Generic drugs in Spain: price competition vs. moral hazard

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Abstract

This paper examines competition between generic and brand-name drugs in the regulated Spanish pharmaceutical market. A nested logit demand model is specified for the three most consumed therapeutic subgroups in Spain: statins (anticholesterol), selective serotonin reuptake inhibitors (antidepressants) and proton pump inhibitors (antiulcers). The model is estimated with instrumental variables from a panel of monthly prescription data from 1999 to 2005. The dataset distinguishes between three different levels of patients' copayments within the prescriptions and the results show that the greater the level of insurance that the patient has (and therefore the lower the patient’s copayment), the lower the proportion of generic prescriptions made by physicians. It seems that the low level of copayment has delayed the penetration of generics into the Spanish market. Additionally, the estimation of the demand model suggests that the substitution rules and promotional efforts associated with the reference pricing system have increased generic market share, and that being among the first generic entrants has an additional positive effect.

Keywords: pharmaceutical industry, generic competition, copayment, moral hazard

JEL classifications: I11, I18, L13, L65

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1. Introduction

Drug expenditure is one of the fastest growing components of health expenditure in most countries (OECD, 2006) and knowing more about the factors that affect generic competition, which is a potential way of reducing spending, is very useful for the design of pharmaceutical policies.

One important feature of the Spanish pharmaceutical market is that it is heavily regulated. The maximum price of each medicine is established individually and since December 1999, there has been a reference pricing system by which the National Health System (NHS) sets the maximum reimbursement for drugs when generic versions are available. This allows the competition of generic medicines to be studied in a regulated context and, since the NHS funds most prescription drug consumption, it is especially interesting to analyse how generic competition is affected by the level of insurance or reimbursement.
The main aim of this paper is thus to analyse to what extent market share depends on the level of patient copayment. The Spanish case, with three different levels of copayment (pensioner, non-pensioner and the chronically ill) is particularly interesting. Additionally, among other factors that may influence the success of generic competition, the effects of the application and modification of the reference pricing system and the order of entry into the market are of special concern.

I contribute with empirical findings regarding these three important issues that affect generic competition. Most of the results I report could be extended to a great number of countries with similar institutional settings and pharmaceutical market characteristics: heavy regulation and a relatively low market penetration of generics.

The outline of the paper is as follows. The next section highlights the idiosyncrasy of the pharmaceutical market and generic competition. The third section explains the main features of the Spanish pharmaceutical market. The fourth section describes the dataset. The section after that presents the demand model and considers estimation issues. In the sixth and seventh sections I present and discuss the estimation results, respectively. Finally, the last section offers the concluding remarks.

2. Generic competition

When brand-name drugs are no longer protected by patents or other legal rules, generic equivalents can enter the market. Such drugs contain the same active
ingredients and have proved bioequivalence with the original product, to the satisfaction of health authorities. However, the manufacturer and certain characteristics (such as colour, shape, inactive ingredients or packaging) may be different. Therefore, they may be considered substitutes for the brand-name drugs but not perfect substitutes: in other words, there is some degree of differentiation.

The expected result of generics entering the market is an increase in the level of competition and possibly a reduction in prices and the brand-name product’s market share. It is also expected that when the number of generics on the market is considerable, prices tend towards the cost of production. However, for brand-name products, the American literature shows some evidence of prices increases after the entry of generics into the market (for instance: Grabowski and Vernon, 1992; Frank and Salkever, 1997): this has been called the “generic paradox” (Scherer, 1993).

In the pharmaceutical industry, the institutional setting is very important and affects market competition. The dispensing process is complex and the physician, the pharmacist, the third-party payer (a public health insurer in most countries) and the patient all play a role. The physician and the pharmacist may be perfect agents for the patient in which case their choices (together with those of the patient) will maximize utility for the patient. In contrast, the physician or the pharmacist may be perfect agents for the third-party payer (ultimately tax-payers when there is a public

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1 Pharmaceutical products are bioequivalent if they are pharmaceutically equivalent or pharmaceutical alternatives, and display comparable bioavailability, when studied under similar experimental conditions. Bioequivalence is considered proven if the bioavailabilities, in terms of peak and total exposure after administration of the same molar dose under the same conditions, are similar to such a degree that the effects of the studied products can be expected to be essentially the same.
insurer) or even, in some countries, for themselves\(^2\). There is also room for intermediate situations.

The process starts when the physician decides to prescribe a drug. He may choose to prescribe a generic or a brand-name drug. Hellerstein (1998) found that physicians play an important role in determining whether patients receive brand-name or generic pharmaceuticals and that some are more likely to prescribe generics while others are more likely to prescribe brand-name products. The practitioner, as the patient’s agent, may choose a brand-name drug if he believes that it is of better quality and is not concerned about the cost of the drug. Moreover, the physician may prefer the brand-name drug because of his experience with the product over the period of exclusivity, during patent protection, or because there are no incentives to change prescription habits (López-Casanovas and Puig-Junoy, 2000). This brand-name loyalty of the practitioner may explain why, in some markets, brand-name products enjoy large market shares even when there are cheaper generic drugs available.

Coscelli (2000) found that in addition to the physician, patient characteristics also affect the prescription decision. Since brand-name and generic drugs may differ in inert ingredients as well as in colour and shape, some patients may wish not to change from the brand-name drug they are used to taking to a generic version. This may be particularly true if they have doubts about quality and do not pay for the

\(^2\) Iizuka (2007) analyzes the trade-off for physicians between being good agents for themselves or for the patients in the Japanese pharmaceutical market.
drug or make only a small copayment; the patient may have a preference to consume brand-name drugs and may influence the physician’s choice.

Apart from the physician and the patient, the pharmacist may participate in the choice of drug, for instance by choosing which generic to dispense. When a generic drug is dispensed, there is competition between different generic products. As stated by Yu and Gupta (2008), the choice at this stage is mainly based on which generics are available at the pharmacy, that is, the pharmacist’s choice of a generic producer within the market defined by the active ingredient.

The dispensing process follows a multi-level market structure, as shown in Figure 1. The first choice is between whether to dispense a drug from a therapeutic subgroup or to prescribe an alternative treatment for the condition, such as a drug from another related therapeutic subgroup, whether to take homeopathic products, whether to take exercise, and so on. If a therapeutic subgroup is chosen, the next step is to decide on an active ingredient. The third decision is to choose a specific presentation from all the possibilities for the molecule, in other words, to choose a combination of the strength and the number of units. The following stage is the choice between branded and generic drugs. And finally, there is the choice from among the different producers.

Furthermore, the public payer may affect the decision by implementing obligatory substitution rules and requirements that limit reimbursements, such as the reference pricing system.
3. The Spanish pharmaceutical market

The Spanish NHS is funded from tax revenue and provides health care services with copayments for prescribed pharmaceuticals. The standard rate of copayment is 40%, but the average copayment is very low and accounts for less than 7% of the total expenditure on ambulatory prescription pharmaceuticals, since prescription drugs for pensioners and some other specific groups, such as the handicapped or people who have suffered occupational accidents and their dependents, have no charge; and drugs indicated specially for chronic diseases have a rate of only 10% with an upper limit.

The prescription market dominates sales: the share of prescription drugs is 85.50% of volume and 92% of total sales, and over-the-counter (OTC) medicines account for the remaining 14.50% of volume and 8% of total sales (Costa-Font and Puig-Junoy, 2005).

Another important feature of the Spanish market is that there are a great number of different presentations of drugs due to there still being considerable numbers of copies and also to the entry of new drugs into the market. In fact, there are three types of prescription drugs in Spain: original brand-name drugs (which might be marketed either by the patent holder or by a licensee), copy brand-name drugs and generics. This is due to the fact that, although Spain joined the European Patent Convention in 1986, it did not grant product patent rights until 8 October 1992, due to a transitional period in accordance with Article 167 of that convention. Before 1992, there were only process patents. Thus, older drugs are marketed
simultaneously in the form of branded original products, branded licensed products, branded copy products and generics.

Although generic drugs were introduced into Spain in 1997, the market share of generic medicines was low at the end of the period analysed: only 14.60% in units and 7.90% in value (IMS Health, 2006b). Generics obtain market authorization when one has already been authorized in another European Union (EU) member state in which the original drug enjoyed product patent protection, or when ten years have passed since the original brand-name drug was released onto the Spanish market (the “ten-year rule”).

Although Spain is a relatively low-price country with limited generic penetration, in December 1999 a reference pricing system was introduced for off-patent drugs with the same active ingredient (chemical equivalence). This policy has gradually been extended to reimburse payment for a growing list of active chemical ingredients.

All versions of off-patent drugs, branded and generics, were included in their respective group of bioequivalent drugs and a group was created once there was at least one generic version of the respective active ingredient. The reference price was determined endogenously as a function of drug prices in the relevant market: for each group, a reference price was calculated as the weighted average selling price of the lowest-priced drug accounting for at least 20% of the market (year on year)\(^3\).

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\(^3\) If the difference between this price and the highest price for the group was less than 10%, the reference price was the result of applying a 10% reduction to the highest price. If the difference between the calculated price and the highest priced product was more than 50%, the reference price was exactly 50% of the highest priced product. Whatever the situation, the reference price was never lower than the generic with the lowest price (López-Casasnoves and Puig-Junoy, 2000).
This system established the maximum price that could be reimbursed by the NHS for any version of the same drug. Whenever the price of any prescribed drug was higher than the reference price, patients could opt for the prescribed drug by paying the difference between its price and the reference price. So, it implied a copayment that depended on the price of the chosen drug and that could be avoided if the drug was cheaper than the reference price⁴.

However, since January 2004 the reference price has been calculated as the average of the three lowest costs per day of treatment, for each form of administration of an active ingredient, according to its defined daily dose (DDD)⁵. With this new system, if prescriptions specify drugs priced higher than the reference price, pharmacists are obliged to substitute them with the cheapest generic version. However, if prescriptions specify drugs priced equal to or lower than the reference price, pharmacists are not obliged to substitute them. When the prescription has been written using the name of the active ingredient, the pharmacist has to dispense the lowest-priced generic drug. In this way, reference pricing has become a system for establishing the maximum reimbursement price that a drug may have without being excluded from the list of publicly financed drugs, that is, a kind of price capping system.

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⁴ In fact, the part of the price under the reference price may also involve a non-avoidable copayment. For instance, non-pensioners pay 40% of the price under the reference price. The avoidable copayment is the total amount above the reference price and is in addition to the non-avoidable copayment.

⁵ A defined daily dose is the average dose per day in adults for a drug when it is used to treat its main indication.
Moreover, the maximum ex-factory price of all drugs (branded and generic) is set during the process of obtaining market approval, and usually the introduction price remains the maximum price for most of the life of the product (Borrell, 2003). The government uses a peculiar form of cost-based price regulation for branded drugs in which manufacturing, marketing and research costs, as well as an industrial profit on invested capital, are allocated to new drugs. However, this is rarely the final price since the legislation allows other factors to be considered, such as the price of the same product in other European countries, the price of drugs that can be considered substitutes or the therapeutic innovation of the medicine. In fact, the legal criteria are that the price has to reflect the therapeutic value of the drug as well as the cost of comparable treatments, the price of the same drug in other countries, and some other political issues such as the contribution to the national economy (Antoñanzas et al., 2007). The wholesalers’ and retailers’ mark-ups are also regulated\(^6\).

4. Data

I use a dataset of monthly prescription drug consumption from 1999 to 2005, provided by the Directorate-General of Pharmacy and Health Products of the Spanish Ministry of Health and Consumer Affairs, which is complemented with data from the *Nomenclator Digitalis* of the NHS Health Information Institute (Ministerio de Sanidad y Consumo, 2005) and from the *Base de Datos del Conocimiento*

I analyse outpatient data for non-paediatric oral prescription drugs containing only one active chemical ingredient. As Table 1 shows, the sample includes 15 market presentations for seven active ingredients in the three most consumed therapeutic subgroups in Spain: statins (HMG-CoA reductase inhibitors), selective serotonin reuptake inhibitors (SSRIs; antidepressants) and proton pump inhibitors (antiulcer agents). The data is not a sample but the entire market for these drugs: all the drugs sold in Spain and financed (at least partially) by the NHS. The active ingredients from the statin subgroup are lovastatin and simvastatin; from the antidepressant subgroup they are citalopram, fluoxetine, fluvoxamine and paroxetine; and from the antiulcer subgroup the active ingredient is omeprazole.

As the Table 1 shows, the different active ingredients have several doses and are sold in different presentations, therefore, all the quantities sold are converted into common units. For each presentation I calculate the total milligrams of the active ingredient and transform this into patient days using the DDD, that is, I calculate the total number of DDDs per package\(^7\). Prices are calculated from the dataset by dividing volumes of sales in euros by the quantities sold. Then, for each product I calculate the price per DDD.

\(^7\) For this purpose I use the DDD of each active ingredient established by the World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology. The use of this international standard dosage enables standardization and comparison of drug quantities across therapeutic groups, active ingredients and presentations.
Table 1 also shows the indications of each active ingredient together with the date of entry of the first generic drug and of the implementation of the reference pricing system for the first time, for each market presentation. Statins are used to lower cholesterol levels in people with, or at risk of, cardiovascular disease. SSRIs are a class of antidepressants mainly used in the treatment of depression, anxiety disorders and some personality disorders. Proton pump inhibitors are a subgroup of antiulcer drugs whose main action is a reduction of gastric acid production and they are used in the treatment of many conditions, such as peptic ulcer.

The panel data is unbalanced since different drugs fulfilled the legal requirements of generic entry and entry happened at different times, however, each market presentation is observed for at least 35 months. There are a total of 23,584 observations involving 318 different presentation forms and 51 manufacturers. A total of 11,839 observations are of pensioners’ consumption, and the remaining 11,745 are from non-pensioners’ prescriptions. Of the latter, 4,410 observations correspond to the consumption of products indicated for chronic diseases.

Each separate market is formed of medicines that compete with other close but not perfect substitute medications. In the pharmaceutical industry, defining the market is not easy since medicines are indicated for treatment of different conditions. Although it is an imperfect approach, some authors (for instance, Aronsson, Bergman and Rudholm, 2001; Dalen, Strøm and Haabeth, 2006; Moreno-Torres,

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8 All the medicines in the antidepressant class are considered for chronic treatment and have a reduced 10% rate of copayment for non-pensioners; the remaining drugs, in other therapeutic groups, have a 40% rate of copayment for non-pensioners.
Puig-Junoy and Borrell, 2009) take the therapeutic active ingredient level according to the WHO’s Anatomical Therapeutic Chemical (ATC) classification as their approach.

In order to tackle the non-linearity of the differently-sized presentation prices and to take advantage of variation among markets to identify parameters, I use the presentation (active ingredient with a specific dosage and size) as the market. Furthermore, the reference pricing system is frequently applied to different presentations, even for the same active ingredient, at different times and therefore these dynamics allow the effects of this system to be identified.

**Figure 2** shows the evolution of the number of generics in three representative markets, one in each therapeutic class. The usual pattern is a marked increase in the number of generic competitors during the first years after the loss of market protection and stabilization at the end of the series.

**Table 2** shows the evolution of the structure of the market at the end of each of the years analysed. There is a clear increase in the number of generic manufacturers for the whole dataset. The increase in their market share was also considerable until 2003; however, since then, the incorporation into the dataset of new markets with less generic penetration is reflected in a recovery of brand-name products. Moreover, there is a reduction in prices per DDD for brand-name and generic products; the latter always have lower prices than the former.
Figures 3 shows the evolution of market shares for the three representative markets and illustrates an interesting issue: in the prescriptions for pensioners, the generic market share is lower than in the prescriptions for non-pensioners. Figure 4 displays the evolution of the average brand-name and generic prices per DDD for the three same markets. Generic prices are almost always lower than brand-name prices although there is some convergence throughout the time. Finally, Figure 5 displays that the market shares of the first three (groups of) generics are usually greater than the average market share from the sixth entrant on for the same sample.

5. Empirical strategy

I use a structural discrete choice model of product differentiation. In this model the utility for consumers depends on product characteristics and individual tastes; firms are modelled as price-setting oligopolists and endogenous market outcomes are derived from an assumption of a Nash equilibrium in prices. This kind of demand model has been applied to many products such as ready-to-eat cereals (Nevo, 2000a and 2001), yogurts (Di Giacomo, 2008), movie theatres (Davis, 2006) and cars (Berry, Levinsohn and Pakes, 1995; Verboven, 1996; or Petrin, 2002). They have also been used to analyse demand for pharmaceuticals by several authors such as Stern (1996), Cleanthous (2004), Dalen, Strøm and Haabeth (2006), Iizuka (2007), Yu and Gupta (2008), Kaiser, Mendez and Rønde (2010) and Coronado (2010).

As my main interest is how copayment affects competition between brand-name drugs and generics, as well as considering competition between generics, I use a
two-level nested logit model based on Berry (1994) and especially on the application of such a model to the pharmaceutical market by Yu and Gupta (2008)\(^9\).

As stated by Berry (1994), in contrast to the simple multinomial logit model, the nested logit model allows consumer tastes to be correlated across products. There is correlation between the idiosyncratic shocks of products in the same segment of the market. This prevents the independence from irrelevant alternatives property and allows for reasonable substitution patterns.

In comparison to the random coefficients alternative\(^10\), the nested logit model may be sensitive to the specification of the nest structure because the researcher chooses the options that are potentially close \(a \text{ priori}\)\(^11\). However, in the case of pharmaceuticals this is not a crucial pitfall since it is possible to use the ATC classification to build the structure of the nests\(^12\).

In this demand model drugs are grouped into mutually exclusive markets. In each market, for instance “omeprazole 20 milligrams 14 capsules”, there are the brand-name and the generic nests. In each generic nest there is a set of drugs denoted \(j = 1, \ldots, J\). I group all the different brand-name drugs within a single nest (original brand-name and copy brand-name drugs) so there is only one possibility available in

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\(^{9}\) An alternative approach is the multistage budgeting model applied by Ellison et al. (1997) to analyze the demand for cephalosporins.

\(^{10}\) The nested logit model can be interpreted as a special case of the random coefficients model with random coefficients only on group-specific dummy variables (Berry, 1994).

\(^{11}\) For those cases in which the order of the nests is important, Bresnahan, Stern and Trajtenberg (1997) developed the principles-of-differentiation general extreme-value model.

\(^{12}\) The therapeutic groups are formed on the basis of the 4th level of the ATC code that approximates the chemical, therapeutic or pharmacological group (for example, N06AB for SSRIs: antidepressants). The pharmaceutical presentations within a group can be considered close substitutes since they have the same active chemical ingredient (5th level of the ATC code: the group for the chemical substance; for instance, N06AB05 for paroxetine).
this nest. The outside good represents the alternative to choose a generic or brand-name drug and is assumed to be the only member of its own group.

I assume that the physician chooses a unit of the drug that maximizes utility for the patient, even though the final consumption may be affected by the substitution rules and the availability of the product at the drugstore.

The indirect utility function for consumer \( i \) of consuming the generic drug \( j \) in the period \( t \) is:

\[
 u_{ijt} = \delta_j + \sum_g [d_{jg} \zeta_{ig}] + (1 - \sigma) \epsilon_{ijt} \tag{1}
\]

where \( \delta_j \) is the mean utility level of product \( j \), which is the same for all consumers, and \( \epsilon_{ijt} \) is an identically and independently distributed extreme value random variable that represents the distribution of consumer preferences about the mean utility. \( d_{jg} \) is a dummy variable that is equal to one for drugs in a specific market, \( g \), and zero otherwise; and so, \( \zeta_{ig} \) is common to all products in market \( g \) and has a distribution function that depends on the parameter \( \sigma \), with \( 0 \leq \sigma < 1 \). This parameter measures the within-nest correlation of utility levels and allows to include the correlation between groups of similar products. If \( \sigma \) approaches 0, the within-group correlation of utility levels is low, and the model tends toward the multinomial logit (Besanko, Gupta and Jain, 1998). When \( \sigma \) tends toward 1, the within-nest correlation of utilities approaches 1. As Cardell (1997) proved, an
additional property of this model is that if \( \varepsilon_{ijt} \) is an extreme value random variable, 
\[ \xi_{ig} + (1 - \sigma)e_{ijt} \] is also an extreme value random variable.

Let me define the indirect utility function for the consumer \( i \) of consuming a brand-name drug as:

\[ u_{ibt} = \delta_{ibt} + \varepsilon_{ibt} \]  \hspace{1cm} (2)

From the derivation by Berry (1994) and following Yu and Gupta (2008), I obtain the following estimating equation:

\[ \ln(s_j / s_{bt}) = (\delta_{jt} - \delta_{bt}) + \sigma \ln(s_{j/g,igt}) + \nu_{jt} \]  \hspace{1cm} (3)

where: \( \ln(s_j / s_{bt}) \) is the log of the relative market share between the generic \( j \) and the group of brand-name products; \( \ln(s_{j/g,igt}) \) is the log of the share of the generic \( j \) in the group of generic products in market \( g \) and \( \nu_{jt} \) is an error term.

I assume that the mean utility of the brand-name drugs depends on the quality that consumers perceive these drugs to have due to their being an incumbent product, and I expect that an increase in the average price per DDD reduces brand-name drugs’ market share. For the generic drugs, I assume that the mean utility depends on the months since it has been on the market and on the price per DDD. The former is expected to affect generics’ market shares positively, because generic producers need time to spread their products through markets; while the price is expected to be inversely related to the market share of generic products.
Thus, the econometric specification to be estimated is:

$$\ln(s_{jt}/s_{gt}) = \alpha + \gamma_j + X\Pi + \sigma \ln(s_{jt}/s_{gt}) + \tau_1 C_0 + \tau_2 C_{10} + \alpha_1 D^{SPI}_{gt} + \alpha_2 D^{PPI}_{gt} + \omega + \nu_{jt}$$  (4)

The first term at the right-hand side is a constant and the second term represents an order-of-entry fixed effect\(^{13}\). The term \(X\) is the matrix of variables that explain the differences in the mean utilities of brands and generics, including the time each generic has been on the market and the logs of prices. Let \(X\) also include other variables that may affect utility for consumers and thus generic penetration, such as the number of indications of the active ingredient, the number of DDDs per unit, the number of units in the package and the number of different brand-name products on the market at the moment of patent expiry. \(\Pi\) is a vector of parameters to be estimated. \(\sigma\) is the parameter that measures the level of substitution between generics in a given market and \(\ln(s_{jt}/s_{gt})\) is the log of the within-generic group market share.

I incorporate two dummy variables related to copayment levels. The first copayment dummy variable, \(C_0\), is equal to one for pensioners’ consumptions, because pensioners do not have any out-of-pocket expenses. The second dummy variable, \(C_{10}\), is equal to one for the consumption of those products designated for the chronically ill, in which non-pensioners have a reduced copayment rate of only 10%. Therefore, the group of comparison is formed of the products with the general 40% rate of copayment.

\(^{13}\) In the strict sense, these are not drug-specific fixed effects because in some cases more than one drug entered the market in the same month and these drugs are grouped into the same dummy variable. Moreover, all the products that enter the market after the 5\(^{th}\) entrant (or group of entrants) are grouped together and act as the comparison group.
My hypothesis is that physicians and pharmacists act as better agents for the patients than for the third-party payer (the NHS or tax-payers) and prescribe and sell more expensive brand-name products to those patients with larger levels of insurance coverage (i.e., lower copayments). Physicians and pharmacists may be influenced by their patients’ interests and thus introduce some degree of moral hazard. Thus, I expect to find larger generic market shares for the chronically ill, with a 10% copayment, and especially for the non-pensioners group, with no copayment reduction, since they have to contribute to the cost of the drug with a copayment rate of 40% and generics are generally cheaper.

Some studies, such as Pavcnik (2002) or Regan (2008), find empirical evidence of the effect of copayment on prices and some theoretical papers try to explain the “generic paradox” by appeal to the level of insurance coverage (Kong, 2008; and Ferrara and Kong, 2008). Some papers find evidence of the effect of copayment on the demand for pharmaceuticals in the US market (such as Esposito, 2005; Coulson and Stuart, 1995; Coulson et al., 1995), although their results cannot be applied directly to Spain because the institutional setting is quite different.

However, in the Swedish market, which is more similar to the Spanish market, Rudholm (2005) found that when the level of pharmaceutical insurance is greater, not only does the quantity consumed increase but so does the price of the products dispensed, and Lundin (2000) showed that patients with high insurance coverage consume more brand-name drugs (relative to generics) than patients with lower insurance coverage. When the cost for the patient of a brand-name product
increases in comparison to the generic version, it is more likely that the doctor will prescribe the generic.

Another important issue addressed by Yu and Gupta (2008) is the effect of the order of market entry of generics on their market shares. In the American pharmaceutical industry there is some evidence that earlier entrants make larger profits (for instance Caves, Whinston and Hurwitz, 1991; Berndt et al., 1995; Cook, 1998). In fact, the “generic paradox” may be interpreted as brand-name loyalty derived from a first-mover advantage. In the pharmaceutical market, first-mover advantage brings pricing power and allows the manufacturer to retain a considerable market share as the number of competitors increases.

This advantage also seems to hold for the first generic entrants; which retain a considerable market share and have higher prices than later generic entrants. Yu and Gupta (2008) and Kalyanaram (2008) in the US and Hollis (2002) in Canada found evidence of larger market shares for the first or earlier generic entrants. This may be interpreted as consumers obtaining more utility from the first generics on the market. That is why I include fixed effects relating to the order of entry. This is also a relevant issue for competition policy, since some brand-name drug producers preempt the generic segment of the market with their own “branded generics” (also known as “pseudo generics” or “authorized generics”). In other words, incumbent brand-name manufacturers sometimes also manufacture the first generic product (Hollis, 2005; Reiffen and Ward, 2007).
In Spain, as Reiffen and Ward (2005) indicated in the US market, the timing of entry into the market is not generally under the control of manufacturers. The date of approval by health authorities is not known with certainty, or indeed even if they will obtain the approval, and neither do they know how many other applications for that market will be approved, or when this may happen. Thus, order-of-entry can be considered as exogenous.

I include a dummy variable, $D_{\text{RPI}}^{gt}$, that is equal to one from the moment the reference price is applied to the market until December 2003, and equal to zero before the implementation of the reference price (or when it is not implemented) and after December 2003. A second dummy variable, $D_{\text{RPI}}^{\text{gt}}$, is equal to one when the reference price is applied to the market from January 2004 onwards, and equal to zero before this moment (or when the reference price is not implemented). In this way, there are three periods for each product: the period previous to the implementation of reference pricing, during which the price capping regulation works; the period in which the first reference price system is applied; and the period of the second reference price system. If a product is not affected by the reference price system, the price capping regulation sets its maximum ex-factory price. The first period acts as the comparison group.

Other policies implemented during the period analysed, such as obligatory reductions of ex-factory prices, reductions of pharmacy and wholesaler price margins, or revisions of reference prices, have no dummy variables since all these effects act through the variation in the prices included in the specification.
It should be considered that, in addition to its effects through the variation of relative prices and copayments, reference pricing is accompanied by specific substitution rules and promotion of generic prescriptions by health authorities. Thus, since prices are introduced in the econometric specification, the parameters $\alpha_1$ and $\alpha_2$ will only capture the effects that are additional to those due to price variations. For instance, the introduction of reference pricing can increase generic market share if it means that brand-name products are relatively more expensive than generics (effect through the prices) but it can also increase generic market share because of obligatory substitution (an effect which is in addition to the price changes).

I also introduce firm-specific fixed effects in the model, $\omega_m$; that is, a variable that is equal to one for a specific firm across drugs and markets and to zero otherwise. The role of these fixed effects is to control for time invariant factors in addition to order-of-entry fixed effects, such as product quality or promotional effort, that are usually common to all the products a firm manufactures. In fact, market shares of competing generic drugs are driven by pharmacists’ choice of a generic producer within the market and generic manufacturers build a reputation and develop idiosyncratic skills in launching and delivering drugs.

The quality of the product together with promotional and marketing activity expenses are observable to the consumer but not to the researcher (that is, they are not totally captured by the variables included). These unobserved factors are correlated with the drug price and with the log of a generic drug’s share within the
group of generics. To partially overcome this pitfall, I use the aforementioned firm-specific dummy variables. These fixed effects capture the mean quality of a drug and the marketing effort invested in it, leaving the time-specific and product-specific deviations as part of the error term. The potential remaining inconsistency in estimation arises from factors that change over time or variation among products from the same firm.

To deal with this remaining endogeneity I use instrumental variables. Following the empirical industrial organization literature (Berry, Levinsohn and Pakes, 1995) and papers that consider the pharmaceutical industry (Iizuka, 2007; Stern, 1996), I considered as possible instruments: the number of products a firm and its competitors manufacture; the product characteristics; and the sums of these at different levels of aggregation. Of these available instruments I chose the set with the strongest correlation with the endogenous variables that did not reject the null hypothesis of exogeneity according to the Sargan-Hansen test (Sargan, 1958; and Hansen, 1982). These instruments are the number of other products from the same firm and the number of products from other firms with the same active ingredient and the sum of the variable time-in-market and the sum of a dummy reference price variable for the therapeutic class.

I use a random-effects generalized two-stage least squares method to estimate equation (4). This method is applied by Yu and Gupta (2008) and also in other papers that study generic competition in the pharmaceutical industry, such as Reiffen and Ward (2005) or Regan (2008). Since some important explanatory variables in the dataset, such as the level of insurance, are constant over time, I
cannot use the alternative fixed effects approach. Hence, the error term, $\eta_j$, is formed of an individual effect, $\varepsilon_j$, and an error term, $\eta_j$, which is assumed to follow a normal distribution with a mean of zero and variance $\sigma^2_\eta$. In addition, following Berry (1994), I use the methodology that has been most used in the empirical industrial organization literature: the (two-stage) generalized method of moments. The results of the two estimations are highly analogous. Table 3 shows the definitions and the descriptive statistics of the variables that I use in the regression analysis.

6. Results

Table 4 shows the estimation of the demand model. The generalized two-stage least squares random effects and the two-stage generalized method of moments estimations are quite similar. The within-generic market share is clearly significant and its coefficient is around 0.50. This result validates the use of the nested logit model instead of a simple multinomial logit model, since the model is consistent with the random utility maximization only when this parameter is significant and between 0 and 1.

Prices per DDD are also significant and have the expected signs. A 1% increase in the generic price reduces the relative market share, that is, the weight of the generic producer market share over the brand-name products market share, between 5.86% and 5.98%. In contrast, a 1% increase of the average price of the brand-name products raises the relative market share by between 3.97% and 4.26%.
I also control for the time the generic product has been on the market, the number of indications of the active ingredient, the number of DDDs per tablet, the number of tablets per package, the number of brand-name presentations in the period before generic entry and for therapeutic subgroups and firm-specific fixed effects. Most of these factors are significant and have the expected signs. For instance, in those markets in which there were a larger number of brand-name drugs, the generics market share is lower. Interestingly, generics gain greater market shares in smaller packet markets (fewer units or lower dosage per unit).

There is a significant and negative effect of the dummy for consumptions without copayment; that is, the mean relative generic market share is smaller in prescriptions dispensed to pensioners. The difference in comparison to the group of non-pensioners, who have a 40% rate of copayment, is a relative market share that is between 68.32% and 69.41% smaller. I find a similar result, but a lower impact, for non-pensioner consumptions of products to treat chronic conditions, which have a reduced rate of copayment of only 10%. In this group, the mean relative market share is roughly 40% smaller than in the group of non-pensioners with the 40% rate of copayment.

The introduction of the reference price system in Spain contributed to the penetration of generic products beyond its effect through prices. Thus, the effect of the implementation of the first system was an increase of the relative market share of 62%-63% in comparison to the period with the price capping regulation. The change in the system, from 2004 on, brought with it a larger effect. The application
of the second reference pricing system raised the relative market share by between 91% and 107%.

The five dummy variables for the first five groups of generic entrants are significant and have a positive coefficient. That means that the first generic entrants in the market have a greater market share than the sixth or later groups of entrants. The coefficients decrease, although not linearly, and in fact the first two groups of entrants have a mean relative market share that is between 84.50% and 93.00% greater than the sixth and later entrants, whereas the following three groups of entrants are only between 26.46% and 35.03% greater than the sixth and later entrants. The coefficients are quite similar in the generalized method of moments estimation, although only the first three groups have a significant coefficient.

7. Discussion

The coefficient of the within-generic market share is significant and has a value of 0.51. However, it is lower than expected: if generic drugs are close substitutes, it should be close to 1. This value is slightly lower than the value of approximately 0.60 found by Yu and Gupta (2008); it seems that there is not only product differentiation between brand-name and generic products, but also among generic medicines.

As expected, prices have a negative effect on the demand for drugs and the effect of high generic prices is greater than the effect on brand-name products. This may be explained by price being a more decisive factor in the consumption of generics,
whereas for brand-name products some other characteristics, such as experience or reputation, are more relevant. The other market and drug characteristics also have the expected effects. The fact that generics gain greater shares in markets of fewer units or lower dose may be due to physicians or patients trusting brand-name products more for intense treatments.

As expected, there is some moral hazard effect. For those patients with greater insurance, that is, with no or a lower rate of copayment, the consumption of generics is lower than for patients with the general rate of copayment. In other words: the greater the level of insurance, the lower the proportion of generic prescriptions. This result seems to confirm the hypothesis that physicians and pharmacists are better agents for the patients than for the NHS or tax-payers and prescribe and sell more expensive brand-name products to patients with higher levels of insurance coverage, or are influenced by the moral hazard of patients. Therefore, the low level of copayment in Spain has affected the penetration of generics negatively. This result is coherent with those of Rudholm (2005) and Lundin (2000).

The positive and clearly significant coefficients of the two reference pricing system dummies indicate that, beyond the effects of these regulations through the variation of relative prices and copayments, the substitution rules and the promotion of generic prescriptions by health authorities has been successful in promoting generic penetration into the market. Moreover, with the second reference pricing system the
increase of generic market shares increased. This may be the result of intensified promotion of generics.

Finally, I find that the order of market entry of generic manufacturers has the expected effect. This confirms that earlier-mover advantage seems to be true for the first generic entrants, which are able to obtain a considerable market share. Similarly to Yu and Gupta (2008), Kalyanaram (2008) or Hollis (2002), I find evidence of larger market shares for the first generic entrants, which is probably explained by the loyalty derived from market experience due to being the first generics.

Furthermore, it seems that in Spain part of the competition occurs in the form of discounts to official prices, as in the cases of France (Kanavos and Taylor, 2007) and the Netherlands (Danzon and Ketcham, 2004). This situation generates profits for pharmacies and wholesalers but no savings to patients or the NHS (Puig-Junoy, 2009; and Borrell and Merino-Castelló, 2007). In this case, first generic entrants, with higher prices than later entrants (since generic prices generally depend on the order of entry\textsuperscript{14}), have a first-mover advantage twice: that obtained from actually being the first generics on the market, and a higher price that allows them to offer higher rebates to pharmacies.

Precisely one of the limitations of this analysis is the lack of information about possible rebates from generic producers and wholesalers to the pharmacies. As mentioned above, a key factor in competition among generic producers is

\textsuperscript{14} The NHS, a monopsony, uses its buying power to negotiate a reduction in the maximum official price of new additional generics. This is similar to the case of New Zealand (Danzon and Ketcham, 2004).
pharmacist choice of a specific generic producer within the market of an active ingredient. However, I only have information about the official prices that were paid by the NHS to pharmacies. This is overcome partially since rebates are part of the promotional efforts of the firms and the endogeneity that this lack of information generates was addressed through the use of firm-specific fixed effects and instrumental variables.

Moreover, the consumption data is aggregated for the entire Spanish market, whereas some regions apply different policies regarding the promotion of generic medicines or active ingredient prescribing. Therefore, it is not possible to control for this geographical heterogeneity.

Finally, I use copayment dummy variables instead of the real copayments due to the difficulties in finding appropriate instrumental variables when the econometric specification includes both the part of the total price paid by the NHS and the part paid by the patient for both the average brand-name product and the generic. This is an issue that will be addressed in future research.

8. Concluding remarks

This paper examines competition between generics and brand-name drugs and among generics in the most consumed Spanish prescription pharmaceutical products: statins (HMG-CoA reductase inhibitors), SSRI antidepressants and proton pump inhibitors (antiulcers), from 1999 to 2005.
The main result is that patients with greater insurance coverage consumed fewer generics than patients with a higher rate of copayment: the greater the level of insurance, the lower the proportion of generic prescriptions. This result seems to confirm the hypothesis that physicians and pharmacists are better agents for the patient than for the third-party payer (tax-payers in Spain) or are influenced by the moral hazard of patients and prescribe and dispense more expensive brand-name products to those patients who have lower rates of copayment. From this result, it seems that the low level of copayment in Spain has affected the penetration of generics negatively.

Secondly, the reference pricing system has had a positive impact on the market shares of generic drugs beyond the effects of these regulations through the variation of relative prices and copayments. This result indicates that the substitution rules and the promotion of generic prescriptions by health authorities have been successful in encouraging generic penetration.

Finally, the order of market entry of generics has important competitive effects. The results confirm that an earlier-mover advantage seems to exist for the first generic entrants, which are able to obtain higher market shares.
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References


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Figures and tables

**Figure 1.** Drug market

```
Statins
  Simvastatin
  Lovastatin
  10MG 28  20MG 28  40MG 28
  Brands
    Gen.1  Gen.2  Gen.3
  Generics
```
**Figure 2.** Evolution of the number of generic manufacturers.

Note: Data from non-pensioner consumption in 3 representative markets is used (fluoxetine 20 mg 14 capsules, omeprazole 20 mg 14 capsules, and simvastatin 40 mg 40 tablets).

**Figure 3.** Evolution of generic and brand-name market share.
Note: Data from consumption in 3 representative markets is used (fluoxetine 20 mg 14 capsules, omeprazole 20 mg 14 capsules, and Simvastatin 40 mg 40 tablets).
Figure 4. Evolution of generic and brand-name prices per DDD
Note: Are used weighted average prices from non-pensioners consumptions of 3 representative markets (fluoxetine 20 mg 14 capsules, omeprazole 20 mg 14 capsules, and Simvastatin 40 mg 40 tablets).

Figure 5. Evolution of average generic market share by order of entry
Note: Data from non-pensioner consumption of 3 representative markets is used (fluoxetine 20 mg 14 capsules, omeprazole 20 mg 14 capsules, and Simvastatin 40 mg 40 tablets).
Table 1. Sample of drugs

<table>
<thead>
<tr>
<th>Therapeutic subgroup (ATC code)</th>
<th>Active Ingredient (ATC code)</th>
<th>Indications</th>
<th>First generic entry</th>
<th>Reference price intro</th>
<th>Market presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proton Pump Inhibitors/Antulcer drugs (A02BC)</td>
<td>Omeprazole (A02BC01)</td>
<td>Gastroesophageal reflux disease, peptic ulcer, nonsteroidal anti-inflammatory drug–induced peptic ulcer, Helicobacter pylori infection and Zollinger-Ellison syndrome.</td>
<td>January 2000</td>
<td>December 1999</td>
<td>20 mg 14 Capsules</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>December 1999</td>
<td>May 2002</td>
<td>20 mg 28 Capsules</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>January 2002</td>
<td>January 2004</td>
<td>20 mg 28 Tablets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>January 2002</td>
<td>January 2004</td>
<td>40 mg 28 Tablets</td>
</tr>
<tr>
<td></td>
<td>Lovastatin (C10AA02)</td>
<td>Dyslipidemia, hypercholesterolemia, hyperlipoproteinaemia and atherosclerotic.</td>
<td>November 2000</td>
<td>May 2002</td>
<td>20 mg 28 Tablets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>December 2000</td>
<td>May 2002</td>
<td>40 mg 28 Tablets</td>
</tr>
<tr>
<td>SSRIs Antidepressants (N06AB)</td>
<td>Fluoxetine (N06AB03)</td>
<td>Depression, bulimia nervosa and obsessive compulsive disorder.</td>
<td>January 1999</td>
<td>December 1999</td>
<td>20 mg 14 Capsules</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>January 1999</td>
<td>December 1999</td>
<td>20 mg 28 Capsules</td>
</tr>
<tr>
<td></td>
<td>Citalopram (N06AB04)</td>
<td>Depression, panic disorder and obsessive compulsive disorder.</td>
<td>August 2002</td>
<td>January 2004</td>
<td>20 mg 14 Tablets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>August 2002</td>
<td>January 2004</td>
<td>20 mg 28 Tablets</td>
</tr>
<tr>
<td></td>
<td>Paroxetine (N06AB05)</td>
<td>Depression, panic disorder, social phobia disorder, generalized anxiety disorder, obsessive compulsive disorder and posttraumatic stress disorder.</td>
<td>October 2002</td>
<td>January 2004</td>
<td>20 mg 14 Tablets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>October 2002</td>
<td>January 2004</td>
<td>20 mg 28 Tablets</td>
</tr>
<tr>
<td></td>
<td>Fluvoxamine (N06AB08)</td>
<td>Depression and obsessive compulsive disorder.</td>
<td>January 2003</td>
<td>May 2003</td>
<td>50 mg 30 Tablets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>January 2003</td>
<td>May 2003</td>
<td>100 mg 30 Tablets</td>
</tr>
</tbody>
</table>
Table 2. Market structure at the end of each year.

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of markets analysed</th>
<th>Number of brand-name manufacturers</th>
<th>Number of generic manufacturers</th>
<th>Average brand-name price per DDD</th>
<th>Average generic price per DDD</th>
<th>Generic market share</th>
<th>Brand-name market share</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>3</td>
<td>30</td>
<td>18</td>
<td>0.9770354</td>
<td>0.7391375</td>
<td>0.080517</td>
<td>0.9194829</td>
</tr>
<tr>
<td>2000</td>
<td>6</td>
<td>62</td>
<td>44</td>
<td>0.9637711</td>
<td>0.963865</td>
<td>0.2409376</td>
<td>0.7590624</td>
</tr>
<tr>
<td>2001</td>
<td>6</td>
<td>74</td>
<td>95</td>
<td>0.8467622</td>
<td>0.6955624</td>
<td>0.3567254</td>
<td>0.6432745</td>
</tr>
<tr>
<td>2002</td>
<td>13</td>
<td>113</td>
<td>186</td>
<td>0.8786461</td>
<td>0.5932166</td>
<td>0.3427948</td>
<td>0.6572052</td>
</tr>
<tr>
<td>2003</td>
<td>15</td>
<td>117</td>
<td>228</td>
<td>0.8335743</td>
<td>0.5467671</td>
<td>0.4720702</td>
<td>0.5279298</td>
</tr>
<tr>
<td>2004</td>
<td>15</td>
<td>119</td>
<td>252</td>
<td>0.4494228</td>
<td>0.3489683</td>
<td>0.6268138</td>
<td>0.3731862</td>
</tr>
<tr>
<td>2005</td>
<td>15</td>
<td>115</td>
<td>292</td>
<td>0.4256382</td>
<td>0.315965</td>
<td>0.6724371</td>
<td>0.3275629</td>
</tr>
</tbody>
</table>

Table 3. Summary statistics for the demand model variables.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
<th>Obs.</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Market share ratio</td>
<td>Generic drug’s market share divided by the brand-names’ market share</td>
<td>23,584</td>
<td>0.058</td>
<td>0.127</td>
<td>0.000</td>
<td>3.249</td>
</tr>
<tr>
<td>Within-generic share</td>
<td>Generic drug’s market share divided by the total generic market share</td>
<td>23,584</td>
<td>0.068521</td>
<td>0.1239926</td>
<td>0.000</td>
<td>1</td>
</tr>
<tr>
<td>Generic price per DDD</td>
<td>Price per DDD of the generic drug</td>
<td>23,584</td>
<td>0.5725827</td>
<td>0.2435079</td>
<td>0.1881696</td>
<td>1.594401</td>
</tr>
<tr>
<td>Average brand-name price per DDD</td>
<td>Average price per DDD of the brand-name drugs</td>
<td>23,584</td>
<td>0.6836283</td>
<td>0.2874202</td>
<td>0.2871252</td>
<td>1.912889</td>
</tr>
<tr>
<td>Time on the market</td>
<td>Number of months since the entry of the generic drug</td>
<td>23,584</td>
<td>25.22278</td>
<td>17.36645</td>
<td>1</td>
<td>84</td>
</tr>
<tr>
<td>No copayment</td>
<td>Dummy equal to one for a pensioner market; 0 otherwise</td>
<td>23,584</td>
<td>0.5019929</td>
<td>0.5000066</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Small copayment</td>
<td>Dummy equal to one for drugs to treat chronic diseases; 0 otherwise</td>
<td>23,584</td>
<td>0.1869912</td>
<td>0.3899127</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Reference pricing I</td>
<td>Dummy equal to 1 from the moment the reference price is applied to the market and until December 2003; 0 before and after</td>
<td>23,584</td>
<td>0.2962178</td>
<td>0.4565979</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Reference pricing II</td>
<td>Dummy equal to 1 from the moment the reference price is applied to the market: December 2003; 0 before</td>
<td>23,584</td>
<td>0.5153494</td>
<td>0.4997749</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Number of indications for the active ingredient</td>
<td>Number of DDDs per tablet or capsule</td>
<td>Units per package</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------------------------------------------</td>
<td>------------------------------------</td>
<td>------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of indications</td>
<td>23,584</td>
<td>3.516494</td>
<td>1.156198</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DDDs per tablet</td>
<td>23,584</td>
<td>1.132802</td>
<td>0.493090</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Units</td>
<td>23,584</td>
<td>24.01942</td>
<td>6.332285</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Presentations</td>
<td>Number of different kinds of presentations in the active ingredient market at the moment of patent expiry</td>
<td>23,584</td>
<td>8.19492</td>
<td>8.28148</td>
<td></td>
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<tr>
<td>1st generic entrant</td>
<td>Dummy equal to one for the first generic entrant; 0 otherwise</td>
<td>23,584</td>
<td>0.1662992</td>
<td>0.3723569</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd generic entrant</td>
<td>Dummy equal to one for the second generic entrant; 0 otherwise</td>
<td>23,584</td>
<td>0.1283497</td>
<td>0.3348597</td>
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<tr>
<td>3rd generic entrant</td>
<td>Dummy equal to one for the third generic entrant; 0 otherwise</td>
<td>23,584</td>
<td>0.089637</td>
<td>0.285667</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4th generic entrant</td>
<td>Dummy equal to one for the fourth generic entrant; 0 otherwise</td>
<td>23,584</td>
<td>0.077171</td>
<td>0.2668682</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5th generic entrant</td>
<td>Dummy equal to one for the fifth generic entrant; 0 otherwise</td>
<td>23,584</td>
<td>0.0474474</td>
<td>0.2125984</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

45
Table 4. Demand model estimation results.

<table>
<thead>
<tr>
<th></th>
<th>G2SLS Random-Effects with IV</th>
<th>2SGMMPooled with IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coefficient</td>
<td>Std. Error</td>
</tr>
<tr>
<td>Log(Within-generic share)</td>
<td>0.5096438***</td>
<td>0.03938</td>
</tr>
<tr>
<td>Log(Generic price per DDD)</td>
<td>-5.97638***</td>
<td>0.406752</td>
</tr>
<tr>
<td>Log(Average brand-name price per DDD)</td>
<td>3.974557***</td>
<td>0.3919272</td>
</tr>
<tr>
<td>No copayment</td>
<td>-0.683159***</td>
<td>0.0283507</td>
</tr>
<tr>
<td>Small copayment</td>
<td>-0.3951118***</td>
<td>0.0410342</td>
</tr>
<tr>
<td>Reference pricing I</td>
<td>0.6243972***</td>
<td>0.0296523</td>
</tr>
<tr>
<td>Reference pricing II</td>
<td>0.9088608***</td>
<td>0.0866061</td>
</tr>
<tr>
<td>Time on the market</td>
<td>0.0091641***</td>
<td>0.0009548</td>
</tr>
<tr>
<td>Number of indications</td>
<td>0.2252446***</td>
<td>0.0203143</td>
</tr>
<tr>
<td>DDDs per tablet</td>
<td>-0.8450448***</td>
<td>0.0591827</td>
</tr>
<tr>
<td>Units</td>
<td>-0.0433392***</td>
<td>0.0033594</td>
</tr>
<tr>
<td>Presentations</td>
<td>-0.1463136***</td>
<td>0.0217165</td>
</tr>
<tr>
<td>1st generic entrant</td>
<td>0.8449423***</td>
<td>0.0881888</td>
</tr>
<tr>
<td>2nd generic entrant</td>
<td>0.9300263***</td>
<td>0.080414</td>
</tr>
<tr>
<td>3rd generic entrant</td>
<td>0.3425538***</td>
<td>0.0496196</td>
</tr>
<tr>
<td>4th generic entrant</td>
<td>0.2645661***</td>
<td>0.0515613</td>
</tr>
<tr>
<td>5th generic entrant</td>
<td>0.3502969***</td>
<td>0.058836</td>
</tr>
<tr>
<td>Constant</td>
<td>-1.571498***</td>
<td>0.446079</td>
</tr>
</tbody>
</table>

Observations: 23,584
R²: 0.5494
Sargan-Hansen statistic (p-value): 1.129 (0.288)
Durbin-Wu-Hausman tests: 12488.85 (0.0000)

Note: Therapeutic subgroups and firm-specific fixed effects are included.
*, **, *** = significant at the 10%, 5%, and 1% level, respectively.
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