



## Original Article

## Resource Use and Economic Impact of Patients With Gout: A Multicenter, Population-Wide Study<sup>☆</sup>

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## ABSTRACT

**Objective:** To determine the use of resources and economic impact of patients with gout at the population level.

**Patients and methods:** Observational design analyzing records belonging to 6 primary care centers and 2 hospitals. We included patients'  $\geq 18$  years with an acute episode of gout over the years 2003–2007. Patient follow-up was 2 years. It produced two study groups: patients with 1–2 attacks/acute recurrences and 3 or more events. Main variables were: demographic, co-morbidity, metabolic syndrome (MS), and resource use and health/non-health costs. Statistical analysis: logistic regression-model ANCOVA,  $P < .05$ .

**Results:** 3130 patients with gout were included. Prevalence: 3.3%, mean age: 55.8 years male: 81.1%. Groups were distributed as follows: 68.4% had 1–2 acute attacks and 31.6% with 3 or more,  $P < .001$ . The prevalence of MS was 28.8% (confidence interval [CI] 95% CI: 27.2%–30.4%). The average/unit cost was € 2228.6 (direct costs: 96.9%), 90.8% in primary care (visits: 23.5%; drugs: 57.7%). For groups, the average corrected model/unit total cost per patient was € 2130.6 vs € 2605.4, respectively ( $P < .001$ ). In all cost components, the results were higher in the group with  $\geq 3$  attacks. The subgroup of diabetic patients (No.=641, 20.5%) had a higher cost (€ 3124.8 vs € 1997.8,  $P < .001$ ).

**Conclusions:** Gout is associated with substantial morbidity, presence of MS and resource consumption. The study provides useful data on the cost of the disease; the costs of outpatient follow up are the highest.

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### Uso de recursos e impacto económico de los pacientes con gota: estudio multicéntrico de ámbito poblacional

## RESUMEN

**Objetivo:** Determinar el uso de recursos y el impacto económico de los pacientes con gota en un ámbito poblacional.

**Pacientes y métodos:** Diseño observacional (multicéntrico) realizado a partir de registros pertenecientes a 6 centros de atención primaria y 2 hospitales. Se incluyó a pacientes  $\geq 18$  años con un episodio agudo de gota durante los años 2003–2007. El seguimiento de los pacientes fue de 2 años. Se confeccionaron 2 grupos de estudio: pacientes con 1-2 ataques/recurrencias agudas y con 3 o más. Principales variables: sociodemográficas, comorbilidad, síndrome metabólico (SM), y uso de recursos y costes sanitarios/no sanitarios. Análisis estadístico: regresión-logística, modelo de ANCOVA;  $p < 0.05$ .

**Resultados:** Se incluyó a 3.130 pacientes con gota. Prevalencia: 3,3%; edad media: 55,8 años; varones: 81,1%. Por grupos: el 68,4% presentó 1-2 ataques agudos y el 31,6%, 3 o más,  $p < 0.001$ . La prevalencia del SM fue del 28,8% (intervalo de confianza [IC] del 95%, 27,2-30,4%). El promedio/unitario del coste fue de 2.228,6 € (costes directos: 96,9%), el 90,8% en AP (visitas: 23,5%; medicamentos: 57,7%). Por grupos, en el modelo corregido el promedio/unitario de los costes totales por paciente fue de 2.130,6 € frente a 2.605,4 €, respectivamente ( $p < 0.001$ ). En todos los componentes del coste los resultados fueron mayores en el grupo con  $\geq 3$  ataques. El subgrupo de pacientes diabéticos (N=641; 20,5%) presentó un mayor coste (3.124,8 € frente a 1.997,8 €;  $p < 0.001$ ).

## Palabras clave:

Gota

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**Conclusiones:** La gota se asocia a una elevada morbilidad, presencia de SM y consumo de recursos. El estudio proporciona datos útiles sobre el coste de la enfermedad; siendo los costes de seguimiento ambulatorio los más elevados.

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## Introduction

Gout is one of the most common causes of arthritis in patients over 40, its prevalence ranges from 0.5% to 5% of the general population.<sup>1,2</sup> It is a disease characterized by the presence of inflammatory episodes, usually monoarticular and recurrent, often intense and self-limited.<sup>3,4</sup> Clinical manifestations of gout occur in three phases: (a) acute attacks, (b) intercrisis periods (tophi are a late symptom of the disease), and (c) chronic arthropathy (multiple and/or persistent attacks).<sup>5–8</sup>

Available studies show that in patients with obesity, hypertension and/or diabetes (high cardiovascular risk), serum urate levels can be considered as a marker of inflammation, ischemia and oxidative stress of the cardiovascular system.<sup>9,10</sup> The association between gout and the metabolic syndrome (MS) is well documented. Studies show that serum urate levels increase as the number of MS components increase, even when set against confounding factors such as age, gender, creatinine clearance, diuretic use and alcohol consumption.<sup>11–13</sup> Overall, the prevalence of MS according to the criteria of the *National Cholesterol Education Program Adult Treatment Panel III* (NCEP-ATP III)<sup>14</sup> ranges from 19% to 71%.

The available evidence regarding the use of resources and costs is limited.<sup>15,16</sup> In the US it is estimated that the annual direct costs for treating new cases of gout in men is approximately \$ 27.4 million.<sup>17</sup> In the few studies reviewed there is a great variability in the methodology used to calculate these resources; moreover, they have been performed in very different groups of patients (cohort of employees, the elderly, etc.),<sup>18–21</sup> circumstances that affect the comparability and external validity of the results. Given this scenario, and given the lack of data available in our country regarding the follow up of patients with gout in routine clinical practice situations, the performance of this type of study may be relevant. The objective of the study was to determine the use of resources and the economic impact (health and non-health costs) of patients with gout in a Spanish population setting with a follow-up period of 2 years.

## Patients and Methods

### Study Population

We performed a multicenter observational design study from the review of medical records, in both outpatients and hospitalized patients. The study population consisted of people from 6 reformed primary care (PC) centers, managed by Badalona Serveis Assistencials (BSA). Information was obtained from the resources of two reference hospitals: Hospital Municipal de Badalona and Germans Trias i Pujol Hospital (specialized). The population assigned to the centers was mostly urban, of middle-low socioeconomic status, predominantly industrial. BSA is an integrated healthcare organization that provides coverage to a reference population of around 120 000 in Badalona (Barcelona, Spain) and has 6 PC centers, one acute care hospital (Hospital Municipal de Badalona) and a health center. Their funding model is public and service providers are private, it is concerted (*contract program*) with the Catalan Health Service (CatSalut).

### Inclusion and Exclusion Criteria

We included in the study all patients consulting for an episode of gout (new or recurrent) from 01/01/2003 to 31/12/2007, and who met the following characteristics: (a) age  $\geq 18$  years; (b) regularly followed the protocol/clinical practice guidelines established in the centers, and (c) met the program requirements of the acute and chronic center. We excluded subjects transferred to other centers, the dead and those displaced or outside the area. Follow up of patients lasted 24 months (2 years) for the calculation of costs (health and non-health related). Depending on the number of episodes/recurrences, two study groups were formed: patients with 1–2 episodes and patients with 3 or more episodes (acute attacks).

### Measures Related to Gout

The diagnosis of gout was obtained from the PC International Classification (CIAP-2), code T92, item 7 of diseases and health problems,<sup>22</sup> and the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)<sup>23</sup> (codes: 274.x). Clinical validation was performed in cases of gout by confirmation of clinical courses in the patient history. Validation consisted of obtaining a random sample of 20 files, where we checked whether the clinical diagnosis of gout was consistent with the ACR criteria.<sup>6</sup> In all cases, diagnostic accuracy was certified.

We estimated the prevalence of the disease as the percentage of individuals in the population presenting an episode of gout during the study period (period prevalence). The cumulative incidence rate was defined as the proportion of healthy individuals who developed the disease (new cases); the cumulative incidence, provides an estimate of the probability or the risk that an individual free from a specific illness develops during a specific period of time. No results were standardized as the population pyramid distributed by age and gender of the patients studied was similar to that of the population of Catalonia (*source*: National Statistics Institute). In addition, we determined the date of onset of illness (years of progression of the disease), the presence of hyperuricemia (dichotomous) and the origin of the patients (PC, hospital and/or outpatient).

### Sociodemographic and Morbidity Data

The main variables were: age (continuous and ranges) and gender, and personal history obtained from the CIAP-2<sup>22</sup>: hypertension (K86, K87), diabetes mellitus (T89, T90), dyslipidemia (T93), obesity (T82), smoking (P17), alcoholism (P15, P16), renal failure, cerebrovascular accident (K90, K91, K93), chronic obstructive pulmonary disease (R95, chronic airflow obstruction), asthma (R96), dementia or memory disorders (P70, P20), neurological diseases: Parkinson's disease (N87), epilepsy (N88), multiple sclerosis (N86) and other neurological diseases (N99); depressive syndrome (P76) and malignancies (all types, A79, B72-75, D74-78, F75, H75, K72, L71, L97, N74-76, R84-86, T71-73, U75-79, W72-73, X75-81, Y77-79).

As a summary variables of overall comorbidity for each patient treated, we used: (a) the Charlson comorbidity index<sup>24</sup> as an approximation to the severity of the patient, and (b) the rate of individual causes, obtained from the Adjusted Clinical Groups (ACG), a

patient classification system for resource self consumption.<sup>25</sup> The ACG provides application resource utilization bands (BUR), so that each patient, based on their overall disease morbidity, is grouped into one of five mutually exclusive categories (1: healthy or very low morbidity, 2: low morbidity, 3: moderate morbidity, 4: high morbidity, and 5: very high morbidity).

The definition of MS was established when the subject met 3 of the 5 NCEP-ATP III modified criteria<sup>14</sup>: (a) triglycerides of 150 mg/dl or greater; (b), high-density lipoprotein cholesterol less than 40 mg/dl in men or less than 50 mg/dl in women; (c) systolic/diastolic blood pressure 130/85 mmHg or higher or antihypertensive treatment, (d) baseline fasting glucose level of 110 mg/dl or more, or treatment with hypoglycemic drugs or previously diagnosed diabetes mellitus, and/or (e) body mass index of 28.8 kg/m<sup>2</sup> or higher (this value was considered equivalent to obesity or abdominal adiposity: waist circumference >102 cm in men and >88 cm in women; rationale used by different authors).<sup>26</sup>

### Resource Use and Cost Model

We considered non health related or indirect costs as those relating to the job productivity losses (job loss and disability days). The system design cost is defined taking into account the characteristics of organizations and the degree of development of the information systems available. The product unit that served as the basis for calculating the outcome (during the study period) was the patient treated and cost expressed in average cost per patient (cost/unit). Different concepts and the economic valuation study are detailed in Table 1 (for 2007). The different rates were obtained from the analytical accounts of the centers except medication and days off work. The requirements were quantified according to the retail price per bottle at the time of prescription. The days of work disability or productivity losses were considered as non-health costs (indirect costs). Cost is measured as the minimum wage (source: National Statistics Institute).<sup>27</sup> Costs will be determined after a 2 year follow-up of patients.

### Confidentiality of Information

We respected the confidentiality of records marked by the Organic Law on Data Protection (15/1999, of 13 December), with the data dissociation. The study was classified by the Spanish Agency for Medicines and Health Products (EPA-OD) and subsequently approved by the Ethics Committee for Clinical Research, University Hospital Germans Trias i Pujol in Badalona.

**Table 1**  
Detail of Costs/Unit and Lost Productivity.

Health care resources and health	Unit costs, €
<i>Doctor visits</i>	
Visit primary care	22.74
Emergency room visit	115.23
Hospitalization (one day)	314.61
Visit to Specialized care	102.36
<i>Additional testing</i>	
Laboratory tests	21.86
Conventional radiology	18.14
Diagnostic/therapeutic tests	36.45
<i>Drug prescription</i>	PVPiva
<i>Productivity job-indirect costs</i>	
Cost per day not worked	54.65

Source of health resources: own analytical accounting. Values expressed in euros. PVP: retail price.

### Statistical Analysis

Statistical analysis was performed with univariate descriptive values of mean, typical/standard deviation (SD) and confidence intervals (CI) of 95%, and with the Kolmogorov–Smirnov test to assess the normal distribution. In the bivariate analysis we not only used ANOVA and chi-square tests, but also Pearson linear correlation. We performed a logistic regression analysis to determine the variables associated with the presence of  $\geq 3$  outbreaks (dependent variable) with procedure *enter* (Statistical Wald). Comparison of outpatient and hospital cost was performed as recommended by Thompson and Barber<sup>28</sup> by analysis of covariance (ANCOVA), with gender, age, BUR, and the Charlson index as covariates (procedure: estimate of marginal means, Bonferroni adjustment). We used SPSSWIN v. 18, establishing a statistical significance of  $P$  values <.05.

### Results

From an initial screening of 96 206 subjects  $\geq 18$  years assigned to the centers, we enrolled 3130 patients with gout. The overall prevalence was 3.3% (95% CI: 2.7%–3.9%). The estimated cumulative incidence rate was 1.1 new cases/1000 inhabitants/year. Regarding study groups, 2142 (68.4%) had 1–2 acute attacks and 988 (31.6%) 3 or more recurrences,  $P < .001$ . The mean  $\pm$  SD age was 55.8  $\pm$  12.2 years and 81.1% were male. Of all patients, 43.6% were hypertensive, 43.1% obese and 40.5% dyslipidemic. The prevalence of MS was 28.8% (95% CI: 27.2%–30.4%).

Table 2 describes the general characteristics of the series and comorbidities associated with gout in patients according to the 2 study groups. Subjects with  $\geq 3$  acute attacks/relapses showed a higher mean age (57.2 vs 55.2 years,  $P < .001$ ), and a higher proportion of males (84.1% vs 79.7%,  $P = .004$ ). These subjects had a higher proportion of comorbidities: BUR (3.1 vs 2.9,  $P < .001$ ) and Charlson index (1.1 vs 0.9,  $P < .001$ ). In the corrected logistic regression model, subjects with  $\geq 3$  acute attacks/relapses were associated with MS (odds ratio [OR]=6.2, 95% CI: 4.6–8.3), obesity (OR=2.1, 95% CI: 1.7–2.5) and hypertension (OR=1.6, 95% CI: 1.3–1.9),  $P < .001$ . MS had a moderate linear correlation with the number of acute attacks ( $r = 0.517$ ), years of disease progression ( $r = 0.321$ ) and initial levels of uric acid ( $r = 0.278$ ),  $P < .001$ . Baseline characteristics of gouty arthropathy are detailed in Table 3, 89.1% of subjects had hyperuricemia and 84.7% of the cases were from PC. Subjects with  $\geq 3$  acute attacks/relapses showed increased monitoring in the rheumatology clinics (3.6% vs 0.8%,  $P < .001$ ). Notably, only 16.9% of patients had a definite diagnosis of gout (displaying monosodium urate crystals under a microscope). Regarding the study groups, in subjects with  $\geq 3$  acute attacks/recurrence was 29.0% vs 11.3%,  $P < .001$ .

The gross prospective and adjusted cost model (up to 24 months) associated with gout according to the study groups is described in Table 4. The total cost of the patients included in the study amounted to 7 million euros, of which 96.9% were direct health costs and 3.1% non-healthcare costs (lost productivity), with an average/€ 2228.6 total unit. For groups, the total costs (health, non-health) of subjects with 1–2 attacks of gout were lower compared with those with  $\geq 3$  attacks (€ 2028.6 vs € 2662.2). The percentage distribution of the cost is 90.8% in PC and 6.2% in specialized care, of these, 23.5% of visits occurred in PC and 57.7% in drug prescription. In the corrected multivariate model, costs were lower in the group with 1–2 attacks, especially total healthcare costs (€ 2101.5 vs € 2517.4,  $P < .001$ ) and in PC (1987.6 € vs € 2331.3,  $P < .001$ ). The average/unit of the total costs per patient was € 2130.6 vs € 2605.4 respectively

**Table 2**  
Baseline Characteristics of the Studied Series.

Groups: Recurrences Number of patients, %	1–2 attacks No.=2142 (68.4%)	≥3 attacks No.=988 (31.6%)	Total No.=3130 (100%)	P
<b>Sociodemographic</b>				
Mean age, years	55.2±13.0	57.2±9.9	55.8±12.2	<.001
Ranges				
18–44 years	23.9%	9.1%	19.2%	
45–64 years	42.9%	62.4%	49.0%	
>64 years	33.3%	28.4%	31.8%	
Gender (male)	79.7%	84.1%	81.1%	.004
<b>General comorbidity</b>				
Average episodes	6.7±3.8	7.6±4.1	7.0±3.9	<.001
Average BUR	2.9±0.6	3.1±0.6	3.0±0.6	<.001
Charlson Index	0.9±0.9	1.1±1.0	0.9±0.9	<.001
<b>Comorbidities</b>				
Hypertension	36.9%	58.3%	43.6%	<.001
Diabetes mellitus	15.5%	31.3%	20.5%	<.001
Dyslipidemia	32.2%	58.6%	40.5%	<.001
Obesity	33.8%	63.5%	43.1%	<.001
Active smokers	17.6%	35.9%	23.4%	<.001
Alcoholism	4.1%	11.4%	6.4%	<.001
Ischemic heart disease	11.6%	23.3%	15.3%	<.001
Cerebrovascular accident	2.9%	8.2%	4.6%	<.001
Renal	1.5%	5.4%	2.7%	<.001
Bronchial asthma	4.4%	4.0%	4.3%	NS
COPD	9.7%	12.6%	10.6%	.015
Neuropathies	0.9%	1.3%	1.1%	NS
depressive syndrome	12.7%	15.2%	13.5%	NS
Malignancies	8.5%	10.7%	9.2%	.040
<b>Metabolic syndrome</b>				
Number of factors	1.5±1.1	2.8±1.2	1.9±1.3	<.001
0	19.3%	4.1%	14.5%	
1	34.3%	10.5%	26.8%	
2	34.6%	19.5%	29.9%	
3 or more	11.8%	65.9%	28.8%	<.001

BUR: resource utilization bands; COPD: chronic obstructive pulmonary disease; NS: not significant; P: statistical significance. Values expressed as percentage or mean±standard deviation.

( $P<.001$ ). In all the cost components results were higher in the group with  $\geq 3$  attacks. During the study period, patients with  $\geq 3$  acute attacks/relapses showed a higher average number of job loss (2.3 vs 1.2,  $P<.006$ ) and days off work (0.6 vs 2.6 days,  $P<.001$ ).

The subgroup of diabetic patients (No.=641, 20.5%, 95% CI: 19.1%–21.9%) compared to non-diabetic ones, had a higher average unit total cost (€ 3124.8 vs € 1997.8,  $P<.001$ ); these patients were older (61.9 vs 54.2 years,  $P=.001$ ), had a higher disease burden (3.1 vs 2.8 BUR,  $P<.001$ ) and frequency of MS (63.2% vs 20.1%,  $P<.001$ ).

## Discussion

The overall results of the study show a prevalence of 3.3% for gout, with a greater male predominance and with 1–2 acute attacks. These features are similar to most of the population-wide studies reviewed.<sup>3,4</sup> Although it should be noted that the natural history of the disease may hinder its diagnosis, especially in primary care and in the emergency department, where the presence of a joint acute attack may mimic other disease entities making for a difficult differential diagnosis.<sup>3,6,8</sup> According to the NCEP,<sup>14</sup> the prevalence of MS was 28.8%, highlighting its association with obesity, hypertension

**Table 3**  
Baseline Characteristics of Gouty Arthropathy.

Groups: Recurrences Number of patients, %	1–2 attacks No.=2142 (68.4%)	≥3 attacks No.=988 (31.6%)	Total No.=3130 (100%)	P
<b>Features</b>				
Progression gout, years	4.4±1.1	5.2±1.4	4.6±1.2	<.001
Average acute attacks	1.4±0.5	4.4±1.5	2.3±1.7	<.001
Presence of hyperuricemia	85.1%	97.9%	89.1%	<.001
<b>Origin of patients</b>				
Primary	88.1%	77.1%	84.7%	
Triage	11.1%	19.2%	13.6%	
Hospital visits	0.8%	3.6%	1.7%	<.001

NS: not significant; P: statistical significance.

Values expressed as percentage or mean±standard deviation.

Distribution of the number of attacks/acute: 1 (No.=1315, 42.0%), 2 (No.=827, 26.4%), 3 (No.=325, 10.4%), 4 (No.=292, 9.3%), 5 (No.=184, 5.9%), 6 (No.=100, 3.2%) 7 (No.=54; 1.7%), 8 (No.=15, 0.5%),  $\geq 9$  (No.=18, 0.6%).

Hyperuricemia is obtained from the first determination of uric acid acute attack.

**Table 4**  
Model of Gross and Corrected Costs.

Groups of arthropathy Number of patients, %	Use, %	PU	1–2 attacks No.=2142 (68.4%)	Use, %	PU	≥3 attacks No.=988 (31.6%)	Use, %	PU	Total No.=3130 (100%)	P <sup>a</sup>	Total cost	%
<b>Cost model uncorrected</b>												
<i>Healthcare costs</i>			1993.6±1538.7			2522.4±1773.8			2160.5±1634.9	<.001	6 762 332.1	96.9%
<i>Costs in primary care</i>			1881.3±1390.4			2328.6±1628.0			2022.5±1484.0	<.001	6 330 381.0	90.8%
Doctor visits	100.0%	22.0	499±383.9	100.0%	25.3	576.7±374.6	100.0%	23.0	523.7±382.6	<.001	1 639 281.1	23.5%
Laboratory tests	95.2%	6.0	130.3±92.6	97.9%	7.3	160.5±91.2	96.1%	6.4	139.8±93.2	<.001	437 571.6	6.3%
Conventional radiology	81.7%	2.1	38.6±38.7	88.8%	2.5	46.1±41.5	83.9%	2.3	41.0±39.8	<.001	128 267.9	1.8%
Other tests	43.1%	0.8	29.2±47.3	55.4%	1.1	39.5±52.5	47.0%	0.9	32.5±49.2	<.001	101 586.2	1.5%
Drug prescription	100.0%		1183.9±1166.4	100.0%		1505.9±1421.8	100.0%		1285.5±1261.3	<.001	4 023 674.1	57.7%
<i>Specialized care costs</i>			112.3±501.8			193.8±545.0			138.0±517.1	<.001	431 951.2	6.2%
Doctor visits	8.8%	0.5	53.9±186.2	20.6%	1.0	97.4±249.7	13.2%	0.7	67.6±209.2	<.001	211 578.1	3.0%
Days in hospital	1.1%	0	42.9±425.6	6.3%	0.3	81.2±436.6	3.1%	0.2	55.0±429.4	.020	172 091.7	2.5%
Emergency	11.0%	0	15.5±49.2	11.6%	0	15.2±44.2	11.2%	0.1	15.4±47.6	NS	48 281.4	0.7%
<i>Nonhealth costs</i>			35.1±550.0	17.3%	2.6	139.8±1116.2	9.8%	1.3	68.1±775.7	<.001	213 189.6	3.1%
<i>Total costs (health/non-health)</i>			2028.6±1661.8			2662.2±2143.1			2228.6±1850.7	<.001	6 975 521.8	100.0%
									<i>Difference</i>			
<i>Healthcare costs</i>			2101.5			2517.4			–415.9	<.001		
95% CI			2024.1–2179.1			2391.2–2643.5						
<i>Costs in primary care</i>			1987.6			2331.3			–343.7	<.001		
95% CI			1917.5–2057.6			2217.3–2445.3						
<i>Specialized care costs</i>			113.9			186.2			–72.3	.006		
95% CI			86.9–141.1			141.9–230.1						
<i>Nonhealth costs</i>			29.1			88.1			9.	.046		
95% CI			11.9–69.8			21.8–154.2						
<i>Total costs (health/non-health)</i>			2130.6			2605.4			–474.8	<.001		
95% CI			2041.18–2220.08			2459.9–2750.9						

CI: confidence interval; NS: not significant; P: statistical significance between the cost of the 2 study groups. Values expressed as percentage or mean±standard deviation.

<sup>a</sup> ANCOVA model: each F-test contrasts the simple effect of the presence of the dose combination in each of the remaining effects shown. These contrasts are based on pair comparisons, linearly independent, among the estimated marginal means. Covariates: age, BUR and Charlson index. Fixed component: gender. Use: percentage of resource use among all patients. PU: average/unit of resource use. Nonhealth costs refer to the days of lost work productivity.

and high baseline levels of uric acid. Our results are similar to data from other studies reviewed.<sup>7,8,11–13</sup> It is worth considering that in our country the prevalence of MS and its association with gout may be higher. Some authors put the figures at around 50% in patients over 60% and 35% in patients with gout in the general population.<sup>29</sup>

In the study, the average/unit cost was € 2228.6. The average corrected model/unit total costs per patient was € 2130.6 (1–2 attacks) vs € 2605.4 ( $\geq 3$  attacks). In all components result costs were higher in the group with  $\geq 3$  attacks and the subgroup of diabetic patients. In this aspect, Brook et al.,<sup>21</sup> demonstrated that the total annual cost in a cohort of employees with gout was \$ 6870, two times higher than patients without gout, noting that only 1% of employees with gout generated the 20% of the costs. Wu et al.,<sup>18</sup> in an excellent study done in elderly patients, related the serum uric acid levels with the cost of patients with gout as being \$ 2555. In the study by Mould-Quevedo et al.,<sup>19</sup> on the main inflammatory rheumatic diseases from the patient's perspective in Mexico, the cost/year was \$ 1006, mostly in outpatient costs. Our results are in line with those reported by Wu et al.,<sup>18</sup> where the methodology was similar to that described in this paper, even when bearing in mind that their patients were older and probably with greater comorbidity. The other two studies mentioned previously (Wu et al.<sup>18</sup> and Mould-Quevedo et al.<sup>19</sup>) are difficult to compare because they are made with older patients and also use different methodologies. All studies are coincident on the weight of the ambulatory costs. In our study, 96.9% were direct health costs and the increased costs were due to follow-up visits and medication. In this regard, increased monitoring of these patients in primary care could reduce costs related to the disease, although undoubtedly the associated morbidity, lack of compliance and possible predisposing factors may affect the use of resources and the cost of these<sup>30</sup> patients.

It is important to note the scarce costs related to lost productivity (sick leave) generated by gout. One possible explanation is that we used a conservative information source (the minimum wage instead of average wage cost, which already in itself is a limitation of the study); it is also possible that temporary job loss was seen (early treatment or decompensation) and not registered by the insurers. The available evidence in this area regarding costs would be consistent with Ferraz<sup>20</sup> and Joish,<sup>31</sup> who show that patients with acute attacks of gouty arthritis lose an average of 3–5 days of work per year, causing significant economic losses to labor productivity that in some cases is a little less quantified. Although, in general, patients with 1–2 attacks are younger and therefore have a lower frequency than most of the associated disease, it may be this which determines the lowest cost of the disease in these patients.

Possible study limitations affect the categorization of the disease, the potential bias of patient classification (due to excess) and operating costs attributable to the information system developed. Therefore, in this paper we show the limitations of retrospective studies, such as underreported data or the possible variability of professionals and patients due to the observational design. Furthermore, the number of acute attacks treated may be compromised because of possible self-medication by patients. The study details the use of resources and the costs associated with gouty arthritis patients in a clinical practice situation. However, note that without adequate standardization of methodologies not only in terms of patient characteristics, but also the number and size of the variables studied, the results should be interpreted with caution forcing us to be cautious regarding the external results validity.

Future research studies call for the availability of cost/effectiveness and efficiency of diagnosis and treatment, in addition to replicating the study in other healthcare organizations. Moreover, the inflammatory property of crystals is not yet fully elucidated and may be linked to the ability to bind immunoglobulins, complement and lipids. It takes long-term clinical trials to test the

hypothesis that uric acid lowering therapy can reduce cardiovascular risk in these patients. No guidelines have been established, derived from clinical trials, for the treatment of acute joint inflammation. The success of interventions for patients with chronic diseases such as gout should be based on multidisciplinary teams that promote effective care in which patients are highly engaged in their own care. Undoubtedly, the diagnosis and treatment of gout should require greater intervention strategy and be monitored by health professionals. In conclusion, gout is associated with substantial morbidity, MS and healthcare resource consumption. This study provides useful data on the cost of gout in Spain. The greatest costs are owed to the follow up of ambulatory patients.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this investigation.

**Confidentiality of Data.** The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

**Right to privacy and informed consent.** The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

## Authorship

A. Sicras and R. Navarro conducted the literature search, extracted the data, performed the analysis and interpretation of the initial results. All authors contributed ideas, interpreted findings and reviewed drafts of the manuscript. All authors approved the final version of the article. A. Sicras is responsible for the study.

## Conflict of Interest

The authors have no conflict of interest to make.

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## References

- Lai SW, Liu CS, Lin T, Lin CC, Lai HC, Liao KF. Prevalence of gout and hyperuricemia in Taiwan: a hospital-based, cross-sectional study. *South Med J.* 2009;102:772–3.
- So A. Epidemiology: gout-bad for the heart as well as the joint. *Nat Rev Rheumatol.* 2010;6:386–7.
- Hamburger M, Baraf HS, Adamson 3rd TC, Basile J, Bass L, Cole B, et al. European League Against Rheumatism. 2011 Recommendations for the diagnosis and management of gout and hyperuricemia. *Postgrad Med.* 2011;123:3–36.
- Wallace SL, Robinson H, Masi AT, Decker JL, McCarty DJ, Yu TF. Preliminary criteria for the classification of the acute arthritis of primary gout. *Arthritis Rheum.* 1977;20:895–900.
- Zhang W, Doherty M, Bardin T, Pacual E, Barskova V, Conaghan P, et al. EULAR Evidence based recommendations for gout Part II. Management. Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCSIT). *Ann Rheum Dis.* 2006;65:1312–24.
- Janssens HJ, Janssen M, van de Lisdonk EH, Fransen J, van Riel PL, van Weel C. Limited validity of the American College of Rheumatology criteria for classifying patients with gout in primary care. *Ann Rheum Dis.* 2010;69:1255–6.
- Perez-Ruiz F, Pascual E, Carmona L, Gonzalez-Gay MA, De Miguel E, Ureña I, et al. Diagnosis of gout in the rheumatology, hospital-based setting lies far from that recommended: results from the GEMA (Gout Evaluation of Management) Study. *Arthritis Rheum.* 2007;56:S639.

8. Schumacher Jr HR, Edwards LN, Perez-Ruiz F, Becker M, Chen LX, Furst DE, et al., OMERACT 7 Special Interest Group. Outcome measures for acute and chronic gout. *J Rheumatol*. 2005;32:2452–5.
9. Ferroni P, Basili S, Paoletti V, Davi G. Endothelial dysfunction and oxidative stress in arterial hypertension. *Nutr Metab Cardiovasc Dis*. 2006;16:222–33.
10. Shah A, Keenan RT. Gout, hyperuricemia, and the risk of cardiovascular disease: cause and effect? *Curr Rheumatol Rep*. 2010;12:118–24.
11. Hjortnaes J, Algra A, Olijhoek J, Huisman M, Jacobs J, van der Graaf Y, et al. Serum uric acid levels and risk for vascular diseases in patients with metabolic syndrome. *J Rheumatol*. 2007;34:1882–7.
12. Choi HK, Ford ES, Li C, Curhan G. Prevalence of the metabolic syndrome in patients with gout: the Third National Health and Nutrition Examination Survey. *Arthritis Rheum*. 2007;57:109–15.
13. Onat A, Uyarel H, Hergenç G, Karabulut A, Albayrak S, Sari I, et al. Serum uric acid is a determinant of metabolic syndrome in a population-based study. *Am J Hypertens*. 2006;19:1055–62.
14. National Cholesterol Education Program-Expert Panel on Detection, Evaluation, Treatment on High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Adult Treatment Panel III final report. *Circulation*. 2002;106:3143–421.
15. Singh JA. Health care costs in gout: what are these emerging data telling us? *J Clin Rheumatol*. 2009;15:1–2.
16. Wu EQ, Patel PA, Yu AP, Mody RR, Cahill KE, Tang J, et al. Disease-related and all-cause health care costs of elderly patients with gout. *J Manag Care Pharm*. 2008;14:164–75.
17. Kim KY, Ralph Schumacher H, Hunsche E, Wertheimer AI, Kong SX. A literature review of the epidemiology and treatment of acute gout. *Clin Ther*. 2003;25:1593–617.
18. Wu EQ, Patel PA, Mody RR, Yu AP, Cahill KE, Tang J, et al. Frequency, risk, and cost of gout-related episodes among the elderly: does serum uric acid level matter? *J Rheumatol*. 2009;36:1032–40.
19. Mould-Quevedo J, Peláez-Ballestas I, Vázquez-Mellado J, Terán-Estrada L, Esquivel-Valerio J, Ventura-Ríos L, et al. El costo de las principales enfermedades reumáticas inflamatorias desde la perspectiva del paciente en México. *Gac Méd Méx*. 2008;144:225–31.
20. Ferraz MB, O'Brien B. A cost effectiveness analysis of urate lowering drugs in nontophaceous recurrent gouty arthritis. *J Rheumatol*. 1995;22: 908–14.
21. Brook RA, Kleinman NL, Patel PA, Melkonian AK, Brizee TJ, Smeeding JE, et al. The economic burden of gout on an employed population. *Curr Med Res Opin*. 2006;22:1381–9.
22. Lamberts H, Wood M, Hofmans-Okkes IM, editors. *The International Classification of Primary Care in the European Community. With a multi-language layer*. Oxford: Oxford University Press; 1993.
23. Ministerio de Sanidad, Servicios Sociales e Igualdad. Portal estadístico del SNS 2010. Clasificación Internacional de Enfermedades, novena revisión, Modificación Clínica (CIE-9-MC). Available from: <http://www.msc.es/estadEstudios/estadisticas/normalizacion/clasifEnferm/home.htm> [accessed December 2011].
24. Charlson ME, Pompei P, Ales KL, Mackenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–83.
25. Weiner JP, Starfield BH, Steinwachs DM, Mumford LM. Development and application of a population-oriented measure of ambulatory care case-mix. *Med Care*. 1991;29:452–72.
26. Sattar N, Gaw A, Scherbakova O, Ford I, O'Reilly DS, Haffner SM, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation*. 2003;108:414–9.
27. Instituto Nacional de Estadística 2010. Encuesta de costes laborales del año 2010. Available from: <http://www.ine.es/infoine> [accessed December 2011].
28. Thompson SG, Barber JA. How should cost data in pragmatic randomised trials be analysed? *BMJ*. 2000;320:1197–200.
29. Fraile JM, García Puig J. Síndrome metabólico, hiperuricemia y gota. *Rev Esp Obes*. 2009;7:85–90.
30. Halpern R, Mody RR, Fuldeore MJ, Patel PA, Mikuls TR. Impact of noncompliance with urate-lowering drug on serum urate and gout-related healthcare costs: administrative claims analysis. *Curr Med Res Opin*. 2009;25: 1711–9.
31. Joish VN, Donaldson G, Stockdale W, Oderda GM, Crawley J, Sasane R, et al. The economic impact of GERD and PUD: examination of direct and indirect costs using a large integrated employer claims database. *Curr Med Res Opin*. 2005;21:535–44.