

Using Chronic Pain to Predict Depressive Morbidity in the General Population

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Background: Pain syndrome is thought to play a role in depression. This study assesses the prevalence of chronic (≥ 6 months' duration) painful physical conditions (CPPCs) (joint/articular, limb, or back pain, headaches, or gastrointestinal diseases) and their relationship with major depressive disorder.

Methods: We conducted a cross-sectional telephone survey of a random sample of 18980 subjects from 15 to 100 years old representative of the general populations of the United Kingdom, Germany, Italy, Portugal, and Spain. Answers provided during telephone interviews using the Sleep-EVAL system were the main outcome measure. Interviews included questions about mental disorders and medical conditions. Data on painful physical conditions were obtained through questions about medical treatment, consultations, and/or hospitalizations for medical conditions and a list of 42 diseases.

Results: Of all subjects interviewed, 17.1% reported having at least 1 CPPC (95% confidence interval [CI],

16.5%-17.6%). At least 1 depressive symptom (sadness, depression, hopelessness, loss of interest, or lack of pleasure) was present in 16.5% of subjects (95% CI, 16.0%-17.1%); 27.6% of these subjects had at least 1 CPPC. Major depressive disorder was diagnosed in 4.0% of subjects; 43.4% of these subjects had at least 1 CPPC, which was 4 times more often than in subjects without major depressive disorder (odds ratio [OR], 4.0; 95% CI, 3.5-4.7). In a logistic regression model, CPPC was strongly associated with major depressive disorder (OR: CPPC alone, 3.6; CPPC+nonpainful medical condition, 5.2); 24-hour presence of pain made an independent contribution to major depressive disorder diagnosis (OR, 1.6).

Conclusions: The presence of CPPCs increases the duration of depressive mood. Patients seeking consultation for a CPPC should be systematically evaluated for depression.

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MAJOR DEPRESSIVE disorder is estimated to occur at a rate of 2% to 6% in the general population of the United States and Western Europe.¹⁻⁶ Variations in prevalence estimates are due partly to the time frame used (previous-year or previous-month basis) and the diagnostic instruments employed (eg, Diagnostic Interview Schedule, University of Michigan Composite International Diagnostic Interview, and Clinical Interview Schedule, Revised). Furthermore, major depressive disorder is one of the most common mental disorders and is the second most common cause of disability in industrial countries.

Some studies have reported associations between depression and a number of long-term medical conditions, including pain syndrome.⁷⁻¹² An epidemiological study in the United Kingdom reported that 16.9% of participants with chronic wide-

spread pain also had a psychiatric diagnosis.¹³ A 7-year longitudinal study reported that the presence of multiple physical symptoms is predictive of a new onset of depression, and, conversely, subjects with depression are 3 to 7 times more likely to develop multiple physical symptoms than are subjects who are not depressed.⁸ More recently, a 1-year longitudinal study reported that nondepressed subjects with a long-term medical condition (eg, migraine headaches, sinusitis, or back problems) were twice as likely to develop major depression within the next year than were subjects without a long-term medical condition.¹¹ Surprisingly, few studies have attempted to determine if a comorbid medical condition in individuals with chronic painful physical conditions increased the likelihood of having major depressive disorder. Similarly, few studies have attempted to determine the role of obesity, a factor found to be associated with in-

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creased pain severity^{14,15} and major depressive disorder,^{16,17} in the association between pain and depression.

In this study, we explored further the relationship of chronic painful physical condition to depression in a large community sample of 18980 Europeans aged 15 years and older. More specifically, we examined (1) the prevalences of pain, depressive symptoms, and major depression in this representative sample; (2) the degree of association between chronic painful physical condition and depressive symptoms and major depressive disorder; (3) whether other factors, such as a comorbid non-painful medical condition, modified the association between pain and depression; and (4) whether pain symptoms are more common than classic vegetative symptoms in a community-based sample of subjects with major depressive disorder.

METHODS

SAMPLING

Participants from the United Kingdom, Germany, Italy, Portugal, and Spain were interviewed by telephone between 1994 and 1999 to investigate sleep habits, sleep-related symptoms, and psychiatric and sleep disorder diagnoses according to the *DSM-IV*. The target population in the United Kingdom, Germany, Italy, and Spain was all noninstitutionalized residents aged 15 years or older; in Portugal, the minimum age was set at 18 years according to the recommendations of the ethics committee. These 5 countries had approximately 206 million inhabitants. The study was approved by an ethics and research committee in Canada, where one of us (M.M.O.) was living at the time the study was conducted. A 2-stage sampling design was used for all 5 countries, using the geographical distribution in the first stage and the Kish selection method¹⁸ in the second stage. The Kish method is based on 8 selection tables. It maintains the age and sex representation of the sample and avoids bias related to noncoverage error.

Participants granted verbal consent before proceeding with the interview. For subjects younger than 18 years, verbal consent was also requested from their parents. Potential participants who had insufficient fluency in the national language, hearing or speech impairment, or an illness that precluded the feasibility of an interview or who were currently hospitalized were excluded.

The participation rate was 79.6% (4972 of 6249 eligible subjects) in the United Kingdom, 68.1% (4115 of 6047 eligible subjects) in Germany, 89.4% (3970 of 4442 eligible subjects) in Italy, 83.2% (1858 of 2234 eligible subjects) in Portugal, and 87.5% (4065 of 4648 eligible subjects) in Spain. Altogether, 18980 subjects participated in the study. The overall participation rate was 80.4%.

INSTRUMENT

The Sleep-EVAL System,^{19,20} a computer program specifically designed for conducting epidemiological studies in the general population and administering questionnaires, was used to perform the interviews. Lay interviewers read subjects the questions displayed on the computer screen and entered their answers into the Sleep-EVAL System.

The Sleep-EVAL System is composed of a standard questionnaire, written by one of us (M.M.O.), and diagnostic pathways covering the *International Classification of Sleep Disorders*²¹ and the *DSM-IV*.²² The questionnaire covers sociodemographic information, the sleep/wake schedule, physical health, and sleep

and mental disease symptoms. Interviews typically begin with general questions about demographic characteristics, followed by questions about sleeping habits and more private questions about mental health. Questions about psychotic symptoms appear near the end of the interview.

The system uses subjects' answers to select a series of plausible diagnostic hypotheses (causal reasoning process) and confirms or rejects these hypotheses based on further questioning and deducing the consequences of each answer (nonmonotonic, level 2 feature). The differential diagnosis process is based on a series of key rules allowing or prohibiting the co-occurrence of 2 diagnoses in accordance with *International Classification of Sleep Disorders* and *DSM-IV* prescriptions. The interview ends once all diagnostic possibilities are exhausted. The system is also endowed with fuzzy logic reasoning, managed by 2 neural networks. The system has been tested in various contexts, including clinical psychiatric settings and sleep disorder clinics.²³⁻²⁶ In psychiatric studies, κ ranged from 0.44 (schizophrenic disorders) to 0.78.^{23,24}

The duration of the interviews ranged from 10 to 333 minutes (mean \pm SE, 40 \pm 20 minutes). The longest interviews involved subjects with multiple sleep and mental disorders. If the duration exceeded 60 minutes, then interviews were completed during 2 or more sessions.

The questionnaire was translated from English to German, Italian, Portuguese, and Spanish. Each translation was verified by at least 3 translators who were native speakers of the targeted language. In all translations, the questionnaire was translated back to English to verify that the questions retained the same meaning.

VARIABLES

Pain Questionnaire

Painful physical conditions were addressed through questions about treatment for a medical condition at the time of the interview (if the subject was being treated, he or she enumerated the conditions), current medication consumption (prescribed or not) and for which disease subjects were taking medication, and hospitalizations in the 12 months before the study and the reason(s) for each hospitalization. Subjects were also provided with a list of 42 diseases and asked if they had one or more of them. Duration of the disease was also determined.

Subjects were considered to have a painful physical condition if the pain had persisted for at least 6 months and they had consulted a health specialist for the pain, whether or not it resulted in a treatment; were taking medication, prescribed or not, for the pain; or reported that pain interfered with functioning. Painful physical conditions were then classified according to 5 categories: (1) joint/articular conditions (arthritic and rheumatoid diseases), (2) limb pain (all nonarticular pains in upper and lower limbs), (3) backache (nonarticular pain in the back regardless of the location on the spine), (4) headache (migraines and all other types of headaches), and (5) gastrointestinal diseases (all types of painful diseases, such as stomach or gastric ulcer, stomach burns, colitis, Crohn disease, gastritis, ileitis, or colonopathy).

Medical conditions were also identified, including both organic diseases (ie, morbid changes in organ structure or the composition of bodily fluids) and functional diseases (ie, diseases in which the symptoms cannot be attributed to any appreciable lesion or structural change).

Depressive Illness Questionnaire

The exploration of depression began with questions assessing whether subjects were feeling sad, downcast, or depressed, feel-

ing hopeless, or had lost interest and lacked pleasure in activities formerly considered pleasant. These questions were answered on an intensity scale (ie, extremely, a lot, moderately, slightly, not at all, does not know), and it was determined whether each symptom was present most of the day and nearly every day. Subjects who had at least 1 of these symptoms were asked another series of questions that assessed changes in appetite or weight; insomnia or hypersomnia symptoms (obtained with the help of the sleep questionnaire and supplemental questions to evaluate their relationship to depressive illness); psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or guilt; difficulties in concentrating, thinking, or making decisions; and suicidal ideations. All these were rated by the subjects on the intensity scale used for the initial symptoms and by whether the symptom was present most of the day and nearly every day. Subjects were also asked about the duration of their depressive mood, current and past use of antidepressant medications, and whether they were currently consulting a health professional for depressive mood or had ever done so.

For a *DSM-IV* diagnosis of major depressive episode, all 5 criteria needed to be met (**Figure 1**). Therefore, in addition to having impaired functioning (criterion C), subjects who meet the criteria for a mixed episode (ie, who had both a major depressive episode and a manic episode) (criterion B; n=32), those who developed depressive symptoms in relation to the use or withdrawal of a drug or medication (criterion D; n=6), or those who developed depressive symptoms in relation to the loss of a loved one (criterion E; n=27) were not considered to have a major depressive episode according to the *DSM-IV*. For example, a subject whose depressive symptoms appeared after the onset of alcohol use (ie, the subject was using alcohol before the onset of the depressive mood) and who reported that his or her mood had changed since using alcohol was not considered to have a major depressive episode. On the other hand, subjects who reported having lost a loved one more than 2 months before the interview and who displayed all the *DSM-IV* criteria were considered to have a major depressive episode.

Subjects with a mood disorder due to a general medical condition (major depressivelike episode; n=76) were included in the analyses.

Sleep Questionnaire

The sleep questionnaire included questions about sleep habits, sleep/wake schedule, sleep quality, and several sleep symptoms (eg, insomnia, hypersomnia, parasomnia, and snoring). Some questions were related to the experience of pain during sleep, such as whether pain awakens the subject and, if so, how many times per night. Sleep disorder diagnoses were made according to *DSM-IV* and *International Classification of Sleep Disorders* criteria. A differential diagnosis procedure was applied prior to the diagnosis attribution.

ANALYSES

A weighting procedure was applied to correct for disparities in the geographical, age, and sex distribution between the samples and each studied country. This procedure compensated for any potential bias from such factors as an uneven response rate across demographic groups. Results were based on weighted n values. Percentages for target variables are given with 95% confidence intervals (CIs) or SEs. Bivariate analyses were performed using the χ^2 test. Logistic regression was used to compute the odds ratios (ORs) associated with major depressive episodes and pain. Logistic regressions were performed using SUDAAN software (Research Triangle Institute, Research Triangle Park, NC), which computes an appropriate

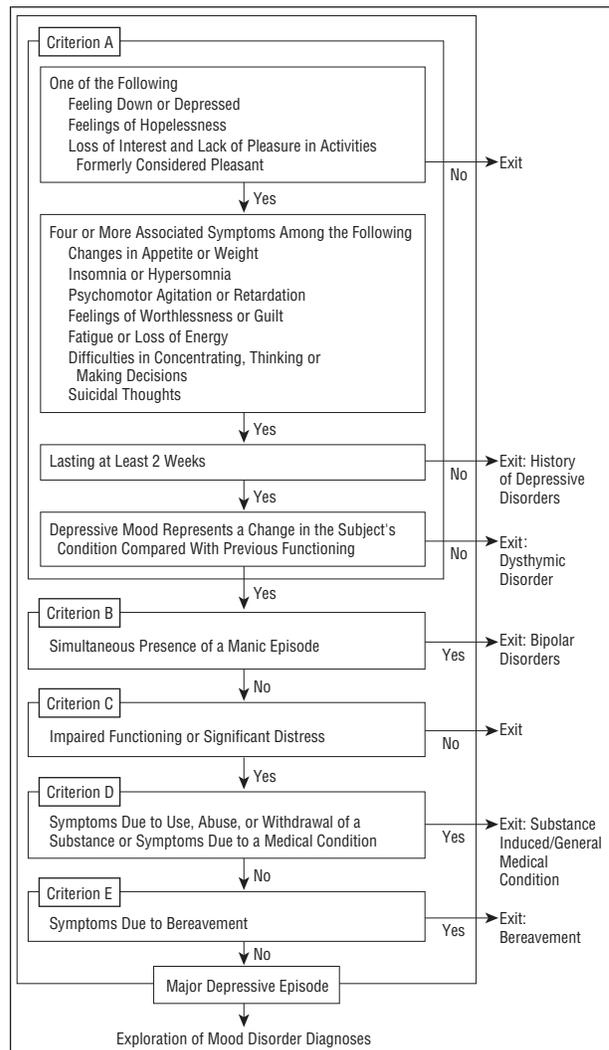


Figure 1. The Sleep-EVAL system schematic tree for exploring a major depressive episode.¹⁹

estimate of the SEs from stratified samples by means of a Taylor series linearization method. $P \leq .05$ was considered statistically significant.

RESULTS

The sample included 18980 subjects from 15 to 100 years old; 26.2% of subjects were from the United Kingdom; 21.7% were from Germany; 21.4% were from Spain; 20.9% were from Italy; and 9.8% were from Portugal.

PREVALENCE OF CHRONIC PAINFUL PHYSICAL CONDITIONS

At the time of the interview, 17.1% of subjects reported having at least 1 chronic painful physical condition (95% CI, 16.5%-17.6%). More women than men had a chronic painful physical condition (20.7% vs 13.2%; $P < .001$). The prevalence increased linearly with age (subjects younger than 25 years, 11.4%; subjects aged 65 years or older, 25.4%; $P < .001$). Headaches were reported by 7.6% of subjects, followed by pain in lower or upper limbs (5.8%), joint/articular disease (3.2%), backaches (3.1%),

Table 1. Prevalence of Chronic Painful Physical Conditions by Sociodemographic Characteristics

Characteristic	No. of Subjects	Pain, % of Subjects (SE)					
		Limb Pain	Backaches	Joint/Articular	Gastrointestinal	Headaches	Any Pain
Men, age, y							
<25	1759	1.9 (0.03)	1.3 (0.03)	0.6 (0.02)	0.6 (0.02)	5.9 (0.06)	9.4 (0.07)
25-34	1807	2.5 (0.04)	0.9 (0.02)	1.4 (0.03)	0.8 (0.02)	4.2 (0.05)	9.1 (0.07)
35-44	1556	2.8 (0.04)	2.0 (0.04)	1.4 (0.03)	1.3 (0.03)	5.4 (0.06)	11.5 (0.08)
45-54	1399	3.5 (0.05)	3.1 (0.05)†	1.9 (0.03)	2.4 (0.04)†	5.2 (0.06)	12.9 (0.09)*
55-64	1228	6.5 (0.07)*	3.7 (0.05)†	4.1 (0.06)*	2.0 (0.04)†	6.0 (0.07)	19.0 (0.11)*
≥65	1367	7.9 (0.07)*	3.4 (0.05)†	6.3 (0.07)*	2.5 (0.04)†	4.3 (0.06)	20.4 (0.40)*
Total	9116	4.0 (0.02)	2.3 (0.02)	2.4 (0.02)	1.5 (0.01)	5.1 (0.02)	13.2 (0.03)
Women, age, y							
<25	1684	3.7 (0.03)	1.1 (0.03)	1.5 (0.03)	1.0 (0.02)	8.6 (0.07)	13.5 (0.08)
25-34	1767	3.1 (0.03)	1.8 (0.03)	1.4 (0.03)	1.0 (0.02)	8.6 (0.07)	13.6 (0.08)
35-44	1554	4.6 (0.05)	2.6 (0.04)	1.7 (0.03)	0.8 (0.02)	9.2 (0.07)	15.7 (0.09)
45-54	1426	9.6 (0.10)*	6.2 (0.06)	3.3 (0.05)†	1.8 (0.04)†	12.8 (0.09)*	24.8 (0.11)†
55-64	1313	11.6 (0.12)*	6.0 (0.07)*	6.1 (0.07)*	2.0 (0.04)†	12.7 (0.09)*	28.2 (0.12)†
≥65	2120	12.7 (0.13)*	5.4 (0.06)*	8.8 (0.06)*	2.5 (0.03)†	8.9 (0.06)	28.6 (0.10)†
Total	9864	7.6 (0.08)	3.8 (0.04)	3.9 (0.02)	1.5 (0.01)	9.9 (0.03)	20.7 (0.04)

* $P < .001$ compared with the lowest figure for that type of pain.

† $P < .05$ compared with the lowest figure for that type of pain.

and gastrointestinal diseases (1.5%). Prevalence of gastrointestinal diseases was comparable between men and women. The other chronic painful physical conditions were more frequent in women than men (**Table 1**). All these conditions significantly increased with age.

ASSOCIATIONS WITH DEPRESSIVE SYMPTOMS

At least 1 of the 3 key symptoms of depression was reported by 16.5% of subjects (95% CI, 16.0%-17.1%), and there was a higher prevalence in women than men (17.8% vs 15.3%; $P < .001$). More than a quarter (27.6%) of subjects with at least 1 of the 3 key depressive symptoms also had at least 1 chronic painful physical condition. Limb pain was reported by 10.5%, whereas 4.9% of subjects without depressive symptoms mentioned limb pain (OR, 2.3; 95% CI, 2.0-2.5; $P < .001$). Joint/articular diseases were reported by 4.9% of subjects with depressive symptoms compared with 2.9% of subjects without depressive symptoms (OR, 1.7; 95% CI, 1.4-2.1; $P < .001$). Backaches were 2 times more prevalent in subjects with depressive symptoms (5.7%) than in subjects without depressive symptoms (2.5%) (OR, 2.3; 95% CI, 2.0-2.8; $P < .001$). Gastrointestinal disturbances were found in 2.4% of subjects with depressive symptoms compared with 1.3% of subjects without depressive symptoms ($P < .001$). Headaches were reported 2 times more frequently in subjects with depressive symptoms (14.0%) compared with subjects without depressive symptoms (6.3%) (OR, 2.4; 95% CI, 2.1-2.7). Overall, subjects feeling sad or depressed were more likely to report chronic painful physical conditions than those who were hopeless or those with loss of interest or lack of pleasure (**Table 2**).

Subjects who reported fatigue or loss of energy more frequently reported all types of chronic painful conditions than did subjects without this symptom (Table 2). Limb pain was more frequently reported by subjects with symptoms of insomnia or hypersomnia, fatigue or loss of energy, and feelings of worthlessness or guilt com-

pared with depressed subjects without these symptoms. Backaches and headaches were not significantly more common among subjects who reported changes in appetite or weight. Only subjects with fatigue or loss of energy reported significantly more gastrointestinal diseases.

The association between chronic painful physical conditions and depressive symptoms increased with the number of depressive symptoms reported. More than a quarter of subjects reporting only 2 depressive symptoms (28.5%) also had a chronic painful physical condition. This rate increased to 37.9% when subjects had 5 depressive symptoms and jumped to 61.9% when at least 8 depressive symptoms were reported ($P < .001$).

Furthermore, 75.3% of subjects with at least 1 chronic painful physical condition reported having 1 of the symptoms associated with somatic depression (fatigue, changes in appetite/weight, or insomnia/hypersomnia).

Subjects with at least 1 key symptom of depression and a chronic painful physical condition reported a longer duration of the depressive mood (19.0 months) than did subjects with at least 1 key symptom of depression without a chronic painful condition (13.3 months; Mann-Whitney U ; $z = -2.99$; $P = .003$).

Finally, 27.6% of subjects with at least 1 key depressive symptom reported having a painful physical condition; 9.3% reported both a chronic painful physical condition and a nonpainful medical condition, and 18.3% reported a chronic painful physical condition alone (**Figure 2A**).

ASSOCIATION WITH DSM-IV MAJOR DEPRESSIVE DISORDER DIAGNOSIS

Major depressive disorder was diagnosed in 4.0% of subjects, including 76 subjects with a mood disorder due to a general medical condition (major depressivelike episode). Women had a higher prevalence of major depressive disorder than did men (4.9% vs 3.1%; $P < .001$).

Table 2. Frequency of Chronic Painful Physical Conditions Among Subjects With Depressive Symptoms

Depressive Symptoms	No. of Subjects	Pain, % of Subjects					
		Limb Pain	Backaches	Joint/Articular	Gastrointestinal	Headaches	Any Pain
Screening Symptoms							
Feeling sad or depressed							
Yes	1353	15.6*	9.8*	5.9*	3.3*	19.3*	37.3*
No	17 627	5.1	2.5	3.0	1.4	6.7	15.5
Hopelessness							
Yes	456	12.8*	5.9†	4.0	1.9	11.9*	27.3*
No	18 524	5.7	3.0	3.2	1.5	7.5	16.8
Loss of interest/lack of pleasure							
Yes	2130	9.3*	5.3*	5.0*	2.1†	13.9*	26.5*
No	16 850	5.4	2.8	3.0	1.5	6.8	15.9
Among Subjects With at Least 1 Screening Symptom							
Changes in appetite or weight							
Yes	882	9.2	6.7	6.4†	2.2	15.8	27.7*
No	2258	11.0	5.3	4.3	2.5	13.3	16.5
Insomnia or hypersomnia symptoms							
Yes	1585	14.6*	9.1*	6.7*	2.9	19.0*	37.3*
No	1554	6.6	2.1	3.1	1.9	8.9	17.8
Psychomotor agitation or retardation							
Yes	567	11.1	10.6*	6.4	3.0	19.6*	35.6*
No	2572	10.4	4.7	4.6	2.3	12.8	16.5
Fatigue or loss of energy							
Yes	356	15.5†	12.4*	8.7*	4.8*	24.4*	43.4*
No	2784	9.9	4.9	4.4	2.1	12.7	16.6
Feelings of worthlessness or guilt							
Yes	209	16.7*	14.3*	6.3	1.8	26.2*	43.5*
No	2910	10.1	5.2	4.8	2.4	13.2	18.2
Difficulties in concentrating, thinking, or making decisions							
Yes	519	11.2	9.4*	5.9	2.2	20.5*	33.2*
No	2621	10.4	5.0	4.7	2.5	12.7	16.6
Suicidal thoughts							
Yes	687	10.3	9.2*	6.3	2.7	18.7*	33.0*
No	2430	10.6	4.8	4.5	2.3	12.8	17.8

* $P < .001$ compared with the lowest figure for that type of pain.

† $P < .05$ compared with the lowest figure for that type of pain.

As indicated in Figure 2B, 43.4% of subjects with major depressive disorder reported having at least 1 chronic painful physical condition; this is 4 times more often than in the remaining sample (16.1%) (OR, 4.0; 95% CI 3.5-4.7; $P < .001$). Conversely, the prevalence of major depressive disorder was 10.2% in subjects with a chronic painful physical condition compared with 2.7% in subjects without chronic painful physical condition ($P < .001$).

Subjects with major depressive disorder were more than 5 times more likely to report backaches than was the rest of the sample (12.8% vs 2.7%; OR, 5.3; 95% CI, 4.2-6.7; $P < .001$). Gastrointestinal diseases (3.0% vs 1.5%; OR, 2.0; 95% CI, 1.3-3.2; $P = .003$) and joint/articular diseases (6.9% vs 3.1%; OR, 2.3; 95% CI, 1.7-3.1; $P < .001$) were 2 times more frequently reported by subjects with major depressive disorder. Headaches were 4 times more frequently reported by subjects with major depressive disorder (24.5% vs 6.9%; OR, 4.4; 95% CI, 3.7-5.2; $P < .001$), and limb pain was 3 times more prevalent in subjects with major depressive disorder (16.3% vs 5.4%; OR, 3.4; 95% CI, 2.8-4.2; $P < .001$).

Most subjects with a major depressive disorder diagnosis (61.6%) reported having either a chronic pain-

ful physical condition or a nonpainful medical condition (Figure 2B). A chronic painful physical condition alone (without another medical condition) was reported by 28.9% of subjects with major depressive disorder. Co-occurrence of a painful physical condition and a nonpainful medical condition was found in 14.5% of subjects with major depressive disorder.

A chronic painful physical condition alone (without a comorbid nonpainful medical condition) was more frequently observed among subjects with a diagnosis of major depressive disorder who reported a change in appetite or weight, psychomotor agitation or retardation, fatigue or loss of energy, or difficulty concentrating, thinking, or making decisions. Comorbid chronic painful physical conditions and nonpainful medical conditions were more frequent in subjects with insomnia or hypersomnia symptoms.

We performed logistic regression to determine if having a chronic painful condition made an independent contribution to major depressive disorder. We included in the model variables most often associated with major depressive disorder: sex, age, occupational status, alcohol intake, smoking, stress, and body mass index (weight in kilograms divided by height in meters

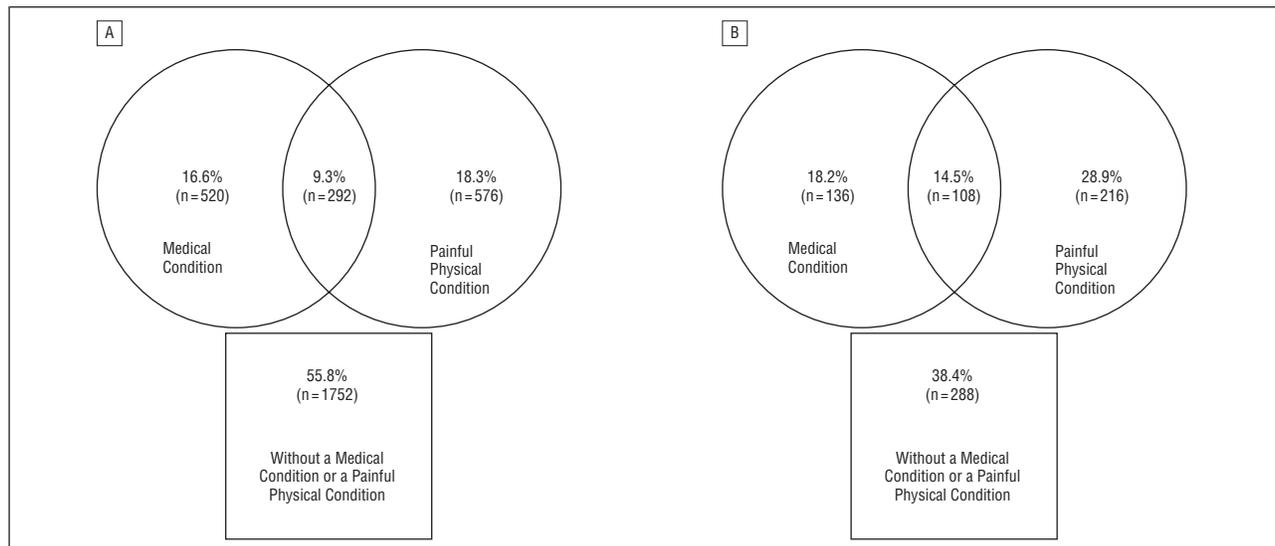


Figure 2. Associations between medical conditions and chronic painful physical conditions in 3140 subjects with at least 1 depressive symptom (A) and 748 subjects with major depressive disorder (B), including 76 subjects with a mood disorder due to a general medical condition (major depressivelike episode: endocrine condition, 9 subjects; heart disease, 53 subjects; cancer, 3 subjects; and another disease, 11 subjects).

squared). Daily caffeine and alcohol intake were not significant in the final model. **Table 3** displays crude and adjusted ORs for subjects with major depressive disorder. Significant adjusted sociodemographic factors included being a woman, being from 45 to 54 years old, working on shifts or at night, being a homemaker, or being unemployed. Being married was a protective factor, as was having a body mass index in the overweight range (25-27). Other significant factors were smoking fewer than 20 cigarettes per day and having a moderately stressful or stressful life.

Illness status was significantly related to the presence of a major depressive disorder diagnosis. The OR for having major depressive disorder was 2.2 for subjects with only a nonpainful medical condition. The OR increased to 3.6 for subjects with only a chronic painful physical condition and 5.2 for subjects with both a chronic painful physical condition and a nonpainful medical condition. Interestingly, the presence of pain during the night and day made an independent significant contribution to major depressive disorder diagnosis.

COMMENT

This study investigated the association between major depressive disorder and pain in a large sample representative of the general populations of 5 European countries (the United Kingdom, Germany, Italy, Portugal, and Spain).

LIMITATIONS OF THE STUDY

This study was primarily designed to address sleep and mental disorders in the general population and the questionnaire did not include extensive questions about the characteristics or location of pain. Therefore, it was not possible to distinguish between the different clinical forms of pain with great specificity.

Second, the data collected on pain and nonpainful medical conditions were self-reported. However, because pain involves mainly subjective perception and experience, self-reports are commonly considered accurate. Studies that have examined the concordance between subjective reports and external measures of pain have found good agreement between the two.²⁷ Furthermore, a physician or other health specialist had already diagnosed the nonpainful medical conditions reported in this study.

PREVALENCE OF PAIN

Nearly 17% of subjects in our sample reported having a chronic painful physical condition. This rate is similar to that reported in epidemiological studies assessing chronic pain²⁸⁻³¹ but lower than the rates reported in studies that addressed both short-term and chronic painful physical conditions.³²⁻³⁴ In this study, the painful physical conditions reported were mostly chronic, and many of these subjects had sought medical assistance for their physical conditions.

PREVALENCE OF DSM-IV DEPRESSIVE DISORDERS

We found a prevalence of 4% for major depressive disorder in this European sample, which is close to the 1-month prevalence of 4.9% reported in the National Comorbidity Survey (NCS).² The differences between this study and the Epidemiologic Catchment Area (ECA)¹ and NCS studies are numerous. First, the age range is broader in this sample (15-100 years) than in the NCS (15-54 years). Second, the time frame is also different (current study, point prevalence; ECA and NCS studies, 1-month, 6-month, 1-year, or lifetime prevalence), and, third, in this study, a differential diagnosis procedure was applied to all the subjects who had experienced a major depressive episode.

THE PAIN-DEPRESSION ASSOCIATION

Major Depressive Disorder

Among the 4% of subjects with major depressive disorder, more than 40% also had a chronic painful physical condition. A third of subjects with major depressive disorder also had a nonpainful medical condition. Therefore, only 38.4% of subjects with major depressive disorder had neither a chronic painful physical condition nor a nonpainful medical condition; approximately 15% had both. In subjects with major depressive disorder, the odds of having a chronic painful physical condition were greater than for subjects with depressive symptoms but no major depressive disorder diagnosis, with crude ORs ranging from 2.0 to 5.0.

Conversely, among subjects with a chronic painful condition, subjects with backaches or headaches had the highest odds of having major depressive disorder. These results confirm the results of other clinical studies that examined the prevalence of depressive disorder in patients with lower back pain or headaches.³⁵⁻³⁸ Interestingly, 24-hour presence of pain made an independent contribution to the presence of major depressive disorder, indicating that continuous pain independently increases the likelihood of having major depressive disorder. Furthermore, when controlling for the presence of a nonpainful medical condition, a chronic painful physical condition remains an important factor related to the presence of major depressive disorder. The influence of 24-hour pain and comorbid chronic painful physical condition and nonpainful medical condition have not previously been investigated in the general population.

Other results are noteworthy. We found that shift work was a predictive factor for major depressive disorder as were unemployment and being a homemaker. Previous epidemiological studies of major depressive disorder did not assess individuals according to their work schedule.¹⁻⁵ However, some studies of shift workers have reported high rates of major depressive disorder in this population.^{39,40} We also investigated the influence of obesity on the association between pain and major depressive disorder because obesity is related to both pain severity^{14,15} and the presence of major depressive disorder.^{16,17} Interestingly, in bivariate analyses, these two associations were observed; ie, obese individuals were more likely to report a chronic painful condition, and they had a higher prevalence of major depressive disorder than individuals whose body mass index was within the normal range. However, when introduced into a multivariate model, the association between obesity and major depressive disorder disappeared. Instead, we found that being overweight was a protective factor for major depressive disorder.

Depressive Symptoms

In this study, 16.5% of subjects reported having at least 1 depressive symptom; of these subjects 27.6%, also reported a chronic painful physical condition. Nonpainful medical conditions also were frequently reported; a

Table 3. Crude and Adjusted Odds Ratios (ORs) for Subjects With Major Depressive Disorder

Variables	Crude OR (95% CI)	Adjusted OR (95% CI)
Female sex*	1.54 (1.33-1.78)†	1.41 (1.20-1.66)†
Age, y		
<25	0.66 (0.50-0.86)†	0.84 (0.54-1.32)
25-34	0.85 (0.67-1.09)	1.15 (0.78-1.69)
35-44	0.95 (0.74-1.21)	1.24 (0.85-1.82)
45-54	1.26 (0.99-1.60)	1.45 (1.01-2.09)
55-64	0.99 (0.76-1.29)	1.05 (0.77-1.43)
≥65	1.00	1.00
Marital status		
Single	1.00	1.00
Married/common law	1.06 (0.89-1.27)	0.76 (0.60-0.95)‡
Separated/divorced	2.28 (1.71-3.04)†	1.34 (0.96-1.88)
Widower	1.79 (1.40-2.28)†	1.33 (0.96-1.85)
Employment status		
Daytime worker	1.00	1.00
Shift/night worker	1.41 (1.04-1.91)‡	1.45 (1.06-1.99)‡
Homemaker	1.60 (1.31-1.94)†	1.55 (1.26-1.91)†
Unemployed	2.23 (1.68-2.96)†	2.17 (1.61-2.92)†
Student	0.78 (0.56-1.10)	1.14 (0.76-1.70)
Retired	1.28 (1.04-1.57)‡	1.21 (0.87-1.69)
Body mass index§		
<20	1.28 (1.02-1.61)‡	1.27 (0.99-1.62)
20-25	1.00	1.00
26-27	0.72 (0.57-0.92)	0.69 (0.54-0.89)
>27	1.10 (0.91-1.32)	0.85 (0.70-1.04)
Refused to disclose	0.92 (0.61-1.38)	0.77 (0.50-1.18)
Caffeine intake, cups/d		
<1	1.00	1.00
1-2	1.09 (0.89-1.33)	1.08 (0.88-1.33)
3-5	1.00 (0.82-1.21)	0.97 (0.79-1.19)
≥6	1.32 (1.05-1.68)‡	1.17 (0.90-1.51)
Smoking, cigarettes/d		
Nonsmoker	1.00	1.00
<20	1.28 (1.07-1.54)	1.27 (1.04-1.54)‡
≥20	1.30 (0.98-1.71)	1.16 (0.86-1.56)
Stress level		
None or low	1.00	1.00
Moderate	1.55 (1.30-1.85)†	1.70 (1.41-2.05)†
High	3.01 (2.50-3.62)†	3.03 (2.47-3.71)†
Illness status		
No illness and no pain	1.00	1.00
Medical condition only	2.15 (1.74-2.65)†	2.24 (1.79-2.79)
Chronic painful physical condition only	4.39 (3.65-5.28)†	3.57 (2.91-4.38)
Medical condition and chronic painful physical condition	6.07 (4.81-7.66)†	5.17 (3.95-6.78)†
Pain present day and night¶	3.56 (2.94-4.30)†	1.60 (1.28-2.01)†

Abbreviation: CI, confidence interval.

*Male sex is the reference category.

† $P < .001$.

‡ $P < .05$.

§Body mass index is calculated by dividing weight in kilograms by height in meters squared.

|| $P < .01$.

¶Absence of pain is the reference category.

quarter of subjects with at least 1 depressive symptom had a nonpainful medical condition. The types of chronic painful physical conditions that were analyzed (limb pain, backache, joint/articular disease, gastrointestinal diseases, and headaches) were strongly associated with the presence of depressive symptoms. The ORs for report-

ing one of these chronic painful physical conditions in subjects with depressive symptoms ranged from 1.7 to 2.4. Similar rates have been reported in other general population studies.^{41,42}

ASSESSING DEPRESSION IN SUBJECTS WITH CHRONIC PAIN

The pain-depression interaction is not yet fully understood. Some argue that chronic pain should be viewed as a potent physical and psychological stressor that may influence mood.⁴³ Thus, pain can be viewed as a potential trigger of depressive illness. Some longitudinal studies partly support that hypothesis.⁸⁻¹² However, the relationship is far more complex. If pain precedes the depressive illness in as many as 40% of cases, then the reverse is also true, and depressive illness often precedes physical pain.^{7,8,10,12} Our data are cross-sectional; therefore, they offer limited information about the course of pain and depression. We found, however, that depressed moods were of significantly longer duration, about 6 months longer, in subjects who reported a chronic painful physical condition. Therefore, pain could also contribute to the prolongation of a depressive episode. This result has also been reported in clinical studies.⁴⁴

In contrast, others argue that depression should be assessed differently in subjects with physical pain or, at least, that special attention should be brought to the somatic symptoms of depression, which are also often associated with physical pain and can in fact be attributable to the painful physical condition rather than to depression.⁴⁵⁻⁴⁷ Therefore, there is a question about the extent to which painful physical conditions can induce a false-positive diagnosis of major depressive disorder.

In this study, we found that changes in appetite or weight, fatigue, insomnia or hypersomnia, and feelings of worthlessness or guilt were frequently associated with pain alone. About 88% of subjects with major depressive disorder reported having somatic depressive symptoms, such as fatigue or sleep and appetite disturbances. If we exclude subjects who reported having both a chronic painful physical condition and somatic symptoms of depression and who did not have sufficient depressive symptoms to fulfill the criteria for a major depressive episode, the prevalence of a major depressive disorder diagnosis drops to 3.4%. Therefore, about 15% of major depressive disorder diagnoses would be discarded. There is no clear consensus about how to manage depressive somatic symptoms in the context of painful physical conditions. Some argue that the overlap between pain and depressive symptoms may even compromise the validity of diagnostic questionnaires in that specific population.⁴⁸⁻⁵⁰ Endicott⁵¹ has recommended that alternative diagnostic criteria be used, such as using nonsomatic substitute symptoms to make the diagnosis of major depression.

In summary, this study clearly shows the importance of chronic painful physical conditions in subjects with major depressive disorder. It is a common symptom that remains strongly associated with major depressive disorder even when controlling for the presence of

nonpainful medical conditions. Furthermore, the co-occurrence of chronic painful physical conditions and nonpainful medical conditions increased the likelihood of having a major depressive disorder. Further studies on the relationship of pain to major depressive disorder are warranted.

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