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Undiagnosed Mood Disorders and Sleep Disturbances in Primary Care Patients with Chronic Musculoskeletal Pain

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Abstract

Objective. The study aims to determine the prevalence of undiagnosed comorbid mood disorders in patients suffering chronic musculoskeletal pain in a primary care setting and to identify sleep disturbances and other associated factors in these patients, and to compare the use of health services by chronic musculoskeletal pain patients with and without comorbid mood disorders.

Design. Cross-sectional study.

Subjects. A total of 1,006 patients with chronic musculoskeletal pain from a representative sample of primary care centers were evaluated.

Outcome Measures. Pain was measured using a visual analog scale and the Primary Care Evaluation of Mental Disorders questionnaire was used to measure mood disorders.

Results. We observed a high prevalence of undiagnosed mood disorders in chronic musculoskeletal pain patients (74.7%, 95% confidence interval [CI] 71.9–77.4%), with greater comorbidity in women (adjusted odds ratio [OR] = 1.91, 95% CI 1.37–2.66%) and widow(er)s (adjusted OR = 1.87, 95% CI 1.19–2.91%). Both sleep disturbances (adjusted OR = 1.60, 95% CI 1.17–2.19%) and pain intensity (adjusted OR = 1.02, 95% CI 1.01–1.02%) displayed a direct relationship with mood disorders. Moreover, we found that chronic musculoskeletal pain patients with comorbid mood disorders availed of health care services more frequently than those without ($P < 0.001$).

Conclusions. The prevalence of undiagnosed mood disorders in patients with chronic musculoskeletal pain is very high in primary care settings. Our findings suggest that greater attention should be paid to this condition in general practice and that sleep disorders should be evaluated in greater detail to achieve accurate diagnoses and select the most appropriate treatment.

Key Words. Chronic Pain; Musculoskeletal; Primary Care; Sleep; Mood

Introduction

Chronic pain and depression are very frequently reported by patients attending primary care centers [1], and they

are often comorbid, with a prevalence ranging from 30% to 60% [2,3]. These comorbid conditions exert a greater negative impact on patient health than either condition alone [2,4], and they are associated with reduced quality of life [5,6], increased use of medical services [7,8], and dissatisfaction with health care providers [9]. Depression is frequently undiagnosed in primary care settings, particularly in patients suffering from chronic pain [10,11], and consequently, this condition is undertreated in these patients. Furthermore, the treatment of somatic complaints often takes precedence over the diagnosis and treatment of depression for primary care physician [12].

Musculoskeletal disease is one of the most common causes of severe long-term disability and protracted chronic pain in industrialized societies [13,14]. These pathologies have a particularly high prevalence, and they account for up to 20% of primary health care consultations [15,16]. While a link between chronic musculoskeletal pain and depression has been reported [11,17], most studies have focused on major depressive disorder (MDD) with only a few studies addressing other mood disorders such as minor depression, dysthymia, or bipolar disorder, all of which are defined as mood disorders in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV). Moreover, few studies have used specific structured interviews to evaluate these conditions in a primary care setting, and to the best of our knowledge, undiagnosed depression has not been previously evaluated in patients with chronic pain caused by musculoskeletal disease.

Most patients with chronic musculoskeletal pain report poor quality sleep, and a mutually deleterious relationship between pain and sleep disorders has been proposed. However, this relationship remains poorly understood and has only been characterized in patients with chronic widespread pain and fibromyalgia [17–19]. Using structured interviews, we investigated the prevalence of undiagnosed mood disorders in patients with chronic musculoskeletal pain in a primary care setting, and we evaluated the occurrence of sleep disorders in these patients. In addition, we identified other factors that may be associated with mood disorders, and we compared the use of health care services by chronic musculoskeletal pain patients with and without comorbid mood disorders.

Methods

Study Design and Sampling Process.

This cross-sectional study was carried out in primary care centers in Spain between April and December 2006, as part of a broader study [20]. To obtain a representative sample, the number of primary care centers chosen in each Spanish region was proportional to their number of inhabitants. In each primary care center, we selected one general practitioner (GP), who participated voluntarily, resulting in a final sample of 600 GPs.

The study was carried out in accordance with the Helsinki Declaration using standard working procedures and protocols, and it was approved by the Clinical Research Ethics Committee at the Clinical and Provincial Hospital in Barcelona, ensuring adherence to the norms of good clinical practice.

Patient Population

The patients participating were men and women over 18 years of age who had attended their Primary Care Center due to musculoskeletal pain that had lasted for at least 6 weeks and who had not previously been diagnosed with any mood disorder. All participants were required to be mentally and physically able to participate in the study, and they provided written informed consent in advance. A total of 1,006 patients fulfilled the earlier requirements.

Measurements

Interviews were conducted at local primary care facilities by GPs who received written guidelines on the data collection procedure. Using a structured questionnaire and the patient's medical records, we gathered data on sociodemographic variables (age, sex, educational level, marital status), clinical variables (cause, duration and intensity of pain, location of pain, interference with daily activities due to pain, treatment such as analgesic and/or psychotropic medication, quality and duration of sleep), and the use of health care resources (number of visits to a doctor and/or hospital due to pain in the previous 6 weeks, pain-related diagnostic tests performed in the previous 6 weeks).

The intensity of pain was measured using a visual analog scale with a range of 0–100, with 0 corresponding to no pain and 100 to the worst pain possible [21]. The extent to which pain interfered with the ability to perform daily activities and the percentage of the day spent in pain during the previous week were also evaluated using scales of 0–100, with 0 corresponding to no disability/no pain and 100 corresponding to total disability/constant pain, respectively.

To detect and evaluate mood disorders, GPs administered the mood state module from the Spanish language version of the Primary Care Evaluation of Mental Disorders (PRIME-MD) questionnaire [22]. This questionnaire was designed by Spitzer and coworkers [23] to diagnose the most common mood disorders in a primary care setting, and it is based on the diagnostic criteria of the DSM-IV. The original version of the questionnaire consist of two components, the patient questionnaire and the clinician's evaluation guide. The PRIME-MD Clinician Evaluation Guide (CEG) is a structured form divided into five modules. The 17 questions in the mood module of this questionnaire allow the clinician to reach a diagnoses of depression according to DSM-IV-text revision. Although the initial questions in the CEG explore the symptoms experienced in the preceding 2 weeks, the algorithm also includes questions about the longitudinal course of symptoms that can aid reaching diagnoses such as dysthymia. The mood

disorders module of CEG used in the study has been shown to have excellent positive predictive value, with satisfactory specificity and sensitivity in terms of diagnosis [24].

In the study, all possible PRIME-MD diagnoses according to DSM-IV criteria were considered: MDD, minor depressive disorder, partial remission from an MDD, dysthymic disorder, bipolar disorder, and depression caused by a general medical condition, medication, or drugs.

Data collection forms were monitored centrally to check for missing data or inconsistencies, and corrected where necessary.

Statistical Analysis

For descriptive analysis, absolute frequencies were calculated for categorical variables, and central trend and dispersion measurements were used for quantitative variables. The prevalence (95% confidence interval [CI]) of undiagnosed mood disorders was calculated as the number of patients with an undiagnosed illness, as determined using the PRIME-MD questionnaire divided by the total number of patients screened using the questionnaire.

To identify factors associated with mood disorders, we used a logistic regression model in which the outcome variable was the presence or absence of mood disorders, and that included the following variables: sex, age, educational level, marital status, location of pain (neck, back, joints, extremities), number of pain locations, intensity of pain, duration of pain expressed as the proportion of each day during the previous week spent in pain, current treatment (non-steroidal anti-inflammatory drugs, analgesic opioids, anxiolytics/hypnotics, other psychotropics); and the quality and duration of sleep. Some interactions were also tested. The variables were selected based on the findings of the univariate analysis ($P < 0.05$) or their association with the dependent variables as described in the literature. The Hosmer–Lemeshow test was used to assess the goodness of fit of the model.

A bivariate analysis was performed to assess the differences between subjects with and without mood disorders and to determine the differences in the use of health care resources between both groups of patients.

Analyses were performed using SPSS Statistics v.17 (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of the Study Sample

Of the 1,006 patients studied, 74.5% were women, with a mean age of 58 years (standard deviation [SD] = 12.7), and 66.2% lived with a partner, while 74.9% had completed primary or secondary education (Table 1). The main causes of pain were osteoarthritis (46.7%) and fibromyalgia (13.2%), although 6.5% of patients reported two or more causes of pain, most commonly osteoarthritis with osteoporosis (44.6%), followed by osteoarthritis with fibromyalgia (36.9%) (Figure 1). The mean duration of pain was 37.6 (SD = 50.1) months, with 96.5% of the patients suffering pain for ≥3 months. The mean intensity of pain was 59 (SD = 19.8), and the average number of pain locations was 3.6 (SD = 1.3), the most common of which was the back (80.5%) (Table 2). The mean inability to perform daily activities was 56.8 (SD = 23.3), and the mean percentage of each day of the previous week spent in pain was 59.4 (SD = 23.3). In addition, 74.9% of patients (N = 1,002) reported sleep disturbances due to pain, while 53.7% (N = 998) reported being awoken by pain (Table 3). Of all the patients studied, 88.8% took some type of analgesic medication (Table 2).

Table 1 Sociodemographic characteristics of the study sample

Variables	N	%
Gender	(N = 974)	
Male	248	25.5
Female	726	74.5
Age	(N = 862)	
<40	69	8
40–49	150	17.4
50–59	257	29.8
60–69	220	25.5
70+	166	19.3
Marital status	(N = 973)	
Living with partner	644	66.2
Divorced/separated	91	9.4
Single	52	5.3
Widow(er)	186	19.1
Education level	(N = 1,002)	
No studies	148	14.8
Primary studies	532	53.1
Secondary studies	218	21.8
University studies	104	10.4

Prevalence of Mood Disorders and Associated Factors

The prevalence of undiagnosed depression was 74.7% (95% CI 71.9–77.4%), and this was higher in women, in patients under 40 years of age, and in patients affected by fibromyalgia, neck or back pain, and osteoarthritis (Table 4). The most common mood disorder was major depression (49.21%), followed by dysthymia (17.39%) and minor depression (17.19%) (Figure 2).

Some important differences were observed between subjects with and without comorbid mood disorders in terms of almost all the variables analyzed, with patients with mood disorders recording more intense pain, more pain sites, more problems in performing daily activities, more time in pain, and more frequent sleep disturbances (Table 2).

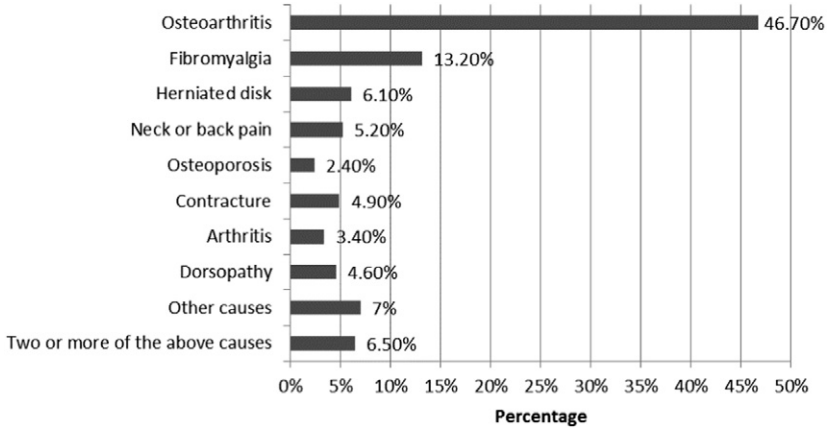

Figure 1 Causes of chronic musculoskeletal pain.

Table 2 Characteristics of chronic musculoskeletal pain and treatment: comparison between subjects with and without comorbid mood disorders

	Total		Without MD		With MD		
Variable	N	%	N	%	N	%	*P*
Duration of pain (months)	(N = 481)		(N = 118)		(N = 363)		0.863‡
1.5–3 months	17	3.5	5	4.2	12	3.3	
3–6 months	86	17.9	20	16.9	66	18.2	
>6 months	378	78.6	93	78.8	285	78.5	
Mean (SD)	37.6 (50.1)		47 (58.1)		34.5 (46.9)		0.027§
Median (P25, P75)	17 (7, 52.5)		22 (8.8, 78.5)		15 (7, 45)		
Intensity of pain (VAS)	(N = 1,006)		(N = 255)		(N = 751)		<0.001§
Mean (SD)	59 (19.8)		53.5 (21.4)		60.8 (18.9)		
Number of pain locations	(N = 955)		(N = 232)		(N = 723)		<0.001‡
1	67	7	28	12.1	39	5.4	
2	162	17	62	26.7	100	13.8	
3 or more	726	76	142	61.2	584	80.8	
Mean (SD)	3.6 (1.3)		3.2 (1.4)		3.7 (1.2)		<0.001§
Location of pain*	(N = 955)		(N = 232)		(N = 723)		
Neck	716	75.0	146	62.9	570	78.8	<0.001§
Back	769	80.5	159	68.5	610	84.4	<0.001§
Joints	703	73.6	151	65.1	552	76.3	0.001§
Extremities	649	68.0	151	65.1	498	68.9	0.282§
Current treatment†	(N = 437)		(N = 111)		(N = 326)		
Analgesics	388	88.8	107	96.4	281	86.2	0.003§
NSAIDs	360	82.4	102	91.9	258	79.1	0.002§
Opioids	84	19.2	17	15.3	67	20.6	0.227§
Psychotropics	216	49.4	42	37.8	174	53.4	0.005§
Anyiolytics/hypnotics	167	38.2	37	33.3	130	39.9	0.221§
Antidepressants, antipsychotics, and mood stabilizers	81	18.5	8	7.2	73	22.4	<0.001§

* May be more than one location; † May be more than one treatment type; ‡ Chi-square test; § Mann-Whitney *U* test.
MD = mood disorders; NSAID = non-steroidal anti-inflammatory drug; SD = standard deviation; P25 = 25th percentile; P75 = 75th percentile; VAS = visual analog scale.

Table 3 Impact of pain on daily activities

	Total		Without MD		With MD		*P*
Variable	n	%	n	%	n	%	
Daily activities interferences due to pain	(N = 1,006)		(N = 255)		(N = 751)		
Mean (SD)	56.8 (23.3)		48.4 (23.6)		59.7 (22.5)		<0.001*
Duration (% of day in pain in the last week)	(N = 1,006)		(N = 255)		(N = 751)		
Mean (SD)	59.4 (23.3)		51.3 (25.1)		62.2 (22.0)		<0.001*
Loss of sleep due to pain							
Yes	1,002	74.9	253	64.4	749	78.4	<0.001†
Awoken due to pain							
Yes	998	53.7	252	42.5	746	57.5	<0.001†

* Mann-Whitney *U* test; † Chi-square test.
MD = mood disorders; SD = standard deviation.

The factors positively associated with the presence of mood disorders were: being female (odds ratio [OR] = 1.91), being a widow(er) (OR = 1.87), being awoken due to pain (OR = 1.60), and experiencing a greater intensity of pain (OR = 1.02) (Table 5).

The Use of Health Services by Patients with Musculoskeletal Pain

Significant differences between patients with and without comorbid mood disorders were only detected for the number of visits made to primary care physicians ($P < 0.001$) (Table 6).

Table 4 Prevalence (95% confidence interval [CI]) of mood disorders according to gender, age, and cause of pain

	N	Prevalence	95% CI
Global	1,006	74.7	(71.9–77.4)
Gender			
Male	248	62.5	(56.3–68.7)
Female	726	78.7	(75.6–81.7)
Age			
<40	69	82.6	(72.9–92.3)
40–49	150	75.3	(68.1–82.6)
50–59	257	71.2	(65.4–76.9)
60–69	220	76.4	(70.5–82.2)
70+	166	72.9	(65.8–79.9)
Cause of pain			
Osteoarthritis	470	75.1	(71.1–79.1)
Fibromyalgia	133	88.7	(83.0–94.5)
Herniated disk	61	65.6	(52.8–78.3)
Neck or back pain	52	78.8	(66.8–90.9)
Osteoporosis	25	72	(52.4–91.6)
Contracture	49	67.3	(53.2–81.5)
Arthritis	35	57.1	(39.3–75.0)
Dorsopathy	46	69.6	(55.2–83.9)
Other causes	70	62.9	(50.8–74.9)
Two or more of the above causes	65	80	(69.5–90.5)

Discussion

The most important finding of the present study was the very high prevalence of undiagnosed mood disorders, not only MDD, in patients with chronic musculoskeletal pain. Factors associated with the presence of comorbid mood disorder included female gender, being a widow(er), high intensity pain, and sleep disruption due to pain.

The estimates available of comorbid depression in patients suffering pain are highly variable ranging from 1.5% to 60% [2]. A study of older patients with musculoskeletal pain reported a prevalence of comorbid depression of 35% [11], while symptoms of moderate depression were reported in 19% of osteoarthritis patients [25]. Similarly, prevalences of depression above 25% were found in osteoarthritis patients [26,27], and the lifetime comorbidity of mood disorders was reported to be 59.9% in patients with fibromyalgia [19]. These results are consistent, although lower than those observed in our study, where patients with fibromyalgia showed 88.7% comorbidity.

The wide variation in these results may be due to differences in the sample populations analyzed, the methodologies employed and the instruments used to evaluate mood disorders.

We assessed the presence of multiple forms of depression, some of which are less symptomatic than major depression, and hence, they are more difficult for a GP to detect [28]. This difficulty can lead to an underestimation of the prevalence of comorbid mood disorders in pain patients and may contribute to the differences between our findings and those of previous studies.

Comorbid mood disorders were more prevalent in female patients in agreement with previous studies in which female gender was identified as a predictor of depression after a 2-year follow-up in subjects with no depression at

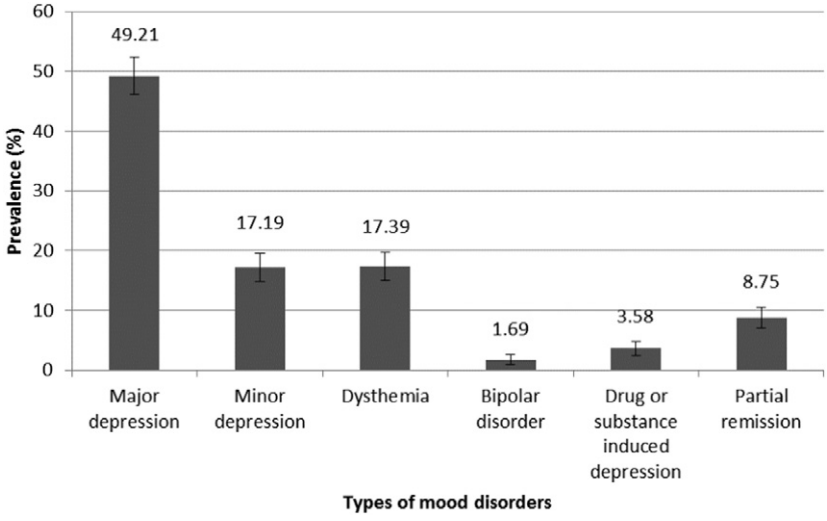

Figure 2 Prevalence of each type of mood disorders.

baseline [29]. While differences in the reporting of pain between women and men are partly attributable to social conditioning and psychosocial factors, such as pain beliefs, coping, and self-efficacy [30], several studies suggest that biological mechanisms may also contribute to this situation [31]. An analysis of sex differences in pain-related disability among patients with musculoskeletal pain demonstrated that women report greater pain intensity and pain-related disability than men, even after controlling for depression, anxiety, and other psychological variables such as self-efficacy [30]. It is plausible that biological and psychosocial influences may predispose males and females to different coping strategies, and indeed, women report a higher degree of catastrophizing than men [32,33]. In a review of pain-related sex differences, substantial differences in clinical and experimental pain responses were reported, and the potential underlying mechanisms were discussed, implicating gonadal hormones, endogenous pain modulatory systems, gender roles, and cognitive/affective factors [34].

Table 5 Binary logistic regression model for the presence of mood disorders in patients with chronic musculoskeletal pain (N = 411)

Variables	B	OR	*P*	95% CI
Sex				
Male*				
Female	0.65	1.91	<0.001	(1.37–2.66)
Marital status				
Living with partner*				
Divorced/separated	0.52	1.68	0.088	(0.93–3.09)
Single	–0.15	0.86	0.652	(0.44–1.67)
Widow(er)	0.62	1.87	0.006	(1.19–2.91)
Awoken due to pain				
No*				
Yes	0.47	1.60	0.003	(1.17–2.19)
Intensity of pain	0.02	1.02	<0.001	(1.01–1.02)

* Reference category.
Hosmer-Lemeshow: $\chi^2 = 4.714$; d.f. = 8; $P = 0.788$.
Dependent variable: Presence of mood disorders.

We found that pain intensity was associated with the presence of comorbid mood disorders, although no such association was detected for the number of pain locations, consistent with previous reports [35]. However, these observations differ from those of Gureje and coworkers, who failed to report an association between the intensity of pain and the severity of depression, but observed a relationship between the number of pain sites and the presence of comorbid mood disorders [36]. It should be noted, however, that the latter study analyzed the general population and not primary care patients.

Comorbid depression in pain patients contributes significantly to poorer outcomes and increased cost of treatment, highlighting the need for a greater understanding of the relationship between pain and depression.

It has been suggested that there are certain connections between depression and chronic pain, as endorsed in several preclinical and clinical studies [37,38]. In fact, the main noradrenergic and serotonergic nuclei in the central nervous system, the locus coeruleus and the dorsal raphe magnus, respectively, are closely associated to the neurobiological mechanisms responsible for the chronicity of pain and the provocation of mood disorders, particularly depression [39,40].

In addition, it is well known that antidepressants that enhance the availability of noradrenaline and serotonin at the level of the synaptic cleft have demonstrated analgesic properties, as well as antidepressant activity [41–44].

Table 6 The use of health services by chronic musculoskeletal pain patients with and without comorbid mood disorders

Variables	Total	Without MD	With MD	*P**
Number of visits to the GP due to pain in the last 6 weeks.	N = 927	N = 224	N = 703	
Mean (SD)	3.20 (1.98)	2.75 (2.26)	3.35 (1.86)	<0.001
Median (P25; P75)	3.0 (2.0; 4.0)	2.0 (2.0; 3.0)	3.0 (2.0; 4.0)	
Number of visits to a specialist due to pain in the last 6 weeks	N = 447	N = 87	N = 360	
Mean (SD)	1.18 (1.38)	1.15 (1.66)	1.19 (1.31)	0.280
Median (P25; P75)	1.0 (1.0; 1.0)	1.0 (1.0; 1.0)	1.0 (1.0; 1.0)	
Number of diagnostic tests for pain in the last 6 weeks	N = 513	N = 117	N = 396	
Mean (SD)	1.49 (1.04)	1.48 (1.21)	1.49 (0.98)	0.602
Median (P25; P75)	1.0 (1.0; 2.0)	1.0 (1.0; 2.0)	1.0 (1.0; 2.0)	
Number of hospitalizations due to pain in the last year.	N = 199	N = 43	N = 156	
Mean (SD)	0.45 (1.03)	0.26 (0.49)	0.51 (1.13)	0.306
Median (P25; P75)	0.0 (0.0; 1.0)	0.0 (0.0; 0.0)	0.0 (0.0; 1.0)	

* Wilcoxon Test.
MD = mood disorders; SD = standard deviation; P25 = 25th percentile; P75 = 75th percentile.

Furthermore, pain modulation is impaired in depressed patients [45,46] probably due to enhanced emotionality, as measured by neuroimanging techniques [46–48].

The link between sleep disturbances and chronic pain described here may have been overestimated due to self-reporting. However, this link is supported by several studies proposing a reciprocal relationship between these phenomena [18,49]. Chronic pain is also associated with a greater number of insomnia symptoms, more severe daytime consequences, and increased chronicity of insomnia [50]. A recent review proposed that sleep disturbances and sleep restrictions result in musculoskeletal pain and increased sensitivity to noxious stimuli [51], while clinical and epidemiological studies have demonstrated a direct influence of sleep disturbances on musculoskeletal pain, fatigue, mood, and overall well-being. Moreover, the relationship between the brain sleep-wake cycle, and cytokine and cellular immune functions, has important implications for the understanding of rheumatic disease pathology and its management with anti-rheumatic drugs.

We found that comorbid mood disorders and pain are associated with increased use of health care resources, particularly primary care consultations. This could be explained by the mood disorder reducing the pain threshold and tolerance, increasing the risk of persistent long-term pain and producing less pain relief through medication [52]. Accordingly, many GPs regard depression and anxiety as the most significant and problematic complications when treating patients with chronic pain [53].

Several limitations of the present study should be borne in mind when considering our findings. First, we did not assess the coincidence of other chronic medical or psychiatric conditions, such as anxiety, which are frequently associated with depression and often prevalent among chronic pain patients [54,55]. Indeed, an association between pain, anxiety, and depression has been reported [55], and the probability of suffering chronic or multiple pain increases in cases of comorbid depression and anxiety, when compared with either condition alone. Second, our survey was conducted as a cross-sectional study and consequently provides no information regarding the direction of causality between chronic pain and mood disorders. Thus, we can only postulate as to how the association between pain and mood is established. Finally, the present study may involve a bias due to the lack of diagnostic confirmation by means of a larger structured psychiatric interview. Nonetheless, the PRIME-MD used is an instrument with tried and tested psychometric properties, and it has proven diagnostic validity in a primary care setting.

It should be noted that this study forms part of another larger study that included patients with pain that had been experienced for at least 6 weeks. Although this criterion does not adjust to the International Association for the Study of Pain (IASP) definition based on the persistence of pain for 12 weeks, it was used as 6 weeks was considered sufficient time to exclude patients with acute pain. In this sense, it should be noted that the criterion of duration is not the only factor that should be considered when defining chronic pain, as indicated by the American Society of Anesthesiologist's Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine [56]. Nevertheless, almost all the patients with pain in this study referred to a duration of pain for at least 3 months.

A key strength of the present study is that our results are based on a large dataset collected from a wide range of

primary care centers where GPs perform their usual clinical work. Furthermore, mood disorders were diagnosed using internationally validated criteria.

Conclusions

In conclusion, we observed a very high prevalence of undiagnosed mood disorders in chronic musculoskeletal pain patients that visit their primary care physician. Detection and treatment of depression and rigorous assessment of sleep disturbances may improve the health status of these patients, as well as providing further pain relief and decreasing the associated disease burden and health care costs.

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