"THE COMPETITIVE IMPACT OF BRANDED GENERIC MEDICINE IN A DEVELOPING COUNTRY"

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Abstract

This paper studies the impact of branded generic competition on 47 molecules recently exposed to competition between January 2002 and July 2017 in the Chilean retail pharmaceutical market. First, making an effort to get the true price differential between branded generics and innovators and its changes through time, we apply the Hausman-Taylor model, controlling for several market and molecule characteristics. The core of our research lies in the estimation of the impact of branded generic competition over prices and quantities of the innovator -testing the market segmentation theory-, and its effect over the total doses dispensed in the market. In doing so, a propensity score matching with a differences in differences approach was adopted, and 26 molecules were involved in this estimation. The results show that in the time lapse of 48 months from the first entrant, the branded generic competition is capable of expanding the retail market supply in 148.1%. This is explained by the lower prices of the branded generic denomination, that in the gross average are 33% cheaper than the innovator alternatives. Finally, no statistically significant effect is observed over prices and quantities of the innovator, validating the generic competition paradox for the Chilean market.

Key words: Branded generic entry; Market segmentation; Differences in differences.

JEL Classification: I11; L11; L65.

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I. Introduction.

In the Chilean pharmaceutical market there are three drug denominations: innovators, branded generics -often called 'similar'-, and unbranded generics. Innovators or originals are drugs that were given a patent protection period of up to 20 years. Once the patent expires generics are allowed to enter the market. The branded generics are copies of the original that are label with a brand, while unbranded generics are sold under the name of the molecule -i.e. the International Common Denomination (ICD)-.

This research has the purpose to contribute with evidence about the impact of the introduction of branded generics in molecules that were previously controlled by the innovator's monopoly. Specifically, we ought to answer what effect is observed over prices and quantities with the branded generic entry. Most of the literature has examined the pharmaceutical markets from developed countries, where unbranded generics rapidly become market leaders. So, little evidence is currently available from contexts where branded competition is the common standard.

First, we trace the changes in the magnitude of the price differential between branded generics and innovators through a set of indicator variables, representing several post-entry periods. For that, the Hausman-Taylor model is adopted in order to account for the correlation of these indicators with the individual fixed effects. Also, controlling for a set of molecule and market characteristics, it is possible to approach to the real price differential between these two denominations. Naturally, an increasing negative coefficient through time is expected, because empirical data supports that branded generics enter the market at a significant lower price.

Second, the effect of branded generic competition over prices and doses dispensed by the innovator, as well as the effect over the total volume dispensed in the market is evaluated. In doing so, a propensity score matching with differences in differences is applied and two treatments are generated. The first treatment captures the impact of passing through the monopoly to a competition regime; while the second one considerers the differentiated impact provoked by the different intensities of the competition; that is, the number of branded generics competitors.

Two hypotheses are suggested to explain the possible response of innovator prices. On the one hand, if the traditional theory of segmented markets (Grabowski and Vernon, 1992; Frank

and Salkever, 1991; Kong, 2000) or the Salop model (Salop, 1979) applied to the pharmaceutical market with a high share of branded generics, then we should see no response on innovator prices or at most a slightly increase. On the other hand, considering the evidence obtained by the Mexico's Federal Economic Competition Commission (2017), if the Chilean pharmaceutical market behaves somehow similar to the Mexican market, it could be possible to observe reductions in the innovator prices. The latter hypothesis it is also supported by the Kong's model if one believed that the elasticity of substitution between branded generics and innovators is higher than that observed with pure generics.

Relative to the effect of the branded competition over the quantities, we do not expect any major shift in the innovator's doses dispensed -no matter what hypothesis is true for their prices. But we do expect a significant increase in the total doses dispensed in the market by all denominations since the data shows a rapid growth in the branded generics doses due to its low prices.

Indeed, the results show that the branded generic entry produces a significant impact in the market in terms of the availability and prices of the drugs. The total doses available in the market experiment an increase of 148.1% in average in the 48 months post-entry period, an effect that is directly attributable to the branded generic competition. The enlargement of the volume of doses it could be explained by the lower prices of branded generics that in the gross average are 33% cheaper than the innovator options; and around 18% cheaper considering the true differential captured by the Hausman-Taylor estimation.

Our results on prices and quantities of the innovator show no response in front of the branded generic entry, validating the generic competition paradox for the Chilean pharmaceutical market.

The paper proceeds in the following manner: section II provides the literature review with the conceptual framework that supports this research. Section III describes the data. Section IV discuss the empirical strategy. Section V presents the main results and section VI the conclusions.

II. Literature review

It is well known in the economic theory that the prices in a competitive equilibrium will be lower than in a monopoly setting, but in the eventuality that the market gets segmented, the monopoly price will have the capacity to prevail. Part of the available evidence agrees that this is the case of the pharmaceutical market. Grabowski and Vernon (1992) were among the first who stated that the incumbents or innovators' prices did not moderate its growth in front of the entrance of generic competition, while these generics exhibited a huge decline to the marginal cost[1]. So, these authors proposed a market segmentation theory that suggests that brand-loyal consumers with an inelastic demand conform a price insensitive segment, while generics attends the segment that is price sensitive (i.e elastic demand).

Understanding that pharmaceutical drugs are credence goods, where the responsibility over the decision to buy the medicine is delegated to the health professional (Danzon, 2014); Frank and Salkever (1991) argue that the market segmentation is produced by the pattern of medical prescription[2]. In this sense, the authors claim that the health professionals who attend patients with a private health insurance are more risk averse and, therefore, are more tied to their prescription habits, associated with the innovators. Moreover, they suggest that these professionals do not have incorporated in their utility function the cost containment of the patient. Consequently, patients attended by this kind of health professional become the brand-loyal segment.

The evidence provides by Crawford and Shum (2005) adds that patients are also risk averse, experiencing a reduction in their utility when the drug that has been historically prescribed to them is replaced by a new one. In this context is reasonable to think that a group of patients will prefer to maintain the consumption of innovator drugs, even though the presence of generics substitutes at a lower cost. In fact, this is equivalent to say that the demand for innovator drugs tends to be more inelastic.

Instead of assuming that the two segments would be independents as in Grabowski and Vernon (1992) and Frank and Salkever (1991); Kong (2000) admits in a more realistic way that there is a factor of cross-substitutability between innovator and generic pharmaceuticals, for both

[1] Innovators are often called 'originals'.
[2] For a detailed description of the principal-agent problem in the pharmaceutical market see Danzon (2014).

segments of the market. According to this model, the 'generic competition paradox', generated by the statu quo or increase of the incumbent prices, occurs as long as the marginal cost of the generic is relativity large[3]. On the other hand, from this framework it can be derived that if competition comes essentially from branded generics, the elasticity of substitution with the innovator could hypothetically be higher than in the pure generic's predominance setting, and hence innovator will not have the capacity to increase[4].

The first-mover advantage is often reported as an alternative hypothesis to explain the reaction of innovator prices. Schmalensee (1982) observes that the first brand that makes its entry to the market has a product differentiation advantage that allows it to stablish higher prices than the upcoming brands and retains a significant portion of the market. Indeed, the early entrant becomes the standard for the consumer in a context of imperfect information, and the upcoming entrants must implement costly actions to minimize the searching cost of consumers and make them forget the brand they are loyally attached to. Empirically, there is ample evidence that in the pharmaceutical market, the innovator has a huge advantage that persist in the post-patent period[5].

The price response to generic entry of innovator drugs has been widely studied in developed countries, in which two actors are market leaders: innovators and unbranded generics[6]. The evidence from these countries has been mixed, without agreement over the competitive effects over innovators from the generic entry.

For the US pharmaceutical market, Regan (2008) approaches to the causal impact of generic competition, however her results are similar to those obtained by Grabowski and Vernon (1992) with more unsophisticated models. Regan (2008), using a panel of monthly data and

[3] From the optimal innovator price derived from the model of Kong (2000), the following condition for the price responsiveness of the innovator demand with the number of generic competitors $\left(\frac{\partial P_b^*}{\partial N}\right)$ can be obtained: $c_g \lessgtr \alpha/(\beta - \gamma)$, where c_g is the cost of the generic pharmaceutical; β is the own-price elasticity; γ is the elasticity of substitution, that is the responsiveness of the drug demand to changes in the substitute drug; and α is a demand parameter. So, the price of the innovator will increase as long as c_g is bigger than the right-hand part of the inequality.

[4] That is $c_g \leq \alpha/(\beta - \gamma)$, because the marginal cost of generics will not be sufficiently large to overcome the right-hand part of the inequality.

[5] For example, Hurwitz and Caves (1988) studied that for a sample of 29 molecules in the US market, the innovator continued to be the leader in the market two years after the expiration of its exclusivity.

[6] Although the share of branded generics is negligible in the majority of developed countries, the researches checked concerning these countries do not distinguish between branded and unbranded generics.

instrumental variables[7], estimates that each additional generic competitor increases the innovator prices in 2%, in average, while it does not have any significant effect over the own generics.

On the contrary, Caves et al (1991), instrumentalizing the number of generic competitors through the volume of sales the year prior to the patent expiration and the time passed since the patent expiration -none of them completely exogenous-, finds that each additional generic provokes a negative significant effect of -0.8%. In the same line, Bergman and Rudhom (2003) studied the price response to the generic entry in the Sweden market, finding that the patent expiration in and of itself has a significant effect of -5% over innovator prices; while each additional competitor reduces the innovator price between a 4% to 7% in average.

The research of the competitive impact of generic entry has been exiguous in developing countries, characterized by the relevant share of branded generics, the presence of which is distinctive of pharmaceutical markets that lack of regulations to fix the market failures (Danzon and Furukawa, 2011; Kaplan et al, 2013). In fact, it has been established that laboratories tend to exploit information asymmetries and the preferences of consumers in a context of uncertainty about the quality and therapeutic efficacy of pharmaceutical products, introducing branded generics at a higher price (Danzon et al, 2013)[8]. Additionally, the unbranded generic share -hence, the displacement of branded generics from the market- depends on the medical tradition, reimbursement insurance policy, and incentives to health professionals, consumers and pharmacists to be prompt to make use of generics of lower cost; aspects that lack of proper deepening in developing countries (Magazzini et al, 2004; Danzon and Furukawa, 2011; Danzon et al, 2013).

From the economic perspective, the role of brands could also be understood through the model of Salop (1979), which is a variant of the Hotelling's model of spatial localization. In this model the products are localized in different points around a circle, which represents the preferences of consumers. For a molecule, each laboratory introduces a brand that is located at some point of the circle. Because of consumers' willingness to pay reduces when the brand is far away

[7] Regan (2008) uses as instruments for the number of generic competitors: (1) The total branded prescriptions dispensed in the month prior to generic entry; (2) A dummy variable indicating whether the initial generic entrants were granted six months of exclusive rights; and (3) The number of Abbreviated New Drugs Applications approved by the FDA.

[8] Indeed, Ganther y Kreling (2000) stated that an important proportion of consumers believe that branded drugs are more effective and safe, and they are willing to pay more for them.

from the one they consider optimal; each laboratory will be interested to differentiate its brand from the other ones around. In other words, there is a vertical differentiation and, then, consumers order their preferences, where one brand is more preferred than other. Thus, if differences in prices are not relevant, each laboratory will capture the consumers near to its brand, for whom the surplus from the acquisition or prescription of that particular brand is superior to any other alternative pharmaceutical brand.

In the last decade, an incipient literature has make explicit reference to branded generics pharmaceuticals. Danzon and Furukawa (2011) build a panel of middle and high-income countries, and only in the case of Mexico – a country with a pharmaceutical market with similar characteristics to the Chilean one- estimates that the number of branded generics manufacturers has a positive significant impact on the average price of generics, but it has no impact on the prices of the innovators. These results would be revealing that Mexican laboratories decide to compete based on brand, avoiding the competition on prices.

Also analyzing the Mexican pharmaceutical market, the Mexico's Federal Economic Competition Commission (2017) reports that in the molecules with presence of branded and unbranded generics, the increase in the innovator price could be 46% lower than in the case where generics are only represented by unbranded alternatives. In other words, contrary to the results obtained by Danzon and Furukuwa (2011), this study demonstrates that branded generics could discipline the innovator prices, an empirical result that corroborates the intuition derived from Kong (2000) considering a large share of branded generics in the model setting.

A line of research has emerged in the market of processed food, testing the response of incumbents to the brand entry and proliferation and, even though it is a market with dissimilar characteristics to the pharmaceutical market, the results observed are coherent with the traditional intuitions obtained in the model of Kong (2000) and Salop (1979)[9]. Putsis (1997) investigates the effect of brand proliferation on national brand of 135 processed food products. Its results show that the number of brands present in the market has a positive effect on the national brand prices, nonetheless the ability to rise its prices decreases when the brands succeeded to achieve high shares. In the same line, Bonfrer et al (2004) state that for each brand that entries the market, the incumbent increases its prices 14.5% in average; but the

[9] In the context of the Salop model, a price-setting firm that does not face a rival keeps its price down to attract customers who are located relatively far from its product characteristic space. However, if a rival locates near to the incumbent, the latter could rise its price to its near consumers until the optimal point to keep them attached to its product. See Salop (1979).

results are heterogeneous when the analysis is done at the product category level, observing a negative effect in half of them.

The evidence about the evolution of the relative prices is merely descriptive, without correcting, for example, for the differences occasioned by the time that a drug has had of exposure in the market, among other things. For the Mexican pharmaceutical market, the Mexico's Federal Economic Competition Commission (2017) reports that on average the prices of generics are 28.6% lower than the innovator alternatives 24 months post-entry. In the highly competitive U.S market, the average relative price at the first quarter post-entry is 60%, that is, generics are 40% cheaper (Ching, 2010). On the other side, the European market reaches a price differential of -40% only at the 24th month from the initial entry of generics (European Commission, 2009).

In general, there is little evidence on the competitive impact of branded generic entry. Moreover, none of the studies cited above has the branded generics as a specific object of study. So too, the studies have been focusing on evaluating the impact on innovator prices, leaving out the effects over the quantities -pharmaceutical doses-, aspect that would bring a complete outlook of the effect of branded generic entry over the social welfare.

III. Institutional framework

Results reported in the literature showed to be sensitive to the institutional framework of the pharmaceutical market, so in this section the main issues that characterize the Chilean market are presented. The chapter is divided into two sub-sections, where the first is dedicated to the regulation issues, and the second to the industrial organization analysis of the market.

3.1 Regulation of the Chilean pharmaceutical market.

The contents presented in this sub-section are based on the Decree N°3 (2011) that approved the Regulation of the National Control System for Pharmaceutical Products (onwards, the Regulation); the Law N° 20.724 (2014) called the Pharmaceutical Act (onwards, the Law); and the Law N°19.039 (2005), also referred as the Industrial Property Act.

3.1.1 Access to the pharmaceutical market.

For any drug to be sold in the market, the laboratory that produces it must request a sanitary registration to the National Health Institute (ISP, for its initials in Spanish). This process consists in the systemic evaluation of the different properties of the drug, guaranteeing its quality, safety, and efficacy[10]. The studies to prove these characteristics are generally required by the Regulation to the innovator's drugs, while generics, under some conditions, could access to an abbreviated procedure of registration[11].

3.1.2 Market exclusivity for innovator molecules.

The sanitary registration is independent from the commercial or industrial property registration. The Law N°19.039 (2005) of industrial property indicates that the owner of a patent will be granted with an exclusivity market period or monopoly, non-renewable of 20 years from the date of the presentation's request for the innovative product[12]. To compensate the period in which the pharmaceutical product was not in the market because of clinical studies, the law

[10] To demonstrate that the drug fulfills these standards, the laboratory must present the toxicological and pharmacological studies in animals and humans, respectively. The efficacy of the drug is measured by its capacity to generate a therapeutic effect, proven in the treatment of some illness. The latter doesn't mean necessarily that generics will have the same effectiveness of the innovator drug.

[11] This is valid for the drugs produced in Chile and those imported. Also, if the pharmaceutical product is incorporated in the list called National Medicine Formulary -which is the list of essential medicines that must be available in every pharmacy-, it could access to an abbreviated procedure that will not exceed the four months of processing.

[12] The Law N°19.039 was approved in 1991, but several modifications were done in 2005.

considers a supplementary period of exclusivity of 5 years, as long as it does not exceed the 20 years of effective economic exploitation of the product.

3.1.3 Publicity and promotion of pharmaceutical products.

The Law indicates that the publicity it is forbidden for those pharmaceutical products whose selling condition is by prescription. The Regulation also states that the only possible way for laboratories to promote their pharmaceutical products is by the medical sample, being forbidden any other incentive to either health professionals or pharmacists. In this sense, the laboratories' sales force plays an important role to influence the medical prescription patterns.

3.1.4 Bioequivalence.

The Regulation defines a bioequivalent medicine as the product that is pharmaceutically equivalent to a reference alternative, and when administered to a patient according to the adequate dose and periodicity, it produces the same effects, being equally safe and effective[13]. From 2008 several molecules have been included in a mandatory list that forces, the pharmaceutical products that contain those molecules, to prove its bioequivalence or otherwise abandon the market after the deadline established[14]. In addition, the Law lays down that pharmacies must have at least one bioequivalent pharmaceutical for each molecule in the mandatory list and allows the interchangeability of the pharmaceutical prescribed by the available bioequivalent[15].

3.1.5 Medical Prescription.

From 2014, with the approval of the Law, it is mandatory that, when a branded pharmaceutical is prescribed, the health professional must add the common international denomination -or the name of the molecule-. However, this only authorize the exchange of the pharmaceutical prescribed when there is a bioequivalent available at the pharmacy. Considering the 829 molecules registered at the ISP, the mandatory list of 168 molecules subject to the bioequivalence policy accounts for the 22% of the market, so in most of the cases the purchase

[13] The therapeutic equivalence implies that the pharmaceutical contains the same active ingredient, salts or esters, although not necessarily the same excipients. Also, it must have the same dosage form and route of administration of the reference pharmaceutical.
[14] The Decree N° 500 (2011), that systematized the previous resolutions from the Ministry of Health, and subsequent Decrees, adds up to 168 active ingredients subject to the bioequivalence policy.
[15] To make the bioequivalent alternatives recognizable the Law establish that the package must have a yellow label.

of the pharmaceutical is still fundamentally determined by the decision of the heath professional.

3.2 Industrial Organization issues.

From the supply perspective, the pharmaceutical industry involves three players: laboratories, wholesale distributors, and pharmacies and/or pharmacy chains; which are going to be explored in this sub-section.

3.2.1 Laboratories.

According to the Centro Nacional de Fármaco-Economía (2013), in the year 2013, in Chile operated 29 laboratories of production and 4 conditioning laboratories[16]. Nevertheless, there are various laboratories that operate as conglomerates attending several niches, so considering the branches, the number of laboratories of production is 43, most of them of national capitals (Vasallo, 2010).

Table 1: Market share of the 10 main laboratories in the ethical market in 2016.

Laboratories	Market Share (%)
Abbott	9.2
Chile (Teva Pharmaceutical)	8.7
Saval Corp	6.9
Merck Sharp & Dohme	6.6
Grunenthal	5.5
Pfizer Corp	5.4
GlaxoSmithkline	3.8
Pharma Investi	3.3
Astrazeneca	3.1
Novartis Corp	2.9
Total	55.3

Source: Authors' own calculations with data from IMS Health.

In the table 1 are reported the 10 main laboratories that operate the ethical market -that is, the market where the prescription is necessary to concrete the purchase- during 2016, considering their market share in the total sales. The main laboratory is Abbott with the 9.2% of the market, followed by Laboratorios Chile -property of Teva Pharmaceutical- and Saval, that captures the

[16] Production laboratories are those dedicated to the production, import, and packaging of pharmaceutical products or its raw material. On the other hand, conditioning laboratories dedicates exclusively to the packaging and labeling of bulk products into finished products.

8.7% and 6.9% of the total sales from the ethical market, respectively[17]. Altogether, the 10 main laboratories account for the 55.3% of the sales.

3.2.2 Wholesale distribution.

According to the ISP register in 2017, 198 distributors -also called 'droguerías'- operates in Chile, that are dedicated to the import and distribution of medicines, providing the logistic for the supply of pharmacies[18] [19]. Despite the apparent atomization, the wholesale distribution is dominated by the distributors vertically integrated with the 3 main pharmacy chains -SalcoBrand, Cruz Verde, and Ahumada-, that control the 82.6% of this market (Court of Defense od Free Competition, 2006).

3.2.3 Pharmacies and Pharmacy chains.

The records from the Ministry of Health (2015) indicate that, at June 2015, there were 3.013 pharmacies in Chile, 48.7% of whom where located in Santiago. From the total pharmacies, 51.2% belongs to 4 pharmacy chains -Ahumada, Cruz Verde, SalcoBrand and Dr.Simi-, and the remaining 48.8% are independent or 'popular' pharmacies. Although the chains account for the half of the stores, they control the 89.8% of the sales in the market, distributed mainly in the 3 leaders.

Table 2: Evolution of the market share (sales) by denomination in the ethical market.

	2012	2013	2014	2015	2016
Innovators	39.6%	38.2%	37.5%	36%	34.6%
Branded Generics	50.9%	51.5%	51.5%	52.7%	53.6%
Unbranded Generics	9.6%	10.2%	11%	11.3%	11.8%

Note: The shares reported correspond to the ethical market of oral solid molecules. Source: Authors' own calculations with data from IMS Health.

The latter is because of the sales of the main 3 pharmacy chains come from innovators or branded generics pharmaceuticals, which have the higher price among the denominations

[17] The leadership of Abbott responds to the acquisition of the national laboratory 'Recalcine' in 2014.
[18] Information extracted from the register of distributors elaborated by the ISP in 2017. Retrieved August 20, 2017, from the website: http://www.ispch.cl/sites/default/files/Droguer%C3%ADas%20VIGENTES%20al%2004-07-2017.xlsx
[19] The huge number of distributors responds to the branches of international laboratories that locally act as exclusive representative of them. This is the case of GlaxoSmithKline, Merck, Synthon, Sanofi-Aventis, among others. It is also interesting to note that most of the municipalities that has adopted a 'farmacia popular', has also adopted its own 'droguería municipal', that for magnitude of the purchase has a low power of negotiation.

available in the market. The table 2 shows that the branded generics and innovators dominate the market with a share of 53.6% and 34.6% of the sales in the year 2016, respectively; experiencing light variations through time.

Another important issue is that pharmacy chains are not only integrated with a wholesale distributor, but also the three of them are vertically integrated with a laboratory that mainly produce generics (Vasallo, 2010)[20].

3.2.4 Relevant characteristics of the market.

The analysis presented in this section allows to extract some relevant conclusions. First, there is a high concentration at the pharmacy level, where 3 chains concentrate 90% of the retail market, situation that also is replicated at the wholesale market. Second, the pharmacy chains are vertically integrated, incorporating areas of production and distribution.

The process of economic concentration modifies the balance of the bargaining power, moving it from the laboratories to the pharmacy chains. It follows then that the big chains, through their vertically integrated structure, are capable to achieve economies of scale and scope, forcing better prices and/or substantial discounts for volume through the negotiation process with the laboratories (Vasallo, 2010)[21] [22].

The situation described above indicates that the retail prices, instead of the factory prices, are relevant in this market and, hence, the analysis should be done at this level. In fact, the available data, presented in the next section correspond to retail prices.

Finally, the third aspect that characterizes the Chilean pharmaceutical market is the leadership of branded generic denomination, that accounts for almost the half of the sales of the ethical market.

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[20] In particular, Mintlab Laboratory is property of Cruz Verde, which is the sixth laboratory in Chile with the highest number of products with sanitary registration; Salcobrand is part of the same conglomerate of Medipharm and Medcell, that belongs to Empresas Yarur S.A.C; and Laboratorios FASA is a branch of Farmacias Ahumada (Vasallo, 2010).

[21] It should be noted that the concentration process that increased the market power of the pharmacy chains could also have generated important efficiencies in the chain of production and distribution.

[22] For molecules that face generic competition there are many pharmaceutical alternatives. In these cases, pharmacies, for space and logistic purposes, must choose the 2 or 3 products that are going to offer to their clients. For example, for the Paracetamol there are 20 options that contain the molecule isolated, and so the bargaining process and the discounts offer by laboratories become relevant in order to select the ones to be offered.

III. Data.

The data base was provided by IMS Health[23] and collects information of monthly sales revenues of the medicines sold in pharmacies between January 2002 and July 2017; that is, 187 months[24]. This data considers all monomolecular medicines dispensed with medical prescription -that is, the so called ethical market- and whose route of administration is oral.

This database reports sales revenues and the number of pills monthly commercialized for each medicine, that allows to determine the average monthly price. For the same molecule there are multiple pharmaceutical products that are being sold in different concentrations (Mg_i: milligram) and number of pills (un_i) – situation that could bias the comparisons-, we proceed to determine the average price per defined daily dose (DDD). The DDD is the assumed average maintenance dose per day for a drug, considering its main indication in adults[25]. With this data, the average price per DDD for the drug i in the period t, was obtained in the following way:

$$p_{it} = \frac{Sale\ Revenue_{it}}{(Mg_i * un_i)/DDD} \qquad (1)$$

The prices got with (1) were deflected to January 2002 prices using the Consumer Price Index (CPI), so the changes reported in this paper correspond to real variations[26].

Among the 618 molecules contained in the database, we identify those that were exposed for the first time to generic competition, removing those molecules that already faced competition before 2002. Also, the molecules with less than a year of exposure to competition were eliminated[27]. According to this, 47 molecules achieved the aforementioned conditions, accounting for 262 drugs. The 72% of the drugs corresponds to branded generics, the 22% to innovators, and 5.7% to unbranded generics. However, unbranded generics are grouped into

[23] IMS Health is an international company specialized in gathering data for the health industry. It is the main source of information for making price research and strategic managing.
[24] The sales revenues are obtained from the 3 main retail chains (FASA, Cruz Verde and SalcoBrand), the independent retail pharmacies, and the 3 main distributors (Toledo, Socofar and Drogueria Ñuñoa).
[25] This unit of measure is determined by World Health Organization (WHO) and it was consulted in website: www.whocc.no/atc_ddd_index. For those molecules that there is no DDD defined by WHO, we used the mode of the different presentations of the molecule available in the market all time. If two or more doses constitute the mode, we opted for the lower concentration.
[26] The monthly CPI data was downloaded from the website of the Central Bank of Chile, in http://si3.bcentral.cl/Siete/secure/cuadros/home.aspx, accessed on October 4th, 2017.
[27] Only 2 cases were in this situation. The Pazopanib and Pirfenidone, with 2 and 4 months of exposure to generic competition.

the 'Generics' denomination, without any identification of the distinct pharmaceutical products sold in this category[28]. In spite of that, in every single of the 47 cases, the first entrant is a branded generic, and the unbranded alternative tends to be a late incoming drug.

A complete description of the main characteristics of the 47 molecules identified is presented Appendix A. Telmisartan shows the higher exposure to branded generic competition with 185 months. By contrast, Capecitabine exhibit the lower exposure with 28 months. In general, the 47 molecules have 119 months, in average, of exposure to branded generic competition.

Table 3 provides descriptive information of the number of competitors through several different post-entry time points. In the first row, the average number of branded generics competitors for the 47 molecules is 1.2 when 6 months has passed since the beginning of competition, reaching 2.3 at 48th month. In the second row the average number of substitutes is reported. The substitutes are those drugs that, under the ATC code level 4, have the same chemical and therapeutic properties[29]. To determine the number of substitutes, the initial 2.188 drugs were considered. Hence, the 47 molecules face an average of 15.6 substitutes – that is, drugs that are elaborated with molecules that belongs to the same chemical subgroup according to the ATC-4- at the 6th month since the beginning of competition, number that is keep relatively constant through the whole post-entry period.

Table 3: Number of average competitors for different periods in the post-entry period.

	6th months	12th months	24th months	48th months
Number of branded generic competitors	1.2	1.4	1.7	2.3
Number of substitutes.	15.6	15.5	15.5	16

Source: Authors' own calculations with data from IMS Health.

Table 4 describes the impact of branded generic competition on innovator prices. Prices reports on the table correspond to the average of the weighted average price of the 47 molecules, where the weights are the monthly doses dispensed by each drug. In the first row, the innovator prices decline 7% in the branded competition period in comparison to the monopoly period. In

[28]Unbranded Generic products are not revealed in detail due to the confidentiality agreement between pharmacies and IMS Health. These pharmacies manufacture their own unbranded generics, which capture an important share of the market.

[29] The Anatomical Therapeutic Chemical (ATC) Classification System classify the molecules according to the system or organ that they affect, and their therapeutic, pharmacological and chemical properties. The system contemplates 5 levels of disaggregation, where the fifth level it's the own-molecule. The 4 level correspond to the family of molecules that belongs to the same chemical subgroup. This ATC system is elaborated by the WHO.

Appendix B it could be seen that, in disaggregated terms, 27 of the 47 molecules (57%) experience a decrease in their prices in the post-entry period in comparison to the pre-entry average.

Table 4: Evolution of average prices by denomination.

		Pre-entry ($)	Post-entry ($)	Variation (%)	6th months ($)	12th months ($)	24th months ($)	48th months ($)	Variation 48th month- 6th month (%)
Average Price	Innovator (1)	4,021	3,758	-7	4,278	4,035	3,917	3,820	-11
	Innovator (2)	4,669	4,663	-0.1	5,321	5,011	4,853	4,574	-14
	Innovator (3)	2,765	2,763	-0.1	3,032	2,941	2,865	2,680	-12
	Branded Generic	-	1,445	-	1,730	1,711	1,661	1,214	-30

Note: The price reported in the table corresponds to the average of the weighted average real price calculated by denomination for each molecule. Row: (1) reports for the 47 molecules that experience entry for the first time in the data; (2) exclude the molecules affected by the collusion of pharmacies; and (3) considers the 26 molecules used in the implementation of the empirical strategy. Source: Authors' own calculations with data from IMS Health.

In the row (2) of table 4, the 11 molecules exposed to the collusive agreement between pharmacies were removed[30]. Assuming that the prices of the remaining 36 of molecules represent a competitive equilibrium, the variation in the innovator prices is almost wiped out with a negligible -0.1%. However, the medium-term variation between the prices of the 48th and 6th month of competition, in the last column, is -14%. Finally, the row (3) reports the evolution of prices of the 26 molecules used in the empirical strategy of the following section. The average price of the molecules drops to almost the half of that found in the previous rows, because of the exclusion of the molecule Temozolomide, with a unitary price of $94,897 per dose. Despite the previous fact, no major variation is registered from the results already mentioned.

Table 5 reports the evolution of the average relative prices, that is, the ratio between the branded generic and innovator prices. Independently of the set of molecules that is considered for the determination of the relative price, no bigger different is visible and, therefore, we are going to refer to the results in row (3). At the 6th month from the beginning of competition, the prices of branded generics are 25% lower than the innovators, difference that increases to the

[30] According to the Court of Defense of Free Competition (2012), 11 out of 47 of the molecules identified were exposed to the collusion of pharmacies between December 2007 and April 2008. This collusive agreement affected the presentations that were market leaders at the time, which correspond mainly to innovators.

-33% at the 48th month. As a benchmark, at the 24th month since the beginning of generic competition, the price differential is -40% in the European Union (European Commission, 2009), that compares with the -30% in the Chilean market, a magnitude that is close to the one reported by the Mexico's Federal Economic Competition Commission (2017) of -28.6%.

Table 5: Evolution of the relative prices in the post-entry period.

		6th month (%)	12th month (%)	24th month (%)	48th month (%)
Average relative price	(1)	74	73	70	67
	(2)	75	72	71	67
	(3)	75	72	71	67
	(4)	75	74	71	67

Note: The average relative price is determined from the branded generic-innovator price ratio of each molecule. (1) reports for the 47 molecules that experience entry for the first time in the data; (2) exclude the molecules affected by the collusion of pharmacies; (3) considers the 26 molecules used in the implementation of the empirical strategy; and (4) excludes the antineoplastics from 26 molecules of (3). Source: Authors' own calculations with data from IMS Health.

Table 6 analyzed the average growth rates in the volume of doses dispensed by innovators in post-entry period. In 19 cases, the innovator exhibits positive rates, and only in two cases the growth rate is higher than 2%. By contrast, in 38 cases branded generics exhibit a positive rate in the volume growth, and in 31 of these cases the rate exceeded the 2%. In average, the monthly growth rate is 0.54% and 2.5% for innovators and branded generics, respectively.

Table 6: Classification of the innovators according to the post-entry growth rate of the volume of doses.

Classification	Rate	Average growth rate (%)	Nº of cases
Strongly reduce	$[-\infty, -0.9]$	-2.9	14
Weakly reduce	$(-0.9, 0]$	-0.3	15
Weakly increase	$(0, 0.9)$	0.4	8
Strongly increase	$[0.9, \infty]$	1.5	11

Note: The growth rates were determined from a regression of the log of the total innovator doses dispensed per month as a dependent variable, and a tendency as an explanatory variable. Source: Authors' own calculations with data from IMS Health.

Finally, table 7 reports the evolution of the average market share by doses. In the first 6 months of competition, branded generics capture an average share of 21% of the market, reaching the 45% at the 48th month of competition. In column (*), for the 26 molecules used in the following sections, branded generics have a share of 41% of the market at the 48th month. The

unbranded generics has an inappreciable share during the first 4 years of competition, with a market share of 0.2% in average at the 48th month[31].

Table 7: Evolution of the average market share by doses in the post-entry period.

	Market Share				
Denomination	6th month	12th month	24th month	48th month	48th month (*)
Innovator	0,79	0,74	0,64	0,54	0,58
Branded Generic	0,21	0,26	0,36	0,45	0,41
Unbranded Generic	-	-	0,001	0,002	0,003

Note: Column (*) considers the 26 molecules used in the implementation of the empirical strategy.
Source: Authors' own calculations with data from IMS Health.

The situation described above let us theorize that the innovative laboratories keep captive a segment of the market -where some molecules are more sensitives tan others to competition- probably through a mechanism argued by Frank and Salkever (1991) associated to the pattern of prescription, or the brand loyalty mention by Grabowski and Vernon (1992). In this sense, it is likely that the placement of new doses by the branded generic laboratories is due to sale efforts to foster loyalty from the health professionals, affecting other therapeutic substitutes. Other possible hypothesis is that the reduction in the pharmaceutical cost of the treatment encourages new patients to incorporate themselves in the pharmacological therapies, being capture by branded generics.

[31] Although we do not know the number of unbranded generic competitors, we do know the total volume of doses sold by this denomination, and hence its share in the retail market.

IV. Methodology

We adopt an impact evaluation technique that combines the properties of Propensity Score Matching (PSM) and Differences in Differences (DiD) methods for estimating the impact of branded generic competition. Using PSM not only allows us to find an appropriate control group for the molecules that are exposed for the first time in the data to branded generic competition, by tackling the problem of selection bias; but also helps us to diminish the concerns over the exogeneity condition of generic entry. That is, controlling for a set of observable characteristics that determine the probability that a particular drug experiences entry, and assuming that no other variable is missing in the model, then the entry becomes a pure lottery event.

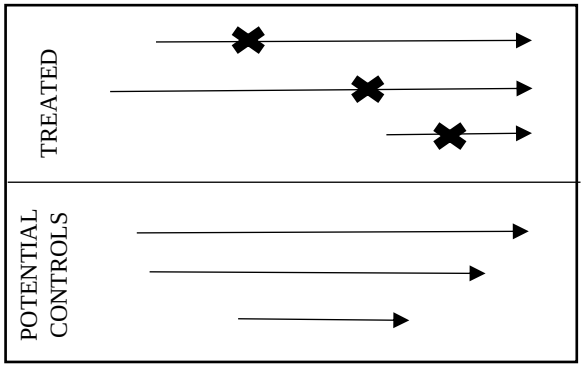
On the other hand, DiD provides a way to deal with unobserved heterogeneity, assuming that the source of that heterogeneity is time invariant, so the bias can be discarded by the differencing process. In this framework, the estimation of the effect of branded generic competition over prices and quantities considers two different treatments. First, a lineal treatment that will provide evidence of the average effect over time associated with the branded generic entry. In other words, the treatment refers to the event of going through a monopoly to a competition regime, where the main source of competition comes from branded generics. Second, taking into consideration that the effect could be non-linear regarding the number of competitors that a particular drug confronts, the next step will contemplate two intensities of competition.

There is one characteristic of the data that hampers us to implement the PSM as the traditional way stated by Rosenbaum and Rubin (1983). The data belongs to an unbalanced panel in response to the differentiated moment of entry of branded generics drugs in the off-patent markets. Of course, the consequence of this is that the beginning and ending of the period of monopoly and competition differs from one molecule to another. By extension, as shown by figure 1, it is not possible to define a certain point in time that will determine a common pre and post treatment period for all molecules. The above means that it's no possible either to identify a priori which is the relevant period for the implementation of the PSM -that is, the pre-treatment

period- for the molecules that have never experienced generic competition and, therefore, are susceptible to become control molecules[32].

A solution for this problem is mention by De Loecker (2007), who considers to leave out the calendar time and rescale the periods so the molecules start experiencing competition at s=0. Then, it is necessary to define the number of periods of pre and post treatment that are going to be considered for each molecule. We opted for 13 and 48 periods of pre-treatment and post-treatment, respectively[33]. Hence, we have 61 periods where prices of branded generics and original drugs are observed. From the initial 47 molecules that experience generic entry for the first time, 33 have sufficient data to cover these periods.

Figure 1: Diagram of the treated and potential control molecules.



Note: The black crosses indicate the beginning of branded generic competition. Source: Authors' own elaboration.

Then, we have to identify a group of molecules that can be used as a potential counterfactual for the treated molecules. In doing so, all the molecules that were under the monopoly of the original between January 2002 and July 2017 were selected, but only keeping those that at least have 61 periods of presence in the data, equivalent to 56 molecules. As the calendar time is no longer relevant, for each potential control molecule we proceed to generate $n - 60$ panels of 61 consecutive periods, where n is the number of months that the molecule has presence in the data base. As a result, 4.492 potential controls were generated for the 33 molecules expose

[32] Besides, it must be noticed that the time length of the potential controls differs from one molecule to another. For example, while some molecules are present in each of the 187 months of the date base, others are only available in less than a quarter of that period extension.

[33] Although the objective was, at least, to have a year of pre-treatment data, considering 13 months of pre-treatment do not imply any extra loss of information. Based on preliminary estimations, the literature, and the criteria of minimizing the loss of information, we considered that 48 months for the post-treatment period were sufficient to detect any effect from competition.

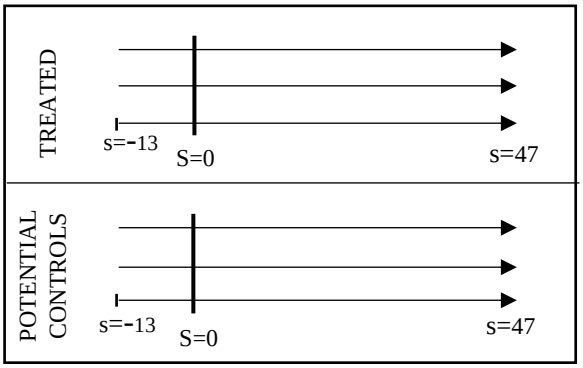
to competition and, as presented in figure 2, it is possible to identify a common pre and post-treatment period for all molecules.

Retaining only the pre-treatment characteristics, corresponding to the first 13 periods for all molecules, the probability of experiencing competition at s=0 is estimated, reshaping the data into a cross-section. The probit model is the following.

$$\Pr\left(Treatment_{i,s=0}=1\right) = g\left\{h\left(cp_{i,-1}\dots cp_{i,-12}, CHRONIC_i, \psi_i, SIZE_{i,-1}, AGE_{i,-1}, NUMsub_{i,-1}, PROL_{i,-1}\right)\right\} \quad (2)$$

The most relevant variables in the estimation of the propensity score are the rates of change of prices during the twelve periods before the beginning of the competition, $cp_{i,-s}$. This set of variables are fundamental in order to dissipate the pre-treatment differences in the evolution of prices. Following Caves et al (1991) we include a specific effect to the therapeutic class ATC-1, which is represented by the vector ψ_i in the specification, that provides a control for aspects that affect the therapeutic class as a whole.

Figure 2: Diagram of De Loecker's solution.



Note: The vertical black line identifies the beginning post-treatment period. Source: Authors' own elaboration.

In addition, a set of variables measured at the month before the beginning of the competition are included, for which the subscript -1 is used. The size of the market of the molecule, $SIZE_{i,-1}$, is included as Grabowski and Vernon (1992) indicates it as one of the main predictor of the generic entry. $NUMsub_{i,-1}$is the number of other available substitute drugs that the molecule i faces it, which contained other active principles but are prescribed for the same illness, according to the therapeutic class ATC-4. $AGE_{i,-1}$corresponds to the number of months since the molecule entered the market, controlling for the life-cycle of the product.

The variable $PROL_{i,-1}$ allows us to control for the proliferation of presentations for the molecule i; that is the number of formats that differs between themselves only in the number of capsules or milligrams. Ellison and Ellison (2007) suggest that the number of presentations available in the market constitutes a strategic tool for entry deterrence; in other words, the more presentations the bigger is the cost for the generic competitor of reproducing the complete line of pharmaceutical products.

Finally, we use the dummy variable $CHRONIC_i$ that takes the value of 1 if the molecule i is prescribed for a chronic illness. Note that laboratories could be more prompt to enter a market that attends chronic patients, as they should exhibit a more inelastic demand for the drug they need. This variable is built upon the definition of Warshaw (2006), who indicates that chronic conditions are those that last for more than a year and require permanent medical attention or limited the activities of daily living.

The model (2) is estimated considering two samples, reflecting two different intensities of competition. Consequently, the sample of molecules that experiences competition was divided into two, considering that the median of the average number of branded generic competitors that the innovator faces in the whole post-entry period is 1.7. It follows, then, that the treatment 1 incorporates all those molecules that on average experience less than 1.7 branded generic competitors, while treatment 2 gather those who exceed 1.7 competitors on average. Then, separately, for each treatment, with the propensity scores obtain in (2), the molecules are matched in the common support. The matching is done applying the nearest neighbor criteria, which is implemented without repetition.

Note that the fundamental assumption behind this method is that, conditional to the observables characteristics mention above, belonging to the group of molecules that experiences competition or the group of control is equivalent to a lottery (Rosenbaum y Rubin, 1983). To put it bluntly, preexistent differences are dissipated and, conditional on the observables, both groups of molecules -treatment and control- are equal on average.

Once the counterfactual group is obtained, we proceed to estimate the causal impact, making use of panel structure of the data. Thus, we employ the DiD method that compares the changes in prices or quantities over time between the treatment and control group. As aforementioned in the article, with DiD we can eliminate any difference that is constant over time, getting a more robust estimation. The first DiD specification to be estimated is (3).

$$Y_{is} = \beta_0 + \beta_1\delta_s + \beta_2\lambda_i + \beta_3\Delta_{is} + \beta_4\Pi_{is} + \beta_5\Omega_i + \beta_6\Psi_{is} + \varepsilon_{is} \qquad (3)$$

Where Y_{is} corresponds to the logarithm of the price (quantity) of the molecule i in the period s; δ_s is a dummy that takes the value of 1 for all $s \geq 0$, that is, the post-entry period; λ_i is a dummy that takes the value of 1 if the molecule i was exposed to competition and, hence, corresponds to a treated molecule; Δ_{is} corresponds to a dummy that takes the value 1 from the entry period ($s \geq 0$) for the treated molecules; accordingly, it is the interaction between δ_s and λ_i.

The Ω_i vector contains a series of level indicator variables to control for the grouping of the molecules after the PSM, and Ψ_{is} controls for the calendar time. In Π_{is} variables are included to control for differences that are generated in the post-entry period such as bioequivalence and the presence of unbranded generics, that only affect the treated molecules. The bioequivalence dummy variable takes the value of 1 from the moment that a therapeutic equivalence study is approved for a pharmaceutical of the molecule i; and the unbranded generic indicator takes the value of 1 if the molecule i faces unbranded generic competition in the month t[34]. Finally, ε_{is} is the stochastic error term.

The coefficient of interest in (3) is β_3, that gives us the estimator of DiD, and therefore the causal impact of branded generic competition over the prices (quantities).

The second DiD specification (4) considers the two intensities defined above.

$$Y_{is} = \varphi_0 + \varphi_1\delta_s + \varphi_2\lambda_{1i} + \varphi_3\lambda_{2i} + \varphi_5 T1_{is} + \varphi_6 T2_{is} + \varphi_7\Pi_{is} + \varphi_8\Omega_i + \varphi_9\Psi_{is} + \mu_{is} \qquad (4)$$

Where Y_{is}, δ_s, Π_{is}, Ψ_{is} and Ω_i are defined in the same terms as in (3), but now λ_i and Δ_{is} were substituted by λ_{1i} and λ_{2i}, and $T1$ and $T2$, respectively. Here, λ_{1i} and λ_{2i} represent dummy variables that take the value of 1 when the treated molecule is associated to the treatment 1 and 2, respectively. T1 is a dummy variable that takes the value of 1 from the moment the molecule i starts experiencing competition, every time the number of the average branded generic competitors is below 1.7; whereas T2 will take the value of 1 for those molecules that exceed that number of average competitors.

[34] The first bioequivalent drug was approved in 2009. Since then, the Public Health Institute has stablished that drugs that contain certain molecules must present studies of their therapeutic equivalence to an approved reference-listed drug. Information and details contained in the Decree-law N°981 from de Ministry of Health.

The estimation of the equations (3) and (4) are made by OLS, and considers robust standard errors clustered at the level of the matching molecules grouped with the PSM, allowing for arbitrary serial correlation within each pair of matched molecules.

To gain further insight into the evolution of the price differential between the branded generics and innovators, we use the information of monthly prices of the initial 47 molecules described in the previous section, during the post-entry period, estimating the equation (5).

$$logP_{mt} = \alpha_i + \beta_1 \sum_{p=1}^{4} BG_{pmt} + \beta_2 Gen_m + \beta_3 Bio_{mt} + \beta_4 NUMsub_{mt} + \beta_5 NUMC_{mt} + \beta_6 HHI_{mt} + \beta_7 Pre_{mt} + \beta_8 AGE_{mt} + \beta_9 AGE_{mt}{}^2 + \beta_{10}\Phi_m + \sum_{r=2}^{47} \xi_{r-1}\Lambda_m + \sum_{t=2}^{187} \theta_{t-1}X_t + \varepsilon_{mt} \quad (5)$$

Where BG_p are dummy variables that capture the price differential between branded generics and innovators at different periods. BG_1 takes the value of 1 if the drug m corresponds to a branded generic during the first 12 months post-entry; BG_2 takes the value of 1 if the drug m corresponds to a branded generic from the 13 month post-entry to the 24; BG_3 takes the value of 1 if the drug m corresponds to a branded generic from the 25 month post-entry to the 47, and finally BG_4 captures the differential price for all the subsequent period from the 48 month post-entry. The variable Gen_{mt} takes the value of 1 if the drug m is an unbranded generic, so the base category is represented by the innovators.

Categorical variables are included in the vector Φ_m to control for time invariant aspects such as the dosage form which can be pills, capsules or tablets; the effect of medication which can be retarded if the drug has a long duration of action, or otherwise ordinary; and the $CHRONIC$ previously explained. Other variables included to control for drug characteristics are Pre_{mt} which corresponds to the number of presentations available in the market for the drug m at time t; Age which is the number of months since the drug was introduced to the market and Age^2 is the squared age. To control for market characteristics, we incorporate $NUMC_{mt}$ which is the number of branded competitors that the drug m faces it at time t; HHI_{mt}, corresponds to the Herfindahl-Hirschman Index to control for the concentration of the molecule market at time t; and $NUMsub_{mt}$ defined as it was previously stated.

Finally, Λ_m is a vector that contains categorical variables for each molecule in order to capture any molecule-specific *s*hocks*;* and X_t is a vector of monthly dummy variables to control for the time, that is, any possible seasonality and common shocks that affect all drugs at time t. Note

that the idea behind this estimation is to get the true price differential between branded generics and innovators, by controlling for the effect of variables that generate differences in prices between these denominations.

It seems natural to recognize the existence of some correlation between the individual specific effects α_i and the price differentials, especially considering the high heterogeneity between the drugs in sample. If this is true, which can be tested by a Hausman Test or other procedure, to get consistent coefficients it is necessary to use the fixed-effects estimator (FE). Although from a statistically point of view this is appropriate, in our case the estimated coefficients on BG_{pmt} would lack the desirable interpretation. This is because, even though the BG_{pmt} varies over time and drugs, the time invariant dummy that identifies the branded generic drugs (=1 if the drug is a branded generic) would be wipe out by the within estimator with all the time invariant heterogeneity. So, in the fixed effect model, the coefficients on BG_{pmt} will capture the little variations from the differential that was precluded.

To circumvent problem, we make use of the so called Hausman-Taylor model that allows us to consistently and efficiently estimate the coefficients of both the time invariant and time-variant variables that are correlated with the individual effects. Basically, Hausman and Taylor (1981) model is based upon an instrumental variable estimator that uses the within and between variation of the strictly exogenous regressors as instruments for the endogenous ones. Following the notation of Wooldridge (2002), this model could be represented by the equation (6):

$$Y_{mt} = \alpha_m + \beta_1 X_{1,mt} + \beta_2 X_{2,mt} + \gamma_1 Z_{1,m} + \gamma_2 Z_{2,m} + \varepsilon_{mt} \qquad (6)$$

The model in (6) considers the partition of time invariant and time-variant vectors of explanatory variables, represented by Z and X, respectively. In this set-up, the variables with the subscript 1 are assumed to be strictly exogenous, whereas the subscript 2 is used to denote those variables that are correlated with the individual fixed effects α_m, but not with ε_{mt}. Hausman and Taylor (1981) proposed to estimate a two-stage least squares (2SLS) considering as instruments the vector $[Q_T, X_1, Z_1]$, where Q_t is the TxT time-demeaning matrix, also called the within transformation matrix[35]. So, essentially the instruments are the time-demeaned variables

[35]The matrix $Q_T \equiv I_T - P_T \equiv I_T - j_T(j_T'j_T)^{-1}j_T'$, where I_T is the identity matrix and P_T is the projection matrix. Intuitively, P_T transform the vector of exogenous time-variant variables into individual means, whereas Q_T into deviation from means.

$Q_T X_1 = X^*_{mt} = X_{mt} - \overline{X_m}$; the individual means or between variation $P_T X_1 = \overline{X_m}$; and the exogenous time invariant variables Z_1. Note that $E[(Q_T X_{mt})' u_{mt}] = 0$, where $u_{mt} = \alpha_m + \varepsilon_{mt}$ is the composite error, thus the matrix $Q_T X_m$ satisfies the exogenous condition that allows it to be an appropriate instrument. The identification condition is satisfied if there are at least many time-varying exogenous variables X_1 to act as instruments for the Z_2 variables.

V. Results

The results reported in table 8, column 1, reports the random effects (RE) model, although the Hausman test significantly reject the null hypothesis of no systematic difference between RE and FE coefficients, so clearly the coefficients in this column are not consistent. In the second column we apply the Hausman-Taylor procedure described above, considering that the price differentials BG_p, the pure generic dummy (Gen), and the brand proliferation are endogenous. According to the results, the coefficient estimated on the price differentials drops to almost the half of the ones reported in the first column, but the Sargan-Hansen test of over-identification reported in the last row indicates that the instruments are no valid.

In the third column we also incorporate the market characteristics as endogenous regressors, that is, the number of competitors $(NUMC)$, the market concentration (HHI) and the bioequivalence dummy (Bio). Note that the age variable and its square are not included because the molecules get older in the market independent of any circumstance. The null hypothesis of the instrument appropriateness is not rejected when we add these variables to the endogenous group.

The results in the column (3) indicate that the prices of the branded generic options are, on average, a 17.6% lower than the innovator options at the first year of branded generic competition, pretty similar to the gross price differential reported in the table 5.[36] This differential keeps relatively constant over a long period of competition, reaching to 18.7% lower than the innovators options beyond the 48 months of competition. On the other hand, the pure generic differential indicates that their prices are 27.4% lower than the innovators.[37]

The chronic dummy and the number of competitors revealed to be significant ant their effects go in the expected direction. Indeed, the chronic drugs are 59.2% more expensive, matching the intuition that this kind of drugs tend to be more inelastic and hence are charged a higher price. Also, each additional branded generic or innovator competitor reduces the drug price in 1.1%, in line with to the low intensity of the branded competition.

[36] As it is a semi-logarithm regression, the impact is estimated as follow: $(\exp(-0.194) - 1) * 100\%$ See Halvorsen and Palmquist (1980).

[37] The price differential of pure generics is not representative of the one observed in the market as whole because this denomination is rarely available in these 47 molecules that experience competition for the first time in the data base.

Table 8: Estimation of the price differential.

VARIABLES	(1) RE	(2) HT-1	(3) HT-2	(4) HT-3
BG_1	-0.412***	-0.211***	-0.194**	
	(0.09)	(0.08)	(0.08)	
BG_2	-0.426***	-0.225***	-0.207***	
	(0.09)	(0.08)	(0.08)	
BG_3	-0.407***	-0.205**	-0.188**	
	(0.09)	(0.09)	(0.09)	
BG_4	-0.426***	-0.224***	-0.207**	
	(0.09)	(0.08)	(0.08)	
Gen	-0.804***	-0.322***	-0.320**	-0.272**
	(0.20)	(0.12)	(0.13)	(0.11)
BG				-0.181**
				(0.08)
$Collusion$				-0.111**
				(0.05)
$Collusion * BG$				0.121**
				(0.05)
Age	0.002	0.004***	0.004***	0.004***
	(0.002)	(0.001)	(0.001)	(0.001)
Age^2	5.68e-06***	5.74e-06***	5.74e-06***	6.07e-06***
	(2.15e-06)	(2.15e-06)	(2.15e-06)	(1.93e-06)
$Chronics$	0.348*	0.464**	0.465**	0.481**
	(0.20)	(0.19)	(0.18)	(0.19)
Bio	-0.014	-0.014	-0.014	-0.014
	(0.02)	(0.02)	(0.02)	(0.02)
Presentations	-0.007	-0.007	-0.007	-0.006
	(0.01)	(0.01)	(0.01)	(0.01)
Effect (= Ordinary)	0.133	0.023	0.013	0.008
	(0.17)	(0.20)	(0.20)	(0.20)
For1(= Capsules)	-0.06	-0.05	-0.06	-0.05
	(0.09)	(0.10)	(0.10)	(0.10)
$For2(= Tablets)$	-0.04	-0.05	-0.05	-0.05
	(0.08)	(0.09)	(0.09)	(0.09)
HHI	-2.85e-06	-2.63e-06	-2.63e-06	-2.55e-06
	(5.61e-06)	(5.61e-06)	(5.61e-06)	(5.56e-06)
$NUMC$	-0.011*	-0.012*	-0.011*	-0.011*
	(0.01)	(0.01)	(0.01)	(0.01)
$NUMsub$	-0.001	-0.0004	-0.0005	-0.0004
	(0.002)	(0.002)	(0.002)	(0.002)
$Constant$	6.439***	6.559***	6.566***	6.578***
	(0.25)	(0.28)	(0.28)	(0.29)
Observations	41,555	41,555	41,555	41,555
R-squared	0.93			
Over-identification test (p-value)		0.04	0.84	0.83

Note: Robust cluster standard error at the level of molecule-denomination. *** significant at 1%, ** significant at 5%, * significant at 10%. Dummy variables to control for time and molecules are included. RE: Random Effects Estimation; HT: Hausman-Taylor Estimation. Source: Authors' own calculations with data from IMS Health.

Finally, in the last column the four price differentials are replaced by a single dummy BG that takes the value of 1 if the drug m is a branded generic. Also, in this estimation we control for the collusion that affected the prices in the short period between December 2007 and April 2008. In doing so, we include the variable $Collusion$ that takes the value of 1 if the molecule *i* was affected by the retail collusion during December 2007 and April 2008, and we interacted this variable with the BG indicator. The coefficient on the interaction indicates that, for the colluded molecules, the price gap between the branded generics and innovators shrinks to -5.8%, which is as expected as the collusion agreement elevates the prices of the affected drugs.[38]

The rest of the section will focus on the results concerning the impact of the branded generic competition. The results from the estimation of the propensity score are provided in the table of Appendix C. According to the distribution of the propensity score of the treated and non-treated molecules, 7 treated molecules were outside of the common support, and so were excluded from the sample. Consequently, from the initial 33 molecules involved in the PSM, 26 molecules were successfully matched with a non-treated molecule applying the nearest neighbor criteria.[39]

The property of balance between treated and non-treated molecules is evaluated in table 9 for 5 observables characteristics that were previously considered in the probit model. From the p-value presented in the last columns of each of these tables it can be seen that there is no significant evidence to sustain that there is a difference between both groups of molecules. Therefore, it can be asserted that they are equals on average.

[38] The marginal effect is obtained as follow: (exp (-0.181+0.121)-1)*100%

[39] The 26 molecules that remain in the final sample are: Cabergoline, Calcitriol, Cefuroxime, Cyclosporine, Ciprofibrate, Clozapine, Duloxetine, Exemestane, Fluvoxamine, Glimepiride, Ibandronic Acid, Imatinib, Leflunomide, Letrozole, Mycophenolate Mofetil, Naratriptan, Olanzapine, Oseltamivir, Oxaprozin, Pramipexole, Rivastigmine, Tolterodine, Topiramate, Trazodone Chlorhydrate, Vildagliptin, Warfarin

Table 9: Property of balance from Treatment 1.

		Average			t-test	
Treatment	Variable	Treated	Control	Sd bias (%)	t	p>t
1	Chronic$_{-1}$	0.64	0.53	23.9	0.68	0.50
	Market Size$_{-1}$ ($MM)	14	23	-74.3	-0.96	0.34
	Age$_{-1}$	119.3	105.31	23.4	-0.73	0.47
	NumSub$_{-1}$	16.9	14.5	12.8	0.32	0.75
	Presentations$_{-1}$	1.6	1.8	-38.5	-0.96	0.34
2	Chronic$_{-1}$	0.78	0.67	24.3	0.50	0.62
	Market Size$_{-1}$ ($MM)	36	30	10.6	0.54	0.60
	Age$_{-1}$	100.1	111.3	-13.7	-0.26	0.80
	NumSub$_{-1}$	12.3	8.9	24.0	0.85	0.41
	Presentations$_{-1}$	1.6	1.3	44.7	1.56	0.14

Note: The standardized bias (sd bias) is the percentage difference of the sample means in the treated and non-treated sub-samples as a percentage of the square root of the average of the sample variances in the treated and non-treated groups.

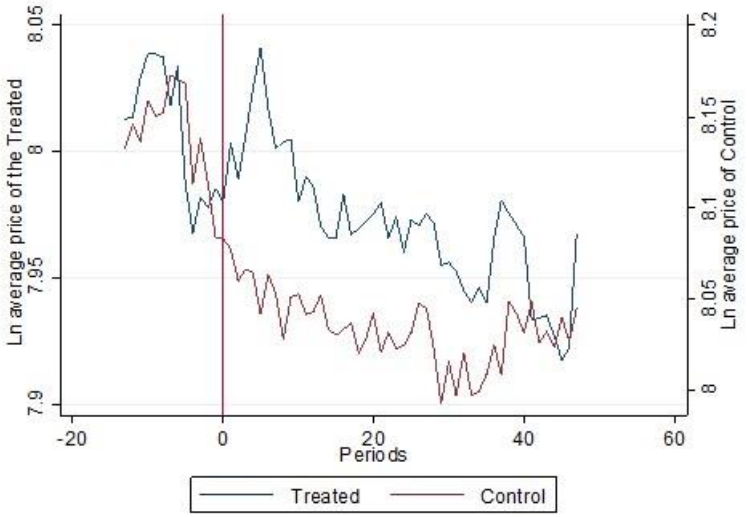
In panel A and B of Figure 3 the evolution of weighing average prices of innovators and total doses sold in the market is presented for treated and non-treated molecules. The pre-treatment tendencies of prices and quantities shown are similar for the treated and control molecules, which allows us to apply the DiD estimation.

Table 10 presents the DiD estimations for the weighing average real prices and doses sold by innovators. In column1, the coefficient of interest estimated on Δ_{is}, in the third row of the table, has a negative sign but shows no statistically significant impact. In other words, the branded generic competition is not able to induce a statistically significant reduction over innovators prices in the post-entry period -considering 48 months- with respect to the molecules that were still under the monopoly regime. In column 2 the same exercise is replicated but excluding the 4 molecules -and its counterfactuals- expose to the collusion of 2009. Again, the results remain almost the same, with no statistical significant effect.

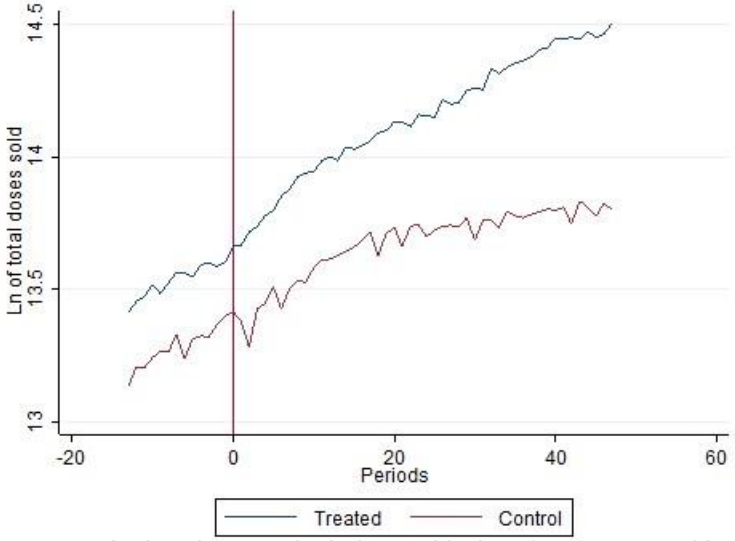
Although the coefficient estimates on Δ_{is} for the doses sold by innovators are positives in columns 3 and 4 of table 10, the branded generic competition does not generate a statistically significant effect over the innovators quantities.

Figure 3

(A) Evolution of weighing average prices of treated and non-treated innovators molecules.



(B) Evolution of total doses sold by treated and non-treated molecules.



Source: Authors' own calculations with data from IMS Health.

These results for the innovators prices are consistent with the theory of segmentation of the market, that claimed that generic competition is unable to lessen the prices of innovators. Furthermore, whereas branded generics provide a significantly cheaper option as shown by results on table 5, branded generic competition seems to be incapable of provoking any major shift in the preferences of innovators consumers. To put it succinctly, as with pure generic competition, the market is divided, with the innovator preserving its loyal consumers who naturally exhibit an inelastic demand.

The pattern follows by the innovator resembles those observed in the food market. As an illustration, Perloff et al (1996) in the context of a Hotelling model, suggests that after the entry of a private label each producer of a national brand -the innovator in our case- may find attractive to sell only to consumer located close to its product in the characteristic space. Therefore, the incumbents' prices and quantities remain unchanged on average.

Table 10: Differences in Differences Estimation for innovators.

VARIABLES	Price		Quantity	
	(1)	(2)	(3)	(4)
After (δ_s)	0.035	0.031	-0.332	-0.383
	(0.15)	(0.17)	(0.33)	(0.37)
Treated (λ_i)	-0.403	-0.222	1.352*	1.259*
	(0.38)	(0.32)	(0.72)	(0.66)
Interaction (Δ_{is})	**-0.122**	**-0.092**	**0.452**	**0.357**
	(0.16)	(0.17)	(0.48)	(0.38)
Constant	8.186***	8.166***	5.770***	5.601***
	(0.44)	(0.37)	(0.86)	(0.78)
Observations	3,156	2,668	3,156	2,668
R-Squared	0.548	0.595	0.528	0.551

Note: Robust cluster standard error at the level of the group of molecules paired with PSM in parenthesis. *** significant at 1%, ** significant at 5%, * significant at 10%. Dummy variables to control for time and the matched molecules are included, as well as controls for post-entry differences (bioequivalence and unbranded generic presence). Columns 2 and 4 report the results excluding the 4 molecules, and its counterfactuals, involved in the collusion of prices. Source: Authors' own calculations with data from IMS Health.

In table 11 we explore the possibility of a non-linear effect deriving from the numbers of branded generic competitors that the innovator faces. So, the two intensities of treatment defined in the preceding section are now considered. In column 1 where reaction on prices is examined no statistical significance is achieved, even though the magnitude associated to the second treatment is considerably higher. Regarding to the supply of medicine doses in column 2 of table 11, the magnitude between both treatment is similar, but again none of them is statically significant.

Table 11: Differences in Differences with distinct intensities for innovators.

VARIABLES	Price (1)	Quantity (2)
After (δ_s)	0.081	-0.458
	(0.16)	(0.36)
Treated 1(λ_{1i})	-0.331	1.012
	(0.43)	(0.81)
Treated 2(λ_{2i})	-0.740	2.492*
	(0.59)	(1.29)
Treatment 1 (T1)	**-0.072**	**0.515**
	(0.14)	(0.44)
Treatment 2 (T2)	**-0.257**	**0.454**
	(0.21)	(0.62)
Constant	8.027***	6.325***
	(0.53)	(0.96)
Observations	3,156	3,156
R-Square	0.559	0.546

Note: Robust cluster standard error at the level of the group of molecules paired with PSM in parenthesis. *** significant at 1%, ** significant at 5%, * significant at 10%. Dummy variables to control for time and the matched molecules are included, as well as controls for post-entry differences (bioequivalence and unbranded generic presence). Source: Authors' own calculations with data from IMS Health.

The evaluation of the branded generic impact would be incomplete without the assessment over the total doses sold in the market, that is the capacity that branded generics have for increasing the market and reach new patients. According to column 1 of table 12, the branded generic competition induces an increment of 148.1% in the supply of medicine doses, magnitude that moderately decrease when the 4 molecules exposed to the collusion are moved away from the estimation. The results in column 3 reveals that a larger number of branded competitors exerts a bigger impact in the market supply. Indeed, the coefficient of the second treatment indicates an increase of 198% in the market supply, in contrast with the 141.1% of the first treatment. Both of them are statistically significant.

The upshot of all the results exposed above is that, even though the market is segmented with the innovators serving a niche with high prices after the branded generic entry, the branded generic competition has an important impact on social welfare. In fact, its prices are nearly one-third lower than the innovators and enhance a dramatically huge expansion of the retail market supply.

Table 12: Difference in difference for the total doses sold in the market.

VARIABLES	(1)	(2)	(3)
After	-0.336	-0.378	-0.479
	(0.33)	(0.37)	(0.36)
Treated	1.444*	1.323*	
	(0.73)	(0.68)	
Treatment	**0.909***	**0.796****	
	(0.46)	(0.37)	
Treated 1			1.119
			(0.80)
Treated 2			2.681**
			(1.28)
Treatment 1			**0.880***
			(0.43)
Treatment 2			**1.093***
			(0.58)
Constant	5.528***	5.369***	6.117***
	(0.87)	(0.79)	(0.95)
Observations	3,156	2,668	3,156
R-Squared	0.570	0.588	0.594

Note: Robust cluster standard error at the level of the group of molecules paired with PSM in parenthesis. *** significant at 1%, ** significant at 5%, * significant at 10%. Dummy variables to control for time and the matched molecules are included, as well as controls for post-entry differences (bioequivalence and unbranded generic presence). Column 2 reports the results excluding the 4 molecules, and its counterfactuals, involved in the collusion of prices; and column 4 considers the two intensities of treatment. Source: Authors' own calculations with data from IMS Health.

VI. Conclusions.

This paper provides empirical evidence of the effects of the branded generic entry over prices and quantities in the retail pharmaceutical market. We identify 47 molecules that experiences branded generic competition for the first time between January 2002 and July 2017. Using a Hausman-Taylor model for the 47 molecules, we trace the changes of the price differential between branded generic and innovators in the post-entry period. Then we study the effect of branded generic competition over prices and quantities of the innovator, as well as the impact over the total doses dispensed in the market. In this case, our empirical strategy considers a propensity score matching with differences in differences estimation, for which 26 molecules were used.

The Hausman-Taylor model allows us to estimate the true price differential between branded generics and innovators, that reaches a -18% the first year of competition, almost 10 percentage points lower from the gross relative price (see table 5). The true price differential keeps relatively stable through the branded competition period, reaching -18.7% in the subsequent period from the 48th month post-entry, that compares with the -33% gross differential.

We find that the branded generic competition has a huge positive effect of 148.1% over the total doses dispensed in the market, with respect to the counterfactual. The expansion of the availability of doses could be explained by the significantly lower prices of branded generics, that reach a gross differential of -33% with respect of the innovators, 4 years after the beginning of the competition period. This allows the incorporation of new patients that were previously excluded from the pharmacological therapies or used less effective drugs. It is important to note that this impact over the social welfare -higher doses sold at a lower price- is directly attributable to the branded generic competition, and to no other factors such as the seasonality that have been properly controlled. Also, when two intensities of treatment were considered, a larger effect was found with the intensity associated with a higher number of branded generic competitors.

Consistent with the literature, our findings indicate that the innovator prices do not react to the branded generic entry, validating the market segmentation theory for the Chilean pharmaceutical market. Indeed, even though the point estimate on the treatment indicator is negative in the different estimations, none of them is statistically significant. When the

estimation is done for the doses dispensed by the innovator the point estimate is positive but lacks statistical significance.

Future research may focus on improving our empirical strategy by replacing the propensity score matching for the exposure to branded competition, finding an exogenous instrument related to the branded generic entry. Although we do not expect a major shift from the results reported in this research, it would make them more robust. Another valuable contribution would be the replication of our approach for a panel of Latin-American countries, that would give the chance not only to evaluate how the estimations variates from one country to another, but also will allow to control for the institutional framework of each country.

VII. References.

Bergman, M. A., & Rudholm, N. (2003). The relative importance of actual and potential competition: empirical evidence from the pharmaceuticals market. *The Journal of Industrial Economics*, *51*(4), 455-467.

Bonfrer, A., & Chintagunta, P. K. (2004). Store brands: who buys them and what happens to retail prices when they are introduced? Review of Industrial Organization, 24(2), 195-218.

Caves, R. E., Whinston, M. D., Hurwitz, M. A., Pakes, A., & Temin, P. (1991). Patent expiration, entry, and competition in the US pharmaceutical industry. Brookings papers on economic activity. Microeconomics, 1991, 1-66.

Centro Nacional de Fármaco-Economía (2013). Medicamentos en Chile: Revisión de la evidencia del mercado nacional de fármacos. Instituto de Salud Pública. Retrieved September 25, 2017, from: http://www.ispch.cl/sites/default/files/EstudioMedicamentos-22012014A.pdf.

Court of Defense of Free Competition (2006). Resolución 15/2006 sobre consulta de la Fiscalía Nacional Económica sobre contrato de franquicia de Socofar S.A, Santiago de Chile, 2 de Agosto de 2006. Retrieved September 6, 2017, from: http://www.tdlc.cl/tdlc/wp-content/uploads/resoluciones/Resolucion-15-2006.pdf.

Court of Defense of Free Competition (2012). Sentencia Nº119/2012, Santiago, Chile, 31 de Enero de 2012. Retrieved September 15, 2017, from: http://www.tdlc.cl/tdlc/wp-content/uploads/sentencias/Sentencia_119_2012.pdf.

Crawford, G. S., & Shum, M. (2005). Uncertainty and learning in pharmaceutical demand. *Econometrica*, 73(4), 1137-1173.

Ching, A. T. (2010). Consumer learning and heterogeneity: Dynamics of demand for prescription drugs after patent expiration. International Journal of Industrial Organization, 28(6), 619-638.

Danzon, P. M., & Furukawa, M. F. (2011). *Cross-national evidence on generic pharmaceuticals: pharmacy vs. physician-driven markets*. National Bureau of Economic Research. Working Paper No. w17226.

Danzon, P. M., Mulcahy, A. W., & Towse, A. K. (2013). Pharmaceutical pricing in emerging markets: effects of income, competition, and procurement. *Health economics*, *24*(2), 238-252.

Danzon, P. M. (2014). Competition and Antitrust Issues in the Pharmaceutical Industry. *CRC America Latina-Centro Regional de Competencia para America Latina.* Retrieved September 11, 2017, from: https://faculty.wharton.upenn.edu/wp-content/uploads/2017/06/Competition-and-Antitrust-Issues-in-the-Pharmaceutical-IndustryFinal7.2.14.pdf.

Decree Nº3 (2011). Establece Reglamento del Sistema Nacional de Control de los Productos Farmacéuticos de Uso Humano. Retrieved August 20, 2017, from: https://www.leychile.cl/Navegar?idNorma=1026879&idParte=0.

Decreto Nº500 (2011). Aprueba norma técnica N°0136, nominada “norma que determina los principios activos contenidos en productos farmacéuticos que deben demostrar sus equivalencia terapéutica y lista de productos farmacéuticos que sirven de referencia de los mismo. Retrieved August 19, 2017, from: http://www.ispch.cl/sites/default/files/decreto_exento_500.pdf.

De Loecker, J. (2007). Do exports generate higher productivity? Evidence from Slovenia. *Journal of international economics*, 73(1), 69-98.

Ellison, G., & Ellison, S. F. (2007). Strategic entry deterrence and the behavior of pharmaceutical incumbents prior to patent expiration. National Bureau of Economic Research. Working Paper No. w13069.

European Comission (2009), Pharmaceutical Sector Inquiry Final Report, de la Comisión Europea. Retrieved March 25, 2018, from: http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf.

Federal Economic Competition Commission of México (2007), Estudio en materia de libre concurrencia y competencia sobre los mercados de medicamentos con patentes vencidas en México, de la Comisión Federal de Competencia Económica de México. Retrieved August 12, 2017, from: https://www.cofece.mx/cofece/attachments/article/769/Estudio-de-Medicamentos_vF-BAJA.pdf.

Frank, R. G., & Salkever, D. S. (1991). *Pricing, patent loss and the market for pharmaceuticals* National Bureau of Economic Research. Working Paper No. w3803.

Ganther, J. M., & Kreling, D. H. (2000). Consumer perceptions of risk and required cost savings for generic prescription drugs. *Journal of the American Pharmaceutical Association (1996)*, *40*(3), 378-383.

Grabowski, H. G., & Vernon, J. M. (1992). Brand loyalty, entry, and price competition in pharmaceuticals after the 1984 Drug Act. *The Journal of Law and Economics*, *35*(2), 331-350.

Halvorsen, R., & Palmquist, R. (1980). The interpretation of dummy variables in semilogarithmic equations. American economic review, 70(3), 474-475.

Hausman, J. A., & Taylor, W. E. (1981). Panel data and unobservable individual effects. Econometrica: Journal of the Econometric Society, 1377-1398.

Hurwitz, M. A., & Caves, R. E. (1988). Persuasion or information? Promotion and the shares of brand name and generic pharmaceuticals. *The journal of law and economics*, *31*(2), 299-320.

Kaplan, W. A., Wirtz, V. J., & Stephens, P. (2013). The market dynamics of generic medicines in the private sector of 19 low and middle income countries between 2001 and 2011: a descriptive time series analysis. *PLoS One*, *8*(9), e74399.

Kong, Y. (2000). Prices and Pricing in Imperfectly Cornpetitive Markets (Tesis Doctoral). Carleton University, Ottawa. Retrieved August 25, 2017, from: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.471.3154&rep=rep1&type=pdf.

Law Nº19.039 (2005). Establece Ley de Propiedad Industrial, Ministry of Economy, Development and Tourism. Retrieved August 30, 2017, from: https://www.leychile.cl/Navegar?idNorma=30406.

Law Nº20.724 (2014). Establece Ley de Fármacos que modifica el Código Sanitario en materia de regulación de farmacias y medicamentos, Ministry of Heath. Retrieved August 25, 2017, from: https://www.leychile.cl/Navegar?idNorma=1058373.

Magazzini, L., Pammolli, F., & Riccaboni, M. (2004). Dynamic competition in pharmaceuticals. *The European Journal of Health Economics, formerly: HEPAC*, *5*(2), 175-182.

Ministry of Health (2015). Distribución de farmacias por región, situación a 2015. División Políticas Públicas Saludables y Promoción, del Ministerio de Salud de Chile. Retrieved August 27, 2017, from: http://web.minsal.cl/wp-content/uploads/2015/09/2015_06-DISTRIBUCI%C3%93N-FARMACIAS-junio-2015-2.pdf.

Putsis, W. P. (1997). An empirical study of the effect of brand proliferation on private label–national brand pricing behavior. Review of industrial Organization, 12(3), 355-371.

Regan, T. L. (2008). Generic entry, price competition, and market segmentation in the prescription drug market. *International Journal of Industrial Organization*, 26(4), 930-948.

Rosenbaum, P. R., & Rubin, D. B. (1983). The central role of the propensity score in observational studies for causal effects. *Biometrika*, 70(1), 41-55.

Salop, S. C. (1979). Monopolistic competition with outside goods. *The Bell Journal of Economics*, 141-15.

Schmalensee, R. (1982). Product differentiation advantages of pioneering brands. *The American Economic Review*, *72*(3), 349-365.

Vasallo, C (2010). El Mercado de medicamentos en Chile: caracterización y recomendaciones para la regulación económica. Ministerio de Salud de Chile. Retrieved August 29, 2017, from: http://web.minsal.cl/wp-content/uploads/2015/09/Informe-Vassallo-2010.pdf.

Warshaw, G. (2006). Introduction: advances and challenges in care of older people with chronic illness. *Generations*, 30(3), 5-10.

Wooldridge, J. M. (2002). Econometric analysis of cross section and panel data MIT Press. Cambridge, MA.

VIII. Appendix.

Appendix A: Description for the 47 molecules.

Molecule	Therapeutic class	Date of the first branded generic entry	(1)	(2)	(3)
Cefuroxime	Antiinfectives	October 2009	2	13	18.9
Efavirenz		December 2014	1	3	64.8
Minocycline		August 2002	3	13	32.8
Oseltamivir		August 2006	3	2	8.4
Capecitabine	Antineoplasic	April 2015	1	4	2.9
Ciclosporin		September 2007	2	18	15.4
Exemestane		January 2013	2	10	11.8
Imatinib		January 2009	1	10	11.7
Letrozole		May 2004	3	8	1.4
Mycophenolate Mofetil		July 2005	3	17	3.2
Temozolomide		October 2007	1	7	6.6
Bisoprolol	Cardiovascular	April 2014	3	25	69.1
Ciprofibrate		November 2010	3	11	38.1
Telmisartan		March 2002	2	30	13.5
Valsartan		September 2002	8	26	63.2
Calcitriol	Alimentary tract and Metabolism	January 2009	1	7	12.7
Glimepiride		May 2009	4	11	23.1
Orlistat		September 2007	5	31	345.0
Pioglitazone		March 2003	2	3	4.6
Racecadotril		May 2007	1	5	1.5
Vildagliptin		December 2010	1	4	7.0
Cabergoline	Genito-urinary	September 2009	1	5	19.9
Tolterodine		March 2009	2	13	9.2
Celecoxib	Musculo-skeletal	January 2015	5	10	454.9
Hydroxychloroquine		June 2009	4	7	53.7
Ibandronic Acid		April 2007	8	16	36.0
Leflunomide		November 2003	3	6	21.6
Oxaprozin		August 2004	1	96	36.0
Warfarin	Blood and blood forming organs	July 2013	1	6	27.5
Agomelatine	Nervous sytem	March 2012	1	27	3.4
Clozapine		November 2007	2	39	26.3
Diphenidol		May 2010	4	7	30.8
Donepezil		October 2002	7	7	22.2
Duloxetine		January 2008	6	17	49.9
Eletriptan		February 2015	3	14	29.9
Escitalopram		March de 2004	14	50	36.3
Fluvoxamine		July 2010	1	57	7.3
Galantamine		July 2007	2	11	1.1
Naratriptan		April 2006	6	10	26.5
Olanzapine		March 2005	7	36	70.2
Pramipexole		May 2007	5	13	34.5
Pregabalin		December 2006	11	63	68.1
Rivastigmine		August 2004	1	11	32.1
Topiramate		March 2003	5	68	6.5
Trazodone Chlorhydrate		May 2003	4	31	36.1
Desloratadine	Respiratory system	July 2003	9	53	56.5
Montelukast		March 2004	5	5	23.4
Average			3.6	20	42

Note: (1): Maximum number of branded generic competitors; (2): Maximum number of substitutes; (3): Total sale revenues (in millions of pesos) the month before first entry. Source: Authors' own calculations with data from IMS Health.

Appendix B: Post-entry variation of innovator prices.

Molecules	Pre-entry ($)	Post-entry ($)	Variation (%)	6th Month ($)	12th Month ($)	24th Month ($)	48th Month ($)	Variation 48th Month – 6th Month (%)
Agomelatine	673	614	-9	637	650	610	605	-10
Desloratadine*	336	170	-49	222	219	176	163	-52
Diphenidol	309	234	-24	237	262	204	239	-23
Donepezilo*	1,936	1,480	-24	1,854	2,029	1,908	1,338	-31
Escitalopram*	580	415	-28	505	492	410	415	-29
Galantamine	2,523	2,091	-17	2,398	1,957	2,400	2,410	-4
Glimepiride	216	225	4	224	209	197	238	10
Ibandronic Acid	361	398	10	260	407	391	419	16
Letrozole	2,717	2,192	-19	2,638	2,673	2,615	2,082	-23
Mycophenolate Mofetil	5,331	4,730	-11	5,236	5,286	5,284	4,511	-15
Montelukast	1,042	1,019	-2	955	1,028	887	1,089	4
Naratriptan	1,198	916	-23	1,108	1,049	1,418	765	-36
Pregabalin*	1,490	1,580	6	1,245	917	1,583	1,635	10
Temozolomide	94,897	85,731	-10	101,921	93,577	90,170	82,282	-13
Topiramate	3,630	3,842	6	4,406	4,446	4247	3,677	1
Valsartan*	232	183	-21	207	240	222	178	-23
Vildagliptin	224	225	0.4	228	221	219	227	1
Warfarin	564	639	13	535	538	625	792	41
Bisoprolol	642	831	30	822	778	794	876	36
Cabergoline	5,456	6,445	18	5,927	6,031	5,799	6,854	26
Calcitriol	1,371	1,452	6	1,519	1,488	1,628	1,414	3
Capecitabine	2,000	1,639	-18	1,610	1,584	1,667	-	-
Cefuroxime	1,325	1,276	-4	1,255	1,235	1,234	1,298	-2
Celecoxib*	456	472	3	522	508	456	-	-
Ciclosporin	5,019	4,325	-14	4,350	4,030	4,173	4,426	-12
Ciprofibrate	397	419	6	432	424	414	417	5
Clozapine	1,803	1,884	5	1,715	1,669	1,829	1,977	10
Duloxetine	601	575	-4	431	571	593	590	-2
Efavirenz	4,148	2,512	-39	2,897	2,702	1,875	-	-
Eletriptan	1,933	2,368	22	2,239	2,313	2,493	-	-
Fluvoxamine*	68	54	-21	67	69	64	45	-33
Exemestane	2,612	2,039	-22	2,271	2,196	2,046	1,826	-30
Hydroxychloroquine	1,083	1,202	11	1,015	1,105	1,269	1,242	15
Imatinib	25,906	28,639	11	34,391	32,248	30,597	26,527	2
Leflunomide*	1,015	1,007	-1	1,106	1,018	877	1,034	2
Minocycline	5.2	6.5	25	5.4	5.7	5.7	7.6	48
Olanzapine*	2,654	1,985	-25	2,329	2,399	2,523	1,837	-31
Orlistat	1,076	991	-8	946	857	873	1,034	-4
Oseltamivir	3,009	2,833	-6	3,255	3,306	2,531	2,817	-6
Oxaprozin	329	371	13	354	357	310	390	19
Pioglitazone	1,088	604	-45	1,327	1,329	954	437	-60
Pramipexole	1,996	1,813	-9	1,094	1,036	1,663	1,866	-7
Racecadotril	435	450	4	448	449	471	442	2
Rivastigmine	2,431	1,799	-26	1,947	1,821	1,654	1,824	-25
Telmisartan*	209	194	-7	193	188	209	195	-7
Tolterodine	521	535	3	536	556	573	527	1
Trazodone Chlorhydrate*	1,144	1,222	7	1,227	1,195	974	1,292	13
Average	4,021	3,758	-7	4,278	4,035	3,917	3,820	-11
Average without *	4,669	4,663	-0.1	5,321	5,011	4,853	4,574	-14

Note: The price reported in the table corresponds to the average of the weighted average real price calculated by denomination for each molecule. With (*) are marked the molecules affected by the collusion of pharmacies. Source: Authors' own calculations with data from IMS Health.

Appendix C: Estimation of the propensity score.

VARIABLES	TREATED_1=1	TREATED_2=1
cp_{-12}	1.747	-2.355
	(1.61)	(4.87)
cp_{-11}	2.396	-1.759
	(2.08)	(5.63)
cp_{-10}	5.337***	6.585
	(1.84)	(4.27)
cp_{-9}	3.604*	7.283*
	(2.04)	(4.14)
cp_{-8}	2.539	-1.122
	(2.07)	(5.22)
cp_{-7}	1.350	-1.345
	(1.97)	(3.78)
cp_{-6}	1.384	-2.015
	(1.86)	(3.60)
cp_{-5}	-2.427	-8.349***
	(1.77)	(2.99)
cp_{-4}	-1.253	-3.968
	(1.87)	(3.29)
cp_{-3}	0.678	-1.188
	(1.96)	(3.71)
cp_{-2}	0.0729	-6.324
	(1.97)	(4.11)
cp_{-1}	0.462	-6.655*
	(1.84)	(3.69)
$\psi_1 (= A)$	1.304***	-7.240
	(0.44)	(302.5)
$\psi_2 (= B)$	2.088***	-
	(0.68)	
$\psi_3 (= C)$	-	-8.374
		(302.5)
$\psi_4 (= G)$	1.133**	-
	(0.57)	
$\psi_5 (= J)$	0.861*	-8.690
	(0.50)	(302.5)
$\psi_6 (= L)$	1.526***	-
	(0.41)	
$\psi_7 (= M)$	1.291***	-7.702
	(0.49)	(302.5)
$\psi_8 (= N)$	-	-8.590
		(302.5)
Chronic$_{-1}$	0.475	-0.696
	(0.30)	(0.43)
Market Size$_{-1}$	9.68e-09	6.57e-08***
	(6.53e-09)	(1.28e-08)
Age$_{-1}$	0.004**	0.002
	(0.002)	(0.002)
NumSub$_{-1}$	0.028***	0.009
	(0.01)	(0.02)
Presentations$_{-1}$	0.300	0.064
	(0.20)	(0.31)
Constant	-5.219***	3.923
	(0.76)	(302.5)
Observations	3,557	3,493

Note: *** significant at 1%, ** significant at 5%, * significant at 10%. TREATED_1 considers the molecules that experience on average less than 1.7 competitors in the post-entry period, while TREATED_2 considers those that exceed that number of competitors. Source: Authors' own calculations with data from IMS Health.