Journal of Psychosomatic Research 203 (2026) 112549

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

journal homepage: www.elsevier.com/locate/jpsychores

Comorbid DSM-5 mental disorders and chronic pain: What kind of relationship? Findings from the P3 cross-sectional study

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ARTICLE INFO

Keywords:
Chronic pain
Mental disorder
Comorbidity
Psychopathology
Depression

ABSTRACT

Purpose: Mental disorders and chronic pain frequently co-occur. The prevalence of this comorbidity varies widely across investigations and is certainly overestimated using screening self-reports. The main aim of this cross-sectional research was to calculate prevalence rates of mental disorders in a chronic pain population during their first consultation in an Italian specialized pain clinic using the narrow diagnostic criteria of the DSM-5. Additionally, we examined the relationship between this psychiatric comorbidity and a broad range of socio-demographic and clinical parameters related to chronic pain.

Procedures: 174 participants were enrolled in the Pain Therapy Service at the Parma University Hospital. They completed the Structured Clinical Interview for DSM-5 mental disorders (SCID-5) and the Brief Pain Inventory (BPI). Associations between psychiatric comorbidity and other parameters were explored using regression analyses.

Main findings: 57 (32.7%) subjects with chronic pain had DSM-5 psychiatric comorbidity, particularly major depression and anxiety disorders. This comorbid psychopathology showed significant associations with BPI pain severity and interference scores, as well as with the presence of widespread chronic pain (including fibromyalgia) and the prescription of anti-neuropathic medication at entry. Notably, only a minority ($n = 18$; 31.6%) of these participants with current comorbid mental disorders were treated in psychiatric services.

Conclusions: A large portion of chronic pain patients with comorbid psychiatric syndromes remain undiagnosed and undertreated. The presence of mental health operators in multidisciplinary chronic pain teams is justified and recommended.

1. Introduction

Mental disorders and chronic pain severely impact the physical and psychological well-being and quality of life of many patients and are responsible for the combined loss of work productivity and income, as well as for increases direct medical expenses, each year [1]. Moreover, these disabling conditions frequently co-occur, with a considerable variance in comorbid prevalence ranging from 10% to 100% [2]. This epidemiological variability is mainly due to different methods in identifying mental disorders, with some investigations using clinical interviews based on standardized classification systems while others administering self-reported screening tools [3]. Indeed, self-reports may overestimate some psychopathological characteristics (e.g., anxiety and depression), without necessarily meeting the diagnostic criteria for a manifest psychiatric category. Additionally, most studies investigating this comorbidity frequently involved patients in specialized care pain services, who generally experienced the most severe pain intensity and/or disability, resulting in a potential overestimation of psychopathology [4].

However, more specific detection of comorbid mental disorders in chronic pain, especially through the lens of international classification systems, may help implement intervention strategies aimed at improving clinical outcomes and treatment response. Psychopathological comorbidity has been found to be associated with pain persistence

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https://doi.org/10.1016/j.jpsychores.2026.112549
Received 30 October 2025; Received in revised form 7 January 2026; Accepted 19 January 2026
Available online 29 January 2026

and diminished pain relief [5]. Because psychiatric symptoms (particularly anxiety and depression) are readily accessible to pharmacological treatments and psychotherapy, improved pain management and prognosis are now more achievable goals, especially when comorbid mental suffering is detected and treated early [6]. Conversely, failing to correctly diagnose patients with ongoing psychiatric illnesses increases the risk of ineffective pain management and poor long-term outcomes. In this regard, a close biological relationship between chronic pain and specific neuroplastic/psychological phenomena has historically been hypothesized and explored. Although a mechanistic explanation is still lacking [7], some pathophysiologic processes in which the central nervous system undergoes changes that alter pain processing and induce maladaptive compensation to aberrant sensory predictive processing (such as central sensitization and predictive processing) have been presented as potentially causing chronic pain [8,9].

Given the inconsistent assessment methods for identifying psychiatric disorders across studies and the relatively limited research using current diagnostic criteria from international classification systems (such as the DSM-5 [Diagnostic and Statistical Manual of mental disorders, 5th Edition]) [10], the main aims of this investigation were: (a) to calculate the prevalence rate of DSM-5-TR mental disorders in a sample of adults with chronic pain during their first consultation at a specialized pain service in Italy, and (b) to explore any relevant associations of this psychiatric comorbidity with a broad range of socio-demographic and clinical pain parameters in the entire population. To our knowledge, this is the first Italian study to examine the clinical relationship of comorbid psychopathology in chronic pain patients and to analyze the need for psychopathological knowledge among physicians treating this disabling condition. In our opinion, the permanent presence of mental health professionals in multidisciplinary chronic pain teams is absolutely justified and desirable, particularly to provide personalized case formulation, to detect concomitant morbidity, and to offer psychopharmacological and/or psychosocial interventions in the treatment of pain syndromes [11].

2. Methods

2.1. Subjects and setting

The sample included adults with chronic pain who visited the Pain Therapy Service (PTS) of the University Hospital of Parma (Northern Italy) between 1 June 2023 and 31 December 2024 for their first specialist consultation as cross-sectional part of the P3 study, a non-pharmacological observational cohort research aimed at investigating the clinical relationships among psychopathology, personality, and pain [12]. Specifically, the Parma PTS is a "hub" clinic offering intensive and highly specialized treatments for chronic pain, serving the entire northern Emilia-Romagna Region: it provides both outpatient and day hospital services [13]. Typically, patients were referred to the PTS by their primary care physicians or other specialists, including professionals working in the "spokes" centers of the area.

Inclusion criteria of this investigation were: (a) age 18–60 years, and (b) first consultation for chronic pain at the Parma PTS. Exclusion criteria were: (a) inability to give a valid informed consent for participation in the study, including known intellectual disability (I.Q. < 70), and (b) not being fluent in Italian language.

All participants gave written informed consent for the inclusion in the research. The participation was voluntary based. Local ethical approvals were obtained for the study (AVEN Ethics Committee protocol no. 20841/2023). This investigation was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments.

2.2. Instruments

In the total sample, any psychiatric diagnoses at entry were formulated by a trained psychiatrist with over 20 years of clinical experience according to the DSM-5 criteria using the Structured Clinical Interview for DSM-5 mental disorders, Clinical Version (SCID-5-CV) [14]. For all participants, the clinical assessment included the "Brief Pain Inventory – short form" (BPI) [15] and the "Twenty-item Toronto Alexithymia Scale" (TAS-20) [16].

The BPI is a 9-item self-reported questionnaire developed to rapidly assess the clinical severity of current pain and its impact on daily functioning. In detail, four specific items related to *pain severity* evaluate the most severe pain in the last 24 h, the mildest pain in the last 24 h, the average pain in the last 24 h, and the current pain. They are rated on a 10-point Likert scale (from 0 = "no pain" to 10 = "the worst pain imaginable"). Moreover, a composite pain severity score ("BPI mean severity score") is calculated as the mean of the subscores of these four items. An additional item regarding the percentage of pain relief obtained by analgesics is also rated on a 10-point Likert scale (from 0 = "no relief" to 10 = "complete relief"). Furthermore, seven specific BPI items related to *pain interference* assess its impact on daily activities and emotions (i.e., general activity, walking, work, mood, enjoyment of life, social relationships, and sleep). They are analogously rated on a 10-point Likert scale (from 0 = "does not interfere" to 10 = "completely interferes"). A BPI pain interference composite score is also calculated as the average of the subscores of these seven items. In this research, we used the Italian version of the BPI, showing good psychometric properties in Italian adults with chronic pain [17].

The TAS-20 is widely used, self-reported instrument specifically developed to measure alexithymia. It is composed of 20 items rating on a 5-point Likert scale (from 1 = "strongly disagree" to 5 = "strongly agree"). A total score is calculated as the sum of all 20 item subscores. The TAS-20 items can be clustered in 3 different cognitive domains: "Difficulty in Identifying Feelings (DIF), "Difficulty in Describing Feelings" (DDF), and "Externally Oriented Thinking" (EOT) style. Individuals with a TAS-20 total score of $\geq$61 were considered as "alexithymic". In the current examination, we used the Italian version of the TAS-20 [18], showing good psychometric properties in adult clinical samples [19,20].

Finally, a sociodemographic/clinical schedule was also completed during the first consultation, capturing a broad range of sociodemographic and clinical parameters (i.e., gender, living status, marital status, employment, years of education, age at entry, family history of chronic pain, diagnosis of chronic pain, duration of chronic pain, medical comorbidity, and pain treatments).

2.3. Procedures

Chronic pain was defined in accordance with the International Association for the Study of Pain (IASP) as "any experiencing pain that persists or recurs for longer than 3 months" [21]. In all patients, psychiatric diagnoses were verified and formulated according to the DSM-5 criteria using the SCID-5-CV. Participants were then divided into two subgroups based on the presence or absence of a psychiatric comorbidity and compared on sociodemographic and clinical parameters. Finally, relevant associations between comorbid psychopathology and clinical variables in the total group were explored.

2.4. Statistical analysis

Data were imported into JASP statistical software (version 0.95.3 for Windows) for analysis [22]. There were no missing data. All tests were two-tailed with a significance level set at 0.05. Where appropriate, p values were corrected for multiple comparisons using the Bonferroni correction [23]. For categorical variables, frequencies and percentages were reported, while for continuous variables, mean and standard deviation were reported. In comparisons between groups, the Chi-squared (X^2) test or Fisher exact-test (where appropriate) was used for qualitative parameters, while the Mann-Whitney U test was used for quantitative parameters. Finally, associations between psychiatric comorbidity

and clinical variables in the total sample were explored using regression multiple linear or binary regression analyses.

3. Results

The study enrolled 174 adults with chronic pain (mean age = 47.02 years [standard deviation = 9.56 years], 115 [66%] females). Of them, 57 (33%) participants met the diagnostic criteria for a DSM-5 mental disorder (Fig. 1). The most common DSM-5 diagnoses were major depressive disorder ($n = 21$), anxiety disorder ($n = 12$), and somatoform disorder ($n = 8$). Psychotic disorder was reported in 5 cases, post-traumatic stress disorder (PTSD) in 4 cases, and substance use disorder in 3 cases. The sociodemographic and clinical features of the two subgroups are shown in Table 1.

Compared to patients who had no psychiatric comorbidity, participants with psychiatric comorbidity had higher prevalence rates of widespread pain (including fibromyalgia), family history of chronic pain, fixed-dose analgesic therapy, and anti-neuropathic pain drug prescription, as well as longer duration of chronic pain (Table 1). Conversely, they had lower prevalence rates of low back pain.

In comparison with participants who had no psychiatric comorbidity, patients with psychiatric comorbidity had a higher BPI mean severity score, as well as higher BPI item 3 ("Worst pain in the last 24 hours"), item 5 ("Average pain in the last 24 hours"), and item 6 ("Current pain") subscores (Table 2). They also showed a higher BPI mean interference score, as well as a higher subscore on each BPI interference item. Finally, participants with psychiatric comorbidity had a higher TAS-20 total score compared to individuals without psychiatric comorbidity, as well as higher TAS-20 DIF and DDF factor subscores (Table 2).

Our binary logistic regression results (Table 3) showed that psychiatric comorbidity was significantly associated with higher BPI mean interference score and TAS total score, as well as with the presence of widespread chronic pain. Moreover, the presence of widespread chronic pain was also significantly associated with female sex and higher TAS-20 total score. No relevant associations of psychiatric comorbidity with duration of chronic pain, family history of chronic pain, fixed-dose analgesic therapy, and anti-neuropathic medication prescription were observed. Finally, the presence of anti-neuropathic pain medication at entry was significantly associated with longer duration of chronic pain and the presence of widespread chronic pain.

Our linear regression analysis results (Table 4) showed that the presence of psychiatric comorbidity significantly predicted higher BPI mean pain severity score (together with female sex), higher BPI mean interference score (together with greater BPI mean severity score), and

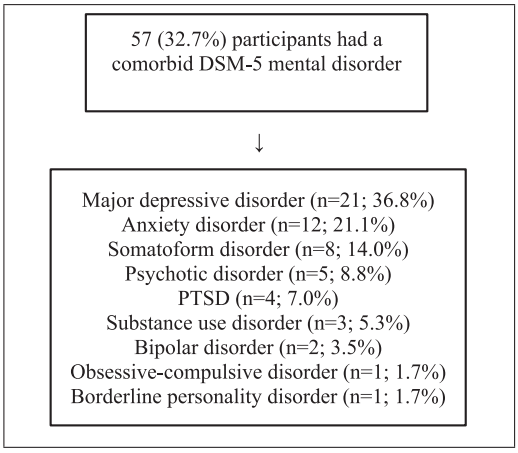

Fig. 1. Comorbid DSM-5 mental disorders in the total sample ($n = 174$).
Note. DSM-5 = Diagnostic and Statistical Manual of mental disorders, 5th Edition; PTSD = post-traumatic stress disorder.

Table 1
Sociodemographic and clinical features in the two subgroups.

Variables	Participants with psychiatric comorbidity ($n = 57$)	Participants without psychiatric comorbidity ($n = 117$)	X^2/U	p
Gender (females)	43 (75.4%)	72 (61.5%)	3.304	0.069
Age at entry (in years)	48.21 ± 9.68	46.44 ± 9.48	3807.500	0.069
Years of education	12.75 ± 3.22	12.73 ± 3.30	3339.000	0.129
Marital status			4.532	0.104
Single	19 (33.3%)	22 (18.8%)	[1.9]	
Married/with partner	31 (54.4%)	76 (64.9%)	[−1.3]	
Separated/divorced	7 (12.3%)	19 (16.2%)	[−0.7]	
Living status			3.062	0.382
Alone	11 (19.3%)	18 (15.4%)	[0.6]	
Living with partner	29 (50.9%)	75 (64.1%)	[−1.7]	
Living with parents	13 (22.8%)	17 (14.5%)	[1.3]	
Other cohabitation	4 (7.0%)	7 (6.0%)	[0.3]	
Employment status			3.026	0.220
Unemployed	11 (19.3%)	15 (12.8%)	[1.1]	
Student	2 (3.5%)	1 (0.8%)	[1.3]	
Employed	44 (77.2%)	101 (86.3%)	[−1.5]	
Nationality (Italian)	54 (94.7%)	107 (91.4%)	0.598	0.439
Migrant status	11 (19.3%)	24 (20.5%)	0.035	0.851
Family history of chronic pain	30 (52.6%)	42 (35.9%)	4.425	**0.035**
Duration of chronic pain (in months)	67.07 ± 80.92	53.48 ± 127.79	4119.000	**0.011**
Localization of chronic pain			23.598	**0.001**
Low back pain	20 (35.1%)	74 (63.3%)	**[−3.5]**	
Widespread pain	24 (42.1%)	15 (12.8%)	**[4.3]**	
Cervical pain	3 (5.3%)	8 (6.8%)	[−0.4]	
Upper arm pain	4 (7.0%)	5 (4.3%)	[0.8]	
Lower arm pain	6 (10.5%)	10 (8.5%)	[0.4]	
Head/facial pain	0 (0.0%)	3 (2.5%)	[−1.2]	
Visceral pain	0 (0.0%)	2 (1.7%)	[−1.0]	
ICD-11 diagnosis of chronic pain			0.309	0.578
Chronic primary pain	49 (85.9%)	104 (88.9%)	[−0.5]	
Chronic secondary pain	8 (14.0%)	13 (11.1%)	[0.5]	
Pharmacological treatment for chronic pain			11.200	**0.004**
Fixed-dose treatment	41 (71.9%)	55 (47.0%)	**[3.1]**	
Treatment as needed	14 (24.6%)	43 (36.7%)	[−1.6]	
No treatment	2 (3.5%)	19 (16.2%)	**[−2.4]**	
–			0.511	0.475
Monotherapy	27 (47.3%)	54 (46.1%)	[0.1]	
Polytherapy	28 (49.1%)	44 (37.6%)	[1.4]	
–			14.868	**0.002**
Opioid medication	20 (35.1%)	28 (23.9%)	[1.5]	
Non-steroidal anti-inflammatory medication	23 (40.3%)	62 (53.0%)	[−1.6]	
Anti-neurophatic pain medication	12 (21.0%)	8 (6.8%)	**[2.7]**	
Non-pharmacological treatment for chronic pain	9 (16.1%)	23 (19.6%)	0.323	0.570

(continued on next page)

Table 1 (*continued*)

Variables	Participants with psychiatric comorbidity (*n* = 57)	Participants without psychiatric comorbidity (*n* = 117)	X^2/U	p
Medical comorbidity	32 (56.1%)	51 (43.6%)	2.420	0.120

Note. Frequencies (and percentages), mean (±standard deviation), Chi-square test (X^2) and Mann-Whitney test (U) values are reported. Adjusted residuals for the subgroup with psychiatric comorbidity are in square brackets. Statistically significant *p* values and adjusted residuals are in bold. Bonferroni corrected *p* values are reported (where applicable).

higher TAS-20 total score (together with the presence of widespread chronic pain). No relevant relationship between psychiatric comorbidity and duration of chronic pain was found.

4. Discussion

Psychiatric comorbidity has long been considered one of the most relevant predictors of a poor prognosis in chronic pain [24]. However, considerable variance in its prevalence rate has been observed, due to inconsistent assessment methods across studies [2]. Indeed, self-reported screening measures have frequently been used, with the risk of overestimating specific psychopathological features (e.g., anxious-depressive symptoms, somatization), without necessarily meeting the diagnostic criteria for a manifest psychiatric category included in international classification systems [25]. The relationship between mental disorders and chronic pain has not been systematically studied using current international psychiatric nosography and thus remains largely debatable [26]. The primary aim of this research was therefore to examine comorbid psychopathology using current DSM-5 diagnostic criteria.

Approximately one-third (33%) of our participants met DSM-5 diagnostic criteria for a comorbid mental disorder at entry, specifically major depressive disorder (13%) and anxiety disorders (9%, including PTSD). These findings are lower than what were reported in previous research (i.e., 30–54% for depression, 20–70% for anxiety) [27–29]. Even considering differences in research design, assessment measures, and sampling characteristics across studies, this supports the need to refer to international classification systems for the diagnosis of psychiatric illnesses, particularly to avoid overestimation of subthreshold symptoms and the risk of overpathologizing psychological distress [30]. However, our investigation included only patients voluntarily recruited from the Parma PTS, who may be particularly sensitive to describing their psychological suffering. At the same time, it was also possible that some participants with mental disorders intentionally avoided assessment due to stigma and/or shame. As both factors can influence (underestimate or further overestimate) the true prevalence of psychiatric illness, future research using the most accepted international nosography on larger chronic pain samples is needed. However, it should also be mentioned that the highest prevalence of mental disorders in chronic pain was reported in specialist pain clinics [31].

Notably, only 18 (32%) of our participants with a current DSM-5 mental disorder were previously treated in psychiatric services. This highlights that a significant portion (*n* = 39; 68%) of chronic pain patients likely do not receive adequate (specialized) treatments for their psychopathology (including psychotherapy) [32], as indicated by the percentage of them (*n* = 18; 46%) who were taking psychopharmacological therapy not prescribed by psychiatrists. Therefore, it is worth noting that there is a relevant proportion of individuals with chronic pain who likely have undiagnosed mental disorders and are treated by professionals other than mental healthcare specialists (such as general practitioners) [33]. Including psychiatrists and/or clinical psychologists in multidisciplinary teams for chronic pain could fill this gap, favor appropriate mental health treatments, and improve prognosis and quality of life.

Table 2
BPI and TAS-20 score comparisons between the two subgroups.

BPI scores	Participants with psychiatric comorbidity (n = 57)	Participants without psychiatric comorbidity (n = 117)	U	p
BPI Pain items				
BPI-3: Worst pain in the last 24 h	7.96 ± 1.61	6.97 ± 2.16	4259.500	**0.003**
BPI-4: Least pain in the last 24 h	5.10 ± 2.42	4.37 ± 2.37	3915.000	0.061
BPI-5: Average pain in the last 24 h	7.05 ± 1.60	5.82 ± 2.13	4447.000	**0.001**
BPI-6: Current pain	7.02 ± 2.06	5.26 ± 2.54	4663.000	**0.001**
Mean severity score	6.78 ± 1.55	5.61 ± 2.03	4423.500	**0.001**
BPI-8: Percentage of pain relief in the last 24 h	34.21 ± 28.84	37.35 ± 26.97	3089.000	0.427
BPI Interference items				
BPI-9 A: General activity	8.26 ± 1.82	7.03 ± 2.67	4241.000	**0.003**
BPI-9B: Mood	7.81 ± 2.80	6.70 ± 2.97	4234.000	**0.003**
BPI-9C: Walking ability	7.23 ± 2.88	5.43 ± 3.19	4511.500	**0.001**
BPI-9D: Normal work (including homework)	8.21 ± 2.63	6.83 ± 2.86	4361.500	**0.001**
BPI-9E: Social relationships	6.91 ± 3.10	4.82 ± 3.41	4600.000	**0.001**
BPI-9F: Sleep	8.00 ± 2.57	6.04 ± 3.24	4670.000	**0.001**
BPI-9G: Enjoyment of life	7.51 ± 2.96	5.33 ± 3.64	4568.500	**0.001**
Mean interference score	7.70 ± 1.78	6.03 ± 2.33	4757.000	**0.001**
TAS-20				
Difficulty in identifying feelings (DIF)	20.26 ± 7.76	13.20 ± 5.84	5140.500	**0.001**
Difficulty in describing feelings (DDF)	14.51 ± 5.06	12.27 ± 4.32	4229.000	**0.004**
Externally oriented thinking (EOT)	23.17 ± 6.40	22.54 ± 6.12	3527.000	0.538
TAS-20 total score	57.95 ± 13.66	48.06 ± 10.87	4731.500	**0.001**

Note. BPI = Brief Pain Inventory; TAS-20 = Toronto Alexithymia Scale-20 items. Frequencies (and percentages), mean ± standard deviation, and Mann-Whitney test (U) values are reported. Statistically significant p values are in bold.

The results of this study further supported the strong association between comorbid psychopathology and some unfavorable clinical aspects of chronic pain, particularly with higher current severity levels, greater current interference with daily activities, and greater likelihood of being prescribed fixed-dose analgesics. Furthermore, intergroup comparisons highlighted a longer duration of pain in patients with comorbid mental disorders. Psychiatric comorbidity confirms its role as an indicator of chronic pain severity at first contact with specialist clinics [34]. However, interesting questions remain open. In this regard, common neurobiological mechanisms (e.g., inflammatory response) have

Table 3
Binary logistic regression analyses in the total sample (n = 174).

Variables	Estimate	SE	OR	p	95% CI for OR	
					Lower	Upper
Intercept	0.746	0.164	2.109	**0.001**	1.530	2.907
Familiarity with chronic pain	0.712	0.426	2.037	0.088	0.884	4.695
Gender (females)	0.203	0.491	1.225	0.679	0.468	3.206
Age at entry (in years)	0.024	0.024	1.034	0.311	0.977	1.068
Marital status (single)	0.429	0.533	1.535	0.421	0.540	4.367
Living status (alone)	−0.090	0.635	0.913	0.887	0.263	3.171
Educational level (in years)	−0.036	0.064	0.965	0.575	0.851	1.094
Widespread chronic pain	1.070	0.516	2.961	**0.038**	1.060	8.023
Duration of chronic pain (in months)	0.001	0.002	1.001	0.690	0.997	1.004
Medical comorbidity	0.320	0.420	1.377	0.447	0.604	3.138
BPI mean severity score	0.100	0.133	1.095	0.454	0.835	1.403
BPI mean interference score	0.390	0.120	1.333	**0.001**	1.144	1.474
TAS total score	0.058	0.017	1.067	**0.001**	1.034	1.088
Dependent parameter: *Psychiatric comorbidity*; $X^2 = 56.021$; df = 158; $p =$ **0.001**; Negelkerke $R^2 = 0.450$; Cox & Snell $R^2 = 0.291$.						

Variables	Estimate	SE	OR	p	95% CI for OR	
					Lower	Upper
Intercept	11.075	0.186	3.266	**0.006**	2.517	5.212
Psychiatric comorbidity	1.054	0.538	2.870	**0.046**	1.000	8.234
Covariates						
Gender (females)	3.261	1.096	1.962	**0.003**	1.671	1.996
Age at entry (in years)	0.057	0.030	1.055	0.061	0.997	1.102
Marital status (single)	1.090	0.612	2.947	0.070	0.896	9.987
Living status (alone)	0.130	0.677	1.122	0.846	0.002	1.767
Educational level (in years)	−0.033	0.077	0.034	0.665	0.021	1.172
Unemployment	0.029	0.632	1.030	0.963	0.298	3.551
Familiarity with chronic pain	−0.620	0.514	0.538	0.228	0.196	1.474
Duration of chronic pain (in months)	0.002	0.002	1.002	0.168	0.999	1.006
Fixed-dose treatment for chronic pain	0.585	0.515	1.795	0.256	0.654	4.930
Medical comorbidity	−0.037	0.490	0.963	0.939	0.369	2.516
BPI mean severity score	0.094	0.156	1.089	0.548	0.236	1.329
BPI mean interference score	−0.055	0.132	0.944	0.678	0.368	1.186
TAS total score	0.048	0.077	1.047	**0.015**	1.009	1.083
Dependent parameter: *Widespread chronic pain*; $X^2 = 58.896$; df = 157; p = **0.001**; Negelkerke $R^2 = 0.448$; Cox & Snell $R^2 = 0.291$.						

Variables	Estimate	SE	OR	p	95% CI for OR	
					Lower	Upper
Intercept	3.740	2.598	1.976	0.150	0.000	2.000
Psychiatric comorbidity	0.810	0.418	2.248	0.053	0.990	5.105
Covariates						
Gender (males)	0.127	0.383	1.135	0.741	0.536	2.404
Age at entry (in years)	−0.009	0.019	0.991	0.660	0.952	1.031
Marital status (single)	0.552	0.446	1.737	0.216	0.724	4.165
Living status (alone)	−0.083	0.567	0.920	0.833	0.303	2.794
Educational level (in years)	−0.085	0.053	0.911	0.110	0.901	1.019
Unemployment	−0.136	0.501	0.873	0.786	0.327	2.331
Familiarity with chronic pain	−0.030	0.359	0.970	0.933	0.480	1.960
Duration of chronic pain (in months)	0.001	0.001	1.001	0.649	0.998	1.003
Medical comorbidity	−0.011	0.345	0.989	0.974	0.503	1.945
BPI mean severity score	0.096	0.108	1.089	0.376	0.977	1.323
BPI mean interference score	0.089	0.090	1.085	0.324	0.992	1.286
TAS total score	−0.017	0.015	0.983	0.238	0.953	1.011
Dependent parameter: *Fixed-dose treatment for chronic pain*; $X^2 = 19.732$; df = 156; $p =$ 0.146; Negelkerke $R^2 = 0.146$; Cox & Snell $R^2 = 0.109$.						

Variables	Estimate	SE	OR	p	95% CI for OR	
					Lower	Upper
Intercept	2.140	0.249	8.500	**0.001**	5.126	13.852
Psychiatric comorbidity	1.241	0.787	3.458	0.115	0.740	16.154
Covariates						
Gender (females)	0.074	0.787	1.031	0.932	0.001	1.838
Age at entry (in years)	−0.017	0.035	0.993	0.618	0.911	1.049
Marital status (single)	−0.178	0.797	0.837	0.823	0.176	3.988
Living status (alone)	−0.126	0.945	0.882	0.894	0.138	5.615
Educational level (in years)	0.035	0.108	1.034	0.745	0.807	1.228
Unemployment	−0.277	1.003	0.758	0.783	0.106	5.412
Familiarity with chronic pain	−1.042	0.731	0.353	0.154	0.084	1.479
Duration of chronic pain (in months)	−0.022	0.011	0.988	**0.042**	0.946	0.999
Widespread chronic pain	2.319	0.729	10.164	**0.001**	2.435	42.421
Medical comorbidity	−0.449	0.641	0.638	0.483	0.182	2.240
BPI mean severity score	−0.345	0.215	0.587	0.108	0.151	1.063
BPI mean interference score	0.309	0.162	1.276	0.057	0.991	1.475
TAS total score	0.001	0.027	1.001	0.985	0.946	1.052
Dependent parameter: *Anti-neurophatic pain medication*; $X^2 = 33.337$; df = 156; $p =$ **0.003**; Negelkerke $R^2 = 0.362$; Cox & Snell $R^2 = 0.177$.						

Note. BPI = Brief Pain Inventory; TAS = Toronto Alexithymia Scale; SE = Standard Error; OR = Odds Ratio; p = statistical significance; 95% CI = 95% Confidence Interval; X^2 = Chi-square value; df = degrees of freedom; R^2 = coefficient for goodness of fit of the statistical model. Statistically significant *p* values are in bold.

been proposed in pain and mental disorders (particularly depression) [35]. From this perspective, chronic pain and psychopathology are considered as comorbid clinical expressions of similar biological alterations, potentially responsive to similar treatments. This may be particularly true in the relevant relationships we further observed in this research between psychiatric illnesses and certain types of chronic pain (such as widespread chronic pain, including fibromyalgia) and in the replicated evidence that psychotropic medications (such as antidepressants) are effective in treating neuropathic pain [36]. Alternatively, considering the "diathesis-stress" model of mental disorders, a pre-existing psychiatric vulnerability could be exacerbated by the stress associated with prolonged pain, resulting in manifest psychopathology [37].

Interestingly, the results of our regression analysis helped to better

Table 4
Multiple linear regression analyses in the total sample (n = 174).

Variables	Unstandardized estimate	SE	t	p	95% CI for estimate	
					Lower	Upper
Intercept	102.184	133.676	6.643	0.446	−161.826	366.194
Psychiatric comorbidity	6.440	21.481	0.300	0.765	−48.865	35.985
Covariates						
Gender (females)	−9.122	20.596	−0.443	0.658	−49.799	31.554
Age at entry (in years)	0.170	1.062	0.160	0.873	−1.928	2.268
Marital status (single)	15.133	23.956	0.632	0.529	−32.181	62.446
Living status (alone)	−41.487	30.106	−1.378	0.170	−100.947	17.972
Educational level (in years)	0.676	2.843	0.283	0.812	−4.939	6.290
Unemployment	9.031	26.806	0.337	0.737	−43.911	61.972
Familiarity with chronic pain	−16.267	19.348	−0.841	0.402	−54.479	21.945
Widespread chronic pain	39.465	25.115	1.571	0.118	−10.138	89.068
Medical comorbidity	14.818	18.803	0.788	0.432	−22.319	51.954
TAS total score	−0.162	0.775	−0.208	0.835	−1.692	1.369

Dependent parameter: *Duration of chronic pain* (in months); F = 0.868; df = 11; $p = 0.810$; $R^2 = 0.044$; Adjusted R^2 = -0.023.

Variables	Unstandardized estimate	SE	t	p	95% CI for estimate	
					Lower	Upper
Intercept	5.578	2.063	2.705	**0.008**	1.504	9.652
Psychiatric comorbidity	0.663	0.337	1.970	**0.049**	1.001	1.329
Covariates						
Gender (females)	0.796	0.317	2.512	**0.013**	0.170	1.422
Age at entry (in years)	−0.001	0.016	−0.056	0.956	−0.033	0.031
Marital status (single)	−0.543	0.370	−1.466	0.145	−1.274	0.188
Living status (alone)	−0.021	0.466	0.045	0.964	−0.941	0.899
Educational level (in years)	−0.006	0.044	−0.131	0.896	−0.093	0.081
Unemployment	0.577	0.412	1.400	0.164	−0.237	1.391
Familiarity with chronic pain	0.345	0.298	1.156	0.249	−0.244	0.933
Widespread chronic pain	0.061	0.391	0.155	0.877	−0.712	0.833
Fixed-dose treatment for chronic pain	0.421	0.289	1.455	0.148	−0.150	0.992
Duration of chronic pain (in months)	0.001	0.001	1.094	0.276	−0.001	0.004
Medical comorbidity	−0.183	0.290	−0.630	0.529	−0.755	0.389
TAS total score	0.014	0.012	1.173	0.243	−0.010	0.038

Dependent parameter: *BPI mean severity score*; F = 2.417; df = 13; $p = \mathbf{0.005}$; $R^2 = 0.408$; Adjusted $R^2 = 0.098$.

Variables	Unstandardized estimate	SE	t	p	95% CI for estimate	
					Lower	Upper
Intercept	5.099	2.244	2.272	**0.024**	0.667	9.531
Psychiatric comorbidity	1.026	0.363	2.831	**0.005**	0.310	1.742
Covariates						
Gender (females)	0.488	0.344	1.420	0.157	−0.191	1.167
Age at entry (in years)	−0.013	0.017	−766	0.445	−0.048	0.021
Marital status (single)	0.243	0.396	0.612	0.541	−0.540	1.025
Living status (alone)	−0.002	0.495	−0.004	0.997	−0.980	0.976
Educational level (in years)	0.037	0.047	0.794	0.428	−0.055	0.130
Unemployment	0.340	0.441	0.771	0.442	−0.531	1.211
Familiarity with chronic pain	−0.164	0.318	−0.517	0.606	−0.793	0.464
Widespread chronic pain	−0.136	0.416	−0.327	0.744	−0.957	0.685
Fixed-dose treatment for chronic pain	0.306	0.310	0.989	0.324	−0.305	0.918
Duration of chronic pain (in months)	−0.001	0.001	−0.292	0.771	−0.003	0.002
Medical comorbidity	0.172	0.308	0.559	0.577	−0.437	0.781
BPI mean severity score	0.531	0.085	6.253	**0.001**	0.363	0.698
TAS total score	−0.008	0.013	−0.611	0.542	−0.033	0.017

Dependent parameter: *BPI mean interference score*; F = 5.845; df = 14; p = **0.001**; $R^2 = 0.344$; Adjusted $R^2 = 0.286$.

Variables	Unstandardized estimate	SE	t	p	95% CI for estimate	
					Lower	Upper
Intercept	60.070	0.970	4.468	**0.001**	33.515	86.626
Psychiatric comorbidity	8.033	2.237	3.592	**0.001**	3.615	12.451
Covariates						
Gender (females)	0.389	2.165	0.184	0.854	−3.878	4.675
Age at entry (in years)	−0.041	0.109	−0.378	0.706	−0.256	0.174
Marital status (single)	0.560	2.483	0.225	0.822	−4.345	5.465
Living status (alone)	−2.818	3.092	−0.912	0.363	−8.925	3.288
Educational level (in years)	0.231	0.293	0.789	0.432	−0.348	0.811
Unemployment	0.072	2.767	0.026	0.979	−5.393	5.537
Familiarity with chronic pain	1.319	1.992	0.662	0.509	−2.616	5.523
Widespread chronic pain	6.454	2.552	2.529	**0.012**	1.413	11.495
Fixed-dose treatment for chronic pain	−2.195	1.937	−1.133	0.259	−6.020	1.631
Duration of chronic pain (in months)	−0.003	0.008	−0.347	0.729	−0.013	0.019
Medical comorbidity	−0.074	1.933	−0.038	0.970	−3.891	3.744
BPI mean severity score	0.780	0.591	1.320	0.189	−0.387	1.947

(*continued on next page*)

Table 4 (*continued*)

Variables	Unstandardized estimate	SE	t	p	95% CI for estimate	
					Lower	Upper
BPI mean interference score	−0.306	0.501	−0.611	0.542	−1.295	0.683
Dependent parameter: *TAS total score*; F = 2.551; df = 14; p = **0.003**; R^2 = 0.186; Adjusted R^2 = 0.113.						

Note. BPI = Brief Pain Inventory; TAS = Toronto Alexithymia Scale; SE = Standard Error; t = t-test value; p = statistical significance; 95% CI = 95% Confidence Interval; F = statistical value; df = degrees of freedom; R^2 = coefficient for goodness of fit of the statistical model. Statistically significant p values are in bold.

clarify the relevance of the relationships between comorbid psychopathology and some clinical aspects of chronic pain. In this respect, psychiatric comorbidity showed crucial associations with levels of pain interference in daily activities and with pain severity (co-mediated by female sex), as well as with the presence of widespread chronic pain (together with female sex and higher levels of alexithymia) and the consequent prescription of anti-neuropathic drugs (co-mediated by shorter duration of pain). Conversely, no direct relationships were found between comorbid psychopathology, pain duration, and prescription of fixed-dose analgesics. In summary, we hypothesize a spiral of "pathoplastic" interaction between psychiatric distress and clinical severity of chronic pain (especially in patients with widespread chronic pain), to which other relevant modulating factors (i.e., female sex, alexithymia) may also contribute in different ways (Fig. 2).

The special link between widespread chronic pain (including fibromyalgia) and comorbid mental disorders also recalls the historical idea that psychological distress can be unconsciously manifested to gain assistance, shifting from psychological to somatic channels [38]. Therefore, as in patients with somatic symptom disorder, even in subjects with pain who are alexithymic and coping poorly with their psychological symptoms, their unhelpful mental reactions can exacerbate physical pain [39]. However, more contemporary neuroscience-based models for explaining the mechanisms of widespread chronic pain mechanisms have gone beyond somatization and described pain that is related to altered processing of pain sensory pathways (e.g., central sensitization phenomenon, "nociplastic" pain) [40,41]. Finally, although the close relationship between psychiatric disorders and chronic widespread pain is also supported by the fact that antidepressants have some evidence in the treatment of neuropathic pain, it should be noted that some forms of neuropathic pain have different mechanisms and pathology than chronic widespread pain [40].

4.1. Limitations

A major limitation is related to sample recruitment within a specialist pain service, which involved subjects suffering from higher pain intensity and pain-related disability. In this way, a highly restricted clinical population was selected, introducing the potential of selection bias, such as the over-representation of concurrent psychopathology.

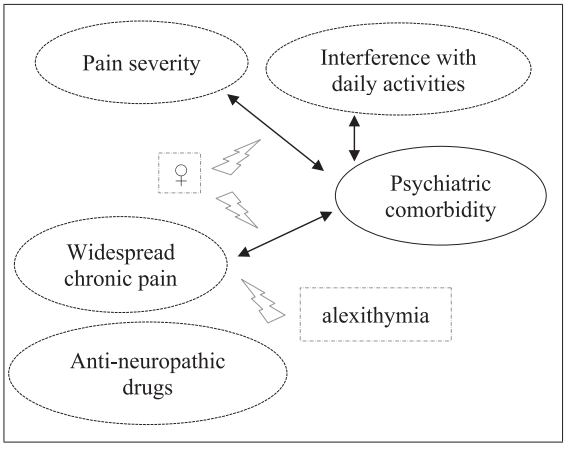

Fig. 2. Hypothesized pathogenic interaction spiral between psychiatric comorbidity and chronic pain.
Note. The relationships between demographic and clinical factors are to be considered as biunivocal.

Another weakness is related to both single-center research design and the relatively small sample size. Our results therefore need to be replicated in multi-center studies and on larger populations of patients with chronic pain, also performing power analyses.

Additionally, we formulated psychiatric diagnoses using DSM-5 criteria. Therefore, our findings may not be systematically generalized and compared with studies that administered other assessment methods (such as self-reports) to evaluate concurrent psychopathology.

Fourth, we considered age between 18 and 60 years among the inclusion criteria. Because the prevalence of chronic pain increases with age [42], its association with psychiatric comorbidity may be underestimated. However, the reason for the cut-off at 60 years was to exclude mental deterioration and psychogeriatric disorders.

Similarly, language barrier was an exclusion criterion. Although a high prevalence of chronic pain and psychiatric disorders has been reported in migrants (probably worse in those with poor language skills) [43], this choice was dictated by the need to complete validated self-report questionnaires in Italian. Future studies that include a wider age range and interpreters for translation are welcome.

Furthermore, participation in our survey was voluntary, and some subjects with psychiatric disorders may have preferred to be reticent and avoid psychopathological assessment. In this regard, 174 patients out of 201 who were referred to the Parma PTS and informed of the study took part in the research.

Finally, although some of the findings in this research are not entirely novel (it has been known for decades that a high, but widely variable, percentage of patients with chronic pain also suffer from comorbid psychiatric symptoms), our cross-sectional clinical and diagnostic results suggest an urgent need for longitudinal and intervention studies (e.g., how to implement multiprofessional treatments in real-world clinical practice, how to best tailor interventions to different patient and diagnostic groups, and how to ensure long-lasting beneficial outcomes). In this respect, this paper was conceived as a "spin-off" of a larger non-pharmacological observational cohort research, which also includes a longitudinal investigation of long-term clinical outcomes (follow-up part of the P3 study) [9,44].

5. Conclusions

The findings of this research demonstrated that a significant minority (approximately one-third) of individuals with chronic pain received a diagnosis of a comorbid mental disorder at their first consultation in a specialized pain clinic. Specifically, a relevant portion of them had never received previous psychiatric consultation and were not currently retained in care within psychiatric services. This is indicative of the presence of undiagnosed and probably undertreated psychiatric syndromes.

Because comorbid psychopathology has been shown to be critical to pain severity and daily functioning, as well as for prognosis, in chronic pain, unmasking undetected mental disorders helps improve outcomes and quality of life. The presence of mental health operators in the multidisciplinary chronic pain team is therefore justified, particularly to offer appropriate assessment strategies, individualized case formulation,

and adequate psychiatric treatments.

CRediT authorship contribution statement

Lorenzo Pelizza: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Simona Pupo:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Camilla Barbi:** Writing – review & editing, Data curation. **Marika Alessia Incardona:** Writing – review & editing, Data curation. **Giovanni Musetti:** Writing – review & editing, Conceptualization. **Marco Menchetti:** Writing – review & editing, Supervision.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors have nothing to declare.

Acknowledgments

The authors thank all participants who actively took part in the P3 study.

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