Associations between DSM-IV mental disorders and subsequent COPD diagnosis

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Abstract

Objectives—COPD and mental disorder comorbidity is commonly reported, although findings are limited by substantive weaknesses. Moreover, few studies investigate mental disorder as a risk for COPD onset. This research aims to investigate associations between current (12-month) DSM-IV mental disorders and COPD, associations between temporally prior mental disorders and subsequent COPD diagnosis, and cumulative effect of multiple mental disorders.

Methods—Data were collected using population surveys of 19 countries (n = 52,095). COPD diagnosis was assessed by self-report of physician's diagnosis. The World Mental Health-Composite International Diagnostic Interview (WMH-CIDI) was used to retrospectively assess

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lifetime prevalence and age at onset of 16 DSM-IV disorders. Adjusting for age, gender, smoking, education, and country, survival analysis estimated associations between first onset of mental disorder and subsequent COPD diagnosis.

Results—COPD and several mental disorders were concurrently associated across the 12-month period (ORs 1.5–3.8). When examining associations between temporally prior disorders and COPD, all but two mental disorders were associated with COPD diagnosis (ORs 1.7–3.5). After comorbidity adjustment, depression, generalized anxiety disorder, and alcohol abuse were significantly associated with COPD (ORs 1.6–1.8). There was a substantive cumulative risk of COPD diagnosis following multiple mental disorders experienced over the lifetime. Conclusions: Mental disorder prevalence is higher in those with COPD than those without COPD. Over time, mental disorders are associated with subsequent diagnosis of COPD; further, the risk is cumulative for multiple diagnoses. Attention should be given to the role of mental disorders in the pathogenesis of COPD using prospective study designs.

Keywords

Alcohol abuse; Anxiety disorders; Comorbidity; COPD; Depression

Introduction

Mental disorders are highly prevalent among those with COPD. [1–3] Mental disorder and COPD comorbidity may negatively affect adaptive functioning, quality of life, exercise capacity, treatment adherence, and mortality. [4,5] A review of studies published between 1968 and 2004 reported that in those with COPD, prevalence of depression ranged from 7%-79% and prevalence of anxiety ranged from 10%–100%; [2] a review of studies between 1966 and 2012, which only included studies using a clinical diagnostic tool to assess mental disorder, found rates ranging between 0%–42% and 10%–55% respectively. [1].

The research investigating mental disorder and COPD comorbidity prevalence is limited by multiple methodological weaknesses including use of small samples, clinical populations of patients with COPD, and symptom rating scales rather than diagnostic clinical measures. Symptom rating scales for mental disorders do not differentiate between diagnostic categories, sometimes overlap with COPD, and may describe negative emotional responses to COPD. Thus, it is not surprising that estimates of the prevalence of mental disorder and COPD comorbidity vary widely. Cross-sectional analysis of general population samples reveals elevated risk of mental disorder in those with COPD. [6–8] However, it is difficult to conclude whether there is an association between COPD and some mental disorders but not others; whether there are differences in the relative strength of association between different mental disorders and COPD, or whether there is a non-specific association between COPD and any mental disorder (that is, mental distress generally).

Moreover, prospective studies that identify the direction of the association between COPD and mental disorders are needed. Understanding the direction of the association between COPD and mental disorders may help clarify the mechanisms that connect these debilitating conditions. The majority of prospective studies have been conducted with participants with COPD at baseline and have determined that mental disorders increase poor outcomes in those with COPD. [3] However, prospective studies investigating mental disorder as a risk factor for COPD onset are lacking. One study provides evidence toward the hypothesis that mental disorder increases risk for COPD, finding that depression doubled the risk for later COPD diagnosis [9].

The World Mental Health (WMH) Surveys comprise cross-national data drawn from the general populations of a range of developed and developing countries, clinically valid assessment of lifetime prevalence of a wide range of DSM-IV mental disorders, and self-reported physician's diagnosis and year of diagnosis of chronic lung disease (referred to herein as COPD). The surveys are cross-sectional in design but collected information retrospectively on age of diagnosis of mental disorders and of COPD, which allows the use of survival analysis to examine associations between temporally prior mental disorders and the subsequent diagnosis of COPD.

The aims of the study were three-fold. First, we estimated concurrent (12 month) associations between lifetime COPD and a wide range of 12 month DSM-IV mental disorders. Second, we investigated associations between first onset of temporally prior mood, anxiety, impulse control, and substance use disorders with subsequent COPD diagnosis, with and without adjustment for mental disorder comorbidity. Third, we investigated whether there was a cumulative effect of multiple mental disorders and subsequent risk of COPD. Adjustment was made for smoking in all analyses.

Method

Samples and procedures

This study uses data from 19 of the WMH surveys (see Table 1). The World Mental Health (WMH) Survey Initiative is a project of the World Health Organization aimed at addressing the global burden of mental disorders. [10,11] A stratified multi-stage clustered area probability sampling strategy was used to select adult respondents (18 years +) in most WMH countries. In most countries, internal subsampling was used to reduce respondent burden and average interview time by dividing the interview into two parts. All respondents completed Part 1 which included the core diagnostic assessment of most mental disorders. All Part 1 respondents who met lifetime criteria for any mental disorder and a probability sample of respondents without mental disorders were administered Part 2 which assessed physical conditions and collected a range of other information related to survey aims. Part 2 respondents were weighted by the inverse of their probability of selection for Part 2 of the interview to adjust for differential sampling, resulting in an unbiased sample.

Analyses in this paper are based on the weighted Part 2 subsample (n = 52,095; person years = 2,167,404). Additional weights were used to adjust for differential probabilities of selection within households, to adjust for non-response, and to match the samples to population socio-demographic distributions. Measures taken to ensure data accuracy, cross-national consistency and protection of respondents are described in detail elsewhere. [11,12] All respondents provided informed consent and procedures for protecting respondents were approved and monitored for compliance by the Institutional Review Boards in each country (see [11] for details).

Measures

Mental disorders—All surveys used the WMH survey version of the WHO Composite International Diagnostic Interview (now CIDI 3.0, [12]) a fully structured interview, to assess lifetime history of mental disorders. Retrospective age-of-onset reports were based on a question series designed to avoid the implausible response patterns obtained in using the standard CIDI age-of-onset question. [13] Disorders were assessed using the definitions and criteria of the DSM-IV. The mental disorders adjusted for in this paper include *anxiety disorders*, *mood disorders*, *substance use disorders*, and *impulse control disorders*. 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. [14].

COPD status—In a series of questions adapted from the U.S Health Interview Survey, [15] respondents were asked about the lifetime presence of selected chronic conditions. Respondents were asked: "Did a doctor or other health professional ever tell you that you had any of the following illnesses… *Other chronic lung disease, like COPD or emphysema*?" If respondents endorsed this question they were classified as having a history of COPD for these analyses. Asthma was not included in this category because it was asked about in a separate question that preceded this 'other chronic lung disease' question.

Although it is possible that some respondents with chronic lung diseases other than COPD/ emphysema may have endorsed this question we use the term COPD as this is likely to comprise the majority of cases captured by this question. Respondents were also asked how old they were when they were first diagnosed with COPD. Only adult-onset COPD (onsets age 21 +) was investigated in this paper on the assumption that pre-adult onsets would reflect congenital processes, rather than any possible influence of temporally prior mental disorders.

Smoking status—Smoking was assessed with one item and respondents were classified according to three-levels, *current smoker*, *ex-smoker*, *or never smoked*.

Statistical analysis

Aim 1—The prevalence of specific mental disorders was estimated separately among respondents with and respondents without a COPD diagnosis. The ORs of the associations between lifetime COPD and specific 12 month DSM-IV mental disorders were calculated in logistic regression equations that adjusted for age, gender, country, smoking, and years of education.

Aim 2—Although the data collection was cross-sectional, there was a time element in the data as we asked for the time of onset of mental disorders and of COPD. We analyzed the associations between mental disorder and COPD diagnosis by using this time-related information. Comparable with previous studies [16,17] using these data we used discrete-time survival analyses [19,20] with person-year as the unit of analysis to investigate sequential associations between first onset of mental disorders and the subsequent diagnosis of COPD. 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 diagnosis of COPD or their age at interview (whichever came first) was treated as a separate observational record, with the year of COPD diagnosis coded 1 and earlier years coded 0 on a dichotomous outcome variable. As stated earlier, we were interested in adults with a COPD diagnosis over the age of 20, therefore the small number of people who reported COPD diagnosis before age 21 were excluded from the analyses. Mental disorder predictors were coded 1 from the year after first diagnosis of each individual mental disorder. This time lag of 1 year in the coding of the predictors ensured that in cases where the first diagnosis of a mental disorder and of COPD occurred in the same year, the mental disorder would not count as a predictor. Only person-years up to the diagnosis of COPD were analyzed so that only mental disorder episodes occurring prior to the diagnosis of COPD were included in the predictor set. Logistic regression analysis was used to estimate associations with the survival coefficients presented as odds ratios, indicating the relative odds of COPD diagnosis in a given year for a person with a prior history of the specific mental disorder compared to people without that mental disorder and people without any mental disorder history at all.

First, a series of single disorder multivariate models were developed including the predictor mental disorder plus control variables to investigate whether each individual mental disorder contributed to an accelerated diagnosis of COPD. Second, a multi disorder model was developed including all mental disorders thereby adjusting for comorbidity to investigate the contribution of each mental disorder over and above the effect of other types of mental disorder.

Aim 3—To investigate the cumulative effect of an increasing number of mental disorders, discrete time survival analysis was used to estimate a model that included number of disorders coded as dummy variable (1, 2, 3, 4, 5 +) without information about type of disorder. For example, those with exactly 1 disorder were coded 1 and the rest of the sample was coded 0 in the exactly 1 disorder category.

All models control for countries, gender, current age, smoking, education level, and cohort (defined by ages at interview 18–29, 30–44, 45–59, 60 +). Our earlier studies of concurrent mental-physical comorbidity in the WMH surveys found that these associations are generally consistent cross-nationally, despite varying prevalence of mental disorder and physical conditions. [10,21] All analyses for this paper were therefore run on the pooled cross-national dataset. As the WMH data are both clustered and weighted, the design-based Taylor series linearization [22] implemented in version 10 of the SUDAAN software system [23] was used to estimate standard errors and evaluate the statistical significance of coefficients.

Results

The survey characteristics are shown in Table 1 together with information about the number of survey respondents reporting a history of COPD (n = 790). Prevalence of COPD diagnosis ranged from 0.1 (Mexico) to 3.4 (Israel) with an averaged prevalence across all countries of 1.3%. It should be noted that prevalence of COPD diagnosis will be underestimated in those 4 countries with upper age limits of 65 relative to the other countries with unrestricted upper ages of respondents. Prevalence of COPD diagnosis is also likely to vary considerably according to country differences in health service availability and assessment procedures. The prevalence of COPD reported in this study is lower than other studies, for example in a US study using a similar method for assessing COPD, the prevalence of COPD was 6.0%. [24].

Twelve-month prevalence of mental health disorders by lifetime COPD status and concurrent comorbidity

As can be seen in Table 2, across a 12-month period, most mood and anxiety disorders were associated with a 50–220% (OR: 1.5–3.2) increased risk of COPD. The impulse control disorders and most substance use disorders were not associated with significantly elevated risk for COPD, excepting drug abuse with dependence, which was associated with a 280% increased risk of COPD diagnosis.

Type and number of mental disorders as predictors of subsequent COPD diagnosis

Results of analysis examining associations between temporally prior mental disorders and subsequent COPD are presented in Table 3. In the single disorder models, with no adjustment for comorbid disorders, all but two mental disorders (binge eating disorder and bulimia nervosa) are associated with COPD with ORs between 1.7–3.5.

In the multi-disorder model, with adjustments for mental disorder comorbidity, the magnitude of associations was reduced (ORs from 1.6–1.8). Depression/dysthymia, generalized anxiety disorder, and alcohol abuse continued to predict diagnosis of COPD over and above the effect of the other disorders.

The global chi square test for the joint effect of all mental disorders was significant (χ^2_{16} = 112.9, $p < 0.001$), however the test for variation in ORs indicates that the associations do not differ significantly in magnitude (χ^2_{15} = 17.4, $p = 0.298$). A cautious interpretation of this latter test result would be that we have found a generalized link between psychopathology and COPD diagnosis, with some suggestion that depression, anxiety, and alcohol abuse may have specific associations with COPD, but these specific relationships would require confirmation in subsequent studies.

Table 4 displays the clear dose–response relationship between number of mental disorders experienced over the life course (prior to COPD diagnosis) and an accelerated COPD diagnosis. At each level of number of mental disorders (1, 2, 3, 4, 5 +) a greater proportion of those with COPD experienced mental disorder (18.3%, 9.0%, 6.2%, 1.9%, 3.8%) compared to those without COPD (16.0%, 6.6%, 2.8%, 1.4%, 1.6%). Further, the results from a multivariate model that considered only number of mental disorders (i.e., not including information about type) are presented in the final columns of data in Table 3., with ORs ranging from 1.6 for one mental disorder to 5.8 for 5 + mental disorders. This model was a better fit for the data than the multivariate type model just presented, again reinforcing the idea that it is psychopathology in general that matters most in terms of increasing COPD risk rather than specific types of mental disorders.

Additional analyses

Multivariate type and number models were developed; other more complex non additive multivariate models were also run, for example including both type and number of mental disorders in the same model, 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 available on request).

Gender differences were examined by including interaction terms between gender and each mental disorder in the multivariate type model but as results were substantively the same for men and women we report results with adjustment for gender.

Minimal changes were observed in the associations between mental disorders and COPD diagnosis after adjustment for nicotine use (data not shown but available on request).

Discussion

This is the first study evaluating the association of a wide range of DSM-IV mental disorders with COPD diagnosis in an international sample. The main finding were that there was an increased likelihood of COPD and mental disorder comorbidity across a 12-month period; those with mood, anxiety, and drug abuse with dependence were 50–280% more likely to also have a COPD diagnosis, which addressed the first aim of the study. The second aim was to investigate associations between temporally prior mental disorders and subsequent COPD diagnosis; significant associations between most mental disorders and COPD were found. After adjusting for comorbidity, depression, generalized anxiety disorder, and alcohol abuse contributed independently to an increased risk of COPD diagnosis at each time point (year of life). Third, there was a marked dose response for cumulative number of mental disorders experienced over the lifetime and the risk of COPD.

The conclusions from this study are constrained by several caveats. COPD status was assessed by self-report of medical diagnosis without verification by clinical assessment and by retrospective report, which may have led to errors in classification and reported age of diagnosis timing. [13] Prevalence of COPD in this study appeared lower than previously reported [24] and rates varied between countries. Moreover, in four countries participation was limited to individuals under the age of 65, which likely excluded the greater proportion of individuals with COPD in those localities. Furthermore, COPD is likely to be markedly under-diagnosed in the general population whereby those who meet criteria for COPD have not received a medical diagnosis. [25] Thus, it is probable that classification errors were made whereby some of those with COPD were classified as not having COPD. Mood has not been found to influence reports of clinician diagnosed conditions [26,27] therefore it is unlikely that current mood disorder moderated self-report of COPD. The result of non-differential, under-reporting would be to weaken possible associations between variables and therefore the findings from this study may be conservative.

The age of mental disorder onset distributions from the WMH surveys are consistent across countries and with other research; [28,29] however, some degree of inaccuracy with the precise timing of onset is likely to remain. Mitigating this, the validity of the survival analysis depends more on the temporal sequence of the mental disorders and COPD being correct, and less on accuracy in their precise onset timing. For most individuals their mental disorders and diagnosis of COPD occurred decades apart, thus the temporal sequence is likely to be correct. To further ensure this though, we do not include as predictors any mental disorders that were reported to occur in the same year as their COPD diagnosis.

Selective classification errors whereby those most affected by mental disorders and COPD are absent from the sample due to hospitalization or early mortality would also influence associations in the direction of a null finding. Finally, this is a retrospective study and although the information on timing of COPD diagnosis and mental disorder onset allowed the estimation of predictive associations that are indicative of specific temporal associations from mental disorder to COPD, these results are regarded as preliminary and await confirmation from prospective studies.

Despite its limitations, this study has a number of unique characteristics that allow for novel contributions to the literature. Controlling for cultural differences was possible through multi-national participation. Selection bias was reduced through surveying the general population. The sample size was sufficient to consider possible associations between COPD and a range of mental disorders, including disorders with lower prevalence rates. Mental disorders were assessed using a clinical instrument allowing for discrimination between diagnostic categories and for adjustment for comorbidity among disorders.

Although as noted, prospective studies will be required to confirm the study findings, it is worth considering the potential causal pathways that mental disorders have in common and how these may increase susceptibility to COPD. One direct, biological mechanism that may connect mental disorders with COPD onset is raised inflammatory response and impaired immune regulation. [5] The immune irregularities in depression are complex and there is evidence for both suppression of cellular immunity through HPA axis mediated hyper-secretion of cortisol, but also of immune activation marked by elevated circulating levels of pro-inflammatory cytokines. [30] To the extent that depression does increase inflammation, it may contribute to the development of COPD in conjunction with other COPD pathogenic factors. Factors that contribute to increased inflammatory response that are common to mental disorders, such as disrupted sleep, may also add to the risk of COPD diagnosis. [6,31].

Smoking is another factor common to mental disorders and to COPD, however minimal changes were observed in the associations between mental disorders and COPD diagnosis after adjustment for nicotine use. Consistent with this, adjustment for smoking did not markedly attenuate the relationship between depression and COPD in other studies. [7,9] Goodwin et al. [8] has argued that it is nicotine dependence rather than nicotine use that is explanatory. Thus our limited assessment of nicotine use may have influenced our findings.

The current study contributes to accumulating evidence that alcohol is involved in the pathogenesis of COPD, independent of nicotine exposure; alcohol abuse doubled the risk of COPD diagnosis after taking into account smoking and other mental disorders. Interestingly, there was no concurrent association between alcohol use and COPD. Alcohol use may no longer be present in older age when COPD is present; however it may be a risk factor for the development of COPD.

Mechanisms that explain the role of heavy alcohol use in impaired lung function include the effects of alcohol and its metabolites and nonalcohol congeners, leading to immunosuppressive effects and compromised mucociliary clearance. [32] Perhaps surprisingly alcohol abuse but not alcohol dependence was associated with an increased risk for COPD. One speculative explanation for this finding may be that those who tolerate alcohol to the extent of developing dependence are genetically less susceptible to alcohol related lung pathology. For example, Asian populations are more likely to have a reduced ability to metabolize alcohol and one of several undesirable results is alcohol triggered asthma. [33].

Although we have discussed possible causal mechanisms thus far, we do not assume these associations are causal as there are also non-causal pathways, common to mental disorder and to COPD, that may explain the association between these conditions such as nutrition and exercise, [5] genetics, [34] and childhood adversities. [35] Moreover, COPD is comorbid with multiple conditions including osteoporosis and coronary heart disease; [5] it may be that diagnosis of other chronic conditions precedes diagnosis of COPD and that the associations we document here reflect in part the associations between mental disorders and these other conditions, or between mental disorders and multiple physical condition comorbidities. Another non-causal pathway may be socio-economic status whereby those with lower SES are more likely to experience mental disorders [36] and are also at greater risk for COPD through several pathways including occupational exposure to lung irritants, exposure to biomass smoke, and poor nutrition and housing. [37] In this study, adjustment was made for education level, which may not have fully controlled for SES.

One further conceivable non-causal connection between mental disorders and COPD diagnosis is that seeking medical attention for mental disorders increases the likelihood of receiving a diagnosis of COPD. For example, panic disorder may increase catastrophic interpretation of dyspnea, thereby increasing the chance of COPD assessment. Additionally, patients seeking attention for any mental disorder may have an increased likelihood of a physician noting symptoms of COPD following greater attendance at a medical practice. Inconsistent with this explanation, adjustment for health care use only slightly attenuated the significant association between COPD and depression observed in another study. [9].

In summary this research contributes new evidence to our understanding of the breadth of associations between mental disorders and COPD. This is the first study to identify the relative contribution of different mental disorders to COPD diagnosis and to identify substantive cumulative risk of COPD diagnosis with the experience of multiple mental disorders. The association between COPD and mental disorders is likely to be bidirectional; however research has focused on identifying COPD as a risk factor for mental disorder [3] rather than mental disorder as a risk factor for COPD. This research indicates that future research should prospectively attend to mental disorders as a risk factor for developing COPD.

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Table 1

Characteristics of WMH samples and percent (and number) with history of chronic lung diseases.

Country	Field dates	Age range[a]	Sample size		Response rate (%)	History of adult onset chronic lung diseases (21+)				
			Part 1	Part 2 sub-sample		N	Weighted %	SE	Mean age of diagnosis	SE
Americas										
Colombia	2003	18–65	4426	2381	87.7	3	0.2	0.1	33.7	2.2
Mexico	2001–2	18–65	5782	2362	76.6	7	0.1	0.0	39.6	6.4
United States	2002–3	18+	9282	5692	70.9	128	2.1	0.3	53.3	1.9
Peru	2005–6	18–65	3930	1801	90.2	4	0.4	0.2	36.8	7.1
Asia and South Pacific										
Japan	2002–6	20+	4129	1682	55.1	16	0.9	0.3	55.1	4.2
PRC Shen Zhen[b]	2006–7	18+	7132	2475	80.0	20	0.4	0.1	36.2	4.5
New Zealand	2003–4	18+	12,790	7312	73.3	107	1.4	0.2	54.3	2.3
Europe										
Belgium	2001–2	18+	2419	1043	50.6	34	2.4	0.5	51.3	4.2
France	2001–2	18+	2894	1436	45.9	51	2.9	0.6	41.6	2.2
Germany	2002–3	18+	3555	1323	57.8	25	1.7	0.4	47.5	3.4
Italy	2001–2	18+	4712	1779	71.3	37	1.6	0.3	48.9	3.0
The Netherlands	2002–3	18+	2372	1094	56.4	20	1.1	0.5	50.8	3.7
Spain	2001–2	18+	5473	2121	78.6	55	1.5	0.3	47.4	2.0
Northern Ireland	2004–7	18+	4340	1986	68.4	11	0.3	0.1	47.0	3.1
Portugal	2008–9	18+	3849	2060	57.3	20	0.8	0.2	43.1	3.4
Romania	2005–6	18+	2357	2357	70.9	31	1.2	0.3	35.8	2.3
Poland	2010–11	18–64	10,081	4000	50.4	26	0.6	0.1	43.5	1.7
Middle East										
Israel	2002–4	21+	4859	4859	72.6	177	3.4	0.3	43.4	1.1
Iraq	2006–7	18+	4332	4332	95.2	18	0.5	0.1	51.9	5.4
Mean age of diagnosis (all countries combined)									47.6	0.8
Prevalence of chronic lung disease (all countries combined)							1.3	0.1		
Weighted average response rate (%)					67.4					

Country	Field dates	Age range[a]	Sample size		Response rate (%)	History of adult onset chronic lung diseases (21+)				
			Part 1	Part 2 sub-sample		N	Weighted %	SE	Mean age of diagnosis	SE
Total sample size			98,714	52,095		790				

[a]For the purposes of cross-national comparisons we limit the sample to 18 + .

[b]People's Republic of China.

Table 2

Prevalence and concurrent associations between 12-month mental disorders and lifetime COPD.

Type of 12-month disorder	Among those with lifetime COPD		Among those without lifetime COPD		Concurrent associations between 12 month disorders and lifetime COPD[1]	
	%	SE	%	SE	OR	(95% C.I)
Mood disorder						
Major depressive episode/Dysthymia	8.7	1.5	5.3	0.1	2.1	(1.5–2.9)
Bipolar disorder (Broad)	1.8	0.5	1.3	0.1	2.3	(1.2–4.2)
Anxiety disorder						
Panic disorder	2.2	0.6	1.1	0.1	2.5	(1.6–3.9)
Generalized anxiety disorder	6.4	1.3	2.0	0.1	2.6	(1.7–4.1)
Social phobia	7.0	1.2	2.8	0.1	2.4	(1.7–3.4)
Specific phobia	8.5	1.4	5.8	0.1	1.5	(1.1–2.1)
Agoraphobia without panic	1.4	0.5	0.5	0.0	3.2	(1.7–5.9)
Post-traumatic stress disorder	3.2	0.7	1.7	0.1	2.3	(1.5–3.5)
Obsessive compulsive disorder	1.6	0.8	1.2	0.1	2.7	(1.0–7.3)
Impulse-control disorder						
Intermittent explosive disorder	3.0	1.1	2.1	0.1	1.6	(0.8–3.5)
Bulimia nervosa	–	–	0.2	0.0	–	–
Binge eating disorder	0.7	0.4	0.6	0.1	1.4	(0.5–3.9)
Substance use disorder						
Alcohol abuse	1.7	0.8	1.6	0.1	1.7	(0.8–3.9)
Alcohol abuse with dependence	0.9	0.3	0.6	0.0	1.7	(0.8–3.5)
Drug abuse	–	–	0.5	0.0	–	–
Drug abuse with dependence	–	–	0.2	0.0	–	–

"–": Unstable estimates due to low number of cases(<5).

[1] Each 12-month mental disorder type was estimated as a predictor in separate logistic regression model controlling for current age, gender, country, smoking (ever/current/never) and years of education.

Table 3

Bivariate and multivariate associations (odds ratios) between DSM-IV mental disorders and the subsequent diagnosis of COPD.

Type of disorders	Single disorder models[1]		Comorbid disorders model[2]	
	OR	(95% C.I.)	OR	(95% C.I.)
I. Mood disorders				
Major Depressive Episode/Dysthymia	2.2	(1.7–2.8)	1.6	(1.3–2.0)
Bipolar Disorder (Broad)	3.5	(2.2–5.7)	1.5	(0.8–2.7)
II. Anxiety disorders				
Panic Disorder	2.1	(1.4–3.3)	1.2	(0.8–1.8)
Generalized Anxiety Disorder	2.8	(2.0–3.9)	1.7	(1.2–2.4)
Social Phobia	2.1	(1.4–3.0)	1.1	(0.8–1.6)
Specific Phobia	1.7	(1.3–2.3)	1.2	(0.9–1.6)
Agoraphobia without Panic	2.7	(1.5–5.0)	1.5	(0.8–2.8)
Post-Traumatic Stress Disorder	2.1	(1.4–3.1)	1.2	(0.8–1.7)
Obsessive Compulsive Disorder	2.7	(1.2–6.5)	1.7	(0.7–4.1)
III. Impulse-control disorders				
Intermittent Explosive Disorder	3.0	(1.8–4.9)	1.6	(0.9–2.8)
Binge Eating Disorder	1.6	(0.8–3.2)	1.0	(0.5–1.8)
Bulimia Nervosa	0.9	(0.3–3.3)	0.4	(0.1–1.5)
IV. Substance disorders				
Alcohol Abuse	2.4	(1.7–3.4)	1.8	(1.3–2.7)
Alcohol Dependence with Abuse	2.9	(1.6–5.0)	1.1	(0.6–2.2)
Drug Abuse	2.3	(1.5–3.8)	1.2	(0.7–2.1)
Drug Dependence with Abuse	2.4	(1.2–4.9)	0.8	(0.4–1.8)
Joint effect of all types of disorders, χ^2_{16}				112.9
Difference between types of disorders, χ^2_{15}				17.4

[1] Single disorder models: each mental disorder type was estimated as a predictor of the physical condition diagnosis in a separate discrete time survival model controlling for age cohorts, gender, person-year, country, smoking (ever/current/never) and years of education.

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

Table 4

Prevalence and association between number of disorders and COPD.

Number of mental disorder	Among those with lifetime chronic lung diseases		Among those without lifetime chronic lung diseases		All		Number of disorders model[1]	
	%	SE	%	SE	%	SE	OR	(95% C.I)
Exactly 1 disorder	18.3	2.0	16.0	0.2	16.0	0.2	1.6*	(1.3–2.1)
Exactly 2 disorders	9.0	1.4	6.6	0.1	6.6	0.1	2.4*	(1.7–3.5)
Exactly 3 disorders	6.2	1.0	2.8	0.1	2.9	0.1	3.8*	(2.6–5.8)
Exactly 4 disorders	1.9	0.5	1.4	0.1	1.5	0.1	3.1*	(1.8–5.6)
5+ disorders	3.8	0.8	1.6	0.1	1.6	0.1	5.8*	(3.5–9.6)
Joint effect of number of disorders, χ^2_5	–	–	–	–	–	–		64.2*

[1] Numberofdisordersmodel:the model was estimated using a discrete-time survival model with dummy variables for number of mental disorders without any information about type of mental disorders, including the controls specified in Table 3.