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IMPACTS OF THE EXTERNAL REFERENCE PRICING IN THE PHARMACEUTICAL INDUSTRY: EVIDENCE FROM COLOMBIA

Juan Felipe Contreras, MSc

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Master thesis

Impacts of the External Reference Pricing in the pharmaceutical industry: evidence from Colombia

Student: Juan Felipe Contreras (12278300)

Email: j.contrerasa94@gmail.com

University of Amsterdam, Amsterdam School of Economics

MSc Economics (Development Economics)

Supervisor: Hessel Oosterbeek, PhD

Second reader: Menno Pradhan, PhD

Date: 15th July 2019

Statement of originality

This document is written by Student Juan Felipe Contreras who declares to take full responsibility for the contents of this document.

I declare that the text and the work presented in this document are original and that no sources other than those mentioned in the text and its references have been used in creating it.

The Faculty of Economics and Business is responsible solely for the supervision of completion of the work, not for the contents.

Contents

1 Introduction

The aim of this thesis is to estimate the impact of the External Reference Pricing (ERP) implemented in the Colombian pharmaceutical industry on the prices and quantities sold of the regulated products and their unregulated closest substitutes using longitudinal data for the period 2011-2018. To achieve this, I investigate the policy designed by the Health Ministry in September 2013 to regulate a set of pharmaceuticals when they were of national interest or considered to be a threat to the financial sustainability of the system. The methodology has been implemented four times since it was established, comprising over 1,000 different commercial presentations. According to the ministry, the main intention of this policy was to contain the recent growth of the pharmaceutical expenditure and to contribute to a better access to drugs.

In general, the pharmaceutical expenditure has become a great concern for health authorities due to its increasing importance to the overall health expenditure. For this reason, a large number of cost-containment measures have been implemented worldwide. In particular, Brekke et al. (2007) defines the two main regulatory regimes that appear in the literature: the Reference Pricing (RP) and the Price Caps (PC). The first one consists on setting a maximum reimbursement price to make demand more elastic. The second one is more straightforward in the sense that it is more common, since it is also used in other markets: it consists on setting a maximum price a firm can charge and its objective is to contain market power. A main difference between the two is that, in the former, the firms can charge any price, however, if it is located above the RP, the consumers have to pay the surcharge.

The ERP is a special case of the PC that differs substantially from the regular RP[1]. The WHO (2016) defines it as "The practice of using the price(s) of a medicine in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country". The implementation of the ERP depends on how the policy is designed in two ways. First, the set of countries to be taken as a reference changes across countries, and second, once it is constructed, the international prices of the product in question are sorted and the ERP is set at a given cutoff according to the methodology of the policy (e.g. the median, the mean, a percentile)[2]. As Leopold et al. (2012) mentioned in their

[1]For this reason, RP is sometimes called as Internal Reference Price.

[2]In Colombia 17 OECD countries were selected and the ERP was set at the 25th percentile, as will be detailly

literature review, the implementation of this system poses several concerns mainly due to the unavailability of international information on prices. A side-effect of this complication is that studying its impacts is challenging and therefore, the literature on this type of regulation is scarce.

Theoretical works have suggested that the need for regulation relies on the characteristic of the health systems of exhibiting market failures. On the one hand, due to high insurance rates (and consequently, low out-of-pocket expenses) the demand is price-inelastic and inversely related to copayment rates (Arrow, 1963; Pauly, 1968, 1978; Zeckhauser, 1970; Nyman, 1999)[3]. On the other hand, the firms are granted market power because of the concession of patents and they are characterized for having large sunk costs due to their high R&D investments[4]. The combination of these characteristics makes it necessary to exert some means of control in order to overcome the drastically increase of the medical expenses in most countries. This is a great concern for policy makers since the purpose of the health system is to guarantee access to health services, but also to ensure its financial sustainability.

In many of the OECD countries, for instance, the pharmaceutical expenditure went from accounting for less than 9 percent of the total health expenditure in the 1980s to 20 percent in 2013, increasing at a faster rate than economic growth (Belloni et al., 2016). For the developing countries, it is estimated that between 10 to 40 percent of the public health budget is forgoing to pharmaceutical expenditures, which is particularly worrying considering that in these countries' health care involves larger amounts of out-of-pocket payments (Govindaraj et al., 2000). In Latin America total drug expenditure in 2003 amounted to about $19 billion, and countries in the region spent between 7 percent and 16 percent of their health sector budgets on pharmaceuticals (Homedes et al., 2005). Thus, understanding the impacts of the different regulatory regimes to contain these costs is important from a policy perspective.

explained in section 2.

[3]There are some notable empirical contributions on estimating the price-elasticy of the demand of health services. A seminal works in the United States are the ones regarding the Rand Health Insurance Experiment (Manning et al., 1987, 1988; Leibowitz et al., 1985; Lohr et al., 1986). In a more recent study Contoyannis et al. (2005) estimated for Quebec (Canada) that the price elasticity was between -0.12 and -0.16.

[4]In fact, the pharmaceutical industry is considered to be the one with the largest ratio of R&D over sales (Shadlen and Guennif, 2011). Some recent studies have suggested that R&D investments are the main determinants of the recent growth of the pharmaceutical costs (Newhouse, 1992; Okunade and Murthy, 2002; Cockburn, 2004, 2006).

Due to the great diversity in the policy designs, building general conclusions is often difficult since each application of either RP or PC varies across countries (Galizzi et al., 2009, 2011; Puig-Junoy, 2010). Moreover, the amount of studies available are regarding different aspects of the policies. An important part of the literature has focused on the impact of the pharmaceutical regulations on the prices of the regulated drugs and its differential impacts between brand-name and generics. Pavcnik (2002), for instance, estimated a Diff-in-Diff for the time frame 1986-1996 to study the gradual implementation of a RP in Germany in two therapeutic groups (oral antidiabetics and antiulcerants) and found that reductions were stronger for brand-names than for generics. Brekke et al. (2009) reached a similar result by conducting a natural experiment in Norway. Estimating also a Diff-in-Diff they found that the RP system reduced prices of brand-names by 18-19 percent and prices of generics by 8-9 percent. An important conclusion of this study, is that they casted doubts on the correct construction of control groups since, as they showed, there may be cross-price effects on unregulated therapeutic substitutes that can potentially bias the results if this is not taken into consideration when selecting the comparison group.

Another part has focused on the effects of regulations on the market structure. For Sweden, Aronsson et al. (2001) used a micro data for the period 1972-1996 to analyze 12 drugs that were subject to generic competition and showed that the introduction of RP decreased the market share of three drugs and they concluded that "the introduction of the reference price system is an important determinant of the price path". For the same policy, Bergman and Rudholm (2003) found that the RP was only effective for products that already faced generic competition at the moment of the introduction of the system: in those cases, the prices fell between 16 and 21 percent. Dalen et al. (2006), assessed the RP in Norway by estimating a structural model using instrumental variables and concluded that as a consequence of the policy, market shares of generic increased and it helped to reduce market power. In a more recent study, Brekke et al. (2011) contribute to this analysis by estimating a significant reduction in the brand-name market share of 14.7 percent.

Although, there are numerous studies on the pharmaceutical regulations in developed countries, most of them focus on RP rather than ERP, despite the fact that this measure has been widely used in state members of the European Union[5], and there are few regarding developing countries. An exception is the analysis conducted by Kaló et al. (2015), who studied the

[5]See for example the overview made by Leopold et al. (2012).

implementation of ERP in the Middle East and concluded that the effects of the regulations differ according to the economic status of each country. Moreover, the literature regarding the effects of pharmaceutical regulations on the demand is scarce, in this sense this study contribute to fill this void.

The Colombian government mostly used a RP regime between 2010 and 2012, and in September 2013 it launched a new round of regulations based on an ERP methodology. Regarding the latter, Prada et al. (2018) conducted a descriptive analysis based on the construction of Laspeyres indices for 90 drugs (both regulated and unregulated) and showed that, even though, the inflation of regulated drugs decreased by 40 percent, the overall pharmaceutical expenditure almost doubled. They suggested that market interventions should be implemented along with market monitoring to prevent unnecessary drug used. A first causal attempt (to my knowledge) of this policy is assessed by Bardey et al. (2018). They estimated a Diff-in-Diff-in-Diff model for 17 therapeutic groups and showed that the policy seemed to only be effective in three of them. Specifically, they argued that there was a reduction in cancer, Alzheimer and diabetes drugs; in 10 groups the prices increased; and in the remaining there were non-statistically significant effects.

Thus, the contribution of this study to the aforementioned is threefold. First, to my knowledge, this is the first causal estimation of the ERP implementation in Colombia on the demanded quantities; second, by providing empirical evidence of cross-price effects on the unregulated therapeutic substitutes of the regulated products; and third, this study includes information since January 2011 up to December 2018, while Prada et al. (2018) and Bardey et al. (2018) only considered data in the time frame 2011-2015 and 2011-2014, respectively, ignoring the inclusion of some drugs that entered price control in 2017 and 2018.

The empirical strategy proposed here consists on exploiting a natural experiment using a platform built by the health ministry called SISMED which contains monthly information of all the pharmaceuticals commercialized in Colombia since 2007. The impact evaluation is motivated by Brekke et al. (2009) and their findings for the Norwegian experience. Since the methodology was established, over 1,000 commercial presentations have been regulated, belonging to 117 different ATC groups[6], some of which contain both regulated and unregulated products, allowing to assess

[6]The Anatomical Therapeutic and Chemical (ATC) system code was proposed by the World Health Organization (WHO) to catalogue drugs within therapeutic classes such that they share the same pharmacological properties. Details will be explained in section 3.

the research question by building two treatment groups. A first one, consisting on the regulated part to estimate the direct impact of the ERP on both prices and quantitites sold; and a second one, on the unregulated commercial presentations that belong to the same ATC as the regulated ones (that by definition are close substitutes) to test for cross-price effects as well as for therapeutic substitution. A valid comparison group is constructed by selecting some ATC that remained unregulated during the whole period and not considered to be substitutes to any of the regulated drugs.

I find that the ERP led to a price reduction of 71 percent of the regulated products and 25 percent of their unregulated closest therapeutic substitutes. However, the results does not support that the policy had induced demand of pharmaceuticals in Colombia, suggesting that changes in the overall expenditure and demanded quantities are not related to the implementation of the policy.

The rest of this document is structured as follows. Section 2 introduces the Colombian health system, its pharmaceutical market and the regulation of 2013. Section 3 a description of the data used for the analysis. Section 4 explains the empirical strategy conducted and its results. Section 5 provides some robustness checks to test the reliability of the results shown in section 4. Finally, section 6 contains some concluding remarks and policy implications.

2 Context and reform

Colombia's health system went through a decentralization process at the end of the twentieth century and was renamed the General System of Social Security (SGSSS, for its Spanish acronym). Enrolment is mandatory for all Colombian residents and, based on one's income level, citizens have to sign up for one of two regimes available: the Contributive Regime (CR), covering workers with a monthly minimum income and their family, or the Subsidiary Regime (SR) covering those classified as poor (using a government test on monthly income) or under vulnerability conditions (Giedion and Villa, 2009; Tafur and Prada, 2019).

Enrollees in both regimes have access to a respective benefit package (POS for CR and POSS for SR, for its Spanish acronyms) that includes services for health promotion, prevention, diagnosis, treatment and rehabilitation. However, there are non-included services and technologies (non-POS) that mostly include experimental and aesthetical procedures. This package can also be made accessible to the Colombians by a judicial mandate if it has been proven that not receiving a certain treatment that falls under this package is life threatening for the person in question. However, these services have to be paid back by the government through a reimbursement scheme (Guerrero et al., 2011; Riascos and Camelo, 2013).

In 2011, the Health Ministry announced that the list of drugs included in the POS would be updated every two years (starting in 2012). The biennial updates are based on a detailed evaluation of the health needs of the Colombians as well as considerations regarding the epidemiological context and the life of Year Lost for Disability by the main diseases, and thus, decide which technologies to include in the POS (Ministry, 2011).

2.1 The Colombian pharmaceutical policy

Colombia's pharmaceutical expenditure experienced a rapid growth over the last decade, going from 1.2 percent of GDP in 2001 to 1.4 percent in 2008 and the non-POS costs on reimbursements went from US$2.8 million in 2001 to US$605.3 million in 2008, reaching US$790 in 2009 (Andia, 2011). The latter is one of the greatest financial threats for the SGSSS; the ministry has reported that the number of reimbursements rose 165.1% in the period 2009-2015 and that the total costs increased by 7.5% in 2015: 74.2% of which corresponded to Non-POS drugs (Ministry, 2015).

This trend is partly explained by the prevalence of the so called "catastrophic diseases" (namely, renal chronic disease, HIV/AID, cancer, hemophilia, arthritis and orphan diseases); according to the Colombian Administrative Statistical Department, malignant tumors are the second cause for death after heart diseases and circulatory diseases. Moreover, the Colombian pharmaceutical expenditure growth is also driven by the fact that Colombia is the first Latin American country achieving almost Universal Health Coverage (Giedion et al., 2014)[7] and that it has one of the lowest out-of-pocket expenses in the region (19 percent) (Chang et al., 2019).

As in most pharmaceutical markets, the Colombian one faces the usual imperfections and the government created in 1994 the National Pharmaceutical Price Commission to correct market failures. Thus, in 2006 three regulatory regimes were imposed: observed liberty, regulated liberty and direct control. The first is for those markets where there was enough competition and there was no need to intervene them. The second is imposed for markets where there was enough evidence of monopolistic competition and therefore, they needed to be observed. The last type of regulatory regime was introduced for drugs with high prices belonging to the second regime; hence they entered to a price control. The intention for each regulatory regime is different; the first two is to prevent producers to charge unreasonable prices in competitive markets and the third one is to keep monopolistic markets under control (Andia, 2011).

In 2004 and 2006 several drugs were put in and pulled from the regulatory regimes and there were adjustments in the methodological framework to place a drug in one of the regimes. Between 2010 and 2012 a RP mechanism called *V*alores Máximos de Recobros was mainly used to a certain number of non-POS ATC to control the rapid growth of the reimbursements.

[7] Enrolment in the SGSSS went from 25% in 1993 to 92% in 2012.

With the spirit of setting a regulatory framework, the Colombian Health Ministry established a National Council of Social and Economic Policy that in 2012 launched a document (called Conpes 155) which objective was to structure the constitutional principles regarding the right to health and the development of the pharmaceutical industry. Its main objective was to contribute to the improvement of health in the long run through some strategies that were intended to achieve during the time frame 2012-2021. The specific objectives were to allow a good informational system to observe prices, to improve access to drugs and to organize the supply into the interests of the domestic pharmaceutical policy. Since 2012, the Conpes 155 has been used as a reference document by the government for all further policy making.

2.1.1 The Regulation of 2013

In 2013 the government launched an ERP system with a new the methodology to include pharmaceutical products into one of the regulatory regimes. Thus, the ministry defined a market as: all the products under the same ATC code and the same pharmaceutical form (e.g. tablets, capsules, powder), and the criterion for concentration was based on the Herfindahl – Hirschman index (HHI) and the number of operating suppliers (N) in the relevant market; specifically if $HHI > 2,500$ or $N < 3$. For those drugs belonging to a concentrated market and which domestic price was higher than the 25th percentile in a ranking of 17 OECD countries[8] were that same drug was commercialized, a price cap equal to such percentile (expressed in COP) was set.

The methodology also stated that when a product was already regulated under the old RP system, it would remain under it, and not be replaced by the ERP. This is an important consideration since some of the pharmaceuticals that enter price control after September 2013 are close substitutes to those that were already regulated.

So far, the methodology has been implemented in four rounds as summarized in table 1. It is important to bear in mind that the pharmaceuticals were not regulated all at the same time for logistic reasons and that the regulatory procedure has been implemented as the relevant information to take decisions became available. Also, that some commercial presentations were regulated after the corresponding ATC had already been regulated in a previous round.

[8]Argentina, Brazil, Chile, Ecuador, Mexico, Panama, Peru, Uruguay, Spain, the United States, the United Kingdom, Australia, Canada, France, Norway, Germany and Portugal.

Table 1: Timeline of the implementation of the ERP in Colombia (2013-2018)

Date	Number of ATC	Number of commercial presentations	Comments
May 21 2013			The methodolody is established.
Sep 3 2013	35	187	The first round of the regulation.
Oct 3 2013	1	3	Kaletra, a drug to treat HIV/AID, was included in the regulation.
Jan 1 2014	33	337	The second round of the regulation.
Apr 16 2014	10	282	The third round of the regulation.
Jan 1 2017	1	18	Glivec, a drug to treat cancer, was included in the regulation.
Mar 1 2018	43	225	The fourth round of the regulation.

Note: Regulatory rounds, number of ATC regulated under each one of them and their corresponding number of commercial presentations.

3 Data description

This section describes the data used in this thesis. The first subsection introduces the system implemented by the WHO to categorizes pharmaceuticals, as this classification will be useful for the rest of the analysis. The second subsection contains a description of the SISMED database and the most relevant information regarding the variables for the empirical strategy of section 4.

3.1 The Anatomical, Therapeutical and Chemical clasification

The WHO (2019) defines a system called the Anatomical Chemical and Therapeutic (ATC) code system to classify drugs for measurement and research purposes. Each code defines a set of drugs such that they share the same pharmacological, chemical and therapeutic properties. The first level corresponds to a letter (among 14) indicating the main organ under which the substance has its effects (anatomical level). The second level has a two-digit number indicating a pharmacological or anatomical group; the third tells the pharmacological or therapeutic subgroup (indicated by one letter). The fourth level is the chemical, therapeutic or pharmacological subgroup (also one letter). The fifth level is what is called as the active ingredient, this is the main ingredient in a pharmaceutical drug, also known as molecule or active principle.

In most health systems and researches regarding the pharmaceutical markets the ATC system is used to categorized drugs according to its therapeutic properties. These also works to define the substitutivity among them according to their closeness in their classification. More specifically, the WHO and some researches like Ellison et al. (1997), Pavcnik (2002) and Brekke et al. (2009) define two drugs as substitutes if they both belong to the same third level in the ATC system (the first four digits are equal). The table 2 summarizes the classification and provides one example for each anatomical level.

In most cases there are more than one medicine (with different commercial names) that fall under the same ATC code (that have the same active ingredient). For example, Candersartan (code C09CA06) is a molecule used to treat hypertension and in the Colombian market there are several products with this ATC: Atacand, Candeprex, Minart, Candersartan (generic), Candam, Candeprex and Europres; each within different commercial presentations (according to the strength

of the active ingredient) and produced by different laboratories[9].

Moreover, since each commercial presentation is substantially different in their pharmaceutical form and the amount of active ingredient, the WHO (2019) also established a standarized measure to make comparisons possible between different products. They defined a Daily Diagnosed Doses (DDD) for a given active ingredient and route of administration (e.g. Oral, Parenteral), such that the quantities sold of each product is converted by multiplying the amount of active ingredient in the corresponding commercial presentation by the DDD defined by WHO (2019)[10]. Although this measure is widely used when studying pharmaceuticals, some authors like Prada et al. (2018) use the total amount of active ingredient as standarized measure. Thus, for instance, a commercial presentation of Atacand that comes in a box with seven tablets, each one with 8 mg of Candarstan, contains 56 mg of active ingredient; and since it has been assigned 8 DDD for each mg of active ingredient, the corresponding measure for this product is 448 DDD.

Table 2: ATC clasification and examples at the anatomical level

Clasification	ATC	ATC1	ATC2	ATC3	ATC4	ATC5
Alimentary track	A11AA03	A	A11	A11A	A11AA	A11AA0
Blood	B01AC11	B	B01	B01A	B01AC	B01AC1
Cardiovascular system	C02KX02	C	C02	C02K	C02KX	C02KX0
Dermatological	D01AE54	D	D01	D01A	D01AE	D01AE5
Genitals	G04CX04	G	G04	G04C	G04CK	G04CK0
Sexual	H01CB03	H	H01	H01C	H01CB	H01CB0
Antiinfective	J05AB14	J	J05	J05A	J05AB	J05AB1
Antineoplastic	L01AX03	L	L01	L01A	L01AX	L01AX0
Musculo-skeletal	M09AX01	M	M09	M09A	M09AX	M09AX0
Nervious system	N03AG04	N	N03	N03A	N03AG	N03AG0
Antiparasitic	P03BX02	P	P03	P03B	P03BX	P03BX0
Respiratory system	R03DX05	R	R03	R03D	R04DX	R04DX0
Sensory organs	S01EB09	S	S01	S01E	S01EB	S01EB0
Various	V08AB02	V	V08	V08A	V08AB	V08AB0

Source: WHO (2019).

[9]For instance, Atacand is produced by the british laboratory Astrazeneca and is commercialized in Colombia in a box with 14 tablets, each one with 32 mg of active ingredient. However, Candam is produced by the Colombian laboratory Lafrancol, and comes in a box with a varying number of tablets with 16 mg of active ingredient each.

[10]In particular the DDD for each ATC can be consulted on `https://www.whocc.no/atc_ddd_index/`

3.2 SISMED

The main source of the data is a platform built by the Health Ministry called SISMED which merges different types of information, from different institutional entities, regarding all the pharmaceuticals commercialized in Colombia. This information includes quantities sold, prices, whether a product belongs to the POS, its pharmaceutical form, its corresponding ATC group, the type of market (institutional or commercial) and the type of seller (laboratory or wholesaler). The information is available monthly since 2007, however, reliable (more complete) data starts from 2010 according to the Health Ministry itself. In addition, the information regarding the specific date in which each regulated drug entered to price control comes from the legal documents produced by the government since the methodology was established. Only the data reported by institutional laboratories was used since the regulation was only implemented in the institutional market, and according to the Ministry, the information from laboratories is more complete than the one from wholesalers.

For the empirical analysis, regulated ATC with both regulated and unregulated products were considered (that by definition are close substitutes). Groups that had no observations prior to the date in which the policy was released (September 2013) or after they were regulated were discarded. In addition, six unregulated ATC were selected to serve as a control group for the natural experiment based on three criteria; that they were not substitutes to any of the regulated drugs; that they had information over the whole period of analysis; and that the trends of both prices and quantities were fairly stable, such that there was no evidence that they could have reacted to the policy.

Here a product is defined as a commercial presentation, and with the time being measured in one-month periods, an observation is a product sold at a given month-year. Thus, the final data is an unbalanced panel, mainly due to the entry of new products (e.g. generic entry). It contains 1,078 different commercial presentations, 37 ATC groups (31 regulated), 96 time periods (January 2011 - December 2018) and 36,939 observations. Finally, to make comparisons valid, real prices (deflated using the Consumer Price Index) and quantities were standardized into a common unit of concentration using the amount of active ingredient[11]. Thus, they were converted into prices

[11]The reason for not using DDD is that the WHO fail to assign a respective value to certain ATC and thus, some health ministries assign their own values after a careful evaluation of the substances. However, this is not the case

per active ingredient and volumes sold of active ingredient, respectively.

Table 3 presents the ATC's selected for the study, their ATC name (active ingredient), the percentage of regulated commercial presentations (in the sample), the date in which they were regulated (empty for the control group) and the number of observations within each group. It is worth noting that among the regulated drugs there are Immunosupressants (ATC3 code L04A), Hemostatics (ATC3 code B02B) and Antineoplastic agents (ATC3 code L01X) that are used to treat catastrophic diseases (cancer and hemophilia). These groups of drugs are relatively important for pharmaceutical policy makers as they have experienced a recent increase in their prices[12].

A natural way to start the data analysis is by exploring the behavior of the relevant variables. Figure 1 plots time series of the mean prices for the regulated drugs, their unregulated closest substitutes and the control group. At first glance it seems that both regulated and unregulated products reacted after the policy was launched (represented by the vertical red line) following a downward trend over the whole period. Also it is important to notice that, the prices of the unregulated substitutes were already decreasing before September 2013; possible explanations for this behavior are pasts cost-containment measures targeted to these products (e.g. the old RP implementation). For the control group, seems to have a constant trend. This information is also shown in the appendix in separated graphs so it is easier to appreciate the individual trend of each one of the series (figure A.1 and figure A.2). Addidionally, the time series of prices and volumes of active ingredient for all unregulated drugs (not substitutes) appear in figures A.3 and A.5, respectively, suggesting that overall the ERP did not have an effect on these drugs.

for Colombia and SISMED does not have information on this. Having used only ATC with a respective value of DDD assigned would have reduced substantially the sample size.

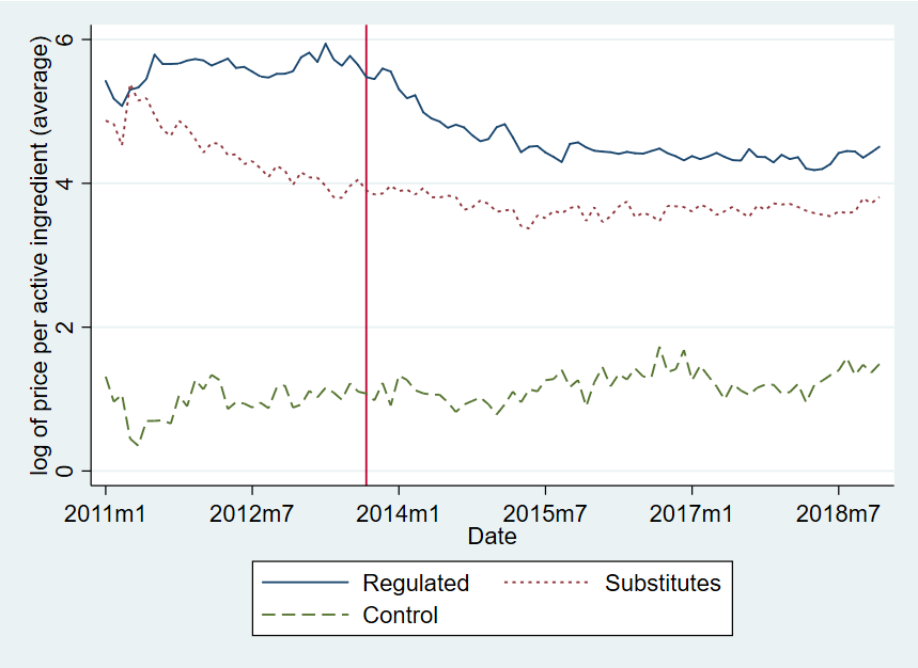
[12]Machado and Moncada (2012), for instance, conducted a descriptive analysis of the evolution in the demand for this type of drugs in Colombia and they found that in recent years there has been a constant increase in the consumption of the most expensive drugs. In a more recent study, Prada and Contreras (2018) estimated cancer costs for patients in their last year of life and found that costs of patients that died and were diagnosed with cancer is $72 - 76$ percent higher than the costs of those that died and had another diagnose.

Table 3: List of the selected ATC and their sample characteristics

ATC code	Active ingredient	Regulated (%)	Date of regulation	Obs.
A02BC05	Esomeprazole	2.41	Jan 2014	3,526
A07EC02	Mesalazine	46.49	March 2018	1,323
A09AA02	Multienzymes	0		923
A10AB06	Insulin	59.42	Jan 2014	308
B01AE07	Dabigatran	33.63	Jan 2014	455
B02BD02	Coagulation	2.52	Apr 2014	2,028
B02BD04	Coagulation	39.12	Apr 2014	685
B02BD05	Coagulation	34.43	Sept 2013	122
B02BD06	Factor VIII	56.86	Apr 2014	503
C07AB02	Metoprolol	0		2,350
C10AB04	Gemfibrozil	0		872
G04BD10	Darifenacin	45.78	March 2018	284
H01CB02	Octreotide	68.68	Jan 2014	364
H02AB04	Methylprednisolone	14.37	Apr 2014	1,016
J01DH02	Meropenem	26.54	Jan 2014	1,315
J01XX08	Linezolid	40.05	Jan 2014	402
J06BB16	Palivizumab	36.00	Sept 2013	200
L01AX03	Temozolomide	43.71	Sept 2013	890
L01BC06	Capecitabine	22.57	Sept 2013	288
L01XE01	Imatinib	21.27	Jan 2017	818
L01XE18	Ruxolitinib	30.00	March 2018	220
L01XX19	Irinotecan	13.51	March 2018	570
L02AE02	Leuprorelin	18.60	Apr 2014	769
L02BB03	Bicalutamide	26.53	Apr 2014	652
L04AA06	Mycophenolic acid	44.76	Jan 2014	563
L04AA13	Leflunomide	79.67	Jan 2014	423
L04AB01	Etanercept	95.46	Sept 2013	286
L04AD01	Ciclosporin	45.71	Jan 2014	711
L04AD02	Tacrolimus	89.15	Sept 2013	673
N01BB02	Lidocaine	0		1,115
N02BE01	Paracetamol	0		2,985
N03AX14	Levetiracetam	11.31	Apr 2014	1,609
N03AX16	Pregabalin	22.85	Apr 2014	2,700
N05AH04	Quetiapine	55.86	Jan 2014	3,099
N06DA03	Rivastigmine	83.94	Jan 2014	691
N06DA04	Galantamine	66.67	Sept 2013	288
R06AX26	Fexofenadine	0		913
Total				36,939

Source: Own computations with SISMED data and the legal documents produced by the Ministry.

Figure 1: Prices per active ingredient 2011-2018



Moreover, figure 2 depicts the expenditure index (base January 2011) following an upward trend[13]. In particular it is noted that even after the policy was implemented, the pharmaceutical expenditure from the regulated drugs continued to grow (it multiplied by four); which is the same result reported by Prada et al. (2018) regarding the regulated ATC. Figure 3 sheds more lights on it: the average volumes sold in the time period has increased during the time horizon and it seems like the implementation of the policy did not change this trend (for neither the regulated drugs nor their unregulated substitutes). For the control group, the volumes sold has a constant trend and seems unaffected by the implementation of the ERP (also projected individually in the supplementary figure A.4 in the appendix, and all unregulated ATC are plotted in figure A.5). These descriptive results seem to suggest that the control group is correctly specified, however it is important to bear in mind that the trends depicted do not control for observables and a deeper analysis is required.

[13]The expenditure index at time t is constructed using the simple indices methodology. Let Y_t be the expenditure at time t, and $t = b$ is the base period. Then the expenditure index at time t, $I_{t/b}$, is $I_{t/b} = \left(\frac{Y_t}{Y_b}\right) * 100$.

Figure 2: Expenditure index (31 regulated ATC) 2011-2018

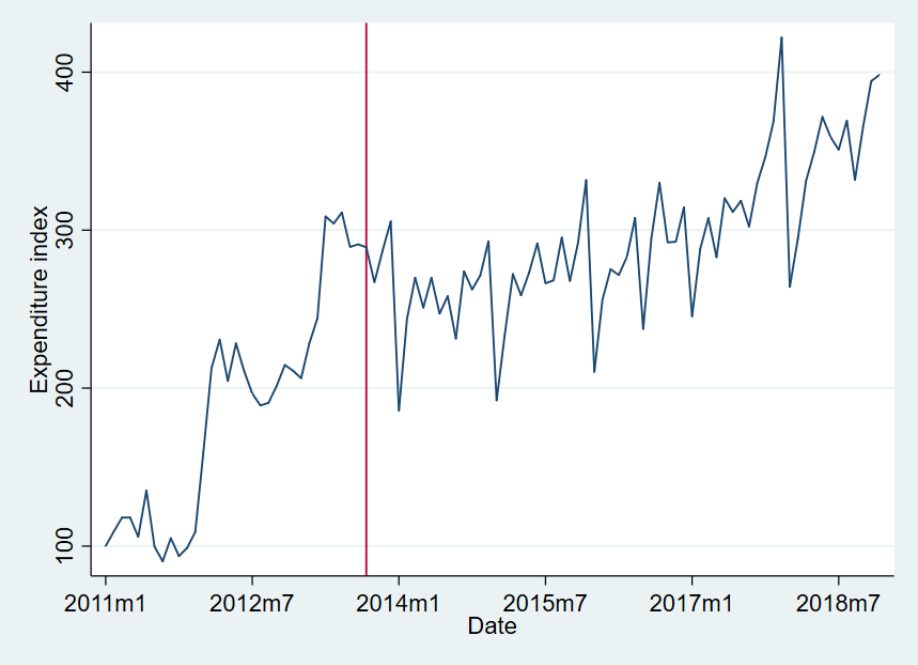
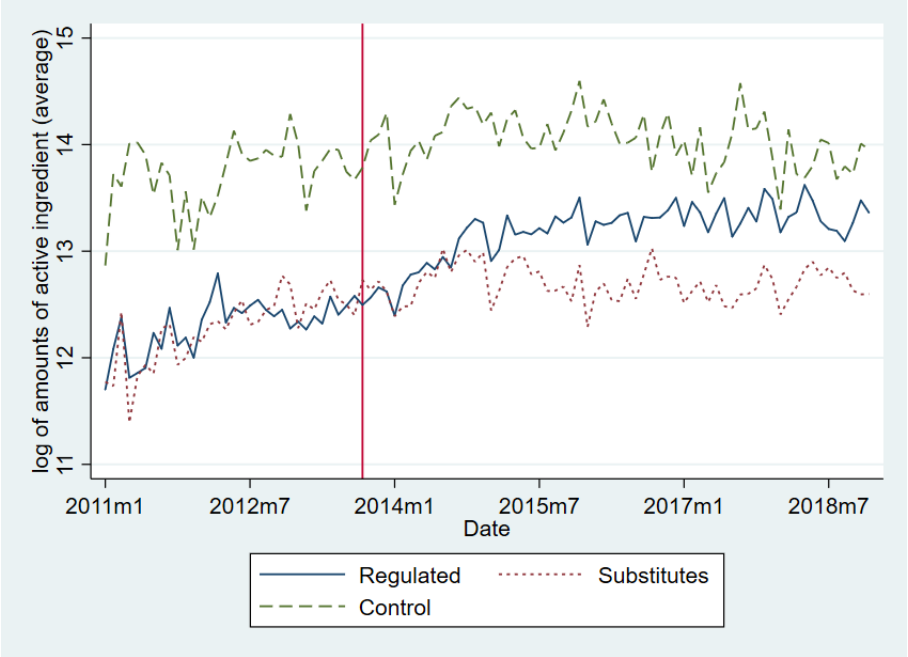


Figure 3: Volumes of active ingredient 2011-2018



4 Empirical strategy and results

4.1 Econometric framework

The identification strategy proposed here is based on many other evaluations of the pharmaceutical regulations (Pavcnik, 2002; Danzon et al., 2005; Dalen et al., 2006; Brekke et al., 2009, 2011, 2015; Bardey et al., 2018). This section complements the descriptive analysis presented in section 3 by estimating a Diff-in-Diff motivated by Brekke et al. (2009). Following the usual procedure in natural experiments, I let the regulated products to be a treatment group to test the direct impact of the ERP on both prices and volumes sold. To test for cross-price effects and therapeutic substitution, the unregulated products belonging to the 31 regulated ATC represent a second treatment group.

Let R_{it} be a dummy variable equal to 1 if product i is being regulated at time t and S_{it} a dummy variable equal to 1 if product i is a close substitute to any product being regulated at time t. The baseline for the estimations proposed here is given by

$$y_{it} = \alpha R_{it} + \beta S_{it} + \gamma HHI_{it} + \lambda_t + a_i + \epsilon_{it} \tag{1}$$

where y_{it} is the outcome variable to be measure (prices or volumes in logarithmic scale), λ_t are time fixed effects and a_i are products fixed effects. HHI_{it} is the Herfindahl - Hirschman index at time t of the market to which the product i belongs to.

In this set up α measures the direct effect of the policy, whereas β tests for cross-price effects (when estimated for prices) and therapeutic substitution (when estimated for volumes). Moreover, some studies have suggested that regulations affect differently brand-names and generics (Brekke et al., 2009; Aronsson et al., 2001; Pavcnik, 2002). To capture this, the extended version of model 1,

$$y_{it} = \alpha_1 R_{it} + \beta_1 S_{it} + \alpha_2 R_{it} * G_i + \beta_2 S_{it} * G_i + \gamma HHI_{it} + \lambda_t + a_i + \epsilon_{it}, \tag{2}$$

is estimated, where G_i is a dummy variable equal to 1 if product i is a generic. In this model $\alpha_1 + \alpha_2$ measures the direct impact of the ERP on generics, and α_2 is the differential effect on

generics compared to brand-names. In a similar way, β_1 and β_2 have the same interpretation for cross-price effects and therapeutic substitution.

For model 1 and model 2 to be correctly specified, it is required that both R_{it} and S_{it} are uncorrelated with ϵ_{it}. Since the regulation was not assigned randomly, controls are important; in particular, the main criterion to regulate was the concentration of the markets, hence the inclusion of HHI is crucial[14]. Furthermore, the prices and demanded quantities of pharmaceuticals could be driven by variables like the epidemiological context in each period, the old RP regulation and the exchange rates (as some products are imported) (Bardey et al., 2018) that could have ultimately led to regulate certain products. However, those have been taken care of by adding time and products fixed effects.

A further central characteristic of these models is that (being correctly specified) it allows to test the effects of the policy in the unregulated therapeutic substitutes by excluding them from the control group. For this to be the case, one needs that the trends, for both treatment groups and the comparison group, once controlled for covariates and fixed effects, to be the same. Thus, I closely follow the usual pre-reform test widely used in the literature (Brekke et al., 2009, 2011, 2015; Pavcnik, 2002; Bardey et al., 2018) and estimate the fixed-effect model:

$$y_{it} = \sum_{t=2}^{33} \delta_t x_i * z_t + \gamma HHI_{it} + \lambda_t + a_i + \epsilon_{it} \qquad \text{(test 1)}$$

where x_i is a dummy variable equal to 1 if product i's treatment status is regulated or substitute. z_t is a dummy variable for each one of the time periods prior to the policy[15]. For the parallel trend assumption to hold, it is necessary δ_t to be statistically insignificant, for $t = 2, ..., 33$. Note that the test 1 is conducted four times, one for each treatment status (regulated or unregulated substitute) per outcome variable (prices or volumes sold).

[14]A better control would have been to add market fixed effects, however if these were used, it would not have been possible to control for specific time-invariant product characteristics.

[15]Note that, time being measured in one-month periods, the time frame prior to the policy in the sample (Jan 2011 - Sep 2013) consists of 33 periods, corresponding to the number of interactions (omitting one).

An additional concern is whether the policy affected the contol group, in which case it would fail to correctly represent the counterfactual. To test for this, the model

$$y_{it} = \eta T_t + \gamma HHI_{it} + \lambda_t + a_i + \epsilon_{it} \qquad \text{(test 2)}$$

is estimated only for the control group, where T_t is a dummy variable equal to one for time periods after September 2013. What is require in this model is η to be statistically insignificant, so the policy did not affect the comparison group.

4.2 Results

Since the empirical strategy proposed here relies on the correct construction of the control group, this subsection starts by showing the results of test 1 and test 2. Table 4 is a complement of what is depicted in figure 1 and figure 3 by controlling for markets concentration and unobservables (each $x_t * z_t$ is labeled as "Interaction t", for $t = 2, ..., 33$). Prices seem to follow the same trend prior to the policy for both treatment groups (column 1 and column 2). For volumes, on the other hand, in some periods the common trend assumption fail to hold (column 3 and column 4). Although this might represent a problem to estimate model 1 and model 2, the availability of enough time periods and levels in the data allow to correct this problem by controlling for specific trends (Angrist and Pischke, 2014). Hence, for volumes, a modified version of equation 2 that accounts for the failure of the common trend assumption is given by the multilevel fixed-effect model

$$log(q_{ikt}) = \alpha_1 R_{ikt} + \beta_1 S_{ikt} + \alpha_2 R_{ikt} * G_{ik} + \beta_2 S_{ikt} * G_{ik} + \sum_{k=1}^{36} \theta_k ATC_k * t + \lambda_t + a_i + \epsilon_{ikt} \qquad (3)$$

where q_{ikt} is the volume of active ingredient sold of product i, which belongs to the ATC k, at time t, and ATC_k is a dummy equal to 1 if the product i belongs to the ATC k.

Furthermore, table 5 shows the estimations of test 2. It is consistent to what was shown in section 3: the control group was not affected by the introduction of the ERP, hence it is correctly specified.

Table 4: Common trend tests (columns 1 and 2 are for prices and columns 3 and 4 are for volumes)

	(1)		(2)		(3)		(4)	
	R vs C		S vs C		R vs C		S vs C	
Interaction 2	0.002	(0.083)	0.097	(0.106)	0.092	(0.290)	-0.045	(0.286)
Interaction 3	-0.137	(0.119)	-0.118	(0.205)	0.563	(0.356)	0.452	(0.317)
Interaction 4	0.452	(0.444)	0.739	(0.510)	-0.476	(0.436)	-0.797*	(0.402)
Interaction 5	0.410	(0.443)	0.710	(0.493)	-0.186	(0.444)	-0.576	(0.393)
Interaction 6	0.493	(0.460)	0.571	(0.470)	0.014	(0.504)	-0.141	(0.422)
Interaction 7	0.395	(0.489)	0.601	(0.542)	1.005	(0.530)	0.110	(0.446)
Interaction 8	0.469	(0.477)	0.632	(0.536)	0.254	(0.522)	-0.161	(0.421)
Interaction 9	0.389	(0.477)	0.512	(0.501)	1.033	(0.526)	0.268	(0.434)
Interaction 10	0.350	(0.479)	0.560	(0.506)	0.903	(0.562)	0.251	(0.435)
Interaction 11	0.335	(0.490)	0.650	(0.539)	0.657	(0.537)	-0.072	(0.437)
Interaction 12	0.329	(0.490)	0.499	(0.504)	0.778	(0.574)	0.354	(0.429)
Interaction 13	0.299	(0.485)	0.567	(0.494)	1.165*	(0.529)	0.177	(0.414)
Interaction 14	0.286	(0.477)	0.587	(0.495)	1.160*	(0.533)	0.257	(0.414)
Interaction 15	0.314	(0.478)	0.554	(0.493)	1.265*	(0.539)	0.316	(0.418)
Interaction 16	0.279	(0.479)	0.458	(0.499)	1.019	(0.560)	0.203	(0.440)
Interaction 17	0.240	(0.487)	0.536	(0.511)	0.844	(0.539)	-0.024	(0.423)
Interaction 18	0.242	(0.480)	0.463	(0.508)	1.123*	(0.532)	0.324	(0.416)
Interaction 19	0.237	(0.487)	0.439	(0.519)	1.151*	(0.557)	0.239	(0.447)
Interaction 20	0.208	(0.482)	0.457	(0.509)	1.231*	(0.555)	0.295	(0.432)
Interaction 21	0.230	(0.482)	0.428	(0.512)	1.078	(0.557)	0.289	(0.434)
Interaction 22	0.181	(0.486)	0.404	(0.501)	0.955	(0.551)	0.292	(0.422)
Interaction 23	0.194	(0.489)	0.427	(0.504)	0.944	(0.574)	0.440	(0.440)
Interaction 24	0.222	(0.491)	0.422	(0.508)	0.845	(0.558)	0.402	(0.435)
Interaction 25	0.128	(0.487)	0.475	(0.480)	1.356*	(0.564)	0.291	(0.441)
Interaction 26	0.193	(0.488)	0.450	(0.500)	1.493*	(0.577)	0.789	(0.444)
Interaction 27	0.174	(0.482)	0.405	(0.498)	1.187*	(0.550)	0.433	(0.430)
Interaction 28	0.145	(0.495)	0.354	(0.513)	1.129*	(0.561)	0.525	(0.424)
Interaction 29	0.163	(0.487)	0.381	(0.505)	1.190*	(0.557)	0.411	(0.431)
Interaction 30	0.295	(0.487)	0.452	(0.515)	1.110*	(0.562)	0.333	(0.445)
Interaction 31	0.245	(0.492)	0.421	(0.515)	1.085	(0.567)	0.384	(0.438)
Interaction 32	0.168	(0.502)	0.452	(0.507)	1.388*	(0.562)	0.443	(0.436)
Interaction 33	0.150	(0.499)	0.537	(0.509)	1.324*	(0.564)	0.674	(0.438)
HHI	-0.570	(0.440)	-0.023	(0.468)	-0.039	(0.926)	0.026	(0.651)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
Observations	5284		7482		5284		7482	
Adjusted R^2	0.050		0.048		0.040		0.031	

Robust standard errors in parentheses

R: regulated; S: substitutes; C: control

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 5: Test for validity of the control group

	Prices (log)		Volumes (log)	
Implementation of the ERP	-0.226	(0.144)	-0.558	(0.474)
HHI	-0.131	(0.174)	-0.549	(0.473)
Time FE	Yes		Yes	
Products FE	Yes		Yes	
Observations	9,158		9,158	
Adjusted R^2	0.030		0.019	

Robust standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

The empirical analysis starts by estimating a reduced version of equation 1 for prices. Column 1 of Table 6 presents the results of a model that ignores the effects on the unregulated substitutes, and it suggests that the ERP reduced prices of regulated drugs by around 60 percent. However, by omitting S, the unregulated substitutes have been included in the control group, biasing the estimations in the case of cross-price effects. The HHI is statistical significant and has a positive sign, which makes sense since firms that supply products in more concentrated markets are granted market power, and thus might charge higher prices. Nevertheless, this estimation should not be taken as a causal impact since there are endogeneity problems arising from the fact that market concentrations are usually correlated with the probability of generic entry, which is simultaneously correlated with prices, as the firms might anticipate higher profits by entering a market where the prices are high (Brekke et al., 2009).

Column 2 and column 3 consider possible cross-price effects by taking the unregulated substitutes out from the control group. As noted, the direct impact of the ERP on the regulated group is now around 70 percent. It also suggests that there is a cross-price effect of 23 percent on the unregulated substitutes. Thus, the estimation in column 1 contains part of these effect. Also note that the introduction of HHI as a control does not change the results by much and does not add too much explanatory power to the estimations (looking at the changes in the adjusted R^2). A possible explanation for this is that some of the markets are characterized for being concentrated, and thus, they include few firms or few pharmaceuticals, in which case by adding products fixed effects part of the concentration of the markets has already been taken care of.

Finally, column 4 reports the estimations of the extended model 2. Contrary to what is found in other countries, there is no statistical evidence to conclude that the ERP affected brand-name different than generics. The coefficients in the non-interacted treatment variables do not change substantially from the previous estimations.

Table 6: Effects of ERP on prices

	(1)		(2)		(3)		(4)	
	Prices (log)		Prices (log)		Prices (log)		Prices (log)	
Products under ERP	-0.599***	(0.058)	-0.715***	(0.057)	-0.708***	(0.057)	-0.714***	(0.059)
Unregulated substitutes			-0.234***	(0.043)	-0.228***	(0.042)	-0.251***	(0.045)
Generics under ERP							0.149	(0.162)
Unregulated generic substitutes							0.103	(0.091)
HHI	0.218*	(0.108)			0.184	(0.103)	0.186	(0.103)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
Observations	36,939		36,939		36,939		36,939	
Adjusted R^2	0.175		0.181		0.181		0.182	

Robust standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

The estimations of the corresponding models for volumes are presented in table 7. By looking at column 1 and column 2, one would naively conclude that the ERP induced demanded quantities by around 57 percent and therapeutic substitution by 30 percent. However, as already been proven, the Diff-in-Diff strategy cannot rely on the common trend assumption. Column 3 and column 4 present the estimation of the corrected model 3 with and without the interaction terms for the differential impacts on generics. In neither case there is statistical evidence to support that pharmaceutical regulation impulsed the demanded quantities. This result is consistent with what was pointed out regarding the series depicted in figure 3. Table A.1 in the appendix also provides the estimations of the corrected model 3 with and without controlling for the HHI and ignoring the unregulated substitutes. The conclusions do not change in any of the specifications.

Table 7: Effects of ERP on volumes

	(1)		(2)		(3)		(4)	
	Volumes (log)		Volumes (log)		Volumes (log)		Volumes (log)	
Products under ERP	0.580***	(0.139)	0.572***	(0.138)	0.137	(0.099)	0.122	(0.100)
Unregulated substitutes	0.326**	(0.125)	0.318*	(0.125)	-0.004	(0.089)	-0.002	(0.095)
Generics under ERP							0.428	(0.348)
Unregulated generic substitutes							-0.007	(0.155)
HHI			-0.232	(0.235)	-0.148	(0.213)	-0.150	(0.212)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
ATC trend	No		No		Yes		Yes	
Observations	36,939		36,939		36,939		36,939	
Adjusted R^2	0.023		0.023		0.067		0.067	

Robust standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

To summarize this section, it was found that the introduction of the ERP system in Colombia led to a reduction of about 71 percent of the prices of the regulated products. The estimations also provide evidence of cross-price effects on the unregulated substitutes of the regulated products of around 23 percent. Contrary to what has been found in other countries (Ellison et al., 1997; Aronsson et al., 2001; Pavcnik, 2002; Brekke et al., 2009, 2011), there was no evidence that the regulation affected differently brand-names than generics. Finally, there was no statistical significant effects of the ERP on volumes sold, suggesting that the increase in the pharmaceutical expenditure and the demanded quantities is not related to the implementation of the ERP system.

5 Robustness checks

This section provides robustness checks for the results presented in section 4. First, since the time horizon in this study is 2011-2018, it comprises all the regulatory rounds that have been implemented in Colombia (see table 1) and the sample contains information of drugs in each round (see table 3). Hence, an interesting aspect is how the estimations would change when considering different time periods and different number of products (depending on whether they have already been regulated in the time frame being considered). Second, a possible concern is that some firms could have reacted to the policy once it was announced (March 2013, see table 1). Third, recent studies have pointed out that the standard errors in Diff-in-Diff estimations are inconsistent due to serial correlation (Wooldrige, 2002; Bertrand et al., 2004) implying that they might be biased downward, overestimating the significance levels.

To take care of each one of these concerns different strategies are implemented in this section. The first one consists on replicating the econometric framework (model 2 for prices and model 3 for volumes) with different time periods, in particular: 2011-2014, 2011-2015, 2011-2016 and 2011-2017 (bounds included), dropping products that have not yet been regulated within each one of these cases. The second one consists on estimating the models where the treatment variables are redefined. In particular, this time let the dummy R_{it} to be equal to 1 if product i was regulated regardless the date in which it entered price control and t is a moment after March 2013 (the respective modification also apply to S_{it} following the same logic). Finally, to overcome possible bias in the standard errors, due to the large number of observations, cluster standard errors are estimated.

5.1 Sensitivity analysis

Table 8 reports the estimations of model 2 for different time frames. The results show that on average the causal effect of the ERP on the prices was near 70 percent, getting larger when more drugs are being added to the sample. These point estimates are close (also the standard errors) to those reported in section 4. One possible explanation for the increase in point estimates is that prices might have adjusted gradually once the regulations took place. A second possible explanation

is that some of the drugs that were included later on were particularly charging unreasonably high prices in comparisson to other drugs, which consequently could have led to implement lower price caps to them (relative to the prices before they enter price control)[16].

On the other hand, impacts on the prices of the unregulated substitutes are not statistical different from zero in the period 2011-2014. After adding the year 2015 the the point estimates starts being statistical significant an getting larger when adding products to the sample. This suggests that cross-price effects might be related to some specific markets and not present in all the ATC under regulation. An additional remark is to note that the impact evaluation proposed by Bardey et al. (2018) for the period 2011-2014 consisted on using the unregulated therapeutic substitutes as a control group. For this to be correctly specified, there should not be cross-price effects (Brekke et al., 2009); thus, the results reported in table 8 confirms that their comparison group is legitimate[17]. Finally, the interactions that test differential effect to brand-name and generics continue to be statistically insignificant.

Table 8: Sensitivity analysis for the impact of the ERP on prices

	2011-2014		2011-2015		2011-2016		2011-2017	
	Prices (log)		Prices (log)		Prices (log)		Prices (log)	
Products under ERP	-0.616***	(0.063)	-0.668***	(0.066)	-0.731***	(0.066)	-0.759***	(0.065)
Unregulated substitutes	-0.088	(0.054)	-0.177**	(0.056)	-0.267***	(0.052)	-0.292***	(0.050)
Generics under ERP	0.184	(0.163)	0.095	(0.137)	0.104	(0.143)	0.132	(0.155)
Unregulated generic substitutes	-0.014	(0.091)	-0.046	(0.084)	0.002	(0.089)	0.057	(0.095)
HHI	0.110	(0.194)	0.269	(0.148)	0.296*	(0.127)	0.183	(0.112)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
Observations	14,585		18,990		23,517		29,136	
Adjusted R^2	0.139		0.182		0.192		0.187	

Robust standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

The corresponding estimations for volumes sold are reported in table 9. The effect on the regulated drugs is the same as the one presented in table 7 except for the time frame 2011-2014. For the unregulated substitutes, on the other hand, the estimations present some counter intuitive results, that even when the regulated drugs did not react to the ERP, they decreased by around 20

[16]For instance, note that Glivec (active ingredient Imatinib) was regulated in 2017 (table 1) which is a drug to treat cancer and was considered to be amongst the most expensive of all. See Experts in Chronic Myeloid Leukemia (2013). Also, the rest of Immunosupressants were added in 2018.

[17]They also showed that the control group is correctly specified by conducting test 2 for the unregulated products in their sample (some of which belong to my second treatment group).

percent for the time frames 2011-2015 and 2011-2016. It is important to note the large standard errors in these estimations, for both the estimated direct impact in the time frame 2011-2014 and the estimated therapeutic substitution in 2011-2015 and 2011-2016. The effects are estimated to be close to the interval $[-0.46, -0.02]$, which is not conclusive at all.

Table 9: Sensitivity analysis for the impact of the ERP on volumes sold

	2011-2014		2011-2015		2011-2016		2011-2017	
	Volumes (log)		Volumes (log)		Volumes (log)		Volumes (log)	
Products under ERP	-0.243*	(0.113)	-0.111	(0.112)	0.012	(0.108)	0.045	(0.113)
Unregulated substitutes	-0.176	(0.106)	-0.230*	(0.109)	-0.224*	(0.107)	-0.147	(0.107)
Generics under ERP	0.377	(0.589)	0.174	(0.482)	0.209	(0.393)	0.292	(0.366)
Unregulated generic substitutes	0.120	(0.136)	0.152	(0.155)	0.135	(0.151)	0.038	(0.158)
HHI	0.270	(0.370)	0.224	(0.267)	-0.040	(0.241)	-0.022	(0.229)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
ATC trend	Yes		Yes		Yes		Yes	
Observations	14,585		18,990		23,517		29,136	
Adjusted R^2	0.105		0.096		0.086		0.073	

Robust standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

5.2 Reactions to the policy

To interpret the results presented in this subsection, one should bear in mind that the strategy consists on taking lagged values of the original dummies R_{it} and S_{it} in equations 2 and 3. However, since not all the pharmaceuticals were regulated at the same time, these variables are lagged a different number of periods for each one of the regulated products (and their unregulated therapeutic substitutes)[18]. Nevertheless, since the time of reference is March 2013, six months before the policy was implemented, it allows to control for behavioral changes that might have happened when none of the products were yet under regulation (the announcement effect).

Table 10 presents the estimated effects for prices. These results do not differ substantially from those reported in table 6, suggesting that the ERP had a negative effect on both the regulated drugs and their unregulated therapeutic substitutes of 69 percent and 32 percent, respectively (column 4). The direct effect being slightly lower implies that part of the price adjustment took place before the implementation of the policy (Brekke et al., 2015).

[18]For the pharmaceuticals regulated in the first round the number of months lagged are six, for the second round ten, for the third round twenty two and for the fourth round thirty four.

Table 10: Impact of the ERP on prices (reactions after March 2013)

	(1)		(2)		(3)		(4)	
	Prices (log)		Prices (log)		Prices (log)		Prices (log)	
Products under ERP (lagged)	-0.495***	(0.067)	-0.697***	(0.073)	-0.688***	(0.072)	-0.694***	(0.074)
Unregulated substitutes (lagged)			-0.317***	(0.062)	-0.309***	(0.060)	-0.321***	(0.064)
Generics under ERP (lagged)							0.141	(0.120)
Unregulated generic substitutes (lagged)							0.055	(0.106)
HHI	0.242*	(0.109)			0.211*	(0.103)	0.211*	(0.102)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
Observations	36,939		36,939		36,939		36,939	
Adjusted R^2	0.157		0.162		0.163		0.163	

Robust standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 11 present the respective estimated impacts on volumes sold. None of the point estimates are statistically different from zero, in the same lines with the results presented in section 4. It is still suggested that the implementation of the pharmaceutical regulation had no impact on the demanded quantitites of neither the regulated products nor their closest unregulated substitutes.

Table 11: Impact of the ERP on volumes (reactions after March 2013)

	(1)		(2)		(3)		(4)	
	Volumes (log)		Volumes (log)		Volumes (log)		Volumes (log)	
Products under ERP (lagged)	0.157	(0.119)	0.073	(0.182)	0.060	(0.184)	0.041	(0.185)
Unregulated substitutes (lagged)			-0.115	(0.175)	-0.126	(0.177)	-0.164	(0.179)
Generics under ERP (lagged)							0.482	(0.443)
Unregulated generic substitutes (lagged)							0.164	(0.190)
HHI	-0.153	(0.211)			-0.167	(0.214)	-0.177	(0.212)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
ATC trend	Yes		Yes		Yes		Yes	
Observations	36,939		36,939		36,939		36,939	
Adjusted R^2	0.067		0.067		0.067		0.068	

Robust standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

5.3 Correction of the standard errors

To overcome potential inconsistency in the standard errors I follow a solution suggested by Bertrand et al. (2004), that in this case might perform well due to the large number of observations in the data: to cluster the standard errors at the ATC level. This alternative takes into account that variables from each products might be correlated if they belong to the same pharmacological or therapeutic groups (Bardey et al., 2018). Note that throughout the document, all the estimations have used robust (Eicker-Huber-White) standard errors, that perform well under the presence of heteroscedasticity, but not under serial correlation (a likely concern in data panel with more than two periods).

Table 12 presents the corresponding estimations for the effects on prices[19]. As expected, the cluster standard errors are larger than the robust standard errors. The point estimates for the impact of the ERP on the prices of the regulated products and their unregulated substitutes continued to be significant at the same level (99 percent) than before. The interacted terms to test differential impacts of the policy on brand-names and generics are still not statistically different from zero. Moreover, note that the point estimate for the HHI in column 1 of table 12 is no longer significant, contrasting with the respecting one in table 6 which supports the interpretation given of potential endogeneity in this variable. Regarding the impact of the ERP on volumes sold, the results reported in table 13 are consistent with the estimations presented in both this section and the previous section.

The appendix also provides the respective estimations using classic (homoscedastic-only) standard errors. It is clear that the significance levels are overestimated which could have led to (incorrectly) conclude that, besides the direct impact of the ERP on prices and cross-price effects, generics had experienced a stronger effect (table A.2). Furthermore, it would have also indicated that the ERP induced demand by 54 percent for generics and 12 percent for brand-names (table A.3).

[19]Note that this strategy will not change the point estimates for the coefficients.

Table 12: Impact of the ERP on prices

	(1)		(2)		(3)		(4)	
	Prices (log)		Prices (log)		Prices (log)		Prices (log)	
Products under ERP	-0.599***	(0.097)	-0.715***	(0.099)	-0.708***	(0.098)	-0.714***	(0.105)
Unregulated substitutes			-0.234**	(0.083)	-0.228**	(0.082)	-0.251**	(0.091)
Generics under ERP							0.149	(0.144)
Unregulated generic substitutes							0.103	(0.101)
HHI	0.218	(0.161)			0.184	(0.148)	0.186	(0.146)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
Observations	36,939		36,939		36,939		36,939	
Adjusted R^2	0.175		0.181		0.181		0.182	

Cluster standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 13: Impact of the ERP on volumes

	(1)		(2)		(3)		(4)	
	Volumes (log)		Volumes (log)		Volumes (log)		Volumes (log)	
Products under ERP	0.572**	(0.175)	0.540**	(0.174)	0.137	(0.115)	0.122	(0.118)
Unregulated substitutes	0.318	(0.186)	0.299	(0.194)	-0.004	(0.130)	-0.002	(0.119)
Generics under ERP			0.794**	(0.227)			0.428	(0.268)
Unregulated generic substitutes			0.094	(0.288)			-0.007	(0.294)
HHI	-0.232	(0.396)	-0.228	(0.395)	-0.148	(0.431)	-0.150	(0.423)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
ATC trend	No		No		Yes		Yes	
Observations	36,939		36,939		36,939		36,939	
Adjusted R^2	0.023		0.024		0.067		0.067	

Cluster standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

6 Conclusions

This study constitutes an attempt to investigate the effects of the ERP system in Colombia on both the pricing behavior and demanded quantities of the products under regulation and their unregulated closest substitutes for the period 2011-2018. The empirical strategy showed that the pharmaceutical policy decreased the prices of the regulated commercial presentations by 71 percent and their unregulated substitutes by 25 percent. In spite of these findings, the results also reported that price reductions do not translate into decreases of the overall pharmaceutical expenditure. However, it can not be concluded that the ERP system in Colombia triggered the demanded quantities.

The estimated direct impact of the ERP is substantially higher than the usual effects found in the literature. Moreover, there is no statistical evidence that the generics were affected differently than brand-names, a result that contrasts with the estimations of Aronsson et al. (2001) for Sweeden, Pavcnik (2002) for Germany and Brekke et al. (2009) for Norway. However, it is important to bear in mind the differences between these policies and the Colombian. Besides the obvious distinction between RP and ERP, the regulation in those countries was implemented on all the commercial presentations within the same ATC.

The presence of cross-price effects on the products that are not covered under the ERP system might have some negative impacts. Some theoretical works have focused on understanding the consequences of developing benchmarks from international references. In particular it has been suggested that the ERP might lead to delays in developing new technologies in small economies because of the international interdependence, since the laboratories can no longer implement differential pricing (Persson and Jönsson, 2016). Thus, the cross-price effects could strengthen this problem by extending it to unregulated commercial presentations. This would not be a concern if only Colombia implements this regime, however, as pointed out by Leopold et al. (2012) the ERP system have become very popular in many state members of the European Union. This is an important consideration from a policy perspective since it might lead to shortages in the supply and reduce incentives for innovation.

A further concern is that even though the regulation was effective in reducing the prices of the regulated products, the pharmaceutical expenditure continued to increased (even if only the regulated ATC are considered), as already shown by Prada et al. (2018). The novelty of this study in relation to theirs is that the empirical estimations ruled out any causal impact of the ERP. This result is consistent with Brekke et al. (2009) who also found a substantial effect in prices (30 percent) but no effects in volumes sold for Norway. This could imply that the increase in demand is represented for better access to medicines instead of unnecessary drug use, in which case it could represent a positive scenario for a developing country like Colombia. However, the empirical analysis proposed here does not allow to disentangle both cases.

Moreover, it is important to emphasize that the results presented here shed lights on the pricing behavior within the regulated ATC but ignore some other aspects of pharmaceutical regulations, like impacts on markets structure and welfare. Thus, a more complete analysis from a policy perspective would require having information of the pharmaceutical firm's innovation and launching incentives, their profits and copayments paid by the consumers. Such analyses are beyond the scope of this thesis and remain as interesting aspects for further research.

Finally, it is important to mention that, this study presents a main shortcut. Although it has been established that every institution that commercialize pharmaceuticals in Colombia must report every four months information on sold products, there is under reported information in the SISMED platform.

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Appendix: Supplementary tables and figures

Figure A.1: Prices per active ingredient (regulated v.s substitutes) 2011-2018

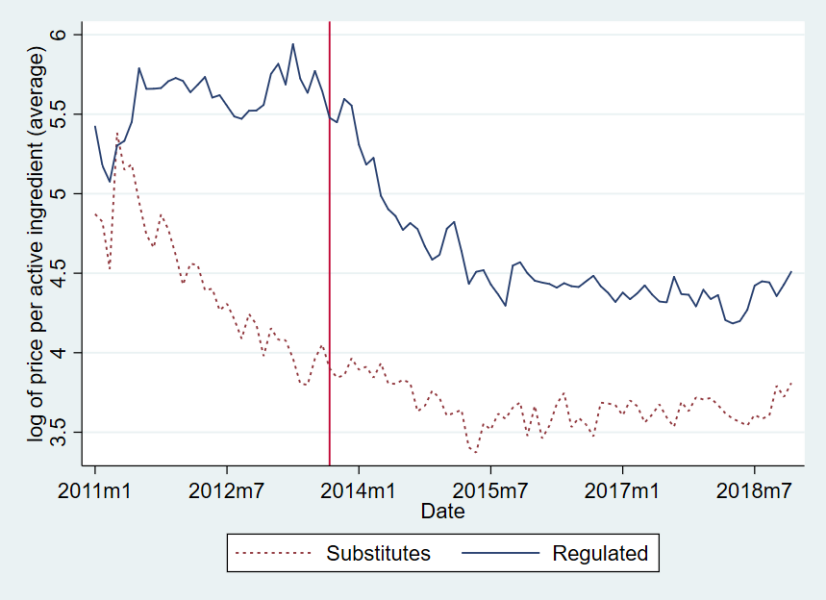

Figure A.2: Prices per active ingredient (control group) 2011-2018

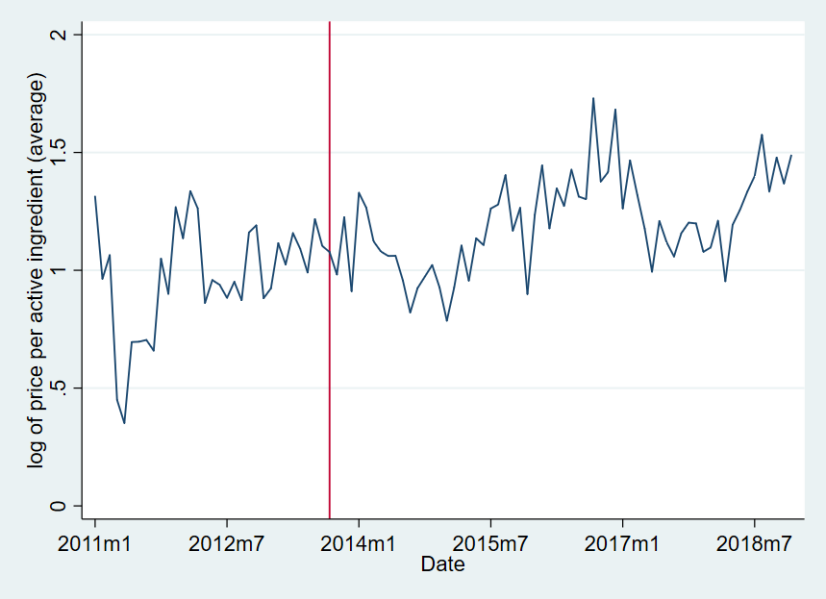

Figure A.3: Prices per active ingredient (all unregulated drugs) 2011-2018

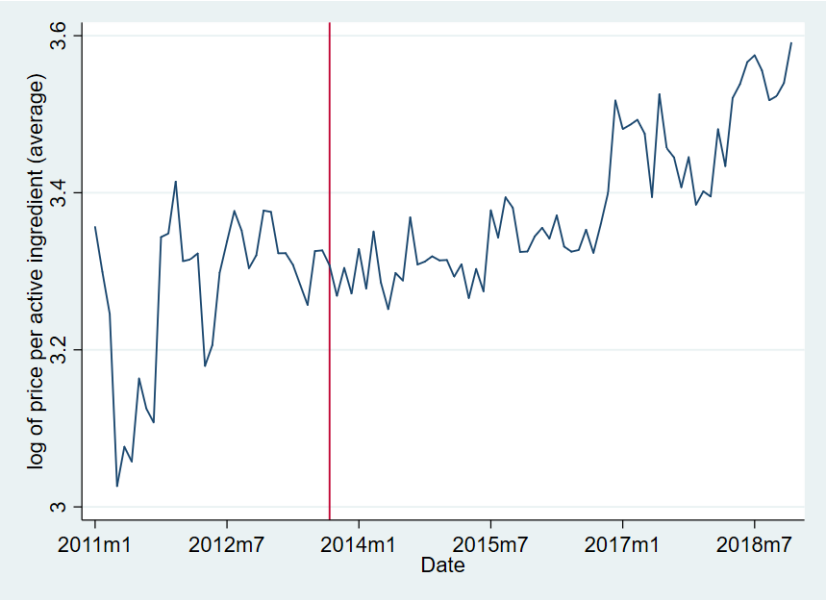

Figure A.4: Volumes of active ingredient (control group) 2011-2018

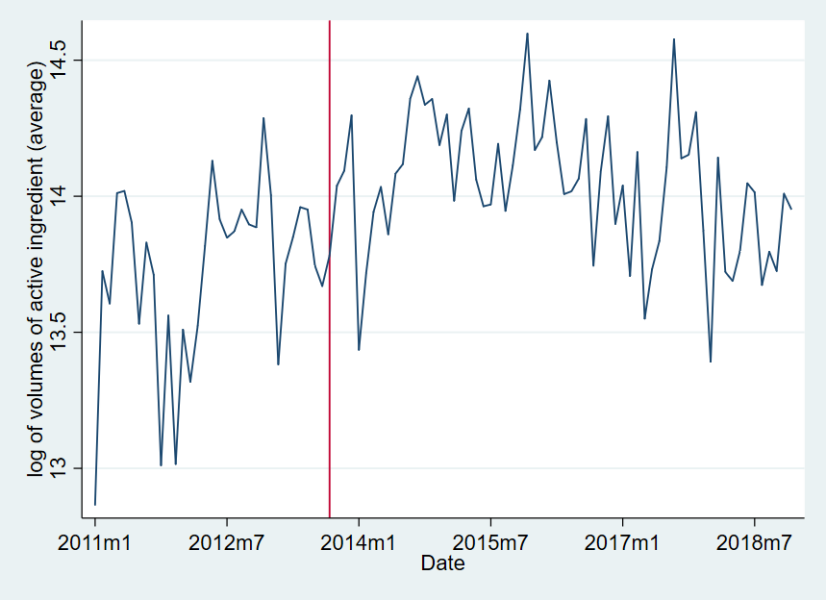

Figure A.5: Volumes of active ingredient (all unregulated drugs) 2011-2018

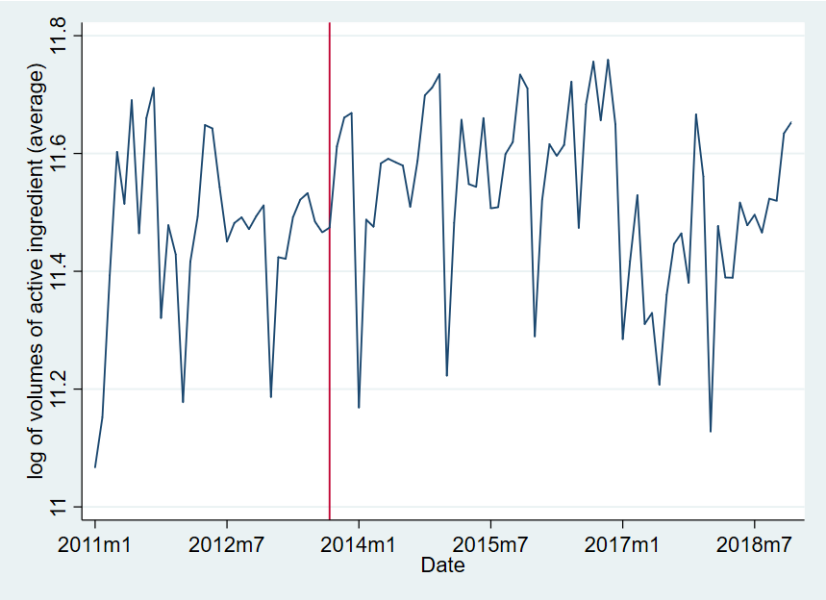

Table A.1: Effects of ERP on volumes (with ATC specific trends)

	(1)		(2)		(3)		(4)	
	Volumes (log)		Volumes (log)		Volumes (log)		Volumes (log)	
Products under ERP	0.139	(0.094)	0.146	(0.098)	0.137	(0.099)	0.122	(0.100)
Unregulated substitutes			0.002	(0.088)	-0.004	(0.089)	-0.002	(0.095)
Generics under ERP							0.428	(0.348)
Unregulated generics substitutes							-0.007	(0.155)
HHI	-0.148	(0.211)			-0.148	(0.213)	-0.150	(0.212)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
ATC trend	Yes		Yes		Yes		Yes	
Observations	36,939		36,939		36,939		36,939	
Adjusted R^2	0.067		0.067		0.067		0.067	

Robust standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table A.2: Effects of ERP on prices (homoscedastic-only standard errors)

	(1)		(2)		(3)		(4)	
	Prices (log)		Prices (log)		Prices (log)		Prices (log)	
Products under ERP	-0.599***	(0.015)	-0.715***	(0.016)	-0.708***	(0.016)	-0.714***	(0.016)
Unregulated substitutes			-0.234***	(0.014)	-0.228***	(0.014)	-0.251***	(0.015)
Generics under ERP							0.149*	(0.063)
Unregulated generic substitutes							0.103***	(0.024)
HHI	0.218***	(0.030)			0.184***	(0.030)	0.186***	(0.030)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
Observations	36,939		36,939		36,939		36,939	
Adjusted R^2	0.151		0.156		0.157		0.157	

Standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table A.3: Effects of ERP on volumes (homoscedastic-only standard errors)

	(1)		(2)		(3)		(4)	
	Volumes (log)		Volumes (log)		Volumes (log)		Volumes (log)	
Products under ERP	0.572***	(0.042)	0.540***	(0.042)	0.137**	(0.050)	0.122*	(0.051)
Unregulated substitutes	0.318***	(0.036)	0.299***	(0.039)	-0.004	(0.045)	-0.002	(0.047)
Generics under ERP			0.794***	(0.162)			0.428**	(0.164)
Unregulated generic substitutes			0.094	(0.062)			-0.007	(0.066)
HHI	-0.232**	(0.078)	-0.228**	(0.078)	-0.148	(0.084)	-0.150	(0.084)
Time FE	Yes		Yes		Yes		Yes	
Products FE	Yes		Yes		Yes		Yes	
ATC trend	No		No		Yes		Yes	
Observations	36,939		36,939		36,939		36,939	
Adjusted R^2	-0.006		-0.006		0.039		0.039	

Standard errors in parentheses

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

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UNIVERSIDAD ICESI

Calle 18 No - 122-135, Universidad Icesi - Casa Rocha
Telefono: +57(2) 321-20-92
Cali - Colombia
www.icesi.edu.co/proesa/