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ORIGINAL PAPER

The impact of repeated cost containment policies on pharmaceutical expenditure: experience in Spain

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Abstract The growth in expenditure on the financing of pharmaceuticals is a factor that accounts for a large part of the increase in public health spending in most developed countries. In an attempt to kerb this growth, many health authorities, particularly in Europe, have introduced numerous regulatory measures that have affected the market, especially on the supply side. These measures include the system of reference pricing, the reduction of wholesale distributors' and retailers' markups and compulsory reductions of ex-factory prices. We assess the impact of these cost containment measures on expenditure per capita, prescriptions per capita and the average price of pharmaceuticals financed by the public sector in Catalonia (Spain), from 1995 to 2006. We apply an autoregressive integrated moving average (ARIMA) time series model using dummy variables to represent the various cost containment measures implemented. Twelve of the 16 interventions analysed that were intended to contain the overall pharmaceutical expenditure were not effective in reducing it even in the short term, and the four that were effective were not so in the long term, thus amounting to a moderate annual saving.

Keywords Pharmaceutical expenditure · Pharmaceutical policy · Cost containment measures · Time series

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Introduction

In recent years, the growth in expenditure on the financing of pharmaceuticals has been one of the factors that accounts for a large part of the increase in public health spending in most developed countries. In an attempt to kerb this growth, health authorities have introduced regulatory measures that have affected the market, especially on the supply side. Some of the most commonly used measures have been the system of reference pricing, the reduction of wholesale distributors' and retailers' markups, compulsory reductions of ex-factory prices, the exclusion of some pharmaceuticals from public financing and incentives to improve prescribing practices.

Demographic factors such as the ageing of the population, the inclusion of new services and innovative treatments, and, in general terms, greater demand for health care, puts increasing pressure on public resources and jeopardise the financial sustainability of the health care system. The administration therefore has responsibility for ensuring the most efficient possible use of available economic resources. Thus, in most countries, it should be of concern to health care payers that have adopted certain measures to know whether they have been effective in containing public expenditure in pharmaceutical products.

The aim of this study is to assess the impact of the measures implemented between 1995 and 2006 on expenditure per capita, average drug prices and the number of prescriptions per capita in Catalonia. In fact, all except one strategy are implemented in the whole country and may have different impacts in each region of Spain, where regional governments control expenditures and organise

health services. This paper contributes to the existing literature by providing an accurate estimation of the impact of repeated pharmaceutical cost containment measures not only on expenditure but also on the accounting factors that explain expenditure growth, i.e. prices and quantities.

The results of the study show how a large part of the measures adopted were not effective, and even when they had a significant impact, it was almost never long term. In the light of the several cost containment measures that have been implemented, the adoption of new measures or the repetition and adjustment of existing ones does not seem to have the expected effect in terms of new reductions. Using a different method, Sood et al. [1]. examine 19 developed countries from 1992 to 2004 and also found that incremental regulation of already regulations in place had a smaller impact on costs. The results presented for Catalonia in this paper may be useful for other highly regulated and tax funded health care systems using similar cost containment measures in the pharmaceutical market.

The study is organised as follows. First, we provide a brief description of the Spanish pharmaceutical market. Then, in the following section, we describe the main cost containment strategies implemented by the health authorities. In the third section, we describe the data and the method used to analyse the interventions, which will allow us to study the impact of the various measures. In the fourth section, we provide the results of the estimates. The next section serves to discuss the results and their implications. Finally, in the last section, we remark the main conclusions of the work.

The Spanish pharmaceutical market

The National Health System (NHS) in Spain, one of the largest markets for pharmaceuticals in the European Union (EU) and the seventh largest worldwide, is funded with taxes and provides health care services to all residents. The health care management system is completely decentralised and regional governments control expenditures and organise health service provision. However, as in many industrialised countries, prices are centrally regulated [2].

Another important feature in Spain is that there are small co-payments for prescribed products. The usual co-payment rate for active population (or their family members) is 40%, but the average co-payment is clearly smaller since prescription drugs for pensioners and some specific groups (retired, handicapped and people who have suffered occupational accidents, and their dependents) are provided free. The co-payment in the case of chronic diseases is only 10%, with a price cap. Then, the effective patient co-payment for pharmaceuticals is very low. Patients cover less than 7% of the total expenditure in ambulatory health care system prescription pharmaceuticals, and the NHS pays all the prescribed drugs in public hospitals. Moreover, the prescription market dominates over-the-counter (OTC) sales: the market share of prescription drugs is 85.50% of volume and 92% of total sales [3].

The average price of drugs in Spain is low compared to that of other EU countries but, although regulated prices increase fall short of the inflation rate, the average brand prescription price has risen steadily, mainly due to drugs recently introduced onto the market at high prices. Maybe as a strategy to avoid parallel trade, the prices for new chemical entities are not much lower than the European average [3]. In fact, low regulated prices for old products have converted the Spanish market into an important source of parallel trade in the EU.

As the NHS is the main payer of ambulatory prescription pharmaceuticals (around 80% of sales are financed by the NHS), budgetary impact of new pharmaceuticals has been an increasing concern for public health service financing sustainability, and cost containment policies have put a great emphasis to maintain traditional low prices, being higher prices for new products increasingly under scrutiny, despite being the increase in consumption the main driver of expenditure rise [4].

In any case, although Spain was still a relatively low-price country and has a limited generic penetration, in December 2000, a reference pricing system was introduced and has gradually been extended to reimburse a growing list of active ingredients.

Moreover, all drugs maximum ex-factory prices are set during the process of obtaining market approval, and usually the introduction price remains as the maximum price for most of the product life [5]. A public agency of the Ministry of Health is responsible for negotiation with firms and price setting. The government used a peculiar form of cost-based price regulation for branded drugs in which manufacturing, marketing and research costs, and an industrial profit on invested capital were allocated to new drugs. However, this is rarely the final price since the legislation allows considering other factors such as the price of the same product in other European countries, the price of drugs that can be considered substitutes or the therapeutic innovation of the medicine. In fact, the legal criterion is that the price has to reflect the therapeutic value of the drug as well as the cost of comparable treatments, the price of the same drug in other countries and some other political issues such as the contribution to the national economy [2].

Finally, it is important to highlight that public expenditure on prescription medicines represented in 2006 almost the 22% of public current health expenditures in Spain, and between 1995 and 2006, the public expenditure

on pharmaceuticals increased a 182%, which represents the fastest growth in overall public service expenditures.

Cost containment policies

Since 1996 the Spanish health care authorities have implemented several measures aimed at containing public expenditure on the supply side. The strategies used can be divided into five groups: adjustment of wholesale distributors' and retailers' markups; exclusion of pharmaceuticals from public financing; compulsory reduction of ex-factory prices; reference pricing; and incentives to improve prescribing practices. After a systematic review of all the cost containment measures applied, we assess those that can have a major quantitative effect on public spending on pharmaceutical products generally. Therefore, we do not assess those measures that can also contribute to the reduction of spending specifically on only certain products, such as prior authorisations for specific medicines [6].

These measures try to impact total costs by affecting price or volume of prescriptions, and as a result of this impact, there is a change in total costs. Table 1 reports the expected effect of each of the 16 cost containment strategies analysed on outcome variables and their period of implementation. Only two measures are expected to have an impact on the number of prescriptions.

Markup adjustment

Markup adjustment can reduce the margins obtained both by wholesalers, who distribute the medicines from the manufacturers to the pharmacies, and by retailers, the pharmacies where the medicines are dispensed to the patients. The expected effect of this measure is a reduction in the consumer price, and therefore in expenditure (per capita) and in average drug prices. In the period analysed, there were five successive markup adjustments.

Negative lists of drugs

Only one major measure was implemented to exclude medicines from public financing, in September 1998, leading to the exclusion of 984 products. A measure of this type should reduce pharmaceutical expenditure (per capita) and prescriptions per patient, by diminishing the number of pharmaceutical products that can be prescribed, but it should not affect average drug prices. Nevertheless, the

Table 1 Description of cost containment measures

Measure	Period	Total cost per capita	Price per prescription	Prescriptions per capita
Markup adjustment 1	March 1997–	☑	☑	
Exclusion of pharmaceuticals	September 1998–	☑		☑
Markup adjustment 2	June 1999–	☑	☑	
Reduction of ex-factory prices 1	November 1999–	☑	☑	
Markup adjustment 3	August 2000–	☑	☑	
Reference pricing system 1	December 2000–December 2003	☑	☑	
Reduction of ex-factory prices 2	July de 2001–	☑	☑	
Reference pricing system 2	May 2002–	☑	☑	
Reference pricing system 3	May 2003–	☑	☑	
Reference pricing system 4	January 2004–	☑	☑	
Economic incentives to improve prescribing practices	April 2004–	☑	☑	☑
Reference pricing system 5	August 2004–	☑	☑	
Reduction of ex-factory prices 3	March 2005–	☑	☑	
Markup adjustment 4	March 2005–	☑	☑	
Reduction of ex-factory prices 4	March 2006–	☑	☑	
Markup adjustment 5	March 2006–	☑	☑	

withdrawal of public funding from some products can also affect the average price of the drugs prescribed if some excluded products are substituted by more expensive drugs or less expensive ones. The sign of the effect cannot be determined a priori.

Compulsory reduction of ex-factory prices

This measure consists of a unilateral reduction of the manufacturer's maximum selling price by the administration. The expected outcome is a reduction in expenditure through a reduction in the price of the drugs prescribed. Therefore, we should observe a reduction in both expenditure per capita and average drug prices, but it should not affect the number of prescriptions, unless the price elasticity is negative.

Reference pricing system

A system of "generic" reference pricing [4] was introduced in December 2000 and remained in operation, with adjustments but without major changes, until December 2003. The number of products affected by the measure was extended in May 2002 and May 2003 with the incorporation of new groups of drugs (homogeneous sets). This system was applied to products with the same active ingredient, pharmaceutical form, dosage and number of units for which there was at least one generic. In fact, a set was created once there was at least one generic version of the respective active ingredient. For each group, a reference price was calculated as the weighted average selling price of the cheapest drug accounting for at least 20% of the market. This system established the maximum price that could be reimbursed by the NHS for any version of the same drug. With this system, if the price of the prescribed medicine was higher than the reference price, the patient could choose either to replace it with another drug priced no higher than the reference price or to pay the difference between the reference price and the price of the medicine.

In January 2004, the reference pricing system was modified, and since then until the final period analysed, as stated by Antoñanzas et al. [1], the system has been ''frozen'' in the sense that no other homogeneous sets have been created and that no other related policies have been implemented. One modification was that the equivalence criterion for drugs affected by the system was extended. All presentations and pharmaceutical forms with the same active ingredient, whether or not they were bioequivalent, came to be grouped in the same set for the purpose of determining their reference price, on condition that there was at least one generic within the set. Thus, the reference price was calculated as the average of the three lowest costs per day of treatment for each form of administration of an active ingredient, according to its defined daily dose.

With the reference pricing system introduced in January 2004, if the price of the prescribed drug was equal to or lower than the reference price, the pharmacist must dispense the prescribed medicine; if the price of the prescribed drug was higher than the reference price and there was a generic version of it available, then the pharmacist was required to dispense the cheapest generic in the same set; and if the price of the prescribed drug was higher than the reference price but there was no generic version of it available, then the pharmacist would have to dispense the prescribed drug at the reference price. If the physician wrote the prescription using the name of the active ingredient, the pharmacist was obliged to dispense the lowest-priced generic. If there was no generic available, the pharmacist must dispense the brand pharmaceutical corresponding to the prescription concerned at the reference price.

The expected outcome of the implementation of a reference pricing system such as the one in place since 2004 is a reduction in total pharmaceutical costs per capita. On the other hand, with a system such as that in force from December 2000 to December 2003, the cost will be reduced for the public insurer, but this is not necessarily the case for total cost, which includes the contribution made by patients to pharmaceutical financing. Kanavos, Costa-Font and Seeley [7], in a study for UK, Germany, France, Italy, US, Canada and Spain pharmaceutical markets, found that reference pricing encourages generic entry and reduces generic prices but only marginally.

Incentives to improve prescribing practices

The last strategy analysed is the Prescription Quality Improvement Programme implemented in Catalonia in April 2004. This measure consisted in giving prescribers an economic incentive, which could amount to as much as 35% of their variable remuneration, to improve the quality of their prescriptions. The aim was to improve physicians' prescribing habits by encouraging the use of drugs with proven efficacy and generics, limiting the use of new drugs, improving the selection of drugs and avoiding over-prescription. The expected outcome of this strategy is a reduction in expenditure, the number of prescriptions per capita and the average price of the drugs prescribed.

Data and method

The data used are the monthly totals charged by pharmacies for ambulatory medical prescriptions from January 1995 to December 2006. These data were provided by the Catalan Health Service. The time series used are total

Table 2 Descriptive statistics of the series analysed

Variable	Average	Standard deviation	Minimum	Maximum	Confidence interval (95%)
Total expenditure per capita (€)	17.21	3.87	9.47	23.92	16.57–17.85
Price per prescription (€)	12.47	1.79	8.99	14.67	12.17–12.76
Prescriptions per capita	1.37	0.14	0.99	1.69	1.34–1.39

pharmaceutical expenditure (including both the cost for the public insurer and the co-payment made by patients) valued at the consumer price that is actually paid and the total number of prescriptions. To assess the growth of the health expenditure devoted to pharmaceutical products, it is important to consider the steep rise in population that took place in Catalonia during the period analysed. This is why the study focuses on analysing the trend in expenditure per capita. We use data for the population covered by the NHS in Catalonia (Ministerio de Sanidad y Consumo, Informe del Grupo de Trabajo de Análisis del Gasto Sanitario, 2005–2007), that is, people insured by the public system, which excludes the civil servants that have a coverage agreement with a private insurance company. Thus, "per capita" simply means that the raw series have been divided by the population that is covered by the NHS in Catalonia. Therefore, the outcome variables for this study on the basis of monthly observations are total pharmaceutical expenditure per capita and the average price per prescription, both valued at the consumer price (i.e. the end price) and the number of prescriptions per capita.

Table 2 shows the descriptive statistics of the variables under study. In the same way as Lee et al. [8], we use the expenditure data in nominal terms, i.e. without accounting for inflation, since drug prices evolve differently from prices in general, and are not regularly adjusted according to any price index (prices are not inflation adjusted over time). The average monthly expenditure per capita over the whole of the period analysed (1995–2006) was €17.21, ranging from €9.47 to €23.92. The average monthly price per prescription was €12.47, ranging between €8.99 and €14.67. The number of prescriptions per capita per month ranged from a minimum of 0.99 and a maximum of 1.69, with an average of 1.37.

Figure 1 shows the monthly trend of the outcome variables and the cost containment strategies applied in the period analysed. There is a clear tendency towards growth of the total pharmaceutical expenditure per capita. This growth trend levelled off notably after January 2004, coinciding with the change in the system of reference pricing. Similarly to expenditure per capita, the average price per prescription followed an upward trend, although less pronounced. In fact, it went from €9.33 in 1995 to €14.46 in 2006, which involves an increase of €0.47 per year although, for the last third of the sample analysed, it remained steady at around €15 per prescription. Lastly, we can see the trend in the number of prescriptions per capita throughout the period analysed.

In order to examine the impact of the cost containment measures on the time series of expenditure per capita, number of prescriptions per capita and price per prescription, we use an observational and retrospective design and the time series models with intervention analysis described by Box and Tiao [9].

The expenditure data are monthly, and show seasonal variations, a trend, and time correlation. Consequently, we specify a time series model of the autoregressive integrated moving average (ARIMA) type. In these models, it is assumed that the observed values of the variable under study are given by two essential elements: the value or values that this variable has taken in the past (autoregressive component); and a stochastic error term, i.e. a random variable, with a structure that can also incorporate its past values (moving average component). In order to apply this type of model, the assumptions of stationarity[1] and ergodicity[2] must be made. The Box–Jenkins methodology [10] enables us to determine which ARIMA model matches the process best. The selected model yields efficient estimates of the parameters, thus avoiding the problems that arise when making estimates using the ordinary least squares method due to the correlation of the dependent variable over time.

The interventions are analysed using dummy variables, which only take the values 0 and 1. In this way, once we have identified the moment in time at which an intervention takes place (for example, the moment the reduction of the wholesalers' distribution markup comes into force), a dummy variable is specified that represents this fact.

Given that in our case, we are interested in using these dummy variables to represent the effects of pharmaceutical policies in force from a particular moment in time, we have to use step variables.[3] Pulse variables, which are equal to one just

[1] In a strict version, it means that the joint distribution function of the process is the same regardless of the moment in time.

[2] The process has a finite memory.

[3] That is, an intervention which effect will last from this period to the final period. In this case, the dummy variable that captures an intensification measure, for example the markup readjustment in June of 1999 that reinforce the previous one in March of 1997, can be interpreted as a interaction variable. In this sense, the dummy variable "June 1999" inform us about the effect in the period in which both interventions overlap and its interpretation is how much adds this second intervention (to the effect of the previous one) to the cost per capita, price per prescription or prescriptions per capita.

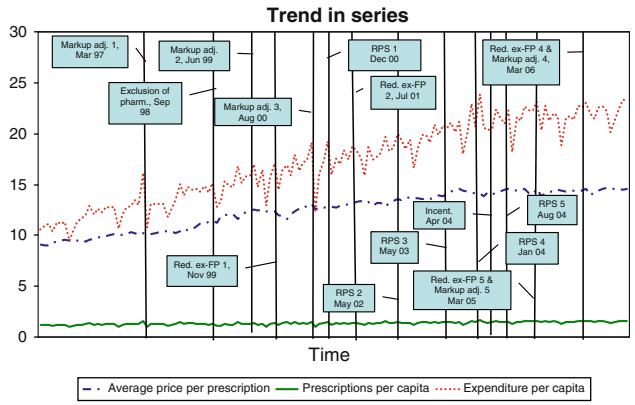

Fig. 1 Trend in time series analysed. Average price per prescription is expressed in terms of Euros per prescription; Prescriptions per capita is expressed as the number of prescriptions per person (covered by the NHS); and Expenditure per capita is expressed in terms of Euros per person (covered by the NHS). *adj* adjustment, *pharm.* pharmaceuticals, *ex-FP* ex-factory price, *RPS* reference pricing system, *Incent.* incentives, *Red.* reduction

one period, can be used to represent isolated events but they are not suitable for representing ongoing measures as of a moment in time. In any case, the intervention can affect the variations of the variable in different ways, as emphasised by Enders [11]. Finally, the coefficients of the dummy variables of the best specification in statistical terms allow us to estimate the effect of the interventions represented by these variables.

The intervention analysis technique and the ARIMA methodology complement each other and enable us to assess the impact of the cost containment policies. Although regression analysis has been used to analyse the effects of drug cost containment measures [12], this is the most appropriate methodology for the analysed data and the purpose of this paper. In fact, this same method has been applied previously to the analysis of pharmaceutical expenditure in Taiwan by Lee et al. [8] and even to analyse the Spanish pharmaceutical expenditure evolution (Barrera, F., Domínguez, D. Perspectivas del gasto farmacéutico en España. Farmaindustria, 2006). Moreover, this methodology has been used to analyse the effect of results of clinical trials on prescribing patterns [13]. In a more general context, ARIMA time series models have also been used, for example, to analyse the impact of a cost sharing drug insurance plan on drug utilisation [14], the effect of administrative restrictions on antibiotic use and expenditure [15] and the impact of increased co-payments on the prescription of antidepressants, anxiolytics and sedatives [16].

On incorporating the intervention analysis into the ARIMA model, the definitive model is

$$\phi_p(L)Y_t = a + \sum_i w_i X_{it} + \theta_q(L)\varepsilon_t \qquad (1)$$

where, on the left-hand side, $\phi_p(L)$ is an autoregressive polynomial of order p (number of delays) and Y_t is the value of process Y at moment t. Indeed, in each equation, Y represents the log of the three outcome variables described above: total pharmaceutical expenditure per capita; average price per prescription; and the number of prescriptions per capita. On the right-hand side, w_i is the effect on Y_t associated with intervention X_{it} and $\theta_q(L)\varepsilon_t$ is a moving average polynomial of order q (number of delays).

Table 3 shows the definition of the dummy variables created to represent each of the 16 cost containment strategies analysed. Some of these variables coincide in time, so at any given moment in time, these dummy variables show the various different measures that are in force.

The ARIMA model will be validated if the total autocorrelation function and partial autocorrelation function of the residuals of the estimated model follow the pattern of a white noise process, i.e. if it is not possible to reject the null hypothesis of non-autocorrelation of residuals for each delay in them by means of the Ljung-Box Q-statistic[17]. To get to this point, first, we have performed the Dickey-Fuller test in which the null hypothesis is that the series is non-stationary. If we can reject this null hypothesis, we have to differentiate the series (as in the case of price per prescription and expenditure per capita). Once we work with a stationary series, we have to find the correct autoregressive or moving average pattern. The correlogram and partial correlogram graphs were used to help in deciding the order of moving average (MA) and autoregressive (AR) terms to include in the model. Then, we incorporate this pattern to explained part of the model—we estimate using maximum likelihood and data analysis was performed in Stata V9.0 (Stata Corporation, College Station, TX, USA). Once the procedure is finished, the residuals obtained will follow the pattern of a white noise process.

At this point, is possible that we computed various permutations of the order of correlation (AR) and order of moving average (MA), which residuals of the estimated model follow this white noise pattern. Among these non-nested models that meet this requirement, if necessary, we use the parsimony principle (that is, we choose the model with less parameter). Finally, to select among the models with the fewest parameters, the Akaike criterion (AIC) or the smallest sum of the squares of the residuals are used. That is, the models selected are those which residuals follow white noise pattern (first step), with less parameters (second step) and, finally, least square error and minimum AIC (third step).

In the case of the series of total expenditure per capita, only the ARIMA$(1,1,0)(1,0,0)_{12}$ model[4] is validated with the least possible number of parameters.[5] That is, first order

[4] Following the form ARIMA$(p,d,q)(P,D,Q)_{12}$, where d and D are the number of integrations in the regular and seasonal part respectively.

[5] This model has a least square error value of 0.0082.

Table 3 Definition of the dummy variables

Dummy variable	Definition
Markup adjustment 1	Value of 1 as of March 1997 and 0 before
Exclusion of pharmaceuticals	Value of 1 as of September 1998 and 0 before
Markup adjustment 2	Value of 1 as of June 1999 and 0 before
Reduction of ex-factory prices 1	Value of 1 as of November 1999 and 0 before
Markup adjustment 3	Value of 1 as of August 2000 and 0 before
Reference pricing system 1	Value of 1 from December 2000 to December 2003 and 0 in any other period
Reduction of ex-factory prices 2	Value of 1 as of July 2001 and 0 before
Reference pricing system 2	Value of 1 as of May 2002 and 0 before
Reference pricing system 3	Value of 1 as of May 2003 and 0 before
Reference pricing system 4	Value of 1 as of January 2004 and 0 before
Economic incentives to improve prescribing practices	Value of 1 as of April 2004 and 0 before
Reference pricing system 5	Value of 1 as of August 2004 and 0 before
Reduction of ex-factory prices 3 and Markup adjustment 4	Value of 1 as of March 2005 and 0 before
Reduction of ex-factory prices 4 and Markup adjustment 5	Value of 1 as of March 2006 and 0 before

differences were applied in order to obtain stationarity with an autoregressive component term in the regular part and an autoregressive component in the seasonal part. As regards the series of average price per prescription, the validated model, which is obtained after differentiating the series once and fulfilling the parsimony principle, is ARIMA$(0,1,2)(1,0,0)_{12}$. With the series of prescriptions per capita, it is not necessary to differentiate the series because it is already stationary.[6] The validated model that satisfies the parsimony principle is ARIMA$(1,0,1)(1,0,0)_{12}$.

The method used in this study makes it possible to estimate two impact measures for each of the analysed cost containment interventions in the period 1995–2006: first, short-term intervention impact is defined as any statistically significant change observed in any of the outcome variables, even if it is a very short-term impact; and second, the medium-term impact of each intervention is estimated as expected expenditure savings in the year following its implementation. This saving is calculated as the effect of the cost containment strategy over the first year of its implementation given the structure of the estimated model and the impact pattern of the dummy variables with the best statistical properties. These figures therefore represent approximations to the true values of the impacts of the measures analysed.

Results

The results of the three estimates (expenditure per capita, average price and number of prescriptions per capita) are shown in Table 4. These results indicate that a large part of the measures applied were not effective in reducing expenditure per capita, the average price of prescriptions or the number of prescriptions per patient. Specifically, the results show that four interventions had a significant negative impact on expenditure per capita, eight interventions had a significant impact on price (7 with a negative impact and one with a positive impact) and three had a positive impact on the number of prescriptions per capita (only one resulted in a reduction).

Expenditure per capita

The containment measures that were effective in reducing pharmaceutical expenditure per capita were the reduction of both wholesale and retail markups in March 1997, the compulsory reduction of ex-factory drug prices in November 1999, the reduction of wholesale and retail markups in August 2000 and the modification of the system of reference pricing in January 2004. These four measures are statistically significant, the first three with a higher level of significance (1%) than the last (10%), and they have a negative coefficient, indicating that they decrease the value of the series of the variable of interest.

Average price per prescription

The containment measures that had an effect on the average price of prescriptions were the reduction of both wholesale and retail markups in March 1997, the exclusion of pharmaceuticals from public funding in September 1998, the decrease in wholesalers' markups in June 1999,

[6] A Dickey-Fuller test has been employed in order to test this hypothesis.

Table 4 Time series intervention analysis of pharmaceutical cost containment measures in Catalonia, 1997–2006

Cost containment measures	Total cost per capita		Price per prescription		Prescriptions per capita	
	Coef.	S.E.	Coef.	S.E.	Coef.	S.E.
Markup adjustment 1 (Mar97)	−0.2211033***	0.0382882	−0.0332327***	0.007053	0.0286596*	0.0161892
Exclusion of pharmaceuticals (Sep98)	−0.0483607	0.0392343	0.0487825***	0.0144618	−0.0380883**	0.017523
Markup adjustment 2 (Jun99)	−0.0979893	0.0760868	−0.027923**	0.0110382	0.0306564	0.0199744
Reduction of ex-factory prices 1 (Nov99)	−0.1482918***	0.03092	−0.0408517**	0.0177371	0.0348064*	0.0196474
Markup adjustment 3 (Aug00)	−0.2200871***	0.0421794	−0.022535***	0.0086722	0.0003795	0.0192393
Reference pricing system 1 (Dec00)	−0.191381	0.1274591	0.0040083	0.0128772	0.0031112	0.0277757
Reduction of ex-factory prices 2 (Jul01)	−0.0838	0.0636944	−0.0129706	0.0159854	0.0364416	0.0224865
Reference pricing system 2 (May02)	−0.0366389	0.0712226	−0.0054509	0.0249085	0.025071	0.0214046
Reference pricing system 3 (May03)	0.0053113	0.1043118	0.0057564	0.0342617	0.0538146***	0.0168228
Reference pricing system 4 (Jan04)	−0.1203447*	0.071266	−0.0211849***	0.007802	−0.0463797	0.0714097
Incentives to improve prescribing practices (Apr04)	0.0437996	0.0831853	−0.0068239	0.0165321	0.0661026	0.0949378
Reference pricing system 5 (Aug04)	−0.0192529	0.038724	0.0024357	0.0158643	−0.0083231	0.0762676
Reduction of ex-factory prices 3 and Markup adjustment 4 (Mar05)	−0.0522066	0.0432004	−0.0296053***	0.0046642	0.0087556	0.0462126
Reduction of ex-factory prices 4 and Markup adjustment 5 (Mar06)	0.0366355	0.3524392	−0.0152262	0.044367	0.0247832	0.0428332
Constant	0.0120838	0.0072279	0.004203	0.0011714	0.2101945	0.0209764
Autoregressive term 1	−0.6047059***	0.061972	–	–	0.2330626**	0.1067027
Moving average 1	–	–	−0.2323268***	0.0890335	−0.3883236***	0.1258053
Moving average 2	–	–	−0.3563633***	0.1076949	–	–
Seasonal autoregressive term 1	0.6295243***	0.051794	0.6709771***	0.0622934	0.592148***	0.0741126
Observations	143		143		144	
Q test (p-value)	50.9890 (0.1142)		42.7722 (0.3530)		52.0930 (0.0953)	
Average of the residuals squared	0.00844976		0.00024552		0.00558583	
AIC	−375.996		−850.5944		−368.4074	
(p,d,q) $(P,D,Q)_{12}$	$(1,1,0)(1,0,0)_{12}$		$(0,1,2)(1,0,0)_{12}$		$(1,0,1)(1,0,0)_{12}$	

*** $p < 0.01$

** $p < 0.05$

* $p < 0.1$

the compulsory reduction of ex-factory prices in November 1999, the reduction of wholesale and retail markups in August 2000, the application of the second reference pricing system as of January 2004 and the compulsory reduction of ex-factory drug prices and reductions of markups that occurred in March 2005. These eight measures (the dummy variable for March 2005 represents two different measures) are statistically significant at a significance level of 1%, except the measures introduced in June and November 1999, which have a significance level of 5%. All the variables have a negative coefficient except the exclusion of pharmaceuticals from public funding in September 1998, which has a positive effect, indicating that the measure actually caused an increase in the average price per prescription.

Prescriptions per capita

A priori, only the exclusion of pharmaceuticals from public funding, in September 1998, and the incentives to improve prescribing practices, in April 2004, were expected to have an effect on the series of prescriptions per capita. However, the estimation result shows that although the measure in September 1998 was effective in reducing the number of prescriptions per capita (negative coefficient, significant at 5%), there are three other dummy variables that have a significant positive coefficient. The reduction of wholesale and retail markups in March 1997, the reduction of ex-factory prices in November 1999 and the revision of reference pricing in May 2003 had a positive impact on the number of prescriptions per capita. This result seems

to indicate the existence of a certain negative price elasticity of demand for pharmaceuticals although Gemmill, Costa-Font and Mcguire [18] found low elasticities when the institutional setting is a tax-based health insurance system as in Spain. In fact, these results indicate that some unilaterally imposed price reductions have been counteracted by increases in the number of prescriptions per capita, which explain the low impact of many interventions on expenditure per capita.

Reduction in expenditure

The impact of the measures that were effective in reducing pharmaceutical expenditure per capita is based on the comparison of the time series predicted by the model estimated with and without the dummy variable that represents the introduction of the containment measures. In all cases, the observed effect was a two-period pulse, i.e. their effect was concentrated at the time of their application and in the following month, then rapidly fading away.

As can be seen in Table 5, which reports estimated annual per capita and annual total cost reductions, the measures that produced the greatest saving per capita during the year after their implementation were the adjustment of markups in August 2000, which caused a reduction of €5.79 per capita, and the adjustment of markups in March 1997, which reduced expenditure per capita by €4.37. The compulsory price reduction in November 1999 and the modification of the system of reference pricing in January 2004 brought with them slightly more modest savings, of €3.40 and €4.06 per capita during the following year, respectively. Aggregate savings range from the €35.59 million of the markup adjustments of August 2000 to the €20.61 million of the ex-factory price reduction of November 1999.

As regards the percentage of annual total pharmaceutical expenditure that these savings represent, in comparison to the time series predicted by the model estimated without the dummy variable that represents the containment measures, the most effective measures were the reductions of wholesale and retail markups in August 2000 and March 1997, with savings of 2.78 and 2.75%, respectively. The compulsory price reduction in November 1999 led to a saving of 1.73%, and the application of the system of reference pricing in January 2004 a saving of 1.54%.

Discussion

Only four cost containment interventions, out of the 16 public interventions analysed in this paper, had a significant impact in the form of a reduction in public pharmaceutical spending. Seven measures were effective in reducing the price per prescription, but since in many cases, the number of prescriptions per capita also increased as a reaction of the agents to the intervention, the effect on prices was offset and the measures did not achieve a decrease in expenditure per capita. These results are not surprising since Darbà [19] found that the government failed to effectively implement cost containment measures in Spain between 1998 and 2001, a period of time also included in our analysis (1995–2006), because the measures introduced were inadequate to control increasing pharmaceutical costs.

Furthermore, one of the interventions, the exclusion of pharmaceuticals in September 1998, actually caused an increase in the average drug price. However, the effect of this measure on expenditure was not significant, as it reduced the number of prescriptions per capita. Previously, in 1993, there was another implementation of a negative list. Then, short-term effects showed a reduction in the number of prescriptions in 1994, but a substitution effect for covered medicines was probably responsible for a subsequent increase in the following years in the number of prescriptions, with a higher average price per prescription. In the 1998 negative list, even the short-term impact was not observed, given the high rate of increase in expenditure occurring in that year. In any case, both experiences have shown limited effectiveness of negative lists of drugs in reducing pharmaceutical expenditure [4]. The effect is that fewer prescriptions are written but they are more expensive because a negative list causes a shift from non-reimbursed drugs to more expensive reimbursed products [19].

Despite being beyond the scope of this study, there are some counterintuitive results in this paper, which deserve more attention and which will have to be addressed in future research. They are the lack of statistical significance of the effect of the application and subsequent adjustments of the first reference pricing system on price per prescription, and also the positive effects of several strategies on the number of prescriptions.

Table 5 Estimated annual per capita and total effects of the pharmaceutical cost containment strategies in Catalonia

Strategy	Saving per insured person (euros)	Total saving (euros)	Percentage saving
Markup adjustment 1 (Mar97)	4.37	25,961,051.41	2.75
Reduction of ex-factory prices 1 (Nov99)	3.40	20,613,039.27	1.73
Markup adjustment 3 (Aug00)	5.79	35,588,212.60	2.78
Reference pricing system 4 (Jan04)	4.06	26,962,738.79	1.54

One possible explanation for these results could be the anticipation and substitution effects that occur between different drugs when cost containment strategies are applied. In the case of the system of reference pricing, the explanation could be the introduction of new more expensive drugs within the same therapeutic subgroup to replace the drugs affected by the price reduction. Darbà [19] found that in Spain, one of the main causes of pharmaceutical expenditure was the introduction of new medicines in areas where no other drugs were previously available and the switch to more expensive products. Moreover, these expensive new products are not always innovative enough and do not offer significant therapeutic advantages over medicines already available.

The only interventions that achieved some fleeting impact on the trend in pharmaceutical expenditure (effective measures) were two reductions of wholesalers' and pharmacists' markups, one compulsory reduction of ex-factory prices and one intervention related to the reference pricing system. The remaining interventions cannot be said to have had any statistically significant impact on the trend in public pharmaceutical expenditure in Catalonia. Furthermore, in the case of the revision of the reference pricing system, the significance level is only 10%.

In any event, none of the effective interventions shows any capacity to reduce expenditure in the medium or long term. Thus, the only types of statistically significant impacts for the effective interventions are pulses lasting two periods (an initial effect that fades almost immediately).

The lack of effectiveness of many of the measures implemented may be explained by the increase in defined daily doses prescribed per capita, parallel to the decrease in prices, and the greater growth in the prescription of pharmaceutical products that are either higher priced or unaffected by the cost containment measures, due to the diversion of prescription from affected drugs to others outside the regulation, e.g. the substitution of a prescribed generic drug with a more expensive one at the pharmacy. The results obtained in this paper point out that the use of repeated cost containment measures based directly or indirectly on imposed price reductions have exhausted their efficacy, and that the main problem to be addressed by clinical management is the sources of appropriate or inappropriate increase in the number of dispensed medicines per capita.

Finally, incentives to improve the prescriptions of general practitioners have not been developed enough as a strategy to contain the pharmaceutical expenditure in Spain. Although the Prescription Quality Improvement Programme implemented in Catalonia in 2004 went in good direction, that is, to improve physicians' prescribing habits by encouraging the use of drugs with proven efficacy and generics, limiting the use of new drugs, improving the selection of drugs and avoiding over-prescription, this measure was no statistically significant in the reduction of expenditure per capita, prescriptions per capita or price per prescription. The lack of significance of this measure may be due to that, in comparison to other immediate strategies such as reduction of margins or ex-factory prices, it may take longer to be effective. As in some European countries, prescribing guidelines, pharmacotherapeutic guides and incentives to general practitioners in relation to total budgets could improve the efficiency of prescriptions.

Conclusions

In the period analysed in this study, we have identified 16 major administrative interventions aimed at containing pharmaceutical expenditure in Catalonia. Of these, one is a negative list (exclusion of pharmaceuticals from public financing), one is an economic incentive to improve prescribing practices and the rest are oriented towards achieving regulatory price cuts by means of repeated revision of dispensers' and/or wholesalers' markups, compulsory reduction of manufacturers' ex-factory price, and the introduction, adjustment and extension of the reference pricing system. Thus, only two of these administrative interventions were not designed to have a direct effect on the consumer price of medicines.

Of these interventions, only four were effective with regard to overall expenditure, i.e. displayed a statistically significant capacity to reduce spending: the reduction of markups for both wholesalers and retailers in March 1997, the compulsory reduction of ex-factory drug prices in November 1999, the reduction of wholesale and retail markups in August 2000, and the revision of the reference pricing system in January 2004. The magnitude of the impact of the effective interventions fell short of 3% of the pharmaceutical expenditure of the following year in all cases, and dropped rapidly after the initial effect, none of them being effective in the medium or long term. Furthermore, neither of the measures that were not designed to have a direct effect on price was effective. Indeed, the negative list, although it reduced the number of prescriptions, caused an increase in the average price per prescription, and so its effect on expenditure per capita was nullified.

Our results indicate that, in a heavily regulated pharmaceutical market such as the Spanish one, incremental price regulation (whether direct or indirect through generic price regulation) has a very limited impact on overall public expenditure and industry revenues. Our results are also in line with those observed by Sood et al. [1] for 19 developed countries, including Spain. The results of this study cast serious doubts on the impact of some repeated price-directed interventions on expenditure, and they also

highlight the short-term nature and low volume of savings that can be attributed to effective interventions. Policy makers should devote more attention to the market factors that drive increases in prescriptions per capita and average consumer prices.

The conclusions of this study should be interpreted taking into account some of its limitations, which are related to the statistical method used and the nature of the data themselves. The method used only identifies statistically significant effects in the behaviour of pharmaceutical expenditure; it is not intended to provide information on the explanatory factors for the effectiveness of the interventions or its magnitude. Moreover, the large number of interventions identified in this study may give rise to problems in attributing impact among interventions when they overlap in excess. With regard to the nature of the data, the fact that they are aggregate data for all active ingredients, together with their limited time horizon, likewise prevent a more detailed analysis of expenditure trends by therapeutic groups or indications.

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