DOCUMENT DE TREBALL

XREAP2011-02

What if there was a stronger pharmaceutical price competition in Spain? When regulation has a similar effect to collusion

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XARXA DE REFERÈNCIA EN ECONOMIA APLICADA

What if there was a stronger pharmaceutical price competition in Spain? When regulation has a similar effect to collusion

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May 2011

Abstract

This paper examines statins competition in the Spanish pharmaceutical market, where prices are highly regulated, and simulates a situation in which there is unrestricted price competition. A nested logit demand model is estimated with a panel of monthly data for pharmaceuticals prescribed from 1997 to 2005. The simulation indicates that the regulation of prices is similar in its effects to cooperation among producers, since the regulated prices are close to those that would be observed in a scenario of perfect collusion. Freedom to set prices and a regulatory framework with appropriate incentives would result in a general reduction in prices and may make the current veiled competition in the form of discounts to pharmacists become more visible. The decrease in prices would be partially offset by an increase in consumption but the net effect would be an overall decrease in expenditure. The counterfactual set-up would also lead to important changes in the market shares of both manufacturers and active ingredients, and a reversal of generic drugs. Therefore, pro-competitive regulation would be welfare-enhancing but would imply winners and losers.

Keywords: pharmaceutical industry, statin drugs, competition, regulation

JEL classifications: I11, I18, L13, L65

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1. Introduction

Due to aging of the population and the inclusion of expensive new products, drug expenditure is one of the fastest growing components of health expenditure in most countries. Since the regulation of the market and certain cost containment measures have not been totally successful in reducing prices, knowing more about drug competition could be very useful for pharmaceutical policy makers.

Although Spain has allowed the introduction of generic drugs since January 1997, that is, drugs that are bioequivalent to brand-name medicines (i.e., their efficacy and

safety are essentially the same) that enter the market when the patents on the original drugs have expired, there is only limited price competition. The pharmaceutical market is highly regulated and prices are driven mainly by modifications and revisions of the regulations.

Therefore, the Spanish case allows a study of competition between pharmaceuticals and also simulations of equilibrium prices in situations without price restrictions or with a regulatory framework with appropriate incentives. The main purpose of this paper is to analyse demand for statin drugs and to perform a counterfactual exercise in price competition *à la* Bertrand. The comparison between the real and the counterfactual situations allows me to evaluate modifications of the strict price regulations in terms of welfare and winners and losers.

This new empirical evidence from Spain, which is one of the largest markets for pharmaceuticals in the European Union (EU) and the seventh largest worldwide, could be applied to a great number of countries with similar institutional settings and pharmaceutical market characteristics: heavy price regulation and low penetration of generic drugs.

The outline of the paper is as follows. The next section explains the main features of the Spanish pharmaceutical market. The third section describes the dataset. The section after that presents the demand and supply models, and the simulation procedure. The fifth section shows the estimation issues and results. The sixth section presents the simulation results. The section after that discusses the results and the last section offers the concluding remarks.

2. The Spanish pharmaceutical market

The Spanish NHS is funded from tax revenue and provides health care services to all residents. The health care management system is decentralized and regional authorities control expenditure and organize health service provision. However, the central government regulates pharmaceutical prices.

Although the NHS provides health care, there are copayments for prescribed pharmaceuticals. The standard rate of copayment is 40%, but the average copayment is less 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 for chronic diseases have a rate of only 10% (with an upper limit). The actual average copayment for prescribed pharmaceuticals is very low and accounts for less than 7% of the total expenditure on ambulatory prescription pharmaceuticals.

Another important feature is that there are a great number of different presentations of drugs. 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 this date, there were only process patents.

Although generic drugs were introduced into Spain in 1997, the market share for generic medicines was low at the end of the period analysed (14.60% in units and 7.90% in value) (IMS Health, 2006b).

The average price of drugs in Spain is low in comparison to that of other EU countries but the average brand prescription price has risen, due mainly to drugs that have been introduced recently at high prices (Costa-Font and Puig-Junoy, 2005). These new high prices may be a strategy to avoid parallel trade, since the low prices for older medicines has led to the Spanish market becoming an important source of parallel trade within the EU.

Although Spain was 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. Reference pricing has gradually been extended to 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 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)[1]. This system established the maximum price that could be reimbursed by the NHS for any version of the same drug. Whenever the price of a

[1] 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 price of the cheapest generic (López-Casasnovas and Puig-Junoy, 2000).

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.

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[2] (DDD). With this system, if prescriptions specify drugs priced higher than the reference price, pharmacists are obliged to substitute them for the cheapest generic version. However, if prescriptions specify drugs whose price is 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.

Moreover, the maximum ex-factory price for all drugs (branded and generics) 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 Ministry of Health and Consumer Affairs is responsible for negotiation with firms. The funding conditions setting and wholesalers' and retailers' mark-ups are also regulated.

[2] A defined daily dose is the average dose per day in adults for a drug when it is used to treat its main indication.

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 criterion is 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).

Finally, it is important to emphasize that, in Spain, public expenditure on prescription medicines represented slightly more than 22% of public health expenditure in 2005, and that between 1997 and 2005, the public expenditure on pharmaceuticals increased by almost 117%.

3. Data

The dataset consists of monthly consumption records of prescription statins from 1997 to 2005. The information was provided by the Directorate-General of Pharmacy and Health Products at the Spanish Ministry of Health and Consumer Affairs, and 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 Sanitario 2005 - BOT PLUS* (Consejo General de Colegios Oficiales de Farmacéuticos, 2005).

The analysis is focused on outpatient consumption of oral prescription drugs containing only one active chemical ingredient. As **Table 1** shows, the sample includes 19 markets for six active ingredients from the group of statins (HMG CoA reductase inhibitors). The active ingredients included are all those commercialized in Spain during the period analysed: atorvastatin, cerivastatin, fluvastatin, lovastatin, pravastatin and simvastatin. However, cerivastatin (marketed in Spain as Lipobay®, Liposterol®, Vaslip®, and Zenas Micro®) was withdrawn from the market in 2001, due to international reports of safety issues.

These drugs are lipid modifying agents that are used to lower high cholesterol levels in people with or at risk of cardiovascular disease. In fact, they are the most potent cholesterol-lowering agents available. The reduction in total cholesterol levels that these drugs are responsible for, and especially in levels of low-density lipoprotein (LDL) cholesterol (commonly known as "bad cholesterol"), implies an important decrease in the number of cardiac events, such as heart attack or sudden cardiac death, and a considerable reduction of the risk of stroke. For this reason, statins are widely prescribed and among the most sold drugs worldwide.

Lovastatin, simvastatin, pravastatin and fluvastatin entered the market before January 1997. Lovastatin was the first statin marketed in Spain; in 1990. In 1991, simvastatin and pravastatin were commercialized. Fluvastatin entered the market in 1996. The first sales of atorvastatin and cerivastatin appear in the dataset in November 1997 and August 1998, respectively.

Table 1 also shows the specific indications of each active ingredient[3], the date of entry of the first generic (in those markets with generic entry before the end of 2005), and the date of the implementation of the reference pricing system (for those markets in which this system of reimbursement was applied).

This dataset is not a sample but the whole outpatient market for these drugs: all statin drugs sold in Spain and financed (at least partially) by the NHS. The panel is unbalanced since atorvastatin and cerivastatin entered in the market after January 1997 and different presentations entered the market at different times. There are, however, observations for at least 56 months for cerivastatin, 98 for atorvastatin and 108 for the remaining active ingredients. There are a total of 10,981 observations for 64 producers.

The different active ingredients have several strengths (quantity of active ingredient per unit) and are sold in different package sizes (number of units); therefore, all the quantities sold are converted into common units. For each presentation I calculate the total number of 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[4]. Prices are calculated from the dataset by dividing volume of sales in euros (€) by the number of DDDs sold: the price per DDD for each product.

[3] The indications for the prescription of statins have broadened over the years, to include for instance the preventative effects of statin use in specific risk groups, such as diabetics (Collins et al., 2003).

[4] 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 dose enables standardisation and comparison drug quantities across therapeutic groups, active ingredients and presentations.

Finally, I calculate the market size as the population who have high cholesterol and therefore, could potentially receive a prescription for a statin. To calculate this potential market I use the number of individuals reported to have been diagnosed with high cholesterol in the 2003 Spanish National Health Survey (*Encuesta Nacional de Salud*). I assume the percentage of population with high cholesterol to be constant over the years analysed and I multiply this percentage by the Spanish population and the number of days in each month. In this way I obtain the number of DDDs potentially consumed.

4. Empirical framework

Two of the most important drivers of pharmaceutical competition are the introduction of new active ingredients for similar indications and the introduction of generic drugs. As mentioned, generics were introduced into Spain in 1997. These products contain the same active chemical ingredient as the original product and have proven bioequivalence[5], to the satisfaction of health authorities. However, the producer and some characteristics such as colour, shape, inactive ingredients or packaging may be different. Therefore, generics may be considered substitutes for the brand-name drugs but not perfect substitutes; in other words, there is some degree of product differentiation.

[5] The WHO defines two pharmaceutical products as bioequivalent if they are pharmaceutically equivalent or pharmaceutical alternatives, and they 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.

The expected result of generics entering the market is an increase in the level of competition in the market and a reduction in the prices and market shares of brand-name products. It is also expected that when the number of manufacturers producing generics in the market is considerable, prices will tend towards the marginal cost of production. However, for brand-name products, the literature in the US shows some evidence of price increases after the entry of generics (for instance Grabowski and Vernon, 1992; or Frank and Salkever, 1997): this has been called the "Generic Paradox" (Scherer, 1993).

Product differentiation is greater if not only the producer, colour, shape, inactive ingredients or packaging are different, but so too is the active ingredient. Indeed, each statin has its own characteristics and entered the market at a different time. For instance, statins may be classified into fermentation-derived and synthetic. The first group includes lovastatin, pravastatin, and simvastatin; the second atorvastatin, cerivastatin, and fluvastatin.

The LDL-lowering potency also varies from one active ingredient to another. Cerivastatin was the most potent, followed by atorvastatin, simvastatin, lovastatin, pravastatin, and fluvastatin. A comparison of the efficacy of atorvastatin, simvastatin, pravastatin, lovastatin, and fluvastatin at reducing LDL and total cholesterol in patients with hypercholesterolemia, found that atorvastatin was the most effective without increasing adverse effects (Shepherd et al., 2003). Finally, the

statins analysed are generally well-tolerated and show similar levels of adverse effect, although the newer statins have a higher ratio of efficacy to adverse effect[6].

Therefore, the statin group is formed of branded and generic medications that compete with other close but not perfect substitute medications. Thus, defining the relevant market is not easy and although it is an imperfect approach, some authors (for instance, Aronsson, Bergman and Rudholm, 2001; Dalen, Strøm and Haabeth, 2006; and Moreno-Torres, Puig-Junoy and Borrell, 2009) take the therapeutic active ingredient level according to the Anatomical Therapeutic Chemical (ATC) classification as the relevant market. I follow this approach to define markets but, in order to tackle the non-linearity of the prices of differently sized presentations and to take advantage of variation between markets and products to identify parameters, I use the product (active ingredient with a specific dosage and size from each manufacturer) as the element of analysis.

Demand

In the pharmaceutical industry the institutional setting is very important and the dispensing process is quite complex; the physician, the pharmacist, the third-party payer and the patient each play a role. I assume that the physician and the pharmacist are perfect agents for the patient and that their choice, together with that of the patient, maximizes utility for the patient.

[6] The risk of myopathy is lowest with pravastatin and fluvastatin probably because they are more hydrophilic and as a result have less muscle penetration. Lovastatin induces the expression of gene atrogin-1, which is believed to be responsible in promoting muscle fibre damage (Hanai et al., 2007).

The dispensing process follows a multi-level market structure, as shown in **Figure 1.** The first choice is between dispensing a statin or prescribing an alternative treatment, such as exercise, a change of diet, homeopathic products or even a drug from another related therapeutic subgroup such as fibrates, bile acid sequestrants or nicotinic acid and its derivatives. In fact, prescription guidelines usually require that the patient has tried a cholesterol-lowering diet before starting to use statins.

If the statin subgroup is chosen, the next step is to decide between the active ingredients based on the medical record of the patient and possible intolerance to some active ingredients. The third decision is to choose a specific presentation from all the possibilities for the active ingredient, in other words, to choose the strength of the product and the package size, given the difference between the actual and targeted cholesterol level, as well as the characteristics of the patient.

The next stage is the choice between branded and generic drugs. 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 branded products. Coscelli (2000) found that in addition to the physician, the patient's characteristics also affect the prescription decision.

When the physician prescribes a brand-name or generic product, there is also a choice between different manufacturers. In fact, as well as the physician and the patient, the pharmacist may participate in the choice of the drug, for instance choosing which product containing the given active ingredient to dispense. The

choice at this stage is mainly based on which products are available at the pharmacy. Finally, the third-party payer may affect the decision by implementing obligatory substitution rules and requirements limiting reimbursements, such as the reference pricing system.

To analyse this market I use a structural discrete-choice model of product differentiation. In this model 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 random utility model has been applied to a great number of products such as ready-to-eat cereals (Nevo, 2000a and 2001), yogurts (Di Giacomo, 2008), movies theatres (Davis, 2006) and vehicles (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 interest is not only in competition between drugs containing the same active ingredient, but also between drugs with different active ingredients, I use a nested logit model based on Berry (1994)[7]. In contrast to the simple multinomial logit model, the nested logit model allows consumer tastes to be correlated across products. Indeed, there is correlation between the idiosyncratic shocks between products of the same segment of the market. This counters the "independence from

[7] An alternative approach is the multistage budgeting model applied by Ellison et al. (1997) to analyse the demand for cephalosporins.

irrelevant alternatives" (IIA) property and allows for reasonable substitution patterns.

In comparison to the random coefficients model[8], 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 priori*[9]. However, in the case of pharmaceuticals this problem does not jeopardize the nested logit model since it is possible to use the ATC classification to build the structure of the nests[10]. It seems reasonable to assume that, within statins, products with the same active ingredient are closer substitutes than products with different active ingredients. Additionally, with the random coefficients model it is necessary that prices or other product characteristics vary across markets (Nevo, 2000b) and in the dataset there are not such variations.

Drugs are grouped into exhaustive and mutually exclusive active ingredient markets. In each of these market, for instance "lovastatin", there is a set of drugs characterized by their strengths, package sizes and manufacturers denoted $j = 1, \ldots, J$. Each set may include brand-name and generic drugs. It is assumed that different presentations with the same active ingredient are highly substitutable and may be

[8] The nested logit model can be interpreted as a special case of the random coefficients model with random coefficients only on segment–specific dummy variables (Berry, 1994). The consumer preference for the segment is the only relevant consumer characteristic and it interacts with only one product characteristic: the segment to which the product belongs.

[9] 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.

[10] The therapeutic groups are formed on the basis of the 4th level of the ATC code that approximates the chemical, therapeutic or pharmacological group (e.g., C10AA for statins or HMG CoA reductase inhibitors) and 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, e.g., C10AA01 for simvastatin).

interchanged; for instance, one daily pill of simvastatin 20 mg with either two pills of simvastatin 10 mg or half a pill of simvastatin 40 mg. Finally, the outside good represents the alternative: not consuming a statin, and is assumed to be the only member of its own group[11].

The physician, jointly with the pharmacist and the patient, chooses a presentation of the drug that maximizes utility for the patient, even though the final consumption may be affected by the reimbursement and substitution rules and the availability of the product at the drugstore. The aggregate demand for each product is obtained by summing over the individual choices.

The indirect utility function of consumer *i* for consuming the drug *j* at the period *t* is:

$$u_{ijt} = \delta_{jt} + \sum_{g} \left[d_{jg} \zeta_{ig} \right] + (1-\sigma)\varepsilon_{ijt} \qquad (1)$$

Where δ_{jt} is the mean utility level of product *j*, which is the same for all consumers. Thus, individual heterogeneity enters the model through the non-deterministic part of the utility, $\zeta_{ig} + (1-\sigma)\varepsilon_{ijt}$. Where $(1-\sigma)\varepsilon_{ijt}$ is the idiosyncratic taste for drug *j* and ζ_{ig} is the individual-specific random term, which is interacted with the dummy variables for each of the active ingredient markets. In fact, ε_{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

[11] In fact, the outside good also includes the consumption of statins by those individuals with private health insurance.

that is equal to one for drugs with a specific active ingredient, *g*, and zero otherwise and ζ_{ig} is common to all products in market *g* and has a distribution function that depends on the parameter σ, with $0 \leq \sigma < 1$. As Cardell (1997) proved, an additional property of this model is that if ε_{ijt} is an extreme value random variable, $[\zeta_{ig} + (1-\sigma)\varepsilon_{ijt}]$ is also an extreme value random variable.

The parameter σ measures the within-nest correlation of utility levels and allows substitution between products with the same active ingredient to be included. If σ 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 σ tends toward 1, the within-nest correlation of utilities approaches 1.

The mean utility, δ_j, is equal to:

$$\delta_{jt} = \kappa + \gamma_g + X\beta + \alpha p_{jt} + \omega_m + \xi_{jt} \qquad (2)$$

Where the κ is a constant term, γ_g is an active ingredient fixed effect, X is a matrix of product characteristics which includes the time of each product in the market and a dummy variable that is equal to 1 if the product is a generic, α is the price coefficient and β is a vector of taste parameters to be estimated. p_{jt} is the price per DDD of drug *j* at time *t*. I also introduce firm-specific fixed effects, ω_m, that is, a variable that is equal to one for a specific firm across drugs and markets and to zero otherwise. ξ_j expresses product characteristics that are observable to

the physicians, pharmacists or patients, but not to the researcher, such as quality, reputation or promotional effort.

One characteristic of this demand model is that wealth effects are not taken into consideration. This would be a problem if the product analysed was a good whose price sensitivity depended on level of income, such as a durable good, but this does not seem to be the case for statin drugs.

After the normalization of the utility of the outside good to 0, $\delta_0 = 0$, and following the derivation in Berry (1994), the econometric specification is:

$$\ln(s_{jt}) - \ln(s_{0t}) = \kappa + \gamma_g + X\beta + \alpha p_{jt} + \sigma \ln(s_{j/gt}) + \omega_m + \upsilon_{jt} \qquad (3)$$

Where s_{jt} and s_{0t} are the market shares of drug *j* and the outside good, respectively, σ is the parameter that measures the level of correlation between products with the same active ingredient, $\ln(s_{j/gt})$ is the log of the share of product *j* in the group of products with active ingredient *g*, and υ_{jt} is an error term.

Supply

In the pharmaceutical industry, firms usually produce more than a single drug. I assume that firms act as multi-product Bertrand profit maximizers and set their prices taking the prices chosen by their competitors as given. Following Nevo (2000a and 2001), each firm produces a subset Γ_f of the *J* products. So, for each period, the profits of the firm *f* are:

$$\Pi_{ft} = \sum_{j \in \Gamma_{ft}} (p_{jt} - mc_{jt}) Ms_{jt}(p) - C_{ft} \qquad (4)$$

Where $s_{jt}(p)$ is the market share of product *j*, which depends on the prices of all products, and *M* is the size of the market, which includes the outside good and implicitly defines its size. As highlighted by Nevo (2000a), this definition allows the market size to be kept fixed while still allowing an increase in the number of the products on the market, since it results in a decrease in the share of the outside good[12]. C_{ft} is the fixed cost of production and mc_{jt} is the marginal operating cost, which is assumed not to depend on the quantity produced.

A unique pure-strategy Bertrand-Nash equilibrium with strictly positive prices is assumed. Thus, the price p_{jt} of product *j* produced by firm *f* at period *t* must satisfy the following first-order condition:

$$s_{jt}(p) + \sum_{r \in \Gamma_{ft}} (p_{rt} - mc_{rt}) \frac{\partial s_{rt}(p)}{\partial p_{jt}} = 0 \qquad (5)$$

These first-order condition equations involve price-costs margins for each drug. Bertrand competition in a context of differentiated products, which is the case in the pharmaceutical industry, is different from a situation of homogenous products. With differentiated products, a firm does not generally lose all of its demand by pricing slightly above the competitors' prices, nor does it steal all rival firms' demand by pricing below their competitors' prices. Thus, in equilibrium, firms may set different prices that exceed the marginal cost and earn positive profits (Baye and

[12] If the potential market size (which was defined in section 3 as the amount of DDDs that would be consumed if all potential patients took a statin) was reduced, for instance, by considering a lower proportion of people with high cholesterol level as potential consumers, it would imply higher elasticities of substitution. Since I assume a relatively large market size for the outside good, it will generate conservative estimates of substitution.

Kovenock, 2008). If products are considered good substitutes, there is more competition and prices should tend towards the marginal cost: with less differentiation, there is a reduction of markups and prices. For instance, the differentiation between brand-name and generic drugs may explain the aforementioned "Generic Paradox" found in the US by some authors.

The markups can be solved for explicitly by defining the following *J* x *J* matrix:

$$\Omega_{jrt}(p) = \begin{cases} -\dfrac{\partial s_{rt}(p)}{\partial p_{jt}}, & if \quad \exists f: \ \{r, j\} \subset \Gamma_{ft} \\ 0, & otherwise \end{cases} \tag{6}$$

Where the own and cross price elasticities of this one-level nested logit model have the following form:

$$\eta_{jjt} = \frac{\alpha}{1-\sigma} p_{jt}(1 - \sigma s_{j/gt} - (1-\sigma)s_{jt})$$

$$\eta_{jrt} = \frac{\alpha}{1-\sigma} p_{rt}(1 - \sigma s_{r/gt} - (1-\sigma)s_{rt}) \tag{7}$$

$$\eta_{jkt} = -\alpha p_{kt} s_{kt}$$

Where *j* and *r* are different products with the same active ingredient and *k* has a different one.

The first-order conditions in (5) can be written in vector notation as:

$$s(p) - \Omega(p - mc) = 0 \tag{8}$$

Simulation

If the marginal costs are not observed, they can be computed from the estimates of the demand system and (8). However, I follow the opposite approach and obtain the vector of prices for each month of 2005 from the inversion of Ω, the market shares and a proxy of the marginal costs. Once the own and cross price elasticities are computed and Ω is inverted, I calculate the prices using the following expression:

$$p = mc^* + \Omega^{-1} s(p) \qquad (9)$$

As a proxy for the marginal operating costs, I use the lowest price per DDD observed for the 19 markets in August 2010, which is €0.07 for the presentation of simvastatin with a dose of 40 mg and 28 tablets. It seems a reasonable marginal cost since the prices tend to the marginal cost when there are a considerable number of competitors and usually, in regulated markets, some years after the introduction of the product. In any case, this price is assumed to be a maximum boundary for the marginal cost. Additionally, I compute prices with a marginal cost equal to zero as a minimum boundary.

In this way, I assume that marginal costs are constant across firms and periods. The assumption of constant marginal cost of production is common in the literature that analyses the pharmaceutical industry. It is also common to assume zero marginal cost, since previous observers have claimed that the marginal cost is extremely low, even that the level of marginal cost is negligible compared to price (Stern, 1996). Therefore, the marginal operating cost per DDD will be €0.07 or zero.

For practical purposes I assume that in each period firms set prices taking into account their own and competitors' market shares in the previous month. After calculating the simulated prices, I compute the corresponding market share of each product for that period with the parameters obtained from the estimation of the demand model. With these market shares, I compute the prices of the following month in a recursive way and with them the market shares for that period[13].

As an alternative scenario, prices in 2005 are computed only for off-patent drugs[14]. Taking the regulated prices of drugs under patent protection as given, I simulate the prices for off-patent products in each period using the previous procedure. Then, I recalculate the market shares of all the products, including those with patent protection.

Finally, I simulate a situation of full collusion among all the firms present in the market. Thus, in these scenarios each producer considers in its first-order condition of profit maximization not only all the products it produces but also its competitors' products. I simulate the prices resulting from this strategy of joint profit-maximization of all the products, which corresponds to monopoly or perfect price collusion, by defining the ownership matrix appropriately and computing the corresponding markups (Nevo, 2001).

[13] I also assume the same number of entries of firms throughout 2005, which is a small number, and that they achieve the same market share in the first month as in the real data.

[14] The inclusion of all the products in the first counterfactual scenario does not mean that active ingredients whose patents have not expired lose their protection, since the entry of new competitors, for instance generics, is not simulated. However, these products are under competitive pressure from other active ingredients in the same therapeutic group and, as will be seen below, their producers are in a better position if they are able to set prices without restrictions when off-patent products can do so.

Welfare variation

In order to evaluate the effects of introducing actual price competition, it is necessary to calculate variations in welfare. Welfare is a monetary measure of the utilities for the patients of the set of products available, including the outside good, minus the price paid by the consumers (the copayment of the patients plus the cost for the NHS).

Some previous work has analysed effects on welfare of the introduction of new products (Petrin, 2002; Di Giacomo, 2008). I only compute welfare variations as a result of price changes for the same set of products, for which it is necessary that there are no welfare variations due to variety effects (Hausman and Leonard, 2002).

Following Small and Rosen (1981), the surplus per consumer in a discrete-choice model may be calculated by integrating over the market share function. Thus, the compensating variation measure of a change in prices for a representative consumer is equal to:

$$W_t = \frac{1}{\alpha} \int_{\delta_t^0}^{\delta_t^1} s_{jt}(\delta_{jt}^r) d\delta \qquad (10)$$

Where δ^0 is the vector of mean utilities calculated with the real prices and δ^1 is the same vector computed with simulated prices of each of the counterfactual scenarios. After integrating the market share formula for the one-level nested logit model (Berry, 1994), the following expression is obtained:

$$W_t = \frac{1}{\alpha} \ln \left(\sum_g \left(\sum_{j \in g} \exp \left(\frac{\delta_{jt}^r}{1-\sigma} \right) \right)^{1-\sigma} + 1 \right) \Bigg|_{\delta_t^0}^{\delta_t^1} \quad (11)$$

Where *g* is the active ingredient subgroup. The total variation in welfare is given by multiplying this compensating variation for a representative consumer by the potential market size. I use the parameter estimates of the demand model to calculate expression (11).

Finally, since the entry costs are sunk costs and fixed costs are the same under any scenario, it is possible to calculate the welfare variation of firms during 2005 as the change in variable profits, i.e. the quantity of DDDs sold multiplied by the difference between the price per DDD and the assumed marginal cost per DDD.

5. Econometric estimation

The quality of the product as well as promotional activities and marketing expenses are observable to the consumer, the physician and the pharmacist, but not to the researcher. These unobserved factors are correlated with the drug price and with the drug's share within the active ingredient and cause endogeneity.

To partially overcome this problem, I include firm-specific dummy variables in the econometric specification. The role of these fixed effects is to control for time invariant factors, which are usually common to all a firm's products, that is, to capture the manufacturers' mean quality and mean marketing effort, leaving the time-specific and product-specific deviations as part of the error term. In fact, the

market shares of competing drugs are driven by physicians' and pharmacists' choices of producer within the market and firms build a reputation and develop idiosyncratic skills in launching and delivering drugs.

So, the remaining potential endogeneity arises from factors that change over time or variation between a manufacturer's products. To deal with this remaining inconsistency in the estimation, I use instrumental variables.

Following the empirical literature on industrial organization (Berry, Levinsohn and Pakes, 1995; Bresnahan, Stern, and Trajtenberg, 1997; and Petrin, 2002) and similar papers dealing with the pharmaceutical industry (for instance Iizuka, 2007; or Stern, 1996), as possible instruments I considered those variables that capture how crowded product space is and the ownership structure at different levels of the market.

From the instruments available I chose the set with strongest correlation to the endogenous variables that did not reject the null hypothesis of the Sargan-Hansen test of exogeneity (Sargan, 1958; and Hansen, 1982). These instruments are: total number of products in the active ingredient market; total time in the market of all a firm's products; and total time in the market of all the competitors' products.

Additionally, I include the order of entry of each product into the active ingredient market as an instrument. In Spain, as Reiffen and Ward (2005) indicated for the US, the timing of entries into the market is largely out of the control of firms; they do not know the date of approval with certainty, or even if they will obtain approval,

neither do they know when, or how many, other applications for that market will be approved. Thus, because of the length and uncertainty of the approval process, order of entry may reasonably be considered as unrelated to firm-specific characteristics.

I use the (two-stage) Generalized Method of Moments (GMM), which is the method most commonly used in the industrial organization literature following Berry (1994), since its estimates are unbiased and consistent. **Table 2** contains the definitions and descriptive statistics of the variables that are used in the estimation.

Table 3 shows the GMM estimation of the demand model. The within-active-ingredient market share is significant and its coefficient is 0.46. This result validates the use of the nested logit model as opposed to a simple multinomial logit model, since the nested model is only consistent with the random utility maximization when this parameter is significant and between 0 and 1.

There is negative price elasticity since the price per DDD parameter is significant and negative. A 1% increase in price reduces the relative statin drug share, that is, the weight of the product share over the outside good share, by 3.46%.

Time in the market has a positive coefficient and is significant. It would seem that products that have been on the market longer have more sales than new products.

The generic dummy variable is significant at the 5% level and has a positive parameter. Thus, being a generic product also seems to have a positive effect on the quantity of DDDs sold.

As expected, the dummy variable for the general withdrawal of cerivastatin until its complete disappearance from the market has a significant large negative coefficient. The remaining active ingredients, except for lovastatin, have significant dummy coefficients in relation to the comparison active ingredient, simvastatin. In fact, atorvastatin and fluvastatin have positive and larger values.

6. Simulation results

Once the own and cross price elasticities given by (8) are computed and Ω is inverted, I calculate the price of each product for each month of 2005 using (9). As proxies for the marginal cost I use the lowest price per DDD observed for the 19 markets in August 2010 and zero. After calculating the simulated prices I compute the corresponding market shares for each product for that month. The 2005 prices are also computed only for off-patent drugs, in order to simulate a scenario in which there is price competition only among products that are not protected by patents.

With these counterfactual prices and market shares, which are obtained from a competition *à la* Bertrand, interest lies in the comparison with the real ones, which are the result of a competition restricted by price among other regulations.

Prices and expenditure

As **Table 4** shows, there is a global decline in unrestricted prices[15]. The weighted average real price per DDD is €0.44 for the whole statin market, while the mean simulated price goes from €0.18 (when the marginal cost is assumed to be zero) to

[15] In order to homogenize comparisons with the real prices and quantities, the real quantities of DDDs are obtained from the predictions of the estimated demand model with the real prices and the real average prices per DDD are weighted by these predicted quantities.

€0.25 (for a marginal cost of 0.07). If there is price competition only between off-patent drugs, the average prices are €0.21 in the first case and €0.27 in the second. Therefore, the price reduction ranges from 39% to 59% depending on the scenario.

As **Table 7** shows, due to the negative price elasticity of demand, there is a slight increase of about 4% in the total quantity of DDDs consumed under any scenario. However, the price decline is enough to compensate this increase in consumption and, as is shown in **Table 5**, there is a considerable decrease in expenditure, especially in those cases where there is no marginal cost. The savings for the NHS and patients ranges from 37% to 57%, depending mainly on the marginal cost assumption.

Active ingredients

Even though there are considerable real price differences between active ingredients, once there is unrestricted price competition, prices are quite similar. The lowest real price is €0.36 for atorvastatin and the highest is €1.00 for pravastatin. When there is competition between all the products and the marginal cost is assumed to be €0.07, the price per DDD is €0.24 for fluvastatins and lovastatins, €0.25 for simvastatins, and €0.26 for atorvastatins and pravastatins. If the marginal cost is assumed to be zero, prices vary between €0.17 and €0.19.

When the competition is restricted to off-patent products, these drugs have almost the same mean prices (in fact they are identical when expressed to two decimals) while the products under patent protection (atorvastatin and fluvastatin) have the

regulated prices. For that reason, the decline in prices is slightly lower for the whole statin market.

Tables 5 and **6** show the distribution of total sales and market shares among active ingredients for each scenario, respectively, and **Tables 7** and **8** show the same information in terms of quantity of DDDs. The data in these four tables are represented in **Figures 2** to **5**[16].

As a consequence of price variations, there are important changes in the total amount of DDDs and market shares of active ingredients. On the one hand, in all the scenarios there is a large increase in consumption of pravastatins, especially when the competition is restricted to off-patent drugs. On the other hand, there are large declines in sales of atorvastatins and simvastatins. The consumption of fluvastatins and lovastatins are relatively stable and fluctuate depending on the assumptions of competition and marginal cost. When the competition is restricted to off-patent drugs, the decline in sales of products under protection is greater. However, as they have relatively high regulated prices, the revenues they generate are less affected than the quantities sold.

[16] Due to space limits, variations in the market shares of different presentation (combinations of dose, quantity and active ingredient) for the same active ingredient are not reported. Active ingredients with considerable variations, in terms of quantities as much as revenues, are atorvastatin, fluvastatin and pravastatin. For the first two active ingredients, not only are there variations in comparison with the real scenario, but also between the situation in which price competition is restricted to off-patent drugs and the one in which it is allowed among all products. These results are available upon request.

Generics vs. brand-name drugs

Taking into account that in 2005 there were no atorvastatin and fluvastatin generics because of patent protection, with the real prices, the generics market share for the whole statin market was 13% in value and 12% in quantity. However, with the introduction of price competition there is a clear decline in these market shares. When there is price competition between all the products, the generics market share is 5% in value and 6% in DDDs, and when there is competition only for off-patent products, the market share is 6% in revenue and between 7% and 8% in quantity (**Tables 9** and **10**). This global decline in generic products is represented in **Figures 6** and **7**.

Among active ingredients, whereas the reduction in the generics market share is not very high for lovastatin and simvastatin (one percent for lovastatin and three percent for simvastatin), it is very marked for pravastatin. In value, the share goes from 34% to 5-6%, and in DDDs, from 41% to 6-7%.

Firms

As **Figures 8** to **12** show, in general terms, the distribution among firms of DDDs sold and revenue are slightly more unequal in any of the hypothetical scenarios than they are with the real prices. In terms of quantity of DDDs, as mentioned above, there is a total increase. However, of the 61 firms active during 2005, only 11 increase their sales when there is competition among all the products, independently of the assumed marginal cost; this becomes 17 or 18 when there is only price

competition for off-patent drugs and the marginal cost is €0.07 and zero, respectively.

In terms of revenue, in spite of the growth of demand and due to the general decline in prices, there is an overall total reduction. These smaller revenues are more concentrated in the hands of some manufacturers, especially for lovastatins and pravastatins (**Figures 13** to **17**). In fact, five of the 61 firms active during 2005 register an increase in their revenues when there is competition for all the products and the marginal cost is €0.07; and three firms do so when there is no marginal cost. When competition is restricted to off-patent products, four producers also experience increased revenue, independently of the marginal cost.

The reduction of aggregate revenue that is reported in **Table 5** is from €44,381,547.88, when there is only price competition among off-patent drugs and the assumed marginal cost is €0.07, to €68,609,032.75, when there is competition for all the products and the marginal cost is equal to zero.

The **Table 11** shows the change in variable profits among active ingredients and overall. The reduction in variable profits is from €31,465,707.95, in the case of price competition only among products not protected by patents and a marginal cost of €0.07, to €38,196,118.95, when there is competition among all the products and the marginal cost is zero. In percentage terms, the variable profits decline by between 36% and 57%.

There is a clear decline in all the active ingredients except for pravastatin, which sees an increase in the number of DDDs sold. In fact, pravastatin experiences a large increase in variable profits in the two hypothetical scenarios in which the marginal cost is assumed to be €0.07. In contrast, the reduction in simvastatin variable profits is very large under all the scenarios and especially when the marginal cost is equal to zero. For atorvastatin, the decline is also large when the marginal cost is assumed to be zero as it is when the marginal cost is equal to €0.07 and all the products experience price competition. In the case of lovastatins and fluvastatins, there are considerable but smaller reductions of variable profits.

Consumer welfare

Table 12 shows the computed changes in the welfare of consumers, understood as the NHS (tax-payers) plus the patients, under each scenario. The price reductions under all the counterfactual scenarios lead to an increase in surplus. This increase is very great when the marginal cost is equal to zero and especially when all the products compete with each other, i.e., in cases in which the decline in prices is great. The decrease in variable profits is also greater under such scenarios. The net effect of the increase in consumers' welfare and the decline in firms' profits is clearly positive in any situation. The net welfare increase ranges from a maximum of €717,343,568.78, when the marginal cost is zero and all the drugs compete, to €538,482,214.06, when the marginal cost is €0.07 and only off-patent products compete.

Regulation and collusion

As **Table 13** shows, average real prices, which are the regulated prices, are very close to those obtained from the simulation of a situation of full collusion among all the firms in the market (joint profit maximization). For the whole market, the weighted mean real price per DDD is €0.44, whereas the weighted mean price resulting from perfect collusion ranges from €0.38, when there is competition only between off-patent drugs and the marginal cost is assumed to be 0, to €0.48, in the scenario where there is competition among all the products and the marginal cost is €0.07.

7. Discussion

As the estimation results show, the within-active-ingredient market share has a significant coefficient of 0.46. Since a value of 1 would indicate a situation of perfect correlation among utilities and a value of 0 no degree of possible substitutions at all, this value shows a considerable degree of differentiation within the active ingredients.

The price has a negative effect on market share, which means that, even though the rate of copayment is quite low in Spain, there is negative price elasticity.

The time in the market has a positive effect on market share. This result is not surprising since in the pharmaceutical market, experience and product reputation are appreciated by patients and healthcare professionals, and there is evidence of an advantage for the first entrants (Yu and Gupta, 2008).

A surprising result is that being a generic drug has a positive effect on market share. It is expected that physicians and patients may prefer brand-name medicines, which usually have a better reputation. The coefficient of this dummy variable may capture the efforts of national and regional health authorities in the promotion of the prescription and consumption of generics.

One limitation of the estimation of the demand model is that the dataset contains no characteristics of the patients or other agents and thus demand depends only on prices and other attributes of the products.

Another pitfall of the dataset is that price rebates are not reflected in it. The prices used in the estimation, and indeed in the real situation in the simulation, are the prices that the NHS actually paid (and the patient when there was a copayment). However, there is some evidence of price discounts in Spain (Borrell and Merino, 2007; Puig-Junoy, 2009), especially for generic medicines, as occurs in other regulated pharmaceutical markets (Kanavos and Taylor, 2007). These price rebates to pharmacists may distort the estimated price elasticity and the subsequent simulations.

As expected, with the simulation of Bertrand price competition, in comparison to the situation of highly regulated prices, there is a notable reduction in prices and, although the price elasticity is negative, the increase in consumption is not enough to compensate for the lower prices. So there is a considerable reduction in expenditure for the whole market.

Among active ingredients there are important variations in market share. One possible explanation is that under the scenarios of unrestricted price competition there are fewer differences between active ingredient prices and the changes in sales may correspond to other characteristics.

Moreover, as the simulations show, when price competition is restricted to off-patent drugs, the decline in sales of products under protection is greater and the overall saving is lower. For this reason, a pro-competitive reform should allow the freedom to set prices for both kinds of active ingredients: with and without patent protection. This would not mean that the former lose their protection, since there is no advance entry for generics. However, it is harder for those active ingredients in a given therapeutic group that enter the market later to recover their R+D expenses since they experience competitive pressure from older active ingredients in markets which may include lower priced generics. On the other hand, their contribution to health improvements is usually also relatively small.

In relation to the reduction of the market share of generics, brand-name producers react to the introduction of generics by reducing prices and the generic products lose their comparative advantage, which is a lower price. Thus, this effect is especially great in those scenarios in which all products compete.

The reduction in prices shown in the previous section may be understood as the capacity to reduce markups from the current regulated prices. This means that if rebates are a common strategy of statin producers or wholesalers, the greatest part of the markups are captured by retailers. In relation to this point, Puig-Junoy (2009)

finds average discounts on the wholesaler price for generic pravastatins and simvastatins to be above 50% in Spain.

In terms of welfare, for the whole market there is a considerable reduction in variable profits. On the other hand, the reduction of prices would increase consumer surplus notably and the net effect would be clearly positive under any of the four scenarios considered. This implies that the liberalization of prices together with pro-competitive regulation would increase welfare.

These results are in line with Kanavos, Costa-Font and Seeley (2008) whose evaluation of the eight top pharmaceutical markets worldwide, which included Spain, found that, when generic drugs are on the market, health insurers (such as the NHS in Spain) do not capitalize totally or save costs quickly due to the lower prices of the generic drugs. One of their explanations is that generic drug prices are closely tied to originator brand-name drug prices and that reference pricing reduces generic prices but only marginally. In order to benefit from the introduction of generics, these authors recommend price competition and avoidance of price-fixing regulation that ties generic prices to those of originator brands.

Additionally, unrestricted price competition may allow discounts to emerge; which currently seem to be captured mainly by pharmacists. If this were to happen, the saving in costs due to price rebates could benefit the NHS (or tax-payers) and patients. With price competition it seems that the main losers would not be the producers and wholesalers in general but the retailers.

Among manufacturers, those producing mainly generics and active ingredients that experience a large reduction in sales, especially simvastatin, would be net losers. In contrast, those selling mainly pravastatin would benefit. Moreover, among firms that produce the same active ingredient, market shares would be distributed more unequally than in the real situation. Similarly to the differences between active ingredients, once the price gap is reduced, other characteristics of the manufacturers should explain those changes.

It is important to note that, in the simulated unrestricted price competition scenarios, prices are reduced because firms are assumed to compete *à la* Bertrand and not to cooperate. In other words, it is assumed that firms do not collude when prices may be freely set. Although collusion is prohibited by Article 101 of the Treaty on the Functioning of the European Union and by the Spanish Law for the Defence of Competition (Act 15/2007), the oligopolistic structure of this industry may facilitate it. Furthermore, it could be argued that cooperation among producers may be relatively high in the pharmaceutical market where a great number of firms meet in different markets.

In some sense, the comparison between the real prices and those obtained in the scenarios of perfect collusion between all the producers suggests that the regulation of prices may have the same effect as cooperation between firms. For instance, the reference pricing system tends to cluster prices at the reference price (Danzon and Liu, 1998), which is not always close to the competitive level. This problem may be

overcome, at least partially, if the reference price is set as the lowest price in the substitution group, as it is in Denmark (Kaiser, Mendez and Rønde, 2010).

However, the relatively high prices of the real situation may be explained by the high prices of entry that are usual in regulated pharmaceutical markets. In the simulation it is assumed that firms always play a one-shot game and therefore they can modify the prices of their products every month: in each period firms set prices taking into account both the fact that they are multi-product firms and the decisions of their competitors in each market, in order to maximize profits. Nevertheless, in the real situation, producers negotiate introductory prices with health authorities and these prices usually remain constant for a long period and decline over time in real terms or are reduced with the implementation of cost containment measures.

Thus, given that price increases are uncommon, the NHS compensates the producers with a relatively high introductory price as Ekelund and Persson (2003) found for the Swedish market. In other words, the regulation of prices impedes penetration strategies, i.e., entry into the market with low prices. For that reason, firms usually opt for a skimming strategy, which involves setting a relatively high introductory price. This may explain why pravastatin experienced such a great increase in market share with price competition. It is a relatively new product with the highest average price and so producers have more of a margin over which to reduce their prices when there is unrestricted competition and therefore sales increase. In fact, fluvastatin, another relatively new product, has the second highest

average price and is the only active ingredient, except for pravastatin, that does not lose part of its market share.

Even with the entry of generic medicines for the first time into the statin market in November 2000, there is currently only limited price competition. One possible explanation is that, as stated by Puig-Junoy (2007), who also analyses the statin market in Spain, the decline in the price of brand-name and generic off-patent products is associated with arbitrary regulatory decisions as to the period for which the product is included in the reference pricing system or the moment at which its reference price is revised. Similarly, Puig-Junoy and Moreno-Torres (2010) concluded that the Spanish reference pricing system results in very little price competition between generic firms and that price reductions are mainly limited to specific regulatory measures.

Moreover, it is possible that companies selling to several countries are reluctant to decrease prices in Spain in order to keep high prices in other countries. A low price in Spain may reduce the bargaining position of firms when they negotiate prices or may even lead to a direct reduction in prices in other countries if they are based on foreign prices. For example, the external reference pricing, which imposes a price cap based on prices of identical or comparable products in other countries, is common in European countries.

What ever the case, the regulation of prices and the application of cost containment measures have not been totally successful in reducing prices and maximizing

welfare. In comparison to the scenarios simulated, it seems that regulation undermines price competition, as was found by Danzon and Chao (2000).

8. Concluding remarks

This paper analyses the demand for statin drugs and reports a counterfactual exercise in unrestricted price competition in the regulated Spanish pharmaceutical market. This comparison between the real and the counterfactual scenarios allows me to evaluate the elimination of price rigidity in terms of welfare, and of winners and losers.

The simulations of price competition *à la* Bertrand under four different scenarios indicate that in a situation with freedom to set prices and a pro-competitive environment of prices, there would be a general reduction in prices. The price reduction for the whole market would range from 39% to 59%, depending on the assumptions regarding the products that compete and the marginal cost.

Due to the negative price elasticity of the demand, there would be an increase in the total quantity of DDDs consumed. However, the decline in prices would more than compensate for it and there would be a considerable expenditure decrease. The savings for the NHS and patients would range from 37% to 57%.

As a consequence of price variations, there would be important changes in the total number of DDDs and market shares among active ingredients. Also, the

counterfactual exercise shows a more unequal distribution of sales among producers and a general reversal of generic drugs.

Finally, there would be a global reduction in revenue and, in fact, most firms would experience reductions in variable profits. For the market as a whole, the reduction in variable profits would range from 36% to 57%. However, the reduction in prices would increase consumer surplus and the net effect would be clearly positive under all the scenarios.

Provided that there is no collusion between firms, the liberalization of prices would enhance welfare and may cause rebates (which at present seem to be captured mainly by retailers) to be reflected in final prices and thus transfer those benefits to the NHS (tax-payers) and patients in the form of cost savings. However, it should be considered that this would involve not only winners but also losers.

In conclusion, in comparison to the scenarios simulated, it seems that regulation of prices, such as reference pricing, may have a similar effect to cooperation among producers and undermine price competition. More freedom to set prices is necessary together with a regulatory framework that includes appropriate incentives to foster competition.

Acknowledgments

The author would like to thank Jaume Puig-Junoy and Joan-Ramon Borrell-Arqué for their guidance and support and Panos Kanavos, Joan Costa-Font and Javier Coronado for helpful comments. I am grateful to the Directorate-General of Pharmacy and Health Products of the Spanish Ministry of Health and Consumer Affairs for data used in this paper and to the LSE Health Centre, London School of Economics and Political Science, London, UK, where part of this paper was developed during a stay in the summer of 2008, which was supported by a BE-DGR grant from the University and Research Grant Management Agency (AGAUR) of the Autonomous Government of Catalonia. I also benefited from the support of grant SEJ2007-66133 from the Spanish Ministry of Education and Science and from the support of an unrestricted educational grant from the Merck Company Foundation, the philanthropic arm of Merck & Co. Inc., Whitehouse Station, New Jersey, USA. The opinions expressed are those of the author and do not necessarily reflect the opinions of the research sponsors.

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Figures and Tables

Figure 1. Drug market

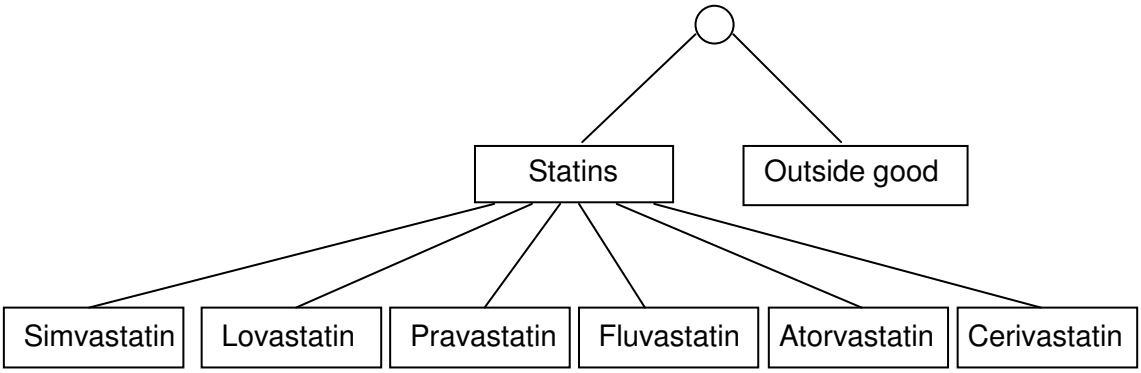

Figure 2. Active ingredients: total amount (€) for 2005

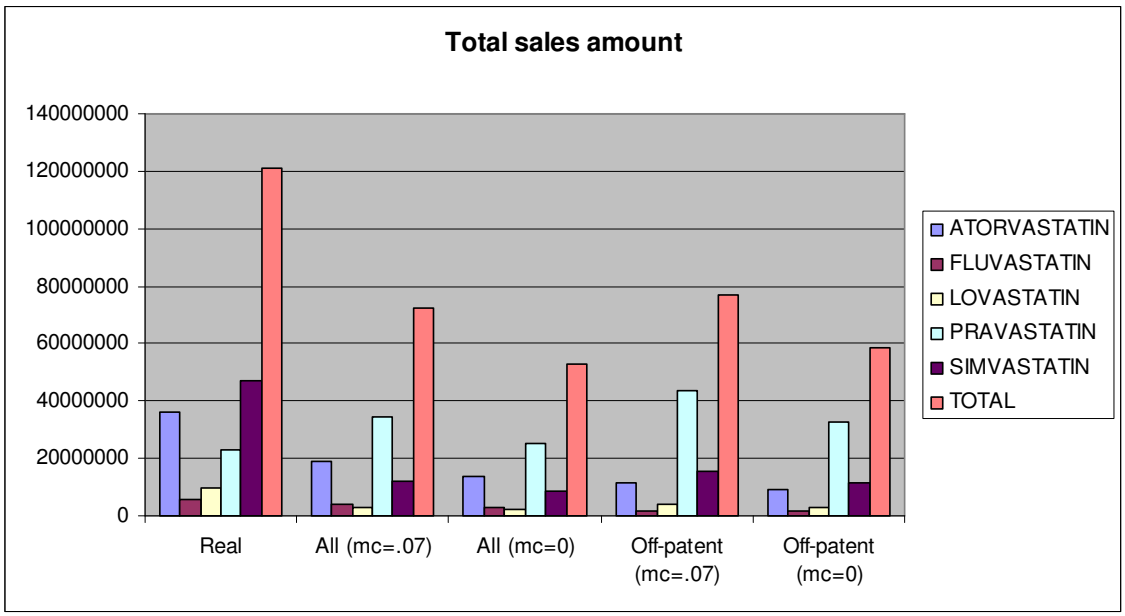

Figure 3. Active ingredient market shares (€) for 2005

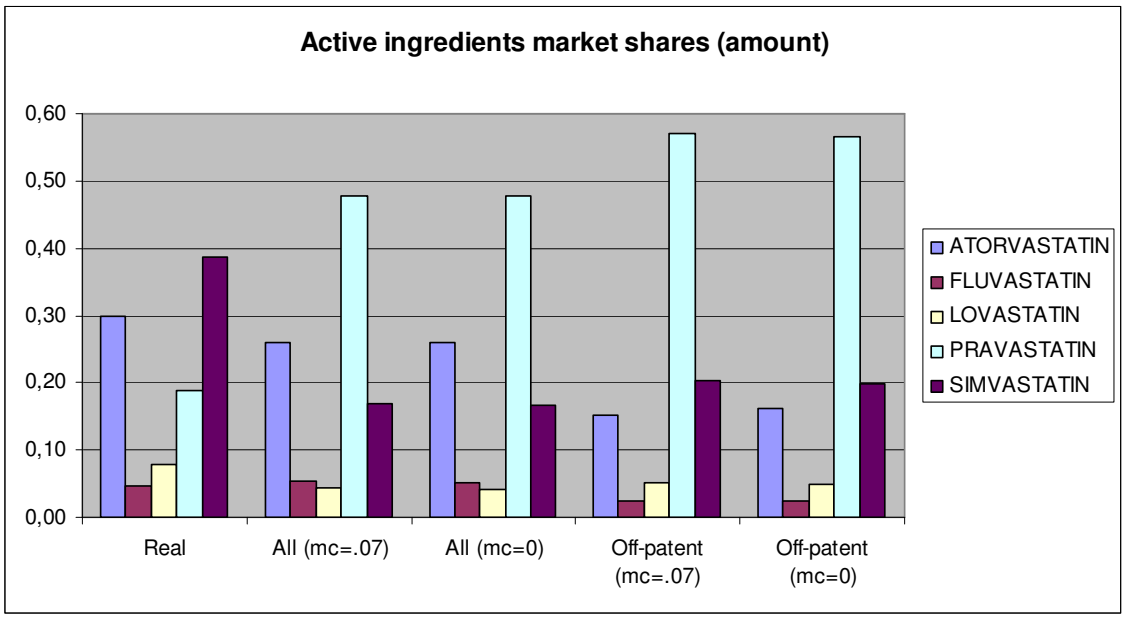

Figure 4. Active ingredients: total quantity (DDDs) for 2005

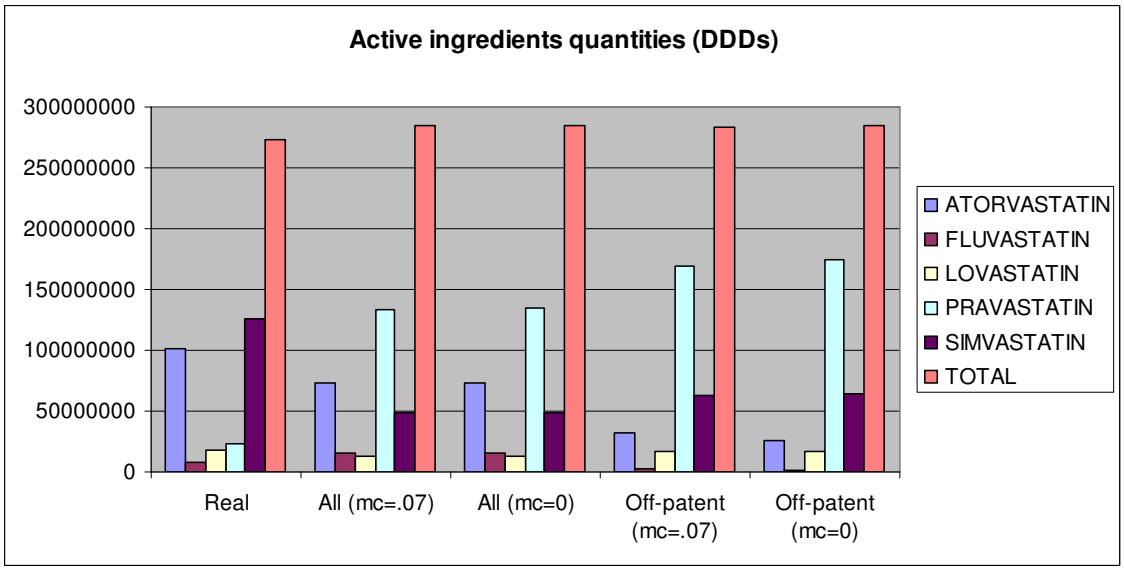

Figure 5. Active ingredient market shares (DDDs) for 2005

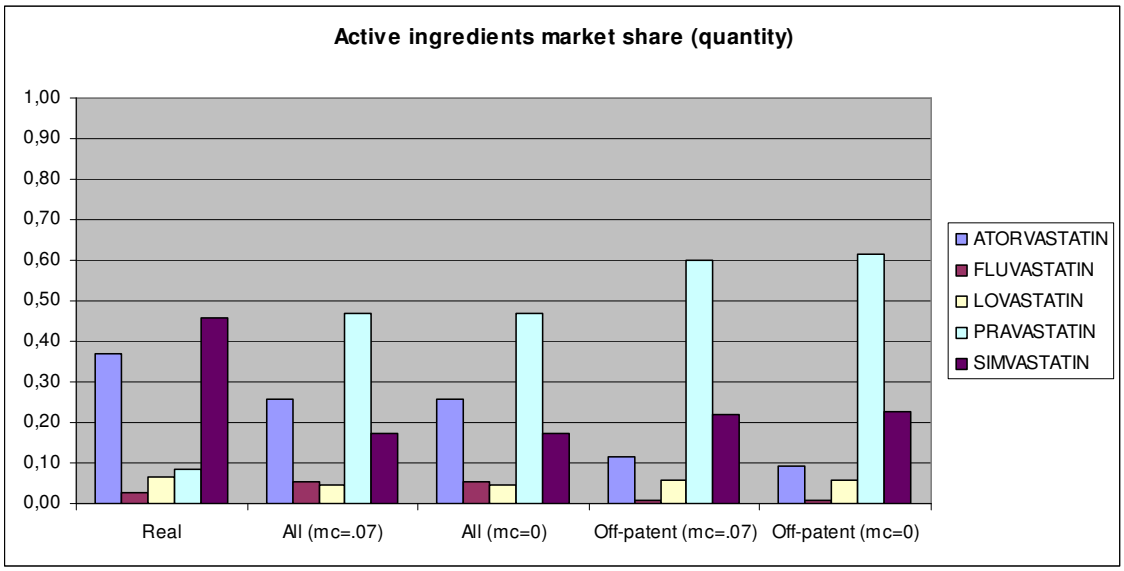

Figure 6. Brand-name and generic drug market shares (€) for 2005

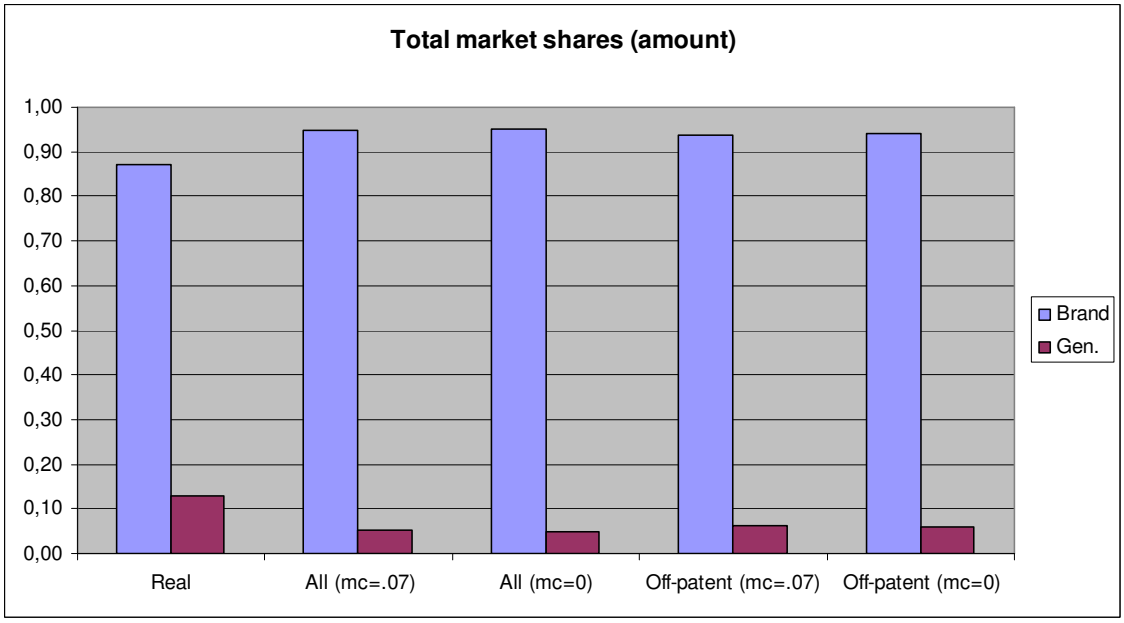

Figure 7. Brand-name and generic drug market shares (DDDs) for 2005

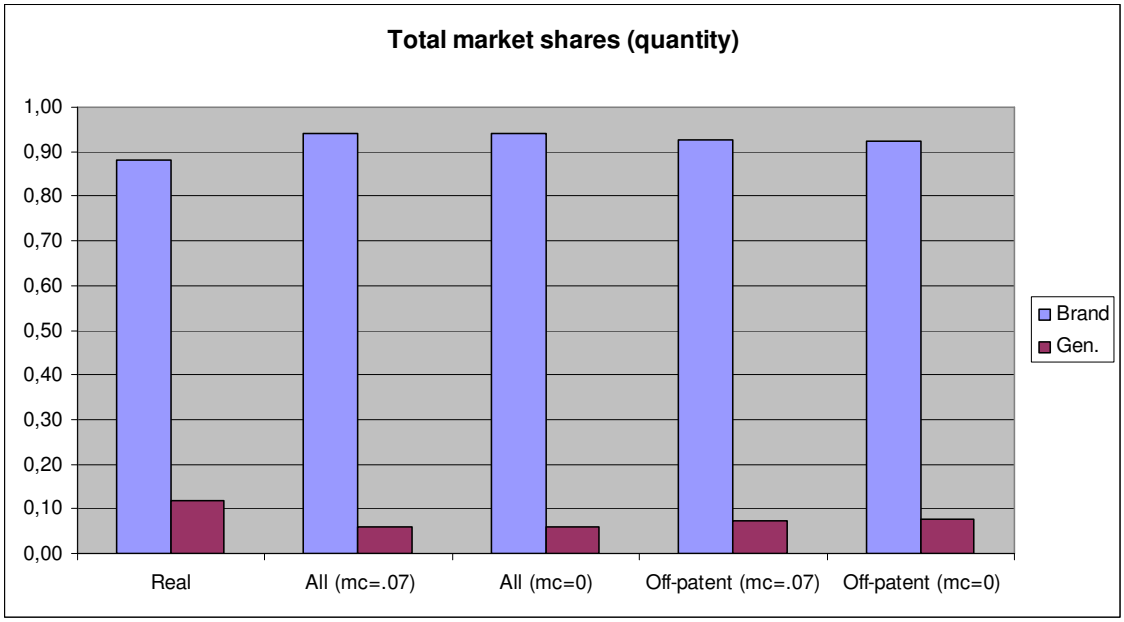

Figure 8. Market shares of atorvastatin manufacturers (DDDs) in 2005

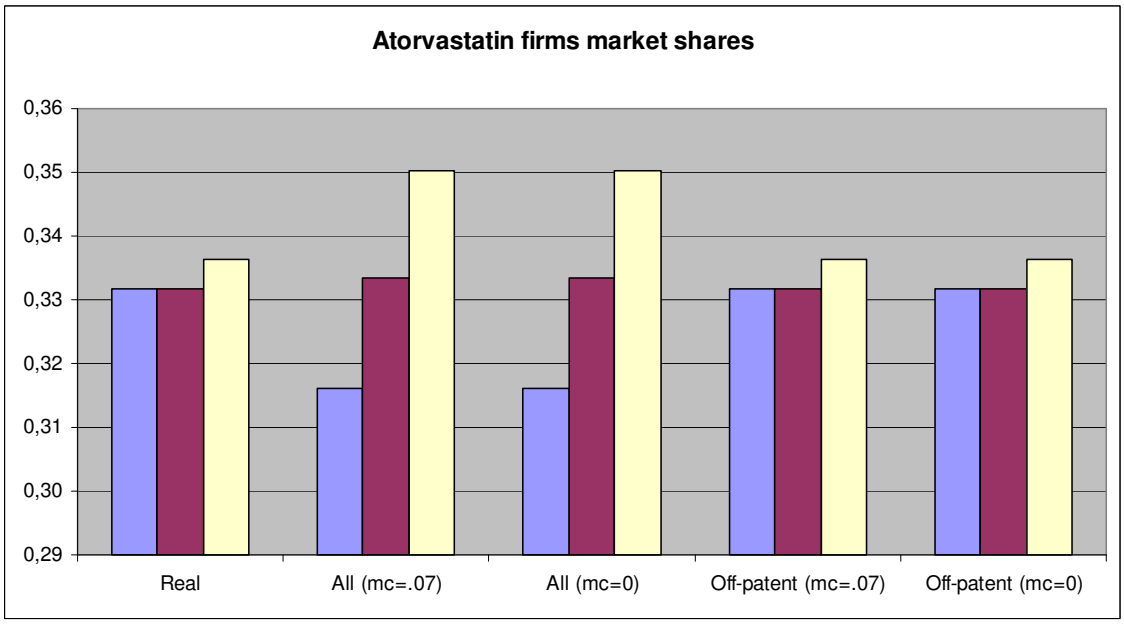

Figure 9. Market shares of fluvastatin manufacturers (DDDs) in 2005

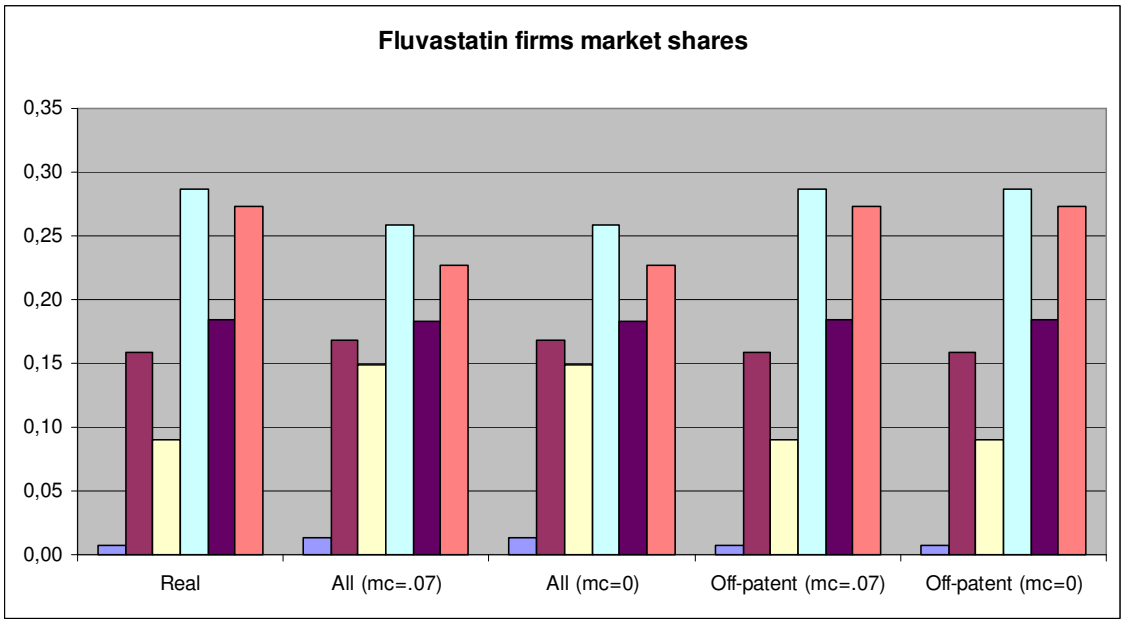

Figure 10. Market shares of lovastatin manufacturers (DDDs) in 2005

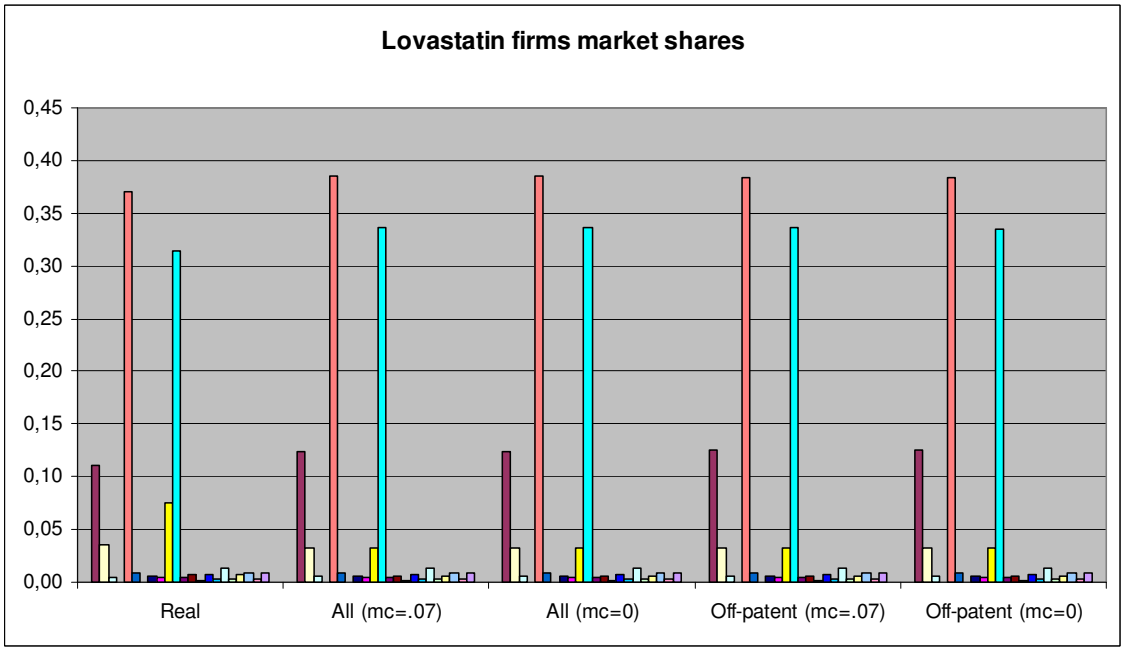

Figure 11. Market shares of pravastatin manufacturers (DDDs) in 2005

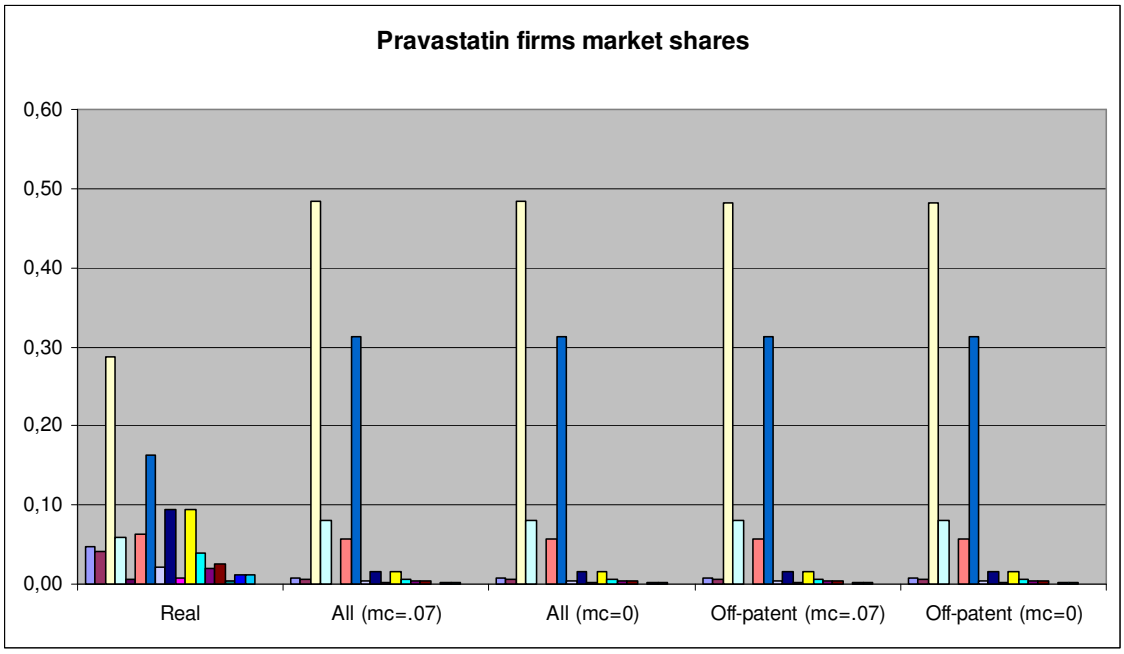

Figure 12. Market shares of simvastatin producer manufacturers (DDDs) in 2005

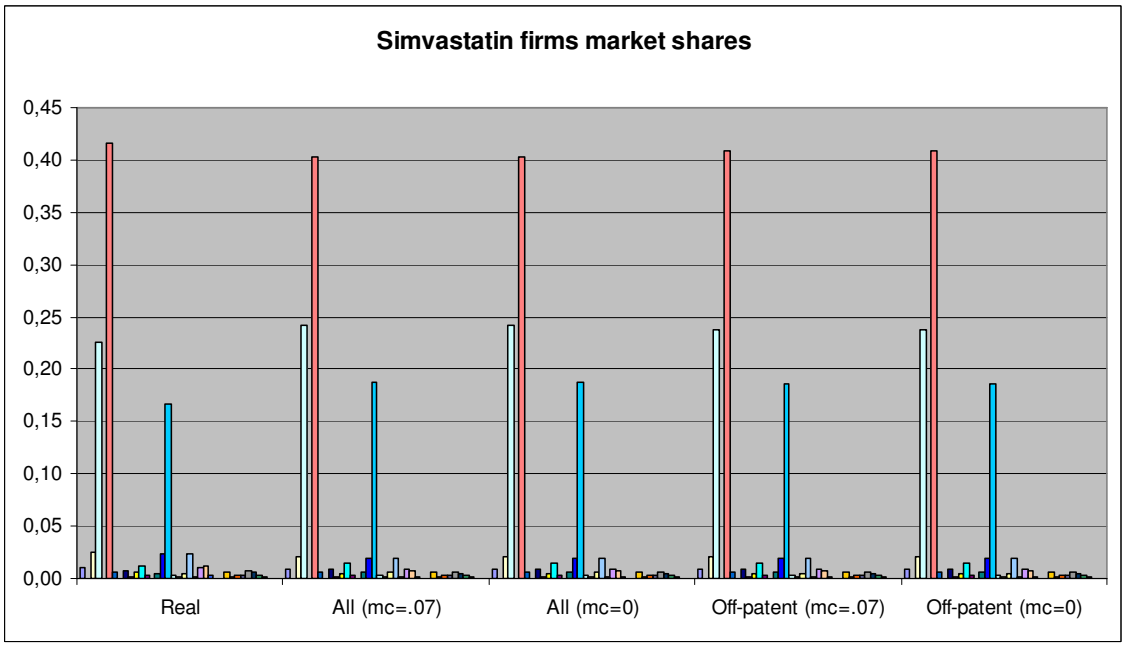

Figure 13. Market shares of atorvastatin manufacturers (€) in 2005

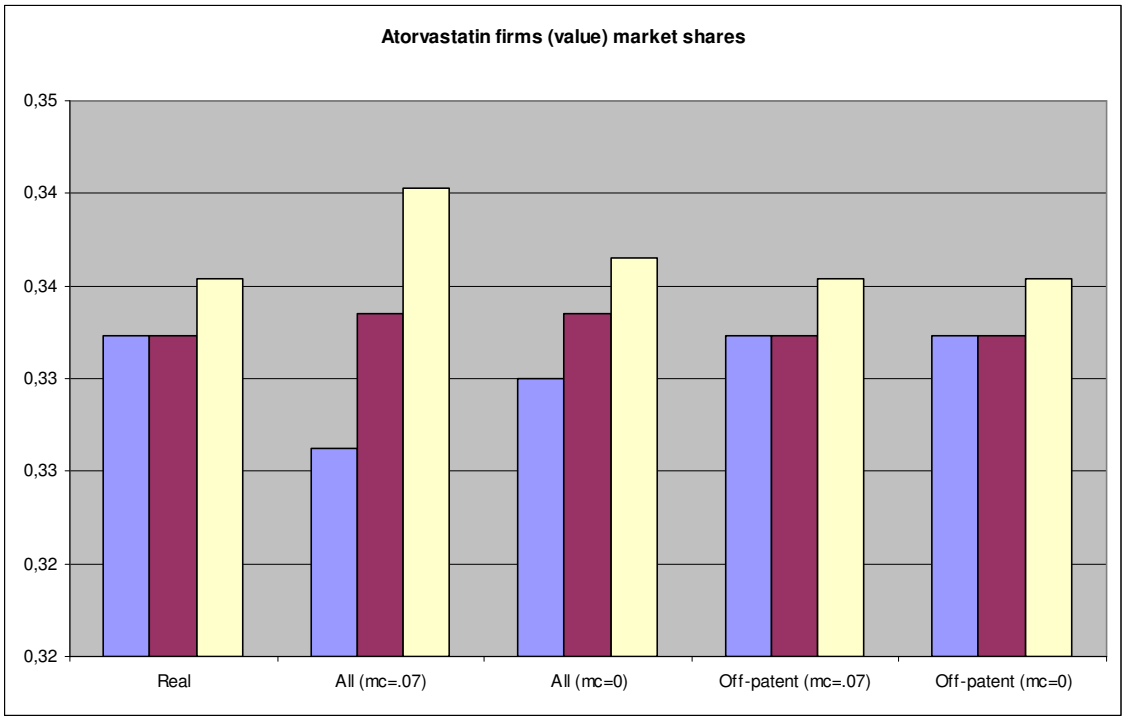

Figure 14. Market shares of fluvastatin manufacturers (€) in 2005

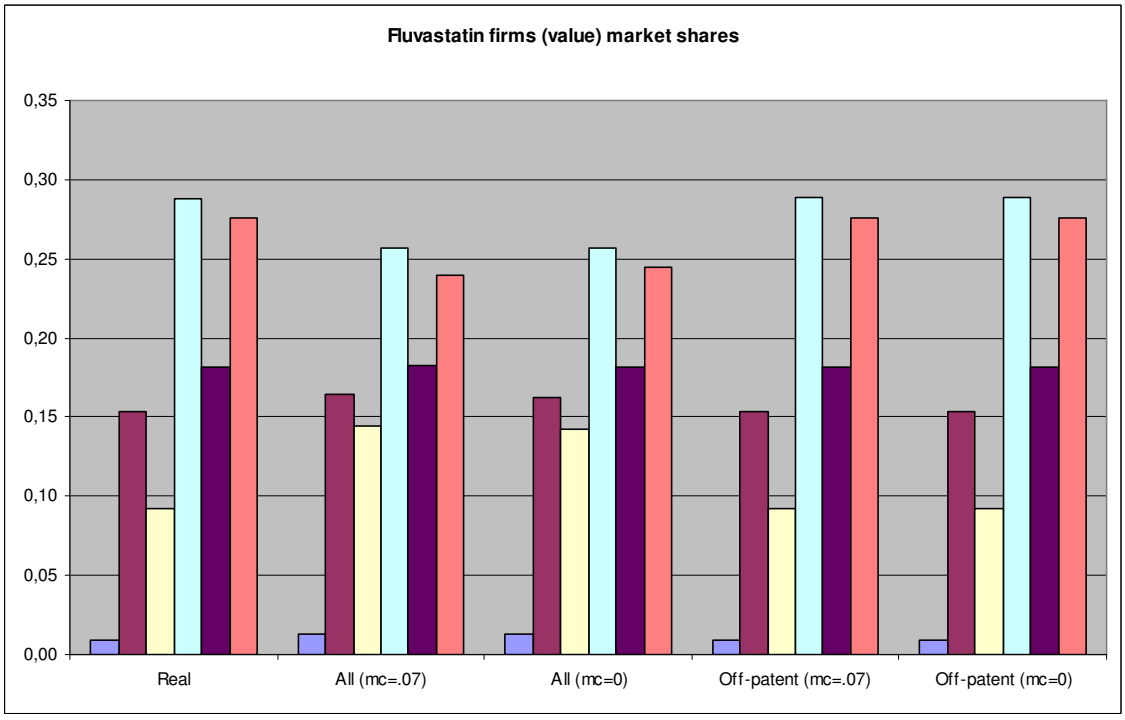

Figure 15. Market shares of lovastatin manufacturers (€) in 2005

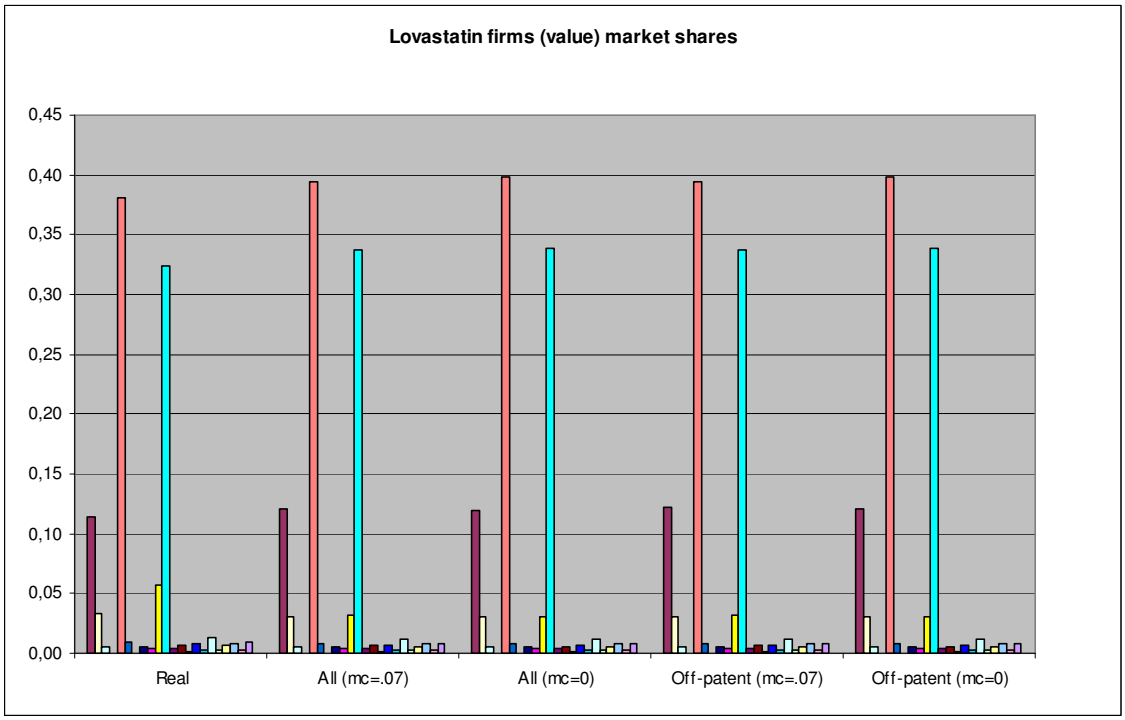

Figure 16. Market shares of pravastatin manufacturers (€) in 2005

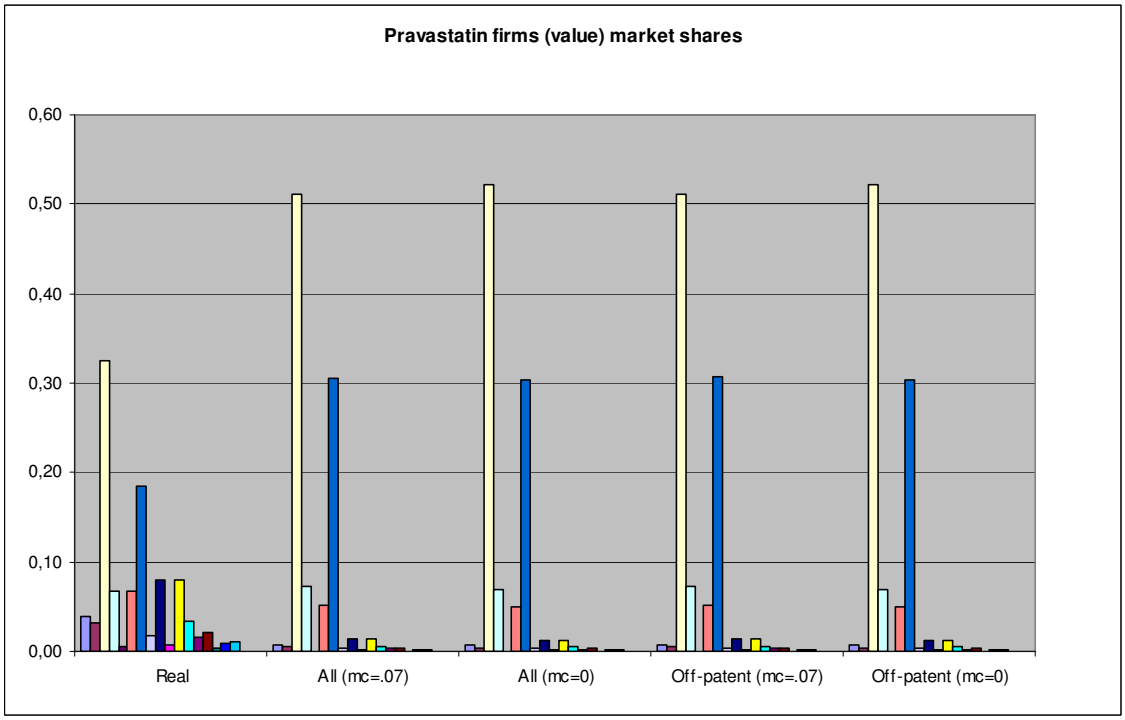

Figure 17. Market shares of simvastatin manufacturers (€) in 2005

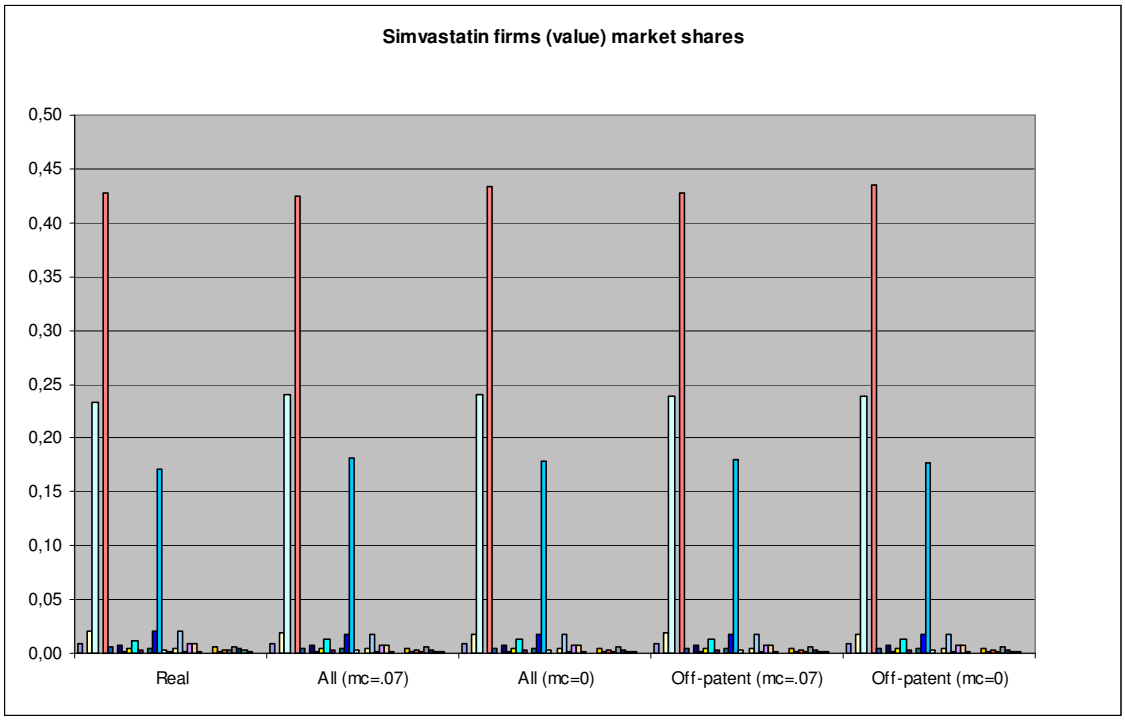

Table 1. Sample of drugs

Active Ingredient (ATC code)	Main indications	First Obs.	Generic entry	Reference pricing	Presentations	
Atorvastatin (C10AA05)	Dyslipidemia, hipercolesterolemia and hypertriglyceridemia.	November 1997	-	-	10 mg	28 Tablets
		May 2001	-	-	20 mg	28 Tablets
		May 2001	-	-	40 mg	28 Tablets
		January 2003	-	-	80 mg	28 Tablets
Cerivastatin (C10AA06)	Hipercolesterolemia.	August 1998	-	-	0.1 mg	28 Tablets
		August 1998	-	-	0.2 mg	28 Tablets
		October 2002	-	-	0.3 mg	28 Tablets
		November 2000	-	-	0.4 mg	28 Tablets
Fluvastatin (C10AA04)	Dyslipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerotic.	January 1997	-	-	20 mg	28 Capsules
		January 1997	-	-	40 mg	28 Capsules
		September 2002	-	-	80 mg	28 Capsules
Lovastatin (C10AA02)	Dyslipidemia, hypercholesterolemia, hyperlipoproteinemia and atherosclerotic.	January 1997	November 2000	May 2002	20 mg	28 Tablets
		January 1997	December 2000	May 2002	40 mg	28 Tablets
Pravastatin (C10AA03)	Dyslipidemia, hypercholesterolemia, hypertriglyceridemia, Atherosclerotic, Ischemic cardiomyopathy and acute myocardial infarction.	January 1997	January 2004	-	10 mg	28 Tablets
		January 1997	January 2004	-	20 mg	28 Tablets
		February 1999	January 2004	-	40 mg	28 Tablets
Simvastatin (C10AA01)	Dyslipidemia, hypercholesterolemia, hypertriglyceridemia, Atherosclerotic, Ischemic cardiomyopathy and diabetes.	January 1997	January 2002	January 2004	10 mg	28 Tablets
		January 1997	January 2002	January 2004	20 mg	28 Tablets
		September 1997	January 2002	January 2004	40 mg	28 Tablets

Table 2. Summary of statistics for the variables in the demand model.

Variable	Definition	Obs.	Mean	Standard Deviation	Minimum	Maximum
Product market share	Product share in the potential market	10981	0.0038	0.0072	0.0000	0.0544
Outside good market share	Outside good share in the potential market	10981	0.4546	0.2004	0.1833	0.9135
Price per DDD	Price per defined daily dose (€/DDD)	10981	0.7880	0.3716	0.1882	1858022
Within active ingredient share	Generic drug's market share divided by the total generic market share	10981	0.0533	0.0908	0.0000	0.8837
Time in market	Number of months since the entry of the generic drug	10981	5257108	387245	0	181
Generic	Dummy equal to one for generics; 0 otherwise	10981	0.4586	0.4983	0	1
Cerivastatin withdrawal	Dummy equal to one for cerivastatins from the withdrawal; 0 otherwise	10981	0.0101	0.1000	0	1
Atorvastatin	Dummy equal to one for atorvastatins; 0 otherwise	10981	0.0670	0.2501	0	1
Cerivastatin	Dummy equal to one for cerivastatins; 0 otherwise	10981	0.0387	0.1929	0	1
Fluvastatin	Dummy equal to one for fluvastatins; 0 otherwise	10981	0.0849	0.2787	0	1
Lovastatin	Dummy equal to one for lovastatins; 0 otherwise	10981	0.2325	0.4224	0	1
Pravastatin	Dummy equal to one for pravastatins; 0 otherwise	10981	0.1616	0.3681	0	1

Table 3. Demand model estimation.

	Coefficient	Std. Error♦
Log(Within active ingredient share)	0.4580***	0.1049
Log(Price per DDD)	-3.4569***	0.2431
Time in market	0.0105***	0.0017
Generic	0.5621**	0.2611
Cerivastatin withdrawal	-7.5984***	0.2670
Atorvastatin	4.8069***	1.0194
Cerivastatin	4.1433***	1.1738
Fluvastatin	3.0647***	0.7986
Lovastatin	-1.0277***	0.1404
Pravastatin	0.9457***	0.1793
Constant	-4.6815***	1.2116
Observations	10981	
R^2	0.8392	
Sargan-Hansen statistic (p-value)	0.0680 (0.7950)	

Note: Fixed firm effects are not shown but are included in the estimation. ♦ Robust clustered standard errors. ** and *** = significant at the 5% and 1% level.

Table 4. Active ingredients: weighted average prices (€/DDD) for 2005

	Real	All		Off-patent	
		MC = 0.07	MC = 0	MC = 0.07	MC = 0
Atorvastatin	0.36	0.26	0.19	0.36	0.36
Fluvastatin	0.77	0.24	0.17	0.77	0.77
Lovastatin	0.55	0.24	0.17	0.24	0.17
Pravastatin	1.00	0.26	0.19	0.26	0.19
Simvastatin	0.37	0.25	0.18	0.25	0.18
Statins	0.44	0.25	0.18	0.27	0.21

Table 5. Active ingredients: total amount (€) for 2005

	Real	All		Off-patent	
		MC = 0.07	MC = 0	MC = 0.07	MC = 0
Atorvastatin	36324392	18755274	13691786	11637822	9415679
Fluvastatin	5603596	3809753	2720561	1795859.125	1452968.125
Lovastatin	9572070	3120487	2224253.25	3971503	2909934.25
Pravastatin	22710510	34466320	25161054	43889544	32988476
Simvastatin	46990844	12194016	8794725	15525136	11498549
Statins	121201412.00	72345850.00	52592379.25	76819864.13	58265606.38
Total variation (Δ%)		-48855562.00 (-40.31%)	-68609032.75 (-56.61%)	-44381547.88 (-36.62%)	-62935805.63 (-51.93%)

Table 6. Active ingredient market shares (€) for 2005

	Real	All		Off-patent	
		MC = 0.07	MC = 0	MC = 0.07	MC = 0
Atorvastatin	0.30	0.26	0.26	0.15	0.16
Fluvastatin	0.05	0.05	0.05	0.02	0.02
Lovastatin	0.08	0.04	0.04	0.05	0.05
Pravastatin	0.19	0.48	0.48	0.57	0.57
Simvastatin	0.39	0.17	0.17	0.20	0.20

Table 7. Active ingredients: total quantity (DDDs) for 2005

	Real	All		Off-patent	
		MC = 0.07	MC = 0	MC = 0.07	MC = 0
Atorvastatin	100779872	72863240	73058784	32292750	26126828
Fluvastatin	7247525	15664540	15706754	2323378.50	1879782
Lovastatin	17378418	12888991	12923670	16428957	16910576
Pravastatin	22783328	133904352	134261536	169790880	174895072
Simvastatin	125385152	48900064	49031480	62408512	64301640
Statins	273574295	284221187	284982224	283244477.50	284113898.00
Total variation (Δ%)		10646892.00 (3.89%)	11407929.00 (4.17%)	9670182.50 (3.53%)	10539603 (3.85%)

Table 8. Active ingredient market shares (DDDs) for 2005

	Real	All		Off-patent	
		MC = 0.07	MC = 0	MC = 0.07	MC = 0
Atorvastatin	0.37	0.26	0.26	0.11	0.09
Fluvastatin	0.03	0.06	0.06	0.01	0.01
Lovastatin	0.06	0.05	0.05	0.06	0.06
Pravastatin	0.08	0.47	0.47	0.60	0.62
Simvastatin	0.46	0.17	0.17	0.22	0.23

Table 9. Brand-name and generic drug market shares (€) for 2005

		Real	All		Off-patent	
			MC = 0.07	MC = 0	MC = 0.07	MC = 0
Lovastatin	**Brand-name**	0.89	0.90	0.90	0.90	0.90
	Generic	0.11	0.10	0.10	0.10	0.10
Pravastatin	**Brand-name**	0.66	0.94	0.95	0.94	0.95
	Generic	0.34	0.06	0.05	0.06	0.05
Simvastatin	**Brand-name**	0.86	0.88	0.88	0.88	0.88
	Generic	0.14	0.12	0.12	0.12	0.12
Statins	**Brand-name**	0.87	0.95	0.95	0.94	0.94
	Generic	0.13	0.05	0.05	0.06	0.06

Table 10. Brand-name and generic drug market shares (DDDs) for 2005

		Real	All		Off-patent	
			MC = 0.07	MC = 0	MC = 0.07	MC = 0
Lovastatin	**Brand-name**	0.88	0.89	0.89	0.89	0.89
	Generic	0.12	0.11	0.11	0.11	0.11
Pravastatin	**Brand-name**	0.59	0.94	0.94	0.94	0.93
	Generic	0.41	0.06	0.06	0.06	0.07
Simvastatin	**Brand-name**	0.84	0.87	0.87	0.87	0.87
	Generic	0.16	0.13	0.13	0.13	0.13
Statins	**Brand-name**	0.88	0.94	0.94	0.93	0.92
	Generic	0.12	0.06	0.06	0.07	0.08

Table 11. Variations in variable profits (€) in 2005

	All		Off-patent	
	MC = 0.07	MC = 0	MC = 0.07	MC = 0
Atorvastatin	-16840717.84	-22632608.00	-23095765.05	-26908714.75
Fluvastatin	-1793843.03	-2883035.17	-3807736.97	-4150627.93
Lovastatin	-6451582.76	-7347816.50	-5600566.89	-6662135.55
Pravastatin	11755809.94	2450544.29	21179033.42	10277965.55
Simvastatin	-34796828.15	-38196118.95	-31465707.95	-35492295.07
Total variation (Δ%)	-48127161.83 (-40.49%)	-68609034.33 (-56.61%)	-42790743.44 (-36.00%)	-62935807.75 (-51.93%)

Table 12. Variation in welfare (€) in 2005

	All		Off-patent	
	MC = 0.07	MC = 0	MC = 0.07	MC = 0
Consumers surplus	669688171.48	785952603.11	552526000.62	655479835.08
Firms' profits	-16290016.45	-68609034.33	-14043786.56	-62935807.75
Net variation	653398155.03	717343568.78	538482214.06	592544027.33

Table 13. Active ingredients: weighted average full collusion prices (€/DDD) for 2005

	Real	All		Off-patent	
		MC = 0.07	MC = 0	MC = 0.07	MC = 0
Atorvastatin	0.36	0.48	0.41	0.36	0.36
Fluvastatin	0.77	0.48	0.41	0.77	0.77
Lovastatin	0.55	0.48	0.41	0.45	0.38
Pravastatin	1.00	0.48	0.41	0.45	0.38
Simvastatin	0.37	0.48	0.41	0.45	0.38
Statins	0.44	0.48	0.41	0.45	0.38

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