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A population-based study on chronic pain and the use of opioids in Portugal

Luís Filipe Azevedo [a,b,c,*], Altamiro Costa-Pereira [a,b,c], Liliane Mendonça [a,c], Cláudia Camila Dias [a,b], José Manuel Castro-Lopes [b,c,d,e]

[a] Department of Health Information and Decision Sciences (CIDES), Faculty of Medicine, University of Porto, Porto, Portugal
[b] Centre for Research in Health Technologies and Information Systems (CINTESIS), University of Porto, Porto, Portugal
[c] Centro Nacional de Observação em Dor (OBSERVDOR; National Pain Observatory), Porto, Portugal
[d] Department of Experimental Biology, Faculty of Medicine, University of Porto, Portugal
[e] IBMC – Institute for Molecular and Cell Biology, University of Porto, Portugal

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ABSTRACT

Although increasing doubts exist regarding the long-term effectiveness and safety of opioids in patients with chronic pain (CP), most guidelines still recognize opioids as an option in effective management of CP. We aimed to describe the prevalence and factors associated with opioid use in subjects with CP in Portugal and to evaluate satisfaction and self-assessed treatment effectiveness. A nationwide study was conducted in a representative sample of the adult Portuguese population. The 5094 participants were selected using random digit dialing and estimates were adequately weighted for the population. The prevalence of opioid use by subjects with CP was 4.37% (95% confidence interval [CI] 3.4–5.5); and in subjects experiencing CP with and without cancer, it was 10.13% and 4.24%, respectively. Use of strong opioids was reported by only 0.17% of CP subjects. Sex, pain severity and symptoms of depression and anxiety were significantly associated with opioid use; however, in multivariate modeling, only pain-related disability remained significant. No significant differences among users and nonusers of opioids were observed regarding treatment satisfaction and self-assessed effectiveness. Although extremely high rates of use of opioids exist in a few countries, it should not be seen as a ubiquitous problem. Indeed, we showed that in Portugal, as in many other regions in the world, opioids are used much less frequently than in those few countries. Moreover, we did not find significant differences among users and nonusers of opioids regarding satisfaction and self-assessed effectiveness, eventually showing the results to be in line with reports that show doubt about opioids' effectiveness. Further research and particular attention to and continuous monitoring of the trends of use and abuse of opioids worldwide are recommended.

1. Introduction

Chronic pain (CP) is recognized as a major public health issue with important physical, psychological and familial consequences [2,22,27,28,62,64,79] and with high social and economic burdens [23,28,31,32,38,47,72,74,77,78]. The focus in most guidelines concerning the treatment and management of patients with CP go beyond pain relief to include goals regarding improvement in physical and social functioning and minimization of disability. The adequate treatment of chronic pain is seen as an important individual and societal problem, and those guidelines are evidence of the effort that has been made to respond adequately to this important issue [9,11,52].

Opioid analgesics have been used for centuries to treat moderate to severe pain; they are accepted and important therapeutic options for those experiencing acute pain and chronic cancer pain [46,48,67,81], and they are still recommended by several chronic noncancer pain (CNCP) treatment guidelines [12,13,15,17,35,42,65,71]. However, increasing reports are shedding doubts on the long-term effectiveness and safety of opioid use in patient with CNCP [4,6,75]. Currently, the available evidence is still insufficient and weak regarding the long-term benefits of opioids for pain relief and even weaker for improvements in physical and social functioning [36,44,50]. Thus, the long-term effectiveness of opioids in patients with CNCP remains an unanswered question. Moreover, there is accumulating evidence of problems of opioid abuse and misuse in some contexts [45,46].

* Corresponding author. Address: Faculdade de Medicina da Universidade do Porto, Departamento de Ciências da Informação e da Decisão (CIDES), Rua Dr. Plácido da Costa, s/n, 4200-319 Porto, Portugal. Tel.: +351 22 5513622; fax: +351 22 5513623.
E-mail address: lazevedo@med.up.pt (L.F. Azevedo).

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Although much has been written about the use, abuse and misuse of opioids in some countries with high frequencies of opioid use [5,9,45,52,56–58,67,76], it is important to emphasize that in most countries in the world opioids are used infrequently in general, particularly in patients with CNCP [1,9,56,58,67,80]. This infrequent use of opioids in many contexts seems to be explained primarily by (1) unscientific beliefs, misconceptions and fears; and (2) scarcity of and difficulties and inequalities in access to health care [1,9,26,46,58,67,80].

Only few population-based studies have described in detail the patterns and factors associated with the use of opioids [21,25,51,73], and none have been done in countries where there is infrequent use of opioids. Thus, in the context of a population-based nationwide epidemiological study focused on chronic pain epidemiology and health services utilization [2], the aims of this study were to describe the prevalence, patterns and factors associated with the use of opioids by subjects with CP in the general Portuguese population and to assess the satisfaction and self-assessed effectiveness of treatment by opioid users.

2. Methods

A cross-sectional nationwide epidemiological study was conducted in a representative sample of the Portuguese population, using random digit dialing (RDD) and computer-assisted telephone interviews. Details regarding the study design, measures and methods used in this project have been described elsewhere [2]. The study was approved by an institutional review board and all subjects gave their informed consent for participation.

2.1. Survey sampling methods

A 3-stage stratified sampling design was used, including 2 steps. First, the Mitofsky-Waksberg 2-stage RDD sampling method [30,40] was used to select a random sample of households with landline telephones. Second, within each selected household, 1 resident was randomly selected.

A comprehensive set of measures was implemented so as to prevent nonresponse. Additionally, to correct for sample imbalances and partially adjust for nonresponse and noncoverage bias, a set of weighting procedures was implemented [29,30,40]. The 2 types of weights used were: (1) weights adapted to the sampling design; and (2) poststratification weights that took into account the geographical region and sex and age distributions of the population [34].

Sample size was determined on the assumption of a CP prevalence of 20%, a CI level of 95%, a margin of error of 2%, and a response rate of 50%. Based on these assumptions, we needed a sample of at least 5000 effective interviews.

2.2. Instruments and methods of data collection

Data collection was carried out between January 2007 and March 2008. A structured questionnaire containing 6 sections was used: (1) introductory section presenting study aims and motivation; (2) CP screening questions; (3) assessment of additional pain characteristics; (4) assessment of health services utilization, management and treatment strategies, self-reported effectiveness of interventions, and patients' satisfaction; (5) assessment of pain-related disability and impact on emotional status; and (6) sociodemographic data. Prior to data collection, a pilot study was performed to test the study questionnaire and evaluate its psychometric characteristics.

The standard criteria of the International Association for the Study of Pain (IASP) were used for CP screening [33]. There were 2 screening questions: whether the respondents experienced pain and how long the pain lasted. Subjects were defined as having CP if they answered positively to the first question, and the pain's duration was $\geqslant$3 months.

Pain severity was assessed using the Brief Pain Inventory [3,18,19,37,70] and categorized using Serlin et al. classification [39,60]. The persistence pattern of pain was classified as continuous (every day or always) or noncontinuous (less often than every day or always). Open questions about pain location and self-reported pain causes were asked and were coded in predefined lists [54,59]. Pain-related disability was assessed using the Pain Disability Index [3,14,53,68,69]. To assess the impact of pain on mood and emotional status, a 5-item questionnaire using a 5-point frequency numerical rating scale (NRS) was used. An additional question was asked regarding the existence of a prior or current medical diagnosis of depression, depressive disorder or both.

A set of questions assessed use of health services, including pain management and treatment. Respondents were also asked about their satisfaction with pain management and treatment using a 5-point satisfaction NRS. Additionally, if subjects reported not being treated for their pain, they were asked to explain why, and answers were coded using a predefined set of options based on the literature and the pilot study. Respondents were asked if they were using any pain medicine and, if the answer was yes, they were asked what drugs they were using and how frequently. Finally, subjects were asked about the self-assessed effectiveness of pain medicines, using a 5-point effectiveness NRS and about frequency of pain while taking their pain medicines, using a 5-point frequency NRS.

2.3. Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences v 18.0 (SPSS, Cary, North Carolina, USA). Parameter estimates and CIs were calculated taking into account the sampling design and the appropriate weights previously described.

Descriptive statistics are presented as frequencies and percentages for categorical variables and as mean and standard deviation (SD) for continuous variables or as median and interquartile ranges, as appropriate. When testing the hypothesis, parametric and nonparametric tests were used as appropriate, taking into account type of variables, normality assumptions and number of groups.

To have a more thorough understanding of the factors associated with the use of opioids, univariate and multivariate logistic regression models were used. In the multivariate regression models, goodness-of-fit was assessed by the Hosmer-Lemeshow statistic and test. The discriminative and predictive powers of the model were evaluated by receiver operating characteristic (ROC) curve analysis. The influence of outlier data values on model fit was estimated using leverage statistics, and collinearity was assessed by evaluation of the coefficients correlation matrix. Logistic regression models were also used to estimate the effects of opioid utilization on treatment dissatisfaction and treatment ineffectiveness and to adjust for relevant confounders. Whenever statistical hypothesis testing was used, tests were 2-sided, and a significance level of $\alpha = 5\%$ was considered. Further details regarding methods, measures and analysis performed may be found elsewhere [2].

3. Results

A total of 25,679 telephone numbers were randomly generated using the Mitofsky-Waksberg RDD sampling method. Of them, 10,005 were residential numbers, and there were 6690 household responses. Of those responding, 5094 randomly selected residents agreed to participate. Thus, the response rate was 76% among responding households and 51% among all identified households.

The general characteristics of the sample, the prevalence of CP and the prevalence of CP with moderate or severe disability are presented in Table 1. The prevalence of CP was 36.7% (95% CI, 35.3–38.2), based on the definition by the IASP. Recurrent or continuous pain was present in 85% of subjects with CP, and moderate to severe intensity and disability were present in 68% and 35%, respectively. A higher prevalence of CP was observed in females; in those who were older, widowed, retired, or unemployed; and in those with lower education levels.

A total of 2213 subjects reporting CP, according to IASP definition criteria, were analyzed in greater detail regarding use of opioids and other relevant variables. Users of opioids were more commonly female, older than 45 years of age, married or widowed, retired, and with low levels of education (Table 1).

The use of opioids and other pain medicines by subjects with CP in the general Portuguese population is described in Table 2. Analgesics of the N02B group, mainly paracetamol, were the most commonly used drugs, followed by nonsteroidal anti-inflammatory drugs of the group M01A (including diclofenac, aceclofenac, nimesulide, ibuprofen, ketoprofen, coxibs, and oxicams) and muscle relaxants of the group M03. The prevalence of opioid use by subjects with CP (Tables 2 and 3) was estimated as 4.37%. Weak-opioid use was reported by 4.20%, and strong-opioid use was reported by 3 subjects (0.17%). Although the large majority of subjects in our study sample had CNCP, a small number of subjects reported cancer as the cause of CP (n = 49); thus, we analyzed the use of opioids (weak and strong) by subjects with noncancer and cancer CP separately (Table 3). Among subjects with chronic cancer pain (Table 3), opioids were used by 4 subjects, 3 of them using weak opioids and 1 a strong opioid.

Pain characteristics among users of opioids and nonusers are presented in Table 4. Pain duration was similar among users and nonusers. Opioid users had continuous CP significantly more often and also had significantly higher pain intensities, higher pain-related disabilities and higher levels of depression and anxiety symptoms. Pain location and self-reported causes of pain had similar distributions among users and nonusers of opioids. Although not statistically significant, opioid users also had a higher number of lost work days.

Factors associated with opioid use by subjects with CP are described in Table 5. Sex, pain persistence, pain intensity, pain-related disability, and depression or anxiety were significantly associated with opioid use. In the multivariate model, only pain-related disability remained a significant and independent predictor of opioid use (OR = 1.23, per increase in 10 units of PDI; $P = 0.035$).

To understand why some of the subjects with CP were not treated for their pain, we analyzed the reasons reported and grouped them into 12 major themes (Table 6). Preferences regarding use of pain medicines (23%) and adverse effects or complications of treatments or medicines (6%–8%) were among the most important reasons for no treatment.

Finally, satisfaction with pain management and self-assessed treatment effectiveness were assessed in all subjects with CP and in the subgroups of users and nonusers of opioid analgesics. When subjects with CP were asked about their general satisfaction with the management of their CP, 19% responded that they were slightly or not at all satisfied, including 12% of users and 19% of nonusers of opioids (OR = 0.56, $P = 0.080$). When asked about the self-assessed effectiveness of pain medicines, 11% reported that their pain medicines were slightly effective or not at all effective, including 12% of users of opioids and 11% of nonusers (OR = 1.16, $P = 0.712$). When adjusting the previous analysis for age, sex, psychological distress (symptoms of depression and anxiety), and pain severity (intensity and disability), both associations remained statistically nonsignificant (adjusted analysis for treatment dissatisfaction; OR = 0.56, $P = 0.195$; and adjusted analysis for treatment ineffectiveness OR = 1.87, $P = 0.128$). Finally, when asked, "In general, how frequently do you feel pain while taking your pain medicines?" 27% responded very frequently or always, with a very similar result among users and nonusers of opioids, 26% and 27% respectively ($P = 0.864$).

4. Discussion

Although opioid therapy for CNCP is currently under scrutiny because of concerns about long-term effectiveness, side effects, potential aberrant drug-related behavior, and addiction [4,6,75], opioid therapy is still a relevant option for the treatment of moderate to severe pain, particularly for acute pain and chronic cancer pain [46,48,67,81]. Moreover, although this is still a "hot" topic [5,9,13,58], several professional societies and guidelines currently recommend opioids for patients with CNCP [12,13,15,17,35,42,65,71], with some expert panels and experienced clinicians indicating that opioids, if adequately used and monitored, may be effective in selected patients with CNCP [9,12,13,15,17,35,42,57,63,65,71].

Based on a critical evaluation of the 6 most recent systematic reviews [16,26,36,43,44,50], it is possible to conclude that there is no satisfactory answer currently available to the question of whether long-term opioid therapy is effective and safe in patients with CNCP [9,13,15,58]. Many of the randomized clinical trials available have low methodological quality [36,44,50] as well as shorter-than-necessary follow-up periods, large rates of withdrawals and dropouts, low compliance, inadequate blinding, insufficient power, and patient-selection criteria that hinder generalizability. Thus, further research is crucial, particularly in improving the follow-up and the methodological quality of studies [13,15,43,58].

A different subject of discussion, one that should not be confused or merged with the analysis of opioid effectiveness, is the objectively demonstrated, and maybe often inadequately demonstrated, extremely high frequency of opioid use in some countries, particularly the United States [45,46]. This has been linked with increasing rates of drug overdoses and attributable deaths [20,41,45,46]. Between 1997 and 2007, the sale of morphine in the United States has increased by 222%, fentanyl by 525% and oxycodone by 866% [46]. Moreover, international statistics show an overwhelmingly excess of use in a few countries in the world. A report from the United Nations shows that 90% of the global consumption of morphine, fentanyl and oxycodone registered in 2009 occurred in the United States, Canada, Australia and New Zealand; and the United States alone, representing 4.6% of the world's population, consumed 83% of the world's oxycodone and 99% of hydrocodone [76]. In 2007–2009, average consumption of opioids was 39,487 defined daily doses per million inhabitants per day (DDD/MID) in the United States, 20,000 in Canada, 19,000 in Germany, 16,000 in Austria, and 13,000 in Denmark [76]. In the United States and other high-use countries, there is indeed an intricate dilemma associated with high and frequently inappropriate use of opioids and, simultaneously, the need to tackle the still frequent and worrying problem of undertreatment of CP [5,9,45,52,56–58,67].

The relevant and difficult scenario of extremely high opioid use that the United States is facing should, however, not be seen as representative or generalizable to the vast majority of the countries in the world. It is interesting that the results of the above-mentioned United Nations report indicate that between 2007 and 2009, the average consumption of opioids in Portugal was 2000 DDD/MID, 20 times less than in the United States; moreover, in the countries of South America and Africa, the average was 220 DDD/MID and 50 DDD/MID [76], respectively.

In the present study we have shown that prevalence of opioid use by subjects with CP in Portugal was 4.37%, with weak opioids used by 4.20% and strong opioids used by only 0.17%. The only

Table 1
General characteristics of the total sample, the subjects with chronic pain, the subjects with chronic pain using opioids, and the prevalence of chronic pain as a function of sociodemographic variables.

Sociodemographic variables	Total sample n (%)[a]	CP subjects[b] n (%)[a]	CP subjects using opioids[b] n (%)[a]	Prevalence (%) of CP (95% CI)	
				CP (IASP)[a,b]	CP with moderate to severe disability[c]
Sex					
Male	1790 (47.7)	540 (35.3)	12 (20.5)	27.0 (25.0–29.2)	5.2 (4.3–6.4)
Female	3304 (52.3)	1673 (64.7)	67 (79.5)	45.7 (43.8–47.6)	15.9 (14.5–17.5)
Age					
18–24 years	407 (12.9)	56 (4.6)	2 (5.1)	13.1 (10.2–16.7)	2.9 (1.6–5.1)
25–34 years	621 (19.1)	133 (10.4)	3 (6.7)	19.7 (16.7–23.1)	6.0 (4.4–8.1)
35–44 years	822 (18.2)	249 (14.4)	7 (9.8)	29.0 (25.7–32.4)	8.5 (6.8–10.7)
45–54 years	866 (16.0)	376 (18.4)	17 (26.5)	42.0 (38.5–45.5)	11.1 (9.1–13.5)
55–64 years	918 (13.5)	496 (18.8)	17 (18.7)	52.0 (48.4–55.6)	15.5 (13.0–18.3)
65–74 years	887 (12.0)	553 (19.6)	23 (21.4)	60.4 (56.8–63.9)	18.8 (16.0–22.0)
75 years or older	573 (8.4)	350 (13.8)	10 (11.8)	62.5 (57.9–66.8)	21.6 (18.0–25.6)
Marital status					
Single	872 (24.8)	210 (13.6)	6 (11.1)	19.6 (17.0–22.3)	5.2 (4.0–6.8)
Married or in a civil union	3183 (61.9)	1390 (66.9)	51 (67.4)	38.9 (37.0–40.8)	11.0 (9.8–12.3)
Divorced or separated	225 (4.2)	93 (4.3)	3 (3.1)	36.9 (30.4–44.0)	12.7 (8.7–18.2)
Widowed	665 (9.1)	420 (15.2)	19 (18.3)	61.5 (57.4–65.4)	23.9 (20.6–27.6)
Professional/occupational status					
Full or part-time worker	2419 (57.9)	779 (45.6)	26 (38.8)	28.2 (26.3–30.1)	7.0 (6.1–8.1)
Student	254 (8.3)	33 (2.7)	1 (2.4)	11.4 (8.1–15.7)	3.1 (1.6–6.0)
Unemployed	198 (4.4)	94 (5.2)	1 (1.3)	41.3 (34.2–48.7)	15.7 (11.2–21.5)
House worker or domestic worker	489 (7.0)	252 (9.6)	8 (7.3)	49.8 (45.0–54.6)	14.7 (11.6–18.4)
Retired	1463 (22.4)	896 (36.9)	41 (50.2)	59.6 (56.8–62.4)	20.3 (18.0–22.9)
Education level					
More than 12 years (higher)	884 (19.9)	241 (13.7)	10 (15.5)	23.9 (21.0–27.0)	5.7 (4.3–7.5)
10–12 years (secondary)	1046 (27.8)	264 (16.6)	4 (6.8)	20.6 (18.3–23.1)	5.1 (4.0–6.6)
5–9 years (basic 2nd and 3rd cycles)	922 (20.3)	367 (20.7)	18 (21.9)	35.3 (32.1–38.7)	9.6 (7.8–11.8)
1–4 years (basic 1st cycle)	1651 (25.9)	975 (42.1)	37 (50.1)	57.3 (54.7–59.9)	19.4 (17.2–21.8)
No education	232 (3.3)	170 (6.9)	5 (5.7)	74.6 (68.2–80.2)	33.3 (26.8–40.5)
Total	5094 (100.0)	2213 (100.0)	79 (100.0)	36.7 (35.3–38.2)	10.8 (9.9–11.8)

CP, chronic pain; IASP, International Association for the Study of Pain; PDI, Pain Disability Index.
[a] Weighted percentages, taking into account the age and sex distribution of the Portuguese population (see Methods section). Differences between the sum of categories and the total sample size is the result of missing data.
[b] Chronic pain was defined using the IASP standard definition as pain present with duration $\geqslant$3 months.
[c] Categorization of disability took into account the mean of items of the voluntary subscale of PDI (excluding sexual behavior) – family/home responsibilities, recreation, social activities and occupation/work. Moderate to severe disability was defined as mean $\geqslant$5.

previous study of primary-care prescriptions of analgesics in northern Portugal found similar estimates [55]. This is in clear contrast to the United States and some other countries, where opioid use by subjects with CP is much higher. In the United States and Canada, the prevalence of opioid use by subjects with CP is above 30% [8,21,49,73], and it is 15% in Denmark and Australia [7,24,25]. In a report of 15 European countries by Breivik et al. [10], the prevalence of strong-opioid use by subjects with CP was 13%; it was 12% and 11% in Ireland and Denmark, respectively, and it was 7% in Belgium, 6% in Norway and 5% in The Netherlands and Austria. In Portugal only 0.17% of subjects with CP reported use of strong opioids. It should be emphasized that the doubts about opioid safety refer mainly to strong opioids. Given these figures, it seems obvious that in Portugal, as probably is true in many other countries in the world, opioids are used infrequently.

We also studied the characteristics of opioid users and further analyzed the factors associated with opioid use. Factors significantly associated with opioid use were sex, pain severity (persistence, intensity and disability) and psychological distress. However, in multivariate analysis, the only factor significantly associated with opioid use was pain-related disability. Other reports have found pain severity, disability, psychological distress, poor self-rated health, and poor quality of life as the main factors associated with opioid use [21,25,51,73]. As in other reports, the cross-sectional nature of our study did not allow us to establish causality, so although it is clear that opioid use is associated with pain severity, disability and psychological distress, we were unable to clarify whether they were causes or effects.

We also studied the reasons some subjects reported not being treated for their pain problems, and we found that preferences regarding use of pain medicines and adverse effects were among the most important reasons. Indeed, individual preferences and adverse effects may be relevant explanations of why patients avoid opioid use [9,25,48,66].

Last, satisfaction with pain management and self-assessed treatment effectiveness were also analyzed. No significant differences were observed in users and nonusers of opioids, even after adjustment for age, sex, psychological distress, and pain severity. Thus, our results failed to show the expected benefits of opioid analgesics and are in line with reports shedding doubt on the effectiveness of opioids in the long-term treatment of patients with CP [25,73]. However, this must be interpreted with caution because

Table 2
Use of pain medicines, including opioids, by subjects with chronic pain.

Are you currently taking any pain medicine (drug) for your pain problem?	n (%)[a]
No	407 (24)
Yes	1428 (76)
Pain medicine use: 15 most frequently reported ATC groups [ATC codes][b]	**n (%)[c]**
N02B Analgesics: other analgesics and antipyretics	381 (21)
M01AB Anti-inflammatory and antirheumatic, nonsteroid, acetic acid derivatives	282 (15)
M01AX Anti-inflammatory and antirheumatic, nonsteroid, other	214 (12)
M01AE Anti-inflammatory and antirheumatic, nonsteroid, propionic acid derivatives	148 (8)
M03 Muscle relaxants, centrally acting agents	99 (5)
N05B Psycholeptics, anxiolytics	80 (4)
N02A Analgesics: pioids	79 (4.37)
Weak opioids	76 (4.20)
Codeine + paracetamol	40 (2.21)
Tramadol + paracetamol	18 (0.99)
Tramadol	17 (0.94)
Dextropropoxyphene + paracetamol	1 (0.06)
Strong opioids	3 (0.17)
Fentanyl	2 (0.11)
Morphine	1 (0.06)
M01AH Anti-inflammatory and antirheumatic products, nonsteroid; coxibs	69 (4)
M02 Topical products for joint and muscular pain	52 (3)
M01AC Anti-inflammatory and antirheumatic products, nonsteroid; oxicams	50 (3)
N06A Psychoanaleptics: antidepressants	39 (2)
N02C Analgesics: antimigraine preparations	21 (1)
N03 Antiepileptics	21 (1)
H02A Corticosteroids for systemic use	17 (1)
N05C Psycholeptics: hypnotics and sedatives	7 (0.4)
Mean number of drugs taken per subject–mean (standard deviation)	1.77 (1.22)

[a] Respondents were participants reporting chronic pain (n = 2213) who responded to the question "Are you currently taking any drug for your pain problem?" (n = 1,835).
[b] The most commonly used active substances for each World Health Organization Anatomical Therapeutic Chemical Classification (ATC) group were: N02B, paracetamol, acetylsalicylic acid and metamizole; M01AB, diclofenac and aceclofenac; M01AX, nimesulide and glucosamine; M01AE, ibuprofen and ketoprofen; M03, thiocolchicoside + paracetamol, thiocolchicoside and cyclobenzaprine; N05B, alprazolam and bromazepam; M01AH, etoricoxib and celecoxib; M02, etofenamate and niflumic acid; M01AC, piroxicam and meloxicam; N06A, amitriptyline and flouxetine; N02A, codeine + paracetamol, tramadol + paracetamol, tramadol, fentanyl and morphine; N02C, zolmitriptan and ergotamine; N03, pregabalin and gabapentin; H02A, prednisolone, betamethasone and prednisone; N05C, estazolam and flurazepam.
[c] Percentages for each ATC group are calculated from subjects who responded to the question "Are you currently taking any drug for your pain problem?" (n = 1835).

Table 3
Prevalence of opioid use by subjects with chronic pain, chronic noncancer pain and chronic cancer pain.

	Prevalence of opioid use[a]		
	All opioids	Weak opioids	Strong opioids
All chronic pain subjects[b]	4.37% 95% CI (3.44–5.54)	4.20% 95% CI (3.30–5.37)	0.17% 95% CI (0.05–0.51)
Chronic noncancer pain subjects	4.24% 95%CI (3.31–5.41)	4.13% 95%CI (3.22–5.31)	0.10% 95%CI (0.02–0.42)
Chronic cancer pain subjects	10.13% 95%CI (3.78–24.46)	7.44% 95%CI (2.33–21.29)	2.69% 95%CI (0.38–16.77)

[a] Weighted percentages, taking into account the age and sex distribution of the Portuguese population (see Methods section).
[b] Chronic pain was defined using the International Association for the Study of Pain (IASP) standard definition, as pain present with duration $\geqslant$3 months.

the cross-sectional nature of our study did not allow us to establish causality.

This study had some major strengths worth noting. First, it was specifically aimed at and designed to study CP epidemiology and health services utilization. Second, rigorous sampling methods were implemented, a large sample size was recruited, and standardized definitions and validated measures were used. Third, it is a population-based nationwide study; thus, it overcomes the common limitation of hospital-based samples, it facilitates generalizability, and it allows comparisons with other country-level studies.

Finally, this study has some limitations that should be taken into account, most of them common to other population-based studies. First, although measures to prevent nonresponse were implemented, the response rate was 76% among responding households and 51% among identified households. Moreover, there was some over-representation of females and middle-aged persons. To overcome this problem and to warrant less biased estimates, a set of weighting procedures was implemented, partially adjusting for nonresponse and noncoverage bias [29,30,40,61]. Second, the subjects with the most severe diseases or impairments (eg, most patients with severe cancer) may have been difficult to recruit, or they refused participation, thus the under-representation of those subpopulations is an inherent limitation of the study design and the sampling methods used. Third, because of low opioid use by subjects with CP, some of the estimates had relatively low precision. Fourth, the study relied on participants' self-reports, which incur the threat of information bias and recall bias, but this was an assumed limitation taken into account in the data collection and analysis. Fifth, the results regarding causal associations

Table 4
Pain characteristics and pain impact in subjects with chronic pain, opioid users and opioid nonusers.

Pain characteristics		Subjects with chronic pain[a] (n = 2213)	Opioid analgesics use		*P* value[b]
			Opioid users (n = 79)	Opioid nonusers (n = 1756)	
Pain duration	Pain duration in year: M (P25–P75)	10 (4–20)	10 (4–20)	10 (5–20)	0.834
Pain-persistence pattern[c]	Noncontinuous CP: n (%)	1038 (47%)	17 (22%)	677 (39%)	0.002
	Continuous CP: n (%)	1167 (53%)	62 (78%)	1073 (61%)	
Pain intensity	Pain on average (0–10 NRS): M (P25–P75)	5 (4–6)	5 (4–6)	5 (4–6)	0.898
	Pain at its least (0–10 NRS): M (P25–P75)	3 (2–4)	3 (2–4)	3 (2–4)	0.686
	Pain at its worst (0–10 NRS): M (P25–P75)	8 (7–10)	9 (7–10)	8 (7–10)	0.232
	Pain right now (0–10 NRS): M (P25–P75)	4 (2–6)	5 (4–6)	4 (2–6)	0.036
	Mild pain intensity[d]: n (%)	685 (53%)	25 (40%)	648 (54%)	0.014
	Moderate pain intensity[d]–n (%)	287 (22%)	23 (37%)	260 (22%)	
	Severe pain intensity[d]–n (%)	322 (25%)	14 (23%)	300 (25%)	
Pain location[e] (top 10)	Lumbar region: n (%)	775 (42%)	37 (47%)	737 (42%)	0.409
	Leg: n (%)	497 (27%)	24 (30%)	470 (27%)	0.492
	Knee–n (%)	445 (24%)	19 (24%)	413 (24%)	0.929
	Cervical region:n (%)	322 (17%)	12 (15%)	301 (17%)	0.641
	Arm: n (%)	268 (15%)	11 (14%)	257 (15%)	0.828
	Hip: n (%)	239 (13%)	11 (14%)	227 (13%)	0.807
	Head: n (%)	226 (12%)	8 (10%)	218 (13%)	0.528
	Shoulder: n (%)	222 (12%)	10 (13%)	212 (12%)	0.886
	Foot: n (%)	217 (12%)	13 (17%)	204 (12%)	0.198
	Dorsal region NOS: n (%)	216 (12%)	11 (14%)	197 (11%)	0.466
	No. of concurrent painful sites: M (P25–P75)	2 (1–3)	2 (1–4)	2 (1–3)	0.745
Pain self-reported aetiology[e] (top 10)	Osteoarthritis/osteoarthrosis: n (%)	737 (47%)	37 (50%)	692 (48%)	0.563
	Intervertebral disk disorders: n (%)	319 (21%)	18 (24%)	301 (21%)	0.496
	Osteoporosis: n (%)	223 (15%)	11 (15%)	207(14%)	0.905
	Unspecified spinal disorders: n (%)	131 (9%)	2 (3%)	129 (9%)	0.062
	Trauma related pain: n (%)	129 (9%)	5 (7%)	125 (9%)	0.567
	Fracture related pain: n (%)	100 (8%)	2 (3%)	97 (8%)	0.197
	Migraine and other chronic headaches: n (%)	116 (8%)	7 (10%)	109 (8%)	0.542
	Peripheral vascular disease: n (%)	104 (7%)	2 (3%)	101 (7%)	0.151
	Pain related to surgical interventions: n (%)	91 (6%)	5 (7%)	86 (6%)	0.796
	Rheumatoid arthritis: n (%)	82 (5%)	4 (5%)	75 (5%)	0.940
Pain-related disability[f]	1. Family/home responsibilities: M (P25–P75)	4 (2–7)	5 (3–8)	4 (2–7)	0.010
	2. Recreation: M (P25–P75)	4 (0–6)	4 (1–6)	3 (0–6)	0.121
	3. Social activities: M (P25–P75)	2 (0–5)	4 (0–7)	2 (0–5)	0.058
	4. Occupation/work: M (P25–P75)	4 (2–7)	5 (3–8)	4 (2–7)	0.128
	5. Sexual behavior: M (P25–P75)	2 (0–5)	4 (0–7)	2 (0–5)	0.071
	6.Self care: M (P25–P75)	1 (0–4)	2 (0–5)	1 (0–4)	0.009
	7. Life-support activities: M (P25–P75)	0 (0–1)	0 (0–4)	0 (0–1)	0.004
	PDI score: M (P25–P75)	18.0 (8.0–28.0)	21.0 (12.0–36.0)	18.0 (8.0–28.0)	0.010
	No disability[f] n (%)	138 (8%)	4 (5%)	135 (8%)	0.338
	Mild disability[f] n (%)	1007 (57%)	41 (52%)	966 (57%)	
	Moderate disability[f] n (%)	350 (20%)	17 (22%)	333 (20%)	
	Severe disability[f] n (%)	272 (15%)	17 (22%)	255 (15%)	
Emotional impact	Sad or depressed: M (P25–P75)	2 (1–3)	3 (2–4)	2 (1–3)	<0.001
	Anxious, nervous or tense: M (P25–P75)	2 (0–4)	3 (2–4)	2 (0–4)	0.001
	Angry or irritated: M (P25–P75)	1 (0–3)	1 (0–3)	1 (0–3)	0.850
	Isolated, solitary or lonely – M (P25–P75)	0 (0–2)	0 (0–2)	0 (0–2)	0.985
	Unable to enjoy life: M (P25–P75)	1 (0–3)	2 (1–4)	1 (0–3)	<0.001
Depressive disorders	Current or previous diagnosis of depression: n (%)	212 (13%)	10 (13%)	201 (12%)	0.812
Impact on occupation[g]	Pain affecting current job or no. of work hours: n (%)	337 (49%)	15 (56%)	322 (48%)	0.449
Lost work days[g]	Mean lost work days in the last 6 months: mean (SD)	4.36 days (16.85)	11.04 days (33.98)	4.07 days (15.70)	0.095

CP, chronic pain; M, median; NRS, numerical rating scale; P25–P75, 25th percentile and 75th percentile; PDI, pain disability index.

[a] Subjects with chronic pain as defined by IASP criteria (pain present with ⩾3 months duration).

[b] *P* value for statistical hypothesis tests comparing users and nonusers of opioids; X^2 test or Fisher exact test was used for categorical variables, as appropriate; Mann-Whitney test was used for numerical variables.

[c] Pain persistence pattern was defined in relation to the question "In general, how frequently is your pain problem present?" Continuous pain was defined as pain present every day or always.

[d] Pain intensity was categorized taking into account "pain right now" (0–10 NRS) and using the Serling classification: mild (1–4), moderate (5–6) and severe pain intensity (7–10).

[e] Multiple pain locations and self-reported aetiologies were recorded for each person. Only the 10 most common are presented.

[f] Pain-related disability was measured by PDI, a 7-item (0–10 NRS) questionnaire. Scores vary from 0 (no disability) to 10 (maximum disability). Categorization of disability had to account for the mean of items of the voluntary subscale of PDI (excluding sexual behavior)–family/home responsibilities, recreation, social activities and occupation/work–and using the following classifications: no disability (0); mild (0–5); moderate (5–7); and severe disability (7–10).

[g] This question was answered only by subjects currently employed or with professional occupations.

Table 5
Predictors of opioid use by subjects with chronic pain.

Variables	Opioid analgesic use (%)[a]	Predictors of opioid analgesics utilization[b]	
		Crude OR (95% CI)	Adjusted[c] OR (95% CI)
Sex		(*P* = 0.047)[d]	(*P* = 0.231)[d]
Male	2.7	1.0	1.0
Female	5.2	1.97 (1.01–3.83)	1.64 (0.73–3.67)
Age		(*P* = 0.761)[d]	(*P* = 0.851)[d]
18–24 years	5.1	1.0	1.0
25–34 years	3.2	0.61 (0.10–3.86)	0.41 (0.06–2.68)
35–44 years	3.2	0.61 (0.12–3.08)	0.40 (0.08–2.10)
45–54 years	6.3	1.25 (0.27–5.83)	0.69 (0.15–3.26)
55–64 years	4.2	0.81 (0.18–3.71)	0.57 (0.12–2.81)
65–74 years	4.6	0.89 (0.20–3.95)	0.73 (0.16–3.42)
75 years or older	3.5	0.68 (0.14–3.27)	0.66 (0.13–3.50)
Marital status		(*P* = 0.928)[d]	–
Single	4.1	1.0	–
Married or in a civil union	4.5	1.10 (0.44–2.77)	–
Divorced or separated	3.3	0.80 (0.18–3.60)	–
Widowed	4.9	1.20 (0.45–3.24)	–
Profession/occupational status		(*P* = 0.324)[d]	–
Full- or part-time worker	4.1	1.0	–
Student	5.0	1.24 (0.16–9.71)	–
House or domestic worker	3.3	0.81 (0.36–1.86)	–
Unemployed	1.1	0.27 (0.04–2.05)	–
Retired	5.7	1.42 (0.82–2.47)	–
Education level		(*P* = 0.314)[d]	–
More than 12 years (higher)	5.7	1.0	–
10–12 years (secondary)	2.0	0.33 (0.09–1.20)	–
1–9 year (basic)	4.8	0.85 (0.40 .80)	–
No education	3.4	0.58 (0.18–1.86)	–
Pain persistence pattern[e]		(*P* = 0.016)[d]	(*P* = 0.083)[d]
Noncontinuous	2.8	1.0	1.0
Continuous	5.6	2.08 (1.15–3.76)	1.64 [0.94–2.86)
Pain intensity[f]		(*P* = 0.008)[d]	(*P* = 0.678)[d]
Mild	3.2	1.0	1.0
Moderate or severe	6.6	2.14 (1.22–3.74)	1.39 [0.29–6.59)
Pain-related disability		(*P* = 0.004)[d]	(*P* = 0.035)[d]
PDI (per increase in 10 units)	–	1.27 (1.08–1.49)	1.23 [1.02–1.50)
Pain duration		(*P* = 0.874)[d]	–
3 months to 1 year	5.2	1.0	–
1 to 10 years	4.4	0.85 (0.35–2.02)	–
More than 10 years	4.2	0.80 (0.33–1.90)	–
Prev. med. diagnosis of depression		(*P* = 0.434)[d]	–
No	4.3	1.0	–
Yes	5.6	1.34 (0.65–2.76)	–
Mood: sad or depressed		(*P* = 0.002)[d]	(*P* = 0.168)[d]
Never, rarely, sometimes	3.1	1.0	1.0
Many times, most times, always	6.9	2.32 (1.38–3.90)	1.61 [0.82–3.19)
Mood: anxious or tense		(*P* = 0.002)[d]	(*P* = 0.858)[d]
Never, rarely, sometimes	2.9	1.0	1.0
Many times, most times, always	6.5	2.28 (1.35–3.87)	1.07 [0.53–2.16)
Total	4.4	–	–

95% CI, 95% confidence interval; OR, odds ratio.

[a] Weighted percentages, taking into account age and sex distribution of the Portuguese population (see Methods section).

[b] Predictors of opioid analgesics use defined by simple and multiple logistic regression; crude and adjusted ORs for categories of sociodemographic variables, pain characteristics and psychological distress variables.

[c] Adjusted ORs were calculated using multivariate logistic regression models. Multivariate models included adjustment for sex, age and all variables with crude association measures with *P* values <0.1 in the univariate analysis.

[d] *P* values for the omnibus tests evaluating the significance of each predictor variable.

[e] Pain-persistence pattern was defined in relation to the question "In general, how frequently is your pain problem present?" Continuous pain was defined as pain present every day or always.

[f] Pain intensity evaluated by the worst pain item (NRS 0–10). Mild intensity was defined as ratings <5 and moderate to severe intensity was defined as ratings >5.

should be interpreted with caution because the cross-sectional nature of our study did not allow us to establish causality clearly.

In conclusion, using validated measures and a set of standardized procedures and definitions, this study showed that in Portugal, as is probably the case in many other countries, there is clearly a low frequency of opioid use, particularly when compared with the countries that have extremely high frequency of use. Moreover, preferences regarding use of pain medicines and consideration of their adverse effects were shown to be among the most important reasons for many patients to avoid opioids. Finally, we observed no significant differences among users and nonusers of opioids regarding satisfaction and self-assessed treatment effectiveness, so we failed to show the expected benefits of opioids in this regard, which is in line with other reports and sheds doubt

Table 6
Reasons for no treatment of chronic pain according to subjects who reported not being treated for their pain.

Reasons for not being treated for your pain problem: major themes Specific reasons reported by participants	n (%)[a] (n = 253)
(1) Pain is not severe enough or no treatment is needed	
My pain is not severe enough	73 (29%)
Pain is only intermittent, not constant	24 (9%)
I think in my case no treatment is needed	14 (6%)
I am better now and I do not need any pain treatment	7 (3%)
(2) Preferences regarding use of pain medicines	
I do not want or do not like to take medicines for my pain problem	57 (23%)
(3) Subject's self-efficacy	
I can manage my pain without help	29 (12%)
I use other alternative methods (exercise, rest, positional changes, etc.)	14 (6%)
(4) Adverse effects or complications of treatments or medicines	
I felt bad with pain treatments I have used in the past	19 (8%)
Pain treatments interfere with other health problems or medicines	17 (7%)
Adverse effects of pain medicines are very frequent.	15 (6%)
(5) Inadequate health system response or quality	
I am waiting for a medical consult, diagnostic tests results or surgery	19 (8%)
I do not have a family physician	10 (4%)
(6) Feelings of hopelessness or accommodation	
I think nothing else can be done to solve my problem	14 (6%)
I rather prefer to live with my pain	7 (3%)
Pain is something normal, or I am used to feeling pain.	4 (2%)
(7) Issues or misconceptions regarding physicians	
I do not like to go to the doctor	13 (5%)
(8) Physician's under-recognition or disregard	
My doctor does not prescribe me pain medicines	9 (4%)
(9) Treatments or medicines ineffectiveness	
The pain treatments I have tried have not been effective	8 (3%)
(10) Subject's under-recognition or disregard	
I do not have the time, I am too busy	6 (2%)
(11) Socioeconomic reasons	
Pain treatments are too expensive	4 (2%)
(12) Treatment refusal	
Because I do not want surgery	3 (1%)

[a] Percentages are calculated from the answers of subjects with chronic pain when responding to the question "Why aren't you being treated for your pain?" (n = 253).

on the effectiveness of opioids in patients with CP. Further research and particular attention to and continuous monitoring of trends of use and abuse of opioids worldwide are strongly recommended, particularly in countries with low rates of opioid use.

Conflict of interest statement

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