

## ***Expenditure, prescription and consumption of analgesic drugs before and during the economic crisis***

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### **ABSTRACT**

**Objective:** The Spanish Health System has undergone many changes as a result of the austerity policies applied during the Spanish economic crisis, specifically in terms of pharmaceutical expenditure, as drugs such as analgesics, which were previously free of charge for a sector of the population, have been affected by the application of co-payment on the sale price. Therefore, our aim is to identify the effects of the economic crisis in Spain in the prescription, expenditure and use of analgesics.

**Method:** A descriptive-cross-sectional study was carried out based on the drug program of the Pharmacy Service of the Almería Health Area, including 18 Primary Care centres. Information on individuals' socio-demographic status, prescription, use, and expenditure on analgesics for the treatment of pain such as opioids (N02A), non-steroidal anti-inflammatory drugs (NSAIDs) (M01A), and antipyretic analgesics (N02B) were collected in 2008 and 2014. We carried out descriptive and comparative analyses of the expenditure, prescription, and use of analgesics between 2008 and 2014, and among Primary Care centres depending on the location of the centres: rural vs. urban areas, and deprived vs. non-deprived areas, reporting mean differences in terms of percentage increase or decrease. To analyse the differences in consumption between 2008 and 2014, parametric (t-Student for paired data) and non-parametric (Wilcoxon test) tests were performed depending on the normality of the quantitative variables, analysed by the Kolmogorov-Smirnov test.

**Results:** A total of 18 Primary Care centres were included, covering 291,024 users in 2008, and 293,498 in 2014. Mean age was 38.5 years old (SD: 4.7) in 2008 and 40.1 (SD: 4.57) in 2014. Overall expenditure on drugs decreased by 23 % in 2014, and expenditure on analgesics decreased by 12 %. However, expenditure on analgesic drugs implied an increase in overall expenditure. Prescription and use of analgesics also decreased in 2014. However, opioids increased in expenditure, use and prescription. A higher increase in the use of analgesic drugs was observed in rural areas, as well as deprived areas.

**Conclusions:** The economic crisis has had a negative effect on the expenditure, use, and prescription of analgesic drugs. However, a change in the profile of pain treatment was observed, increasing the expenditure and use of opioids prescribed.

**Key words:** Prescription, use, expenditure, analgesics, economic-crisis.

### **RESUMEN**

**Objetivos:** El sistema sanitario español ha sufrido muchos cambios como consecuencia de las políticas de austeridad llevadas a cabo durante la crisis económica, concretamente en lo que se refiere al gasto farmacéutico; medicamentos como los analgésicos, que previamente eran gratuitos para un sector de la población, se han visto afectados por la aplicación de un copago sobre el precio de venta. Por ello, nos planteamos identificar el efecto de la crisis económica en España sobre el gasto, prescripción y consumo de analgésicos.

**Material y métodos:** Se realizó un estudio Observacional Descriptivo Transversal, basado en programa de gestión de medicamentos del Servicio de Farmacia del Distrito Sanitario de Almería, que incluye 18 centros de Atención Primaria (AP). Se

recogió información sociodemográfica, prescripción, gasto farmacéutico y consumo de opiáceos (N02A), antiinflamatorios no esteroideos (AINE) (M01A) y analgésicos antipiréticos (N02B) en 2008 y 2014. Se realizó un análisis descriptivo y comparativo del gasto, prescripción y consumo entre 2008 y 2014, y entre centros de AP dependiendo de su ubicación: rural o urbana, y con o sin necesidad de transformación social, reportando diferencias de medias en términos de aumento o disminución porcentual. Para analizar las diferencias en el consumo entre 2008 y 2014 se llevaron a cabo pruebas paramétricas (t-Student para datos apareados) y no paramétricas (Test de Wilcoxon), según la normalidad de las variables cuantitativas analizadas mediante el test de Kolmogorov-Smirnov.

**Resultados:** Se incluyeron 18 centros de AP que daban cobertura a 291.024 usuarios en 2008 y 293.498 en 2014. La edad media de la población fue 38,5 años (DT: 4,7) en 2008 y 40,1 años (DT: 4,5) en 2014. El gasto global de medicamentos disminuyó un 23 % en 2014, y el de analgésicos un 12 %. Sin embargo, el gasto de analgésicos supuso un aumento en el gasto general farmacéutico. La prescripción y consumo de analgésicos también disminuyeron en 2014. A pesar de la disminución generalizada de analgésicos, los opioides aumentaron el gasto, la prescripción y el consumo. En el área rural, así como en las zonas de necesidad de transformación social, hubo un mayor aumento del consumo.

**Conclusiones:** La crisis económica ha tenido un efecto negativo en la prescripción, consumo y gasto de analgésicos. Sin embargo, se observa un cambio de perfil en el tratamiento, aumentando el gasto y el consumo de opiáceos respecto a otros analgésicos.

**Palabras clave:** Prescripción, consumo, gasto, analgésicos, crisis económica.

## INTRODUCTION

The economic crisis has been a problem affecting almost all European countries in recent years, and which has had major consequences in Spain (1). The crisis that began in 2008, apart from being a scourge for the labour and business sector, also affected the Spanish health system, which since then has seen a drop in investment in median annual health expenditure per inhabitant (2). Among the austerity policies implemented in these years, and specifically as regards pharmaceutical expenditure, it may be seen that as from 2012 (3) a change took place in the price of drugs, so medications that had previously been free for one sector of the population (pensioners), were affected by the application of co-payment on sale price, which ranged between 10% in the case of pensioners, and 40-60% in the rest of the population. It is clear that access to appropriate treatment is essential for adequate disease control (4), and that said access will depend to a large

extent on the sick person's economic situation (5-7), so it seems reasonable to assume that the applied measures could have negative consequences for patients' health care.

Chronic pain (CP) is a complex problem that affects 16.6% of the general Spanish population, and 70% of patients who suffer it are receiving some kind of analgesic treatment (8,9). With the assumption that economic measures adopted during the crisis period could affect the prescription and use of analgesic drugs to treat pain, this work's main objective is to compare the prescription, expenditure and consumption of analgesics used at the outset of the economic crisis (2008) and after its establishment (2014), in a geographical area in southern Spain, characterized as having agriculture as its main economical driving force (10) and showing a prevalence of CP in 17.5% of the general population (11).

## MATERIAL AND METHODS

A cross-sectional, descriptive study was carried out. The information was obtained from the drug management program of the Pharmacy Service in the Health District of Almería under the Andalusian Health Service (Microstrategy), which comprises a coverage area of 291,288 inhabitants. Information was obtained regarding consumption, prescription and pharmaceutical expenditure of pharmacological groups in the classification Anatomical-Therapeutic-Chemical (Anatomical Chemical Classification, ATC) which included opiates (N02A), non-steroid anti-inflammatory drugs (M01A) and antipyretic analgesics (N02B). The aggregated data was used added for each of the 18 Primary Health Care centres in the health district of Almería for the years 2008 and 2014 regarding:

- Pharmaceutical expenditure of the health-care district, which was measured by recommended retail price (RRP) of each container, by the number of containers dispensed.
- Pharmaceutical prescription, measured by the number of containers dispensed with medical prescription in the health-care district.
- Consumption rate of each pharmacological group analysed, which was measured in daily dose defined by a thousand health cards per day (DDC).

Information was also collected on socio-demographic characteristics (age, gender) of the population in the district's coverage area, and the geographical environment of the Primary Health Care centres included, differentiating whether they had a rural or urban location. Additionally, a difference was made between Areas with Needs for Social Transformation (ZNTS) or Without Needs for Social Transformation (SNTS), according to the

definition established by the Council for Equality and Social Welfare of the Regional Government of Andalusia (12,13), which considers an Area with Needs for Social Transformation (ZNTS) as clearly defined geographical areas, whose population exhibit structural situations of serious poverty and social exclusion, and which significantly show problems in:

- Housing, urban deterioration and deficit in public infrastructure, equipment and services.
- High rates of school absenteeism and dropout.
- High unemployment rates along with a serious lack of professional training.
- Significant hygienic health-care deficiencies.
- Conditions of social disintegration.

A descriptive analysis was carried out on the variables studied, using frequency measurement in the case of categorical variables and weighted averages by number of inhabitants of each PHC centre in the case of continuous quantitative variables. Furthermore, changes in expenditure, prescription and consumption were described between the years 2008 and 2014, reporting differences of averages in terms of percentage increase or decrease. To analyse differences in consumption between 2008 and 2014 parametric (t-Student for paired data) and non-parametric (Wilcoxon) tests were carried out, according to the normality of quantitative variables analysed using the Kolmogorov-Smirnov test.

Analyses were carried out with the IBM SPSS V.24 statistics package.

The study was conducted in accordance with the agreements of the Helsinki Declaration and with authorization from the Research Ethics Committee of the District of Almería.

## RESULTS

### General characteristics of the population

The population in the study in the year 2008 belonging to the area of health-care coverage, comprised 50.9% of males. In the year 2014, the population increased by 0.85%, corresponding to 50.1% men and 49.9% women. The population's median age was 38.5 years old (SD: 4.75) in 2008 and 40.1 years old (SD: 4.57) in 2014. Of the 18 centres analysed, 7 (39%) were rural centres and 11 (61%) urban; 10 (55.6%) were SNTS, and 8 (44.4%) ZNTS (Table I).

### Expenditure, prescription and consumption of analgesic drugs in 2008 and 2014

In 2008, total pharmaceutical expenditure of the district was of €64,932,855 and in 2014 was €49,956,631, which represents a drop of 23%. The 18 health-care centres spent an average of €3,607,381 (SD: 1,747,168) in 2008 and €2,775,368 (SD: 1,310,519) in 2014. Expenditure on the pharmacological groups included in the study (N02A,

N02B and M01A) in 2008 was €4,250,827, which represents 6.5% of the district's total expenditure in pharmacy, and €3,744,006 in 2014, which is 7.5% of the year's total pharmaceutical expenditure.

Total number of drugs prescribed was 5,226,559 in 2008, and 4,628,333 in 2014, which represents a drop of 11.1%. Prescriptions issued by therapeutic groups analysed in the study were of 683,393 in 2008 and 652,202 in 2014, that is, there was a drop of 4.6%. As regards the total, prescription by analysed groups represented 13.1% in the year 2008 and 14.03% in 2014.

In the weighted average consumption of analgesic drugs, expressed in DDC, a fall can be seen from 2008 to 2014, from 80.7 DDC to 72.5 DDC. Especially significant is the increase in the consumption of opiates and the drop in NSAIDs during the period analysed (Table II).

In the analysis of weighted expenditure according to PHC centres, it was observed that in 2014 the expenditure on opiates increased mainly in suburban Almería, Bajo Andarax, Ciudad Jardín and Torrecárdenas. Expenditure on analgesics and antipyretics did not undergo major changes, except in clinics of Almería centre, Cruz de Caravaca, Oliveros and Virgen del Mar, where there was lower expenditure than in 2008. NSAIDs were what suffered the greatest drop in expenditure, mainly in centres in Ciudad Jardín, Oliveros, Plaza de Toros and Virgen del Mar (Figure 1).

Despite the general drop in the number of analgesic drug prescriptions in 2014, the prescription of opiates in particular increased considerably in some PHC centres, such as Bajo Andarax and Ciudad Jardín, as well as antipyretic analgesic in suburban Almería, Bajo Andarax, Nijar and Torrecárdenas. The prescription of the NSAIDs only increased in one PHC centre, Torrecárdenas, characterized as being in an urban environment and SNTS (Figure 2).

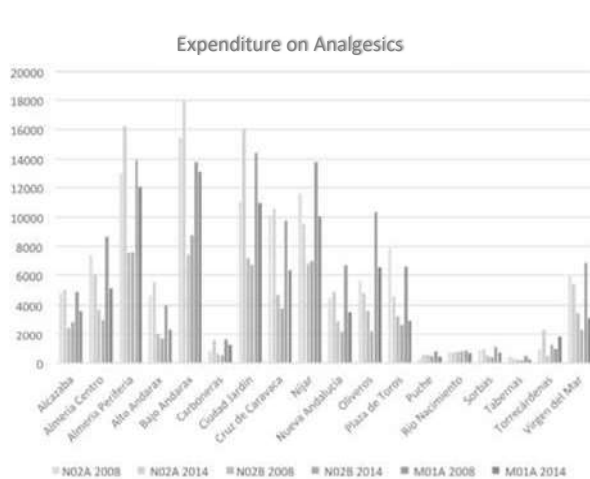
TABLE I  
PHC CENTERS ACCORDING TO ENVIRONMENT AND  
GEOGRAPHICAL AREA

	ZNTS	SNTS
<i>Rural</i>	- Bajo Andarax - Nijar - Río Nacimiento	- Alto Andarax - Carboneras - Sorbas - Tabernas
<i>Urban</i>	- Alcazaba - Suburban Almería - Cruz de Caravaca - Plaza de toros - Puche	- Almería Centro - Ciudad Jardín - Nueva Andalucía - Oliveros - Torrecárdenas - Virgen del mar

**TABLE II**  
PHARMACEUTICAL EXPENDITURE, PRESCRIPTION AND CONSUMPTION OF N02A, N02B AND M01A IN 2008 AND 2014 IN THE HEALTH-CARE DISTRICT OF ALMERÍA

ATC GROUP	Year	Pharmaceutical group (€)	Difference in pharmaceutical expenditure (%)	No. of prescriptions issued	Difference in No. of prescriptions issued (%)	Average weighted consumption (DDC)	p-value (DDC)
N02A	2008	1,578,905	+6.9 %	83,657	+50.4 %	8.7	< 0.001a
	2014	1,688,364		125,809		13.61	
N02B	2008	875,538	-7.3 %	327,626	+1.2 %	19	0.002a
	2014	811,722		331,520		21.62	
M01A	2008	1,796,384	-30.7 %	270,708	-29.2 %	52.7	< 0.001b
	2014	1,243,921		191,515		37.2	

ATC Groups: N02A: opiates; N02B: antipyretic analgesics; M01A: non-steroid anti-inflammatory drugs (NSAIDs). DDC: Total daily dose. <sup>a</sup> Wilcoxon Test. <sup>b</sup> T-Student for paired data.

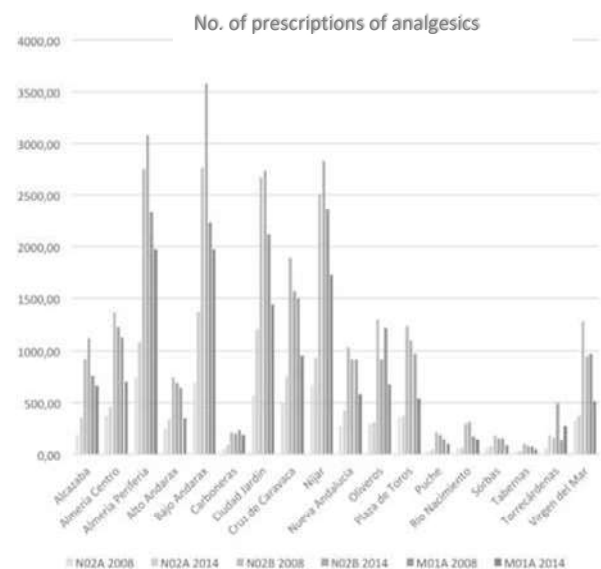


**Fig. 1.** Expenditure on analgesics N02A, N02B and M01A in the years 2008 and 2014 according to Primary Health Care centers.

The consumption of analgesics weighted by number of users attended in PHC centres follows the same pattern in all centres in 2014: the consumption of opiates, of antipyretic analgesics increases and the consumption of NSAIDs falls, although this continues to be by far the analgesic most consumed (Figure 3).

#### Expenditure, prescription and consumption of analgesic drugs in urban vs. rural centers.

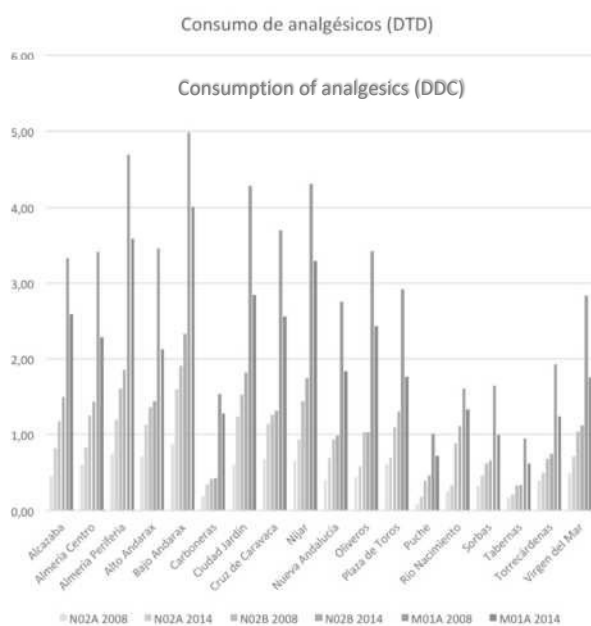
In the analysis of differences according to rural or urban location of PHC centres, it was found that, during the



**Fig. 2.** No. of prescriptions of analgesics N02A, N02B and M01A in the years 2008 and 2014 according to Primary Health Care centres.

study period, in urban centres, expenditure on analgesics fell by 14.5% compared with a drop of 7% in rural centres. Conversely, an increase in expenditure on analgesics regarding total expense on pharmacy was seen in both urban and rural areas.

The number of prescriptions issued and the consumption of analgesics also showed a drop, although in urban centres, the fall was larger (Table III).



**Fig. 3.** Consumption of analgesics N02A, N02B and M01A in the years 2008 and 2014 according to Primary Health Care centres.

### Expenditure, prescription and consumption of analgesic drugs in areas with and without needs for social transformation

The drop in expenditure on analgesics was greater in the SNTS areas (12.8 vs. 11.1%) than in ZNTS areas in study period. However, the percentage of expenditure on these analgesics regarding total pharmaceutical expenditure increased slightly both in SNTS and in ZNTS. In SNTS areas, the decrease was greater both in the number of prescriptions issued (10% vs. 4% in rural centres), and in consumption of analgesics (13.5% vs. 3,6% in ZNTS).

By therapeutic groups, although an increase was seen in the prescription and consumption of opiates and a drop in NSAIDs, there was also a rise in prescription and consumption of antipyretic analgesics (N02B) in the ZNTS (Table IV).

**TABLE III**  
EXPENDITURE, PRESCRIPTION AND CONSUMPTION BETWEEN SNTS AND ZNTS AREAS IN THE YEARS 2008 AND 2014.  
THERAPEUTIC GROUPS N02A, N02B AND M01A

ATC GROUP	Areas	Years	Pharmaceutical expenditure (€)	Difference in pharmaceutical expenditure (%)	No. of prescriptions issued	Difference in No. of prescriptions issued (%)	Average weighted consumption (DDC)	p-value (DDC)
N02A	Urbano	2008	1,023,266	+5.2 %	53,005	+49.5 %	5.5	0.004 <sup>a</sup>
		2014	1,076,957		79,236		8.6	
	Rural	2008	555,639	+10.04 %	30,652	+51.9 %	3.2	0.018 <sup>a</sup>
		2014	611,407		46,573		5	
N02B	Urbano	2008	568,934	-10.3 %	212,320	-2 %	12	0.026 <sup>a</sup>
		2014	510,124		207,988		13.6	
	Rural	2008	306,604	-1.6 %	115,306	+7.1 %	7	0.028 <sup>a</sup>
		2014	301,598		123,532		8,1	
M01A	Urbano	2008	1,203,503	-33.2 %	173,750	-30 %	34.3	<0.001 <sup>b</sup>
		2014	803,674		121,368		23.6	
	Rural	2008	592,881	-25.7 %	96,958	-27.6 %	18.6	0.003 <sup>b</sup>
		2014	440,247		70,147		13.6	

ATC Groups: N02A: opiates; N02B: antipyretic analgesics; M01A: non-steroid anti-inflammatory drugs (NSAIDs). DDC: Daily dose by card. <sup>a</sup> Wilcoxon test. <sup>b</sup> T-Student for paired data.

**TABLE IV**  
EXPENDITURE, PRESCRIPTION AND CONSUMPTION BETWEEN SNTS AND ZNTS AREAS IN THE YEARS 2008 AND 2014.  
THERAPEUTIC GROUPS N02A, N02B AND M01A

ATC GROUP	Areas	Years	Pharmaceutical expenditure (€)	Difference in pharmaceutical expenditure (%)	No. of prescriptions issued	Difference in No. of prescriptions issued (%)	Average weighted consumption (DDC)	p-value (DDC)
N02A	SNTS	2008	746,866	+15.41 %	41,651	+50.1 %	4.3	0.007 <sup>a</sup>
		2014	861,983		62,531		6.7	
	ZNTS	2008	832,039	-0.7 %	42,006	+50.6 %	4.4	0.012 <sup>a</sup>
		2014	826,381		63,278		6.9	
N02B	SNTS	2008	424,547	-14.9 %	156,769	-5.3 %	9.2	0.059 <sup>a</sup>
		2014	361,412		148,491		.0	
	ZNTS	2008	450,991	-0.1 %	170,857	+7.1 %	9.8	0.012 <sup>a</sup>
		2014	450,309		183,029		11.6	
M01A	SNTS	2008	951,188	-34 %	133,100	-34.4 %	26.2	<0.001 <sup>b</sup>
		2014	627,936		87,365		17.4	
	ZNTS	2008	845,196	-27.1 %	137,608	-24.3 %	26.5	<0.001 <sup>b</sup>
		2014	615,985		104,150		19.8	

ATC Groups: N02A: opiates. N02B: antipyretic analgesics. M01A: non-steroid anti-inflammatory drugs (NSAIDs). DDC: daily dose by card. <sup>a</sup>Wilcoxon Test. <sup>b</sup>T-Student for paired data. ZNTS: areas with needs for social transformation. SNTS: areas without needs for social transformation.

## DISCUSSION

To our knowledge, this is the first study to analyse prescription, expenditure and consumption of analgesic drugs, before and during the economic crisis. Furthermore, it examines these results in accordance with two social indicators, one related with the needs of social transformation in the geographical areas included in the study, and another depending on the rural or urban nature of the centres studied. Among the results obtained, we should highlight the drop in expenditure, consumption and prescription of analgesics in the year 2014 regarding 2008. However, we can see an increase in expenditure, prescription and consumption of these drugs with respect to total pharmaceutical expenditure in the health-care district.

Additionally, it is worth noting the increase in opioids, particularly with regard to the outset of the crisis. These results are in line with the findings presented in the recent report on the use of opioid drugs in Spain between 2008 and 2015 (14), which justified the increase in the use of opiates due to the extensive offer of pharmaceutical presentations and forms that appeared over these years. According to the analgesic scale of the World Health Organization (WHO), among drugs suitable for palliating moderate and severe pain intensity (15), their use has been

fostered in numerous studies (16,17). Additionally, some studies have shown that the increase in opioid consumption is directly related with a greater prevalence of CP among the population (18). This circumstance could also explain our results, as although it does not show the prevalence of chronic pain over these years in health-care in the district under study, the prevalence of chronic pain is known to have increased in Spain in recent years, rising from 12% in 2006 (9) to 16.6% in 2014 (19).

Also significant is the result seen in the group N02B, where there is a drop in expenditure, despite an increase in consumption. This result could be explained by the application of the Act approved in 2011 (20), obliging health-care professionals to prescribe according to active ingredient. If we bear in mind that generic compounds have a lower cost, this could justify the increase in consumption despite the fall in expenditure.

NSAIDs are mainly the drugs where a more marked fall in expenditure, prescription and consumption was observed. Similar results have been seen in countries like Greece (21), where despite increasing consumption of drugs associated with mental illnesses, hypertension or gastric pathology, consumption of NSAIDs has fallen during the crisis period. These authors argue that this decrease could be associated with austerity policies implemented in the health-care system, and the reduction

in users' income. Nevertheless, these results should be interpreted as an estimate in consumption, as different measurements were used.

The differences observed according to rural/urban environment of health-care centres were another aspect analysed in the study, finding a lower drop in consumption of analgesics in rural centres over these years. Although other studies show that living in rural or urban areas is not associated with differences in the use of analgesics (22), reports show that the prevalence of musculoskeletal chronic pain is greater in rural environments (23) and that patients who live in this environment fall ill at an earlier age (24). It is significant that in the study area, the main economic activity is greenhouse farming, with 45,000 people working in this sector (10), where working conditions (lack of mechanization, concentration of work, long working days, heat stress inside the greenhouse) are especially unfavourable, and these circumstances may justify the results observed. However, the information necessary to prove this has not been collected in the study.

Regarding the parameters analysed in the areas with or without needs for social transformation, it is significant that expenditure on analgesics in ZNTS has remained practically the same from the outset of the crisis. The application of pharmaceutical co-payment, implemented in 2012 in Spain (3), could be the cause of this variability in expenditure in SNTS with respect to ZNTS, as the latter are characterized as having a population in structural situations of serious poverty and social exclusion with high unemployment rates where co-payment is 0%, thus not affecting expenditure. Furthermore, consumption has fallen less in the ZNTS during the crisis. It may be assumed that the prevalence of pain is greater in these areas, as the relationship between the presence of pain and more disadvantaged social and cultural levels has been broadly described. According to the literature (25), persons with pain that live in areas of social deprivation suffer greater multimorbidity. Additionally, housing conditions and key health factors, such as tobacco use, alcoholism, poor quality nutrition, among others, have been shown to affect these populations more (26). However, future studies would be necessary in order to demonstrate this hypothesis.

Certain limitations should be mentioned in this work. Firstly, the aggregated nature of the data has not shown prescription and consumption of these drugs among patients who suffer chronic pain. Therefore, pain is assumed to be the only reason for prescription and consumption of analgesics, though there may be other reasons for such prescription. Furthermore, and although indicators of social interest have been used, the lack of information on other aspects related with lifestyles mentioned above makes the provided information limited. Despite the above, and since the subject study area has a

high rate of vulnerable population, the study's implementation seems justified.

In conclusion, we could say that the Spanish economic crisis has had a negative effect on the expenditure, prescription and consumption of analgesic drugs commonly used for treating pain. Nevertheless, we have observed a change in profile in treatment, as increases in the consumption of opiates with respect to the outset of the crisis and a reduction in NSAIDs. Additionally, differences have been shown according to the social indicators analysed, with higher consumption of analgesics in rural areas and with needs for social transformation.

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## CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

## BIBLIOGRAPHY

- Gili M, Roca M, Basu S, McKee M, Stuckler D. The mental health risks of economic crisis in Spain: Evidence from primary care centres, 2006 and 2010. *Eur J Public Health* 2013;23(1):103-8. DOI: 10.1093/eurpub/cks035.
- Quaglio GL, Karapiperis T, Van Woensel L, Arnold E, McDaid D. Austerity and health in Europe. *Health Policy (New York)* 2013;113(1-2):13-9. DOI: 10.1016/j.health-pol.2013.09.005.
- Boletín Oficial del Estado. Real Decreto-Ley 16/2012, de 20 de abril, de medidas urgentes para garantizar la sostenibilidad del Sistema Nacional de Salud y mejorar la calidad y seguridad de sus prestaciones. *Boletín Oficial del Estado* 2012 p. 31278.
- Timmerman L, Stronks DL, Groeneweg JG, Huygen FJ. Prevalence and determinants of medication non-adherence in chronic pain patients: A systematic review. *Acta Anaesth-sciol Scand* 2016;60(4):416-31. DOI: 10.1111/aas.12697.
- Markotic F, Cerni Obrdalj E, Zalihic A, Pehar R, Hadziomanovic Z, Pivic G, et al. Adherence to pharmacological treatment of chronic nonmalignant pain in individuals aged 65 and older. *Pain Med* 2013;14(2):247-56. DOI: 10.1111/pme.12035.
- Geitona M, Daniil Z. The pharmacological cost of COPD during Greek economic crisis. *Int J COPD* 2017;12:461-6. DOI: 10.2147/COPD.S123095.
- Benach J, Tarafa G, Muntaner C. El copago sanitario y la desigualdad: Ciencia y política. *Gac Sanit* 2012;26(1):80-2. DOI: 10.1016/j.gaceta.2011.12.001.
- Dueñas M, Salazar A, Ojeda B, Fernández-Palacín F, Mico JA, Torres LM, et al. A nationwide study of chronic pain prevalence in the general Spanish population: identifying clinical subgroups through cluster analysis. *Pain Med (United States)* 2015;16(4):811-22. DOI: 10.1111/pme.12640.
- Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain* 2006;10(4):287-333.
- Callejón-Ferre AJ, Montoya-García ME, Pérez-Alonso J, Rojas-

- Sola JJ. The psychosocial risks of farm workers in south-east Spain. *Saf Sci* 2015;78:77-90.
11. Asociación Andaluza del tratamiento del dolor y asistencia continuada. Estudio sobre la Incidencia del Dolor en la Comunidad Autónoma de Andalucía; 2010.
  12. Consejería de Igualdad y Políticas sociales. Junta de Andalucía. Definición de Zona de Necesidad de Transformación Social (ZNTS).
  13. Dirección General de Asistencia Sanitaria. Atención a La Salud En Las Zonas Con Necesidades De Transformación Social De Andalucía (Znts); 2004.
  14. Agencia española de medicamentos y productos sanitarios. Utilización de medicamentos opioides en España durante el periodo 2008-2015; 2017.
  15. Siebenhuener K, Eschmann E, Kienast A, Schneider D, Minder CE, Saller R, et al. Chronic pain: how challenging are ddis in the analgesic treatment of inpatients with multiple chronic conditions? *PLoS One* 2017;12(1):e0168987. DOI: 10.1371/journal.pone.0168987.
  16. Scholten W. Improving access to adequate pain management in Taiwan. *Acta Anaesthesiol Taiwanica* 2015;53(2):62-5. DOI: 10.1016/j.aat.2015.05.004.
  17. Gooberman-Hill R, Heathcote C, Reid CM, Horwood J, Beswick AD, Williams S, et al. Professional experience guides opioid prescribing for chronic joint pain in primary care. *Fam Pract* 2011;28(1):102-9. DOI: 10.1093/fampra/cmq083.
  18. Birke H, Kurita GP, Sjögren P, Højsted J, Simonsen MK, Juel K, et al. Chronic non-cancer pain and the epidemic prescription of opioids in the Danish population: Trends from 2000 to 2013. *Acta Anaesthesiol Scand* 2016;60(5):623-33. DOI: 10.1111/aas.12700.
  19. Dueñas M, Salazar A, Ojeda B, Fernández-palacín F, Micó JA, Torres LM, et al. A nationwide study of chronic pain prevalence in the general spanish population: identifying clinical subgroups through cluster analysis. *Pain Med* 2014;16(4):811-22. DOI: 10.1111/pme.12640.
  20. Boletín Oficial del Estado. Real Decreto-Ley 9/2011, de 19 de agosto, de medidas para la mejora de la calidad y cohesión del sistema nacional de salud, de contribución a la consolidación fiscal, y de elevación del importe máximo de los avales del Estado para 2011. Boletín Oficial del Estado 2011 p. 93143-68.
  21. Thomaidis NS, Gago-Ferrero P, Ort C, Maragou NC, Alygizakis NA, Borova VL, et al. Reflection of socioeconomic changes in wastewater: licit and illicit drug use patterns. *Environ Sci Technol* 2016;50(18):10065-72. DOI: 10.1021/acs.est.6b02417.
  22. Hernández-Cáceres AE, Rodríguez-amado J, Peláez-balles I, Vega-morales D, Garza-elizondo MA. Factors associated with treatment of osteoarthritis: Analisis of a COPCORD study in Nuevo León, Mexico. *Reumatol Clínica* 2015;11(4):204-9. DOI: 10.1016/j.reuma.2014.08.001.
  23. Docking RE, Beasley M, Steinerowski A, Jones E, Farmer J, Macfarlane GJ, et al. The epidemiology of regional and widespread musculoskeletal pain in rural versus urban settings in those > 55 years. *Br J Pain* 2015;9(2):86-95. DOI: 10.1177/2049463714527438.
  24. Dowsey MM, Petterwood J, Lisik JP, Gunn J, Choong PFM. Prospective analysis of rural-urban differences in demographic patterns and outcomes following total joint replacement. *Aust J Rural Health* 2014;22(5):241-8. DOI: 10.1111/ajr.12100.
  25. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: A cross-sectional study. *Lancet* 2012;380(9836):37-43. DOI: 10.1016/S0140-6736(12)60240-2.
  26. Novoa AM, Amat J, Malmusi D, Diaz F, Darnell M, Trilla C, et al. Changes in health following housing improvement in a vulnerable population in Spain: a follow-up study. *Int J Heal Serv* 2017;47(1):83-107.