Paying for Formerly Free Medicines in Spain after one Year of Co-payment: Changes in the Number of Dispensed Prescriptions

Short running title: One year of co-payment for medicines in Spain

Jaume Puig-Junoy[1], Santiago Rodríguez-Feijoó[2], Beatriz G Lopez-Valcarcel[2]

[1]Department of Economics and Business, Pompeu Fabra University, Barcelona, Spain.
[2]Departament of Quantitative Methods in Economics and Management, University of Las Palmas de Gran Canaria, Spain.

Correspondence to: PhD Jaume Puig-Junoy, Department of Economics and Business, Universitat Pompeu Fabra, Ramon Trias Fargas 25-27, 34-08005 Barcelona, Catalunya. Tel.: +34 93 542 18 57. Fax: +34 93 542 17 46. E-mail: jaume.puig@upf.edu.

Word count (text only): 2,971 words.

ABSTRACT

Background: After more than three decades of free medicines for the elderly in Spain, in the context of heavy austerity reforms of public financing, a set of cost sharing reforms on pharmaceutical prescriptions with regional variants were established in Spain since July 2012.

Objective: The purpose of this analysis is to present the first attempt to provide accurate estimates of the overall impact at the regional level of this these cost sharing reforms.

Method: We estimated the reform´s impact on the quantity of dispensed medicines during the first fourteen months. We estimated seventeen autoregressive integrated moving average (ARIMA) time series models of the monthly number of prescriptions dispensed in pharmacies for the period January 2003-May 2012 in each one of the 17 regions (Autonomous Communities) of Spain. We calculated dynamic forecasts for the horizon June 2012-July 2013 in order to estimate the *counterfactual* (number of prescriptions that would had been observed without the intervention), and we estimated the impact of cost sharing changes as the difference between the observed number of accumulated prescriptions at 3, 6, 12 and 14 months and the number predicted by our time-series models (in percentages).

Results: During the last decade the number of dispensed prescriptions experienced rapid and continuous increases. In the 14 first months after the copayment reform, the total number of prescriptions decreased dramatically, by more than 20% in Catalunya, Valencia and Galicia, by more than 15% in 9 other regions and by more than 10% in 15 out of the 17 Spanish regions. Our model results suggest that the new copayment caused an abrupt shift in the mean level of the time series. No shift in trend has been detected; the previous positive trend remains unchanged in most of the Autonomous Communities.

Conclusion: After decades of unsuccessfully trying to reduce drug spending in the Spanish National Health System through actions on prices and on prescribers, the copayment established in mid-2012 led to a dramatic reduction in the use of drugs. The health effects of this reduction are not known.

Key Points for Decision Makers

- After a decade of rapid and continuous increases, the number of dispensed prescriptions decreased dramatically in the first year after the copayment reform.

-
  The new copayment appeared to cause an abrupt downward shift in the number of dispensed prescriptions, although the previous positive trend appears unchanged in most regions.

-

- Although the level of the new national coinsurance rate is dependent on income, a small portion of patients supports a large part of the expense.

- Regional differences in copayment policies are also consistent with the hypothesis that the first Euro of cost sharing has a large impact on drug use.

- Further research is needed to determine the change in distribution of prescriptions across different patients groups, any reductions in moral hazard, the financial impact on patients, and any effects on health, both positive and negative.

INTRODUCTION

The sudden fall of public revenues after 2008 and the long-lasting economic crisis have led many public health systems in European countries to cut public health financing through high copayments or coinsurance rates on drug prescriptions dispensed in pharmacies[1-6]. This is specially the case in Spain, where until July 2012 nearly three out of four prescriptions where dispensed free of charge, being Spain until then one of the European countries with the highest number of prescriptions per capita[7].

In some national health systems funded primarily though taxation, as the Spanish one is, medical treatments are free for a large part of the population. That is because those systems are concerned with equity of access to healthcare. Since 1978, Spanish pensioners, whether they were in a low, middle or high-income bracket, had enjoyed free access to practically all medicines prescribed by physicians of the national health system. As a consequence, there was a significant increase in the number of prescriptions, and public expenditure per patient rose by around 25% in the first year of free medication[8]. Potential moral hazard – the increase in consumption by those who acquire the right to free medicines, attributable solely to this change in status – was concentrated in the consumption of those medicines affected by 40% coinsurance before the medication became free, i.e., those that had been most expensive for the patient. Over-prescription[9] *–a prescription is given without the pertinent indication-* is a common form of inappropriate utilization of healthcare which does not cause only an inefficient increase in costs but also a higher number of adverse events and related health problems[10]. There is broad evidence that over-prescribing is associated with an increased risk of adverse drugs events, morbidity, mortality and health care utilization, such as emergency visits[11,12].

Free medication for all Spanish pensioners has also been shown to be clearly inequitable. As it was independent of financial circumstances, a pensioner who received a large pension or had assets worth millions would pay nothing, while an unemployed person or a family with young children and an income of barely €1,000 per month, would pay their share. Half of all the cost sharing contributed by patients is concentrated in a small group of sick people: it was provided by just 5% of users, for whom it can represent a heavy burden[13].

But the severe economic crisis in Spain and the subsequent need for a reduction in public expenditure were the main drivers of change[1]. After more than three decades of free medicines for elderly, in mid 2012 a new co-payment policy was adopted.

In July 2012 a combined set of cost sharing policies (*"three-payment"*) described in Table I abruptly ended this scenario by first introducing a national coinsurance rate of 10% for retirees with a monthly income-related cap. The individual monthly contribution was limited by a cap of 8, 18 or 60 Euros, depending on income. Additionally, two regions (Catalunya and Madrid) charged temporarily a one-euro copayment per prescription. Finally, the national reform stopped funding a long list of medicines indicated for minor symptoms, which is equivalent to a 100% coinsurance rate for those medicines. Under the new co-insurance formula medicines remain free

for disadvantaged people. A region (the País Vasco) did not apply the national co-insurance reform until one year later. These "three-payment" reforms have been applied to the population covered by the National Health System, excluding civil servants, which are covered under a different health insurance plan.

[Insert Table I about here]

The monthly limit encourages chronic patients to concentrate their prescriptions in the minimum number of months. To avoid this opportunistic behavior would be advisable to set annual limits, which also are easier to manage. In some Autonomous Communities patients had to pay as if there's no monthly limit, and they have to wait for the reimbursement some months later. This is an expensive bureaucratic procedure and overrides the protective effect of co-payment ceiling. This was the case of most Autonomous Communities during the first months of the new system, since only Catalunya and Andalusia had been able to apply the coinsurance caps in real time since the first moment.

Coinsurance rates for non-pensioners increased from 40% to 50% or 60% depending on income. There is no cap for them. Some medications for chronic treatments have a co-payment rate of 10% with a maximum per prescription. In the new scheme, the percentage of the price paid depends on income, but, contrary to what might appear at first glance, the new copayment is not progressive, because a small number of seriously ill patients that require a lot of medication and are not pensioners bear the greatest load.

The regional fee of 1 € per prescription might be an appropriate tool for reducing the over-consumption associated with the cost-free status. It was universal (with few exemptions for the most deprived), it established an annual limit per person, quite low and reasonably easy to manage. This low intensity fee was suspended in January 2013 by the Spanish Constitutional Court, not because of a lack of effectiveness or any side effects, but because of a conflict in the scope of the competences of the Spanish government and the Regions.

No other demand-side measures--besides the three described above concerning copayment-- were implemented after July 2012.

This is the first attempt to estimate the short term overall impact at the regional level of the three combined cost-sharing reforms on the quantity of dispensed medicines during the first fourteen months after their establishment.

DATA AND METHOD

We used monthly data of NHS dispensed prescriptions in each Autonomous Community from January 2003 to July 2013. They are available at the webpage of the Spanish Ministry of Health[14].

First, we estimated seventeen autoregressive integrated moving average (ARIMA) time series models of the monthly number of prescriptions dispensed in pharmacies for the period January 2003-May 2012. More specifically, for each Autonomous Community we used a univariate ARIMA model. In order to identify the models, following the Box-Jenkins method[15] we estimated average-rank regressions with annual data (for deciding between logarithmic or linear models) and we used the standard integration tests to specify the needed number of regular and seasonal differences. The significance of the regression coefficients and the residual correlograms guided the interactive process of selection of regressors. In some Autonomous Communities we included specific dummy variables for certain months or time intervals with extreme – outlier- residuals (more than two standard deviations in absolute value). We also calculated the Q test by Ljung-Box-Pierce (Portmanteau test) in order to verify the white noise condition for the residuals. We selected the model with the best fit among alternative specifications that had passed all the tests described above. The fit was measured with the Aikake Information Criterion (AIC) and the coefficient of determination.

Second, we calculated dynamic forecasts for the post-sample period June 2012-July 2013 in order to estimate the *counterfactual* number of prescriptions that would have been observed if the reform had not taken place.

And, third, we estimated the impact of cost sharing changes as the difference between the observed number of accumulated prescriptions at 3, 6, 12 and 14 months and the number predicted by our time-series models (in percentages). 95% Confidence Intervals adjusted by correlations between subsequent forecasts have been also calculated. For each Autonomous Community we calculated 95% confidence intervals of the predicted effects on the overall impact of the copayment reform. To estimate confidence intervals for the cumulative effects of the new copayment we derived the specific formulas (available upon request), based on the monthly forecasts resulting from the ARIMA models and taking into account that the standard errors of consecutive predictions are correlated.

Although the reform came into force in July 2012, our forecast horizon starts in June 2012 to consider the anticipation effect (stockpiling) in the month before the reform.

RESULTS

The time series for the monthly number of prescriptions from January 2003 to July 2013 point to a dramatic change in July 2012. Figure I presents three of those time series for three selected regions that represent three "models" of cost sharing being implemented: Catalunya (regional fee of 1 € per prescription and new co-insurance rates), Castilla-León (only national co-insurance), and País Vasco (no change in cost sharing until July 2013). According to these descriptive data, an anticipation effect (stockpiling) happened in all regions the month before the measure was enacted . And, also, it appears that in Catalunya there was a large drop in the number of prescriptions in July 2012 despite the fact that only the regional 1 € fee was applied in this region

from July to September to pensioners. This immediate drop was equal or higher than in other regions where the national co-insurance rate was applied, as it is the case of Castilla-León.

[Insert Figure I about here]

The Appendix table shows the detailed estimates of the 17 ARIMA models, their coefficients of determination and the Q6 and Q12 statistics of the Ljung-Box-Pierce test Portmanteau.

According to the results of our ARIMA models, a significant, dramatic and sudden reduction in the number of dispensed prescriptions compared to the counterfactual has been estimated for all regions (Table II) with the exception of the País Vasco, where only the delisting policy had been applied until July 2013.

[Insert Table II]

The highest impact of the intervention has been observed in Catalunya, where the coinsurance reform and the new regional copayment were applied concurrently. Our estimation of the impact in Catalunya is a 23.7% decrease in the number of prescriptions after 14 months [95% Confidence interval -27.0, -20.5]. Applying the cap in the moment of purchase reduces the impact of the co-payment. That means that if patients have already reached their maximum for the month, they get their prescription from the pharmacy free of charge. Among the regions that only applied the state copayment, Andalucía was the only able to manage the cap in time. In the remaining regions patients were required to prepay and they were reimbursed afterwards. Andalucía showed the smallest reduction in that group (9.4% [95% CI -13.4, -5.5]).

In summary, concurrent copayment policies had a dramatic impact, statistically significant when applied to a NHS system that used to provide free drugs to retired patients. Catalunya, where the one-euro per prescription was first applied and then the state copayment was added (see details in Table I), suffered a 23.9% reduction in the number of prescriptions in twelve months. By contrast, the País Vasco, that did not apply any copayments until July 2013, had a reduction of only 3.8%.

DISCUSSION AND POLICY IMPLICATIONS

Spain had become one of the countries with the highest per capita pharmaceutical usage in the world: a comparison of per capita usage levels in 14 developed countries for 14 disease areas concluded that France, United States and Denmark have generally high levels of usage, although this is not uniform across all diseases or drug categories. Spain appeared as one of the three countries with higher per capita usage for the treatment of osteoporosis, hepatitis C, cancer, antipsychotics and dementia[7]. However, mainly due to lower prices, Spanish per capita expenditure (adjusted by purchasing parity power) was only 3.5% above the OECD average in 2011[16]. Several

studies have shown that medication over-prescription does not only affect costs, it induces adverse health outcomes, particularly in the elderly, being the reduction in the number of drugs given the main preventable factor[12,17].

The severe economic crisis in Spain and the subsequent need for a reduction in public expenditure were the main drivers of change. After more than three decades of free medicines for the elderly, in mid 2012 co-payment was established.

A notable contribution of this analysis is to provide evidence of the important changes in the demand for prescription of medicines as a response to increases in the price paid by the patient and to the fact that a small linear co-payment (1€ per prescription) has a large impact on medicine´s use. Our results exploiting regional differences in copayment policies are also consistent with the hypothesis that the first Euro of cost sharing has a large impact on drug use [18].

The estimates reported in this paper provide an aggregate measure of the impact at the regional level of the concurrent measures that came into force with the Decree 16/2012. This impact has been measured on the number of prescriptions issued in the NHS. Despite the fact that the "three-payment reforms" are the most notable, other measures taken during the period, such as the exclusion from healthcare coverage to undocumented immigrants, may have had also some influence on the number of prescriptions.

Our results should be cautiously taken, We do not know whether this reduction in prescriptions was the result of a reduction in the practice of overprescribing and useless stockpiling, which would indicate a positive effect, or rather the result of some patients not being able to access medicines they needed (which would be a negative effect) or a mix of the two. Also, another obvious limitation of our results is that they are based on the dynamics in the number of prescriptions at the regional level, but there is no available information on changes in the number of a more homogeneous consumption measure such as Defined Daily Doses (DDD) prescribed.

Copayment reform could change both the level and the time trend of the number of prescriptions, but for now we cannot make reliable statements about the magnitude of these changes. Rigorous evaluations should wait until the NHS discloses the data to researchers. In fact, our models suggest that the new copayment caused an abrupt shift in the mean level of the time series of dispensed prescriptions. However, our data and methods do not allow us so far to test rigorously the hypothesis of an unchanged trend, an issue that clearly deserves further research. Our provisional results show that in most of the Autonomous Communities the previous positive trend, i.e. the monthly growth rate, seems to remain unchanged after the reform. This may be due to the fact that other prescription incentives have not been altered. The effects of various interventions on drug prices [19] applied in Spain from 1995-2006, provide another example of temporary impact, which is diluted over a year or so,

If prescribing still shows upward trends after typical demand-side measures, such as the copayment reforms adopted since July 2012, it would advisable to adopt a wider

range of policy measures directed to influence prescription practices. Among those, an appropriate mix of financial incentives (such as indicative or coactive prescribing budgets included or not in comprehensive budgets) and non-financial incentives (such as information, training, prescription monitoring, formularies and treatment protocols) may be appropriate. Those policies have been nearly neglected in Spain until recently, but they should play a more prominent and urgent role[9].

Even though the reform does not change the underlying trend, as we provisionally conclude, this does not mean that the impact of the copayment is being progressively diluted, it rather means that the underlying causes of the proclivity to demand/prescribe/dispense an ever increasing number of medicines has not gone away. That is because the dynamics of prescriptions depends on other many factors besides copayment: industry pressure on prescribers, GP workload, training and incentives for prescribers, etc. Even more, it could happen that the initial effect, i.e. the sudden shift in the mean level of the number of prescribed medicines, is non permanent, once the awareness of paying a price is instilled in patients' minds. If that is the case, we will see in a few months the series back in their pre-reform levels. This will eventually be revealed with an impact analysis with more appropriate assessment techniques and more disaggregated data.

Finally, some regions were not able to manage effectively individual's monthly caps because they lack individual income data and information technology. Those regions implemented an expensive and lengthy administrative reimbursement process for those patients that had paid over their cap. It would have been better either to wait or to design a simpler procedure.

It would be a mistake to increase cost sharing on medication across chronic and effective treatments. If one thing is clear from randomized and natural experiments, it is that cost sharing should be lower the greater the need for the treatment and the more effective that treatment is[20]. The high concentration of expenditure in patients with chronic conditions recommends the maintenance of low rates, together with the application of upper limits to the amount payable out of the patient's pocket, either as a monetary amount that would be the same for all, or – a finer adjustment – as a percentage of each patient's income. Otherwise, the cost in the form of greater use of emergency and hospital services may more than cancel out the savings attained through cost sharing for chronic patients[21].

CONCLUSIONS

This article provides empirical evidence that after a continuous increase in the number of dispensed prescriptions in Spain during the last two decades, insensitive to the many price control measures, the total number of prescriptions has been dramatically cut by nearly a quarter after 14 months of the "three payment" reforms in Catalunya, and by more than one tenth in 15 out of 17 Spanish regions.

Overall our results provide new information on the price sensitivity of the prescriptions issued in a NHS, and they also raise several new questions relevant to policies. It is necessary and urgent to know which groups of patients and therapeutic groups have been most affected, in order to evaluate the potential reduction in the abuse (*moral hazard*) attributable to free medicines and the equity issues.

These questions deserve urgent attention from health policy makers in order to evaluate overall welfare effects of these financial oriented reforms and to redefine copayment policies. Potential unwanted side effects on adherence, health and use of other health resources should also be investigated.

Conflict of interest: There is no relevant conflict of interest to disclose.

The plan for the analysis of data was designed by all the authors. Beatriz G Lopez-Valcarcel and Santiago Rodríguez-Feijoó conducted the statistical analysis. Jaume Puig-Junoy wrote a substantial proportion of the manuscript. He is the guarantor for the overall content of the manuscript and was also in charge of coordinating the manuscript preparation and submission process. All of the authors critically reviewed drafts of the manuscript prior to submission.

REFERENCES

1. Legido-Quigley H, Otero L, la Parra D, Alvarez-Dardet C, Martin-Moreno JM, McKee M. Will austerity cuts dismantle the Spanish healthcare system?. *BMJ* 2013;346:f2363.
2. Urbanos R, González B, Puig-Junoy J. La crisis económica llega a la sanidad. *Economistas* 2012;131:158-7.
3. Thomson S, Mossialos E. Primary care and prescription drugs: coverage, cost-sharing, and financial protection in six European countries. Issues in International Health Policy. *Commonwealth Fund pub.* 2010;1384:82.
4. Carone G, Schwierz C, Xavier A. Cost-containment policies in public pharmaceutical spending in the EU. Economic Papers 461, *European Commission* 2012.
5. Vandoros S, Stargardt T. Reforms in the Greek pharmaceutical market during the financial crisis. *Health Policy* 2013;109:1-6.
6. Smith PC. Universal health coverage and user charges. Health Economics, Policy and Law 2013;8(4):529-535.
7. Richards M. Extent and causes of international variation in drug usage. A report to the Secretary of State for Health 2010. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/151987/dh_117977.pdf.pdf.
8. Puig-Junoy J, García-Gómez P, Casado-Marín D. Free Medicines thanks to Retirement: Moral Hazard and Hospitalization Offsets in an NHS. *TinBergen Institute Discussion Paper* TI, 2011;108/3.
9. Cabiedes L, Ortún V. Prescriber incentives. Chapter 9 in: Puig-Junoy J. The public financing of pharmaceuticals. Northampton MA: *Edward Elgar Pub*; 2005.
10. Meneu R, Peiró S. Elementos para la gestión de la prescripción y la prestación farmacéutica. Barcelona: *Masson Ed*; 2004.
11. Xu KT et al. Over-prescribing of antibiotics and imaging in the management of uncomplicated URIs in emergency departments. *BMC Emergency Medicine* 2013;13:7.
12. Sanfelix-Gimeno, G., S. Peiro, et al. "[Pharmaceutical prescription in primary care. SESPAS report 2012]." Gac Sanit 2012;26 Suppl 1: 41-45.
13. Puig-Junoy J. Paying for free healthcare. The role of prices in our healthcare decisions. Barcelona: *Libros del Lince*; 2013.
14. Ministerio de Sanidad, Servicios Sociales e Igualdad. http://www.msssi.gob.es/
15. Box GEP, Jenkins GM, Reinsel GC. Time series analysis: forecasting and control, 4th edition. San Francisco: *John Willey & Sons;* 2008.
16. OECD. Health at a glance 2013: OECD Indicators. Paris: *OECD Publishing*; 2013.
17. Laroche M-L et al. Is inappropriate medication use a major cause of adverse drug reactions in the elderly? *Br J Clin Pharmacol* 2007;63(2):177-86.
18. Ellis RP. Five questions for health economists. *Int J Health Care Finance Econ.* 2012;12:217-33.
19. Moreno-Torres, J. Puig-Junoy, J.M. Raya. The impact of repeated cost containment policies on pharmaceutical expenditure: experience in Spain. Eur J Health Econ 2011;12:563-573.

20. van de Vooren K, Curto A, Garattini L. Optional copayments on anti-cancer drugs. *BMJ* 2012;346:f349.

21. Chandra A, Gruber J, McKnight R. Patient cost sharing in low income populations. *AER: P&P* 2010;100:303-8.

Table I
Spanish national and regional cost sharing.
Comparison of the regulation before and after the 2012 reform

| Cost sharing measure	Description	Regional implementation
Changes in drug co-insurance rates at national level from July 1st 2012 (RD 16/2012)	Before July 2012: - PENSIONERS: exempted from any coinsurance rate. - NON-PENSIONERS: co-payment of 40% of consumer price (10% for drugs indicated for chronic diseases). After July 1st 2012: - Exempted population: unemployed without any subsidy, and beneficiaries of some very low pensions. - PENSIONERS: a new 10% co-insurance rate on consumer price with a monthly cap depending on annual income (€8 and €18); 60€ co-insurance rate for pensioners with income ≥ €100,000. - NON-PENSIONERS: 40%, 50% or 60% co-insurance rate on consumer price depending on income with no cap. 10% co-insurance rate for drugs indicated for chronic diseases (max. €4.13 per prescription).	New co-insurance rates in all regions from July 1st 2012. Exceptions: - País Vasco: not applied until 1 year later. - Catalunya: applied to non pensioners since August 1st 2012 and to pensioners since October 1st 2012. During the first months of implementation of the reform, most regions were not able to apply the cap for pensioners in real time. They paid the co-insurance rate even though they had reached their month's cap. They requested the reimbursement afterwards. Exceptions: in some regions (i.e., Catalunya and Andalucía) coinsurance caps were applied in real time without reimbursements since initial implementation.
Delisting of a list of medicines from public coverage from September 1st 2012 (RD16/2012)	417 medicines indicated for minor symptoms were excluded from public subsidy	In all regions from September 1st 2012. No exceptions.
A new co-payment rate of one € per prescription in two regions	All patients pay a 1€ rate per prescription with a maximum cap of 61€ per year, independent of income. Exempted population: beneficiaries of some very low pensions.	Catalunya: from June 23th 2012 to January 15th 2013 Madrid: from January 1st 2013 to January 29th 2013

Sources: Puig-Junoy et al[8]; Puig-Junoy[13]; Law 5/2012 of the Catalan Parliament; Law 16/2012 of the Spanish Congress.

Table II
Average estimated impact of the cost sharing measures adopted in July 2012
Reduction in the number of prescriptions after the first 3, 6, 12 and 14 months (since June 2012)

AUTONOMOUS COMMUNITY	Percentage of reduction			After 14 months		
	After 3 months	After 6 months	After 12 months	Prescriptions (million)		Percentage of reduction Mean [95% Confidence Interval]
				Real	Prediction without co-payment	
ANDALUCIA	-2.4	-7.6	-9.8	188.23	206.01	-9.4 [-5.5;-13.4]
ARAGON	-3.2	-11.3	-14.5	30.61	34.96	-14.2 [-10.7;-17.4]
ASTURIAS	-4.0	-11.3	-13.4	26.62	30.26	-13.7 [-11.1;-16.2]
BALEARES	-6.0	-12.9	-15.7	19.07	22.15	-16.2 [-9.0;-23.3]
CANARIAS	-7.7	-13.6	-15.3	44.36	51.34	-15.7 [-9.4;-21.3]
CANTABRIA	-5.4	-10.5	-11.6	12.17	13.52	-11.1 [-7.8;-14.2]
CASTILLA-LEON	-6.5	-12.4	-15.4	55.68	64.1	-15.1 [-13.4;-16.8]
CASTILLA-MANCHA	-8.6	-16.2	-18.2	48.55	57.51	-18.5 [-15.7;-21.3]
CATALUNYA	-13.3	-22.6	-23.9	152.64	188.85	-23.7 [-20.5;-27.0]
COM VALENCIANA	-12.1	-19.7	-19.9	112.08	134.99	-20.4 [-16.4;-24.5]
EXTREMADURA	-6.0	-13.6	-14.8	28.72	32.98	-14.8 [-10.1;-19.6]
GALICIA	-6.0	-17.3	-22.1	67.42	82.11	-21.8 [-19.5;-24.0]
MADRID	-2.2	-10.4	-14.1	115.39	131.295	-13.8 [-10.5;-16.8]
MURCIA	-9.8	-14.9	-17.5	32.44	38.21	-17.8 [-14.6;-21.0]
NAVARRA	-5.3	-11.6	-13.9	12.84	14.65	-14.1 [-10.4;-17.9]
PAIS VASCO	+3.8	-2.4	-3.8	47.56	49.42	-3.9 [-2.5;-5.3]
RIOJA	-7.5	-13.3	-15.6	6.68	7.74	-15.8 [-13.0;-18.6]

Figure I
Monthly number of prescriptions from January 2003 to July 2013 in three Autonomous Communities
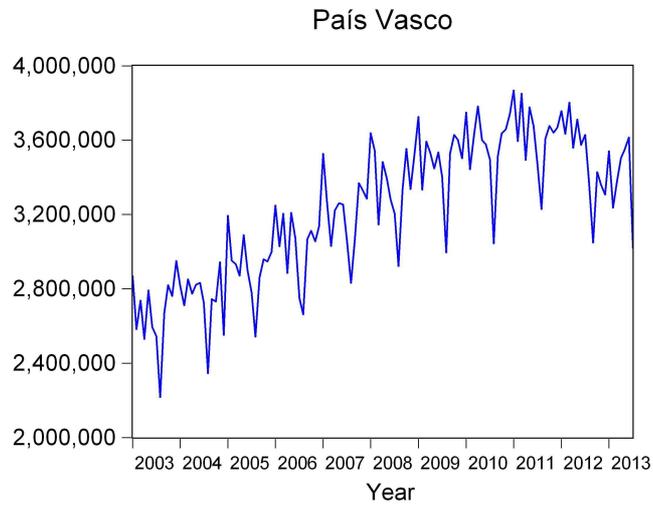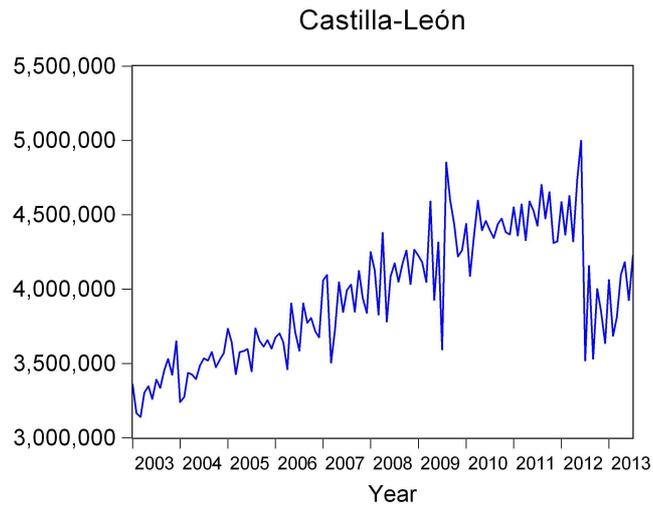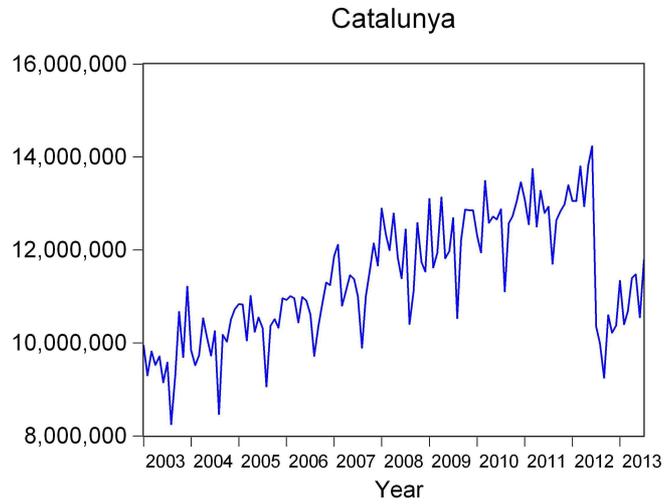
APPENDIX

Y_t is the number of prescriptions in month t

t={1(January 2003), 2(February 2003),...,}

Log(Y_t) is the natural logarithm of Y_t

ε_t is a white noise series

Definition of dichotomous variables for the treatment of external effects

$$D_t^{\{Month\ Year\}} = \begin{cases} 1 & \text{if } t = \{Month\ Year\} \\ 0 & \text{in other case} \end{cases}$$

$$D_t^{\{Month\ Year1\}\_\{Month\ Year2\}} = \begin{cases} 1 & \text{if } \{Month\ Year1\} \le t \le \{Month\ Year2\} \\ 0 & \text{in other case} \end{cases}$$

$$D_t^{\{Month\ Year\}\_\{End\}} = \begin{cases} 1 & \text{If } t \ge \{Month\ Year\} \\ 0 & \text{in other case} \end{cases}$$

$$D_t^{\{Month\}} = \begin{cases} 1 & \text{if } t = \{Month\} \\ 0 & \text{in other case} \end{cases}$$

ϕ_j, Autoregressive parameters

θ_j, Moving Average Parameters

γ_j, Other model parameters (constant, dichotomous and linear trend)

L is the lag operator

ARIMA Estimated Models

Autonomous Community	Model	R^2	Q_6	Q_{12}
Andalucía	$(1-\phi_1 L - \phi_2 L^2 - \phi_4 L^4)(1-\phi_{12}L^{12})(1-L)Y_t =$ $= \gamma_1 D_t^{\{January\ 2010\}} + (1-\theta_1 L)\varepsilon_t$	0.82	0.83(0.4)	5.58(0.6)
Aragón	$(1-\phi_1 L - \phi_2 L^2)(1-\phi_{12}L^{12})(1-L)\log(Y_t) =$ $= \gamma_1 D_t^{\{January\ 2005\}} + (1-\theta_1 L - \theta_3 L^3)\varepsilon_t$	0.72	4.2(0.04)	9.7(0.2)
Asturias	$(1-\phi_1 L - \phi_4 L^4)(1-\phi_{12}L^{12})(1-L)Y_t =$ $= (1-\theta_1 L)\varepsilon_t$	0.72	3.5(0.06)	10.2(0.3)
Baleares	$(1-\phi_1 L - \phi_2 L^2 - \phi_4 L^4)(1-\phi_{12}L^{12})(1-L)Y_t =$ $= \gamma_0 + \varepsilon_t$	0.55	3.1(0.08)	12.4(0.1)
Canarias	$(1-\phi_2 L^2)(1-\phi_{12}L^{12})(1-L)\log(Y_t) =$ $= \gamma_0 + \varepsilon_t$	0.53	3.0(0.4)	11.4(0.2)

Cantabria	$(1-\phi_1 L - \phi_2 L^2)(1-\phi_{12}L^{12})(1-L)\log(Y_t) =$ $= \gamma_1 t + \gamma_2 t * D_t^{\{January\ 2011\}-\{December\ 2012\}} + \gamma_3 D_t^{\{April\ 2011\}-\{End\}} + (1-\theta_3 L^3)\varepsilon_t$	0.78	5.4(0.07)	9.2(0.3)
Castilla León	$(1-\phi_{13}L^{13})(1-\phi_{12}L^{12})(1-L)Y_t = \gamma_0 + \gamma_1 D_t^{\{July\ 2009\}} + \gamma_2 D_t^{\{August\ 2009\}} +$ $+ \gamma_3 D_t^{\{January\ 2012\}-\{December\ 2012\}} + (1-\theta_1 L - \theta_2 L^2 - \theta_3 L^3)\varepsilon_t$	0.85	2.8(NA)	7.6(0.3)
Castilla La Mancha	$(1-\phi_4 L^4)(1-\phi_{12}L^{12})(1-L)Y_t =$ $= \gamma_0 + \gamma_1 D_t^{\{November\ 2011\}-\{December\ 2011\}} + (1-\theta_1 L - \theta_3 L^3)\varepsilon_t$	0.73	0.8(0.6)	3.0(0.9)
Catalunya	$(1-\phi_3 L^3 - \phi_{10}L^{10})(1-\phi_{12}L^{12})(1-L)Y_t =$ $= \gamma_0 + (1-\theta_1 L)\varepsilon_t$	0.75	1.1(0.6)	7.4(0.5)
Valencia	$(1-\phi_{12}L^{12})(1-L)Y_t =$ $= \gamma_0 + \gamma_1 D_t^{\{November\ 2011\}} + \gamma_2 D_t^{\{April\ 2008\}} + (1-\theta_1 L - \theta_3 L^3)\varepsilon_t$	0.55	6.8(0.08)	10.3(0.3)
Extremadura	$(1-\phi_1 L^1 - \phi_2 L^2 - \phi_4 L^4)(1-\phi_{12}L^{12})(1-L)Y_t =$ $= (1-\theta_1 L)\varepsilon_t$	0.67	0.4(0.5)	4.6(0.7)
Galicia	$(1-\phi_1 L^1 - \phi_3 L^3)(1-\phi_{12}L^{12})(1-L)Y_t =$ $= \gamma_0 + (1-\theta_1 L)\varepsilon_t$	0.76	4.8(0.1)	12.8(0.1)
Madrid	$(1-\phi_{12}L^{12})(1-\phi_4 L^4)(1-L)\log(Y_t) =$ $= \gamma D_t^{\{August\}} + (1-\theta_1 L - \theta_2 L^2)(1-\theta_{12}L^{12})\varepsilon_t$	0.90	0.6(0.4)	5.4(0.5)
Murcia	$(1-\phi_1 L^1 - \phi_5 L^5)(1-\theta_{12}L^{12})(1-L)Y_t =$ $= \gamma_0 + \gamma_1 D_t^{\{April\ 2011\}} + (1-\theta_1 L)\varepsilon_t$	0.71	3.5(0.2)	5.9(0.7)
Navarra	$(1-\phi_1 L^1 - \phi_2 L^2)(1-\phi_{12}L^{12})(1-L)Y_t =$ $= \gamma_0 + \gamma_1 D_t^{\{April\ 2011\}} + \gamma_2 D_t^{\{November\ 2011\}} + (1-\theta_1 L)\varepsilon_t$	0.65	5.3(0.08)	11.2(0.2)
País Vasco	$(1-\phi_{12}L^{12})(1-\phi_4 L^4)(1-L)\log(Y_t) = \gamma_1 D_t^{\{August\}} + \gamma_2 D_t^{\{December\ 2004\}} +$ $+ \gamma_3 D_t^{\{April\ 2011\}} + \gamma_4 D_t^{\{May\ 2011\}-\{End\}} + (1-\theta_1 L - \theta_2 L^2)(1-\theta_{12}L^{12})\varepsilon_t$	0.86	4.6(0.03)	5.5(0.6)
Rioja	$(1-\phi_1 L^1 - \phi_2 L^2 - \phi_4 L^4)(1-\phi_{12}L^{12})(1-L)Y_t =$ $= \gamma_0 + \gamma_1 D_t^{\{February\ 2010\}} + (1-\theta_1 L)\varepsilon_t$	0.81	1.0(0.3)	1.8(1.0)

Note: the Portmanteau statistics for residual correlation is shown for 6 and 12 lags (Q6 and Q12 respectively). In brackets, p-value