Date of Entry	Molecule	Brand Name	Category	New Producer
3/91	*gemfibrozil*	GENLIP	2	NO
6/91	*gemfibrozil*	GEMLIPID	2	NO
6/91	*gemfibrozil*	GENLIP	2	NO
6/91	*gemfibrozil*	LIPOZID	2	NO
6/91	*gemfibrozil*	LOPID	2	NO
12/91	*meglutole*	MEVALON	2	NO
6/92	*cholestyramine*	COLESTROL	2	NO
5/93	*pravastin*	APLACTIN	1	YES
5/93	*pravastin*	PRASTEROL	1	YES
6/93	*detastrane*	RATIONALE	2	NO
7/93	*gemfibrozil*	FIBROCIT	2	NO
6/94	*simvastin*	MEDIPO	1	YES

Category: 1-New firm, and bio-equivalent drug; 2-new presentation form by an incumbent. New producer is NO if the firm was already in the molecule market, YES otherwise. Sample period: January, 1991 to December, 1994. Source: Informatore Farmaceutico [19].

prescribing only one brand for each molecule.[14]

When does adoption usually occur? One of the standard methodologies used to describe the reaction of doctors to the entry of a new drug over time, when there is censoring (i.e., some doctors retire before the end of the sample period), is a Kaplan-Meier estimation. Kaplan-Meier is a generalization of the sample survivor function to the case with censored data. The estimated survivor function, $\hat{S}(t)$, takes the following value at time t:[15]

$$\hat{S}(t) = \prod_{j|t_j \leq t} (n_j - d_j)/n_j \qquad (1)$$

where n_j is the number of doctors in the market who have not prescribed the new drug until time j, and d_j is the number of doctors who adopt[16] at time j. These Kaplan-Meier estimates widely differ for the drugs in my sample. For example, figure 3 estimates the adoption of a new drug (ANTRA) entering a growing molecule market (*omeprazole*) with three producers already in it. More than 75% of the doctors adopt before the end of the sample period. The vertical steps represent the hazard rate of adoption in each month. Conversely, figure 4 shows the adoption pattern for another "homogeneous" product (NEO-GASTRAUSIL) entering a mature molecule market (*cimetidene*) with more than fifteen vendors in it. Only a few doctors ever prescribe it, and adoption occurs in the first few months after entry, when most of the advertising budget for the product is spent.

These differences pose a series of questions: which doctors immediately adopt? Are these doctors only experimenting, or are they permanently moving from one producer to another? Is doctors' behavior related to some time-invariant characteristic, such as seniority and/or to their past prescribing behavior? In order to answer these questions, I need a multivariate statistical model that holds constant various factors that affect doctors' decision to adopt new drugs.

4.2 Introduction to Duration Models

My estimation strategy uses continuous-time duration models. The advantage of these models is the extreme flexibility that they allow in estimating the effect of various doctors' characteristics on the rate of adoption of new drugs. I estimate one drug at a time, therefore the identification comes from the variation in doctors' responses to the entry of the new drug. The only kind of information I have about patients is the monthly number of them listed with each doctor in two large age groups (14–65, and over 65).

An observation is a doctor's duration until the first prescription of the new drug. That is, the dependent variable is the number of months elapsing between the entry of the new drug in the market, and its prescription by each doctor. This choice of dependent variable allows me to estimate the temporal path of diffusion of the drug in the market. The basic object of the analysis is the hazard rate of adoption, which specifies the rate of adoption of the new drug at t in the doctors' population, conditional upon the absence of prescription until time t, and the doctors' observed characteristics.

4.3 Cox Estimation–Proportional Hazards Model

The economic literature estimating duration models[17] uses both parametric and semiparametric specifications. In the parametric case (e.g., exponential or Weibull estimation) the adoption time distribution is assumed to be known except for a few parameters. Conversely, the semiparametric specifications use unspecified functions based on the idea that many components of the model are uncertain, or arbitrary from the point of view of economic theory. [18] Since my approach is primarily empirical, I use a semiparametric modeling strategy.

Separately for each entry episode, I estimate different specifications of a duration model, in order to find out which doctors' covariates are responsible for their different time of adoption. More specifically, to model the time it takes a physician to adopt a new drug, I will use a marginal likelihood method, which is described below.

Likelihood function To begin, for each single entry episode j,[19] I define the order statistic, $O(t) = [t_{(1)}, t_{(2)}, \ldots, t_{(n)}]$ as a vector ordering the different times of adoption from the shortest to the longest. The rank statistic, $r(t) = [(1), (2), \ldots, (n)]$, indicates which doctor corresponds to the *ith* order statistic. So for example: $t_{(1)}$ indicates the number of months before the first doctor actually prescribes the drug, and (1) denotes the rank of the doctor who prescribes the drug. In the special case when there is no right-censoring and the time of adoption is recorded so frequently (e.g., day of the prescription) that there are no ties, it is possible to show that only the rank statistic, r, carries information about the vector

[14] This result is common to other molecule markets: doctors prescribe many brands in *any* molecule market.

[15] Here t is the number of months after entry.

[16] By adoption, I always mean first adoption unless otherwise specified.

[17] Lancaster [18] provides a good survey of the duration models used by economists, with a special focus on the analysis of duration of unemployment.

[18] Han and Hausman [13], and Kiefer [17] discuss the relative merits of the two statistical approaches for economic analysis.

[19] I will not use the superscript j in defining the variables below, but it should be remembered that this analysis is conducted separately for every entry episode.

of coefficients to be estimated, $\hat{\beta}$ (Kalbfleisch and Prentice [16]). In the estimations below, though, I need to take into account both censoring and ties. A tie is a situation where two or more doctors adopt at the same time. More precisely, ties occur when the time-unit of observation is such that there is some grouping. In my sample I cannot distinguish among the doctors who adopt the drug during the same month. Furthermore, there is a censoring problem, since I do not know whether the doctors in the sample will prescribe the drug after the end of the sample period. In particular, there is right-censoring in my dataset, because I observe doctors' prescriptions only until December 1994. Additionally, since I can observe the exact date of entry and exit from the market for each single doctor in my sample, I know that some of them retire or otherwise exit the market before December 1994. This is defined as *type I censoring*, that is, a situation where the time of exit from the sample is independent from the decision to adopt a new drug or not.

To summarize: for each single entry episode j, I observe an ordered vector of adoption times $[t_{(1)}, t_{(2)}, \cdots, t_{(n)}]$, and the total number of doctors, $d_{(i)}$, who adopt in each month $t_{(i)}$. The elements of the vector of adoption times are the ordered months after entry when adoption occurs; for example, if three doctors adopt in the first month, and six doctors adopt during the second month, the first nine elements of the vector are $[1, 1, 1, 2, 2, 2, 2, 2, 2, \cdots]$. Moreover, in the likelihood function, I need to incorporate the information that, even if I do not know the rank of adoption among the $d_{(i)}$ doctors who adopt at time $t_{(i)}$, I know that they adopt the drug before every doctor adopting at $t_{(s)}$ if $s > i$. Therefore, the marginal likelihood in this general case takes the following form (Kalbfleisch and Prentice [16]):

$$L = \prod_{i=1}^{n} \exp\Big(\sum_{k \in D_{(i)}} x_k \beta \Big) \left[\sum_{p \in Q_{(i)}} \prod_{r=1}^{d_{(i)}} \left(\sum_{l \in R(t_{(i)}, p_r)} \exp(x_l \beta) \right)^{-1} \right] \tag{2}$$

where i indexes the ordered adoption times $t_{(i)}$ $(i = 1, \ldots, n)$ for the n doctors in the sample; $\sum_{k \in D_{(i)}} x_k$ is the sum of the covariates for the set of doctors, $D_{(i)}$, adopting at time $t_{(i)}$; and $d_{(i)}$ is the number of doctors adopting at time $t_{(i)}$.

The component included in the square bracket takes into account that I do not know the order of adoption among the doctors who adopt during the same month. Therefore, $Q_{(i)}$ indicates the set of permutations of $D_{(i)}$, and $p = (p_1, \ldots, p_{d_{(i)}})$ is an element of $Q_{(i)}$. Moreover, $R(t_{(i)}, p_r) = R(t_{(i)}) - \{p_1, \ldots, p_{r-1}\} = \{(i), (i+1), \ldots, (n)\} - \{p_1, \ldots, p_{r-1}\}$ is the set difference between the risk set and one possible permutation for the doctors who actually adopted. The risk set $R(t_{(i)})$ consists of all doctors that could have adopted at time $t_{(i)}$ (i.e., all j such that $t_{(i)} \leq t_j$). Equation (2) above is extremely difficult to compute, therefore the Peto-Breslow approximation (Peto [22], Breslow [3]) is used in the estimation routine performed with STATA:

$$L = \prod_{i=1}^{n} \frac{\exp\left(\sum_{k \in D_{(i)}} x_k \beta \right)}{\sum_{l \in R(t_{(i)})} \exp(x_l \beta)^{d_{(i)}}} \tag{3}$$

Basically, the estimation routine avoids the cumbersome treatment of all the possible permutations for each set of doctors adopting at the same time. Kalbfleisch and Prentice [16] claim that if the number of doctors that adopt in each month, $d_{(i)}$, is small compared to the number of doctors at risk, $R(t_{(i)})$, the approximation will be good. Nevertheless, the Peto-Breslow approximation will generate some asymptotic bias in both the estimation of the coefficients, $\hat{\beta}$, and in the estimation of the variance-covariance matrix.

After maximizing equation (3), I obtain a vector of estimated coefficients, $\hat{\beta}$, that allows me to compute the estimated hazard rate of adoption at time t for a doctor whose vector of observed characteristics is x:

$$\lambda(t; x) = \lambda_0(t) \exp\left(x(t) \hat{\beta} \right) \tag{4}$$

Where t is the time of adoption or censoring, $x(t)$ is the vector of covariates, $\hat{\beta}$ is the estimated vector of coefficients, and $\lambda_0(t)$ is the arbitrary baseline hazard function, which is not estimated.[20] This is how the estimated coefficients should be interpreted: the coefficient $\hat{\beta}_i$ of a time-invariant covariate x_i increases (if positive), or decreases (if negative) the estimated probability that the doctor adopts the new drug by the same amount in every month.

5 The Data

5.1 Overview

I use a new dataset, provided by the Health Department of the Emilia-Romagna Regional Government in Italy, that records all the prescriptions of anti-ulcer (A02B) and cholesterol-lowering drugs (B04A) in the province of Parma[21] from January, 1991 to December, 1994. For each doctor, I know the total number of units prescribed in each month for every presentation form and the total monthly expenditure on each presentation form. Since the prescription data are collected at the pharmacy level, they indicate exactly the drugs bought by a doctor's patients. In addition, I have another dataset, which lists for each

[20] The baseline hazard function is a peculiar characteristic of the non-parametric estimation method that I use; it depends on the *absolute* number of adoptions over time, that I am not explicitly modeling.

[21] Parma is one of the nine provinces in the region. The overall population in the province is about 400,000.

doctor: gender, year of birth, year of graduation from medical school and the total monthly number of patients listed with them. The National Health Service (NHS) requires every resident in a particular geographical area to list a general practitioner in the area to whom they must always refer for prescriptions. There is a total of 180 doctors working for the NHS in the province of Parma during the sample period, whose prescriptions I observe.[22] Some of these doctors (about 10% of the sample) retired or moved to other places during the sample period, so that the censoring for these doctors takes place before December 1994.[23]

5.2 Definition of the Covariates

To construct the likelihood function, I need to know how many months the doctor waited before prescribing the drug. TIMEADOP records the number of months to adoption, while ADOPTION is an indicator variable taking value 1 if the doctor ever prescribes the drug, and 0 otherwise. I define adoption as the first prescription of the drug by the doctor. Section 7 discusses alternative definitions.

Time-invariant doctors' characteristics I test whether time-invariant variables like gender, seniority in the profession,[24] and quantity of drugs prescribed by the doctor prior to entry have any systematic effect on the doctors' likelihood to adopt a new drug. That is, I analyze whether these variables help explain the observed heterogeneity in the doctors' adoption decisions. More specifically, I use the following variables:

- GENDER indicates the sex of the doctor. In my sample 88% of the doctors are men: it is equal to 1 if female, 2 if male.
- YSG indicates the seniority in the profession, i.e., the number of years since the doctors graduated from medical school. For the 180 doctors in the sample, seniority ranges from six to fifty years, and it is nineteen years on average.
- QUANTITY is the average monthly quantity prescribed by the doctor in the therapeutic market prior to entry of the new drug. Following Stern [26], I normalize the quantity prescribed using the *defined daily doses*.[25] This covariate distinguishes between heavy and light prescribers.

[22] I did not consider pediatricians, because there are only a few prescriptions in the entire sample by these doctors. This is clearly what I expected given the two markets that I am considering.

[23] There are 20 more doctors who joined the NHS in Parma during the sample period, but I have information on their prescriptions for only a short amount of time, so that I was forced to disregard them.

[24] Age and seniority in the profession are extremely correlated, therefore I only use seniority in the profession (YSG) in the estimates.

[25] According to this international measurement unit, an average patient requires a certain amount of the chemical compound every day. For example if an *average* patient requires two tablets of 150 mg of *ranitidine* a day, then the *defined daily dose* of *ranitidine* is 300 mg per day. If a doctor prescribes 10 boxes containing 10 pills of 300 mg ZANTAC in a month, then she prescribes (300 × 10 × 10)/300 = 100 patient-day units of ZANTAC.

[26] It is probably a combination of therapeutic and "economic" reasons, but for identification purpose, I define it as being driven by therapeutic considerations only.

These three covariates are used in all the estimations. Other covariates are built according to the specific characteristics of the entry episodes.

6 Results

6.1 Entry of "Homogeneous" Drugs

This section studies the entry episodes where the new drug is identical to some of the existing drugs. There are two groups of doctor covariates that I use in the estimations: (i) time-invariant covariates, described in the previous section, and (ii) covariates built using information from doctors' past prescribing behavior. What kind of information from past prescribing behavior helps me predict doctors' likelihood of adoption?

I want to test whether doctors who showed a preference for prescribing across brands in the past are more likely to prescribe a new homogeneous product (Hypothesis 2, H2). To build an index of dispersion for *each* doctor in the sample I compute the market share of each brand both in the therapeutic market, and in the molecule market. I use these market shares to compute the herfindahl index of concentration within a market, that is, the sum of the squares of the market shares. Higher values of the herfindahl index mean higher levels of concentration (or lower dispersion) in the market. Moreover, I compute the herfindahl index of dispersion at the *molecule* level (THERDISP) for each doctor in the sample. My main identifying assumption is that, after controlling for dispersion across molecules (THERDISP), which I assume driven by therapeutic reasons and by the heterogeneity of the patients' pool,[26] the dispersion at the *brand* level in the therapeutic market (HERFBRAND) depends only on the doctors' preference to prescribe across brands. That is, while a doctor may prescribe a high proportion of *ranitidine*, since *ranitidine* offers the best therapeutic properties to a large proportion of her patients, the choice to prescribe many different brands of *ranitidine* or only one depends only on the distribution of the doctors' benefits across brands—there is nothing medical in the choice between two brands of the *same* molecule. For example, a doctor might prescribe *ranitidine* to 60% of her patients, while another doctor prescribes *ranitidine* to only 35% of her patients; I assume that this depends on the characteristics of the patient. What I am interested in is whether these doctors prescribe only ZANTAC to all the patients receiving *ranitidine*, or whether they prescribe ZANTAC to 33% of the patients, RANIDIL to 33% and ULCEX to the remaining 33%.

Therefore, I expect a higher dispersion across brands (a lower value of HERFBRAND) to be positively correlated with adoption.

Doctors' preferences to prescribe multiple brands for each molecule (dependent on the distribution of the benefits) can also be proxied using other covariates: (i) TOT#BRANDS indicates the total number of different brands prescribed by the doctor in the therapeutic market before entry takes place. Since there are only a few chemical compounds in each market, if the doctor prescribes many brands, this means that the doctor is willing to prescribe across brands.[27] (ii) HERFMOL indicates the value of the herfindahl index *within the molecule market*.[28] If the doctor wants to specialize with one incumbent, they would just prescribe that brand; on the other hand, if they heavily prescribe across brands, this could mean that (a) the doctors find it optimal not to specialize, and (b) that these doctors are ready to prescribe many brands for the same molecule, therefore, these doctors should be more likely to prescribe a new brand for the same molecule.

Finally, since I have information on doctors' prescribing behavior in two therapeutic markets, I can also use the information on the other therapeutic market when studying a particular entry episode. That is, I can test whether doctors who are willing to prescribe across brands in *any* market are more likely to prescribe a new identical drug. (iii) THERDISP$_{-i}$ indicates the herfindahl index at the molecule level in the *other* therapeutic market; it is used as a control for unobserved patients' heterogeneity. HERFBRAND$_{-i}$ is the value of the herfindahl index at the *brand* level in the *other* therapeutic market.

Results Ten episodes of entry in my dataset deal with new vendors entering particular molecule markets with a perfectly homogeneous good sold at the same price as the incumbent drugs. Table 3 indicates the adoption rate of the ten drugs in my sample over time. That is, it shows the proportion of doctors that have adopted before (or at) t. Three entry episodes took place during the last six months of the sample period; moreover, two other entry episodes are relative to molecules rarely prescribed by doctors, therefore they elicited a very limited response. Therefore, I report the estimates of four of the five most relevant entry episodes: ANTRA in the *omeprazole* market; APLACTIN and PRASTEROL, in the *pravastatine* market; and CITOGEL in the *sucralfate* market.[29] The first three drugs entered exactly at the same time (May 1993), while CITOGEL entered in June, 1992. I

[27] Since HERFBRAND and TOT#BRANDS proxy exactly for the same underlying variable, they are used interchangeably.

[28] All the indexes are computed for the molecule market and the therapeutic market the new drug belongs to, unless otherwise specified.

[29] The results for entry of GASTROGEL are very similar to those for CITOGEL, therefore I do not report them.

Table 3: Adoption Rate of the New Drugs

Drug	Molecule	Entry	Months after entry		
			3	6	9
			12	18	20
Anti-ulcer Drugs					
CITOGEL(⋆)	*sucralfate*	6/92	5.56%	20.56%	28.33%
			37.37%	55%	57.78%
GASTROGEL	*sucralfate*	7/92	12.22%	38.33%	48.89%
			57.78%	70%	76.11%
ANTRA(⋆)	*omeprazole*	5/93	11.67%	31.67%	47.22%
			57.78%	72.78%	75.56%
NEO-GASTRAUSIL	*cimetidene*	7/93	1.11%	3.33%	3.33%
			3.33%	3.33%	
ROTIL	*niperotidine*	8/93	0.05%	6.11%	7.78%
			7.78%		
CRAFILAI	*sucralfate*	6/94	4.14%	7.69%	
PERULTID	*niperotidine*	9/94	11.6%		
Cholesterol-lowering Drugs					
APLACTIN(⋆)	*pravastatine*	5/93	7.87%	18.54%	32.02%
			34.27%	37.08%	39.33%
PRASTEROL(⋆)	*pravastatine*	5/93	6.18%	8.43%	10.67%
			14.04%	18.54%	19.1%
MEDIPO	*simvastatine*	6/94	4.79%	10.78%	

(⋆) Duration model estimates for these entry episodes are reported below.
Estimates for the remaining entry episodes are available from the author upon request.
Source: author's computations using the data described in section 5.

observe adoption rates ranging from 20% to 76% in the first 20 months after entry. There were three incumbents selling *omeprazole*, two incumbents selling *pravastatine*, and five incumbents selling *sucralfate* when entry occurred.

Table 4 reports the results of four different specifications for ANTRA. The first specification is the baseline model, since it includes the three covariates (GENDER, YSG and QUANTITY), that I use in every specification, and TOT#BRANDS, that is, the standard proxy for doctors' willingness to prescribe across brands. In the second specification, HERFBRAND is used instead of TOT#BRANDS as a proxy for preference to prescribe across brands; in the third specification a second index of dispersion (HERFMOL) is included; finally, the fourth specification uses the information about the doctors' preference to prescribe across brands in the *cholesterol-lowering* drug market.

The reported coefficient in the tables below is $e^{\hat{\beta}}$, and the reported t-statistic is a test that $e^{\hat{\beta}}$ is equal to 1. The vector of coefficients, $\hat{\beta}$ is obtained by maximizing equation (3) above. The interpretation of the coefficients derives from equation (4): a coefficient of 1.03, for example, indicates that a unit increase in the covariate implies a 3% increase in the hazard rate of prescribing the drug in *every* month. Time-invariant covariates increase or decrease the baseline hazard rate of adoption by the same amount in every month.

GENDER and YSG never have any significant impact on the likelihood of prescribing the new drug. The QUANTITY of anti-ulcer drugs prescribed by the doctor always increases the hazard rate of adoption in every month; the estimate is statistically significant in two of the four specifications. For example, in the second specification, an increase of 50 days[30] of anti-ulcer drugs prescribed on average in the months prior to entry, leads to an increase in the likelihood of adopting ANTRA in any month by 3%. The two proxies (HERFBRAND and TOT#BRANDS) for the preference to prescribe across brands always have the expected sign: doctors who chose to prescribe more brands in the past are more likely to prescribe ANTRA. The coefficient on TOT#BRANDS in the two specifications indicates that one additional brand prescribed prior to entry of ANTRA increases the hazard rate of adopting in every month by 3.5-4%. The sample average for TOT#BRANDS is 24, therefore this covariate has an important impact as a predictor of the decision to adopt ANTRA. In specification (2), the coefficient on HERFBRAND indicates that a unit increase in concentration causes a 2% reduction in the likelihood of adopting ANTRA; it is not precisely estimated though. Moreover, doctors more dispersed across the incumbent brands of *omeprazole* (HERFMOL) are more likely to adopt ANTRA. This coefficient is not precisely estimated, either. Finally, in the fourth specification, the coefficient on the doctors' herfindahl index in the cholesterol-lowering drug market is negative and statistically

[30]The mean value of QUANTITY in the sample is about 800 days.

Table 4: Cox Estimations–Antra

Product–ANTRA ; molecule market–*omeprazole* (A02B); Entry–5/1993; Adoption rate–75.56%;
Producers already in the market–3.
Asymptotic t-statistic in parenthesis.

Specifications	(1)	(2)	(3)	(4)
Dependent Variable–# Months before First Prescription				
Doctors' time-invariant characteristics				
Gender: 1 if Female,	.811	.845	.836	.889
2 if Male	(-.67)	(-.54)	(-.58)	(-.38)
Years since Graduation	.959	.962	.957	.949
(YSG)	(-.83)	(-.77)	(-.88)	(-.77)
Quantity of Anti-ulcer drugs prescribed				
Average Quantity				
Prescribed Monthly/50	1.025	1.03	1.014	1.028
(QUANTITY)	(1.36)	(1.73)	(.68)	(1.64)
Anti-ulcer drug market; (*)Cholesterol-lowering drug market				
Herfindahl at				
the Molecule level	.989	.991	.993	1.005(*)
(THERDISP)	(-1.12)	(.82)	(-.73)	(.38)
Herfindahl at				
the Brand level		.98		.973(*)
(HERFBRAND)		(-.68)		(-1.901)
Total #Brands	1.04		1.035	
(TOT#BRANDS)	(1.84)		(1.637)	
Molecule Market				
Herfindahl within the				
molecule market		.989	.989	
(HERFMOL)		(-1.18)	(-1.21)	
Log-likelihood	-610.62	-610.02	-608.91	-611.56
# Observations	177	174	174	177

significant. This means that doctors who showed a preference for prescribing across brands in the *cholesterol-lowering* drug market, have a higher propensity to prescribe ANTRA.

These results imply that Hypothesis 1 (H1) is rejected in two of the four specifications. On the contrary, Hypothesis 2 (H2) is not rejected by these estimates. Doctors' willingness to prescribe across brands is a good predictor of the doctors' likelihood of adopting a new identical drug. Finally, GENDER and seniority (YSG) are not related to the likelihood of adopting. Do these results hold for the other entry episodes as well?

Table 5 reports the results of similar Cox estimations for the two new *pravastatines* (cholesterol-lowering drugs): APLACTIN and PRASTEROL. A dummy variable controls for the differences in supply side characteristics (such as size of the firm, and advertising levels) between the two drugs. APLACTIN is prescribed much more often: the average doctor is two and a half times more likely to adopt APLACTIN in every month. The results are very similar to those for ANTRA, reported in table 4. The variables proxying for the preference to prescribe across brands are even more significant and with larger coefficients. An increase of one unit of TOT#BRANDS increases the hazard rate of adoption of 9.8-9.9% in *each* month. In the third specification, I include a new covariate proxying for existing ties with the incumbents. This variable counts the number of different brands of *pravastatine* prescribed at least once by the doctor before entry (which can be 0,1 or 2). This covariate *does not* have any statistically significant effect. There are probably counteracting effects: doctors who prescribed more brands of *pravastatine* before are more likely to prescribe *pravastatine*, but at the same time they might have developed a habit for prescribing the incumbent brands. Finally, QUANTITY prescribed by the doctors does not seem to have any statistically significant effect on the likelihood of prescribing a new brand of *pravastatine*.

Finally, there are two entry episodes (CITOGEL and GASTROGEL) where new firms entered the *sucralfate* market with presentation forms not previously available. The incumbents reacted by introducing the same presentation forms shortly afterwards.[31] Therefore, these entry episodes are very similar to the others analyzed in this section. The minor innovation could have simply contributed to a faster adoption. Since patient heterogeneity could have been a factor in the doctor's decision whether to adopt the new drug, I include an additional covariate which should proxy for some of the heterogeneity in the patients' pool. PATHET is the ratio of the number of patients listed with the doctor whose age is greater than 65 over the number of patients aged between 14 and 65. This is because doctors who have patients that on average might receive a higher benefit from the new presentation form could be more likely to adopt (e.g., a higher proportion of old patients whose compliance

[31] The new presentation form was a syrup containing 150 milliliters of *sucralfate* that entered before one of the incumbents, SUCRATE, started marketing the new presentation form a month later.

Table 5: Cox Estimations–Aplactin & Prasterol

Products–APLACTIN and PRASTEROL; molecule market–*pravastatine* (B04A); Entry–5/1993; Adoption rate–39.33% APLACTIN, 19% PRASTEROL; Producers already in the market–2.
Asymptotic t-statistic in parenthesis.

Specifications	(1)	(2)	(3)	(4)
Dependent Variable–# Months before First Prescription				
Doctors' time-invariant characteristics				
Gender: 1 if Female, 2 if Male	1.719 (1.24)	1.742 (1.27)	1.736 (1.26)	1.625 (1.108)
Years since Graduation (YSG)	.954 (-.85)	.966 (-.61)	.956 (-.82)	.985 (-.26)
Quantity of Cholesterol-Lowering Drugs Prescribed				
Average Quantity Prescribed Monthly/50 (QUANTITY)	1.036 (1.33)	.991 (-.26)	1.036 (1.36)	1.063 (2.6)
Cholesterol-lowering drug market; (+)Anti-ulcer drug market				
Herfindahl at the Molecule level (THERDISP)	.985 (-1.34)	1.031 (2.08)	.985 (-1.37)	1.017(+) (1.54)
Herfindahl- Brand level (HERFBRAND)		.920 (-4.17)		.950(+) (-2.92)
Total #Brands (TOT#BRANDS)	1.098 (2.73)		1.099 (2.74)	
Molecule Market				
Herfindahl within the Molecule market (HERFMOL)		.998 (-.206)		
# Different Brands of *pravastatine* Previously Prescribed: 0, 1, 2			.891 (-.28)	
Dummy: 0 if PRASTEROL, 1 if APLACTIN	2.515 (4.38)	2.587 (4.51)	2.517 (4.39)	2.508 (4.37)
Log-likelihood	-565.08	-558.16	-565.05	-558.55
# Observations	350	344	350	350

with syrup is higher than the compliance with tablets). Patient heterogeneity was not an issue in the previous entry episodes analyzed, since the presentation forms were exactly identical to those offered by the incumbents.

Table 6 presents the results for CITOGEL. PATHET does not have any statistically significant effect on the likelihood of prescribing CITOGEL. This could be either because patient heterogeneity is not an important factor, or because the available proxy does not adequately capture patient heterogeneity. Otherwise, the results are very consistent with those for ANTRA, APLACTIN and PRASTEROL: doctors who were more dispersed across brands prior to entry are more likely to adopt CITOGEL.

Together the results from this section imply that (i) QUANTITY prescribed by doctors does not have a significant impact on their hazard rate of prescribing an identical drug; that is, Hypothesis 1 (H1) is rejected, and (ii) Hypothesis 2 (H2) holds in all the specifications: previous dispersion across brands, once controlled for dispersion across molecules, is a good predictor of the likelihood of adopting a new "homogeneous" drug. This means that some doctors are more likely to prescribe a new identical drug than others, and that this is dependent on their past prescribing behavior, rather than on age, gender or seniority. This indicates that pharmaceutical firms cannot base their marketing policies on easily observable doctor characteristics (such as age and seniority), but they need to infer doctors' "willingness-to-experiment" from their past prescribing behavior. Finally, these regressions only estimate the *relative* likelihood of adopting one drug by the different doctors; my estimates do not explain why the actual number of doctors who adopt different drugs differs (this is because the baseline hazard function is not estimated).

6.2 Introduction of a New Presentation Form by an Incumbent Firm

In my sample, there are many instances of incumbents introducing new presentation forms. Tables 1 and 2 list the fifteen entry episodes in this category. When I estimate doctors' reaction to the introduction of a new presentation form by an incumbent firm, I need to take into account a few differences from the entry episodes studied in the previous section. First, the firm introducing the new presentation form is an incumbent, therefore I want to use the information I have about past prescriptions of the *brand* by the doctors. Second, doctors might have heterogeneous preferences about prescribing different presentation forms (i.e., some doctors tend to prescribe one presentation form for each brand, while others might prescribe all the presentation forms available). Therefore, I make the following changes to the covariates that I use in section 6.1:

HERFBRAND I compute the herfindahl index at the *presentation form level*, because I want to take into account both the preference for prescribing across brands, and the

Table 6: Cox Estimations–Citogel

Product–CITOGEL; molecule market–*sucralfate* (A02B); Entry–6/1992; Adoption rate–73.69%; Producers already in the market–5.

Asymptotic t-statistic in parenthesis.

Specifications	(1)	(2)	(3)	(4)
Dependent Variable–# Months before First Prescription				
Doctors' time-invariant characteristics				
Gender: 1 if Female, 2 if Male	.504 (-2.23)	.531 (-2.05)	.571 (-1.69)	.477 (-2.47)
Years since Graduation (YSG)	1.03 (.64)	1.03 (.63)	1.01 (.211)	1.013 (.29)
Ratio of Old to Young Patients (PATHET)	1.805 (1.16)	1.651 (.98)	1.422 (.62)	1.858 (1.18)
Quantity of Anti-ulcer drugs Prescribed				
Average Quantity Prescribed Monthly/50 (QUANTITY)	1.004 (.35)	.992 (-.41)	1.003 (.24)	.983 (-1.07)
Anti-ulcer drug market; (•)cholesterol-lowering drug market				
Herfindahl at the Molecule level (THERDISP)	1.004 (.43)	.997 (-.308)	1.004 (.39)	1.01(•) (.69)
Herfindahl at the Brand level (HERFBRAND)	.973 (-2.05)		.984 (-1.06)	.968(•) (-2.281)
Total #Brands Prescribed (TOT#BRANDS)		1.052 (2.126)		
Molecule Market				
Herfindahl within the Molecule (HERFMOL)			.989 (-1.627)	
Log-likelihood	-607.71	-607.65	-579.38	-602.29
# Observations	177	177	168	175

preference to prescribe many presentation forms for the same brand expressed by each doctor prior to entry.

TOTAL#PF counts the total number of *different presentation forms* prescribed by the doctor prior to the introduction of the new presentation form. It is an alternative to using HERFBRAND as a proxy.

FREQPDT is a *brand loyalty* variable for the doctor. It counts the number of months prior to entry when the doctor prescribed the brand at least once. The idea is that these doctors might receive higher benefits when they prescribe the brand, therefore they should be more likely to prescribe the new presentation form (H3).

Results Table 7 presents the results for the introduction of a new presentation form of SUCRATE,[32] an anti-ulcer drug already available in the market in a different presentation form.[33] GENDER and seniority (YSG) do not have a statistically significant effect. The quantity of anti-ulcer drugs prescribed by the doctor (QUANTITY) does not have any effect on the likelihood of adoption. Doctors who heavily prescribed across presentation forms in the entire market have a much higher likelihood of prescribing the new presentation form. TOT#PF in specification (2) indicates that doctors who prescribed many different presentation forms in the past have a higher likelihood of adopting: one additional presentation form prescribed before entry increases the likelihood of adopting by 5.6% in each month. In the fourth specification, I compute the herfindahl index at the presentation form level in the cholesterol-lowering drug market. Doctors more dispersed in the cholesterol-lowering drug market are more likely to prescribe a new presentation form of SUCRATE in the anti-ulcer drug market. The most important covariate is FREQPDT: doctors who often prescribed SUCRATE in the past have a much higher likelihood of adopting the new presentation form of SUCRATE in every period. An additional month of prescription in the past implies about a 33% increase in the conditional hazard rate of adoption in every month. These results show that Hypothesis 3 (H3) is consistent with the empirical findings: doctors show strong brand loyalty.

Overall, the results are consistent with the findings for entry of new vendors discussed in section 6.1: doctors have heterogeneous preferences; knowing the doctors' age or seniority does not help predict their likelihood of adoption; knowing their past prescribing

[32] The results for the other fourteen entry episodes are similar. They are available from the author upon request.

[33] It was being sold in boxes of 30 packages, each containing 1 gram of *sucralfate*. The new presentation form is a syrup containing 150 milliliters of *sucralfate*.

Table 7: Cox Estimations–Sucrate

Product–SUCRATE; molecule market–*sucralfate* (A02B); Entry–7/1992; Adoption rate–59.44%; Producers already in the market–6.

Asymptotic t-statistic in parenthesis.

Specifications	(1)	(2)	(3)	(4)
Dependent Variable–# Months before First Prescription				
Doctors' time-invariant characteristics				
Gender: 1 if Female, 2 if Male	.835 (-.51)	.818 (-.56)	.988 (-.03)	.95 (-.14)
Years since Graduation (YSG)	.964 (-.63)	.953 (-.82)	.917 (-1.52)	.928 (-1.32)
Quantity of Anti-ulcer drugs prescribed				
Average Quantity Prescribed Monthly/50 (QUANTITY)	.995 (-.295)	.967 (-1.553)	.997 (-.174)	.998 (-.089)
Anti-ulcer drug market: (•)Cholesterol-lowering drug market				
Herfindahl at the Molecule level (THERDISP)	1.019 (1.722)	1.023 (2.034)	.995 (-.504)	1.000(•) (1.462)
Herfindahl at the Brand level (HERFBRAND)	.945 (-3.201)	.966 (-1.833)		.972(•) (-2.163)
Total #Pres. Forms (TOT#PF)		1.056 (2.431)		
Molecule Market				
Total # Presentation Forms in the molecule (#PRESFORM)			1.226 (3.024)	
Brand-Loyalty by the Doctor				
Frequency of Adoption of the Brand in the past (FREQPDT)	1.331 (6.64)	1.315 (6.29)	1.317 (6.34)	1.342 (6.88)
Log-likelihood	-483.75	-480.75	-485.33	-487.22
# Observations	177	177	177	175

behavior is very useful to infer who are the doctors most likely to adopt. The main difference with the previous section is that the additional information available regarding the frequency of prescription of the brand in the past is very useful to predict who will adopt.

7 Additional Empirical Analyses

Choice of the Dependent Variable In the duration model estimated above, I use as a dependent variable time until the first prescription. The risk in analyzing the first prescription only is to mix adoption and mere experimentation by the doctors. In order to check whether this is the case, I re-estimated the model for some entry episodes using as a dependent variable a threshold percentage of units of the new brand prescribed by the doctor over the total prescriptions for the molecule. I used 10%, 20%, and 40% market share thresholds.[34] Table 8 compares the results I obtained using the different dependent variables for two entry episodes: ANTRA and APLACTIN. The alternative specification that I report uses a 40% threshold as a dependent variable. In the ANTRA specification, I use the average number of patients listed with the doctor, AVG, instead of QUANTITY to control for the amount of anti-ulcer drugs previously prescribed. Since AVG and QUANTITY are very collinear, this choice does not change the estimated coefficients for the other variables. The results are very similar both in terms of point estimates and statistical significance, therefore I conclude that the same factors drive both experimentation and larger scale adoption.

Firm loyalty Pharmaceutical firms tend to operate in most therapeutic markets. Since I observe doctors' prescriptions in two therapeutic markets, I investigate whether general practitioners tend to prescribe the products of some firms more often than others. The best possible tests for firm loyalty are clearly those involving the same firms operating in the two therapeutic markets, since within the same therapeutic market there is also competition among products offered by the same firm taking place (e.g., a firm marketing two different molecules treating the same diagnosis), which makes identification more difficult.

The best natural experiment in my dataset concerns two molecules (*famotidine* and *simvastatine*), marketed in the two different therapeutic markets (anti-ulcer drugs and cholesterol-lowering drugs) by the same three firms (Merck, Sigma-tau, and Neo-Pharma, a small Italian producer). I test whether the sample averages of the market shares for the firms across doctors are significantly correlated in the two markets. I expect to see a positive correlation between market shares for the same doctor in the two markets in case

[34] The threshold is computed using the defined daily doses normalization.

Table 8: Cox Estimations–Different Dependent Variables

Entry Episodes	(ANTRA)		(APLACTIN)	
Specifications	(*)	(**)	(*)	(**)
Dependent Variable–(*): # Months before First Prescription; (**): 40% Threshold				
Doctors' time-invariant characteristics				
Gender: 1 if Female 2 if Male	.901 (-.26)	.918 (-.27)	.963 (-.06)	1.306 (.55)
Years since Graduation (YSG)	1.055 (.828)	.959 (-.826)	.9 (-1.11)	.946 (-.801)
Average Number of Listed Patients (AVG)	.953 (-2.57)	1.007 (.591)		
Quantity of Anti-ulcer drugs prescribed; (*)Cholesterol-Lowering				
Average Quantity Prescribed Monthly/50 (QUANTITY)			.999(*) (-.007)	1.008(*) (.22)
Anti-ulcer drug market; cholesterol-lowering drug market				
Herfindahl at the Molecule level (THERDISP)	.997 (-.197)	.993 (.599)	1.036(*) (1.521)	1.031(*) (1.679)
Herfindahl at the Brand level (HERFBRAND)	.961 (-1.904)	.97 (-1.947)	.891(*) (-3.43)	.905(*) (-3.86)
Molecule Market				
Herfindahl within the Molecule Market (HERFMOLE)			1.003(*) (.24)	.997(*) (-.239)
Log-likelihood	-354.813	-615.04	-210.23	-323.65
# Observations	177	177	172	172

Asymptotic t-statistic in parenthesis.

(**) The dependent variable is 1 when the doctor prescribes a proportion of the brand under study equal to at least 40% of the total amount prescribed for the molecule.

Table 9: Firm Loyalty

FAMOTIDINE(A02B)-SIMVASTATINE(B01A)

Average monthly market shares across doctors

CORRELATIONS

	Merck *simvastatine*	SigmaTau *simvastatine*	NeoPH *simvastatine*
Merck *famotidine*	.0195		
SigmaTau *famotidine*		.0425	
NeoPh *famotidine*			.1094

Source: Author's computations using the data described in section 5. Sample period: 48 months (January, 1991 to December, 1994).

of an unobservable relationship between the doctor and the firm. This is because the three firms started marketing the brands at the same time with equal prices; therefore, there nothing prevented a doctor from specializing. Table 9 reports the correlation coefficients across doctors for the sample average of the market shares: they range from .0195 to .1094. Therefore, the hypothesis of positive correlation (H4) is rejected at the 95% significance level for all three firms.[35] Figure 5 graphs the correlation of the sample averages across the two markets for one of the three firms (Sigma-Tau).

There is another similar situation in my data: two Italian firms (Firma, and Lusofarmaco) purchased the license to produce the same two molecules (*ranitidine* in the anti-ulcer drug market, and *gemfibrozil* in the cholesterol-lowering drug market) in two different markets. Table 10 reports the correlation between the market shares in the two markets across doctors: they are respectively 18.46%, and 2.32%. The same test previously described fails to reject the hypothesis of firm loyalty (H4) at the 95% significance level for Firma, while it allows me to reject the hypothesis of firm loyalty for Lusofarmaco. Together the results indicate that doctors do not specialize across firms.

I can further test the hypothesis of firm loyalty (H4) by analyzing the entry episodes.

[35] The hypothesis is tested assuming that $p = \text{invt}(n-2, r\sqrt{1-r^2})$, where *invt* indicates the inverse two-tailed cumulative t-distribution, n is the number of observations and r is the correlation coefficient.

Table 10: Firm Loyalty (2)

RANITIDINE(A02B)-GEMFIBROZIL(B01A)

Average monthly market shares across doctors

CORRELATIONS

	Firma *gemfibrozil*	Lusofarmaco *gemfibrozil*
Firma *ranitidine*	.1846(*)	
Lusofarmaco *ranitidine*		.0232

Source: Author's computations using the data described in section 5. Sample period: 48 months (January, 1991 to December, 1994). (*) significant at 95%

Under the null hypothesis of firm loyalty, once I control for doctors' heterogeneity, the doctors who more often prescribe a drug produced by a firm in other molecule markets, should be the ones more likely to adopt a *new* drug introduced by the same firm. The evidence is summarized in table 11 and it is puzzling. The Cox estimations are the same baseline specifications reported in the section 6.1 with the inclusion of an additional covariate whose statistical significance I am interested in. Table 11 shows that the hypothesis of firm loyalty (H4) is generally rejected in my data: the effect that familiarity with the firm has on the likelihood of the new drug being adopted by the doctor is either negative or positive, but not statistically significant. This is true both when I analyze the introduction by the firm of new brands in a therapeutic market where it already operates, and when I analyze the introduction of new brands in a therapeutic market where the firm was not operating.

The evidence of firm loyalty reported above is puzzling especially under the hypothesis of unobservable benefits going to the doctor. A possible explanation is that the optimal distribution of prescriptions for the doctors (given the pool of patients) might require that they prescribe a certain threshold quantity from as many vendors as possible, instead of developing very strong ties with only some of them. In order to have more definite results, I would need to look across more drug markets.

From my sample to national level data This study so far has analyzed first adoption by doctors. Figure 6 summarizes the in-sample movement in market shares for the vendors

Table 11: Firm Loyalty (3)

Summary of Cox Estimations

Effect of the market share of Merck's *simvastatine* (B04A) on the adoption of a new presentation form of *famotidine* (A02B) introduced by Merck	negative
Effect of the market share of Sigma-Tau's *simvastatine* (B04A) on the adoption of a new presentation form of *famotidine* (A02B) introduced by Sigma-Tau	positive (not significant)
Effect of the quantity prescribed of *omeprazole* (A02B) by Malesci on the adoption of a new presentation form of *sucralfate* (A02B)	positive (not significant)
Effect of the quantity prescribed of *omeprazole* (A02B) by Bracco on prescriptions of a new *sucralfate* (A02B) by Bracco	negative
Effect of the frequency of prescriptions of *omeprazole* (A02B) by Bracco on prescriptions of a new *sucralfate* (A02B) by Bracco	positive (significant*)
Effect of the frequency of prescriptions of anti-ulcer drugs by Malesci on prescriptions of a new cholesterol-lowering drug (*pravastatine*) by Malesci	positive (not significant)
Effect of the prescribed quantity of anti-ulcer drugs by Malesci on prescriptions of a new cholesterol-lowering drug (*pravastatine*) by Malesci	positive (significant*)

By frequency, I mean number of previous months when the drug was prescribed by the doctor. Quantity is defined in terms of *defined daily doses*. A02B: anti-ulcer drug market; B04A: cholesterol-lowering drug market. Source: estimations by the author; they are not reported, but they are available upon request.

of *omeprazole* during my sample period. Figure 7 shows the corresponding movement in market shares in the Italian market for the vendors of *omeprazole* during my sample period. The dynamics are very similar. This shows that the behavior of the doctors in my sample could be representative of the behavior of Italian doctors. The market share for ANTRA constantly increases over time, although it takes two years to reach a 20% market share, which is the market share of LOSEC, the least successful of the three incumbents. According to my findings, one component of the slow increase in market share is the heterogeneity of doctors in terms of different preferences for prescribing a new identical drug. Coscelli and Shum [6] show that adoption, and widespread prescription is much faster for innovative drugs.

8 Conclusions

My analysis of doctors' reaction to entry of new drugs has produced three distinct sets of results. First, I find that new entrants with therapeutically equivalent products fail to win large market shares (the baseline hazard rate of adoption is generally low). Moreover, doctors who prescribe many different drugs in a therapeutic market are more likely to prescribe new drugs: for those doctors the hazard rate of adoption is significantly higher in every period. Together these findings indicate that, since price competition is ruled out, an entrant would be able to compete with the incumbents more effectively if it were able to single out the doctors who have a higher likelihood to adopt a new *identical* drug in any time period (that is, those doctors who showed a "willingness-to-experiment" across brands in the past). The observed slow growth in market shares for new products is consistent with the findings by Hellerstein [14]. Moreover, in Coscelli [5], I find very strong brand loyalty by consumers and habit persistence by doctors, together creating order of entry effects in the market. On the other hand, some previous researchers (e.g., Frank and Salkever [8] and Stern [26]) explain the slow growth in market shares for generic drugs vis-a-vis the more expensive pioneer drug in the US market by assuming that there is a "perceived" quality difference between the products. In this paper, I observe the entry of a new drug (ANTRA) marketed by the patent-holder of *omeprazole*, Astra, three years after *omeprazole* started being marketed by three licensees. ANTRA experienced the same problems in gaining market shares that licensees encounter; even if probably ANTRA's entry episode was, relatively speaking, one of the most successful during the sample period I analyze. Notwithstanding, ANTRA's struggle to win a large market share suggests that the brand-loyalty effect is a crucial factor in explaining changes in market shares over time in the Italian pharmaceutical market. The US market could differ in terms of brand loyalty

effects since there is not a licensing system. Patent-holders and generic producers tend to be more differentiated, and the "perceived" quality difference between the products might play an important role in the market.

Second, we observe the introduction of many new presentation forms by the incumbents. This is consistent with what economic theory (Schmalensee [23]) predicts: incumbents want to cover every niche of the market to prevent potential entrants from gaining a foothold in the market with minor innovations. I find that the incumbents are very successful at convincing the doctors who usually prescribe the brand to adopt the new presentation forms.

Third, this study analyzed doctors' prescription patterns across drug classes. Doctors show little firm loyalty *across* drug classes. Even when the doctors are free to choose the vendor of a new molecule, they fail to select those whose products they prescribe the most in other drug classes. This important finding seems to suggest either that *unobservable* benefits from drug companies are not a very important factor in the doctors' decision process, or that doctors maximize their objective function by reaching a threshold level of prescriptions for many firms.

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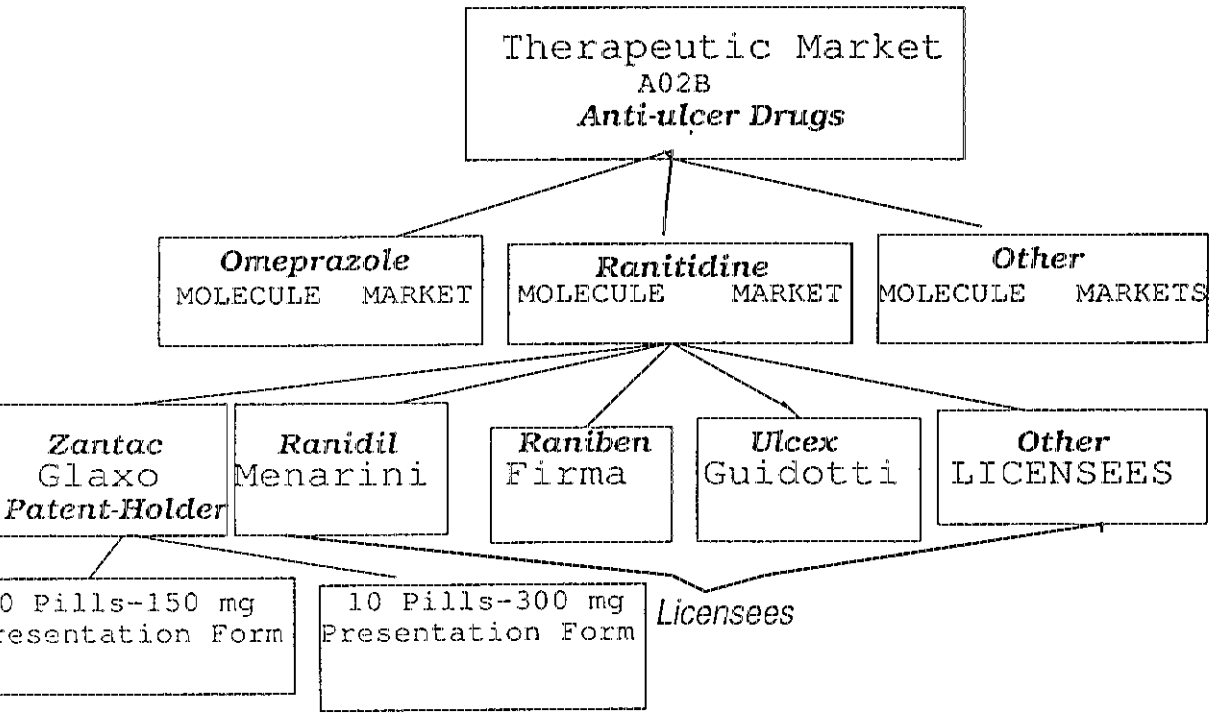
Market Structure and Terminology



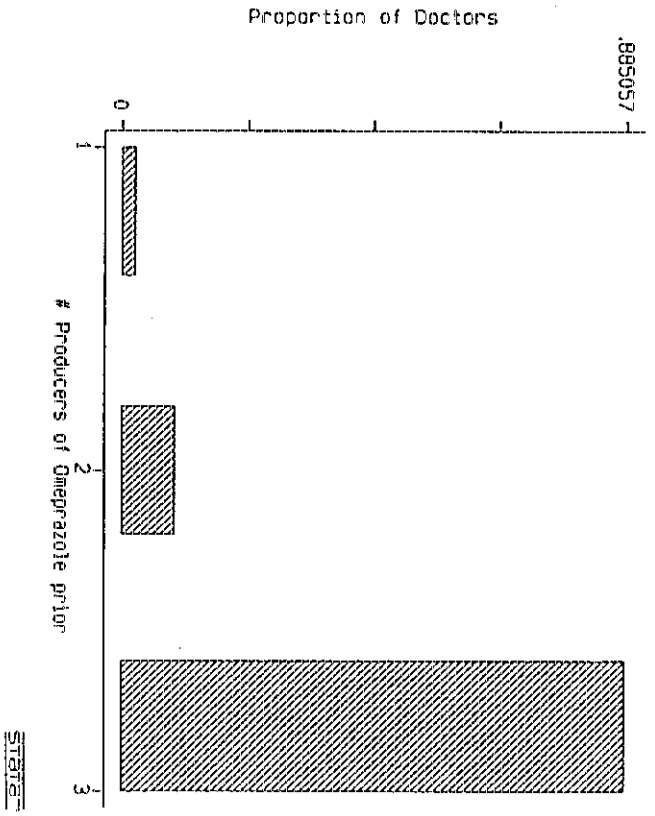


Figure 2: On the y-axis, proportion of the 180 in-sample doctors, who prescribed (0, 1, 2, or 3) brands of *omeprazole* at least once in the 28 months between the beginning of the sample (January, 1991), and entry of the fourth producer (May, 1993).

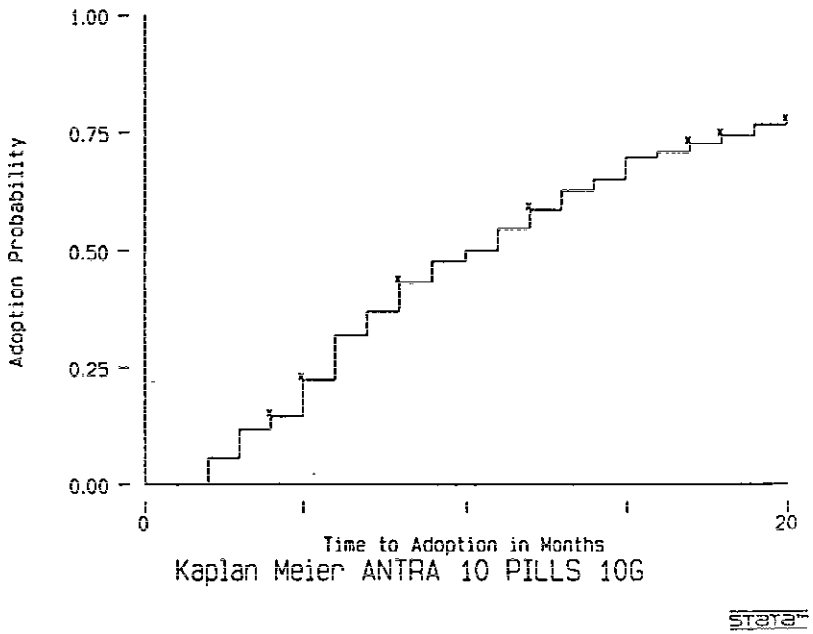


Figure 3: Kaplan-Meier: estimation of doctors' adoption of ANTRA. On the x-axis, number of months after entry. On the y-axis, estimated proportion of doctors who adopted before t, or at t. The vertical steps represent the fraction of doctors who adopted at t. The x signs indicate doctors who were censored before the end of the sample period.

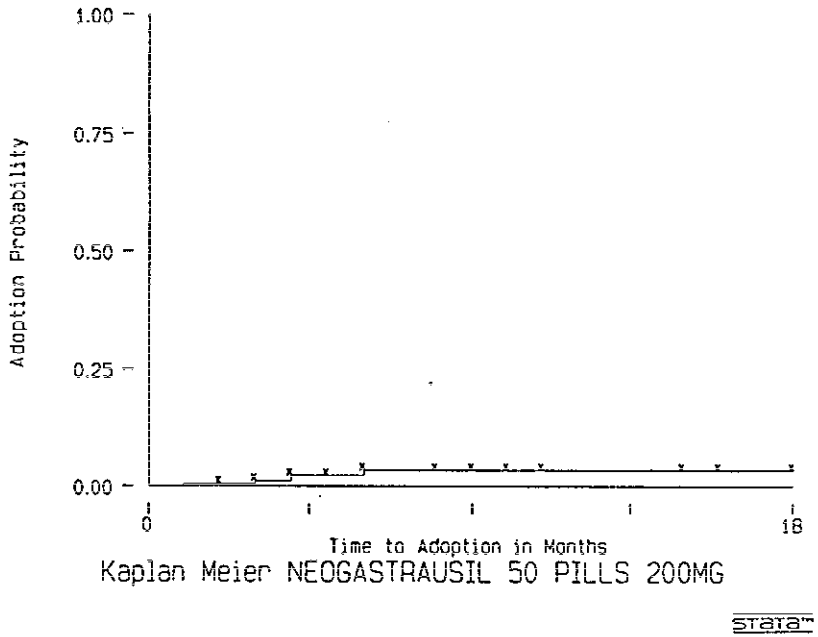


Figure 4: Kaplan-Meier: estimation of doctors' adoption of NEO-GASTRAUSIL. On the x-axis, number of months after entry. On the y-axis, estimated proportion of doctors who adopted before t, or at t. The vertical steps represent the fraction of doctors who adopted at t. The x signs indicate doctors who were censored before the end of the sample period.

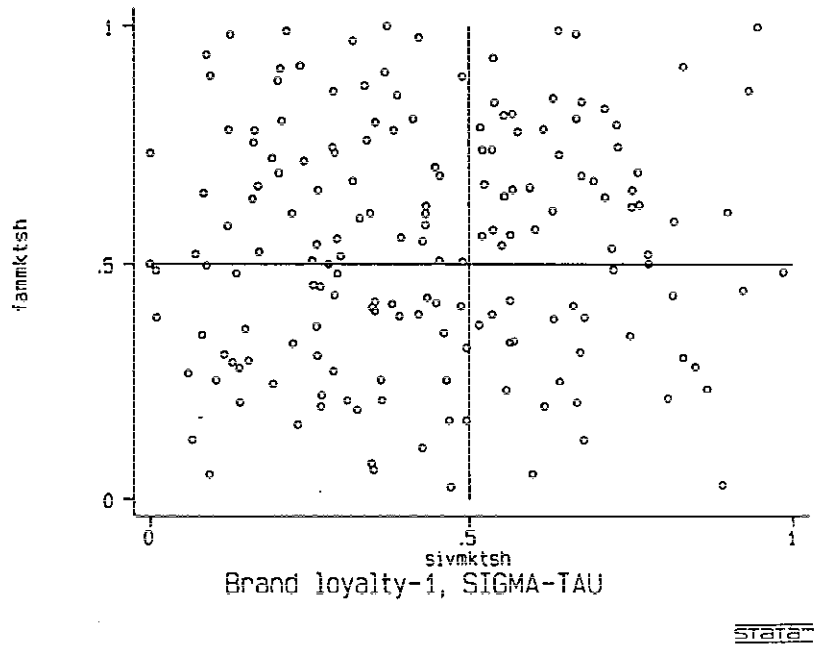


Figure 5: On the x-axis, in-sample monthly averages of the market shares of *simvastatine* marketed by Sigma-Tau (other two competing brands were available) for each doctor; on the y-axis, in-sample monthly averages of the market shares of *famotidine* marketed by Sigma-Tau (other two competing brands were available) for each doctor.

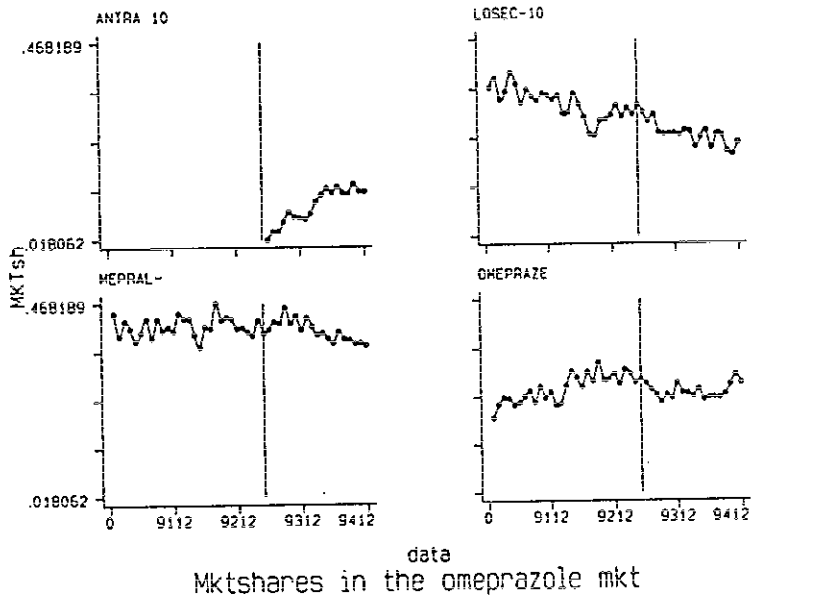


Figure 6: *In-sample* market shares for the four brands available in the *omeprazole* market. The vertical bar for May 1993 indicates the date of entry of ANTRA, the fourth brand. Sample period: January, 1991 to December, 1994. Source: Author's computations using the data described in section 5.

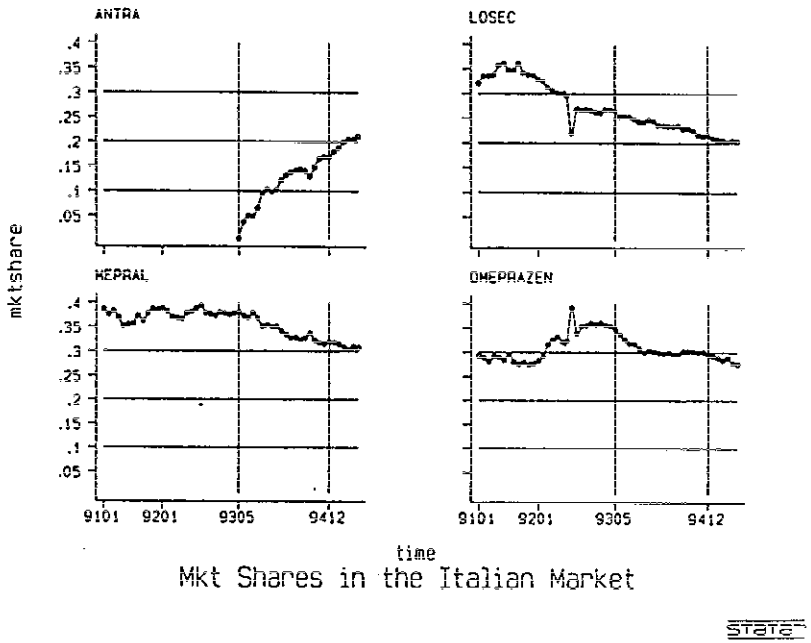


Figure 7: *National* market shares for the four brands available in the *omeprazole* Italian market. The vertical bar for May 1993 indicates the date of entry of ANTRA, the fourth brand. The second vertical bar (December, 1994) indicates the end of the sample period. Sample period: January, 1991 to June, 1995. Source: IMS Italy.