Diffusion of new pharmaceuticals: is there a first-mover advantage?*

Victoria Serra-Sastre
Alistair McGuire

LSE Health
London School of Economics and Political Science
Houghton Street
London WC2A 2AE
(e-mail: v.serra@lse.ac.uk)

***Work in Progress**
Please do not quote without authors' permission

HESG September 2007
Brunel University

1. Introduction

The study of the diffusion of medical technology has been growing over the last few years mainly due to the identification of innovation as the main driver of the health care expenditure increase experienced in many developed countries over the last decades. Among different technologies, pharmaceuticals are of particular interest because they represent a significant percentage of the total health expenditure – around 15% in OECD countries - and also because of the growth in the pharmaceutical expenditure which fluctuated on average between 3.5% and 4.6% annually over the 80s and 90s. In the UK, for instance, the expenditure in pharmaceuticals was 12.8% of the total health care expenditure in 1980 and 16.1% in 1996 (Jacobzone, 2000).

This paper studies the diffusion of new pharmaceuticals through examination of the different information mechanisms used by physicians to assimilate the uncertain quality attributes of these new products into their treatments. In particular, the paper looks at the diffusion of different molecules within the same therapeutical class as to explain differences in the diffusion paths of products that are close substitutes. Molecules in the group were sequentially introduced and despite being similar in composition they competed in the market as treatment for the same condition. However, there are observed differences in the uptake of molecules with the expectation that the first product to be introduced has a clear market advantage with respect to products introduced later. This paper looks at the determinants of these differences and examines the diffusion path of the competing molecules as potential products that could destabilize the advantage of the pioneer drug. This is motivated by the fact that the prescription rates associated with the last entrant were significantly higher than a number of incumbents. The decision by the physician to prescribe the molecules is examined through analysis of the competition between the different branded molecules. The competition

between these branded molecules and their equivalent generics are not considered here as over the study period these molecules enjoyed patent protection and generic competition was non existent[1].

The entry of a new product in any market and especially in the pharmaceutical market has been of interest in economics as it provides a clear example of first-mover advantage with respect to later entrants. The optimal price setting followed by the manufacturer of the pioneer product has been at the core of the analysis as a means of understanding the behaviour of the producer when facing the projection of potential competitors entering the market. In general, a monopolist's objective function would adopt the optimal price path which prevented entry by competitors. An incumbent firm would defend a monopoly position, established through patent protection for example, and only when the patent expired would competitors enter the market and face such a racing strategy. A major difference in the pharmaceutical context is that close drug substitutes may enter the market even when the incumbent holds patent protection and although they are not direct competitors in terms of being bioequivalent products they are close enough as to compete for the prescription demand.

In this study, we look at the diffusion of statins, a class of cholesterol lowering drugs that have been shown to be highly effective in the primary and secondary prevention of cardiovascular disease. Diffusion is examined within the UK NHS primary care sector at the practice level using IMS prescription data for the period 1991-2004. After simvastatin was firstly introduced in the UK in 1989, several molecules within the same therapeutical class were introduced over time. Simvastatin as the initial entrant may have enjoyed first mover competitive advantage in this market with respect to the other molecules. Thus differences in uptake across the various molecules may be explained because of supply and demand factors. The body of literature that looks at the importance of being first in the market normally addresses the problem analysing the manufacturer characteristics and the elements of the production function that could generate the competitve advantage. However, this paper looks at the diffusion pattern of molecules within the statins group comparing the different mechanism used by doctors as they acquire information on the quality characteristics of the product and the resultant differences that arise in uptake rate, placing emphasis on the micro components that explain individual behaviour in the drug choice. The study addresses questions such as: Which are the determinants of the diffusion of the molecules? How do we explain differences in demand

[1] This allows to focus on the pure competition effects between molecules and eliminates any competitive issue between branded drugs and generics.

of products that are close substitutes? Why is the prescription of simvastatin (the first molecule to be marketed) higher than the other competing molecules specially after long after the first molecule is introduced? Is there a first-mover advantage?

Section 2 outlines the relevant evidence from the literature on the first-mover advantage and the approaches used in the literature on the diffusion process. Section 3 presents the diffusion model. The following section describes the data used and the panel data methods for the estimation of the demand equations. Section 5 presents the results and conclusions are set out in the final section.

2. The advantage of being first and the diffusion process

A number of studies have analysed the importance of being the first entrant in the industry. Firms that are predominant in the market are usually the first to enter and this has generated an increasing interest in the analysis of the mechanisms perpetuating this advantage. Both demand and supply-related factors have been identified as driving the inertia of the leading producers in pricing and market shares. As such Mueller (1997) identifies several demand-related factors as the existence of switching costs, network externalities, consumer persistence due to uncertain product quality and habit persistence. On the supply-side, the producer may have efficiency advantages that help to keep costs down and be dominant in the market. Incumbent firms may have advantages with respect to the potential entrants due to network externalities and economies of scale or because of cost reductions arising from production experience.

Much of the literature has focused on the effect of advertising on the product advantage of the first entrant. Advertising is a form of non-price competition that helps provide information regarding the existence and price of the product. However, different perspectives arise in the definition of advertising according to its final goal: advertising may be seen as a purely informative action to enhance rational choices or it may be perceived as a persuasive action to generate habit persistence. In the particular case of pharmaceuticals, the difference in these points of view has been subject to discussion and empirical evidence has been brought in support of both perspectives (Leffler, 1981; Hurwitz and Caves, 1988).

In addition to the advertising effects on product differentiation other mechanisms have been found that perpetuate the competitive advantage of the first entrant into the market. The

consumer's experience and information may, for example, act as an alternative mechanism for the existence of first-mover advantage. Uncertainty regarding the quality of the pioneer brand could allow the monopolist to set a high price and still maintain large market share as new entrants arrive (Schmalensee, 1982; Conrad, 1983). Uncertainty in this scenario refers to the unknown quality of the product prior to consumption. These goods have been labelled experience goods by Nelson (1970) and refer to the products whose characteristics are learnt only after the consumer purchases the product. In these two seminal models, the price setting strategy adopted by the pioneer brand is such that once consumers learn about the pioneer product quality they do not have any incentives to invest in gaining information on a new entrant's product quality. This acts as a barrier to entry and perpetuates the predominance of the incumbent firm.

These models use consumer aversion to the uncertain quality of entrants product as a channel to generate a competitive advantage even though the incumbent firm sets prices higher than its potential competitors. A different approach looks at the first-mover advantage as a strategic process in which prices are set optimally with the incumbent firm benefiting from learning by doing in the production process. Smiley and Ravid (1983) model the optimal price setting of an incumbent firm in a context in which there is learning by doing in the production of a new product and the monopoly advantage is threatened by the entry of potential competitors. The learning process in this model includes the concepts of proprietary or firm-specific learning developed by Rosen (1972) and industry wide learning process discussed in Arrow (1962). This process hence benefits from the own production experience and from the experience gained in observing the competitors performance and it is used as a mechanism to reduce the production costs that generate the incumbent's competitive advantage.

The learning process is inherently linked to the use of a newly developed product. However, the introduction of a new product into a market is normally a slow process with empirical evidence supporting an S-shaped adoption curve over time as the diffusion path followed by the new product. In the health care sector the diffusion of medical technologies has attracted attention not only as an explanation of increasing health care expenditure but also given the fast technological adoption rates experienced in this market. As with any technology, the use of a new product in health care requires learning about its functioning and characteristics. In the particular case of pharmaceuticals a new product within a new therapeutical class will compete not only with the existing products but over time it is likely that different molecules will be introduced leading to competition within the class of molecule over the diffusion

process with any specific advantages helping to determine their relative ranking in the market share.

Within the pharmaceutical market the advantages presented to the first-movers have also captured the interest of scholars. On the one hand, pioneer branded products face the entry of generics and the new market composition experiences changes in prices and market shares. Empirical evidence has shown that despite the entry of competitors, the pioneer branded products did not decrease their prices and still kept a substantial market share whereas the competitors experienced a decreasing price trend over time (Grabowski and Vernon, 1992). First-mover advantages have also been examined within the generic pharmaceutical market showing that the first generic to be introduced into the market will benefit from large market shares (Hollis, 2002).

This paper now turns to look at the diffusion of four molecules within the same therapeutical class considering not only at the determinants of diffusion but also at the determinants of first-mover advantage with a special emphasis on the role of information. The approach used here is that of a learning process as outlined by Smiley and Ravid (1983) from the perspective of the decision-maker in the drug choice: the physician. Among other informational channels available to doctors, their own experience and market signals on the acceptance of the drug (labelled here as consumption externalities) will be part of the learning process in which consumers also engage and in the present paper learning will represent a decrease in the cost of uncertainty[2] and information seeking. Diffusion of new products within the pharmaceutical market has been modelled in the literature as learning process in which physicians obtain information through direct experience (Coscelli and Shum, 2004; Crawford and Shum, 2005). In these studies, however, the new product was compared to the products classified in other therapeutical groups. In the present paper, we are interested in the comparison of molecules within the same group.

There are six molecules within the statins therapeutical class as shown in Table 1 that were introduced between 1989 and 2003 in the UK under a branded name with no generic competition. The evidence regarding statins is incontrovertible. Their effectiveness in reducing total and LDL-cholesterol have been extensively shown in the literature. Several clinical trials showed a positive effect of statins in lowering the onset of patients with high risk of coronary

[2] Over time the degree of uncertainty will be reduced though the acquisition of information and individuals will have a better knowledge of the characteristics and quality of the drug.

events and stroke in primary prevention. Moreover, in secondary prevention statins demonstrated reductions in cerebrovascular disease and cardiovascular events. Also, it has been shown that statins are cost-effective in lowering cholesterol and overall are well tolerated[3] (Palmer et al., 2003; NICE, 2006).

This study examines the first four statins to be marketed: simvastatin, pravastatin, fluvastatin and atorvastatin. Cerivastatin is excluded from the analyses mainly because it was withdrawn because of safety issues and rosuvastatin is excluded because it was introduced in 2003 a year prior to the end of the data set period of study therefore not allowing the dynamic nature of the diffusion process to be captured.

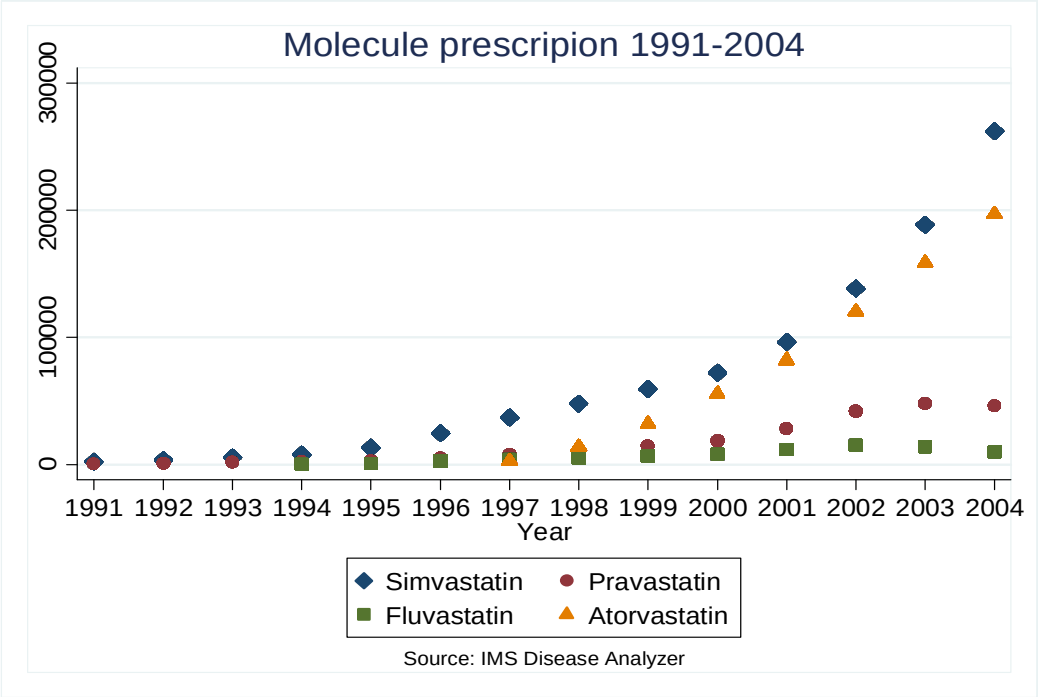
Table 1. Year of molecule launch

Substance		Launch Year
Simvastatin	Zocor	1989
Pravastatin	Lipostat	1990
Fluvastatin	Lescol	1994
Atorvastatin	Lipitor	1997
Cerivastatin	Lipobay	1997
Rosuvastatin	Crestor	2003

Figure 1 shows the prescription path of each molecule. The diffusion path moves slowly during the initital years of introduction. Over the first four years, and with the third statin just being introduced, the demand for this new class of drugs remained low. The take off in prescription coincides with the publication of randomised control trials in 1994 with evidence on their cost-effectiveness. Despite being therapeutically equivalent, simvastatin seems to enjoy some degree of competitive advantage with respect to pravastatin and this seems to hold when the third statin (fluvastatin) is introduced. There is a predominance of the first-mover simvastatin that is only threatened by the entry in 1997 of the fourth molecule atorvastatin. The figure also shows that despite the much later entrance of the fourth molecule, the demand for this drug increases and reaches level of demand very close to those for the incumbent drug. The entry of atorvastatin seems to threaten the dominant position of simvastatin as the molecule with first-mover advantage.

[3] Recent evidence (Palmer et al., 2003) shows that atorvastatin is the most cost-effective, followed by simvastatin, fluvastatin and pravastatin.

Figure 1. Molecule diffusion



3. The model

The pharmaceutical market is characterised as being dynamic with drug producers engaging in the development of new drugs. When a successful innovation is brought into the market there will be negotiations between the manufacturer and a third-party funding agency regarding the reimbursement price of the drug. The contractual agreement between the manufacturer and the insurer represent interaction from the supply-side that certainly will have an influence in the final consumption. Nevertheless, this paper is focused on the demand-side of the diffusion of new drugs and the process of the supply-side is treated as exogenous. Demand in the health care sector presents a peculiarity in that the individual that decides the treatment is not the final consumer – the patient. The doctor-patient agency relationship arises because of the asymmetry of information that prevents the patient to make decisions regarding diagnosis and treatment. The fact that doctors are the key decision-makers in the drug choice determines the extend to which a new drug will be accepted over time. Several forces will reach the doctor that may well determine his uptake of the new medicine.

The diffusion of new pharmaceuticals has been studied in the literature as one in which information plays a central role. Recently some papers have approached the issue of diffusion as one of being a learning process in which doctors learn about the drug only through direct

experience (Coscelli and Shum, 2004; Crawford and Shum, 2005). However, other sources of information, not drawn from direct experience are also available to doctors. The cost associated in acquiring information will differ and the risk aversion of doctors will define the uncertainty attached to new products with greater aversion entailing a higher search for information. Marketing is a well-known source of information to doctors however the extend to which this mechanism is used as a purely information exchange or to assure future consumption has been disputed in the literature as discussed in the previous section. It has been argued, in a rational expectations manner, that the anticipation of competition from later entrants by the pioneer product manufacturer provides incentives for the incumbent to provide correct information on the product (Klein and Leffler, 1981).

In addition, information is also provided through the scientific literature available to the public through the publication of clinical studies. There is a strong structure of incentives to researchers and bodies responsible for technology evaluation for the publication of clinical studies to be purely informative. Empirical evidence suggests that these publications do have an impact on the demand of new drugs and it is accepted that generally this information is objective (Azoulay, 2002). However, the doctors/decision-makers operate in a market that will send signals regarding the overall acceptance of the drug, in what has been named as consumption externalities (Berndt et al., 2003). All these factors have been analysed separately in the literature and the results may be biased because they are excluding individual elements that should be taken into account jointly.

Because there are four molecules, the research presents pair-wise comparisons of the molecules to see the relative advantage of each of the informational factors in the diffusion of each product and the main determinant of the competitive advantage, if any. Hence, the estimated dynamic demand equations are modelled as follows:

$$\left(\frac{simva}{simva+k}\right)_{it} = \left(\frac{simva}{simva+k}\right)_{it-1} + sales\left(\frac{simva}{k}\right)_{it} + mkt\left(\frac{simva}{k}\right)_{it} + cle_{it} + se\left(\frac{simva}{k}\right)_{it}$$

for $k = pravastatin,\ fluvastatin, atorvastatin$ and $t = 1991,...,2004$.

The dependent variable is the relative prescription share of simvastatin with respect to the sum of simvastatin and the competing molecule. It is the prescription share of each doctor in

practice *i* at time *t*[4]. The lagged value of the dependent variable represents learning through the doctor's own experience. Consumption externalities are captured by the market sales of each molecule. The informational role of the manufacturer is captured by the marketing variable. In the estimation the advertising efforts of each manufacturer are proxied by the percentage of the employees in the sales/marketing department over the total number of employees employed by the manufacturer of the molecule[5] and the clinical evidence is expressed as the cumulative number of papers published of molecule *k* to year *t*. The last three variables are expressed in terms of the value of simvastatin relative to the competitor. Finally, in order to capture qualitative differences we include a variable that captures different aspects of the quality of the product such as side effects or dosage. The model also includes number of GPs and population over 65 as control for demographic variables.

Higher prescription of the pioneer with respect to the competing molecules could be explained by demand inertia (Mueller, 1997). On the one hand, the uncertainty over the quality of the product is overcome over time through direct or indirect information acquisition. On the other hand, it could be explained as a habit persistence generation process in which the time the molecule is in the market in monopoly will determine the future path of prescription since the doctors will prescribe the first molecules they had the first contact with. If new molecules are introduced, although there will be common features in the characteristics of the molecules, individuals will face switching costs arising from the investment required in getting information regarding the differential features of the molecule. For that reason and because of the sequential introduction of the molecules that would involve constant information gathering to keep up-to-date, physicians may choose to stick to the first drug.

4. Data and methodology

Data

The data used in this study were provided by Intercontinental Medical Statistics (IMS) a company that collects pharmaceutical sales and volume data. Specifically, we use a dataset called the IMS Disease Analyzer-UK consisting of prescription data from a sample of over 130 practices throughout the UK covering three million patients. The first data record was in 1991

[4] The prescription per doctor represents the prescription per capita per practice. Due to identification issues a prescription in practice *i* could not be linked to the doctor id and only the total number of prescriptions per year could be computed. Having the information on the number of doctors per practice, the number of prescriptions per capita was calculated and used in the estimation.

[5] These information was retrieved from the Annual Accounts presented by the manufacturers to the Companies House.

and the data collection runs monthly at the practice level. As the first statins –simvastatin and pravastatin - were first marketed in 1989 and 1990, respectively, and the study period starts in 1991 there is a two year gap between the availability and the use reflected in the demand equations. However, data within sample have been compared with external data in prescription use to verify the low uptake of statins over the first years.

Each observation recorded in IMS Disease Analyzer is a patient visit and it tracks doctors, patients and therapies over time. The data contains information on practice-specific characteristics, patient demographics and diagnostic and therapy information. The prescription data includes the date of event, the anatomical therapeutic chemical (ATC) code of the drug, the form, strength and manufacturer of the product and the quantity prescribed. The data were exported identifying the patients that were prescribed one of the drugs and then all the prescription history of those patients was extracted. Hence, the datasets analysed in this paper includes all patients' visits in one of the participating GP practices in which a statin, was prescribed.

There were 1,987,598 observations in the prescription of statins in the Disease Analyzer-UK for the 14 years of the study period. The data were then manipulated to obtain the longitudinal dataset that includes the prescriptions per year of each practice and the final panel has 1758 observations that indicate for each practice and year the prescription of each of the four molecules included in the present study. This is an unbalanced panel with information on practices that provided information during consecutive periods. The participation prescription patterns differ among practices in the number of periods available and in terms of the year they enter the sample.

Panel data methods

Due to the dynamic nature of the analysis of the diffusion process of statins we use dynamic panel data methods. The specification outlined in the previous section is captured using autoregressive distributed lag models. The dynamic element is introduced here as a measure of the learning experience gained by past prescription use. We consider the dynamic demand equation of the form:

$$y_{it} = \alpha \cdot y_{it-1} + \beta \cdot x_{it} + c_i + u_{it}$$

The model includes the lag of the dependent variable and independent explanatory variables. c_i denotes the unobservable cross-section specific effect and u_i is the disturbance term. The

individual effects and the disturbances are assumed to be independently distributed and have the following structure:

$$E[c_i] = 0,\ E[u_{it}] = 0,\ E[u_{it}c_i] = 0 \text{ for } i = 1,...,N \text{ and } t = 2,...,T$$

and under the assumption of lack of serial correlation among the errors

$$E[u_{it}u_{is}] = 0 \text{ for } i = 1,...,N \text{ and } s \neq t$$

The OLS estimator of α will be inconsistent because the lagged value of the dependent variable is correlated with the error component and this will give an upward biased estimator. By first-differencing the equations, the unobserved effect is eliminated. Applying OLS to the transformed equation gives the Within Group estimator. However, the first difference will introduce correlation between the transformed lagged dependent variable and the transformed error term and the estimator will be downward biased (see Bond (2002) for an extended discussion). In order to obtain consistent estimators we need a transformation that removes the bias caused due to the correlation of the individual effect and the lagged dependent variable. The most common transformation used is to first difference to eliminate the individual effect

$$\Delta y_{it} = \alpha \cdot \Delta y_{it-1} + \Delta u_{it} \qquad i = 1,2,...,N\ ; \qquad t = 3,...,T$$

where $\Delta y_{it} = y_{it} - y_{it-1}$ and $\Delta u_{it} = u_{it} - u_{it-1}$. However, the first difference of the lagged dependent variable is now correlated with the first differenced error component. Instrumental variables estimators can be used in order to obtain consistent estimates with the only assumption that y_{i1} is not correlated with future error terms

$$E(y_{i1}e_{it}) = 0 \quad \text{for} \quad t = 2,...,T \quad (*)$$

If there are at least three time periods, there are a number of valid instruments that can be used to consistently estimate α. The assumption of no serial correlation and (*) on the initial condition y_{i1} imply that there are $\frac{1}{2}(T-1)(T-2)$ ortogonality conditions:

$$E[y_{t-s}\Delta u_{it}] = 0 \text{ for } t = 2,...,T \text{ and } s \geq 2$$

These conditions are exploited in the first-differenced generalised method of moments (GMM) developed in (Arellano and Bond, 1991). The exact form of the matrix of instruments will

depend on the assumptions on the explanatory variables x_{it} and the elements of the error component. There will be different extra moment condition depending on whether x_{it} is assumed to be endogenous, predetermined or strictly exogenous.

In addition to the moment conditions for the first-differenced equations, there are some extra conditions as possible instruments for the level equations.

$$E[u_{it}\Delta y_{it-1}] = 0 \quad \text{for} \quad t = 3,...,T$$

$$E[u_{it}\Delta x_{it-1}] = 0 \quad \text{for} \quad t = 3,...,T$$

This method was first proposed by (Arellano and Bover, 1995) and further developed by (Blundell and Bond, 1998). These conditions applied to the level equations together with the moment conditions for the first-differenced equations give the so-called system GMM estimator. Monte Carlo simulations in Blundell and Bond (1998) suggest that this estimator is more robust than first-differenced estimators to the presence of weak instruments when the series are highly persistent. The estimator has been found to have poor finite sample properties when the lagged levels are weakly correlated with the first differences. Using additional assumptions available in the system GMM can improve and have superior finite sample properties.

Unit Root tests

Instruments used in the difference GMM may be weak instruments in presence of highly persistent series. In order to test for non stationarity there are several tests available. Bond et al. (2002) study the performance of different unit root tests and conclude that the t-test based on the OLS estimation of the parameter α is robust for cases where the variance of the unobserved heterogeneity is low. The OLS estimator of the following first-order autoregressive model

$$y_{it} = \alpha \cdot y_{it-1} + e_{it}$$

$$e_{it} = (1-\alpha)\cdot c_i + u_{it}$$

The simple t-test will tell us whether or not to reject the null hypothesis of unit root $\alpha = 1$. under the null hypothesis the OLS estimator is consistent. An alternative test was proposed by (Breitung et al., 1994) and is based on the OLS estimation of the following transformed model:

$$y_{it} - y_{i1} = \alpha \cdot (y_{it-1} - y_{i1}) + \varepsilon_{it} \qquad t = 3,...,T$$

$$e_{it} = u_{it} - (1-\alpha)\cdot (y_{i1} - c_i)$$

under the null hypothesis of $\alpha = 1$ the t-statistic is a valid test for testing whether the individual series are a random walk.

5. Results

This section reports the results of the diffusion equation among competitors with the role of different informational sources with the aim to explain the observed differences. All results are obtained using the system GMM estimator due to the presence of persistent series (first-difference results are not reported here). These are estimates considering the marketing and sales as endogenous (misspecification tests support the endogeneity of these two variables). Overall, the results suggest that the relative performance of simvastatin with respect to the other molecules is driven by higher information availability and drug attributes. Only the introduction of atorvastatin introduces potential competition to the pioneer drug.

The first three columns in table 2 show the results of the demand equations that include the relative number of side effects of simvastatin with respect to any of the other competing drugs as a measure of the molecules' quality. All molecules have the same contra-indications and differences arise largely due to the side-effects. It is expected that qualitative differences will be rooted in differences in the molecule performance. The lag of the dependant variable indicates the presence of a strong effect of the doctor's own experience over the learning process. At the same time, the fact that there are no generics competing with this variable will be uniquely capturing the habit persistence generated by the doctor's molecule loyalty.

For the case of the simvastatin-pravastatin equation we see that the persistence in prescription is lower than for the simvastatin-fluvastatin equation. The year of difference between the introduction of simvastatin and pravastatin could explain the lower effect of the prescription share in the future use of the drug. However, this gap in time between the molecules introduction seems to be sufficient to generate prescription habit of the pioneer molecule. In the case of fluvastatin the prescription share is showing a clear gain of simvastatin in being the first-mover in the market. As for the simvastatin-atorvastatin equation, the experience brought forward as a result of the prescription of these two molecules indicates the rising competitive advantage of atorvastatin. Indeed, the evidence obtained from the own experience on the higher atorvastatin effectiveness was the driver of the increasing prescription share in the market. This may well indicate the effect of spillover effects regarding the common attributes of the molecules through the accumulation of experience and marginal

quality variations would explain that a new entrant increasingly captures a higher prescription share. Over the study period the process of competition between simvastatin and atorvastatin is just starting and the faster diffusion process experienced by atorvastatin suggests spillover effects in experience and clinical evidence. Being close substitutes means that by the time the molecule is introduced the main characteristics of the drug are learnt and the marginal cost of investing in acquiring information regarding the new product is decreasing over time.

Table 2. Dynamic equations: product quality

Variable	Sim/Pra	Sim/Flu	Sim/Ator	Sim/Pra	Sim/Flu	Sim/Ator
Share(t-1)	0.7204	0.9808	0.67413	0.720725	0.980813	0.674838
	1.90E-25	1.30E-65	4.10E-14	1.40E-25	4.20E-66	4.50E-14
Sales	0.14698	-0.07056	0.05122	0.146399	-0.025750	0.022446
	0.0015	0.2936	0.1471	0.0027	0.6068	0.6098
CEvidence	0.10383	0.04611	0.02576	0.102617	0.025028	0.031589
	0.1825	0.2189	0.0021	0.1937	0.3697	2.00E-04
Marketing	0.0258	0.02616	-0.0058	0.047441	0.078460	-0.024066
	0.1262	0.2796	0.7774	0.0338	0.0072	0.1904
Side Effects	0.01379	0.02043	0.1617	0.007225	0.017261	0.148910
	0.003	0.0954	1.30E-06	0.3406	0.0756	4.30E-05
Dosage				0.000020	-0.000022	0.000017
				0.2378	0.0155	0.3109
Hansen Test	0.984	0.039	0.451	0.984	0.071	0.535
N	1605	1413	917	1605	1413	917

Notes: Standard errors below the coefficients
P-value reported for the Hansen test
GMM results are one-step robust estimates

The last three columns include the side effects and the number of dosage forms available for each molecule as measure for the product quality that would capture any dosage effect specific to the molecules. The underlying assumption is that higher variability in dosage forms will facilitate the matching process of the product with the patient. Results are stable when including this variable in the demand equation and the dosage effects are only negative for the simvastatin-fluvastatin equation. Simvastatin and fluvastatin are the molecules with wider availability of dosage forms and in that respect the negative sign of the estimate could be explained by the fluvastatin competing with simvastatin in that specific characteristic of the drug.

As an additional product quality we include the inverse of the age of the pioneer drug into the prescription share equation. The idea behind that is to capture any inverse relationship between the relative demand of simvastatin with respect to the competing molecules. The

results show that any increase in the pioneer's age would have a positive effect on the prescription share of the competing molecule. In the case of atorvastatin this effect would suggest that the presence of the pioneer in the market for a longer time does not prevent the later entrant to capture a higher prescription share.

Table 3. Demand equations with age

Variable	Simva/Prava	Simva/Fluva	Simva/Ator
Share(t-1)	0.72072237	0.98620634	0.55899835
	3.40E-25	3.70E-67	9.50E-04
Sales	0.14846632	0.02393569	0.04438456
	0.0013	0.5031	0.1953
CEvidence	-0.05156966	0.01258973	0.00242535
	0.9199	0.5133	0.9006
Marketing	0.02260631	0.04589947	0.00870364
	0.312	0.0288	0.5646
Side Effects	0.03097813	-0.01227284	0.46208662
	0.5806	0.5015	0.0779
1/Age	0.00046713	-0.00088309	0.01117367
	0.7589	0.2441	0.2507
Hansen test	0.982	0.120	0.484
N	1605	1413	917

Notes: Standard errors below the coefficients
P-value reported for the Hansen test
GMM results are one-step robust estimates

The marketing variable has been introduced to capture the advertising effort made by the manufacturer. The positive sign in all estimates except for the equation simvastatin-atorvastatin reflects that the marketing effort in promoting simvastatin helped to consolidate its competitive advantage. The negative sign of the estimate for the atorvastatin equation may be reflecting the higher marketing effort made by the manufacturer of atorvastatin. In marketing we would expect some degree of free riding from later entrants. However, the marketing effort is relatively higher for the last entrant than for the existing molecules. Previous to the introduction of atorvastatin the marketing efforts by the competing molecules are in accordance to the order of entry. This hence shows how in a market with k products the marketing activity becomes rivalrous (Berndt et al., 1997).

As discussed in the literature marketing may have different goals: an informational role and as loyalty generation. With the aim to differentiate between those two effects we generate a variable that interacts the relative marketing effort with time. The marketing variable is partitioned in two periods with the aim to see if during the first years after introduction there is

a stronger effect on prescription than when it has been in the market for some time. If t_0 is the time in which the competing molecule was introduced (1991 is assumed for pravastatin instead of 1990 (the actual year of introduction), 1994 for fluvastatin and 1997 for atorvastatin), t^* is the midpoint between the introduction of the molecule and the end-year and t_{04} is the end of the study period, the marketing variable is defined as follows for the first period:

$m_{tt^*} = mkt * year$ if $t_0 \le t \le t^*$

$m_{t^* t_{04}} = 0$ if $t > t^*$

And for the second period:

$m_{tt^*} = 0$ if $t_0 \le t \le t^*$

$m_{t^* t_{04}} = mkt * year$ if $t > t^*$

For the simvastatin-pravastatin case we take the marketing from 1991 to 1994 because the latter is the year in which a third molecule is introduced and this will capture the role of the marketing when there are only the first two competitors. For the other two equations, t^* is the midpoint between introduction of the competing molecule and the end year.

How is the marketing related to diffusion? Is it market-expanding or pure informational effect? It seems that at early stages of the diffusion there is a positive effect that then turns negative. This maybe an indication that initially the marketing efforts provide evidence on the availability and characteristics of the drug whereas at later stages, and specially in relative terms, the negative sign of the marketing is an indicator of the decrease of advertising suggesting that information provision is embedded in the marketing activity. The simvastatin-atorvastatin equation shows an exception to that trend. Probably the threat of atorvastatin having superior characteristics combined with high levels of marketing effort determines the positive effect of the simvastatin relative marketing over the entire period as a mechanism to guarantee future prescription.

Table 4. Demand equations: marketing

Variable	Simva/Prava	Simva/Fluva	Simva/Ator
Share(t-1)	0.71876255	0.96233213	0.6186811
	6.80E-25	7.10E-63	1.80E-06
Sales	0.320279	-1.09E-02	0.03176185
	5.00E-05	0.7832	0.37
CEvidence	0.13175893	0.01785177	0.03943467
	0.0797	0.4059	0.0051
Side Effects	0.03914965	0.02222622	0.14685132
	0.0051	0.0015	5.30E-05
Marketing 91-94	0.00007224		0.00006491
	0.0207		0.4679
Marketing 95-04	-0.0000188		0.00012293
	0.6098		0.3023
Marketing 94-99		0.00002227	
		0.3039	
Marketing 00-04		-4.40E-06	
		0.8363	
Marketing 97-00			0.00006491
			0.4679
Marketing 01-04			0.00012293
			0.3023
Hansen test	0.98	0.451	0.606
N	1605	1413	917

Notes: Standard errors below the coefficients
P-value reported for the Hansen test
GMM results are one-step robust estimates

6. Conclusions

This paper has addressed the diffusion of new drugs from a micro perspective with special emphasis on the role of information over the diffusion process. A longitudinal dataset on prescription has been used to analyse whether there is any kind of competitive advantage for the first-mover in comparison with later entrants in the market. Evidence showing higher prescription of the pioneer drug over time suggests the first entrant to have competitive advantage. The empirical analysis is based on the pairwise comparison of the prescription of the pioneer drug focusing on two sets of variables: information and product quality.

Of the four mechanisms included in the analysis, the own experience of the doctor seem to shape the prescription pattern of physicians when facing the drug choice between the incumbent and the alternative later entrant. These molecules are marketed under brand names and there is no generic competition under the study period setting a framework in

which doctors only face the molecule choice. Other sources of information also favour the prescription of the pioneer and the marketing efforts are shown to have an informational role rather than a persuasive element. Among the competitors only atorvastatin appears as a true competitor undermining the first-mover advantage enjoyed by simvastatin as seen by the higher prescription volume of atorvastatin.

The results of the analysis of the statins market suggest that the pioneer drug enjoys competitive advantage for a certain period of time and after that a new entrant presenting additional product quality characteristics captures a high market share. Despite the marginal contribution in quality of the later entrant, there are spillover effects on the learning process since the later entry by the competitor means that doctors will have a low cost in information search since the molecules share the main characteristics and the learning process will be focused on the additional product characteristics.

References

Arellano, M. and Bond, S. (1991). Some Tests of Specification for Panel Data: Monte Carlo Evidence and an Application to Employment Equations. *The Review of Economic Studies* 58, 277-297.

Arellano, M. and Bover, O. (1995). Another look at the instrumental variable estimation of error-components models. *Journal of Econometrics* 68, 29-51.

Arrow, K. J. (1962). The Economic Implications of Learning by Doing. *The Review of Economic Studies* 29, 155-173.

Azoulay, P. (2002). Do Pharmaceutical Sales Respond to Scientific Evidence? *Journal of Economics & Management Strategy* 11, 551-594.

Berndt, E. R., Bui, L. T., Lucking-Reiley, D. H. and Urban, G. L. (1997). The roles of marketing, product quality, and price competition in the growth and composition of the U.S. Antiulcer drug industry. In *The economics of new goods*(Eds, Bresnahan, T. F. and Gordon, R. J.). Chicago: The University of Chicago Press.

Berndt, E. R., Pindyck, R. S. and Azoulay, P. (2003). Consumption Externalities and Diffusion in Pharmaceutical Markets: Antiulcer Drugs. *The Journal of Industrial Economics* 51, 243.

Blundell, R. and Bond, S. (1998). Initial conditions and moment restrictions in dynamic panel data models. *Journal of Econometrics* 87, 115-143.

Bond, S., Nauges, C. and Windmeijer, F. (2002). Unit Roots and identification in autoregressive panel data models: a comparison of alternative tests. *Mimeo* Institute for Fiscal Studies, London.

Bond, S. R. (2002). Dynamic panel data models: a guide to micro data methods and practice. *Portuguese Economic Journal* 1, 141-162.

Breitung, J., auml, rg and Meyer, W. (1994). Testing for unit roots in panel data: are wages on different bargaining levels cointegrated? *Applied Economics* 26, 353-361.

Conrad, C. A. (1983). The advantage of being first and competition between firms. *International Journal of Industrial Organization* 1, 353-364.

Coscelli, A. and Shum, M. (2004). An empirical model of learning and patient spillovers in new drug entry. *Journal of Econometrics* 122, 213-246.

Crawford, G. S. and Shum, M. (2005). Uncertainty and Learning in Pharmaceutical Demand. *Econometrica* 73, 1137-1173.

Grabowski, H. G. and Vernon, J. M. (1992). Brand Loyalty, Entry, and Price Competition in Pharmaceuticals after the 1984 Drug Act. *Journal of Law and Economics* 35, 331-350.

Hollis, A. (2002). The importance of being first: evidence from Canadian generic pharmaceuticals. *Health Economics* 11, 723-734.
Hurwitz, M. A. and Caves, R. E. (1988). Persuasion or Information? Promotion and the Shares of Brand Name and Generic Pharmaceuticals. *Journal of Law and Economics* 31, 299-320.
Jacobzone, S. (2000). Pharmaceutical Policies in OECD Countries: Reconciling Social and Industrial Goals. *OECD Labour Market and Social Policy Occacional Papers* No. 40, OECD Publishing
Klein, B. and Leffler, K. B. (1981). The Role of Market Forces in Assuring Contractual Performance. *The Journal of Political Economy* 89, 615-641.
Leffler, K. B. (1981). Persuasion or Information? The Economics of Prescription Drug Advertising. *Journal of Law and Economics* 24, 45-74.
Mueller, D. C. (1997). First-mover advantages and path dependence. *International Journal of Industrial Organization* 15, 827-850.
Nelson, P. (1970). Information and Consumer Behavior. *The Journal of Political Economy* 78, 311-329.
NICE (2006). Statins for the Prevention of cardiovascular events.
Palmer, S. J., Brady, A. J. and Ratcliffe, A. E. (2003). The cost-effectiveness of a new statin (rosuvastatin) in the UK NHS. *International Journal of Clinical Practice* 57, 792-800.
Rosen, S. (1972). Learning by Experience as Joint Production. *The Quarterly Journal of Economics* 86, 366-382.
Schmalensee, R. (1982). Product Differentiation Advantages of Pioneering Brands. *The American Economic Review* 72, 349-365.
Smiley, R. H. and Ravid, S. A. (1983). The Importance of Being First: Learning Price and Strategy. *The Quarterly Journal of Economics* 98, 353-362.