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Prior mental disorders and subsequent onset of chronic back or neck pain: findings from 19 countries.

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Abstract

Associations between depression/anxiety and pain are well established, but its directionality is not clear. We examined the associations between temporally prior mental disorders and subsequent self-reported chronic back/neck pain onset, and investigated the variation in the strength of associations by timing of events during the life course, and by gender. Data were from population-based household surveys conducted in 19 countries (n=52,095). Lifetime prevalence and age-of-onset of 16 DSM-IV mental disorders, and the occurrence and age-of-onset of back/neck pain were assessed using the Composite International Diagnostic Interview. Survival analyses estimated the associations between first onset of mental disorders and subsequent back/neck pain onset. All mental disorders were positively associated with back/neck pain in bivariate analyses; most (12/16) remained so after adjusting for psychiatric comorbidity, with a clear dose-response relationship between number of mental disorders and subsequent pain. Early-onset disorders were stronger predictors of pain; when adjusting for psychiatric comorbidity, this remained the case for depression/dysthymia. No gender differences were observed. In conclusion, individuals with mental disorder, beyond depression and anxiety, are at higher risk of developing subsequent back/neck pain, stressing the importance of early detection of mental disorders, and highlight the need of assessing back/neck pain in mental health clinical settings.

Keywords

back or neck pain; mental-physical comorbidity; psychiatric epidemiology; cross-national studies; mental health

Introduction

Back and neck pain are amongst the most common pain conditions in the general population [24,25,55], being, respectively, the leading and the 4th cause of years lost due to disability worldwide [55]. Twelve-month prevalence estimates of back pain range between 12% and 56% [35,41,37,53,11,12], and of neck pain, from 12% to 34% [30,3,12]; co-occurrence is frequent [10]. Furthermore, back/neck pain is often associated with other pain conditions, physical diseases and mental disorders [2,5,8,22,9,23,53,45].

Comorbidity of back/neck pain with depression has been widely reported [29,15,16], but with other mental disorders it has been less studied. Only more recently, associations with anxiety and comorbid anxiety/alcohol-related disorders have been reported [53,42]. Population-based estimates from 18 countries participating in the World Mental Health (WMH) surveys [12] reported 12-month prevalence of chronic back/neck pain ranging from 10% to 42%, and positive associations with mental disorders were found, across both developed and developing countries. However, the investigation of such associations did not take into account the temporal sequence of events, leaving it unclear whether mental disorders precede or follow the development of chronic back/neck pain, or both.

Prospective studies examining such association in the general population are less common, and mostly assessed only depression or special populations. Studies from clinical samples typically focused on identifying determinants of transition from acute to chronic pain or

addressed the effect of mental disorders on pain prognosis. In a systematic review of 20 prospective studies evaluating 10,842 patients with acute low back pain, the presence of psychiatric comorbidities were among the most important predictors of persistence of disabling pain [7]. Increased risk of chronicity, with persisting pain and disability, was also associated with psychological factors, such as distress, depressive mood and somatization [38]. Among primary care patients with acute low back pain, depression was found to be a significant baseline predictor for persistence of pain in a 6-month follow-up period [31]. A bidirectional association between depressive symptoms and chronic back/neck pain was reported in a two-year follow up study of the elderly living in the community [32], with similar results being observed in the English Longitudinal Study of Ageing [6].

Our study used the cross-national WMH surveys dataset [28] to assess the presence and extent of the associations between a wide range of common mental disorders and back/neck pain in population-based samples from 19 countries. Although the WMH surveys are cross-sectional in design, systematic information on the timing-of-onset of these conditions was collected, allowing the use of survival analysis methods to examine associations between temporally prior DSM-IV psychiatric disorders and subsequent onset of back/neck pain. Furthermore, we investigated the impact of psychiatric comorbidity in modifying the risk of subsequent pain onset, and whether there is variation in risk magnitude by gender or over the life span (i.e. whether the age-of-onset of mental disorders modifies the risk of subsequent pain onset).

Methods

Samples and procedures

This report is based on data obtained from 19 participating countries of the WMH community-based epidemiological surveys that assessed the occurrence of chronic back/neck pain and its age-of-onset (Table 1). Stratified multi-stage clustered area probability sampling strategies were used to select adult (18+ years of age) household respondents in most of the participating countries (Belgium, Israel and Japan used a national registry for one-stage sampling). All surveys were based on multi-stage, clustered-area probability household resident samples that were nationally representative, with the exception of two samples of only urban areas (Colombia, Mexico) and one of a specific Metropolitan area (PRC Shenzhen). Sample sizes ranged from 2,357 (Romania) to 12,790 (New Zealand), with a total of 98,714 participating adult respondents (Table 1). Response rates ranged from 45.9% (France) to 95.2% (Iraq), with a weighted average of 78% (Table 1). Weights were utilized to adjust for differential probabilities of selection within all sampling stages, to non-response and to match samples with population demographic distributions in all countries. Detailed information about WMH sampling and weighting procedures is presented elsewhere [21].

All respondents were assessed in their homes with face-to-face interviews using the WMH Surveys version of the Composite International Diagnostic Interview (CIDI 3.0) [27] by trained non-clinical interviewers. Standardized WHO translation, back-translation, and harmonization procedures were used to translate and adapt the instruments and other study

materials into the different languages used in the surveys, so as to maximize comparability of assessments across countries [18].

In most surveys, random sub-sampling was used, depending on allocation and availability of resources, in order to reduce respondent burden and average interviewing time. Within this framework, the CIDI 3.0, composed by clinical and non-clinical sections, was arranged in Part 1 and Part 2. All respondents received Part 1, and those who met lifetime diagnostic criteria (according to the DSM-IV and ICD-10) for any of the core disorders assessed in Part 1 (mood, anxiety, substance use and impulse-control disorders, as well as suicidal cognitions and behavior) and a probability sample of non-cases were administered also Part 2, which is composed by sections assessing risk factors, additional less common mental disorders (e.g. Obsessive Compulsive, Post Traumatic Stress and Eating Disorders), use of services, and physical conditions. Part 2 respondents were additionally weighted by the inverse of their probability of selection for Part 2 of the interview, thus adjusting for differential sampling. Analyses in this paper are based on the weighted Part 2 subsample, which was composed of 52, 095 respondents.

Consistent field quality control procedures, described in detail elsewhere [36], were implemented in all countries. Interviews were conducted after informed consent was given by respondents. All surveys were carried out strictly in compliance with procedures approved by local institutional review boards or ethical committees.

Measures

Mental disorders—All surveys used the WMH survey version of the above mentioned World Health Organization Composite International Diagnostic Interview (now CIDI 3.0) [27], a fully structured interview, developed to assess lifetime history of mental disorders, based on the DSM-IV definitions and criteria. A total of 16 mental disorders were assessed, including anxiety disorders (panic disorder, agoraphobia without panic, specific phobia, social phobia, post-traumatic stress disorder, generalized anxiety disorder, obsessive compulsive disorder); mood disorders (major depressive disorder/dysthymia, and bipolar disorders I and II); substance use disorders (alcohol and drug abuse and dependence); and impulse control disorders (intermittent explosive disorder, bulimia nervosa and binge eating disorder). CIDI organic exclusion rules were applied in making diagnoses. Clinical reappraisal studies conducted in some of the WMH countries indicate that lifetime diagnoses of anxiety, mood and substance use disorders based on the CIDI have generally good concordance with diagnoses based on blinded clinical interviews [19].

Chronic back or neck pain status—In a series of questions about physical health, adapted from the U.S Health Interview Survey [33], respondents were asked about the lifetime presence of selected chronic conditions. For the ascertainment of chronic back/neck pain, respondents were asked if they ever had serious chronic back/neck pain. Although all studies on chronic pain are reliant on self-assessment and self-reporting of symptoms and their intensity, as well as its age of onset (AOO), in an attempt to reduce information and recall biases and improve the quality of data collected, the question was carefully worded: “Serious chronic pain is defined as pain lasting six months or longer that is severe enough

either to interfere with your normal activities or to cause emotional distress. With that definition in mind, did you have serious chronic pain in the past 12 months in the neck/back region?"; if this was endorsed, they were further encouraged to best estimate the first age-of-onset of the condition). One major concern in self-reporting age of onset (AOO) is the occurrence of telescoping bias, which was explored through the analyses of AOO distributions across age cohorts, and there were not significant differences in reporting early onset chronic back/neck pain across age cohorts (data available on request). Therefore, if respondents endorsed having had the condition, they were classified as having a history of chronic back/neck pain and the age of onset was used to create the person-year dataset.

Statistical Analysis

Discrete-time survival analyses [47] with person-year as the unit of analysis were used to test sequential associations between first onset of mental disorders and the subsequent onset of chronic back/neck pain. For these analyses, a person-year data set was created in which each year in the life of each respondent up to and including the age-of-onset of chronic back/neck pain or their age at interview (whichever came first) was treated as a separate observational record, with the year of chronic back/neck pain onset coded 1 and earlier years coded 0, on a dichotomous outcome variable. Mental disorder predictors were coded 1 from the year after first onset of each individual mental disorder. This time lag of 1 year in the coding of the predictors ensured that in cases where the first onset of a mental disorder and of chronic back/neck pain occurred in the same year, the mental disorder would not count as a predictor. Only person-years up to the diagnosis of chronic back/neck pain were analyzed, so that only mental disorder episodes occurring prior to the onset of chronic back/neck pain were included in the predictor set. Logistic regression was used to analyze these data with the survival coefficients presented as odds ratios, indicating the relative odds of chronic back/neck pain onset in a given year for a person with a prior history of mental disorder compared to a person without that mental disorder, or without any history of mental disorder.

A series of bivariate and multivariate models were developed, including the "predictor" mental disorder plus control variables. Bivariate models investigated association of specific mental disorders with subsequent onset of chronic back/neck pain, where only one mental disorder at a time was considered as a predictor of chronic back/neck pain onset, each disorder in a separate discrete time survival model controlling for age-cohort, gender, person-year and country. The next model, a multivariate model, estimated the associations of each mental disorder with chronic back/neck pain onset, adjusting also for mental disorder comorbidity (that is, for other mental disorders occurring at any stage prior to the onset of chronic back/neck pain), with all mental disorders considered simultaneously in the model. A second multivariate model included a series of predictor variables for number of mental disorders (e.g., one such variable for respondents who experienced exactly one mental disorder, another for respondents who experienced exactly two mental disorders, and so on), as well as the control variables. Other more complex non-additive multivariate models were also run, for example, including both type and number of mental disorders, but model fit statistics did not indicate these provided a better fit for the data, so the simpler models are reported here (model fitting statistics are available on request). Our general approach was to

not control for covariates that could be on the causal pathway between mental disorders and subsequent chronic back/neck pain.

We examined life course variation in two ways. First, we examined whether early versus late-onset mental disorders differed significantly in their associations with chronic back/neck pain through creation of mental disorder-specific dummy variables for early-onset mental disorder (<= 21 years) and late-onset disorder (>21 years) (see table footnotes for model specifications). Second, we assessed whether associations varied by when in the life course chronic back/neck pain started by including cross-product terms between person-years (coded as a continuous variable) and each type of mental disorder in the multivariate type model. Gender differences were examined by including cross-product terms between gender and each mental disorder in the multivariate type model.

Our earlier studies of concurrent mental-physical comorbidity in the WMH surveys found that their associations are generally consistent cross-nationally, despite varying prevalence of mental disorder and physical conditions [54,12]. All analyses for this paper were therefore run on the pooled cross-national dataset. As the WMH Surveys data are both clustered and weighted, the design-based Taylor series linearization [44] implemented in version 10 of the SUDAAN software system [49] was used to estimate standard errors and evaluate the statistical significance of coefficients.

Results

Sample characteristics and history of chronic back or neck pain

Characteristics of the WMH samples and history of chronic back/neck pain are presented in Table 1. A total of 52,095 respondents (Part 2 sub-sample) were included in the analyses. From those, 14,609 respondents reported history of chronic back/neck pain, with a global prevalence of 24.7%. Although the prevalence range across countries was quite wide, from 9.7% in Peru to 50.5% in Italy, chronic back/neck pain was reported by one-fifth to one-third of the population in most countries (Table 1).

Prior mental disorders and subsequent onset of chronic back or neck pain

All mental disorders assessed were positively associated with subsequent onset of chronic back/neck pain (Table 2) in bivariate models, with odds ratios (ORs) ranging from 1.7 for alcohol abuse to 2.9 for bulimia nervosa.

Considering that comorbidity among lifetime mental disorders may play a role in the associations with chronic back/neck pain onset, the results of multivariate models are shown in the second data column of Table 2. It can be seen that, although the magnitude of the associations diminished, most disorders remained significantly associated with subsequent onset of chronic back/neck pain, with ORs ranging between 1.3 and 1.6 (Table 2); only bipolar disorder, agoraphobia without panic, and alcohol and drug dependence (i.e. 4 out of 16 disorders assessed) was not associated with subsequent pain in this model. The global chi square value for testing the joint effect of all types of mental disorders was large and highly significant ($Chi_{\mathbf{16}}$= 934.2; $p \leq 0.001$). Moreover, the test for variation in the ORs was also significant ($Chi_{\mathbf{15}}$= 67.3; $p \leq 0.001$), indicating that the hypothesis that the ORs are the same

for all disorders should be rejected, supporting the interpretation that those mental disorders remaining significant have specific associations with pain onset, rather than expressing just a global effect of emotional distress.

The next multivariate model considered the number of mental disorders, regardless of their type, with results presented in the last column of Table 2. There is a clear dose-response relationship in the association between the number of mental disorders experienced and subsequent onset of chronic back/neck pain, with ORs for pain of 1.8 in respondents with one mental disorder, increasing to 3.2 among those with five or more lifetime mental disorders (Table 2). The global chi square test for the joint effect of the number of mental disorders was large and highly significant ($Chi_{\mathbf{5}}$= 760.3; $p \leq 0.001$)

Timing of mental disorder onset (early versus late-onset)

We investigated whether early-onset mental disorders (defined as having first onset occurring prior to the age of 21) were more or less strongly associated with onset of chronic back/neck pain compared to later-onset mental disorders (Table 3). Results from the bivariate models, where early-onset and late-onset variants of each mental disorder were both included in the model as predictors of subsequent onset of chronic back/neck pain, with the usual control variables but with no adjustment for other mental disorders are presented in the first two columns of data in Table 3. Most (12 out of 16) early-onset mental disorders showed quantitatively larger associations with subsequent chronic back/neck pain compared to their later-onset equivalents. When formally tested, the differences (early versus later-onset ORs) were significant for depression/dysthymia, bipolar disorder, panic disorder, generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD), alcohol abuse and alcohol dependence. The magnitude of ORs for early-onset mental disorders leading to subsequent pain ranged from 1.8 for OCD to 2.6 for GAD and 2.8 for bulimia. For later-onset mental disorders, ORs ranged from 1.5 for all mood disorders, social phobia, and alcohol abuse, to 3.2 for bulimia (Table 3).

In the multivariate models (second set of columns in Table 3), when accounting for comorbid mental disorders, the only significant difference was for depression/dysthymia, as early-onset depression (ORs 1.5; 95% CI 1.3-1.5) was more strongly associated with subsequent pain onset compared to later-onset depression (ORs 1.3; 95% CI 1.2-1.4). Although variation in the timing of onset of the mental disorder evaluated does significantly affect the strength of association with subsequent chronic back/neck pain onset, most of the associations disappeared when accounting for comorbid mental disorders, as the earlier the onset of mental disorders, the greater the occurrence of lifetime comorbidity. Taken together, the joint effect of all early-onset mental disorders was large and highly significant ($Chi_{\mathbf{16}}$= 746.2; $p \leq 0.001$), and larger than the joint effect of the later-onset disorders ($Chi_{\mathbf{16}}$= 122.3; $p \leq 0.001$).

Variation across the life course regarding timing of chronic back or neck pain onset

To examine whether there were variations in the associations between mental disorders and pain onset, as a function of when in the life course the chronic back/neck pain onset occurred, we conducted a series of multivariate analyses including an interaction term

between person year and each mental disorder assessed as predictor, adjusting for the occurrence of other mental disorders (Table 4). There were strongly significant negative interactions between all mental disorders and person-year, indicating that the strength of associations do vary according to the timing (age) of pain onset for all mental disorders, seen in the first three columns of Table 4. The negative interaction indicates that the younger the age-of-onset of chronic back/neck pain, the stronger the role of mental disorders as determinants of pain occurrence. To better illustrate the nature of these interactions, the person-year dataset was then stratified into quartiles according to the age-of-onset of pain and the multivariate models were re-estimated for each quartile. These results, shown in the remainder of Table 4, indicate that associations between most mental disorders and subsequent chronic back/neck pain were stronger when the pain condition occurred earlier rather than later in life. This is illustrated by either the reducing magnitude of the associations or the loss of significance in older onset cohorts, as seen, for example, in depression/dysthymia (ORs 1.8 to 1.3, all significant) or in panic disorder (ORs 1.4 to 0.9). For a few disorders, this pattern is not evident with the categories applied in the stratified analyses. However, the negative interaction between person year and these disorders indicates that the general pattern of stronger association with earlier pain onset holds true for these disorders also.

Gender differences

There were no significant interactions of gender with any of the mental disorders in predicting chronic back/neck pain onset, indicating that associations of mental disorders and the pain condition were similar for men and women (results available on request).

Discussion

Using a large general population-based sample, this study corroborated the assumption that self-reported chronic back/neck pain is a frequent condition, affecting 20-30% of the general adult resident population in most countries (ranging from 10-50%). Due to the large number of respondents, the rigorous diagnostic assessment of common mental disorders, and systematic information on age-of-onset of both conditions, this is the first study able to examine the role a wide range of DSM-IV mental disorders may play in increasing the risk of subsequent onset of chronic back/neck pain, and to further adjust for mental disorder comorbidity. Indeed, all mental disorders studied were positively associated with subsequent onset of chronic back/neck pain in bivariate analyses, and, for most (12/16), the associations remained significant after adjusting for psychiatric comorbidity, including depression/dysthymia, all anxiety disorders (except agoraphobia), all impulse-control disorders, and alcohol and drug abuse. A clear dose-response relationship between the number of mental disorders experienced and the associated risk of subsequent onset of chronic back/neck pain was observed.

When examining the age-of-onset of DSM-IV mental disorders, almost all disorders (with the exception for late-onset specific phobia and agoraphobia) were associated with subsequent pain, regardless of age-of-onset; however, those with early-onset were more strongly associated with subsequent pain compared to their later-onset counterparts. When

adjusting for psychiatric comorbidity, the differential associations for early versus later-onset typically disappeared, due to the more frequent occurrence of psychiatric comorbidity following early-onset psychiatric disorders. The differential association only remained significant for depression/dysthymia, indicating that early-onset depression may create a specific vulnerability to later-onset back pain. Another important novel finding was that the earlier the onset of chronic back/neck pain, the stronger the role of mental disorders as predictors of pain occurrence, for most mental disorders. And finally, although women are more likely to report pain and to suffer from mood and anxiety disorders, there were no gender differences in the associations of mental disorders and subsequent onset of chronic back/neck pain.

Despite the strengths of this study, it is also important to emphasize a number of limitations, which may influence the interpretation of the findings. Retrospective information regarding mental health symptoms, collected in a cross-sectional design, is likely to be susceptible to recall bias, which may result in underestimating diagnosis of psychiatric disorders [56] and/or inaccurate timing estimation of age-at-onset of symptoms [46]. Attempting to reduce recall bias, the CIDI 3.0 version developed to be used in the WMH surveys was modified to improve precision in timing events and age-of-onset of symptoms [27]. The occurrence of chronic back/neck pain was self-reported, based on a limited number of questions based on a stated definition of “serious chronic pain”, which might have led to the underestimation of mild pain conditions, as more severe and lasting pain is more likely to be reported [26]. Previous findings have suggested that self-reporting might be less distorted than behavioral pain measures, which are likely to be influenced by cultural and social norms or coping strategies [20,48]. Additionally, self-report methods have shown to present moderate to high agreement with medical records [33]. However, reporting pain may be influenced by current mood status, especially if respondents are currently depressed [51]. To assess for this potential limitation, we re-ran the analyses excluding respondents with DSM-IV 30-day MDD and essentially the same results were observed, i.e. the associations remained the same regardless of current depressive mood (data available on request). Since back/neck pain are not conditions commonly associated with premature death, it is unlikely that these finding may have been affected by survival bias. However, the most severe and impairing cases were probably not included in the surveys, as they either would not be able to participate in such a complex assessment or may have been admitted into healthcare facilities; in both cases this would have led to underestimation of the strength of the associations examined. Finally, control for multiple comparisons were not carried out, as its use has been the subject of considerable scientific debate [40].

These findings, based on the survival analysis framework used in this study, cannot be paralleled by any other single previous report in the literature for several reasons: the range of mental disorders assessed in this study was wider than previous research (which mostly focused on depression and anxiety), and these were ascertained through the systematic investigation of symptoms based on diagnostic criteria; a specific temporal direction of associations was investigated i.e. mental disorders as predictors and chronic back/neck pain as the outcome; the impact of timing of onset of mental disorders in the occurrence of pain, as well as the influence of mental disorders in the timing of pain onset, have never been

investigated. However, given the retrospective nature of the data, these findings will require confirmation in prospective designs.

Prior investigation has been mostly devoted to assessing the relationship of pain and major depression, with reports of bi-directional relationships or co-occurrence [13,17], with, in all cases, worse clinical prognosis, poorer treatment response, and increased disability [2,43]. In this study, depression, examined together with dysthymia, was found to be significantly associated with subsequent onset of back/neck pain, even after controlling for comorbidity with other mental disorders, and regardless of age-at-onset of back/neck pain, not only corroborating previous findings, but establishing novel information. Depression, among all disorders studied and after controlling for psychiatric comorbidity, was the only mental disorder conveying differential magnitude of risk for pain, when occurring early, compared to late-onset.

The relation between chronic pain and mental disorders is not easy to disentangle, as there are many mechanisms involved in the pain process, such as interaction in the central nervous system neurotransmitters and receptors, genetic influences, inhibition of pain circuitry, turning the understanding of pain expression and comorbidity extremely complex [4]. Evidence from translational research suggests that the neuroanatomical and functional overlap between pain and emotion/reward/motivation brain circuits support integration and mutual modulation of these systems [14]. Behavior-related mechanisms might also be relevant, as psychiatric conditions are related to being sedentary and poorer diets, leading to dyslipidemia and obesity, causing inflammation, in turn associated with both pain and psychiatric morbidity, especially depression [1,39,50]. However, as we found associations with most mental disorders, lifestyle and/or behavior-associated mechanisms may play a generic, non-specific role across mental disorders. Other lifestyle-related behaviors, such as occupational stress and tobacco smoking, may also contribute to psychoimmune dysfunctions and inflammation [34]. Psychiatric disorders are frequently associated with alterations in pain processing, whereas chronic pain may impair emotional and cognitive functioning [14]. And indeed, beyond depression, we documented that most mental disorders assessed are significantly associated with subsequent chronic back/neck pain onset, with important implications for prevention and care provision. Although there is a robust literature on depression being associated with inflammation, there is less agreement on the causal nature of this association, or if there might underlying factors causing both, mental disorders and pain.

It is well established that early onset mental disorders take longer to be diagnosed and treated, often present with greater severity of symptoms, and have generally poorer prognosis and more disabling course [38,42,43]. They are also more likely to be associated with comorbid medical/physical conditions, as well as with other psychiatric disorders later in life [43]. The stronger association of early onset mental disorders with subsequent pain (compared to later onset mental disorders) may help explain part of the burden associated with the more pervasive course of early-onset psychiatric conditions. It may also indicate the deleterious role that inflammatory processes associated with more severe mental disorders may pose to physical conditions [34,39]. Moreover, since comorbidity of mental disorders is common, and the number of disorders over the lifetime is a marker of severity of

psychopathology, it is of interest that the strength of association with pain increases as the number of disorders experienced increases, as demonstrated by the dose-response relationship found.

The public health importance of chronic back/neck pain is unquestionable [55,52]. Its consequences are vast and affect individuals, families, health-care systems, industry, and the economy [52], attributed to restrictions in physical capabilities, individual participation, work-related and financial burden, and use of health-care resources [55,52]. This report points out the great importance of all mental disorders as associated risk factors for subsequent onset of chronic back and neck pain, and these findings should be taken into account to improve early identification and management of mental health disorders and pain symptoms, thereby reducing comorbidity and disability.

Disclosures

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Table 1.

Characteristics of WMH samples and percent (and number) with history of chronic back or neck pain.

Country	Data Collection	Age Range	Sample Size (N)		Response Rate (%)	History of Chronic back or neck pain	
			Part 1	Part 2 sub-sample		Number Unweighted (N)	Weighted prevalence (%)
Americas							
Colombia	2003	18–65	4426	2381	87.7	516	17.3
Mexico	2001-2	18-65	5782	2362	76.6	682	23.6
Peru	2005-6	18-65	3930	1801	90.2	201	9.7
United States	2002-3	18+	9282	5692	70.9	1905	29.3
Asia and South Pacific							
PRC* Shenzhen	2006-7	18+	7132	2475	80.0	555	14.8
Japan	2002-6	20+	4129	1682	55.1	501	25.3
New Zealand	2003-4	18+	12790	7312	73.3	2463	30.2
Europe							
Belgium	2001-2	18+	2419	1043	50.6	368	31.0
France	2001-2	18+	2894	1436	45.9	586	38.2
Germany	2002-3	18+	3555	1323	57.8	395	28.5
Italy	2001-2	18+	4712	1779	71.3	947	50.5
The Netherlands	2002-3	18+	2372	1094	56.4	329	24.2
Northern Ireland	2004-7	18+	4340	1986	68.4	435	21.3
Poland	2010-11	18-64	10081	4000	50.4	888	18.8
Portugal	2008-9	18+	3849	2060	57.3	542	22.4
Romania	2005-6	18+	2357	2357	70.9	550	20.7
Spain	2001-2	18+	5473	2121	78.6	641	23.7
Middle East							
Iraq	2006-7	18+	4332	4332	95.2	860	18.2
Israel	2002-4	21+	4859	4859	72.6	1245	25.1
Weighted average response rate (%)					67.4		
Total sample size			98714	52095		14609	24.7

*People's Republic of China

Table 2.

Bivariate and multivariate associations (odds ratios) between lifetime DSM-IV mental disorders and the subsequent onset of chronic back or neck pain (N=52095).

	Bivariate Models[1]		Multivariate Type Model[2]		Multivariate Number Model[3]	
Mental disorders[#]	**OR**	**(95% C.I.)**	**OR**	**(95% C.I.)**	**OR**	**(95% C.I.)**
I. Mood disorders						
Major Depressive Episode/ Dysthymia	1.8*	(1.7-1.9)	1.4*	(1.3-1.5)	-	-
Bipolar Disorder (Broad)	2.1*	(1.8-2.4)	1.1	(1.0-1.4)	-	-
II. Anxiety disorders						
Panic Disorder	2.1*	(1.8-2.3)	1.3*	(1.1-1.4)	-	-
Generalized Anxiety Disorder	2.2*	(2.0-2.4)	1.4*	(1.3-1.6)	-	-
Social Phobia	1.9*	(1.7-2.0)	1.3*	(1.1-1.4)	-	-
Specific Phobia	1.8*	(1.7-2.0)	1.5*	(1.4-1.6)	-	-
Agoraphobia without Panic	1.8*	(1.5-2.2)	1.0	(0.8-1.3)	-	-
Post-Traumatic Stress Disorder	2.0*	(1.7-2.2)	1.3*	(1.1-1.4)	-	-
Obsessive Compulsive Disorder	1.9*	(1.5-2.5)	1.4*	(1.1-1.8)	-	-
III. Impulse-control disorders						
Intermittent Explosive Disorder	2.2*	(1.9-2.5)	1.5*	(1.3-1.7)	-	-
Binge Eating Disorder	2.1*	(1.6-2.8)	1.5*	(1.1-2.0)	-	-
Bulimia Nervosa	2.9*	(2.2-3.7)	1.6*	(1.2-2.1)	-	-
IV. Substance disorders						
Alcohol Abuse	1.7*	(1.6-1.9)	1.3*	(1.2-1.5)	-	-
Alcohol Dependence with Abuse	2.0*	(1.7-2.3)	1.0	(0.9-1.2)	-	-
Drug Abuse	2.2*	(1.9-2.5)	1.4*	(1.2-1.6)	-	-
Drug Dependence with Abuse	2.1*	(1.7-2.6)	0.8	(0.6-1.0)	-	-
Joint effect of all types of disorders, χ^2_{16}				934.2*		
Difference between types of disorders, χ^2_{15}				67.3*		
V. Number of disorders						
None (reference)					1.0	
Exactly 1 disorder	-	-	-	-	1.8*	(1.7-2.0)
Exactly 2 disorders	-	-	-	-	2.2*	(2.0-2.4)
Exactly 3 disorders	-	-	-	-	2.5*	(2.2-2.8)
Exactly 4 disorders	-	-	-	-	2.5*	(2.2-2.9)
5+ disorders	-	-	-	-	3.2*	(2.7-3.7)
Joint effect of number of disorders, χ^2_5						760.3*

*Significant at the 0.05 level, two-tailed test.

[#]The reference category for all disorders is the absence of each diagnosis.

[1]Bivariate models: each mental disorder type was estimated as a predictor of the physical condition onset in a separate discrete time survival model controlling for age cohorts, gender, person-year and country.

[2]Multivariate Type model: the model was estimated with dummy variables for all mental disorders entered simultaneously, including the controls specified above.

[3]Multivariate Number model: the model was estimated with dummy predictors for number of mental disorders without any information about type of mental disorders, including the controls specified above.

Table 3.

Associations (odds ratios) between early vs. late mental disorder onset and the subsequent onset of chronic back or neck pain.

	Bivariate Models[1]				Multivariate Model[2]			
	Early	Late	Test of the difference between early and late		Early	Late	Test of the difference between early and late	
	OR (95% C.I)	OR (95% C.I)	χ_1^2	[p]	OR (95% C.I)	OR (95% C.I)	χ_1^2	[p]
I. Mood disorders								
Major Depressive Episode/Dysthymia	2.2* (2.0-2.4)	1.5* (1.4-1.7)	31.8*	[0.000]	1.5* (1.3-1.6)	1.3* (1.2-1.4)	4.6*	[0.032]
Bipolar Disorder (Broad)	2.5* (2.1-3.0)	1.5* (1.2-2.0)	8.3*	[0.004]	1.2 (1.0-1.5)	0.9 (0.7-1.2)	3.0	[0.085]
II. Anxiety disorders								
Panic Disorder	2.4* (2.0-2.8)	1.7* (1.4-2.0)	7.2*	[0.007]	1.3* (1.1-1.6)	1.2 (0.9-1.4)	0.9	[0.358]
Generalized Anxiety Disorder	2.6* (2.3-3.0)	1.8* (1.6-2.1)	15.4*	[0.000]	1.5* (1.3-1.7)	1.3* (1.2-1.5)	1.6	[0.213]
Social Phobia	1.9* (1.8-2.1)	1.5* (1.1-2.0)	2.9	[0.090]	1.3* (1.1-1.4)	1.0 (0.7-1.4)	1.6	[0.203]
Specific Phobia	1.9* (1.7-2.0)	1.4 (1.0-1.9)	3.2	[0.075]	1.5* (1.4-1.7)	1.2 (0.8-1.7)	1.7	[0.197]
Agoraphobia Without Panic Disorder	1.9* (1.5-2.4)	1.4 (1.0-2.0)	2.4	[0.125]	1.0 (0.8-1.3)	0.9 (0.6-1.3)	0.4	[0.544]
Post-Traumatic Stress Disorder	2.2* (1.9-2.6)	1.6* (1.3-2.1)	4.9*	[0.028]	1.3* (1.2-1.6)	1.2 (1.0-1.5)	0.8	[0.372]
Obsessive Compulsive Disorder	1.8* (1.4-2.5)	2.3* (1.3-4.3)	0.4	[0.549]	1.4* (1.0-1.8)	1.6 (0.9-3.0)	0.2	[0.642]
III. Impulse-control disorders								
Intermittent Explosive Disorder	2.3* (2.0-2.6)	1.8* (1.3-2.6)	1.6	[0.210]	1.5* (1.3-1.8)	1.3 (0.9-1.9)	0.4	[0.525]
Binge Eating Disorder	1.9* (1.4-2.7)	2.4* (1.5-3.9)	0.5	[0.467]	1.4 (1.0-1.9)	1.6 (1.0-2.7)	0.3	[0.620]
Bulimia Nervosa	2.8* (2.1-3.7)	3.2* (2.0-5.1)	0.3	[0.598]	1.4* (1.0-2.0)	2.0* (1.2-3.3)	1.0	[0.317]
IV. Substance disorders								
Alcohol Abuse	1.9* (1.7-2.2)	1.5* (1.3-1.7)	10.1*	[0.002]	1.4* (1.2-1.7)	1.2* (1.0-1.4)	2.7	[0.102]
Alcohol Dependence with Abuse	2.3* (1.9-2.7)	1.6* (1.3-2.1)	5.1*	[0.023]	1.1 (0.9-1.3)	1.0 (0.8-1.3)	0.3	[0.612]
Drug Abuse	2.1* (1.8-2.5)	2.2* (1.7-2.9)	0.0	[0.896]	1.3* (1.0-1.6)	1.4* (1.1-1.9)	0.4	[0.521]
Drug Dependence With Abuse	2.2* (1.7-2.8)	2.0* (1.3-3.0)	0.2	[0.660]	0.7 (0.5-1.0)	0.8 (0.5-1.3)	0.2	[0.651]

	Bivariate Models[1]				Multivariate Model[2]			
	Early	Late	Test of the difference between early and late		Early	Late	Test of the difference between early and late	
	OR (95% C.I)	OR (95% C.I)	χ_1^2	[p]	OR (95% C.I)	OR (95% C.I)	χ_1^2	[p]
V. Joint Effect of all Early Onset Disorders, χ^2_{16}					746.2*			
VI. Joint Effect of all Late Onset Disorders, χ^2_{16}						122.3*		
VII. Joint Effect of Early Onset Disorders independent of joint effect of any disorders,χ^2_{16}							30.8*	

*Significant at the 0.05 level, two-tailed test.

[1]Models include dummy variables for early onset mental disorders (= first onset < 21 years of age) and for late onset disorders, plus control variables (age-cohort, person years, gender and country). A second bivariate model was estimated to test the significance of the difference between early and late onset disorders. This model included the dummy variables for the early onset disorder and the dummy variable for the disorder itself (i.e, having it at all), plus controls.

[2]Multivariate models paralleled the bivariate models in design but included dummy variables for all mental disorders entered simultaneously.

Table 4.

Variations in associations between mental disorders and chronic back or neck pain by lifecourse timing of chronic back or neck pain onset.

Type of Mental Disorders	Mental disorder*Person-year interaction[1]			Stratified Models[2]			
				Up to Age 24	Age 25-35	Age 36-47	Age 48+
	OR (95% C.I.)	χ^2_1	[p]	OR (95% C.I.)	OR (95% C.I.)	OR (95% C.I.)	OR (95% C.I.)
Major Depressive Episode/ Dysthymia	0.98*(0.98-0.98)	87.7*	[0.000]	1.8*(1.6-2.0)	1.4*(1.2-1.5)	1.3*(1.2-1.5)	1.3*(1.1-1.5)
Bipolar Disorder (Broad)	0.98*(0.97-0.99)	11.8*	[0.001]	1.3*(1.0-1.7)	1.0 (0.7-1.4)	1.0 (0.6-1.4)	1.5 (0.9-2.4)
Panic Disorder	0.97*(0.96-0.98)	37.3*	[0.000]	1.4*(1.1-1.8)	1.5*(1.2-1.9)	1.2 (0.9-1.5)	0.9 (0.6-1.3)
Generalized Anxiety Disorder	0.98*(0.97-0.99)	23.5*	[0.000]	1.4*(1.1-1.7)	1.2*(1.0-1.5)	1.7*(1.4-2.1)	1.5*(1.2-1.9)
Social Phobia	0.98*(0.97-0.98)	68.4*	[0.000]	1.3*(1.1-1.5)	1.3*(1.1-1.5)	1.0 (0.9-1.3)	0.9 (0.7-1.2)
Specific Phobia	0.99*(0.99-1.00)	16.4*	[0.000]	1.4*(1.3-1.6)	1.5*(1.3-1.7)	1.5*(1.3-1.7)	1.5*(1.2-1.9)
Post-Traumatic Stress Disorder	0.98*(0.97-0.99)	21.6*	[0.000]	1.2 (1.0-1.5)	1.4*(1.1-1.8)	1.3*(1.0-1.7)	1.2 (0.9-1.6)
Intermittent Explosive Disorder	0.99*(0.97-1.00)	7.8*	[0.005]	1.5*(1.2-1.9)	1.5*(1.2-1.9)	1.3 (0.9-1.8)	1.5 (0.9-2.3)
Alcohol Abuse	0.97*(0.96-0.98)	59.0*	[0.000]	1.4*(1.1-1.7)	1.3*(1.1-1.6)	1.3*(1.0-1.7)	1.0 (0.7-1.3)
Alcohol Dependence with Abuse	0.98*(0.96-0.99)	11.7*	[0.001]	1.0 (0.8-1.4)	1.0 (0.7-1.4)	1.0 (0.7-1.4)	1.5 (1.0-2.5)
Drug Abuse	0.97*(0.95-0.99)	13.2*	[0.000]	1.3 (1.0-1.8)	1.1 (0.8-1.4)	1.7*(1.1-2.4)	2.1*(1.2-3.7)
Drug Dependence with Abuse	0.96*(0.93-0.98)	11.1*	[0.001]	0.8 (0.6-1.2)	0.9 (0.6-1.3)	0.6 (0.3-1.1)	0.2*(0.1-0.9)

*OR significant at the 0.05 level, 2-sided test

[1]A series of multivariate models were estimated. For example, the model for depression included the dummy variables for all mental disorders plus the cross-product term for depression and person-year (as a continuous variable), plus the controls specified for earlier models.

[2]The multivariate model was estimated in the four person-year datasets corresponding to quartiles of the chronic back or neck pain onset distribution.