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Market Effects of Generic Entry: The Role of Physicians and of Non-Bioequivalent Competitors

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THE ROLE OF PHYSICIANS AND OF NON-BIOEQUIVALENT COMPETITORS

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MARKET EFFECTS OF GENERIC ENTRY: THE ROLE OF PHYSICIANS AND OF NON-BIOEQUIVALENT COMPETITORS

Abstract

Patent expiration represents a turning point for the brand losing patent protection as bioequivalent generic versions of the drug quickly enter the market at reduced prices. In this paper, we study how physician characteristics and their prescribing decisions impact the competition among molecules of a therapeutic class, once generic versions of one of these molecules enter the market. Specifically, we study the evolution of the Selective Serotonine Reuptake Inhibitors (SSRIs) after the introduction of generic versions of fluoxetine (brand name Prozac) in the United Kingdom (UK).

Our results suggest that, to fully understand the market evolution after generic entry, public health officials need to consider the marketing activities of pharmaceutical companies and determine how (1) individual physicians prescribe *all* competing drugs, and (2) respond to drug prices and marketing actions. For example, we find that a group of physicians sensitive to detailing switch from fluoxetine to non-bioequivalent branded alternatives after patent expiration, as Prozac significantly reduces its marketing support. Consequently, the market share of fluoxetine decreases despite being available at significant price discount under generic form, and despite the increase of prescriptions by price-sensitive physicians. Hence, governments interested in assessing generics diffusion should consider the prescribing across *all* competitors, whether or not bioequivalent, and determine the size of physician segments sensitive to pharmaceutical marketing activity and prices.

Key words: Generic entry, Pharmaceuticals, Heterogeneity, Competition

1. Introduction

With a significant number of major blockbuster molecules no longer protected by patents, or nearing patent expiration, drug companies have demonstrated an increased interest in studying generic drug competition and its market penetration. For example, over the next five to ten years about US$40 billion of prescription revenue is expected to be affected by patent expiration and consequent generic entry (Van Arnum, 2004). Drug companies are not the only market agents interested in better understanding the substitution patterns between generic versus branded versions of a molecule. Rising health care costs have become a major public concern in recent years.

Prescription drugs represent a significant component of such costs, with shares ranging from four percent in the United States (US) to nearly 18 percent in France and Italy (Kyle, 2003). As a result, one of the avenues pursued by public health officials to reduce health-related expenditures has been to foster the substitution of branded molecules with lower priced generic versions (Gleckman, 2002). The benefits from such substitution can be substantial. For example, Fischer and Avorn (2003) analyze state-by-state Medicaid prescription drug spending in the US for the year 2000 and find that states would have saved US$229 million with a greater use of generic drugs. Total savings would have reached US$450 million if the best available prices from each state had been used nationally.

The interest of both drug companies and public health officials has spurred significant research efforts in the area of generic drug competition and adoption. A significant portion of this recent literature has focused on the institutional factors and supply side issues that affect generic demand (e.g., Caves, Whinston & Hurwitz 1992; Scott-Morton, 1999, 2000 and 2002; Danzon & Chao 2000), and on the aggregate effects of generic entry on the branded drug losing patent protection (e.g., Frank & Salkever, 1992 and 1997; Magazzini, Pammolli, Riccaboni & Magazzini, 2004; Lexchin, 2004). The role of physicians on the demand for generics and on generic competition has received far less attention (e.g., Hellerstein, 1998), though a critical feature of prescription pharmaceuticals is that the end consumer, the patient, does not select the drug she will consume. Instead, the physician decides the drug therapy and, in

most western countries, whether the patient will receive a branded drug or its generic alternative, once generics become available in the market.

Using a unique panel data that tracks physician prescription behavior before and after entry of a generic drug, we study how physician characteristics (observable and unobservable) and their prescribing decisions impact the competition among molecules of a therapeutic class, once generic versions of one of these molecules enter the market. Specifically, we study the evolution of the Selective Serotonin Reuptake Inhibitors (SSRIs), a subcategory of antidepressants, after the introduction of generic versions of fluoxetine (brand name Prozac) in the United Kingdom (UK).

Unlike previous research, we analyze simultaneously the competition between the entering generics and the brand that faces patent expiration (within-molecule competition), and the competition among all of the molecules in the therapeutic class (between-molecule competition). In the analysis, we control for the marketing activity targeted to physicians and for drug similarity due to bioequivalence as in the case of branded molecules and their generic counterparts. These are factors ignored by previous research. In addition, we compare the behavior of physicians before and after patent expiration. This allows us to study how physician characteristics, measured before patent expiration (e.g., drug preference, sensitivity to marketing activity, and sensitivity to prices) are predictive of the market evolution of generics, of the brand facing patent expiration, and of the remaining brands in the therapeutic class.

Our findings are of interest for both managers and policy makers. For example, in this empirical application we find that the market share of the molecule losing patent protection, (also called the multi-source molecule because of its availability under branded and generic versions) decreased after patent expiration, a pattern undesirable by most governments but not uncommon (see Caves et al., 1992). This reduction occurred despite the availability of generics at significant price discounts, and despite the more favorable price differential for the multi-source molecule versus the remaining drugs in the category. We argue that this is due to a significant reduction of marketing support by the brand losing patent protection, in expectation of significant free-riding from generics. As a result, physicians sensitive to marketing activities switch from the multi-source molecule to other (branded) non-bioequivalent molecules. A

smaller segment of price-sensitive physicians, who increase prescribing of the multi-source molecule, is however unable to fully compensate for the behavior of physicians who are sensitive to marketing activities, like detailing.

These results suggest that, to fully understand the market impact of generic drug entry and its subsequent adoption, it is essential to (1) study the full competitive market dynamics (both the within- and the between-molecule competition), (2) account for the marketing activity of pharmaceutical companies, and determine how physicians respond to the marketing actions and drug prices at the individual level, and (3) investigate the prescription habits of physicians even before drugs lose patent protection.

Our findings also suggest that the design of proper incentive schemes by companies and governments should carefully consider the responsiveness of physicians to prices *and* to marketing activity, the size of the different physician segments, and the likely competitive responses of all players in the market (e.g., in this case non-bioequivalent competitors had little reason to fear from generic entry and a deep price cuts would have not been warranted). Even if very detailed information is not available for the all physicians, companies and governments could determine which physicians to target using observable physician characteristics. In this data set, for example, women prescribe generics more often than men, and physicians working in larger practices prescribe more generics than those in smaller practices.

This paper is organized as follows. Next, we present the literature review and the findings relevant to this work. Then we describe the adopted methodology, present the data used, and provide more information on the empirical application setting and estimation issues. Finally, we present the results and elaborate on the implications for policy makers and drug companies. We then conclude with limitations and areas for future research.

2. Literature Review

The importance of generic consumption has created a fertile ground for research on generic drug

competition and adoption. These studies rely mostly on aggregated data and rarely consider the individual physician influence.

2.1 Aggregate Level Studies

A significant portion of the recent literature on generics has focused on the effect of institutional and supply side factors. Such work comprises the analysis of topics such as: the effect of regulation on competition (Danzon & Chao, 2000; Aronsson, Bergman & Rudholm, 2001; Kyle, 2003), the role of buying system characteristics such as insurance and Medicaid coverage (Jayachandran, Nevins & Bearden, 2003), advertising and licensing as entry deterrents (Grabowski & Vernon, 1992; Scott-Morton, 2000; Königbauer, 2005), the integrated production of generics and branded drugs (Ferrándiz, 1999; Scott-Morton, 2002), and factors influencing generic entry (Bae, 1997; Scott-Morton, 1999 and 2000).

Another significant stream of research investigates the dynamics of market shares, quantity sold, and prices after generic entry (e.g., Hurwitz & Caves, 1988; Caves et al., 1992; Frank & Salkever, 1992 and 1997; Aronsson et al., 2001; Reiffen & Ward, 2003; Lexchin, 2004; Magazzini et al., 2004). Results have not always been in agreement, depending often on data and methodology employed, though several important conclusions can be made. For example, most studies report a significant decrease in market share of the original brand after patent expiration, with major brand names in recent years typically losing half of their market share within one year of patent expiration (e.g., Grabowski & Vernon, 1996). In contrast, prices of original brands increase (e.g., Grabowski & Vernon, 1992; Frank & Salkever, 1997) or remain mostly unchanged (e.g., Caves et al., 1992; Lexchin, 2004) though the net effect is an average price reduction for a prescription (Frank & Salkever, 1997).

2.2 Physician Role

With few exceptions, the role of physicians' characteristics and physician decision-making is often ignored, despite the central role that physicians play in prescription drug markets. Recently the few studies that analyze physician-level prescribing data have shed some light on the influence of physicians on generic adoption. Hellerstein (1998) uses US physician prescription data to examine physician choice

of drug version (branded vs. generic) for molecules whose patents had recently expired. She concludes that some physicians are significantly more likely to prescribe generics whereas others are more likely to prescribe brands (though almost all physicians prescribe both versions), and that physicians are indeed important agents in shaping the fate of generics. Two other studies on physician role in generic prescribing, Coscelli (2000) and Lundin (2000), draw similar conclusions. Mainly, these studies show that physician habit has a significant influence on generic versus brand-name choices.

Though these recent studies provide important insights regarding the role of physician in shaping within-molecule competition, several questions remain unanswered. First, competition in pharmaceuticals exists both within a molecule (branded vs. generic, prescription vs. over-the-counter) and between different molecules that treat the same condition. Hellerstein (1998), Coscelli (2000), and Lundin (2000) do not incorporate nor study the competition among non-bioequivalent drugs in the same therapeutic class (between-molecule competition), despite previous studies that show the importance of intermolecular competition. For example, Stern (1996) shows that cross-price elasticities between branded and generic versions of a molecule are low and that the cross-price elasticities between therapeutic substitutes are high. Lichtenberg and Philipson (2000) find also that the loss in sales due to the entry of new drugs to the therapeutic class reduces the value of a drug considerably more than the entry of bioequivalent generics.

Second, the works of Hellerstein (1998), Coscelli (2000), and Lundin (2000) have not incorporated pharmaceutical marketing and individual physician response to marketing actions. Marketing actions have a real impact on physician prescribing (e.g., Gönül, Carter, Petrova & Srinivasan, 2001; Wittink, 2002; Venkataraman & Stremersch, 2007) and constitute a major competitive force by which firms strive to differentiate their products and soften price competition. Pharmaceutical firms invest heavily in product promotion, spending as much on marketing as they do on research and development (promotion-to-sales ratios are among the highest of all manufactured goods; Hurwitz & Caves, 1988). Prior studies have also shown that physicians differ in their drug preferences and in their responsiveness to marketing activities and prices (e.g., Venkataraman & Stremersch, 2007), making it essential to incorporate physician heterogeneity in studying generic adoption. Incorporating individual level heterogeneity is also important

from the perspective of brand and generic managers, as the brand losing patent protection tends to significantly reduce its marketing effort, and generic versions do not invest in goodwill building activities (Caves et al., 1992).This structural change is likely to alter the incentives of some physicians and transform the competitive landscape.

In this study we investigate how physician characteristics (observable and unobservable) and physician prescribing decisions impact the competition among *all* molecules of a therapeutic class (e.g., SSRIs, a subcategory of antidepressants), once generic versions of one of these molecules (e.g., fluoxetine) enter the market. In our analysis, and unlike previous research, we will study both within- and between-molecule competition and account for drug price changes. In addition, we control for pharmaceutical marketing activity, physician heterogeneity in response, and drug similarity due to bioequivalence. Next we will present the modeling approach and describe the setting of the empirical application.

3. Modeling Approach

We adopt a two-step approach to investigate how both physician characteristics and prescribing decisions impact the competition among molecules of a therapeutic class, once generic versions of one of these molecules enter the market. In the first phase, we study physician prescribing behavior to characterize physicians in terms of unobservable characteristics like brand and drug preference, responsiveness to marketing activity, and price sensitivity. In the second phase, we study drug prescribing after the initial market settling period, and model the prescribing of the molecule losing patent expiration versus (1) all other drugs in the therapeutic category (between-molecule competition) and (2) the generic competitors (within-molecule competition). For the second phase, we use as covariates the estimates from the first phase and test whether the level of physician detailing sensitivity and other unobservable physician characteristics allow a better understanding of physician prescribing after patent expiration.

3.1 Phase 1: Random Effects Multinomial Nested Logit Model

In the first phase, we model the physician decision of drug choice for each patient visit given a

prescription in the focal therapeutic category as a two-level process: physicians select which molecule to prescribe given a prescription in the category (e.g., fluoxetine versus citalopram given an SSRI prescription) and then which version (e.g., branded versus generic). This modeling approach creates a two-level tree structure (Figure 1) that can be estimated using the well-known multinomial nested logit (for model details and derivation please see Appendix A). We estimate individual level parameters (e.g., underlying preferences, responsiveness to marketing activity and prices) via a random effects formulation and use these to characterize physicians. The model is estimated using Bayesian simulation methods (for details see Appendix B).

During this first phase we observe physicians for a significant period before generic entry and during the initial stages of generic entry while the market settles (we call this Period 1). This allows the reliable measurement of physician characteristics and the measurement of physician's preference for drug version (generic vs. branded). Physicians are not always indifferent between the two because generics do not benefit from previous investments in goodwill (e.g., advertising) and from years of market presence and experience as do branded versions. Physicians can then see generics as a trade-off between cost and (perceived) quality (see Caves et al., 1992).

We believe that the proposed random effects multinomial nested logit approach is the most appropriate. First, multinomial logit models are well known, robust, and widely used to study choice behavior when full competitive information is available. Previous applications include the analysis of pharmaceuticals (e.g., Narayanan, Manchanda & Chintagunta 2005; Gönül et al., 2001), transportation mode (e.g, Ben-Akiva & Lerman, 1985), and packaged goods (e.g., Bucklin & Gupta, 1992). Prior studies of drug performance (Jayachandran et al., 2003) also suggest that the entry of generic pharmaceuticals does not lead to appreciable market expansion and the data used for this study also supports this contention. As a result, we can account for the full competitive actions when modeling drug choice conditional on a prescription using a multinomial choice model. In addition, previous studies on pharmaceuticals have shown that, at a given patient visit, physicians are influenced by their own previous prescription choices (e.g., Janakiraman, Dutta, Sismeiro & Stern, 2007). As a result, by modeling the

prescription decision for each individual patient, we can account for these carryover effects.

Finally, the nested structure avoids the Independence of Irrelevant Alternatives property (IIA) that is present in standard multinomial logit models. Government agencies evaluate and approve the bioequivalence of generic drugs, and though controversy persists about the bioequivalence of a handful of medications, nearly all other generic drugs provide identical therapeutic benefits (Fischer & Avorn, 2003). In contrast, different branded molecules in a therapeutic class can be used to treat the same illness, but are not therapeutically equivalent, and patients can differ in their susceptibility towards them. Standard models cannot account for this closer similarity of two or more alternatives[2] because of the IIA property (see Ben-Akiva & Lerman, 1985). This is avoided using the nested structure.

3.2 Phase 2: Binomial Models

In the second phase of the analysis, we study drug prescribing after the initial market settling period. We will denote this time period as Period 2 (the same physicians are tracked in Period 1 and 2). Using the data in Period 2, we model (1) the prescribing of the *molecule* losing patent protection, generic and branded versions combined, versus all other drugs in the therapeutic category (between-molecule competition) and (2) the prescribing of the *brand* losing patent protection versus its generic competitors (within-molecule competition). In these between- and within-molecule competition analyses we will study whether *observable* (e.g., gender and practice size) and *unobservable* (e.g., responsiveness to marketing actions and price) physician characteristics can predict the market evolution after generic entry. To measure the unobservable physician characteristics we will use the physician parameters obtained in the first modeling phase (using the random effects multinomial nested logit model).

To study prescriptions of the *molecule* losing patent expiry versus *all other drugs* in the therapeutic category (between-molecule competition), we estimate a binomial model (details in Appendix A). We

[2] Though generics and branded drugs are bioequivalent with respect to their active ingredients, they do not necessarily contain the same inactive ingredients, nor are sold under the same dosages or formats. That is why the two versions are "more similar" and not "exactly the same". For example, Fridman, Jaffe, and Steinhardt (1987) found that only half of 245 physicians surveyed believed that generic drugs are as effective as the original branded version. As explained before, the structure of the nested multinomial logit will also allow us to test the level of substitution within and between molecules by looking at the inclusive value parameter.

assume that, after patent expiration, for physician i and across all n_i prescriptions in the category, the probability of prescribing the multi-source molecule irrespective of its form (p_i) is a function of (1) physician-specific unobservable (estimated in the first phase) and observable characteristics, and (2) a prescription baseline. Hence, the prescription probability is then given by:

$$p_i = \frac{\exp(s_i + \alpha + Z_i\theta)}{1 + \exp(s_i + \alpha + Z_i\theta)}, \quad (1)$$

where, Z_i is a ($1\times q$) vector of physician characteristics (observable and unobservable), θ is the ($q\times 1$) vector of parameters, α represents the model intercept, and s_i is the prescription baseline.

We estimate two alternative model formulations that correspond to two alternative baselines. One model formulation will allow the study of prescribing *changes* from Period 1 to Period 2. To do so we set as prescription baseline the logit transformation of the prescription share of the multi-source drug for each physician, that is, $s_i = \log(SHARE_i / (1\text{-}SHARE_i))$ where $SHARE_i$ is the prescription share for the multi-source molecule (vs. all molecules of the category) during Period 1 (we call this Model I; see Table 1). The interpretation is straightforward (assume for simplicity that $\alpha = 0$): if the observable and unobservable physician characteristics are not predictive of prescribing changes from Period 1 to Period 2, then the θ will *not* be significantly different from zero and the best model will set the probability of prescribing the molecule equal to the previous prescribing share for that physician ($p_i = SHARE_i$), otherwise θ will be significantly different from zero and it will shift the prescription probability of each physician away from her own previous prescribing share.

The second model formulation will allow the study of how physicians split their prescribing into the different drug alternatives in Period 2. In this case, we set to zero the prescribing baseline ($s_i = 0$; we call this Model II) and are able to study how different physicians prescribe the drug after patent expiry. We adopt similar model formulations to study within-molecule competition. In this case the variables of the binomial likelihood will correspond to branded prescriptions of Period 2 versus total multi-source

prescriptions of Period 2. Both baseline formulations are possible for the within-molecule binomial model and these models are called Model IV and Model III (see Table 1 for a summary).

4. Data

We use a dataset on physician prescribing behavior and competitive marketing activity from a continuous panel of General Practitioners (GP) in the UK, tracked from September 1998 to September 2000. The category of prescriptions tracked are those of Selective Serotonin Reuptake Inhibitors (SSRIs), a subcategory of antidepressants, and the time-period under analysis covers the patent expiration of fluoxetine (brand name Prozac), which occurred in January 2000.

4.1 The Selective Serotonine Reuptake Inhibitors Category in the UK

Fluoxetine Hydrochloride was the first SSRI, marketed worldwide under the name of Prozac. It was launched in 1988 and quickly became a success. Proclaimed as a wonder drug, it benefited from the unprecedented media attention, the marketing efforts of Eli-Lilly (its manufacturer), milder side effects, and the novel benefit of non-lethal overdoses. This success led to introductions of more SSRIs during the 1990s: Seroxat (Glaxo-Smithkline-Beecham) and Lustral (Pfizer) both introduced in 1991, and Cipramil (Lundbeck) introduced in 1995.[3] On January 2000, the last patent held by Eli-Lilly in the UK on its blockbuster drug ended, and 14 companies launched generic versions of fluoxetine. At the end of 2000 generic versions of fluoxetine had overcome Prozac in unit sales, and the amount of money paid by the UK National Health System for Prozac 20mg (the most common format) plunged from £88.1 million in 1999 to £61 million in 2000. In 2000, the average prescription price for Prozac was £26.12 whereas generic versions were priced at £15.29 (Department of Health UK, 2002).

The UK market development after the entry of generic fluoxetine is similar to those in other markets and pharmaceutical categories: the original brand tends to lose market share rapidly because generics are offered at deep discount; however, the molecule as a whole does not necessarily grow. This makes the example of Prozac/fluoxetine in the UK an ideal case to study. In addition, the specific features

of the UK market are also especially appealing for this study. First, direct to consumer advertising of prescription drugs is not allowed in the UK and drugs can only be advertised in medical journals. Also medical insurance and the actions of Health Management Organizations (Gönül et al., 2001) do not play a significant role in the UK due to the ubiquity of the National Health Service (NHS). Patients pay a flat rate for prescription drugs, regardless of the cost of the drug (e.g., in 2004 UK patients paid £5.25 per prescription, which covered 40% of the average prescription cost). Thus patients tend to exert a weak influence on physician prescription decisions due to weak cost-related incentives and lack of information.

Furthermore, in the UK, prices of drugs under patent are the outcome of negotiations between pharmaceutical companies and the NHS, translating into small price variations across drugs and for each drug across time. For example, in this sample there was only one significant price change across all brands during the two-year period under analysis, and this change was motivated by exogenous and not strategic reasons (NHS Report, 2002).[4] Hence, there is little incentive for patients to keep track of prices.

Lastly, physicians in the UK (as in most Western economies) play an important role in deciding under which format, generic or branded, patients will receive the multi-source drug. If a prescription is written under the molecule name the pharmacist can dispense any product containing the molecule; if a brand name is prescribed, the pharmacist has to dispense the brand. Because pharmacists have strong incentives to dispense generics if they want to remain competitive[5], the format choice of a specific molecule will be mostly at the hands of the physician.

4.2 Detailed Data Description

For each physician we have information on (1) new SSRI prescriptions and changes of SSRI

[3] The brand names in the US are Paxil (Seroxat), Zoloft (Lustral) and Celexa (Cipramil).

[4] The Pharmaceutical Price Regulation Scheme (PPRS) regulates the prices that drugs protected by patents receive from the NHS. Under the PPRS, companies are obliged to reduce prices of a drug if the financial returns for that drug exceed certain threshold. One of the price reductions observed in the data was indeed imposed by PPRS; the other significant change was due to the entry of generics.

[5] Legislation in the UK fosters competition at the retail level. Generally speaking, the NHS calculates an average price for each drug in the UK and reimburses the pharmacist according to this price. Therefore, drugstores feel the pressure to be efficient in buying, and the cheapest alternatives tend to be generics. A complete description of how this system works is beyond this manuscript. For details, shortcomings and suggested ways of improving the system, read "Fundamental Review of the Generic Drugs Market," a Report prepared by OXERA on behalf of the Department of Health (July 2001).

medication for each patient treated, (2) frequency and timing of sales representatives' visits to physicians from all competing drugs in the market, and (3) physician specific information (gender and practice size). We retained all the records in which Prozac (fluoxetine), Seroxat (paroxetine), Lustral (sertraline), and Cipramil (citalopram) had been prescribed. These are the four key players for this category during the two years covered by the data, and represent over 98% of all SSRI prescriptions. We do not include the remaining (much smaller) drugs in the analysis because of their limited impact, although our approach could be easily extended to include them.

In addition, we analyze only those physicians who are active in the category. This is common practice in the industry and allows for the estimation of reliable individual-level parameters. Hence, we retained the prescription choices of physicians who wrote at least ten new SSRI prescriptions and received at least one sales call from any of the four key players in the two-year period under analysis. This subset of 170 physicians provides a good indicator of the whole sample as it accounts for more than 80% of all SSRI prescriptions in the time period under analysis.

Table 2 provides the summary statistics of prescriptions and detailing visits per molecule for the final dataset. Period 1 includes the 19 months from September 1998 till March 2000, and Period 2 includes the 6 months from April 2000 till September 2000. The final dataset comprises the records of 170 physicians, who wrote a total of 10,079 SSRI prescriptions. Over the entire sample period, SSRIs were prescribed about 403 times each month and engaged in 100 detailing visits monthly. There was significant heterogeneity both in the number of prescriptions and the number of detailing visits across physicians. The minimum number of total prescriptions per physician for Period 1 and 2 combined was 11, and the maximum was 236; for the number of detailing visits, the minimum was two and the maximum 66.

Fluoxetine (Prozac) and paroxetine (Seroxat) were the two market leaders, followed by Citalopram (Cipramil), with Sertraline (Lustral) the fourth largest SSRI brand. An important change in

Period 2 is the reduction in prescription share of 2.2 percent points of fluoxetine as a whole (generic plus brand name) after generic entry. Aggregate data from the NHS also confirms this declining trend (details are available from the authors upon request). Though not novel in the literature (e.g., Caves et al., 1992), this is a surprising result considering that the average prices of fluoxetine dropped 37% immediately after generic entry.

A possible explanation for such market evolution could be the changes in the marketing activity by the branded drugs which retain patent protection. In Period 1 all drugs have similar detailing levels. In contrast, detailing shares shift dramatically in Period 2: Lundbeck increased the detailing of citalopram reaching a share of voice of 39%, Eli Lilly virtually stops Prozac detailing, and generic versions of fluoxetine do not engage in detailing activities. As a result, the detailing share of fluoxetine drops to 4%. This first statistic is very significant as it suggests the importance of analyzing the competition from non-bioequivalent molecules, before and after a patent expires, to study the impact of generic entry. Next, we describe the variables we extracted from the final dataset that were used in the analysis of within- and between-molecule competition.

4.3 Variable Definition for the Random Effects Multinomial Nested Logit Model

A long stream of literature has demonstrated that detailing visits have a major impact on physician prescribing (e.g., Gönül et al., 2001; Wittink, 2002; Venkataraman & Stremersch, 2007). Following previous research (e.g., Gönül et al., 2001), we account for the effect of detailing using a parsimonious and flexible exponential smoothing formulation that allows detailing meetings to have an impact on prescriptions even if they did not occur immediately before a prescription occasion, though it will give more weight to recent detailing visits. Hence, we define the detailing variable, SD_{ijt} as:

$$SD_{ijt} = SDD_{ij\omega(t)}, \text{ for } I = 1, \ldots, N, j = 1, \ldots, J, \text{ and } t = 1, \ldots, T_i, \text{ and} \quad (2)$$

$$SDD_{ij\kappa} = \sum_{\tau=1}^{\kappa} \delta_D^{\kappa-\tau} D_{ij\tau}, \quad (3)$$

where J is the number of alternative molecules, N is the number of physicians observed, T_i is the number of times the physician i prescribes in the category, $\omega(t)$ is a function that maps the *prescribing occasion* t to its corresponding *calendar day* τ, δ_D is the parameter of daily decay ($0 < \delta_D < 1$)[6], and $D_{ij\tau}$ is a dummy variable that takes the value of one if molecule j is detailed to physician i in calendar day τ, the value zero otherwise. With this formulation, the mean of the stock of detailing variables was between 0.18 (Cipramil) and 0.27 (Lustral).

Unlike detailing, price effects have been subject to greater controversy. For example, the results of Arosson et al. (2001) and Lundin (2000) suggest that physicians consider the price patients effectively pay for the drugs when deciding which drug to prescribe. The results of Newhouse (1993) and Gönül et al. (2001) suggest the opposite. Because it is yet unclear whether physicians are or not price sensitive, we will measure physician sensitivity to price. During the time-period under analysis there was only one significant price change unrelated to the entry of generic fluoxetine in the market: a price reduction of 38% of Lustral in June 1999 imposed by the government (Department of Health UK, 2002). We account for this price cut by incorporating a dummy variable, PD_{jt}, that takes the value of one if j = *Lustral* and if a prescription occasion takes place after Lustral's price reduction; PD_{jt} will then be zero all other times. (We do not add a second price dummy for the price reduction of fluoxetine after generic entry because this is part of the overall market impact of generic entry and cannot be modeled independently; the nested structure of the model will account for such changes.)

Finally, another important factor affecting physician prescribing is state-dependence in physician choices which affects the correct measurement of marketing and price responsiveness (Janakiraman et al., 2007). Following previous research we incorporate information about physicians' past prescriptions using a dummy variable, SX_{ijt}, that takes the value of one if physician i selects drug j in prescribing occasion t-1, and that takes the value of zero otherwise (we have tested alternative state dependence specifications and

[6] In our empirical application the daily decay parameter of detailing is fixed so that a detailing visit has a halftime life of 1 month, which means that if detailing is one on the day of the visit, it will be about one half, 30 days after ($\delta_D = 0.997$). We tested for alternative values of the decay parameter and concluded that for halftime lives between 15 and 45 days final results do not change significantly. These are values consistent with previous research.

found that the lagged dummy provides the best fit; details available from the authors upon request).

The final model formulation can then be written as:

$$V_{ijt} = \beta_{0ij} + \beta_{1ij} SD_{ijt} + \beta_{2ij} SX_{ijt} + \beta_{3ij} PD_{jt} + G_{ij} + \varepsilon_{ijt} \quad , \qquad (4)$$

where V_{ijt} is the valuation of molecule j for physician i at prescription occasion t, ε_{ijt} is a general extreme value distributed error term (Train, 2003), and β_{0ij}, β_{1ij}, β_{2ij} and β_{3ij} represent the intercepts (baseline preference), the responsiveness to detailing, the effect of past prescriptions, and the responsiveness to price, respectively. The term G_{ij} is an extra factor that is only present if the molecule is available in generic form. It represents the change in valuation due to the trade-off between the significant price discounts of generic versions and their perceived quality. Finally, all of the parameters are physician and drug specific though some constraints are necessary in the nested multinomial logit model for identification purposes (see Appendix A for details on the constraints).

4.4 Variable Definition for the Binomial Models of Within- and Between-Molecule Competition

We model the within- and between-molecule competition as a function of observable and unobservable physician characteristics. For the observable characteristics we use as covariates physician gender and practice size: gender is defined as a dummy variable that takes the value of one if the physician is male and zero if female; practice size is defined as the number of physicians working in the physician's practice. For the unobservable characteristics we include as explanatory variables the values of the individual-level parameters estimated using the multinomial nested logit. To reduce noise, we build 90% probability intervals for each physician-parameter combination based on 2000 draws from the posterior distribution, and kept only the mean values significantly different from zero. All others were set to zero. The parameters of interest that were included are: the responsiveness to Prozac detailing (β_{1i_Prozac}), the responsiveness to Lustral's price cut (β_{3i}), and the inclusive value parameter (λ_i). We also included the intrinsic attractiveness of Prozac for all the physicians as indicator of the preference for fluoxetine. The other individual level parameters provided little information.

To prevent confounding the responsiveness to detailing and the intrinsic physician preference with

the level of detailing activity and the prescribing levels, we have also included several control variables. These include the number of detailing visits from Prozac and from its competitors during Period 1 and Period 2, and the level of physician prescribing of drugs competing with the multisource molecule during Period 1. Next, we discuss in detail the results, highlight the potential explanations for the market evolution, and elaborate on the implications for policy makers and drug companies. Finally, we conclude with the limitations and areas for future research.

5. Results

First we will discuss briefly the results from the first modeling phase. Then we will discuss in more detail the results from the binomial model that uses as covariates the parameters estimates from the first phase.

5.1 Random Effects Multinomial Nested Logit Model

Table 3 presents the posterior means and 95% probability intervals for the population level estimates of the random effects multinomial nested logit. Consistent with previous research we find significant state-dependence across physicians' drug choices (the posterior mean of the population-level parameter of past prescriptions, β_2, is 0.31 with a probability interval of [0.23, 0.39]). The parameter associated with the price cut of Lustral, β_3, is also positive but marginally significant, with a posterior mean of 0.29 and a probability interval of [0.03, 0.54]. This positive but weak effect is consistent with mixed results in prior studies on the impact of prior cuts. Regarding the intercepts, we find an overall preference for Prozac (fluoxetine) and Seroxat (paroxetine), consistent with their market shares (36% and 33% respectively).

The parameter associated with Prozac detailing has a posterior mean of 0.15, with a wide 95% probability interval that includes zero. The parameters associated with the detailing of the remaining molecules are all significant (i.e., have 95% probability intervals that do not include zero) and positive. Hence, on average for Period 1, Prozac detailing has little or no impact which is consistent with its high level of brand awareness. Detailing from the remaining, newer, and less popular drugs has a positive and significant impact on physician prescribing. In addition, and consistent with previous research, we find

considerable heterogeneity across physicians which confirms the need of modeling individual physician response and of using individual physician data to study physician prescribing (e.g., 12% of the physicians have positive and significant individual parameters for Prozac detailing, with posterior mean values that range from 0.57 to 2.93; the remaining physicians have parameters that were not significant).

Regarding the parameters associated with the nested structure of the model[7], we find the posterior mean of the factor associated with generic versions of fluoxetine (G) to be 2.15, with the 95% probability interval of [1.64, 2.69]. This means that fluoxetine generics are being prescribed more often than Prozac, on those occasions that the molecule fluoxetine is prescribed. This is consistent with previous findings in the literature that describe a very fast share erosion of brand name molecules once generics become available.

The posterior mean of the inclusive value parameter (λ) is related to the degree of within-molecule competition[8]. When λ equals unity, the model tree collapses to a multinomial logit without a nested structure (consistent with generic versions of a multi-source molecule being viewed as completely different drugs from the branded alternative). If, in the limit, λ equals zero ($\lambda \to 0$), each *molecule* (irrespective of format) represents separate choice alternatives. Finally, if λ is positive, but less than one, physicians are indeed influenced by the low price of the generic alternative once generic versions of a given molecule enter the market and will change the valuation of the molecule nest and prescribe more of the molecule losing patent protection[9] (the molecule as a whole becomes more competitive compared to the other molecules). Hence, the magnitude of the λ parameter provides a measure of how generics are perceived by physicians and of their impact once they enter the market. In our case the parameter is very

[7] To test for the use of the nested structure, and for the absence of serious structural breaks in the data, we have also estimated the multinomial logit model with only the data before generic entry. The model parameters and the remaining results for the binomial models remain largely unchanged from the results we present in the paper. This suggests that the multinomial nested logit is a valid model to capture the introduction of a generic in a category as we do in this analysis.

[8] We also estimated a multinomial logit (without nested structure) for the choice of molecule (irrespective of format) with a dummy variable for prescriptions after generic entry (as an alternative model formulation). The posterior mean estimates of the inclusive value parameters and the generic entry dummies are highly correlated, which indicates that a nested logit model is able to capture the changes at the molecule level after patent expiration. The nested logit has the added advantage of modelling also the prescription of the version (branded vs. generic) of the multi-source that is prescribed.

close to zero (posterior mean of 0.02 with a 95% probability interval of [0.01, 0.05]) suggesting that the introduction of fluoxetine in generic format, with the corresponding price reduction, had little or no impact on most physician choices after patent expiry.

We can infer from these results that most physicians perceive generic and branded alternatives of a molecule as very similar in terms of price-quality tradeoffs (they are almost indifferent in prescribing one or the other), and that generic entry does not change significantly the overall perception of the molecule as a whole, that is, similar in terms of price-quality tradeoffs (they are almost indifferent in prescribing one or the other), and that generic entry does not change significantly the overall perception of the molecule as a whole, that is, it did not lead to an expansion in molecule prescription due to its lower price after patent expiration. In addition, even for those physicians who change their behavior, changes are quite small (the posterior means for the inclusive value parameters range from 0.01 to 0.08).

5.2 Binomial Model Estimations Post Generic Entry

Tables 4 and 5 present the results of the binomial regressions of between- and within-molecule competition, respectively, estimated after generics have been introduced (what we called Period 2). All variables in the binomial models deemed non-significant at a 5% significance level were dropped from further analysis, and we only present the parameters estimated for the retained variables. Based on Bayesian Information Criterion (BIC) comparisons the full models are also significant.

In these binomial models, we use as covariates the estimates of unobservable characteristics obtained from the nested logit (these include the sensitivity to detailing and prices). Because such estimates have significant measurement error (e.g., the individual-level parameters obtained from the first stage of the analysis have wide confidence intervals) we need to assess the robustness of our estimates. To do so we use a bootstrap procedure. We re-estimate the binomial models 100 times including as covariates the posterior means of the parameters from the nested logit computed using 100 different random samples of physician-specific draws (we retained 2000 draws during estimation of the nested

[9] Note that in applications with little price variation and with generics entering the market at deep price discounts, it will be

logit for each physician and each sub-sample has 200 draws; re-sampling was performed with replacement). We report the parameters of the binomial models (posterior means used as covariates are computed across the 2000 draws) and the range of the empirical distribution of the t-statistic for the different replications.

Physicians Sensitive to Prozac Detailing Decrease Fluoxetine Prescribing A first significant result from the binomial models is the reduction of fluoxetine prescribing (Prozac plus generics) in Period 2 by those physicians sensitive to Prozac detailing in Period 1. The first and second columns of Table 4 present the results of Model I (model of between-molecule competition that uses the share of fluoxetine prescribing from Period 1 as baseline). This model is adequate to explain the changes in prescribing of fluoxetine (Prozac plus generics) versus other SSRIs from Period 1 to Period 2. The binomial parameter associated with Prozac detailing is –0.22 and significant across all replications. This means that those physicians who are more sensitive to Prozac detailing are the ones who 'move away from' fluoxetine the most (Prozac plus generics) in Period 2 compared to Period 1.

This prescription reduction is quite significant. Based on physician's individual probability intervals for the parameter of Prozac detailing, we have classified physicians into those sensitive to Prozac detailing (HIGH Group) and those not sensitive (LOW Group). About 12% of the physicians were classified as being sensitive (HIGH) and on average these physicians prescribe 8.08% less fluoxetine (Prozac plus generic versions) in Period 2 than what would have been expected considering their prescribing levels from Period 1. Using a Chi-square test we conclude this is a significant change at a 5% significance level. The remaining 88% of physicians classified as LOW, (that is, not responsive to Prozac detailing) did not exhibit any significant change in their prescription behavior in Period 2 from what would have been expected given their prescribing behavior in Period 1 (the average change in fluoxetine prescriptions was –1.30% and not significant).

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impossible to separate the effects due to price sensitivity for the molecule, and those effects due to perceived quality differences between a generic version and the brand name alternative.

The reaction of detail sensitive physicians is perhaps due to the sudden reduction, and subsequent elimination, of Prozac detailing (generics do not engage in marketing activities in this market). Physicians who were greatly influenced by marketing activities end up reducing their fluoxetine prescribing once the marketing actions of Prozac stop, switching to the other SSRIs that maintain (or even increase) their marketing effort like detailing. This means that predictions of generic impact must consider the marketing reactions of the incumbent brands which will retain patent protection and not just the direct effects of generics on the brand losing patent protection.

With respect to the cross-sectional variation of prescribing in Period 2, we note that the responsiveness to Prozac detailing does not explain the physician prescribing split into fluoxetine and other drugs across all physicians (the variable is not significant in Model II; see Table 4) though it explains the prescribing \of Prozac versus generic versions of fluoxetine, once fluoxetine is the prescribed molecule. Physicians responsive to Prozac detailing in Period 1 prescribe generics fewer times, given that the fluoxetine molecule is chosen (the variable has a negative impact, $\theta_{ResponseProzacDetailing} = -0.82$, and is significant in Model IV, the within-molecule model without baseline; see Table 5). This is an interesting result from a public policy point of view. Though physicians sensitive to Prozac detailing (all else constant) do not prescribe the molecule fluoxetine differently from those not responsive (only the changes from Period 1 to Period 2 at the individual-level are affected), once the molecule is chosen physicians prescribe fewer generics if they were sensitive to Prozac detailing. In this case, detailing has a long lasting effect on the market even after it is no longer used by the company: it created loyalty to the brand. This result would have not been discovered had we used traditional regression based techniques using aggregate level data.

Price Sensitive Physicians Increase Fluoxetine Prescribing Physicians with higher inclusive value switch from other SSRI molecules to fluoxetine in Period 2 ($\theta_\lambda = 18.73$ in Model I; recall that this parameter measures also the responsiveness of physicians to price, i.e., the farther away from zero, the more physicians increase the use of fluoxetine because of the presence of low cost generics). The same

pattern is present for physicians sensitive to Lustral's price cut ($\theta_{ResponsePriceCut} = 0.27$ in Model I), even though the effect is less pronounced (this parameter was not significant in 13 replications, out of 100, and we should consider the result cautiously). This pattern is simple to explain: price sensitive physicians see a greater advantage in using fluoxetine, versus all other drugs in the category, because of its reduced price after generic entry. These physicians will then prescribe more fluoxetine than before, and reduce the use of the remaining molecules (switch from other SSRIs to fluoxetine).

Again, the prescription changes are significant. For example, physicians classified as LOW with respect to the inclusive value parameter (about 80% of the sample) *reduce* their fluoxetine prescriptions by 3.83%; those classified as HIGH (about 20%) *increase* the use of fluoxetine by 5.07% more than would have been expected given their prescribing in Period 1. Both changes are statistically significant. However, the increase in fluoxetine prescribing (a result desired from a public policy perspective after generic entry) was not able to compensate the reduction of fluoxetine prescription from other physicians that are not especially price conscious and might be sensitive to other marketing actions such detailing. In addition, the move towards fluoxetine is fuelled by generic prescribing and not Prozac prescribing (as expected and hoped for by most public officials). This can be seen from the results of Model IV (Table 5): physicians with higher inclusive values and higher response to the price cut prescribe more generics than those with lower values for these parameters ($\theta_{ResponsePriceCut} = 0.93$ and $\theta_{\lambda} = 42.78$ in Model IV).

<u>*Observable Physician Characteristics can help to predict Generic Use*</u> Consistent with previous research (e.g., Hellerstein 1998), we find that observable physician characteristics can explain part of the variance of format choice decisions. The results in Table 5 (models of within-molecule competition) provide clear evidence that though there is a total increase in generic prescribing, male doctors and those working in smaller practices are less proactive in increasing these levels ($\theta_{Gender} = -2.34$ and $\theta_{PracticeSize} = 0.22$ in Model III). In addition, all else constant, we find that physicians in smaller practices and male physicians prescribe fewer generics than the remaining physicians In Period 2, when fluoxetine is the chosen molecule we get similar results ($\theta_{Gender} = -1.07$ and $\theta_{PracticeSize} = 0.178$ in Model IV).

However, it is not clear why we obtain such result. One possible explanation, for example, is that smaller practices are not as well informed about the potential cost benefits of generic prescribing. Another possible explanation for the practice size result is that current incentives are designed to benefit mostly bigger practices. It is difficult to find explanations for why male physicians prescribe fewer generics. It is possible that gender is working as a proxy for some other factor we are not accounting for and that further research is required to fully understand this result. Such understanding will be important if the UK government is to increase generic prescribing.

6. Conclusion

Patent expiration represents a turning point for the brand losing patent protection as generic versions of the drug, certified to be bioequivalent, quickly enter the market at reduced prices. Consequently, for managers of branded drugs this entry changes market dynamics and could be a threat for some while it could provide an opportunity for others. For public health officials it also represents an opportunity to reduce healthcare costs without jeopardizing therapeutic effectiveness. In studying what factors might influence the adoption of generic drugs, and provide an opportunity for cost reduction from new generic entry, previous research has focused mostly on how generics impact prices and market shares of the drug losing patent protection (within-molecule competition). In this paper, we suggest that if managers and public officials want to get a more comprehensive idea of the impact of generic entry, they need to look beyond within-molecule competition. In particular, we suggest that they need to study the full competitive landscape in the relevant therapeutic class, and include the actions of non-bioequivalent competitors. In addition, managers and policy makers need to consider carefully the role of individual physicians and their prescribing behavior across all competing molecules, and study not only their reaction to prices but also to marketing activity.

To provide support for this contention, we study the evolution of Selective Serotonin Reuptake Inhibitors (SSRI) in the UK after generic versions of fluoxetine (brand name Prozac) were introduced. Using a data set on physician prescribing and competitive marketing activity, we study how the

prescribing decisions of physicians and their characteristics (observable and unobservable) impact the competition among all molecules after generic entry. We find that the market share of the molecule losing patent protection (fluoxetine) decreased after patent expiration, despite the availability of generics at significant price discounts. Our approach allows us to offer new insight to managers about the market share of fluoxetine. We suggest that this reduction occurred because a segment of physicians prescribed less of the multi-source molecule and more of other drugs in the category after generic entry (between-molecule effect). These were physicians sensitive to the marketing activities of Prozac, which were significantly reduced after generic entry. We also find that a segment of price sensitive physicians did increase prescribing of fluoxetine due to its lower average price, but this increase was unable to compensate the reduction of fluoxetine prescribing by physicians sensitive to marketing activities.

Our findings suggest that introduction of generics could be an opportunity for managers of competing brands that are still under patent protection. For example, when the US appeals court in Washington D.C. set a sooner-than-expected end to the Prozac patent protection in the US, analysts warned that the sales of one of the most important competitors to Prozac, Cipramil also known in the US as Celexa, could be damaged by competition form generic versions of Prozac. Our results might explain why Celexa managers were not disturbed by such predictions (McCarthy, 2000): perhaps Celexa managers anticipated a reduction of Prozac marketing efforts and an increase in prescribing of their own molecule by a significant number of physicians given the responsiveness profile of physicians. Indeed, this article shows that it is necessary to study physicians' choice behavior and their responsiveness to price and detailing to fully understand and better predict the market events.

We also show an approach that managers could use to simulate outcomes of both generic entry and incumbent responses to assess resource allocation decisions post generic entry. In addition we provide a rationale for one manufacturer to market more than one drug in the same category, with different patent protection timescales (which could be achieved through acquisition or in-licensing). When one of the patents expires, the manufacturer could switch marketing support to other brands still under patent protection. There is a parallel here in the way that manufacturers in fast moving consumer goods markets

such as detergents, offer multiple brands within the category and use one or more of the brands to protect the market position of the portfolio.

In addition, from a public policy perspective, this study reveals that cost-reduction strategies promoting the increase of generic prescribing should study both within- and between-molecule dynamics and determine physician characteristics and their segmentation. Analyses that consider only within-molecule dynamics or that are performed at the aggregate-level would be myopic and could lead to the development of ineffective incentive schemes. For example, to impose the substitution of branded versions by their generic alternatives at pharmacies might not produce the expected and desired cost reductions if physicians switch to other branded molecules of the same category that are still under patent protection. The importance of between-molecule competition and the responsiveness to marketing activity is perhaps what explains why some states in the US engage in counter-detailing activities (Mizik and Jacobson, 2004), that is, encourage detailing visits promoting the generic versions of molecules.

The analyses in this paper were based solely on UK data for the SSRI category because this was the only dataset available with the level of detail required to answer our research question: our analyses require the use of individual level physician data covering a significant period of time and comprising information on drug choice for each patient visit, and on the marketing activity targeted to physicians. Datasets with such detail are not common for a multitude of categories and countries. Previous research indicates that institutional features of each market have a great influence on prescribing behavior and on the effects of generic entry. In addition, each pharmaceutical category might reveal different market evolutions and dynamics (e.g., Danzon & Chao, 2000). It might then be difficult to extrapolate our results to other countries and drugs.

However, given the importance of side effects in the use of SSRI's, we believe this empirical example is conservative regarding the impact of price and detailing changes, which is likely bigger in contexts where drugs have fewer and less severe side effects. We also believe that the impact of detailing in this empirical application is particularly small because of the age of the drugs and the experience of physicians. We would expect that physicians starting their professional career, and those considering the

adoption of new drugs, would be more influenced by the informative role of detailing (Narayanan et al., 2005). In addition, we would also expect price effects to be more important in those countries or situations in which final consumers are more price sensitive (e.g., countries in which final consumers bear a greater share of the cost).

An area for future research is the replication of our approach in different countries and across multiple categories. It would then be possible to understand how institutional features of each market interact with the physician segmentation and the competitive dynamics. Specifically, it would be very interesting to establish which kind of incentives drive physicians to be more price conscious and what drive physicians away from generic prescribing. Further analysis of these issues is warranted to articulate more effective policies that can significantly reduce healthcare expenditures without affecting patient welfare.

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APPENDIX A

A.1 Multinomia Nested Logit Model: Define V_{ijt} as physician i valuation of drug j for patient-visit t as:

$$V_{ijt} = X_{ijt}\beta_{ij} + G_{ij} + \varepsilon_{ijt}\text{ , for } i = 1, \ldots, N, j = 1, \ldots, J, \text{ and } t = 1, \ldots, T_i, \tag{A.1}$$

where X_{ijt} is a (1×k) vector of explanatory variables, β_{ij} is the corresponding (k×1) vector of physician specific parameters, J is the number of alternative drugs, N is the number of physicians observed, T_i is the number of prescription occasions of physician i, and ε_{ijt} is a general extreme value distributed error term (Train 2003). The term G_{ij} is an extra factor that is only present if the molecule is available in generic form. It represents the change in valuation due to the trade-off between the significant price discounts of generic versions and their perceived quality.

If we assume that physcians prescribe the drug with the maximum valuation, we obtain a nested multinomial logit model. Physician's i probability of prescribing molecule j at occasion t is then defined as:

$$p_{ijt} = \frac{\exp\left(X_{ijt}\beta_{ij} + \lambda_i I_{ijt}\right)}{\sum_{l=1}^{J}\exp\left(X_{ilt}\beta_{il} + \lambda_i I_{ilt}\right)}, \tag{A.2}$$

The term I_{ijt} is the "inclusive value" of physician i, which is equal to $\ln\left(1+\exp\left(G_{ij}/\lambda_i\right)\right)$ if a generic version is available for molecule j at patient visit t, or equal to zero if a generic is not available; λ_i is the physician-specific inclusive value parameter. Note that these inclusive value parameters should lie between zero and one. For those molecules available under generic and brand-name formulations, the probability of prescribing molecule j under generic version is:

$$p_{iG_jt} = p_{ijt}\frac{\exp(G_{ij}/\lambda_i)}{1+\exp(G_{ij}/\lambda_i)}, \tag{A.3}$$

and the probability of prescribing molecule j under brand version is:

$$p_{iB_jt} = p_{ijt}\frac{1}{1+\exp(G_{ij}/\lambda_i)}\ . \tag{A.4}$$

The final choice probability is decomposed in two parts: one is the probability of selecting the molecule (p_{ijt}) which corresponds to the upper level nests, and the other is the probability of selecting the format of the molecule given molecule choice (choice of format within the molecule nest).

Finally, we adopt a random effects formulation to model physician-specific effects and estimated the final model via Bayesian simulation methods (estimation details presented in Appendix B). Random effects are commonly used in economics and management to account for differences across individual units. Previous models of pharmaceutical demand have also used a random effects formulation to account for heterogeneity (e.g., Manchanda et al 2004; Narayanan et al., 2005). Specifically, we assume that physician-specific parameters are normally distributed, $\beta_{ij} \propto MVN(\overline{\beta}, \Sigma)$ where $\overline{\beta}$ is the (k×1) vector of population level means and Σ is the corresponding (k× k) variance-covariance matrix.

Finally, all of the parameters are physician and drug specific though some constraints are necessary for identification purposes. Physician specific intercepts for Seroxat (Paroxetine) are set to zero for each physician, and price effects are set to be equal for all molecules ($\beta_{3ij} = \beta_{3i}$, for all j). Because we are doing an individual level analysis we are also interested in reducing the number of parameters to a minimum. After several tests, we have further constrained past prescription parameters to be equal across all drugs ($\beta_{2ij} = \beta_{2i}$, for all j and for all physicians). This final specification requires the estimation of only 11 parameters for each one of the 170 physicians and is very similar to the unconstrained version in terms of fit (details available from the authors upon request).

These parameters are estimated using traditional Markov Chain Monte Carlo (MCMC) methods with a Gibbs-Sampler to draw from the closed-form conditional distributions, and a Metropolis-Hastings step to explore the posterior distribution of the parameters without closed form conditionals (Appendix B presents the detailed description of priors and estimation procedure).

A.2 Binomial Models: Define p_j as physician i probability of prescribing the option u_1 in Period 2 across all prescriptions occasions. The likelihood for each physician is then given by:

$$l(n_i, r_i, p_i) = \frac{n_i!}{r_i!(n_i - r_i)!} p_i^{r_i} (1 - p_i)^{n_i - r_i}, \tag{A.5}$$

where, r_i is the number of prescriptions of option u_1 for physician i during Period 2 and n_i is the number of prescription occasions; p_i is the probability of prescribing u_1. The proposed models (see Table 1 in the paper for the different alternatives) are estimated via maximum likelihood. Variables are tested for inclusion using a 5% significance level and if deemed non-significant are removed from the final model.

APPENDIX B

1. Specification of Priors.

We specify a multivariate normal prior for the between-physician conditional mean parameters and an inverted Wishart for the variance-covariance matrix of the random coefficient nested logit model. We take diffuse priors to induce a mild amount of shrinkage. We did a robustness check estimating the models with three different priors. Some of the physicians were classified in different groups with the different prior specifications but agreement rate was above 93%; findings were also the same regardless of the prior used.

The likelihood for physician i with the proposed random coefficient nested logit model has the following form:

$$L_i(\beta_i | data) = \prod_{j=1}^{4} \prod_{t=1}^{T_i} p_{iG_jt}^{y_t} p_{iB_jt}^{y_t} \tag{B.1}$$

with the probabilities defined in Equations A.3 and A.4 and y_t defined as a dummy variable equal to one when drug j in generic/brand version was chosen by physician i in prescription occasion t. Heterogeneity is introduced in the model as $\beta_i \propto MVN(\overline{\beta}, \Sigma)$ and we use the following priors

- $\overline{\beta} \propto MVN(a_0, b_0)$ where $a_0 = \bar{0}_k$, $b_0 = 100 I_k$ and $k = 9$ (# parameters)
- $\Sigma \propto IW(n_0, s_0)$ where $n_0 = k + 2 = 11$, and $s_0 = \frac{n_0}{10} I_k$

2. Full conditionals and simulation algorithm.

(1) Set starting values for the unknown parameters.

(2) Draw β_i from a Metropolis-Hasting algorithm. Let us denote $\beta^p{}_i$ the previous draw for β_i and $\beta^n{}_i$ the candidate draw. The acceptance probability of the candidate draw is given by:

$$\pi_i = \min\left[\frac{\exp\left[-\frac{1}{2}(\beta^n{}_i - \overline{\beta})\Sigma^{-1}(\beta^n{}_i - \overline{\beta}) L_i(\beta^n{}_{ij})\right]}{\exp\left[-\frac{1}{2}(\beta^p{}_i - \overline{\beta})\Sigma^{-1}(\beta^p{}_i - \overline{\beta}) L_i(\beta^p{}_{ij})\right]}, 1 \right] \tag{B.2}$$

(3) Draw $\overline{\beta}$ from the conditional distribution:

$$\overline{\beta}\left|\beta_i,\Sigma \propto MVN\left(\sum_{i=1}^{N}\beta_i\Big/N,\left(N\Big/\Sigma+(b_0)^{-1}\right)^{-1}\right)\right. \tag{B.3}$$

(4) Draw Σ from the conditional distribution:

$$\Sigma\left|\beta_i,\overline{\beta} \propto IW\left(N+n_0,\sum_{i=1}^{N}(\beta_i-\overline{\beta})(\beta_i-\overline{\beta})'+s_0^{-1}\right)\right. \tag{B.4}$$

Figure1: Choice tree of multi-source drugs

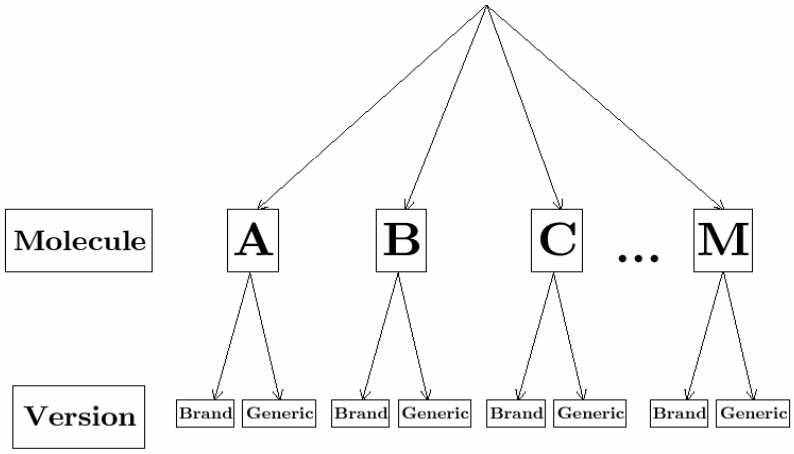

Table 1: The Four Binomial Models Estimated

	With Baseline **Analyze Prescription Change**	**With No Baseline** **Analyze Prescription Split**
Between-Molecule Competition Model the number of times the multi-source molecule (e.g., branded fluoxetine and generic fluoxetine) has been prescribed across all prescriptions in the category (e.g., SSRIs)	**Model I** $s_i^I = \log\left(SHARE_i / \left(1 - SHARE_i\right)\right)$ *SHARE* = share of multi-source molecule prescriptions (fluoxetine) across all prescriptions in the category	**Model II** $s_i^{II} = 0$
Within-Molecule Competition Model the number of times the generic version of the multi-source molecule (e.g., generic fluoxetine) has been prescribed across all prescriptions of fluoxetine (e.g., branded fluoxetine and generic fluoxetine)	**Model III** $s_i^{III} = \log\left(SHARE_i / \left(1 - SHARE_i\right)\right)$ *SHARE* = Share of generic prescriptions of the multi-source molecule across all multi-source molecule prescriptions	**Model IV** $s_i^{IV} = 0$

Table 2: Summary Statistics of Prescriptions and Detailing Visits for our Sample*

Molecule (Brand Name)	Monthly Prescriptions By All 170 Physicians				Monthly Detailings To All 170 Physicians			
	Number		Percentage		Number		Percentage	
	Period 1	Period 2	Period 1	Period 2	Period 1	Period 2	Period 1	Period 2
Fluoxetine (Prozac)	145	142	36%	34%	28	3	26%	4%
Paroxetine (Seroxat)	137	128	34%	31%	25	19	23%	26%
Citalopram (Cipramil)	78	106	20%	26%	25	29	23%	39%
Sertraline (Lustral)	39	40	10%	10%	29	23	27%	31%
Total	399	417	100%	100%	108	74	100%	100%

* Cipramil is the brand name of citalopram produced by Lundbeck; Lustral is the brand name of sertraline produced by Pfizer; Prozac is the brand name of fluoxetine produced by Eli-Lily; and Seroxat is the brand name of paroxetine produced by GSK. For fluoxetine, Period 2 prescription values include the prescriptions of branded and generic alternatives.

Table 3: Random Effects Multinomial Nested Logit

(Posterior Means and 95% Probability Intervals)*

	Posterior Mean	**95% Probability Intervals**
Intercepts (β_0)		
Prozac+Fluoxetine	0.02	[-0.19, 0.23]
Lustral	**-1.91**	[-2.23, -1.66]
Cipramil	**-1.09**	[-1.35, -0.85]
Detailing (β_1)		[0.00, 0.00]
Prozac	0.15	[-0.22, 0.53]
Lustral	**0.58**	[0.36, 0.86]
Cipramil	**0.83**	[0.59, 1.05]
Seroxat	**0.47**	[0.29, 0.64]
Past Prescription (β_2)	**0.31**	[0.23, 0.39]
Price Dummy Lustral (β_3)	**0.29**	[0.03, 0.54]
Inclusive Value (λ)	**0.02**	[0.01, 0.05]
Generic Fluoxetine (G)	**2.15**	[1.64, 2.69]

*Values in bold mean the 95% probability interval for the parameter does not include zero.

Table 4: Summary of Results for the Binomial Models of Between-Molecule Competition*

	Model I: With Baseline (Analyze Change) $s_i^I = \log(SHARE_i/(1-SHARE_i))$			**Model II : With No Baseline (Analyze Levels)** $s_i^{II} = 0$		
	Estimate	**Standard Error**	**t-statistic***	**Estimate**	**Standard Error**	**t-statistic***
Intercept	-0.745	0.198	[–4.45, –2.92]	-0.733	0.185	[–4.64, –2.94]
Observable Characteristics						
Gender	n.s.	n.s.	—	n.s.	n.s.	—
Practice Size	–0.061	0.026	[–2.62, –2.04]	-0.085	0.024	[–3.8, –3.17]
Unobservable Characteristics						
Response to Prozac Detailing	–0.220	0.075	[–3.89, –1.98]	n.s.	n.s.	—
Response to Price Cut	0.272	0.120	[1.5, 2.74] (87)	n.s.	n.s.	—
Inclusive Value	18.731	4.595	[3.04, 5.37]	18.967	4.407	[2.88, 5.56]
Preference for Prozac	n.s.	n.s.	—	0.763	0.053	[13.67, 14.73]
Control Variables						
# Prescriptions Period 1	0.018	0.007	[4.2, 4.96]	n.s.	n.s.	—
# Details Period1	0.007	0.002	[2.13, 2.66]	n.s.	n.s.	—
# Details Period2	n.s.	n.s.	—	–0.064	0.022	[–3.18, –2.75]
Model BIC	873.94			NA		
Null Model** BIC	911.52			NA		

* Range of the t-statistic for the 100 replications of the posterior mean of the Unobservable Characteristics. In parenthesis, number of times that |t-stat|>1.96 (i.e. 95% significant cut-off point).
** Null Model is a binomial model in which we allow physicians to change their prescriptions by a constant.

Table 5: Summary of Results for the Binomial Models of Within-Molecule Competition*

	Model III: With Baseline (Analyze Change) $s_i^{IV} = \log(SHARE_i/(1-SHARE_i))$			**Model IV : With No Baseline (Analyze Levels)** $s_i^{III} = 0$		
	Estimate	**Standard Error**	**t-statistic***	**Estimate**	**Standard Error**	**t-statistic***
Intercept	2.382	0.697	3.42	–0.614	0.439	[–2.28, –0.08] (5)
Observable Characteristics						
Gender	–2.337	0.629	–3.72	–1.074	0.270	[–4.41, –3.48]
Practice Size	0.219	0.111	1.97	0.178	0.048	[3.35 4.27]
Unobservable Characteristics						
Response to Prozac Detailing	n.s.	n.s.	—	–0.821	0.125	[–7.21, -5.15]
Response to Price Cut	n.s.	n.s.	—	0.930	0.356	[2.00, 3.99]
Inclusive Value	n.s.	n.s.	—	42.784	10.306	[2.25, 5.64]
Preference Prozac (β_{0_Prozac})	n.s.	n.s.	—	n.s.	n.s.	—
Control Variables			—			—
# Prescriptions Period 1	n.s.	n.s.	—	0.031	0.006	[4.91, 5.8]
# Details Period1	n.s.	n.s.	—	0.037	0.016	[1.65, 2.71] (62)
# Details Period2	n.s.	n.s.	—	n.s.	n.s.	—
Model BIC	347.39	—	—	NA	—	—
Null Model** BIC	375.64	—	—	NA	—	—

* Range of the t-statistic for the 100 replications of the posterior mean of the Unobservable Characteristics. In parenthesis, number of times when |t-stat|>1.96 (i.e. 95% significant cut-off point).
** Null Model is a binomial model in which we allow physicians to change their prescriptions by a constant.