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The Competitive Impact of Branded Generic Medicine in a Developing Country

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Abstract[4]

This paper studies the effect of the entry of branded generic medications — representing 47 molecules — between January 2002 and July 2017 in the Chilean retail pharmaceutical market. Using a differences-in-differences approach, we measure the impact on prices and quantities on the market after the entry of branded generic pharmaceuticals, following the patent expiration of innovator drugs. The results show that in a period of 48 months from the first entry, the quantities sold in the retail market increased by 148.1%. This is explained by the lower prices of the branded generics, as the gross average price is 33% cheaper than the innovator alternatives. Finally, no statistically significant effect is observed on prices and quantities for innovators, suggesting that the segmented market theory might apply to the Chilean pharmaceutical market.

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

JEL Classification: I11; L11; L65.

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I. Introduction.

The population's access to drugs at affordable prices has been a constant concern for governments. An important research topic for this is the evaluation of changes experienced in markets where generics enter the market once the original patent has expired. Most of the literature has focused on the price effect of entry, specifically whether the incumbent reacts to the presence of competition once the patent expires, yet no attention has been paid to the impact on quantity. Even if the incumbent does not react to the entry of generics, there may still be a positive impact on welfare if more consumers acquire the drugs from the entrants.

In addition, existing research has examined pharmaceutical markets in developed countries, where unbranded generics rapidly penetrate the market after patent expiration. However, there is little evidence currently available from environments where branded competition is the common standard, as is the case of Latin American countries.

In Latin America, pharmaceutical markets are usually divided in three segments or drug denominations: innovators, branded generics — often called "similar", — and unbranded generics. Innovators are drugs whose creators were granted patent protection for a period of at most 20 years. Once the patent expires, generics are allowed to enter the market. The branded generics are copies of the original that have a brand name, while unbranded generics are sold under the name of the molecule, i.e. the international common denomination (ICD).

Our research provides novel evidence on this issue using data for Chile, contributing to the discussion on the impact of the introduction of branded generics of medicines. With this purpose, we analyze the effect of generic branded entry — in prices and quantities — of 47 molecules between January 2002 and July 2017 in the retail pharmaceutical market in Chile. We look at the causal effect of branded generic competition on innovator prices and amount sold, as well as the effect on the total volume sold. We use a propensity score matching with differences-in-differences, and two types of treatments are considered. The

first treatment captures the impact of passing through the monopoly to a competition regime; while the second considerers the differentiated impact provoked by the different degrees of competition, e.g. the number of branded generic competitors.

What that impact might be isn't clearly shown by theory. Two hypotheses are suggested to explain the possible response of innovator prices to generic competition. On the one hand, if the theory of segmented markets (Grabowski and Vernon, 1992; Frank and Salkever, 1991) applies to pharmaceuticals, we should see no response in innovator prices. This theory hinges on the fact that the innovator kept the inelastic part of the demand, while more price sensitive customers switch to the generic competitor. On the other hand, branded generics could exert a greater competitive pressure on innovators, because they also have a brand and make a sales effort to penetrate the market, thus becoming closer substitutes of innovators for most of the customers.[5]

Our results show that the branded generic entry produces a significant impact on the market in terms of the availability and prices of the drugs. The total doses available in the market increase 148.1% on average in the 48 months post-entry period, an effect that is directly attributable to the branded generic competition. This increase could be explained by the lower prices of branded generics that, in the gross average, are 33% cheaper than the innovator options. These results suggest a significant impact on welfare due to the entry of branded generics in the market. Regarding the reaction of innovators to the entry of competitors, we found no evidence of variations in the prices and quantities of the incumbent, a result that would validate the hypothesis of segmented markets for the case of Chile

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 discusses the empirical strategy. Section V presents the main results and Section VI the conclusions.

[5] According to Kong (2000) the elasticity of substitution between innovators and branded generic drugs is larger than the same elasticity between innovators and pure generic medicines.

II. Literature Review

It is a tenet in economic theory that the entry of competitors into a market controlled by a monopolist causes prices to fall. However, if the market is segmented after entry, pre-entry monopoly price may prevail. Part of the available evidence agrees that the latter is true for the pharmaceutical market. Grabowski and Vernon (1992) were among the first who stated that the incumbents or innovators' prices did not alter its pattern in front of the entrance of generic competition, although these generics drugs exhibited a huge decline in the marginal cost. So, these authors proposed a market segmentation theory that suggests that brand-loyal consumers with an inelastic demand care 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 for the decision to buy the medicine is delegated to health professionals (Danzon, 2014), Frank and Salkever (1991) argue that the market segmentation is produced by the pattern of medical prescription.[6] In this sense, the authors claim that the health professionals whose patients have private health insurance are more risk averse and, therefore, are more tied to their prescription habits of prescribing innovation drugs. Moreover, they suggest that these professionals have not incorporated in their utility function the cost containment of the patient. Consequently, patients using this kind of health professional become the brand-loyal segment.

Crawford and Shum (2005) add that patients are also risk averse, suffering a reduction in their utility when a new drug replaces the one that has been historically prescribed to them. In this context, it is reasonable to think that a group of patients will remain loyal to innovative medicines, even though they could save money by switching to generics.

Instead of assuming that the two segments would be independent as in Grabowski and Vernon (1992) and Frank and Salkever (1991), Kong (2000) suggests that realistically there is some degree of cross-substitutability between innovator and generic pharmaceuticals.

[6] For a detailed description of the principal-agent problem in the pharmaceutical market see Danzon (2014).

According to this model, the generic competition paradox occurs as long as the marginal cost of the generic drug is relativity large.[7] On the other hand, from this framework, it can be suggested 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 have to react by lowering prices.

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 enters the market has a product differentiation advantage that allows it to establish higher prices than following brands, and it retains a significant portion of the market. Indeed, the incumbent 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 for consumers and overcome their brand loyalty. Empirically, there is ample evidence that in the pharmaceutical market, the innovator has a huge advantage that persists in the post-patent period.[8]

The price response of the innovator to generic entry has been widely studied for rich economies.[9] The evidence from these countries has been mixed, without agreement on the competitive effects on innovators from the generic entry. For the US pharmaceutical market, Regan (2008) approaches 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 instrumental variables, estimates that each additional generic competitor increases innovator prices by 2% in average, while it does not have any significant effect on other generics. [10]

[7] 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 can be obtained: , where is the cost of the generic pharmaceutical; is the own-price elasticity; is the elasticity of substitution, that is the responsiveness of the drug demand to changes in the substitute drug; and is a demand parameter. So, the innovator's price will increase as long as is bigger than the right-hand part of the inequality.

[8] 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 patent.

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

[10] 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

To the contrary, Caves et al (1991), instrumentalizing the number of generic competitors through the volume of sales the year before the patent expiration and the time passed since the patent expiration, finds that each additional generic reduces prices by 0.8%. In the same line, Bergman and Rudhom (2003) studied the price response to generic entry in the Swedish market, finding that the patent expiration in and of itself has a significant effect of -5% on innovator prices, while each additional competitor reduces the innovator's price between 4 and 7% on average.

The research of the competitive impact of generic entry has been exiguous in developing countries. These markets differ from the richest economies because they have a significant share of branded generic products. In the last decade, an incipient literature has made explicit reference to branded generic pharmaceuticals. Danzon and Furukawa (2011) build a panel of middle and high-income countries, and found only in the case of Mexico — a country whose pharmaceutical market has similar characteristics to Chile —that the number of branded generic manufacturers has a positive significant impact on the average price of generics, but has no impact on the prices of the innovators. These results might suggest that Mexican laboratories decide to compete based on brand, avoiding the competition on prices.

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

The evidence of the evolution of the relative prices is merely descriptive without correcting, for example, for the differences caused by the time that such drugs have been on the market among others. For the Mexican pharmaceutical market, Mexico's Federal Economic Competition Commission (2017) reports that on average the prices of generics are 28.6%

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the initial generic entrants were granted six months of exclusive rights; and (3) the number of Abbreviated New Drugs Applications approved by the FDA.

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 24 months from the initial entry of generics (European Commission, 2009).

III. Data

The database was provided by IMS Health[11] and collects information on monthly sales revenues of the medicines sold in pharmacies between January 2002 and July 2017 — 187 months.[12] This data considers all monomolecular oral medicines dispensed with medical prescription.

The database reports sales revenues and the number of pills sold monthly for each medicine, allowing us 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). This is situation that could bias t comparisons, thus 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 prescription in adults[13]. With this data, the average price per DDD for the drug i in the period t, was obtained in the following way:

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

[11] IMS Health is an international company specializing in gathering data for the health industry. It is the main source of information for price research and strategic managing.

[12] The sales revenues are obtained from the 3 main retail chains (FASA, Cruz Verde, and SalcoBrand), independent retail pharmacies, and the 3 main distributors (Toledo, Socofar, and Drogueria Ñuñoa).

[13] This unit of measure is determined by World Health Organization (WHO), we created it with using information from www.whocc.no/atc_ddd_index. For those molecules that there is no DDD defined by WHO, we used the mode of the different options of the molecule available in the market all time. If two or more doses constitute the mode, we opted for the lower concentration.

The prices obtained with (1) were deflected to January 2002 prices using the Consumer Price Index (CPI), so the changes reported in this paper correspond to actual variations.[14]

Among the 618 molecules in the database, we identify those that faced generic competition for the first time, removing those molecules that already faced competition before 2002. Molecules with less than a year of exposure to competition were eliminated.[15] Thus our data set consists 47 molecules, accounting for 262 drugs. Seventy-two percent of the drugs are branded generics, 22% are innovators, and 5.7% are unbranded generics. We group unbranded generics into the "Generics" category, without any identification of the distinct pharmaceutical products.[16] Note that in every one of the 47 cases, the first entrant is a branded generic, and unbranded alternatives tends to be late to the market.

A complete description of the main characteristics of the 47 molecules identified is presented Appendix A. Telmisartan has the longest branded generic competition with 185 months, while Capecitabine has the lowest of 28 months. In general, the 47 molecules have 119 months of exposure to branded generic competition.

Table 1 provides descriptive information of the number of competitors at different post-entry time points. In the first row, the average number of branded generic competitors is 1.2 after 6 months 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.[17] 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 whose molecules belongs to the same chemical

[14] The monthly CPI data was downloaded from the website of the Central Bank of Chile — http://si3.bcentral.cl/Siete/secure/cuadros/home.aspx — accessed on October 4th, 2017.
[15] Only 2 cases were in this situation: Pazopanib and Pirfenidone, with 2 and 4 months of generic competition.
[16] There is not much data about unbranded generic products 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.
[17] The Anatomical Therapeutic Chemical (ATC) Classification System classify 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 is its own molecule. The fourth level corresponds to the family of molecules that belongs to the same chemical subgroup. This ATC system is elaborated by the WHO.

subgroup according to the ATC-4 — at 6 months after the beginning of competition, a number that is keep relatively constant through the whole post-entry period.

Table 1: 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 2 describes the impact of branded generic competition on innovator prices. Price reports on the table correspond to the average of the weighted average price of the 47 molecules, where the weights are the monthly doses for each drug. In the first row, the innovator prices decline 7% in the branded competition period compared to the monopoly period. In Appendix B it could be seen that, in disaggregated terms, 27 of the 47 molecules (57%) experience a comparative price decrease in the post-entry period.

Table 2: 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 prices for the 47 molecules that experience entry for the first time in the data; (2) excludes 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 2, the 11 molecules exposed to the collusive agreement between pharmacies were removed.[18] Assuming that the prices of the remaining 36 molecules represent a competitive equilibrium, the variation in the innovator prices is negligible with a change of -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, row (3) reports the price evolution \ 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 Temozolomide, which has a unitary price of $94,897 per dose. Despite the previous, no major variation is registered from the results previously mentioned.

Table 3 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 being considered for the relative price determination, no bigger difference 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 continues to decrease to 33% less 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), compared with 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%.

[18] According to the Chilean Competition Tribunal (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 market leaders at the time, which were mainly innovators.

Table 3: 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 to innovator price ratio of each molecule. (1) Reports average relative price for the 47 molecules entering the market for the first time in the data; (2) exclude the molecules affected by the pharmacy collusion; (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 4 analyzed the average growth rates in the volume of doses sold by innovators in post-entry period. In 19 cases, the innovator exhibits positive rates, but only in two of the cases is 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%. On average, the monthly growth rate is 0.54% for innovators and 2.5% for branded generics.

Table 4: Classification of the innovators according to the post-entry growth rate by sales 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 sold per month as a dependent variable, and a trend as an explanatory variable. Source: Authors' own calculations with data from IMS Health.

Finally, Table 5 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 45% at the 48th month of competition. In column (*), for the 26 molecules used in the following sections, branded generics have a 41% share of the market at the 48th month. Unbranded generics have an inappreciable share during the first 4 years of competition, with a market share of 0.2% on average at the 48th month.[19]

Table 5: 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 lets us theorize that the innovator laboratories keep captive a segment of the market —although some are more sensitive to competition than others — probably through a mechanism argued by Frank and Salkever (1991) associated with the pattern of prescription, or the brand loyalty as mentioning 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. Another possible hypothesis is that the reduction in the

[19] Although we do not know the number of unbranded generic competitors, we do know the total volume of doses they sell, and hence their share in the retail market.

pharmaceutical cost of the treatment encourages new patients to try the medication, who will only be open to use generics due to their price sensitivity.

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 of interest by tackling the problem of selection bias, but also helps us to diminish the concerns about the exogeneity condition of generic entry. That is, after controlling for a set of observable characteristics that determine the probability that a particular drug experiences in entry, and assuming that no other variable is missing in the model, the entry becomes a pure lottery event.

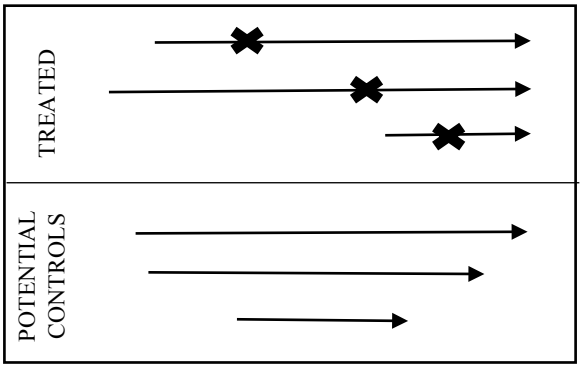
On the other hand, DiD provides a way to deal with unobserved heterogeneity, assuming that the source of that heterogeneity is time invariant so the bias can be discarded by the differencing process. In this framework, the estimation of the effect of branded generic competition on prices and quantities considers two different treatments. First, a linear 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 changing from 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, the next step will contemplate two intensities of competition.

There is one characteristic of the data that hampers us in implementing the PSM in 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 into the off-patent markets. Of course, the consequence is that the beginning and the ending of the monopoly period and competition one 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 is not possible either to identify *a priori* 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 becoming control molecules.[20]

A solution to this problem is mention by De Loecker (2007), who suggests leaving calendar time, rescaling the periods so the molecules start experiencing competition at s=0. Thus 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.[21] Hence, we have 61 periods showing the effect of competiton on prices. 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.

[20] Besides it must be noted 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 database, others are only in the market for less than a quarter of that period extension.

[21] Note that the objective was, at least, to have a year of pre-treatment data, considering 13 months of pre-treatment does 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.

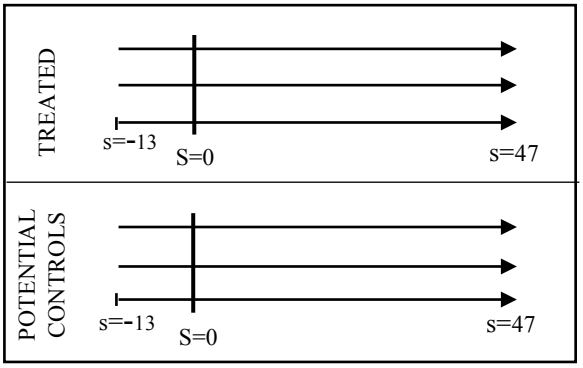
Then we have to identify a group of molecules that can be used as potential counterfactuals for the treated molecules. When doing so, all the molecules that were under monopoly between January 2002 and July 2017 were selected, but we only kept those that at least have 61 periods of presence in the data, ending with 56 molecules. As 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 is in the database. As a result, 4.492 potential controls were generated for the 33 molecules exposed 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:

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

The most relevant variables in the estimation of the propensity score are the rates of price changes during the twelve periods before the beginning of the competition, $cp_{i,-s}$. This set of variables is fundamental in order to dissipate the pre-treatment differences in the evolution of prices. Following Caves et al. (1991) we include a specific effect in 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 in the month before the beginning of the competition is included, for which the subscript -1 is used. The size of the market of the molecule, $SIZE_{i,-1}$, is included as in Grabowski and Vernon (1992), which is suggested as one of the main predictors of the generic entry. $NUMsub_{i,-1}$is the number of other available substitute drugs that the molecule i faces, which contain other active principle 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 of the molecule i; that is the number of forms that differs 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 larger the cost for the generic competitor to reproduce 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 may more quickly enter a market for chronic patients, as they should exhibit a more inelastic demand for the drug they need.[22]

Model (2) is estimated considering two samples, reflecting two different intensities of competition. Consequently, the sample of molecules that experience 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. Thus treatment 1 incorporates all those molecules that on average experience less than 1.7 branded generic competitors, while treatment 2 includes those that exceed an average of 1.7 competitors.

[22] 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 daily life activities

Then, separately for each treatment with the propensity scores obtained in (2), the molecules are matched in the common support. The matching is done by applying the nearest neighbor criteria, which is implemented without repetition.

Note that the fundamental assumption behind this method is that, conditional to the observable characteristics mentioned above, belonging to the group of molecules that experiences competition or the control group is equivalent to a lottery (Rosenbaum and Rubin, 1983). To put it bluntly, pre-existent 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 changes in prices or quantities over time between the treatment and control group. As previously mentioned, 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):

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

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 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 and accordingly 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 the calendar time. Variables are included in Π_i 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 medication of molecule i; and the unbranded generic

indicator takes the value of 1 if the molecule i faces unbranded generic competition in the month t.[23] Finally, ε_{is} is the stochastic error term.

The coefficient of interest in (3) is β_3, which gives us the DiD estimator, and therefore the causal impact of branded generic competition over the prices (quantities). The second DiD specification (4) considers the two intensities defined above:

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

Where Y_{is}, δ_s, Π_i, and Ω_i are defined in the same terms as in (3), but now λ_i and Δ_{is} are substituted with 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 with 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, when the average branded generic competitors is below 1.7. Meanwhile T2 takes the value of 1 for those molecules that exceed that number of average competitors.

The estimation of equations (3) and (4) are made by OLS, and considers robust standard errors clustered at the level of the matching molecules grouped by 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 branded generics and innovators, we use the information of monthly prices of the initial 47 molecules described in the previous section, estimating equation (5):

[23] The first bioequivalent drug was approved in 2009. Since then, the Public Health Institute has established that drugs that contain certain molecules must present studies of their therapeutic equivalence to an approved reference-listed drug. Information and details can be found in the Decree-law N°981 (2011) from the Ministry of Health.

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

Where BG_p are categorical 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 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 vector Φ_m to control for time invariant aspects such as the dosage form. i.e. 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 $CHRONIC$ as previously explained. Other variables included to control for drug characteristics are: Pre_{mt} which corresponds to the number of dosage options available in the market for drug m at time t; *Age* which is the number of months since the drug was introduced to the market; and Age^2, which is the squared age. To control for market characteristics, we incorporate $NUMC_{mt}$ which is the number of branded competitors that drug m faces 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 previously mentioned.

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 calendar time, that is, any possible seasonality or common shocks that affect all molecules at time t. Note that the idea behind this estimation is to find the true price

differential between branded generics and innovators by controlling for the effect of variables that generate differences in prices that are not based on the competition between the two types.

It seems natural to recognize the existence of some correlation between the individual specific effects α_i and price differentials, especially considering the high heterogeneity between the drugs in the sample. If this is true, which we can find using a Hausman Test or similar procedure, 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 wiped 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 would be precluded.

To circumvent this problem, we make use of the 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 the 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 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 estimating 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.[24] So, essentially the instruments are the time-demeaned variables $Q_T X_1 = X^*_{mt} = X_{mt} - \overline{X_m}$, the individual means or between variation $P_T X_1 = \overline{X_m}$, and the exogenous time invariant variables Z_1. Note that $E\left[\left(Q_T X_{mt}\right)' u_{mt}\right] = 0$, 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

Table 6, column 1 reports the random effects (RE) model, although the Hausman test significantly rejects the null hypothesis of no systematic difference between RE and FE coefficients; 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 for the price differentials drops to almost half of those in the first column, however the Sargan-Hansen test of over-identification reported in the last row indicates that the instruments are not valid.

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

[24]The matrix , where is the identity matrix and is the projection matrix. Intuitively, transform the vector of exogenous time-variant variables into individual means, whereas into deviation from means.

Table 6: Estimation of the price differential.

	(1)	(2)	(3)	(4)
VARIABLES	RE	HT-1	HT-2	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**	-0.278**
	(0.20)	(0.12)	(0.13)	(0.11)
BG				-0.201**
				(0.08)
Collusion				-0.111**
				(0.05)
$Collusion * BG$				0.121**
				(0.05)
Age	0.001	0.004***	0.004***	0.004***
	(0.001)	(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
	(0.19)	(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*	-0.012*	-0.012*
	(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 months and molecules are included. RE: Random Effects Estimation; HT: Hausman-Taylor Estimation. Source: Authors' own calculations with data from IMS Health.

The results in the column (3) indicate that the prices of the branded generic options are, on average, 17.6% lower than the innovator after the first year of branded generic competition, similar to the gross price differential reported in Table 3.[25] This differential keeps relatively constant over a long period of competition, reaching 18.7% lower than the innovator options after 48 months of competition. On the other hand, the unbranded generic differential indicates that their prices are 27.4% lower than the innovators.[26]

The chronic dummy and the number of competitors are significant, and their effects go in the expected direction. Indeed, drugs for chronic conditions are 59.2% more expensive,

[25] As it is a semi-logarithm regression, the impact is estimated as follow: See Halvorsen and Palmquist (1980).

[26] The price differential of unbranded generics is not representative of that observed in the overall market because this option is rarely available for these 47 molecules when they first experience competition.

matching the intuition that the demand for these drugs tends be more inelastic, and hence are more expensive. Additionally, each additional branded generic or innovator competitor reduces the drug price by 1.2%, in line with the low intensity of the branded competition.

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. Note that in this estimation we control for the collusion that affected the prices between December 2007 and April 2008. In doing so, we include the variable ***Collusion*** that takes the value of 1 if molecule *i* was affected by the retail collusion, and we interacted this variable with the ***BG*** indicator. The coefficient for the interaction indicates that, for the colluded molecules, the price gap between the branded generics and innovators shrinks to -7.6%, which is as expected as the collusion agreement elevated the prices of the affected drugs.[27]

The rest of the section will focus on the results concerning the impact of branded generic competition. The results from the estimation of the propensity score are provided in 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 via the nearest neighbor criteria.[28]

The property of the balance between treated and non-treated molecules is evaluated in Table 7 for the 5 observable 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 suggest that there is a difference between both groups of molecules. Therefore, it can be asserted that they are, on average, equals.

Table 7: Property of balance from Treatment 1.

	Average	t-test

[27] The marginal effect is obtained as follow: (exp (-0.201+0.121)-1)*100%.

[28] The 26 molecules remaining 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, and Warfarin.

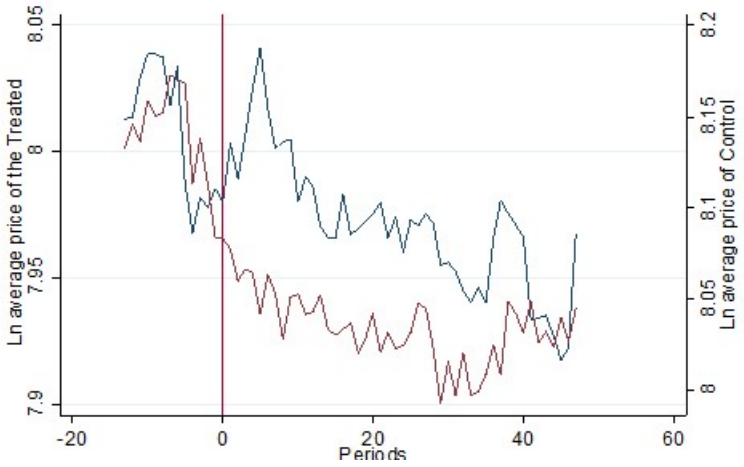
Treatment	Variable	Treated	Control	Sd bias (%)	t	p>t
1	$Chronic_{-1}$	0.64	0.53	23.9	0.68	0.50
	Market $Size_{-1}$ ($MM)	14	23	-74.3	-0.96	0.34
	Age_{-1}	119.3	105.31	23.4	-0.73	0.47
	$NumSub_{-1}$	16.9	14.5	12.8	0.32	0.75
	$Presentations_{-1}$	1.6	1.8	-38.5	-0.96	0.34
2	$Chronic_{-1}$	0.78	0.67	24.3	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.

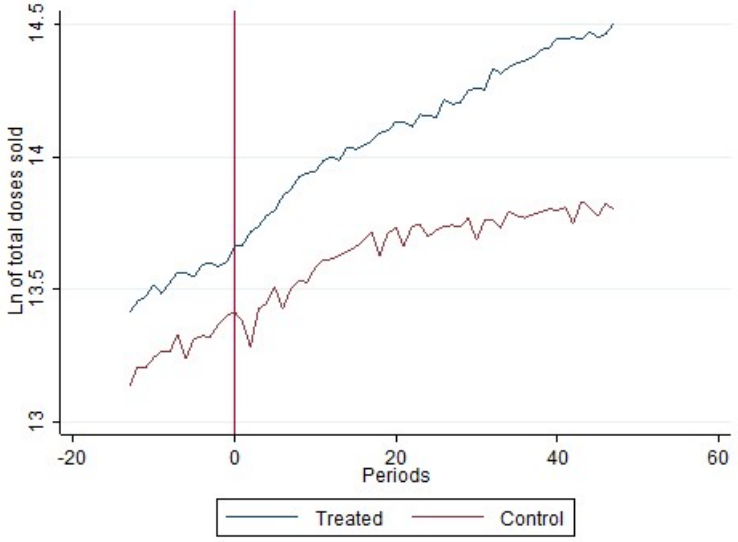
In panels A and B of Figure 3 the evolution of weighing average prices of innovators and total doses sold in the market is presented for treated and non-treated molecules. The pre-treatment trends of prices and quantities shown are similar for both the treated and control molecules, which allows us to apply the DiD estimation. A formal test for the parallel trends assumption is done in Appendix D by using a flexible specification or event study regression, where the treatment variable is replaced by a series of dummies taking a six-month period for each one. The model shows that the there is no statistical difference between the groups before the treatment.

Figure 3

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



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



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

Table 8 presents the DiD estimations for the weighting average real prices and doses sold by innovators. In column 1, the coefficient of interest estimated by Δ_{is}, is in the third row of the table, and 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 in innovators prices in the post-entry period — 48 months — with respect to the molecules that still had monopoly protection. In column 2 the same exercise is replicated

but excluding the 4 molecules and their counterfactuals exposed 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 positive in columns 3 and 4 of Table 8, the branded generic competition does not generate a statistically significant effect on innovator quantities either.

These results for the innovator prices are consistent with the theory of market segmentation that suggests that generic competition is unable to affect innovator prices. Furthermore, whereas branded generics provide a significantly cheaper option as shown by results in Table 6, branded generic competition seems to be incapable of provoking any major shift in the preferences of innovator consumers. To put it succinctly, the market is divided with the innovator preserving its loyal consumers who naturally exhibit an inelastic demand.

Table 8: 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 months 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 their counterfactuals, involved in the price collusion. Source: Authors' own calculations with data from IMS Health.

In Table 9 we explore the possibility of a non-linear effect deriving from the amount of branded generic competitors faced by the innovator. The two intensities of treatment defined in the preceding section are now considered. In column 1 where the reaction effect on prices is examined, no statistical significance is achieved even though the magnitude associated with the second treatment is considerably higher. Regarding the supply of medicine doses in column 2 of Table 9, the magnitude between both treatments is similar, but again none of them is statically significant.

Table 9: 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 months 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.

This evaluation of the branded generics' impact would be incomplete without an assessment of the total doses sold in the market, that is the capacity that branded generics have for increasing the market and reaching new patients. According to column 1 of Table 10, branded generic competition increases the supply of medication doses by 148.1%, a magnitude that moderately decreases when the 4 molecules exposed to collusion are removed. The results in column 3 reveal that a larger number of branded competitors exert a larger 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 discussed above is that — even though the market is segmented with the innovators serving a high-price niche after branded generic entry, — the branded generic competition has an important impact on social welfare. In fact, their prices are nearly one-third lower than the innovator ones and create a dramatically huge expansion of the retail market supply.

Table 10: Differences-in-differences 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 months 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 collusion molecules, and their counterfactuals, and column 4 considers the two treatment intensities. Source: Authors' own calculations with data from IMS Health.

VI. Conclusions.

This paper provides empirical evidence of the effects of branded generic entry over prices and quantities of drugs in the retail pharmaceutical market. We identify 47 molecules that experienced 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 on innovator prices and quantities, as well as the impact over the total doses sold. 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 17.6% the first year of competition, almost 10 percentage points lower from the gross relative price (see Table 3). The true price differential remains relatively stable through the branded competition period, reaching -

18.7% in the subsequent period from the 48 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% on the total doses sold with respect to the counterfactual. The expansion of the availability of doses could be explained by the significantly lower prices of branded generics, which reach a gross differential of-33% with respect to the innovators 4 years after the start of competition. The price allows for new patients who were previously excluded from the pharmacological therapies or used less effective drugs. It is important to note that this impact on the social welfare — more doses sold at lower prices — is directly attributable to the branded generic competition, and not other factors such as the seasonality as those have been controlled for. Also, when two intensities of competition were considered, a greater effect was found from more branded generic competitors.

Consistent with the literature, our findings indicate that the innovator prices do not react to the branded generic entry, validating 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 innovator doses, the point estimate is positive but lacks statistical significance.

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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	-3	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)

ψ_2 (= *B*)	2.088***	-
	(0.68)	
ψ_3 (= *C*)	-	-8.374
		(302.5)
ψ_4 (= *G*)	1.133**	-
	(0.57)	
ψ_5 (= *J*)	0.861*	-8.690
	(0.50)	(302.5)
ψ_6 (= *L*)	1.526***	-
	(0.41)	
ψ_7 (= *M*)	1.291***	-7.702
	(0.49)	(302.5)
ψ_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.

Appendix D: Parallel trends test.

VARIABLES	(1) Innovator Price	(2) Innovator quantity	(2) Total quantities
After (=1)	0.0339	-0.361	-0.322
	(0.156)	(0.356)	(0.344)
Treated (=1)	-0.404	1.437*	1.421*
	(0.377)	(0.715)	(0.724)
Pre2	0.0155	-0.0483	-0.0592
	(0.0800)	(0.202)	(0.200)
Post1	-0.0746	0.516	0.626
	(0.134)	(0.401)	(0.394)
Post2	-0.102	0.605	0.811**
	(0.133)	(0.386)	(0.374)
Post3	-0.137	0.555	0.855*
	(0.130)	(0.435)	(0.421)
Post4	-0.140	0.612	0.962**
	(0.136)	(0.432)	(0.414)
Post5	-0.123	0.469	0.876*
	(0.152)	(0.468)	(0.454)
Post6	-0.102	0.518	1.026**
	(0.179)	(0.503)	(0.479)
Post7	-0.119	0.428	1.028*
	(0.211)	(0.568)	(0.541)
Post8	-0.146	0.393	1.030*
	(0.229)	(0.594)	(0.569)

Bioequivalent (=1)	0.305	-0.664	-0.939
	(0.255)	(0.755)	(0.802)
Generic	0.576*	-1.569*	-1.403
	(0.307)	(0.899)	(0.893)
Constant	8.172***	5.786***	5.602***
	(0.477)	(0.955)	(0.964)
Control			
Paired molecules	Yes	Yes	Yes
Time	Yes	Yes	Yes
Observations	3,156	3,158	3,158
R-Squared	0.548	0.535	0.571

Note: *** significant at 1%, ** significant at 5%, * significant at 10%. Each Pre and Post variable takes a six-month period, where Pre and Post refer to the pre-treatment and post-treatment periods, respectively. So, for example, Post1 takes the value of 1 if the molecule is exposed to competition during the first six-month post-entry. The omitted dummy is Pre1, and so it is the reference category. Source: Authors' own calculations with data from IMS Health.