Information and Diffusion of New Prescription Drugs

Victoria Serra-Sastre[a1], Alistair McGuire[b]
[a]City University London
[b]London School of Economics and Political Science

June 2011

Abstract

This paper examines the role of different product information flows on the diffusion of new pharmaceuticals. Given the innovative nature of pharmaceutical drugs and their impact on health care expenditure there is a surprisingly small literature devoted to this topic. Some information flow mechanisms have been examined individually in the literature, but very few have captured the simultaneous impact of these mechanisms on up-take and diffusion. This paper uses the up-take of statins as an example. Diffusion of this therapeutical group is expressed as a function of four specific informational channels: self-experience, consumption externalities, scientific evidence and marketing. In addition to this, the influence of economic factors is tested to examine whether they have any role in drug diffusion. Prescription data from over 130 GP practices in the UK during 1991-2004 are used to test the econometric specification applying dynamic panel data methods. Results suggest individual self-experience and clinical evidence are major factors promoting diffusion, while there is an inverse relationship with GP practice size and diffusion. Having controlled for these factors financial incentives and marketing appear to play little role.

JEL classification: I11, I18, L65

Keywords: Technology diffusion, information, new prescription drugs, system GMM estimator

Acknowledgements: We would like to than Martin Knapp, Matt Sutton and various members of the European Health Economics Association who have commented on earlier drafts of this paper. Responsibility for the final product remains our proprietary right of course.

[1] Corresponding author. Department of Economics, City University London, Northampton Square London, EC1V 0HB.Email: v.serra-sastre@city.ac.uk

I. Introduction

There has been little examination of the processes driving the adoption and diffusion of new pharmaceutical drugs despite their innovative nature and the complexity of the pharmaceutical market structure. Only a small number of studies formally assess the role of information, which naturally accompanies new product launches, in this diffusion process. A number of studies focus on physician behaviour highlighting either learning through self-experience or the influence of peer-group effects, yet others on the direct influence of scientific evidence on the uptake process (Coscelli and Shum, 2004; Crawford and Shum, 2005, Bikchandani et al., 2001, Azoulay, 2002). Berndt et al. (2003) examined the positive impact of consumption externalities on the adoption of new anti-ulcer drugs using market level data, while Nair et al (2010) have considered the impact that peer-effects have on the slow adoption of new drugs. Ching and Ishihara (2010) consider the role of clinical evidence in a structural learning model based on individual manufacturer and physician behaviour. These analyses of pharmaceutical drug diffusion generally adopt an aggregate perspective based on the total volume of pharmaceutical sales, although the learning process models based on self-experience do analyse individual physician behaviour. Moreover most empirical work to date restricts consideration to specific, individual informational flows to explain diffusion. Undoubtedly this partly reflects data restrictions and the collinear movements that exist across a range of informational variables and their empirical proxies. Chintagunta et al (2009) and Bradford and Kliet (2010) do consider the role of competing information such as any available public information and the doctor's learning process obtained from patients' experience.

This paper extends these studies of competing information flows on the diffusion of new medicines through an empirical analysis from the physicians' perspective. The analysis covers the diffusion process from the early stages of market entry, when drugs are newly launched, to a later stage of diffusion in which demand is established and specific treatments are commonly prescribed by physicians. Four specific information channels are indentified: clinical evidence on the treatment, self-experience, pharmaceutical company marketing efforts, and consumption externalities.

Existing evidence suggests a positive relationship between increased scientific evidence and the diffusion of pharmaceuticals as shown by Azoulay for the anti-ulcer drug market (2002)[2]. Personal experience, through prescribing, seems likewise important as product quality associated with efficacy and safety will be revealed through usage. Empirical evidence suggests that direct prescription experience does indeed impact on up-take (Currie and Park, 2002; Coscelli and Shum, 2004). Company marketing efforts confer an additional information source. The focus in this study is on the diffusion of statins as a drug class therefore we are not interested in whether advertising is informative or manipulative, we merely note that pharmaceutical sales have been positively associated with advertising efforts and this effect has been shown to be positive (Azoulay, 2002; Berndt et al., 2003). Lastly, consumption externalities, reflecting peer group acceptance (or rejection) either at the market or physician practice level, also seem to affect new product diffusion rates. Berndt et al. (2003) provide positive empirical support on such market externalities, while a number of studies are suggestive of practice level externalities (Banerjee, 1992; Bikhchandani et al., 1992; Shiller, 1995).

[2] Azoulay (2002) uses the stock of scientific information as proxy to study the relationship between clinical evidence in the sales pattern in the anti-ulcer drug market.

The diffusion framework is tested with a dynamic empirical model using prescription data on statins within the UK primary care market. Statins are cholesterol-lowering drugs for the prevention and treatment of coronary heart disease and cerebrovascular disease[3]. Diffusion of this new therapy is explored at the therapeutic class level[4]. This is justified on the basis that once a new therapeutic class is introduced there is aggregate information acquired on the drug class[5]. This will always hold unless there is substantial within-class variation in product; which is not an issue here, as individual statin products all exhibit the same therapeutic (class) effects. Figure 1 shows the total number of prescription statins dispensed in the community in England from 1991 to 2004 outlining an increasing diffusion of statins beginning with slow up-take at the early stage of market entry and then an accelerated up-take rate over later years. Saturation, as normally indicated by a logistic type (S-shaped) curve, has obviously not occurred yet for statins and these drugs still seem to be diffusing widely across the NHS.

Finally, note that although there are several individual drugs within the therapeutical group all were branded products during the examination period. Generic competition against branded statins began in 2003, when patent protection for simvastatin expired. In 2004, a generic product for pravastatin also started being marketed. As the generic market only opened in the last two years of the study period 1991-2004, branded-

[3] Heart disease and cerebrovascular disease are the first two leading causes of death not only in the UK but also worldwide. In 2004 statins represented around 4% of all prescriptions items dispensed in England and approximately 10% of the overall net ingredient cost. The evidence regarding statins is incontrovertible and NICE has published technology appraisal promoting the use of statins to prevent cardiovascular disease (NICE, 2006).

[4]Within the statins therapeutical group there are six different molecules. The first statin to be marketed in the UK was simvastatin and it was introduced in 1989. Other statins like pravastatin and fluvastatin were introduced early in the 90s and during the second half of the 90s atorvastatin and cerivastatin emerged in the market. In 2003 rosuvastatin was launched, this is a year before the end of the study period however its prescription is included into the analysis as part of the diffusion process.

[5] Molecules within therapeutical class share common features and informative inter-molecular spillovers are assumed to exist: once the first molecule within the same therapeutical group is marketed, information will spill over subsequent molecules. Within-class product variation is not an issue with the drug classes studied below where individual products all exhibit the same therapeutic class effects.

generic competition is discarded given that our interest lies in the overall diffusion patterns of statins as a therapeutical group, and these drugs are still diffusing widely.

Figure 1

II. Model Specification

The up-take of these new prescription drugs is analysed within a dynamic empirical model. The general model specification includes the price of statins as it might be expected that new prescription drug demand by physicians is explained by, amongst other factors, drug prices. However, in the UK primary care sector there is evidence to suspect that general practitioner's (GP) knowledge of drug price is poor and does not affect prescription rates per se[6]. The UK Office of Fair Trading (OFT) in an extensive evaluation of the UK Pharmaceutical Pricing and Reimbursement Scheme (PPRS) undertook an analysis of 1,000 GPs and their ability to rank branded drugs by price. They found no evidence consistent with GP price awareness (OFT, 2007). Given that we are dealing with a single therapeutic class such a finding casts doubt on the general influence of price on volume, which of course is also affected by co-payment levels and the level of compliance. Moreover there is generally little price variation after a drug is launched other than adjustment for inflation, in some cases even beyond patent expiry (Kanavos et al., 2007). Nonetheless we include price in our general specification to test

[6]In the context of the UK National Health System (NHS), in which we analyse demand, it is not evident that price will in any case enter the demand function. Under the public health insurance system of the type existing in the UK the prescribing physician has little incentive to incorporate price as a factor affecting demand. On the consumer (patient) side, the cost borne, regardless of the actual drug price, is a relatively low, fixed co-payment and thus it is unlikely that demand is affected.

whether physicians do react to drug price in their decision to prescribe.[7] Demand for statins, which is taken to be synonomous with diffusion, is thus given as follows:

$$q_{it} = \alpha.p_t + \delta \cdot I_{it} + \beta \cdot x_{it} + \gamma \cdot d_{it} + c_i \qquad (2.1)$$

The dependent variable q_{it} is the average prescription volume per physician in practice i at time t. The dependent variable is constructed as the total number of prescriptions in practice *i* in year t divided by the number of GPs in the practice (in logarithmic terms). Ideally, the analysis would pursue examination of diffusion at the individual GP level. This was not possible due to coding issues within the data set as the prescriptions issued in each individual practice were mostly coded under the identifier of the "leading prescriber" rather than the individual GP. The number of drugs prescribed by each GP could therefore not be calculated and an average measure was used as a proxy for the number of prescriptions issued by each doctor in the practice. The first variable in the right-hand side of equation 2.1 represents the price element. As we are considering the analysis at the therapeutical level the price is a weighted average of the drugs within the group. The main component in 2.1, I_{it}, represents a matrix of variables defining product information flows and is expanded as follows:

$$I_{it} = (q_{it-1}, me_t, pe_i, ce_t, m_t) \qquad (2.2)$$

q_{it-1} is the lagged value of the dependent prescription volume variable and captures the physician's own self-experience. The underlying idea is that prescriptions issued in the previous year yield knowledge on drug performance, primarily efficacy and safety. The

[7] Although a reduced form model is estimated endogeneity of price remains an issue and is addressed in our empirical specification below.

second element, me_t, captures informational externalities relating to the general market acceptability of the drug. This is represented as the log of total statins sales in the pharmaceutical retail market. The practice information externality, pe_i, represents the information that potentially may be derived from peers in the same practice[8]. It is measured as the count of GPs in the same practice and intends to capture whether number of peers in the practice will affect uptake.

The fourth element in (2.2), ce_t, measures available scientific evidence. In order to capture this an index of the cumulative published clinical evidence available each year was constructed. As analysis is undertaken at the therapeutical group that comprises different individual drugs, scientific evidence was adjusted by individual contributions corrected by their relative weight within the drug group. This weight is proxied by the market share of each individual drug within the statins group. This index is therefore defined as the cumulative number of scientific papers published (cum_{kt}) for each molecule within any of the drug classes weighted by their market share ($mshare_{kt}$):

$$CE_t = \sum_{i=1}^{k} (cum_{kt} * mshare_{kt}) \quad \text{for} \quad t = 1991,...,2004$$

Where *k* represents each of the six molecules within the statins class. The variable cum_{kt} refers to all scientific papers published up to year t. In order to obtain the

[8] It could be argued that externalities could also arise from information sharing among patients generating consumer externalities. However, as we are examining the prescription decision what matters are physician-related externalities. Including potential consumer externalities would introduce elements of the doctor-patient relationship that are beyond the scope of this paper. In any case these types of externalities are not observed by the researcher and any potential influence would be captured by the unobserved fixed-effect c_i shown in equation 2.1.

cumulative number of papers the following strategy was followed. A search was carried out in PubMed for papers that had any of the statins molecules in the title or abstract[9]. Following Azoulay (2002) the definition of this variable reflects the stock of clinical evidence as the evidence provided is expected to have long-term effects. Relevant publications may appear before the introduction of the product and consequently the variable includes clinical evidence prior to the year of entry in the market.

The last of the information flow variables in (2.2), m_t, reflects the marketing efforts made by statins manufacturers[10]. Published studies have generally used specific data source that captures detailing minutes spent by sales representatives with physicians (Berndt et al., 1995, 1997, 2003; Azoulay, 2002). Such data is not publicly available and was not accessible for this study. Thus marketing activity was proxied using information on employment and the size of the pharmaceutical sales force for each statin manufacturer. This information was retrieved from their Annual Accounts, which were accessed from UK Companies House which registers and provides basic information on all UK-operating companies. Data on manufacturers' total employment, distribution or sales/marketing employment was retrieved as a basis to proxy advertising effort. This data is used to construct a marketing variable ($eindex_t$) that captures the percentage of

[9] Azoulay (2002) labels the articles as "marketing-expanding science" to the articles that compare the drug with placebo and "comparative science" when they compare two or more drugs within the same group. This distinction is not made here as we are not examining within group patterns but the influence of clinical evidence on statins diffusion as a whole. Regardless of the benchmark drug, clinical articles will be informative in nature.

[10] Note that in characterising marketing as an informative source we do not refer to the goals that marketing efforts may pursue. It has been discussed in the literature whether marketing has a pure information (knowledge dissemination) objective or it aims at ensuring prescription persistence over time. Evidence in support of both objectives has been empirically shown (Leffler, 1981; Hurwitz and Caves, 1988; Azoulay, 2002; Windmeijer et al., 2006). In the context of the current model, the interest is not about the discussion regarding the final goal of advertising efforts but rather what is the market mechanism used to inform physicians on availability and product characteristics.

sales/distribution employment of each manufacturer as a proportion of the manufacturer's total employment weighted by the market share of their product[11]

$$eindex_t = \sum_{i=1}^{k} (\%employ_{kt} * mshare_{kt}) \quad \text{for} \quad t = 1991,...,2004$$

where $\%employ_{kt}$ is the proportion of employment force devoted to sales/distribution by manufacturer producing drug *k* within statins therapeutical class and $mshare_{kt}$ is the market share of drug *k* at period *t*[12]. Given extensive data limitations and a lack of publicly available data from pharmaceutical companies sales employment measures represent a viable proxy.

The vector x_{it} in equation (2.1) represents confounding institutional factors defining a set of financial incentives, $x_{it} = (fh_i, dd_i)$. fh_i reflects fundholding status of the GP practice and captures whether the practice joined the fundholding scheme in 1991. In the UK, between 1991 and 1999 practices could hold a budget for outpatient and hospital referral as well as prescribing costs. Any savings could be used to transfer the budget surplus from one category to another (savings in prescription costs could be used against any costs in specialist referral) or it could be used in the following year[13]. Incentives to prescribe new prescription drugs are thus expected to differ for those

[11] Although each manufacturer will have a different marketing strategy, this variable only intends to account for the total effect of marketing on diffusion. Note that the present analysis is interested in the association between marketing and diffusion as a general trend for different therapeutical groups.

[12] Whether it is specifically sales or distribution employment figures will depend upon the information provided by individual manufacturers in their Annual Accounts.

[13] Studies published early after the scheme was introduced showed evidence of prescription cost containment for the first waves of fundholding practices (Maxwell et al., 1993; Bradlow and Coulter, 1993; Wilson et al., 1995). It was suggested that even though there was a general increase in prescribing costs, the growth rate was lower for the practices with fundholding status (Gosden and Torgerson, 1997; Delnoij and Brenner, 2000).

practices that were fundholders. The second practice characteristic dd_i relates to whether or not the practice was a drug dispenser. Drug dispensing practices are allowed to dispense prescribed drugs to patients within the practice. These are generally practices that are located in rural areas with no near pharmacy. Given that dispensing physicians have a two-tier income, salary and revenue from drugs sold, this variable explores whether economic incentives enhance new drug prescriptions, especially when new drugs have a higher unit cost than existing treatment options.

Finally, specification (2.1) also includes a vector of controls d_{it} for various characteristics of the regional health authority where the practice is located: percentage of population aged 45-64 and older than 65 and number of GPs in the regional health authority. The final component c_i captures systematic unobserved heterogeneity of the average physician in practice i.

III. Data and Panel Data Methods

The primary data used for the empirical analysis was obtained from Intercontinental Medical Statistics (IMS Health). Data was retrieved from their database IMS Disease-Analyzer containing prescription data from a sample of over 130 GP practices throughout the UK during the period 1991-2004[14]. Each observation recorded is a patient visit in one of the participating GP practices in which a statin was prescribed. Price data was also obtained from IMS Health. It contains quarterly price data for the period 1991-2002. Prices refer to the average price of all products within the therapeutic

[14] These practices were selected to be representative of the GPs distribution in the UK. The demographics (age and gender) of the patients covered by the panel of doctors in Disease-Analyzer are similar to UK population demographics when figures are compared to the census population from the Office of National Statistics (ONS).

group[15]. Sales data were also provided by IMS Health and refer to wholesaler and manufacturer distribution to retail pharmacy and dispensing doctors[16]. This data was supplemented by basic GP organisational and demographic data taken from the Office for National Statistics. Table 1 summarises these variables and summary statistics.

Table 1

The learning process held to influence diffusion discussed above is well suited to a dynamic panel data approach. Given that past prescription experience is used as explanatory variable the selection of an autoregressive-distributed lag model to estimate the coefficients of the variables seems appropriate. Using an AR(1) structure the model can be expressed as follows

$$q_{it} = \alpha.p_t + \delta \cdot q_{it-1} + \beta \cdot z_{it} + c_i + e_{it}; \quad i = 1,2,...,N; \quad t = 2,...,T$$

where q_{it} is the series for cross-section i at time period t with p_t the weighted real therapeutic price variable and q_{it-1} is the lagged value of the dependent variable. In addition to the self-learning effect captured by the lag of the dependent variable, vector z_{it} includes all the other informational, organisational and control variables in equation (2.1), i.e. I_{it}, x_{it} and d_{it}. The idiosyncratic term is e_{it} and c_i denotes unobservable practice-specific effects capturing heterogeneity across GP practices.

[15] Note that the available price data covers a shorter period than the prescription data, thus when obtaining estimates of demand equations with prices the study period will be restricted by the price data availability.

[16] Price series and sales were deflated using the CPI.

In order to obtain consistent estimators first-differences are taken to eliminate c_i and remove any bias caused by the correlation of c_i and the lagged dependent variable. So the estimating equation becomes:

$$\Delta q_{it} = \alpha \cdot \Delta p_t + \delta . \Delta q_{it-1} + \beta \cdot \Delta z_{it} + \Delta e_{it} \qquad i = 1,2,...,N\,; \qquad t = 3,...,T$$

where $\Delta q_{it} = q_{it} - q_{it-1}$, $\Delta z_{it} = z_{it} - z_{it-1}$ and $\Delta e_{it} = e_{it} - e_{it-1}$. As the first difference of the lagged dependent variable is now correlated with the first-differenced error component, instrumental variable (IV) estimators must be used in order to obtain consistent estimates. If $T \geq 3$, there are a number of valid instruments that can be used to consistently estimate equation coefficients with a General Methods of Moments (GMM) estimator (Arellano and Bond, 1991; Blundell and Bond, 1998; Bond, 2002). Here we use a vector of the levels of prescribing quantities, and where appropriate price, sales and marketing data across different time periods (up to T-2) as instruments for the first-differenced equations. Due to the highly persistent prescription series, the preferred estimation method is the "system GMM" estimator, as the first-differences GMM estimator has been found to have poor finite sample properties when the lagged levels are weakly correlated with the first differences (Blundell and Bond, 1988).

IV. Results

All results refer to the estimates obtained using system GMM assuming endogeneity of the price variables, sales and marketing efforts. The prescription volume series, q_{it}, are found to be persistent but unit root tests rejected stationarity. The persistence of the series supports use of the system GMM estimators, combining equations in differences and levels for estimation. The first column in Table 2 presents the results when price (in

logarithms) is included[17]. Note that these results refer 1991-2002, the time frame for which price data was available. The instruments used are the following $(p_{i,t-2}, p_{i,t-3},..., p_{i1}; q_{i,t-2}, q_{i,t-3},..., q_{i1}; me_{t-2}, me_{i,t-3},..., me_1; m_{t-2}, m_{i,t-3},..., m_1)$ for the equations in differences and $(\Delta p_{i,t-1}; \Delta q_{i,t-1}, \Delta me_{t-1}, \Delta m_{t-1})$ for the equations in levels[18]. The vector of instruments is adjusted according to the variables included in the various specifications.

Results reported in column 1 Table 2 show the price elasticity to be negative but not statistically significant, and is therefore consistent with the OFT (2007) findings of no evidence of price responsiveness in the demand for new drugs by GPs in the UK. *Ceteris paribus* new drug prescription would not necessarily be driven by prices, as it is the price effect on marginal treatment cost that would matter. Given the lack of significance of price elasticity in statin prescription, the lack of influence of price on diffusion and the potential simultaneity across price and volume defined variables attention is now given to the diffusion equations that exclude prices. Note however that the coefficients on the variables reflecting self-experience and practice externalities, which we return to below, are significant and consistent across all specifications.

Interestingly, although practices that are fund-holders and drug-dispensers are expected to have a faster up-take of statins there is no significant estimated impact and this result

[17] Alternative specifications with one and two lags of the dependent variable (Pres(t-1) and Pres(t-2)) and sales (Sales and Sales(t-1)) were also considered to explore alternative dynamic specifications but to no great effect.

[18] A large number of instruments included in the estimation may lead to a problem of weak instruments and the Sargan test of the validity of additional moment conditions may not be reliable. In the results presented, all possible instruments were included. However, we also run the model using five lags as instruments. Results did not change and the Sargan test confirmed the validity of the additional moment conditions used in the estimation procedure.

is robust across all the specifications presented[19]. Therefore, there is no evidence from our data that organisational factors influence diffusion[20]. One could potentially pursue between and within GP practice differences, but the use of dynamic longitudinal models allows the control for unobservable heterogeneity. Consequently, other managerial attitudes that cannot be measured are captured by the unobserved practice-specific effect c_i, and are not further pursued here.

Table 2

Column 2 in Table 2 shows the results for the estimation of the diffusion equation for the period 1991-2004 without the price variable. Overall, the results suggest that self-experience from direct prescription and cumulative clinical evidence have a positive impact on the up-take and diffusion of pharmaceutical drugs, while the number of GPs within a practice appears negatively related to up-take and diffusion.

The estimate that refers to self-learning through prescribing indicates a strongly significant and positive impact of past experience on current new drug up-take for statins. The logarithmic specification of the functional form makes it possible to interpret the coefficient as an elasticity, therefore implying that diffusion has an elasticity of 0.63

[19] The fundholding and drug dispensing practice characteristics present the peculiarity that are both constant over time. The prescription data collected by IMS Disease-Analyzer recorded at the beginning of the data collection whether the practice was classified as fundholder and/or drug dispenser; however, this information was not updated in the subsequent years. Although practices might have changed status, these characteristics indicate the managerial attitude that the practice might have. In the case of fundholding, in 1999 all GP practices were required to join into Primary Care Groups (PCGs) but this change can be considered to happen in a mature stage where the efficacy of the prescription drugs was better known.

[20] A further possibility was inspected to detect whether the interaction of these two effects may be strong enough to show a significant result that could support the hypothesis of organisational factors. This might indicate that in these cases the combination of having a budget could be counterbalanced by the additional set of incentives that can be derived from having extra revenue arising from selling the drug in-site. Results could not support the effect of the interaction of these two factors and thus corroborates the lack of influence of the managerial strategy that defined the activity of each practice.

with respect to self-experience. We also find that accumulated scientific evidence also has a strongly significant positive impact on statins diffusion. The number of GPs within a practice appears to be negatively related to diffusion. Whilst initially surprising, having controlled for other factors, this negative impact might reflect greater efficiency in practice externalities, with smaller practices leading to easier flow of information across GPs within the practice reinforcing the self-learning product information flow. Conversely, it might reflect that larger GP practices have tighter controls over up-take. In this specification marketing efforts also have a pronounced effect on diffusion.

The estimate for sales retains statistical significance but the sign of its coefficient changes. This counter-intuitive negative sign on sales is possibly reflecting contamination with the now excluded price variable. Consequently, a further estimation also excludes this variable to consider the stability of the independent effect of the other covariates. These results are reported in column 3 in Table 2. All other variables of interest remain stable apart from the marketing variable, which now becomes insignificant. All other variables reflecting informational flows retain their sign with self-experience and cumulative clinical evidence on statins having a positive impact on up-take and diffusion, and GP practice size again being negatively associated with diffusion. All institutional variables remain insignificant.

While the four informational channels are clearly conceptually different there is apparent statistical overlap. While the paper is attempting to disentangle the different impacts of these informational flows on diffusion, estimation of an integrated dynamic model becomes difficult given the implied multicollinearity between some of the individual

proxies for our informational flows. Price and sales levels are obviously collinear; sales is then seemingly contaminated in regression runs where the price variable is excluded. When the variable sales is dropped, the marketing variable becomes affected, presumably through the causal relationship which will exist between sales and marketing[21]. Consequently, and as a robustness check on the other variables, the marketing variable is dropped from the specification shown by the final column of Table 2. The remaining sub-set of information flow variables appears stable and consistent; their coefficients and significance appear robust to the dropping of these other variables.

Note that for the results presented in this section, specification tests support the empirical model. As Arellano and Bond (1991) argue the consistency of the estimators depends on the lack of second-order serially uncorrelated error terms. Tests on first- and second-order autocorrelation indicated that we could not rule out the presence of first-order autocorrelation but the presence of second-order autocorrelation was rejected at 1% significance level. In addition, the validity of the additional moment conditions imposed by the instruments used to control for the presence of AR(1) and endogenous variables is also tested. The Hansen/Sargan test accepts the validity of the overidentifying restrictions. The results presented are one-step robust estimates given that two-step estimators have been shown to bring little efficiency gains and the trade-off that using a two-step matrix weight brings in terms of asymptotics (Bond, 2002).

As discussed above the marketing variable does not reflect product-specific marketing efforts or the manufacturer's firm size. In constructing a composite index with the intent

[21] The contamination between these two variables is further confirmed by the fact that the same specification as in column 3 but excluding sales instead of marketing gives an insignificant and negative coefficient of the variable sales.

of capturing marketing effort for the whole therapeutical class it may be that we are averaging out marketing effort. In an attempt to further investigate the impact of marketing, given the data restrictions imposed on both the overall data set as noted above, we pursued further estimation using two additional proxies of pharmaceutical company marketing effort [22] . We first consider a variable that reflects the marketing effort by the manufacturer of the initial statin introduced onto the market, simvastatin. Being the first entrant brings clear potential long-term benefits to advertising. The first mover faces initial entry barriers, but may also capture brand loyalty in subsequent periods. The underlying idea here is that the initial marketing activity of the first product may be an important indicator of the impact of marketing more generally but will be less correlated with general therapeutic sales levels as it is product-specific. To further test this idea we also examine the marketing effort of the fourth statin to be introduced, atorvastatin. This specific product has come to be seen as the most direct competitor of the initial statin, given its therapeutic advantage, on the market and again, while the product specific marketing is held to be less correlated with the sales variable, it may also reflect the role of marketing generally in the diffusion process. Both of these alternative proxies were again measured by the proportion of employees in the sales/distribution department using data from the Companies House as detailed above. Results are presented in Table 3 and the sales variable is excluded to control for contamination between sales and marketing.

Table 3

[22] This measurement difficulty is not aided by a general reluctance of the industry to release product specific marketing data due to commercial sensitivities.

As can be seen from the results of Table 3 these additional proxies did not introduce any further insight. Both proxies indicate a positive impact on diffusion but the effect is not significant. The variables on self-experience and GP size remain significant and robust when compared to earlier results. The clinical evidence variable remains relatively robust, although it becomes insignificant when the marketing levels of the first entrant are proxied.

V. Concluding Remarks

The results obtained suggests that prices are not an important driving force in the diffusion of statins within the UK, in line with the most recent evidence provided by the OFT (2007) on the lack of drug price awareness by GPs. The evidence provided with respect to financial incentives given to GPs as measured by the fund-holding and drug-dispensing status is also in line a finding of no relationship between volume and prices. The results robustly suggest that self-experience through prescribing plays an important role. This is a result consistent with the characterisation of drugs as experience goods and with physicians acquiring knowledge about the product safety and efficacy through drug prescription. Cumulative clinical evidence is also found to play a significant and independent role in aiding statins diffuse across the health sector. The size of the GP practice appears to be inversely related with diffusion. This aspect warrants further investigation in order to determine exactly the explanation behind this negative causal relation, although it is consistent with GP practice externalities being more efficient when GP numbers are small.

Careful interpretation is required given the proxies used for marketing efforts. In considering the various specifications the impact of marketing effort is generally in the presumed *a priori* direction and diffusion does appear to be augmented by pharmaceutical company marketing, although the relationship could not be statistically fully supported. The estimates for marketing activity were highly conditioned on the variable measurement and the proxy used to capture advertising. Despite the fact that we did not hold accurate marketing data, proxies were included to control for this influence. Improved marketing data, which is undoubtedly collected but of high commercial value, would be most useful in investigating this impact further. Conceptually diffusion could also be explained by general market consumption externalities, although empirically this could not be statistically determined as the variable used as proxy (sales) appeared to be contaminated by others covariates; specifically price and marketing.

The data available for this paper were specific to the statins therapeutical class, being a new drug class with a highly innovative therapeutical contribution. However, analysis of diffusion of other new therapeutical classes ought to be pursued to improve the results reported here. Other drug classes would present different characteristics that could lead to dynamics that shape diffusion differently. Also the data used here had the limitation that individual prescription patterns could not be observed because prescriptions were generally tagged under the leading prescriber in the practice. The analysis therefore had to be focused on the prescription pattern of the GP practice instead. Ideally, additional research would examine the prescription patterns of individual physicians. This could possibly be analysed using survey data on prescriptions, but would have the limitation of

short period of observational data, something that our dataset overcomes as there are fourteen years of data.

This research used a dynamic model to simultaneously test various influences on pharmaceutical diffusion within the UK GP sector. However, empirically there were data limitations that could not provide full robust evidence on some of the individual informational aspects. This was an ambitious aim given the inherent complexities of the diffusion process and the lack of primary data. The data restrictions reflect the indicative nature of our results, although it is clear that independent influences are at work in the diffusion process. Thus, further work on this area is necessary to confirm the determinants of the diffusion of health care technology generally and pharmaceuticals specifically, before full understanding can be given to the process of diffusion in this area.

References

ARELLANO, M., and S. BOND (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.

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

BANERJEE, A. V. (1992): "A Simple Model of Herd Behavior," *The Quarterly Journal of Economics*, 107, 797-817.

BERNDT, E. R., L. BUI, D. R. REILEY, and G. L. URBAN (1995): "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," *The American Economic Review*, 85, 100-105.

BERNDT, E. R., L. T. BUI, D. H. LUCKING-REILEY, and G. L. URBAN (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*, ed. by T. F. Bresnahan, and R. J. Gordon. Chicago: The University of Chicago Press.

BERNDT, E. R., R. S. PINDYCK, and P. AZOULAY (2003): "Consumption Externalities and Diffusion in Pharmaceutical Markets: Antiulcer Drugs," *The Journal of Industrial Economics*, 51, 243.

BIKHCHANDANI, S., A. CHANDRA, D. GOLDMAN, and I. WELCH (2001): "The Economics of Iatroepidemics and Quakeries: Physician Learning, Informational Cascades and Geographic Variation in Medical Practice," *Paper prepared for the 2001 NBER Summer Institute*.

BIKHCHANDANI, S., D. HIRSHLEIFER, and I. WELCH (1992): "A Theory of Fads, Fashion, Custom, and Cultural Change as Informational Cascades," *The Journal of Political Economy*, 100, 992-1026.

BLUNDELL, R., and S. BOND (1998): "Initial Conditions and Moment Restrictions in Dynamic Panel Data Models," *Journal of Econometrics*, 87, 115-143.

BOND, S. R. (2002): "Dynamic Panel Data Models: A Guide to Micro Data Methods and Practice," *Portuguese Economic Journal*, 1, 141-162.

BRADFORD, W. D., and A. N. KLIET (2010): "The Impact of Public Information and FDA Issued Warnings on the Utilization of Antidepressants in Adolescents and Young Adults," *Presented at the Third Biennial American Society of Health Economists Conference*.

BRADLOW, J., and A. COULTER (1993): "Effect of Fundholding and Indicative Prescribing Schemes on General Practitioners' Prescribing Costs," *British Medical Journal*, 307, 1186-9.

CHING, A., and M. ISHIHARA (2010): "The Effects of Detailing on Prescribing Decisions under Quality Uncertainty," *Quantitative Marketing and Economics*, 8, 123-165.

CHINTAGUNTA, P., R. JIANG, and G. JIN (2009): "Information, Learning, and Drug Diffusion: The Case of Cox-2 Inhibitors," *Quantitative Marketing and Economics*, 7, 399-443.

COSCELLI, A., and M. SHUM (2004): "An Empirical Model of Learning and Patient Spillovers in New Drug Entry," *Journal of Econometrics*, 122, 213-246.

CRAWFORD, G. S., and M. SHUM (2005): "Uncertainty and Learning in Pharmaceutical Demand," *Econometrica*, 73, 1137-1173.

CURRIE, G. R., and S. PARK (2002): "The Effects of Advertising and Consumption Experience on the Demand for Antidepressant Drugs."

DELNOIJ, D., and G. BRENNER (2000): "Importing Budget Systems from Other Countries: What Can We Learn from the German Drug Budget and the British GP Fundholding?," *Health Policy*, 52, 157-169.

GOSDEN, T., and D. J. TORGERSON (1997): "The Effect of Fundholding on Prescribing and Referral Costs: A Review of the Evidence," *Health Policy*, 40, 103-114.

HURWITZ, M. A., and R. E. CAVES (1988): "Persuasion or Information? Promotion and the Shares of Brand Name and Generic Pharmaceuticals," *Journal of Law and Economics*, 31, 299-320.

KANAVOS, P., FONT, J. C. and MCGUIRE, A. (2007) Product differentiation, competition and regulation of new drugs: the case of statins in four European countries. *Managerial & Decision Economics,* 28**,** 455-465.

LEFFLER, K. B. (1981): "Persuasion or Information? The Economics of Prescription Drug Advertising," *Journal of Law and Economics*, 24, 45-74.

LUNDIN, D. (2000): "Moral Hazard in Physician Prescription Behavior," *Journal of Health Economics*, 19, 639-62.

MAXWELL, M., D. HEANEY, J. G. HOWIE, and S. NOBLE (1993): "General Practice Fundholding: Observations on Prescribing Patterns and Costs Using the Defined Daily Dose Method," *Bmj*, 307, 1190-4.

NAIR, H., P. MANCHANDA, and T. BHATIA (2010): "Asymmetric Social Interactions in Physician Prescription Behavior: The Role of Opinion Leaders," *Journal of Marketing Research*, Forthcoming.

NICE (2006): "Statins for the Prevention of Cardiovascular Events."

OFT (2007): "The Pharmaceutical Price Regulation Scheme," *Office of Fair Trading*.

SHILLER, R. J. (1995): "Conversation, Information, and Herd Behavior," *The American Economic Review*, 85, 181-185.

WILSON, R. P., I. BUCHAN, and T. WALLEY (1995): "Alterations in Prescribing by General Practitioner Fundholders: An Observational Study," *British Medical Journal*, 311, 1347-50.

WINDMEIJER, F., E. DE LAAT, R. DOUVEN, and E. MOT (2006): "Pharmaceutical Promotion and GP Prescription Behaviour," *Health Economics*, 15, 5-18.

Table 1. Summary Statistics

Variable	Description	Mean	Std. Err.
Pres	Average Prescription per physician (logs)	2.25	0.047
Sales	Market externalities proxied by market sales (logs)	18.90	0.031
NGP	Practice externalities (number of GPs in practice)	5.13	0.053
Ce	Clinical Evidence	806.19	10.14
Mkt	Marketing efforts	0.487	0.001
Fh	Fund-holding (=1 if practice is fundholder)	1.48	0.012
Dd	Drug dispensing (=1 if drug dispenser)	0.20	0.010
GPs	General Practitioners by regional health authority	2459	20.98
Pop45_64	Percentage population aged 45-64 by regional health authority	0.23	0.0005
Pop65	Percentage population aged 65 and above by regional health authority	0.16	0.0004

Table 2. Diffusion Equations

Dep. Variable: Pres(t)	(1) All	(2) No Price	(3) No price and no sales	(4) No price, no sales, no Mkt
Price	-2.310596			
Pres(t-1)	0.624707***	0.636175***	0.636175***	0.611009***
Sales	0.431009	-0.557860*		
NGP	-0.026837**	-0.027890**	-0.027890**	-0.029758**
Ce	-0.000228	0.001051***	0.000295**	0.000538***
Mkt	0.645699	0.728427**	-0.547026	
Fh	0.005221	0.01735	0.01735	0.017041
Dd	0.087716	0.093058	0.093058	0.100084
GPs	-0.000053	-0.000046	-0.000046	-0.00005
Pop45_64	-1.77288	-1.15118	-1.15118	-1.215463
Pop65	1.31778	1.002882	1.002882	1.062023
Time Dummies	Yes	Yes	Yes	Yes
N	1334	1594	1594	1594
m1	0	0	0	0.001
m2	0.069	0.04	0.04	0.04
Hansen/Sargan	0.74	0.998	0.998	0.239

Notes: Legend: * p<0.05; ** p<0.01; *** p<0.001
m1 and m2 are the first and second order serial correlation tests
p-value reported for the Hansen/Sargan test
GMM results are one-step robust estimates

Table 3. Diffusion equations with marketing proxied by advertising efforts by first and fourth entrant.

Dep. Variable: Pres(t)	(1) No sales/1st entrant	(2) No Sales/4th entrant
Pres(t-1)	0.636175***	0.643720***
Sales		
NGP	-0.027890**	-0.027414**
Ce	0.000183	0.000404***
Mkt 1st/ 4th entrant	1.102233	2.222887
Fh	0.01735	0.016682
Dd	0.093058	0.091575
GPs	-0.000046	-0.000046*
Pop45_64	-1.15118	-1.214521
Pop65	1.002882	1.085545
Time Dummies	Yes	Yes
N	1594	1594
m1	0	0.001
m2	0.04	0.039
Hansen/Sargan	0.997	0.553

Note: see legend in Table 2