## **PHARMACOECONOMICS**

# Healthcare costs associated with elderly chronic pain patients in primary care

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#### Abstract

Objective This study aimed to estimate the total healthcare costs associated with elderly chronic pain (CP) patients, define cost-related factors in this population, and examine cost evolution over two years.

Method This is an ancillary study from the CP S.AGE subcohort, including non-institutionalized patients aged over 65 suffering from CP. 1190, 1108, 1042, and 950 patients were reviewed with available healthcare data at follow-up visits at 6, 12, 18, and 24 months, respectively. Healthcare components included medical and paramedical visits, medication prescription, and hospitalization.

Result The mean total cost in the first semester was estimated at &2548 $\pm\&$ 885 per patient. Hospitalization represented the largest cost component (50 %) followed by paramedical care (24 %), medications (21 %), and medical visits (5 %). Significant cost-associated factors were comorbidity (OR 1.49, 95 % CI 1.35–1.64), dependency

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in daily activities (OR 1.85, 95 % CI 1.39–2.47), probable depression (OR 1.71, 95 % CI 1.09–2.69), permanent pain (OR 1.48, 95 % CI 1.18–1.86), neuropathic pain (OR 1.94, 95 % CI 1.38–2.73), living alone (OR 1.45, 95 % CI 1.16–1.82), chronic back pain (OR 1.35, 95 % CI 1.07–1.71), and vertebral fracture/compression (OR 1.47, 95 % CI 1.08–2.01). Healthcare costs increased significantly by 48 % (p<0.0001) during follow-up namely due to hospitalizations. Elevated costs were associated with a higher risk of future hospitalization (OR 1.95, CI 95 % 1.33–2.87).

Conclusion Healthcare costs increased rapidly over time, largely due to hospitalization. Prevention strategies to limit hospitalizations in elderly appear to be the most useful in order to achieve cost savings in the future.

**Keywords** Healthcare · Cost · Chronic pain · Elderly patients

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## Introduction

Chronic pain (CP) is a major public health issue as it affects physical and mental health, limits functional status, and adversely impacts quality of life [1]. It is also thought to be one of the most common reasons for medical consultations, medication use, and hospital admissions, in addition to other healthcare services [2–4]. CP-attributable healthcare costs are reported to exceed those of cardiovascular disease, diabetes, and cancer [1]. The socioeconomic costs of CP are well established for the general population. In a recent study conducted in the USA, Gaskin et al. found that the total costs associated with CP ranged from \$560 to \$635 billion in 2010. He also reported that incremental healthcare costs for pain range from \$261 to \$300 billion annually [1]. In Sweden and Ireland, the costs associated with CP reached €32 and €5.34 billion nationally in 2008 [5, 6]. In France, few studies estimate financial costs in CP populations. They are also limited to specific pain conditions such as back pain, osteoarthritis, migraine, fibromyalgia, or rheumatoid arthritis [7–11]. Depont et al. reported that the total direct cost for chronic low back pain (CLBP) was over €2.7 billion in 2007 among a patient population aged between 35 and 64 years [7]. Bertin et al. reported that the total annual cost of osteoarthritis in community patients is €3.4 billion [11].

Although older people are at higher risk of pain-related diagnosis, little is known about healthcare use and costs among the elderly. Therefore, it is important to identify cost-associated factors in the CP population since the aging of the western population will likely result in significant increase in medical costs in the future [3].

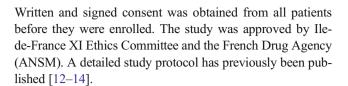
The aim of this S.AGE CP subcohort ancillary study was to describe the total financial costs among elderly CP patients, identify factors associated with healthcare costs, and examine the risk of subsequent clinical events in the future.

## Methods

The S.AGE cohort [12] is a French study of non-institutionalized patients over 65 years old. This cohort (n= 3434) is composed of three sub-cohorts of patients suffering from either atrial fibrillation (n=1072), type 2 diabetes mellitus (n=983), or chronic pain (n=1379) [12–14].

From 51,179 general practitioners (GPs) contacted all over France, 760 GPs accepted to participate in this cohort and then were randomized into one of the three S.AGE sub-cohorts. Patients were recruited between June 2009 and September 2011, and the follow-up of patients was planned for three years with six-monthly visits.

GPs entered the patients' data into electronic case report forms (e-CRF). All prescriptions were recorded using the Anatomical Therapeutic Chemical (ATC) classification code.



## Study population

One thousand three hundred seventy-nine patients, meeting the following inclusion criteria, were enrolled in the CP subcohort: aged 65 or over and living in France, able to understand the objective of the study, registered with a social security scheme or equivalent insurer, presenting pain lasting more than 3 months and requiring treatment, and signing the informed consent form. Patients could not participate if they were nursing home residents and could not be monitored after inclusion or had a short life expectancy. CP was defined as pain that motivated visits to a general practitioner (GP), had been developing for more than 3 months, and for which the GP prescribed a treatment. The primary objective of CP subcohort was to describe the pharmacotherapeutic management of patients. Estimation of the resources' consumption according to the medical and nonmedical management constitutes an ancillary objective of this cohort.

In the CP subcohort, 1190, 1108, 1042, and 950 patients were reviewed with the available healthcare data at the successive six-monthly follow-up visits. The reasons why patients did not attend the follow-up visits were as follows: death, removal, institutionalization, withdrawal of consent, withdrawal from the study because their GP stopped participating, and unknown (Supplementary Figure 1).

## Baseline study variables

Socio-demographic data included the following: gender, age, educational level, living area and situation, and professional activity.

Pain variables are as follows: type (mechanical, inflammatory, or neuropathic), chronology (permanent or intermittent), and severity (scored visual analogue scale (VAS)). Pain severity was categorized into none or minimal (0–3), moderate [4–6], and severe [7–10].

The impact of pain on mood, sleep, walking, relationships with others, and daily activities was assessed by each GP on a 0- to 4-point scale. A total pain impact score was then calculated (addition of the 5 scores), varying from 0 to 20 (0 indicating no impact of pain on the five items and 20 indicating major impact) with good internal consistency (Cronbach's alpha coefficient=0.74). Physical function was assessed using the activities of daily living (ADL) scale [15]. A score of 6 indicates that the patient is independent while 0 indicates that the patient is dependent. A simplified four-item instrumental activities of daily living (IADL) scale was also used [16]. A



score of 4 indicates that the patient is independent while 0 indicates that the patient is dependent. The presence of depressive symptoms was assessed using the 15-item geriatric depression scale (GDS) [17], with a score of  $\geq$ 5 indicating some depressive symptoms divided into two categories: possible ([5–10]) and probable ( $\geq$ 10) clinical depression. Comorbidities included the following: arterial disease, atrial fibrillation, high blood pressure, T2DM, heart failure, central nervous system disease, cancer, and obesity.

#### Healthcare data

Four main healthcare components were recorded between each successive six-monthly visit: paramedical care visits, medical visits, medication prescriptions, and number of hospitalization days. We estimated the total healthcare costs, whether related or unrelated to CP.

(a) Paramedical care visits involving assistance at home (washing, eating, going to the toilet, dressing, etc.), nursing at home or in nurses' offices, physiotherapy, and pedicure care visits were recorded by each GP. (b) The number of medical visits either to GPs or specialists was assessed by each GP every 6 months. (c) All medications (ATC classification) prescribed by the GPs at each six-monthly visit were taken into account except over-the-counter medications. (d) Hospitalizations were categorized as day or inpatient, and the admission departments were divided into three groups: general medicine, intensive care, and surgery.

Costs were calculated using a societal perspective, i.e., independently of the payer. In France, the cost of paramedical and medical visits, drugs, and hospitalization are fixed either nationally or regionally. Therefore, we took into account the official total cost, whatever the payer was (patient, national healthcare system, region, or additional private health insurance). Costs were calculated for each patient by multiplying the number of visits, medications, and days of hospitalization by unit costs. To convert euros into dollars, multiply by 1.35 [18].

The cost of each medication was based on the selling price provided from the national drug registry [19], which is unique in France. The cost of each pill (or injection or patch) was multiplied by the number of units taken each day.

A home assistance visit costs  $\in$ 30, a nursing at home visit costs  $\in$ 14.95, a physiotherapist visit costs  $\in$ 22.26, a pedicure visit costs  $\in$ 27, a GP visit costs  $\in$ 23, and a specialist MD visit costs  $\in$ 30 [20].

Average daily hospitalization costs of stay were obtained from Assistance-Publique Hôpitaux de Paris (AP-HP), representing forty teaching hospitals in and around Paris. For each patient, its cost was obtained by multiplying the average daily cost of stay in each department by the number of days spent in the department in the last 6 months.

Daily average inpatient hospital costs of stay in general medicine, geriatric, cardiology, neurology, other specialties (oncology, endocrinology, hematology, gastroenterology, infectious disease, nephrology, pulmonology, rheumatology, psychiatry), orthopedic surgery, other surgery (visceral surgery, neurosurgery, gynecology, ophthalmology, otolaryngology), and neurovascular departments were  $\epsilon$ 428,  $\epsilon$ 302,  $\epsilon$ 583,  $\epsilon$ 518,  $\epsilon$ 537,  $\epsilon$ 651,  $\epsilon$ 855, and  $\epsilon$ 740, respectively, and  $\epsilon$ 922 in intensive care units. An average day hospitalization cost was considered to be  $\epsilon$ 870, which is the mean of day hospitalization costs in the aforementioned admission departments.

## Statistical analysis

Categorical variables were presented as frequencies and percentages. Group differences were tested using the chi-square test. Continuous variables were presented as mean±standard deviation. Group differences were tested using ANOVA and Kruskal-Wallis tests for normally and non-normally distributed variables, respectively. The dependent variable was healthcare cost, which was ranked into three categories (low, intermediate, and elevated). The identification of the independent cost-associated factors in the first semester was performed through the two following steps: (1) in the univariate analyses, the association of all study variables with the cost variable was analyzed and only variables associated to cost at  $p \le 0.20$  were considered to be entered in the multivariate analyses. (2) In the multivariate analyses, variables with  $p \le 0.20$ were introduced in the multiple logistic regression model with a background selection procedure at a threshold of 0.05 and resulting factors with  $p \le 0.05$  were considered as independent cost-associated factors.

The predictive power of the model was described using the area under the receiver-operating characteristics (ROC) curve (AUC). The p value of the changing healthcare use and costs was calculated using repeated measures ANOVA which accounts for a potential heteroskedasticity using a command SAS: "proc mixed" with "Repeated" function. Correlation between observation times was modeled with a compound symmetry structure (type = cs) which assumes one overall variance and one common pairwise covariance. Due to a significant percentage of missing values in the multivariate model, mainly related to GDS, the latter was imputed according to the SAS multiple imputation procedure (PROC MI). The association between healthcare costs in the first semester and the occurrence of clinical events between the 6th and 24th months was performed using logistic regression after adjusting for the identified independent cost-associated variables. Statistical analyses were conducted using SAS (Statistical Analysis System, version 9.3).



#### Results

## **Baseline patient characteristics**

From the 1379 patients included in the CP subcohort, 1190 underwent complete cost evaluation during the first semester (between baseline and the sixth month of follow-up). Table 1 shows the characteristics of these 1190 patients, who had a mean age of 78. Most (71 %) were females, 20 % had a high level of education, and nearly 43 % lived alone at home. The majority (89 %) experienced mechanical pain (19 % experienced both mechanical and inflammatory pain), and 57.5 % presented permanent CP with 73 % of moderate to severe pain. Almost a quarter were considered dependent by the ADL scale, and nearly half had depressive symptoms (GDS ≥5). The CP diagnosis included the following: limb osteoarthritis (66 %), common back pain (60 %), vertebral fracture/ compression (16 %), inflammatory arthropathy (12 %), peripheral neuropathy (10 %), migraine (3 %), post-herpetic (1.4 %), and psychogenic pain (4 %). The 1190 selected patients did not differ significantly from the 189 excluded patients based on the criteria presented in Table 1 (supplementary table 1).

#### Total healthcare use and costs in the first semester

The mean number of paramedical care visits per patient was  $26.4\pm52.4$  with the majority of visits for home assistance followed by nursing visits. The mean number of medical visits per patient was  $5.1\pm4.1$  with more visits to GPs than to specialists. The mean number of medications taken per patient was  $5.0\pm3.3$  with the highest number for the cardiovascular system (ATC C) followed by the nervous system (ATC N).

The mean number of days spent in hospital per patient for any type of hospitalization was  $1.9\pm12.9$  days  $(0.5\pm5.1$  for day hospitalization and  $1.4\pm9.7$  for inpatient hospitalization) (supplementary table 2).

Most costs resulted from hospitalization, with a mean cost per patient of  $\[ \in \] 1270\pm \[ \in \] 8672$  (median=0, interquartile range (IQR)=0), followed by paramedical care  $\[ \in \] 624\pm \[ \in \] 1218$  (median=81, IQR=674), medications  $\[ \in \] 529\pm \[ \in \] 730$  (median=381, IQR=398), and medical visits  $\[ \in \] 125\pm \[ \in \] 100$  (median=115, IQR=108) (Table 2).

## Cost-related factors in the first semester

Table 1 shows 17 factors associated with total healthcare costs with a p value of <0.20. In the ordinal multiple logistic regression model, eight of these factors remained independently associated with costs (Table 3): comorbidity, dependence defined by the IADL and ADL scales, depression, permanent pain, neuropathic pain, living alone, CBP, and vertebral fracture/compression (AUC=0.72).



#### Evolution of healthcare use and costs

From baseline to the 24th month, the mean numbers of all four healthcare components increased significantly (supplementary table 2). During semesters 1, 2, 3, and 4, the mean healthcare cost per patient was  $\[ \] 2548\pm \[ \] 8885$  (median=858, IQR=1361),  $\[ \] 2848\pm \[ \] 67723$  (median=941, IQR=1535),  $\[ \] 3176\pm \[ \] 611$ ,949 (median=1011, IQR=1741), and  $\[ \] 63761\pm \[ \] 611$ ,977 (median=1059, IQR=1692), respectively. The mean of all four cost components increased significantly during the follow-up period with a 7, 14, 26, and 78 % rise for paramedical care, medical visit, medication, and hospitalization costs, respectively (Table 2).

Of the 950 patients seen at every six-monthly visit, the individual mean number of comorbidities and functional disability increased significantly while pain severity decreased significantly over the same period (Supplementary online Table 3).

### Healthcare costs and risk of future clinical events

The association between healthcare costs in the first semester and the risk of several clinical events (hospitalization, death, institutionalization, arterial disease, or cancer) during the next 18 months was analyzed in supplementary table 4. Elevated healthcare costs in the first semester were associated with 1.95, CI 95 %1.33–2.87 higher risks of hospitalization at 2 years of follow-up after adjusting for the independent costrelated factors obtained in Table 3. However, no significant association was found between increased costs in the first semester and the occurrence of death, institutionalization, arterial disease, or cancer at 2 years.

## **Discussion**

This is one of the few studies aiming to estimate the financial cost of healthcare over time among non-institutionalized elderly CP patients, irrespective of the cause. We found that total healthcare costs averaged €2548 per patient in the first semester following inclusion and increased substantially throughout the follow-up period.

Many healthcare cost studies have been conducted in France using a societal perspective in general populations with specific pain conditions. In a retrospective study conducted in primary care in France, including 796 adults, Depont et al. found that the mean six-monthly cost attributed to CLBP per patient was €716 [7]. This was lower than ours for two possible reasons: our study took into account total healthcare costs, whether related or unrelated to CP, while Depont et al. considered only the costs attributable to CLBP. Furthermore, patients in the Depont et al. study were younger (53 versus 78 here) and had fewer comorbidities. In another French study,

Table 1 Patients' characteristics according to total healthcare costs in the first semester

	Total, <i>n</i> =1190, <i>n</i> (%)	Low cost, median 326, IQR <sup>a</sup> 214, min–max (0–548) <i>n</i> =396, <i>n</i> (%)	Intermediate cost, median 857, IQR <sup>a</sup> 356, min–max (549–1341) <i>n</i> =397, <i>n</i> (%)	Elevated cost, median 3419, IQR <sup>a</sup> 4105, min–max (1344–212,223) <i>n</i> =397, <i>n</i> (%)	p
Female versus male	848 (71.3)	260 (30.7)	286 (33.7)	302 (35.6)	0.005
Age	$78.0 \pm 6.2^{b}$	$77.1\pm6.1^{b}$	$77.8 \pm 5.9^{b}$	$79.2 \pm 6.5^{b}$	< 0.0001
High level of education (vs. low) <sup>c</sup>	237 (20.1)	85 (35.9)	91 (38.4)	61 (25.7)	0.02
Living alone (vs. with someone)	511 (42.9)	143 (27.9)	174 (34.1)	194 (37.9)	0.001
Urban (vs. no) Professional activity <sup>d</sup>	688 (57.8)	213 (30.9)	235 (34.2)	240 (34.9)	0.13 0.47
Ongoing	18 (1.5)	9 (50.0)	6 (33.3)	3 (16.7)	
stopped	914 (77.1)	298 (32.6)	305 (33.4)	311 (34.0)	
Never worked	254 (21.4)	88 (34.6)	84 (33.1)	82 (32.3)	
Mechanical pain (vs. none) <sup>d</sup>	1053 (88.8)	344 (32.7)	354 (33.6)	355 (33.7)	0.41
Inflammatory pain (vs. none) <sup>d</sup>	309 (26.1)	108 (34.9)	115 (37.2)	86 (27.9)	0.05
Neuropathic pain (vs. none) <sup>d</sup>	164 (13.8)	34 (20.7)	52 (31.7)	78 (47.6)	< 0.0001
Permanent pain (vs. Intermittent) <sup>e</sup> Pain severity <sup>f</sup>	680 (57.5)	184 (27.1)	235 (34.6)	261 (38.4)	< 0.0001
[0–3]	327 (27.6)	134 (41.0)	111 (33.9)	82 (25.1)	< 0.0001
[4–6]	663 (55.9)	219 (33.0)	218 (32.9)	226 (34.1)	
[7–10]	197 (16.6)	43 (21.8)	67 (34.0)	87 (44.2)	
Pain impact score <sup>g</sup>	$8.9 \pm 3.5^{b}$	$8.3 \pm 3.5^{b}$	$9.0 \pm 3.4^{b}$	$9.7 \pm 3.4^{b}$	< 0.0001
Diagnostic of chronic pain					
Limb osteoarthritis h	782 (66.1)	249 (31.8)	266 (34.0)	267 (34.1)	0.39
Common back pain i	717 (60.4)	208 (29.0)	261 (36.4)	248 (34.6)	0.0004
Vertebral fracture/compression i	197 (16.6)	38 (19.3)	77 (39.1)	82 (41.6)	< 0.0001
Migraine i	31 (2.6)	12 (38.7)	10 (32.3)	9 (29.0)	0.78
Herpes zoster i	16 (1.4)	5 (31.3)	8 (50.0)	3 (18.8)	0.30
Inflammatory arthropathy j	145 (12.2)	43 (29.7)	55 (37.9)	47 (32.4)	0.42
Peripheral neuropathy j	113 (9.5)	18 (15.9)	39 (34.5)	56 (49.6)	< 0.0001
Psychogenic pain i	50 (4.2)	10 (20.0)	16 (32.0)	24 (48.0)	0.05
ADL <sup>k</sup> : <6 (vs. 6)	288 (24.3)	54 (18.8)	73 (25.3)	161 (55.9)	< 0.0001
IADL <sup>1</sup> : <4 (vs. 4)	366 (30.8)	69 (18.9)	102 (27.8)	195 (53.3)	< 0.0001
GDS-15 <sup>m</sup>					
<5	503 (53.5)	209 (41.5)	175 (34.8)	119 (23.7)	< 0.0001
[5–10]	348 (37.0)	85 (24.4)	109 (31.3)	154 (44.3)	
≥10	89 (9.5)	16 (17.9)	33 (37.1)	40 (44.9)	
Number of comorbidities <sup>n</sup>	$1.67 \pm 1.24^{b}$	$1.22 \pm 1.04^{b}$	$1.67 \pm 1.13^{b}$	$2.13\pm1.37^{b}$	< 0.0001

<sup>&</sup>lt;sup>a</sup> Interquartile range

<sup>&</sup>lt;sup>n</sup> Arterial disease, atrial fibrillation, high blood pressure, type 2 diabetes mellitus, heart failure, central nervous system diseases, cancer, obesity (BMI>30) The p value determines if an explicative variable has the same or a different distribution between the three tertiles of cost



 $<sup>^{\</sup>rm b}$  Mean $\pm$ SD

<sup>&</sup>lt;sup>c</sup> 7 missing values (MV)

<sup>&</sup>lt;sup>d</sup> 4 MV

e 7 MV

<sup>&</sup>lt;sup>f</sup>No or minimal pain (0-3), moderate pain (4-6), severe pain (7-10), 3 MV

<sup>&</sup>lt;sup>g</sup> Impact of pain on mood, walking, sleep, daily activities, relationships with others, 1 MV

<sup>&</sup>lt;sup>h</sup> 6 MV

i 3 MV

<sup>&</sup>lt;sup>j</sup> 2 MV

<sup>&</sup>lt;sup>k</sup> Activities of daily living scale (0-6 dependence, 6 independence), 3 MV

<sup>&</sup>lt;sup>1</sup>Instrumental activities of daily living scale (0-4 dependence, 4 independence), 2 MV

<sup>&</sup>lt;sup>m</sup> Geriatric depression scale: normal <5, possible (5–10), and probable clinical depression ≥10, 250 MV

Table 2 Evolution of healthcare costs during the follow-up period

	Baseline to 6 months follow-up (semester 1)	6th to 12th month follow-up (semester 2)	12th to 18th month follow-up (semester 3)	18th to 24th month follow-up (semester 4)	p
Paramedical cost	624±1218 (0-8065)	633±1184 (0–7286)	638±1220 (0–7662)	669±1286 (0–9155)	<0.0001
	81 (674)	89 (711)	84 (671)	89 (697)	
Medical cost	125±100 (0-868)	137±103 (0–976)	135±104 (0–950)	143±109 (0–912)	< 0.0001
	115 (108)	122 (106)	115 (106)	122 (115)	
Hospitalization cost	1270±8672 (0–210,870)	1515±7518 (0–96,600)	1741±11,664 (0–223,995)	2259±11,537 (0–156,408)	< 0.0001
	0 (0)	0 (0)	0 (0)	0 (0)	
Drug cost	529±730 (0–9099)	622±925 (0–11,179)	645±981 (0–13,667)	667±953 (0-13,667)	< 0.0001
	381 (398)	421 (429)	451 (455)	471 (487)	
Total cost	2548±8885 (0–212,223)	2848±7723 (7–104,236)	3176±11,949 (29–226,853)	3761±11,977 (0–161,977)	< 0.0001
	858 (1361)	941 (1535)	1011 (1741)	1059 (1692)	

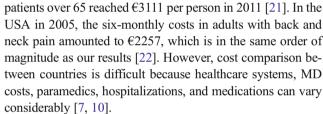
Results are presented as mean ±SD, (min-max), median (interquartile range)

Kobelt et al. found considerably higher six-monthly individual costs (€5879) among rheumatoid arthritis (RA) patients with a mean age of 62, which was explained by the authors to be related to the high disease severity and high proportion of patients receiving expensive biological treatment [9]. Bertin et al. found that the six-monthly cost of medications and medical consultations for osteoarthritis reached €438 [11]. In Germany, Huscher at al. reported that six-monthly costs for RA

 $\begin{tabular}{ll} \textbf{Table 3} & Factors independently associated with total healthcare costs in the first semester \end{tabular}$ 

Final $n$ of the model=1164	OR	95 % CI	p value*
Number of comorbidities <sup>a</sup>	1.49	1.35–1.64	< 0.0001
IADL (<4 vs. 4) <sup>b</sup>	1.67	1.27-2.19	< 0.0001
GDS-15 <sup>c</sup>			< 0.0001
Possible depression	1.63	1.27-2.08	
Probable depression	1.71	1.09-2.69	
ADL (<6 vs. 6) <sup>d</sup>	1.85	1.39-2.47	< 0.0001
Permanent (vs. intermittent)	1.48	1.18-1.86	0.0001
Neuropathic pain (vs. none)	1.94	1.38-2.73	0.001
Living alone (vs. none)	1.45	1.16-1.82	0.001
Common back pain (vs. none)	1.35	1.07-1.71	0.01
Vertebral fracture/compression (vs. none)	1.47	1.08-2.01	0.01

<sup>&</sup>lt;sup>a</sup> Arterial disease, articular fibrillation, high blood pressure, diabetes, heart failure, central nervous system, cancer, obesity



In this study, the main cost component in the first semester was hospitalization (50 %) followed by paramedical care (24 %). Medication and medical consultation costs accounted for 21 and 5 %, respectively. These findings are consistent with the systematic review of RA patients; Lubeck et al. concluded that hospitalization was the highest component of direct costs followed by medications and physician visits [23]. Numerous additional studies have previously observed that hospitalization ranges from 25 to 62 % of the total cost, mainly depending on the type of disease responsible for the pain and the patient's age [4, 6, 22, 24].

The second aim of this study was to analyze which factors are associated with healthcare costs. In a multivariate analysis, costs were independently associated with the number of comorbidities, dependency, depression, permanent pain, neuropathic pain, living alone, CBP, and vertebral fracture/compression. These results are generally consistent with the determinants identified in previous studies examining healthcare use and costs, remembering that we considered multiple pain conditions in elderly patients while most studies examined just one [2, 25–31].

In this study, healthcare costs increased by 48 % over the follow-up period. This dramatic cost increment was mainly due to an increase in the number of days spent in hospital which costs raised by 78 %. Several studies have found an



<sup>&</sup>lt;sup>b</sup> Instrumental activities of daily living scale (0–4 dependence, 4 independence)

<sup>&</sup>lt;sup>c</sup> Geriatric Depression Scale: normal <5, possible (5–10), and probable depression ≥10 (obtained after imputation)

<sup>&</sup>lt;sup>d</sup> Activities of daily living scale (0–6 dependence, 6 independence)

<sup>\*</sup>Significant when  $p \le 0.05$ 

increase in healthcare costs over time ranging from 47 to 129 % depending on the study period, pain condition, and population age [22, 21, 32–34]. Furthermore, our results revealed that elevated costs in the first semester are associated with an increased risk of hospitalization during the next 18 months. Therefore, healthcare costs and hospitalizations seem to be closely linked. As a consequence, prevention of hospitalization might be one of the most effective interventions to reduce the burden of costs in such elderly patients. A meta-analyses conducted by Fox et al. found that geriatric units were associated with less functional decline, shorter length of hospital stay, and lower cost. Therefore, such units might be useful for our study patients in order to reduce the functional decline, length of stay in hospital, and at last, the costs [35].

This study is one of the few to develop longitudinal cost estimates among elderly CP patients. The societal perspective is considered the most comprehensive and avoids underestimating costs when only considered from a narrower perspective.

Some study limitations should be mentioned as follows: (1) the retrospective method used to collect healthcare data in the last 6 months may underreport the number of healthcare visits. (2) The sample in this study is based on elderly patients consulting primary care physicians and does not represent institutionalized elderly patients, thereby limiting the generalization to all elderly CP patients. (3) Although the data made it possible to examine multiple components of healthcare services, other important aspects of medical care such as over-thecounter medications, medical imaging techniques, biological analysis, or complementary and alternative therapies were not taken into account. (4) The way of calculating hospitalization costs was based on an average daily cost of stay in specific admission departments which does not necessarily represent the cost calculated by the French healthcare system (based on an average cost for a specific disease). (5) Other variables such as patient's belief about pain, treatment, healthcare services, and treatment adherence which have been associated with variations in healthcare use and costs [36] were not assessed and might therefore represent an additional confusion bias. Finally, as we only assessed total healthcare costs, we were unable to define the proportion of costs attributed to CP versus those generated by unrelated coexisting diseases.

## Conclusion

This study highlights high healthcare costs in elderly CP patients, which increased dramatically over 2 years mainly due to hospitalizations. It provides also for GPs a quick and easy

tool for identifying patients at high risk of healthcare costs. For such patients, interventional geriatric units might be very useful to prevent hospitalizations and achieve cost savings in the future.

**Author contributions** Lazkani A: study design, data analysis, and manuscript preparation.

Becquemont L: study design, data analysis, and manuscript preparation.

Delespierre T: study design, data analysis, and manuscript preparation.

Bauduceau B: study design, manuscript revision, and approval of the final version for publication.

Pasquier F: study design, manuscript revision, and approval of the final version for publication.

Bertin P: study design, manuscript revision, and approval of the final version for publication.

Berrut G: study design, manuscript revision, and approval of the final version for publication.

Corruble E: study design, manuscript revision, and approval of the final version for publication.

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Doucet J: study design, manuscript revision, and approval of the final version for publication.

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Hanon O: study design, manuscript revision, and approval of the final version for publication.

Benattar-Zibi L: study design, manuscript revision, and approval of the final version for publication.

Piedvache C: data analysis, manuscript revision, and approval of the final version for publication.

### Conflicts of interest Lazkani A has no conflict of interest.

Becquemont L received consulting fees from Sanofi-Aventis, Pfizer and Servier, and lecture fees from Genzyme, GlaxoSmithKline, Bristol-Myers Squibb, and Merck Sharp & Dohme; close family member working at Sanofi France.

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Bertin P received consulting fees from Sanofi-Aventis, Pfizer, Ethypharm and Reckitt Benckiser, and speaking fees from Genevrier, Roche, Bristol-Myers Squibb, and Merck Sharp & Dohme.

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Pasquier F is an investigator for Pfizer, Piramal, Roche, Lilly, Astra Zeneca, Noscira, Pharmext, Forum Pharmaceutical, and GE Healthcare and received consulting fees from Lilly, Novartis, Nuticia, and Sanofi.

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### References

- Gaskin DJ, Richard P (2012) The economic costs of pain in the United States. J Pain 13(8):715–724
- Andersson HI, Ejlertsson G, Leden I, Schersten B (1999) Impact of chronic pain on health care seeking, self care, and medication. Results from a population-based Swedish study. J Epidemiol Community Health 53(8):503–509
- Dominick KL, Ahern FM, Gold CH, Heller DA (2004) Healthrelated quality of life and health service use among older adults with osteoarthritis. Arthritis Rheum 51(3):326–331
- Lalonde L, Choiniere M, Martin E, Berbiche D, Perreault S, Lussier D (2014) Costs of moderate to severe chronic pain in primary care patients—a study of the ACCORD Program. J Pain Res 7:389–403
- Gustavsson A, Bjorkman J, Ljungcrantz C, Rhodin A, Rivano-Fischer M, Sjolund KF, Mannheimer C (2012) Socio-economic burden of patients with a diagnosis related to chronic pain—register data of 840,000 Swedish patients. Eur J Pain 16(2):289–299
- Raftery MN, Ryan P, Normand C, Murphy AW, de la Harpe D, McGuire BE (2012) The economic cost of chronic noncancer pain in Ireland: results from the PRIME study, part 2. J Pain 13(2):139– 145
- Depont F, Hunsche E, Abouelfath A, Diatta T, Addra I, Grelaud A, Lagnaoui R, Molimard M, Moore N (2010) Medical and nonmedical direct costs of chronic low back pain in patients consulting primary care physicians in France. Fundam Clin Pharmacol 24(1): 101–108
- Pradalier A, Auray JP, El Hasnaoui A, Alzahouri K, Dartigues JF, Duru G, Henry P, Lanteri-Minet M, Lucas C, Chazot G, Gaudin AF (2004) Economic impact of migraine and other episodic headaches in France: data from the GRIM2000 study. Pharmacoeconomics 22(15):985–999
- Kobelt G, Woronoff AS, Richard B, Peeters P, Sany J (2008)
   Disease status, costs and quality of life of patients with rheumatoid arthritis in France: the ECO-PR Study. Joint Bone Spine 75(4):408–415
- Knight T, Schaefer C, Chandran A, Zlateva G, Winkelmann A, Perrot S (2013) Health-resource use and costs associated with fibromyalgia in France, Germany, and the United States. Clinicoecon Outcome Res 5:171–180
- Bertin P, Rannou F, Grange L, Dachicourt JN, Bruel P, Emery C, Grandfils N, Ch T (2014) Annual cost of patients with osteoarthritis of the hip and knee in France. J Musculoskelet Pain 22(4):356–364
- 12. Becquemont L, Benattar-Zibi L, Bertin P, Berrut G, Corruble E, Danchin N, Delespierre T, Derumeaux G, Falissard B, Forette F, Hanon O, Pasquier F, Pinget M, Ourabah R, Piedvache C (2013) National observatory on the therapeutic management in ambulatory care patients aged 65 and over, with type 2 diabetes, chronic pain or atrial fibrillation The S.AGES cohort, design and baseline characteristics of the study population. Therapie 68(4):1–19
- Bertin P, Becquemont L, Corruble E, Derumeaux G, Falissard B, Hanon O, Pinget M, Forette F (2013) The therapeutic management of chronic pain in ambulatory care patients aged 65 and over in France: the S.AGES Cohort. Baseline data. J Nutr Heal Aging 17(8):681–686
- Bucher S, Bauduceau B, Benattar-Zibi L, Bertin P, Berrut G, Corruble E, Danchin N, Delespierre T, Derumeaux G, Doucet J,

- Falissard B, Forette F, Hanon O, Ourabah R, Pasquier F, Piedvache C, Pinget M, Ringa V, Becquemont L (2014) Primary care management of non-institutionalized elderly diabetic patients: the S.AGES cohort—baseline data. Prim Care Diabetes. doi:10.1016/j.pcd.2014.07.004
- Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW (1963) Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. JAMA 185:914– 919
- Barberger-Gateau P, Dartigues JF, Letenneur L (1993) Four instrumental activities of daily living score as a predictor of one-year incident dementia. Age Ageing 22(6):457–463
- Marc LG, Raue PJ, Bruce ML (2008) Screening performance of the 15-item geriatric depression scale in a diverse elderly home care population. Am J Geriatr Psychiatry 16(11):914–921
- http://www.insee.fr/fr/bases-de-donnees/bsweb/serie.asp?idbank= 000642334.
- 19. http://base-donnees-publique.medicaments.gouv.fr/.
- http://www.ameli.fr/professionnels-de-sante/medecins/votreconvention/tarifs/index.php.
- Huscher D, Mittendorf T, von Hinuber U, Kotter I, Hoese G, Pfafflin A, Bischoff S, Zink A (2014) Evolution of cost structures in rheumatoid arthritis over the past decade. Ann Rheum Dis 74(4): 738–745
- Martin BI, Deyo RA, Mirza SK, Turner JA, Comstock BA, Hollingworth W, Sullivan SD (2008) Expenditures and health status among adults with back and neck problems. JAMA 299(6): 656–664
- Lubeck DP (2001) A review of the direct costs of rheumatoid arthritis: managed care versus fee-for-service settings. Pharmacoeconomics 19(8):811-818
- Yelin E, Wanke LA (1999) An assessment of the annual and longterm direct costs of rheumatoid arthritis: the impact of poor function and functional decline. Arthritis Rheum 42(6):1209–1218
- Michaud K, Messer J, Choi HK, Wolfe F (2003) Direct medical costs and their predictors in patients with rheumatoid arthritis: a three-year study of 7,527 patients. Arthritis Rheum 48(10):2750– 2762
- Sabariego C, Brach M, Stucki G (2011) Determinants of major direct medical cost categories among patients with osteoporosis, osteoarthritis, back pain or fibromyalgia undergoing outpatient rehabilitation. J Rehabil Med 43(8):703–708
- Margolis JM, Juneau P, Sadosky A, Cappelleri JC, Bryce TN, Nieshoff EC (2014) Health care resource utilization and medical costs of spinal cord injury with neuropathic pain in a commercially insured population in the United States. Arch Phys Med Rehabil 95(12):2279–2287
- Walen HR, Cronan PA, Bigatti SM (2001) Factors associated with healthcare costs in women with fibromyalgia. Am J Manag Care 7 Spec No:SP39-47
- Dellaroza MS, Pimenta CA, Lebrao ML, Duarte YA (2013) Association of chronic pain with the use of health care services by older adults in Sao Paulo. Rev Saude Publica 47(5):914–922
- Evans RL, Hendricks RD, Lawrence KV, Bishop DS (1988) Identifying factors associated with health care use: a hospital-based risk screening index. Soc Sci Med 27(9):947–954
- Dagenais S, Caro J, Haldeman S (2008) A systematic review of low back pain cost of illness studies in the United States and internationally. Spine J 8(1):8–20
- Liotta G, Brenna A (2007) Evolution of the in-patient hospital expenditure for the elderly in Italy: 1996–2001 comparison. Arch Gerontol Geriatr 45(2):169–177
- Blanco-Moreno A, Urbanos-Garrido RM, Thuissard-Vasallo IJ (2013) Public healthcare expenditure in Spain: measuring the impact of driving factors. Health Policy 111(1):34–42



- Smith M, Davis MA, Stano M, Whedon JM (2013) Aging baby boomers and the rising cost of chronic back pain: secular trend analysis of longitudinal Medical Expenditures Panel Survey data for years 2000 to 2007. J Manipulative Physiol Ther 36(1):2–11
- 35. Fox MT, Persaud M, Maimets I, O'Brien K, Brooks D, Tregunno D, Schraa E (2012) Effectiveness of acute geriatric unit care using
- acute care for elders components: a systematic review and metaanalysis. J Am Geriatr Soc 60(12):2237–2245
- Thompson E, Broadbent J, Bertino MD, Staiger PK (2015) Do pain-related beliefs influence treatment adherence? A systematic review. Clin J Pain. doi:10.1097/AJP.0000000000000035

