Disease Burden on Healthcare in Treated and Untreated Patients with Osteoarthritis Pain: A Spanish nationwide survey

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Abstract

Objectives: To estimate disease burden on healthcare in osteoarthritis (OA) pain patients in Spain, and to determine whether frequency of healthcare resource utilisation (HRU) and related costs differ by pain severity and treatment with usual analgesics.

Methods: The 2017 Spanish National Health Survey (ENSE), a large, nationwide, cross-sectional general health survey, was used to abstract data on adult patients with a self-reported physician diagnosis of OA. Patients were cross-classified according to pain severity in the last 4-weeks (no/mild, moderate, severe) and use of usual analgesia in the last 2-weeks (treated/untreated). Per patient per year (PPPY) HRU included medical visits, other healthcare visits, diagnostic/laboratory tests, days of hospitalisation, days in day hospital facilities, and surgical procedures. Costs were computed by multiplying unit price by annual frequency of HRU.

Results: 5,234 OA patients were analysed (women 70.8%; age 69.9 [SD:13.1]; 66.5% treated). Significant associations were observed in treated and untreated OA patients between pain severity and adjusted PPPY mean utilisation of medical visits, days of hospitalisation, other healthcare visits, and related costs: the greater the pain severity, the greater the HRU and costs, with treated showing higher HRU and costs than untreated patients. Average total healthcare costs were €2,274 (5,461) PPPY, with costs associated with outpatient healthcare visits being the major driver.

Conclusions: HRU and related costs were seen to increase as pain severity increased in patients with OA in a nationally representative sample in Spain. These findings seem to be more consistent in treated versus not treated patients with usual analgesics.

Keywords: osteoarthritis, burden, treated, pain, healthcare resource utilisation, costs

Introduction

Osteoarthritis (OA) is a heterogeneous, degenerative and frequently painful and seriously debilitating disease that affects the joints, requiring joint replacement under some circumstances[1,2]. This gradually progressing health condition is currently the most common rheumatologic disease[1,3-5]. In Spain, according to most recent epidemiologic studies, OA in any location affects up to 29.4% of people aged 40 or older[5], with pain as a core symptom in many patients[6,7]: up to 56.5% of OA patients suffered from moderate to severe pain in last four weeks, according to the 2017 Spanish National Health Survey (ENSE)[8,9]. The disease may have a commensurate tremendous individual and socioeconomic burden[1,4,10-17], and as it is usually accompanied by pain, it is a significant cause of burden to society, both from a humanistic point of view (contributing to poor quality of life) and in economic terms (impacting the limited healthcare budgets of national health systems)[10]. The consequences of OA pain include limitations in activities of daily living and restrictions on participation in activities[11,13], and it is responsible for many primary care visits and other healthcare resource utilisation (HRU) as well as joint replacement surgeries[14-17]. However, it is well known that the socio-economic burden of osteoarthritis, particularly in painful subjects, is not exclusively limited to direct healthcare costs; it also entails significant non-healthcare costs related to loss of occupational productivity and associated with the formal and informal care needed when osteoarthritis patients lose their independence[10,14-18].

OA treatment guidelines recommend a wide variety of pharmacologic and non-pharmacologic treatments[4,19,20]. However, these treatments are, for the moment, ineffective in halting disease progression, and are focused on modifying symptoms and managing pain, with debated effectiveness[3,20]; moreover, they are associated with high rates of treatment discontinuation due to side effects and/or lack of effectiveness[21]. Despite this disease's high social burden, it has traditionally received moderate interest and has historically been studied as a part of a group of rheumatologic diseases, not an independent entity. Also, the relationship of pain in OA to HRU and corresponding costs has not been documented extensively. Recent findings of significant relationships between patients' self-reported OA severity and other outcomes, including pain, function, productivity, and

costs in both US and European populations suggest that self-reporting of OA severity provides an accurate and tangible assessment of patients' perceptions of their disease[18,19,22]. Patients' self-reporting of OA severity thus may be a useful approach for evaluating the impact and burden of OA on the patient[18,19,22]. Therefore, the objective was to estimate disease burden on healthcare in patients with OA pain in Spain from the perspective of the Spanish National Health System, and to determine whether frequency of HRU and related costs differs by pain severity and treatment with usual analgesics, based on the data collected in the 2017 ENSE[9].

Methods

Study design

This study has a cross-sectional design developed according to the STROBE checklist (***See supporting information***, https://www.strobe-statement.org)[23].

Data source

The most recent ENSE survey (from 2017) was used as the source from which data were abstracted[9]. The ENSE is funded every five years by the Spanish Ministry of Health and constitutes the main source of information on health perceived by the population residing in Spain. It is highly representative of Spain as a nation according to population geographic density and collects an extensive set of disaggregated aspects of health according to demographic and socio-economic characteristics. The information was obtained through interviews in homes throughout the country using computer-assisted personal interviews (CAPIs) as a method of information collection after obtaining the consent of those surveyed[9]. The 2017 ENSE collected information for a representative sample of 23,089 men and women over 15 years of age in the Spanish population.

Study population

For this study, a subsample of the ENSE was used comprising survey participants of both sexes aged 18 or older with a self-reported physician diagnosis of OA who completed the survey. Pain

severity was assessed by the pain domain of the Spanish version of SF-36v2 questionnaire included in the ENSE questionnaires (***See supporting information***). To analyse the study objectives, the OA subsample of the 2017 ENSE was grouped by presence of pain in the past four weeks, assessed according to the question on pain severity in the past four weeks from the Spanish version of the SF-36v2 questionnaire included in the ENSE (***See supporting information, Question 45***), into three categories: no pain/mild pain (response 1, 2 or 3 to Q45), moderate pain (response 4), and severe pain (response 5 or 6). These were then grouped by use or non-use of prescribed usual pain medications in the past two weeks according to the ENSE (***See supporting information, Question 87_2a***), such that six subgroups were formed based on pain severity in the past four weeks and use of pain medication in the past two weeks.

Assessment of healthcare utilisation and cost

To assess disease burden on healthcare, average healthcare resource utilization (HRU) per patient per year (PPPY) was collected in terms of medical visits to primary care, medical visits to specialist physicians, medical visits to the emergency department, visits to other healthcare professionals (psychotherapist, physiotherapist, nurse/midwife), diagnostic and laboratory tests (X-ray, CT scan, ultrasound, MRI, CBC, clinical chemistry and urinalysis), days of hospitalisation in an inpatient hospital (where duration of hospitalisation was more than 24 hours), days of hospitalisation in an outpatient hospital facility (where duration of hospitalisation was less than 24 hours), and surgery-related procedures. HRU was derived from the healthcare module of the ENSE, using questions from Modules N (Medical visits and other outpatient services) and O (Hospitalisations, emergency care and health insurance, ***See supporting information***). Once HRU was recorded, the economic burden arising from the use of those resources was calculated using their corresponding unit costs. The Oblikue Consulting e-Health database was used to obtain unit costs for different healthcare departments (***See supporting information, Table S1***)[24]. Once the quantity of resources used and the unit costs in euros (€) for 2017 had been obtained, they were multiplied by each other to determine the economic burden arising from healthcare in the study population. Costs of prescribed pain

medications could not be imputed due to the limited information collected in the ENSE regarding doses, names of active substances and treatment durations.

Statistical analysis

The statistical analysis included a preliminary analysis of the study sample groups performed by preparing dynamic tables and conducting a descriptive univariate analysis of relevant socio-demographic variables and characteristics related to the study objectives. Prior to any analysis, the rate of response or proportion of people interviewed who had provided a response on the variable to be analysed was estimated. Missing data were not imputed due to the cross-sectional design of the survey and the fact that the loss of data in the variables studied was very low (range 0.0%-0.6%). The descriptive analysis included the percentage distribution for categorical variables as well as measures of central tendency and dispersion for continuous variables, including normality tests. IBM SPSS (version 26.0, New York, United States), a software program for statistical processing, was used (https://www.ibm.com/analytics/spss-statistics-software).

To analyse the study objectives, we applied generalised linear models (GLMs) with covariates with estimation of effects using a factorial model with covariates to analyse HRU (negative binomial regression for counts), surgical procedures (binary logistic regression), and monetary costs (gamma regression). The percentage of patients with at least one medical visit (primary care, specialist or any) in the last year was compared with a GLM (binary logistic regression) with covariates. The covariates included in the models were the survey participant's geographic region of residence, age, sex, marital status, level of education, accidents in the past 12 months, smoking status, alcohol use, level of physical activity, and Functional Comorbidity Index (FCI)[25]. The FCI was used to correct the individual's HRU and costs weighted by the density of comorbidities deemed significant in terms of their impact on the individual's healthcare burden, such as obesity. It was calculated as a count of affirmative responses to the 18 items or comorbidities that comprise it as recommended by its authors Groll DL et al.[25], and that are included, amongst others, in the ENSE survey questionnaire. The sequential Bonferroni correction was applied in case of multiple comparisons.

To interpret the results obtained, when statistically significant differences were found between pairs, the magnitude of the difference was calculated by estimating the effect size with Cohen's *d*

statistic[26]. Effect size was estimated by dividing the mean difference between groups by the overall standard deviation and was interpreted according to the recommendations of Cohen and Kazis[26,27]: 0.20-0.50 = small effect size; 0.50-0.80 = moderate effect size; and $\geq$ 0.80 = large effect size. A sensitivity analysis was also performed in which the main statistical analyses were replicated in subgroups of patients with large sample sizes, as was the case for women and patients aged 65 or older (comprising 70.8% and 67.4%, respectively of the entire sample analysed, ***See supporting information***).

RESULTS

A total of 5,234 patients with a self-reported physician diagnosis of OA were analysed: 70.8% women, with a mean age of 69.9 (SD: 13.1) years (67.4% aged 65 or older). Of these, 43.5% (95% CI: 42.2-44.8) had no pain/mild pain, 32.8% (31.6-34.1) moderate pain, and 23.7% (22.6-24.9) severe pain. Most of them had been treated with usual oral pain medications in last two weeks: 66.5% (65.2-67.8). **Table 1** describes the main demographic characteristics of the population analysed by study group. The overall average (standard deviation) for utilisation of all types of medical visits was 12.8 (17.7) PPPY, with a significant association with increased pain severity ($p < 0.001$), regardless of whether or not one was treated with pain medications; the greater the pain, the greater the utilisation of medical visits (Table 2). OA patients with either mild or severe treated pain showed more utilisation of visits than OA patients with untreated pain (Table 2). The magnitude of these differences was small to moderate, with effect sizes ranging from 0.12 to 0.54. On average, 46.8% of OA patients used visits to primary care, 19.4% used visits to specialists, 37.5% used visits to the emergency department, and 41.3% used other healthcare visits. Treated OA patients with mild or severe pain showed significantly more utilisation of these resources than untreated OA patients (Tables 2 and 3, Figure 1). Utilisation of diagnostic and laboratory tests was 1.8 (1.2) units per OA patient, with no statistically significant differences between subgroups by pain severity or by treatment or non-treatment with analgesics in the last two weeks. Overall days of hospitalisation were 1.2 (6.4) PPPY, with a significant association with increased pain severity ($p < 0.001$), regardless of whether was treated. Again, the greater the pain, the greater the number of days of hospitalisation (Table 2).

Treated OA patients had more days of hospitalisation than untreated OA patients; this was independent of pain severity (Table 2). These differences were small in magnitude, with effect sizes always below 0.25. Days of hospitalisation in a day hospital were 0.4 (4.3) PPPY (only 12.7% of patients used this resource), with significantly greater utilisation in treated patients with mild or severe pain than in untreated patients (Table 2). However, there was an association in untreated OA patients regarding this resource utilisation, with utilisation decreasing as pain severity increased, whereas treated OA patients with severe pain used more days in a day hospital than patients with either no pain/mild pain or moderate pain (Table 2). The magnitude of these differences was negligible, with effect sizes ranging from 0.09 to 0.12. Surgical procedures were used by 7.0% of patients on average, with treated OA patients showing numerically greater utilisation of this resource than untreated, without reaching statistical significance (Table 2). Utilisation of surgical procedures was also numerically greater with increased pain severity, being more obvious in treated than in untreated patients.

Average total healthcare costs were €2,274 (5,461) PPPY, with a significant association with increased pain severity ($p < 0.001$) in treated patients, but not in untreated patients (Table 4). Nonetheless, the magnitude of these differences was small, with effect sizes ranging from 0.07 to 0.28. Costs of all types of healthcare visits were €981 (1,124) PPPY (43.1% of all healthcare costs), with a significant association with increased pain severity, either treated or untreated, within the group, and significant differences in both no/mild and severe pain between treated patients and untreated patients in the group (effect sizes ranging from 0.11 to 0.44). By type of visit, treated OA patients with severe pain accounted for significantly greater costs than untreated patients with severe pain (Figure 2), regardless of the type of visit, with a significant association by pain severity in treated and untreated patients in primary care and emergency department visits (Figure 2). Costs of diagnostic and laboratory tests were €201 (221) PPPY (8.8% of all healthcare costs). These were also significantly associated with increased pain severity ($p < 0.001$), regardless of whether was treated with pain medications, although no significant differences were seen regarding utilisation analgesics within each group by pain severity (Table 4). Costs of hospitalisation were €813 (4,303) PPPY (35.8% of all healthcare costs), with treated OA patients with severe pain showing significantly

greater costs than treated OA patients with no pain/mild pain or moderate pain. Effect sizes were negligible (0.12 to 0.15). Costs of surgical procedures were €459 (1,668) PPPY, accounting for 20.2% of total healthcare costs on average, with treated OA patients with severe pain showing the highest costs in this component of healthcare costs (Table 4).

Findings from replication of the main statistical analyses in subgroups of patients with large sample sizes (sensitivity analysis), i.e. women and patients aged 65 or older, were consistent with those seen in the entire study sample, particularly in women. In women, the major driver of HRU was medical visits, in both treated and in untreated patients, and was significantly associated with increased pain severity, although treated patients showed greater utilisation of medical visits than untreated patients, apart from those with moderate pain (***See supporting information, Table S2***). Average total healthcare costs were €1,999 (3,994) PPPY, with a significant association with increased pain severity ($p < 0.001$) present both in treated and untreated patients, but significantly greater in treated patients (***See supporting information, Table S3***). The sensitivity analysis in OA patients aged 65 or older showed that the major driver of HRU was again medical visits in both treated and untreated patients, although a significant association was seen in patients with severe pain only (***See supporting information, Table S4***). Average total healthcare costs were €2,038 (4,140) PPPY, and healthcare costs increased numerically as pain severity increased (with a trend toward statistical significance) mainly in individuals with severe pain (***See supporting information, Table S5***).

DISCUSSION

This study was conducted with the objective of examining the healthcare burden of treated and untreated OA pain in the Spanish population with a focus on HRU and its costs from the perspective of the Spanish National Health System. To do this, the data from the latest available ENSE survey was used[9]; this could be considered a strength of this study due to the large size of the sample analysed and its nationwide representativeness, even though data capture was based on persons surveyed. Nonetheless, self-reported OA severity and other outcomes, including pain, function, productivity, and costs in both US and European populations suggest that self-reporting of

OA severity provides an accurate and tangible assessment of patients' perceptions of their disease[18,19,22,28]. Another strength of using the ENSE survey was that self-reported OA prevalence was the same as the OA prevalence found in a physician-based Spanish prevalence study of rheumatologic diseases (the EPISER study) conducted recently by the Spanish Association of Rheumatology[5]; the prevalence of OA in people aged 40 or older was 29.4% in the EPISER study versus 29.8% in the ENSE survey in the same age range group. In the analysis included here, a large sample comprising a total of 5,234 OA patients aged 18 or older was analysed; as expected, most were women (70.8%) and older (67.4% over age 65), as seen in the EPISER study[5]. The main finding of our analysis was an increased burden in HRU (frequency) PPPY corresponding to a non-fatal health condition resulting in deterioration of patients' ability to go about basic and instrumental activities of daily living[29-33]. Significant associations were observed in OA patients between pain severity and PPPY adjusted mean utilisation of medical visits, other healthcare visits and days of hospitalisation, as well as corresponding costs, regardless of whether or not patients were on analgesic treatment: the greater the pain severity, the greater the HRU and costs, although the magnitude of differences were of small to moderate effect size in most comparisons. Also, patients receiving usual pain medications showed greater HRU and costs than untreated patients in these regards, except in hospitalisation costs, which were numerically greater but did not reach statistical significance. Surgical procedures with hospitalisation and diagnostic and laboratory tests showed a trend toward greater HRU and costs in patients with the most severe pain.

The main driver of HRU consisted of visits to medical and other healthcare professionals, with an average number of any type of medical visit of 12.8 PPPY and with 39.8%-68.2% of subjects (depending on pain severity) visiting a physician (a family physician, specialist or any other type) in last year. Visits to family physicians accounted for approximately 2/3 of all medical visits, regardless of pain severity or analgesic treatment, although treated patients made more visits to family physicians than untreated patients. Patients with OA pain receiving usual analgesics showed a 7%-49% increase in frequency of medical visits in comparison to untreated subjects. Days of hospitalisation comprised the other component of HRU that showed a significant increase in association with pain severity and analgesic treatment. Although the values observed were small in

terms of PPPY utilisation, the increase in days of hospitalisation in treated subjects ranged from nearly 40% to 120%, depending on pain severity. Due to such HRU, total healthcare costs were also associated with pain severity, regardless of analgesic utilisation, with numerically greater values in treated patients than in untreated patients. The analyses in two subgroups of patients, women and persons aged 65 or older, largely replicated the findings seen in the entire sample, although the reduction in sample size impacted attainment of statistical significance in associations in some comparisons (***See supporting information***). One possible explanation for these findings is that the treated patients might have been in later disease stages; this would have affected the results. Another is that existing analgesic treatment strategies do not meet all patient needs for adequate pain management. In fact, the most recent OA treatment guidelines do not recommend a wide variety of pharmacologic treatments currently used for managing pain in these patients due to their debated effectiveness or poor outcomes in pain management[20].

High HRU has been identified in previous studies. In 2010 in the US, nearly 10% of all outpatient visits were for a diagnosis of arthritis or other rheumatic conditions; of these, 58% were estimated to be for a diagnosis of symptomatic OA[14], thus, accounting for a major portion of healthcare costs, as reported by other authors[14,15]. The social burden of OA is expected to grow as population ageing increases and life spans lengthen, and the economic burden of OA is expected to grow along with it. Our frequency data were consistent with such studies; however, they diverged from the values reported by the EPISER study (28.9%), which was conducted in Spain around the same time as the ENSE[34]. The discrepancy might have arisen from the fact that the EPISER study considered medical visits related to osteoarticular problems only, whereas the ENSE asked about medical visits in general, not for a specific health problem. Another study conducted in Spain in patients with knee and hip OA (the ARTROCAD study) also found that the most important component of healthcare costs is time dedicated by medical professionals to patients, accounting for 24% of total healthcare costs[17]. This finding, although far from that of our analysis, could be explained again by the type of patients enrolled in ARTROCAD study, as it was limited to knee and hip OA patients, and the fact that the study investigated resources related to those OA conditions only. Another possibility is that both the EPISER study and the ARTROCAD study were managed by

physicians, whereas the ENSE is a Spanish national health survey conducted by interviewers using a CAPI methodology[9]. Nonetheless, we were unable to find any studies analysing the impact of pain severity and treatment with usual analgesics on disease burden on healthcare. Therefore, the analysis herein offers new findings to the scientific community in the field of rheumatology.

Our study found that total unadjusted healthcare costs PPPY in OA patients were substantial: €2,274 (€1,492 with a 5% trimmed mean), with increased costs in treated OA patients compared to untreated patients that ranged from 26% to 51%, depending on pain severity. Near 43% of total costs corresponded to outpatients visits, as this was the major driver of the burden of OA on the Spanish National Health System, particularly in treated patients and patients with more severe pain. These findings are aligned with the results of The Burden of Musculoskeletal Diseases in the United States, which showed that OA costs account for a significant portion of healthcare spending in that country[14]. In addition, the ARTROCAD study[17] showed the magnitude of healthcare costs in knee and hip OA. The researchers found that average total annual costs were €1,502 per patient in 2007 and estimated national costs of €4,738 million, accounting for 0.5% of the Spanish gross domestic product. In our analysis based in the ENSE survey, if we projected the actual prevalence of OA, regardless of location, and average healthcare costs PPPY, the actual national costs would be €11.2 billion, or 0.96% of the 2017 Spanish gross domestic product[35].

This study is not free of possible limitations. For example, OA diagnosis according to the ENSE as a data source could be considered a study limitation, as the data therein are self-reported by survey participants rather than drawn from medical databases or directly from medical personnel. Nonetheless, as mentioned, self-reporting may be a robust way of capturing patients' perceptions of their health[12,15,17,19], and the prevalence of OA in the ENSE was the same as that observed in a more formal Spanish study on the prevalence of rheumatic diseases conducted by the Spanish Association of Rheumatology[5]. In addition, other authors have previously selected a similar approach to their research on OA and have also found the disease to have a considerable burden on society[32]. Moreover, although the size of the sample analysed was large, some subgroups of patients (particularly untreated OA subjects with severe pain) could be under-represented in the study. Another possible limitation is that the study failed in computing the costs of analgesia, since information related to types of active

substance, dosages and treatment durations was not collected in the ENSE. Finally, for some variables, we had to interpolate annual utilisation from a shorter period in accordance with the data collected in the ENSE.

Despite the limitations of the study, from the results obtained it may also be concluded that pain severity is the major determinant of HRU and costs to the Spanish National Health System, regardless of whether or not analgesics are used, although treated versus untreated OA pain was usually associated with increased HRU and costs in other components of disease burden. Therefore, it seems that this health condition, the prevalence and burden of which are growing, merits more attention in the form of research on new treatments to reduce HRU and costs. In conclusion, HRU was clearly related with pain severity in patients with OA in a nationally representative sample in Spain. These findings appear to be more obvious in patients treated with analgesics than in untreated patients.

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DECLARATIONS

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Conflicts of interest/Competing interests: The authors declare that they have no conflicts of interest with regard to this research. The analysis was conducted by Natalia Llopart and Sofia García to obtain their master's degree in Health Economics and Market Access at Universidad Carlos III, Madrid, Spain, under the direction of Javier Rejas, an Associated Professor for this master's degree program. Javier Rejas is also employed at Pfizer, SLU, Alcobendas, Madrid, Spain. Josep Darbá is a Professor of Economics at Universitat de Barcelona and participated in the health economics part of the analysis.

Availability of data and material: Data and analysis are available upon request.

Code availability: Not applicable.

Authors' contributions: Each author agrees that the manuscript represents honest work. The manuscript was prepared jointly by all authors, and all of them had the right to review, comment on, and approve the manuscript prior to submission. The data reported within the manuscript are not the property of any of the authors. Javier Rejas was responsible for the study concept. Natalia Llopart, Sofia García, Javier Rejas, and Josep Darbá were responsible for data analysis, abstraction, and interpretation.

Ethics approval: The analysis performed in this study used aggregate dated available in the public domain only; thus, de-identification was guaranteed to prevent anyone's personal identity from being revealed. Therefore, studies as this one are exempt from IRB submission or classification by the Spanish Agency for Medicines and Medical Devices (AEMPS) according to current regulations for post-authorization observational studies (https://www.aemps.gob.es/investigacionClinica/medicamentos/estudiosPostautorizacion.htm#norEstatal).

Consent to participate: The confidentiality of the (anonymous and dissociated) records was respected in accordance with the existing Law on Personal Data Protection in Spain (Law 15/1999, of 13 December 1999, on Personal Data Protection). Individuals included in the ENSE survey participated voluntarily and gave their personal consent prior to their participation in the survey (see

details on survey implementation at https://www.mscbs.gob.es/estadEstudios/estadisticas/encuestaNacional/encuesta2017.htm).

Consent for publication: The manuscript has been read and approved by all authors who also meet the requirements for authorship. All of them agreed to submit the manuscript for publication, and that decision pertains solely to all authors.

Table 1: Demographic characteristics of the study population.

TOTAL N = 5,234	No/mild pain (N = 2,276)		Moderate pain (N = 1,717)		Severe pain (N = 1,241)	
Analgesia within the last two weeks Yes = 3,481 (66.5%); No = 1,753 (33.5%)	Yes N = 1,031 (19.7%)	No N = 1,245 (23.8%)	Yes N = 1,342 (25.6%)	No N = 375 (7.2%)	Yes N = 1,108 (21.2%)	No N = 133 (2.5%)
Age (mean, SD), years	69.4 (13.4)	68.4 (12.8)	70.8 (12.9)	69.2 (12.5)	71.5 (13.4)	68.8 (13.3)
Sex (female), %	70.1	59.0	76.7	60.8	81.3	68.4
Marital status, %						
Single	9.6	12.4	9.7	9.1	8.1	8.3
Married	52.9	53.8	48.1	53.6	46.4	55.6
Widowed	31.6	28.0	34.5	30.9	39.6	25.6
Legally separated	1.8	1.9	2.5	1.6	1.9	3.8
Divorced	4.1	3.6	5.1	4.5	4.0	6.0
Level of education, %						
None	5.0	2.8	4.4	4.0	8.1	9.8
Primary	54.4	49.6	58.7	52.5	59.4	49.6
Secondary	25.5	26.3	24.3	26.7	22.4	29.3
Professional formation	6.9	8.2	5.9	7.5	5.9	5.3
University education	8.1	13.2	6.7	9.3	4.1	6.0
Smokers, %	11.4	13.3	13.6	10.4	11.9	15.8
Alcohol use, %	49.6	60.1	47.6	57.3	36.0	50.4
Physical activity, %						
Does not exercise	40.4	31.5	55.3	47.5	67.0	66.2
Exercises on occasion	48.3	53.0	35.5	40.5	26.4	26.3
Exercises several times per month	5.6	8.0	4.8	6.1	3.6	0.8
Exercises several times per week	5.6	7.6	4.4	5.9	3.0	6.0
Accident in past 12 months, %	9.8	7.8	13.3	9.9	21.2	15.8
Functional Comorbidity Index (mean, SD)[a], counts	3.0 (2.2)	2.3 (1.9)	3.8 (2.3)	3.4 (2.2)	5.2 (2.6)	4.1 (2.3)

[a] Maximum number of comorbidities 18, minimum 0 (see reference 17 with list of comorbidities deemed significant in term of their impact on the individual's functioning according to Groll DL et al.; J Clin Epidemiol 2002; 58: 595-602); SD = Standard deviation.

Table 2: Healthcare burden in patients with osteoarthritis by pain severity and analgesic treatment: Healthcare resource utilisation (HRU) (frequency) per patient per year (PPPY).

TOTAL N = 5,234	No/mild pain (N = 2,276)		Moderate pain (N = 1,717)		Severe pain (N = 1,241)	
Healthcare resource	Analgesia within the last two weeks; Yes = 3,481 (66.5%); No = 1,753 (33.5%)					
	Yes N = 1,031 (19.7%)	No N = 1,245 (23.8%)	Yes N = 1,342 (25.6%)	No N = 375 (7.2%)	Yes N = 1,108 (21.2%)	No N = 133 (2.5%)
Medical visits (units)[1]	10.7‡ (10.1-11.4)	7.9 (7.5-8.4)	12.9$$$ (12.2-13.7)	12.1$$$ (10.9-13.4)	20.2‡, $$$,§§§ (19.0-21.5)	13.6$$$ (11.4-16.2)
Visits to other healthcare professionals (%)[2]	39.3† (36.3-42.3)	32.2 (29.6-34.8)	42.1 (39.5-44.8)	41.7$$ (36.8-46.7)	52.5†,$$$, §§§ (49.6-55.5)	36.8 (29.1-45.3)
Diagnostic and laboratory tests (units)[3]	1.7 (1.6-1.8)	1.6 (1.5-1.7)	1.8 (1.7-2.0)	1.8 (1.5-2.0)	2.2$$$, §§ (2.1-2.4)	1.9 (1.5-2.3)
Hospitalisation (days)	1.1‡ (1.0-1.2)	0.5 (0.4-0.5)	1.3‡, $ (1.2-1.4)	0.9$$$ (0.8-1.0)	2.0†, $$$,§§§ (1.9-2.2)	1.4 $$$,§§ (1.1-1.8)
Day hospital facilities (days)	0.3‡ (0.3-0.3)	0.4 (0.4-0.5)	0.4 (0.3-0.4)	0.4 (0.3-0.5)	0.7‡,$$$,§§§ (0.6-0.8)	0.2$$$,§§§ (0.1-0.3)
Surgical procedures (%)[4]	6.3 (5.0-8.0)	5.2 (4.1-6.6)	7.4 (6.1-9.0)	5.6 (3.7-8.5)	9.6 (8.0-11.5)	9.0 (5.2-15.2)

[1]Include visits to family physician, specialist, and emergency department; [2]Psychotherapist, Physiotherapist, Nurse/Midwife; [3]X-ray, CT, ultrasound, MRI, CBC, clinical chemistry, urinalysis; [4]With hospitalisation for more than 24 hours; ‡ = $p < 0.001$; † = $p < 0.01$; * = $p < 0.05$ analgesia versus no analgesia within pain severity subgroup; $$$ = $p < 0.001$; $$p < 0.01$; $p < 0.05$ versus no/mild pain within analgesic treatment subgroup; §§§ = $p < 0.001$; §§p < 0.01; §p < 0.05 versus moderate pain within analgesic treatment subgroup; not significant when not specified. Values expressed as mean (95% CI) adjusted with covariates (see Methods section for a list of covariates included in the GLM model).

Table 3: Percentage of patients with osteoarthritis having visited a physician (primary care physician [PCP] and/or specialist) in last year by pain severity and analgesic treatment.

TOTAL N = 5,234	No/mild pain (N = 2,276)		Moderate pain (N = 1,717)		Severe pain (N = 1,241)	
Type of medical visit (%)	Analgesia within the last two weeks; Yes = 3,481 (66.5%); No = 1,753 (33.5%)					
	Yes N = 1,031 (19.7%)	No N = 1,245 (23.8%)	Yes N = 1,342 (25.6%)	No N = 375 (7.2%)	Yes N = 1,108 (21.2%)	No N = 133 (2.5%)
Medical visits (PCP and/or any specialist)	49.6‡ (46.5-52.6)	39.8 (37.2-42.6)	57.0$$ (54.3-59.6)	52.8$$$ (47.7-57.8)	68.2†, $$$,§§§ (65.4-70.9)	51.9$ (43.4-60.2)
Visits to PCP	42.4† (39.4-45.4)	33.9 (31.3-36.6)	49.9$$ (47.3-52.6)	45.6$$$ (40.6-50.7)	61.8*,$$$, §§§ (58.9-64.6)	47.4$ (39.0-55.8)
Visits to any specialist	17.1 (14.9-19.5)	13.4 (11.6-15.4)	19.6 (17.6-21.8)	19.7$ (16.0-24.1)	27.8$$$, §§ (25.2-30.5)	20.3 (14.3-28.0)

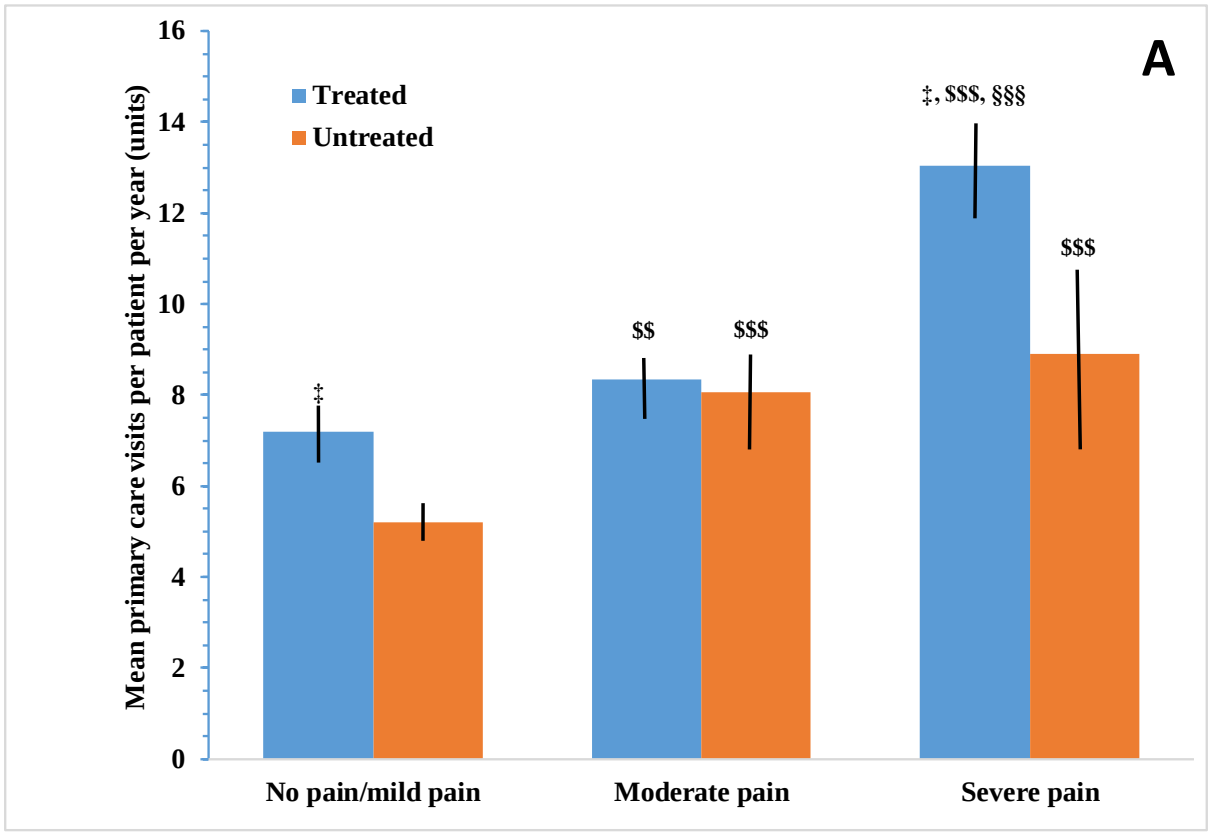
‡ = p < 0.001; † = p < 0.01; * = p < 0.05 analgesia versus no analgesia within pain severity subgroup; $$$ = p < 0.001; $$p < 0.01; $p < 0.05 versus no/mild pain within analgesic treatment subgroup; §§§ = p < 0.001; §§p < 0.01; §p < 0.05 versus moderate pain within analgesic treatment subgroup; not significant when not specified. Values expressed as % (95% CI) adjusted with covariates (see Methods section for a list of covariates included in the GLM model).

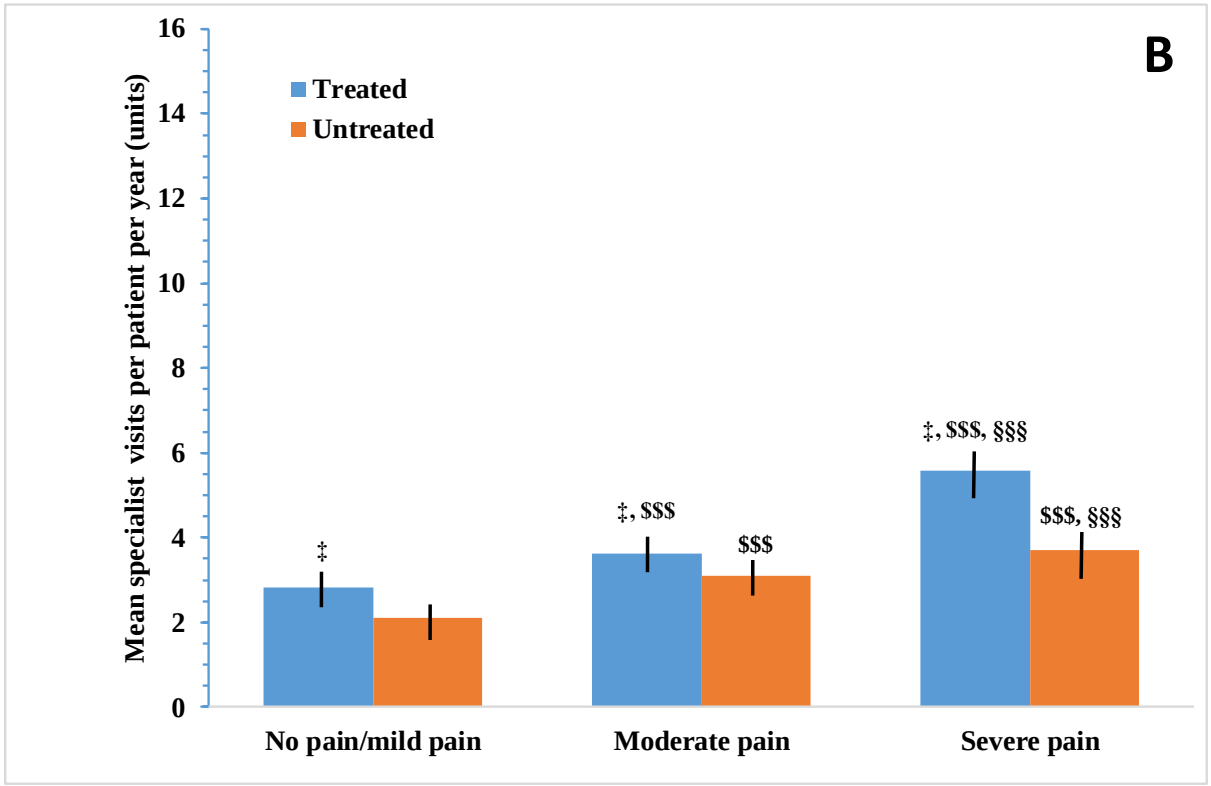
Table 4: Healthcare burden in patients with osteoarthritis by pain severity and analgesic treatment: Costs of healthcare resources per patient per year.

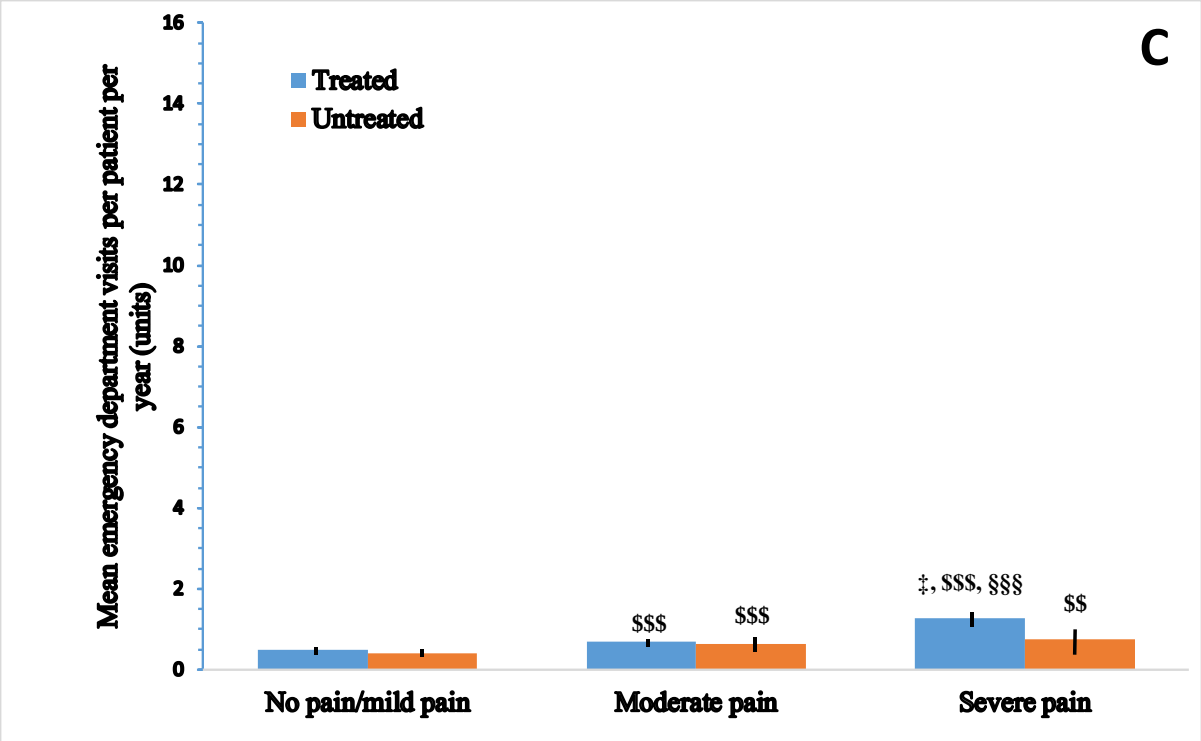
TOTAL N = 5,234	No/mild pain (N = 2,276)		Moderate pain (N = 1,717)		Severe pain (N = 1,241)	
Healthcare resource costs (€)	Analgesia within the last two weeks; Yes = 3,481 (66.5%); No = 1,753 (33.5%)					
	Yes N = 1,031 (19.7%)	No N = 1,245 (23.8%)	Yes N = 1,342 (25.6%)	No N = 375 (7.2%)	Yes N = 1,108 (21.2%)	No N = 133 (2.5%)
Medical and other healthcare visits[1]	848† (799-899)	728 (687-772)	965$^{\$\$}$ (918-1,015)	898$^{\$\$}$ (816-989)	1,336*$^{,\$\$\$,\S\S\S}$ (1,267-1,409)	1,062$^{\$\$}$ (900-1,253)
Diagnostic/laboratory tests[2]	180 (170-190)	166 (158-175)	201$^{\$}$ (192-211)	194$^{\$}$ (177-212)	258$^{\$\$\$,\S\S\S}$ (245-271)	211$^{\$}$ (181-246)
Hospitalisation	744 (483-1,006)	315 (77-553)	896 (666-1,125)	593 (159-1,027)	1,392$^{\$\$,\S}$ (1,140-1,644)	963 (235-1,692)
Hospital-day facility	43 (5-80)	61 (28-95)	50 (17-82)	56 (–6-118)	98 (62-134)	22 (–81,126)
Surgical procedures[3]	418 (316-519)	335 (243-427)	481 (392-570)	365 (197-534)	624$^{\$}$ (526-722)	588 (306-871)
Total healthcare costs	2,009* (1,679-2,339)	1,341 (1,041-1,641)	2,381 (2,091-2,670)	1,899 (1,352-2,447)	3,534$^{\$\$\$,\S\S\S}$ (3,216-3,853)	2,562 (1,642-3,481)

[1]Include visits to family physician, specialist, emergency department and other healthcare professionals (psychotherapist, physiotherapist, nurse/midwife); [2]X-ray, CT, ultrasound, MRI, CBC, clinical chemistry, urinalysis; [3]With hospitalisation for more than 24 hours; ‡ = $p < 0.001$; † = $p < 0.01$; * = $p < 0.05$ analgesia versus no analgesia within pain severity subgroup; \$\$\$ = $p < 0.001$; \$\$p < 0.01; \$p < 0.05 versus no/mild pain within analgesic treatment subgroup; §§§ = $p < 0.001$; §§p < 0.01; §p < 0.05 versus moderate pain within analgesic treatment subgroup; not significant when not specified. Values expressed as mean (95% CI) adjusted with covariates (see Methods section for a list of covariates included in the GLM model).

Figure 1: Frequency (units) of healthcare visits of patients with osteoarthritis by pain severity and analgesic treatment: A = Primary care visits, B = Specialist visits, C = Emergency department visits.

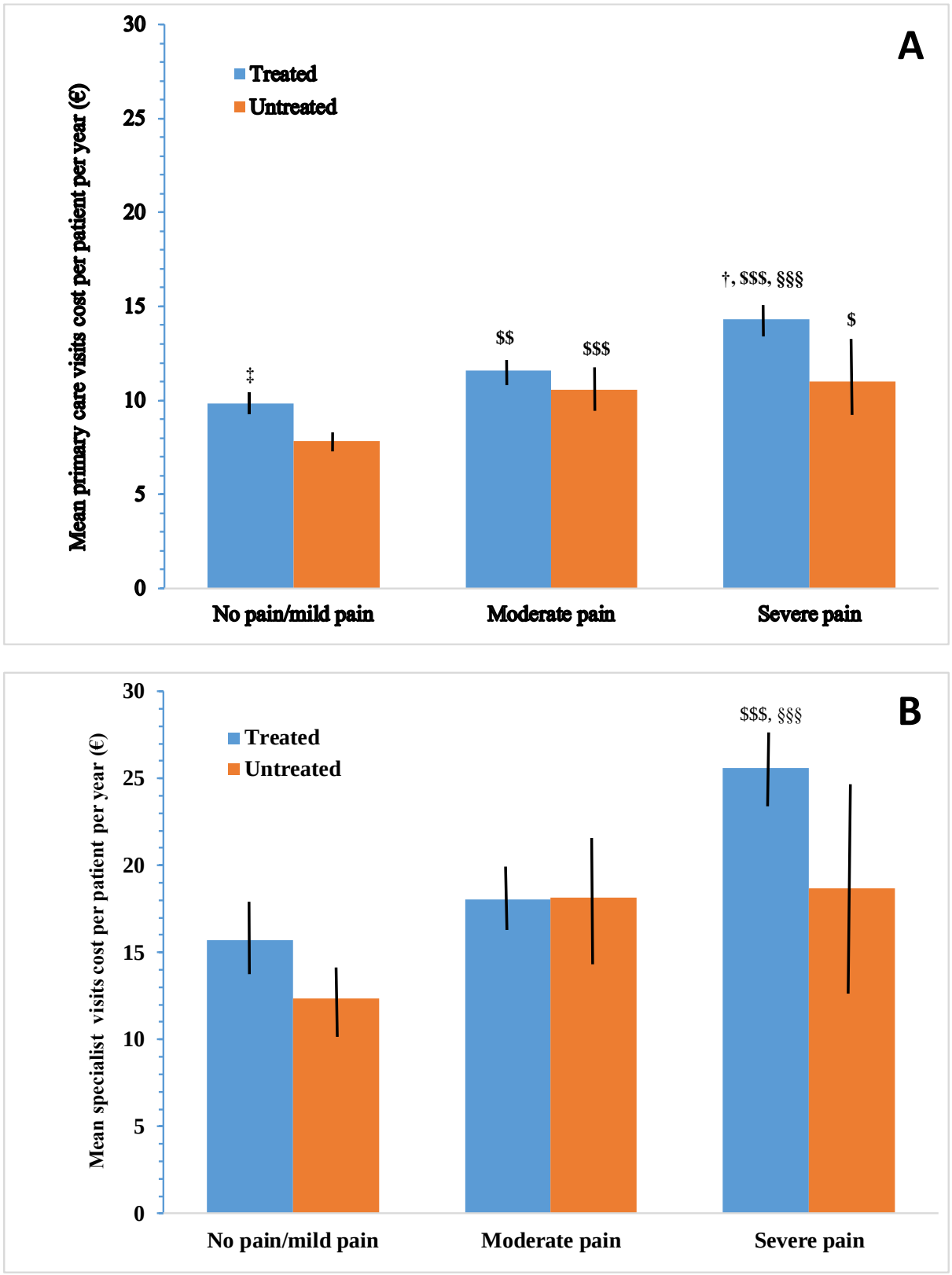


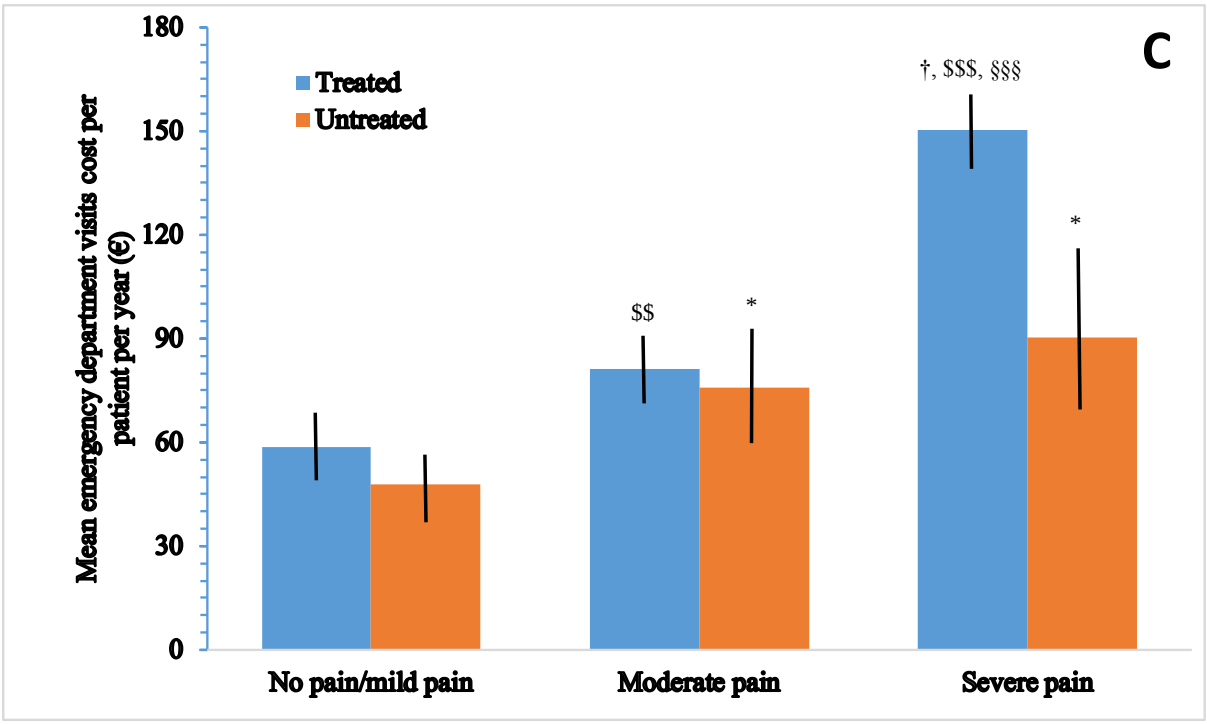




‡ = p < 0.001; † = p < 0.01; * = p < 0.05 analgesia versus no analgesia within pain severity subgroup; $$$ = p < 0.001; $$p < 0.01; $p < 0.05 versus no/mild pain within analgesic treatment subgroup; §§§ = p < 0.001; §§p < 0.01; §p < 0.05 versus moderate pain within analgesic treatment subgroup; not significant when not specified. Values expressed as mean (95% CI) adjusted with covariates (see Methods section for a list of covariates included in the GLM model).

Figure 2: Costs (€) of healthcare visits of patients with osteoarthritis by pain severity and analgesic treatment: A = Primary care visits, B = Specialist visits, C = Emergency department visits.





‡ = p < 0.001; † = p < 0.01; * = p < 0.05 analgesia versus no analgesia within pain severity subgroup; $$$ = p < 0.001; $$p < 0.01; $p < 0.05 versus no/mild pain within analgesic treatment subgroup; §§§ = p < 0.001; §§p < 0.01; §p < 0.05 versus moderate pain within analgesic treatment subgroup; not significant when not specified. Values expressed as mean (95% CI) adjusted with covariates (see Methods section for a list of covariates included in the GLM model).