Original Investigation

Association of Mental Disorders With Subsequent Chronic Physical Conditions
World Mental Health Surveys From 17 Countries

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IMPORTANCE It is clear that mental disorders in treatment settings are associated with a higher incidence of chronic physical conditions, but whether this is true of mental disorders in the community, and how generalized (across a range of physical health outcomes) these associations are, is less clear. This information has important implications for mental health care and the primary prevention of chronic physical disease.

OBJECTIVE To investigate associations of 16 temporally prior *DSM-IV* mental disorders with the subsequent onset or diagnosis of 10 chronic physical conditions.

DESIGN, SETTING, AND PARTICIPANTS Eighteen face-to-face, cross-sectional household surveys of community-dwelling adults were conducted in 17 countries (47 609 individuals; 2 032 942 person-years) from January 1, 2001, to December 31, 2011. The Composite International Diagnostic Interview was used to retrospectively assess the lifetime prevalence and age at onset of *DSM-IV*–identified mental disorders. Data analysis was performed from January 3, 2012, to September 30, 2015.

MAIN OUTCOMES AND MEASURES Lifetime history of physical conditions was ascertained via self-report of physician's diagnosis and year of onset or diagnosis. Survival analyses estimated the associations of temporally prior first onset of mental disorders with subsequent onset or diagnosis of physical conditions.

RESULTS Most associations between 16 mental disorders and subsequent onset or diagnosis of 10 physical conditions were statistically significant, with odds ratios (ORs) (95% CIs) ranging from 1.2 (1.0-1.5) to 3.6 (2.0-6.6). The associations were attenuated after adjustment for mental disorder comorbidity, but mood, anxiety, substance use, and impulse control disorders remained significantly associated with onset of between 7 and all 10 of the physical conditions (ORs [95% CIs] from 1.2 [1.1-1.3] to 2.0 [1.4-2.8]). An increasing number of mental disorders experienced over the life course was significantly associated with increasing odds of onset or diagnosis of all 10 types of physical conditions, with ORs (95% CIs) for 1 mental disorder ranging from 1.3 (1.1-1.6) to 1.8 (1.4-2.2) and ORs (95% CIs) for 5 or more mental disorders ranging from 1.9 (1.4-2.7) to 4.0 (2.5-6.5). In population-attributable risk estimates, specific mental disorders were associated with 1.5% to 13.3% of physical condition onsets.

CONCLUSIONS AND RELEVANCE These findings suggest that mental disorders of all kinds are associated with an increased risk of onset of a wide range of chronic physical conditions. Current efforts to improve the physical health of individuals with mental disorders may be too narrowly focused on the small group with the most severe mental disorders. Interventions aimed at the primary prevention of chronic physical diseases should optimally be integrated into treatment of all mental disorders in primary and secondary care from early in the disorder course.

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Much evidence has accrued from record linkage and clinical studies attesting to the higher incidence of chronic physical conditions and associated earlier mortality among individuals with severe mental illness,[1-3] as well as among those with common mental disorders.[4-7] However, the findings of these studies are limited to those who receive treatment,[1] so it is less clear whether mental disorders in the community (untreated and treated) might be linked with subsequent risk of chronic physical conditions. It also remains unclear as to how generalized these associations might be across a range of physical health outcomes. This information has important implications for mental health care and the primary prevention of chronic physical disease.

Ideally, associations between mental disorders in the general population and subsequent physical conditions should be investigated in studies with prospective designs. However, to examine associations between a wide range of mental disorders and physical conditions prospectively is challenging because it requires very large cohorts with information on both mental and physical disorders to be followed over many decades. As an interim approach, we have investigated mental-physical sequential associations using retrospectively collected data from the World Mental Health (WMH) surveys. The collection of information on age at onset of mental disorders and age at onset or diagnosis of chronic physical conditions in these surveys allows the use of survival analysis to examine predictive associations between temporally prior mental disorders and the subsequent onset or diagnosis of physical conditions. Previous publications have reported on associations between mental disorders and specific physical conditions.[8-12] The present study provides a broader overview by describing associations between mental disorders and a wide range of physical condition outcomes collectively. It is from this broader perspective that important clinical and public health implications emerge.

Methods

Samples and Procedures

This study used all WMH surveys with the requisite data conducted in 17 countries (**Table 1**). Translation protocols and measures taken to ensure data accuracy, cross-national consistency, and protection of respondents are described in detail elsewhere.[14] All respondents provided written informed consent, and the study was approved by the institutional review boards in each country; there was no financial compensation.[14] The study was conducted from January 1, 2001, to December 31, 2011.

A stratified, multistage, clustered-area, probability-sampling strategy was used to select adult respondents (≥18 years) in most WMH countries. Most of the surveys were based on nationally representative household samples; Colombia, Mexico, and Shenzhen were based on nationally representative household samples in urbanized areas. In most countries, internal subsampling was used to reduce respondent burden by dividing the interview into 2 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 given part 2 of the instrument (at the same interview), which assessed the remaining mental disorders and collected information on physical conditions and covariates. Data acquired from the part 2 respondents were weighted by the inverse of their probability of selection to adjust for differential sampling.[14]

Analyses in this article are based on the weighted part 2 subsample (47 609 individuals; 2 032 942 person-years). Additional weighting was used to adjust for differential probabilities of selection within households, to adjust for nonresponse, and to match the samples to population sociodemographic distributions.

Measures

Mental Disorders

All surveys used the WMH-Composite International Diagnostic Interview (CIDI, 3.0[14]), a fully structured interview, to assess lifetime history of mental disorders. Disorders were evaluated using the definitions and criteria of the *DSM-IV*. Age-at-onset reports (obtained in connection with the first onset of clusters of symptoms indicative of the disorder) were obtained using a probing strategy that experimental research[15] has shown yields responses with a more plausible age-at-onset distribution than the standard CIDI questionnaire. Clinical reappraisal interviews using the Structured Clinical Interview for *DSM* Disorders (SCID) in several WMH countries documented generally good CIDI-SCID concordance, with the CIDI being conservative compared with the SCID for lifetime estimates.[16]

Chronic Physical Conditions

Respondents were asked whether a health professional had ever told them they had any of a series of medical conditions (eg, heart disease, stroke, cancer, diabetes mellitus, hypertension, asthma, other chronic lung disease, and peptic ulcer) or whether they had a lifetime history of a chronic symptomatic condition (eg, arthritis, chronic back or neck pain, chronic or severe headaches, and any other chronic pain). Respondents were asked how old they were when the condition was first diagnosed (for the medical conditions) or first experienced the condition (for the symptomatic conditions). This year is referred to herein as the *age at onset* of these conditions, although it is recognized that the underlying disease process of many of these conditions usually develops over many years. For all but 2 of these conditions (chronic pain and ulcer), people with childhood onset (aged <21 years) of the physical condition were excluded from analyses because early onset of these conditions is likely to be congenital.

Statistical Analysis

Data analysis was performed from January 3, 2012, to September 30, 2015. Discrete-time survival analyses[17] with person-year as the unit of analysis were used to investigate associations between temporally prior lifetime history of a mental disorder and the subsequent onset of a physical condition. Separate models were estimated for each physical condition.

Table 1. World Mental Health Sample Characteristics by World Bank Income Categories[a]

Income Category	Survey	Sample Characteristics	Field Dates	Age Range, y[b]	Sample Size, No.		Response Rate, %
					Part 1	Part 2	
Low-lower middle							
Colombia	NSMH	All urban areas of the country (approximately 73% of the total national population)	2003	18-65	4426	2381	87.7
Iraq	IMHS	Nationally representative	2006-2007	≥18	4332	4332	95.2
Peru	EMSMP	Nationally representative	2004-2005	18-65	3930	1801	90.2
Shenzhen, China	Shenzhen	Shenzhen metropolitan area Included temporary and household residents	2006-2007	≥18	7132	2475	80.0
Upper middle							
Colombia (Medellin)[c]	MMHHS	Medellin metropolitan area	2011-2012	18-65	3261	1673	97.2
Mexico	M-NCS	All urban areas (approximately 75% of the total national population)	2001-2002	18-65	5782	2362	76.6
Romania	RMHS	Nationally representative	2005-2006	≥18	2357	2357	70.9
High							
Belgium	ESEMeD	Nationally representative	2001-2012	≥18	2419	1043	50.6
Italy	ESEMeD	Nationally representative	2001-2012	≥18	4712	1779	71.3
Japan	WMHJ	Eleven metropolitan areas	2002-2006	≥20	4129	1682	55.1
New Zealand	NZMHS	Nationally representative	2003-2004	≥18	12 790	7312	73.3
Northern Ireland	NIMHS	Nationally representative	2004-2007	≥18	4340	1986	68.4
Poland	EZOP	Nationally representative	2010-2011	18-64	10 080	4000	50.4
Portugal	NMHS	Nationally representative	2008-2009	≥18	3849	2060	57.3
Spain	ESEMeD	Nationally representative	2001-2002	≥18	5473	2121	78.6
Spain (Murcia)	PEGASUS-Murcia	Murcia region	2010-2012	≥18	2621	1459	67.4
The Netherlands	ESEMeD	Nationally representative	2002-2003	≥18	2372	1094	56.4
United States	NCS-R	Nationally representative	2002-2003	≥18	9282	5692	70.9
Total					93 287	47 609	
Weighted mean response rate, %							69.3

Abbreviations: EMSMP, La Encuesta Mundial de Salud Mental en el Peru; ESEMeD, European Study of the Epidemiology of Mental Disorders; EZOP, Epidemiology of Mental Health and Access to Care Survey; IMHS, Iraq Mental Health Survey; M-NCS, Mexico National Comorbidity Survey; MMHHS, Medellín Mental Health Household Study; NCS-R, National Comorbidity Survey Replication; NIMHS, Northern Ireland Mental Health Survey; NMHS, Portugal National Mental Health Survey; NSMH, National Study of Mental Health; NZMHS, New Zealand Mental Health Survey; PEGASUS, Murcia, Psychiatric Enquiry to General Population in Southeast Spain-Murcia; RMHS, Romania Mental Health Survey; WMHJ World Mental Health Japan.

[a] World Bank categorization was used.[13]

[b] For the purposes of cross-national comparisons, we limited the sample to individuals 18 years or older.

[c] The newer Colombian survey in Medellin was classified as an upper-middle–income country (owing to a change of classification by the World Bank), although the original survey in Colombia was classified as a low- to lower-middle–income country.

Initial models included each of the 16 mental disorders as predictors, but given the similarity in the pattern of findings across mental disorders, mental disorder classes (any mood disorder, anxiety disorder, substance use disorder, and impulse control disorder) were included as predictors in subsequent models. For these analyses, a person-year data set was created with each year in the life of each respondent treated as a separate observational record up to and including the age at onset of the physical condition or their age at interview (whichever came first), with the year of physical condition onset coded as 1 and earlier years coded as 0 on a dichotomous outcome variable. Mental disorders were coded as 1 from the year after first onset of each mental disorder. This time lag ensured that first onsets of a mental disorder in the same year as the physical condition did not count as a predictor. Only person-years up to the diagnosis or onset of the physical condition were analyzed so that only mental disorder episodes occurring before the onset of the physical condition were included in the predictor set. Survival coefficients are presented as odds ratios (ORs), indicating the relative odds of the physical condition onset for a person with the mental disorder compared with people without that disorder (including those without a history of any mental disorder).

A series of bivariate and multivariate models were developed, including the predictor mental disorder (or disorder class), plus covariates. Covariates included in the statistical models were age cohorts (18-29, 30-44, 45-59, and ≥60 years), sex, person-years, country, educational level (low, low-average, high-average, and high based on the number of years of education), and smoking history (current, ever, or never). Multivariate models included controls for other mental disorders and also investigated associations between the number

of mental disorders experienced over the life course and the onset of the physical condition.

Evaluation of whether associations varied by age at physical condition onset or diagnosis was undertaken by including interaction terms between person-years (coded as a continuous variable) and mental disorder classes in the multivariate models. Population-attributable risk proportions (PARPs) calculated the proportion of the outcome variables associated with the predictor mental disorders in the bivariate models (eTable 1 in the Supplement reports the method). Country variation in the associations was evaluated in 2 ways. First, the I^2 level was calculated to describe the percentage of total variation in multivariate associations across countries that is due to heterogeneity rather than chance.[18] For most models, significant ($P < .05$) heterogeneity was not observed (eTable 2 in the Supplement), but 2 examples of where country variation was significant (in the associations of mood and anxiety disorders with heart disease) are shown in funnel plots in eFigure 1 and eFigure 2 in the Supplement. Second, interaction terms of mental disorders with individual countries were included in the multivariate models; most of the interaction coefficients were not significant (eTable 3 in the Supplement). All further analyses were conducted on the pooled all-countries data set. Because the WMH data are both clustered and weighted, the design-based Taylor series linearization[19] implemented in version 10 of the SUDAAN software system was used to estimate SEs and evaluate the statistical significance of coefficients.

Results

Bivariate Associations of Specific Mental Disorders

After adjustment for age, sex, country, smoking, and educational level, a history of depressive disorder was associated with an increased odds of subsequent onset of arthritis (OR, 1.6; 95% CI, 1.5-1.8) (**Table 2**). Most associations between the 16 mental disorders and the subsequent onset/diagnosis of the 10 physical conditions were statistically significant. Depression, some of the anxiety disorders (panic disorder, specific phobia, and posttraumatic stress disorder), and alcohol abuse were associated with all 10 physical conditions; bipolar disorder, social phobia, intermittent explosive disorder, and alcohol dependence were associated with 9 of 10 physical conditions. Significant associations ranged from a low OR of 1.2 (95% CI, 1.0-1.5) between depression and subsequent cancer to a high OR of 3.6 (95% CI, 2.0-6.6) between bulimia nervosa and subsequent diabetes mellitus, with the ORs for most associations falling between 1.5 and 2.0.

Bivariate and Multivariate Associations of Mental Disorder Classes

The bivariate models reported in **Table 3** include the same controls as the models in Table 2 to allow comparison with the results for individual disorders. All mental disorder classes were associated with all of the physical condition outcomes, with ORs ranging from 1.2 to 2.6. The single physical condition most strongly associated with temporally prior mental disorders was chronic lung disease, with ORs (95% CIs) ranging from 1.7 (1.3-2.3) (anxiety disorder) to 2.6 (1.7-3.8) (impulse control disorder). Cancer had the weakest associations with mental disorders, with ORs (95% CIs) from 1.2 (1.0-1.4) for anxiety disorder to 1.6 (1.2-2.1) for impulse control disorder. Mental disorder comorbidity was not taken into account in these associations.

Analysis using multivariate models demonstrated associations from models adjusting for mental disorder comorbidity, with the effect that the magnitude of associations was reduced by approximately 50%. This finding indicates that some of the strength of the bivariate associations was the result of the multiple disorders that many individuals experience over the life course rather than to one disorder. The multivariate ORs (95% CIs) ranged from 1.2 (1.0-1.4) for the association of mood disorder with subsequent heart disease and 1.2 (1.1-1.3) for the association of substance use disorder with subsequent chronic pain to 2.0 (1.4-2.8) for the association of substance use disorders with subsequent stroke. Substance use disorders remained significantly associated with all 10 of the physical condition outcomes, mood disorders remained associated with 8 of the physical condition outcomes, and anxiety disorders and impulse control disorders remained associated with 7 outcomes. Mood and anxiety disorders were no longer significantly associated with cancer after comorbidity adjustment.

Associations between an increasing number of mental disorders experienced over the life course and subsequent onset or diagnosis of chronic physical conditions were demonstrated (Table 3). Associations (ORs [95% CI]) for 1 mental disorder ranged from lows of 1.3 (1.0-1.5; 1.1-1.6) for cancer and asthma, respectively, to highs of 1.8 (1.7-1.9; 1.4-2.2) for chronic pain and chronic lung disease, respectively. Associations (ORs [95% CI]) with 5 or more disorders ranged from 1.9 (1.4-2.7) with cancer to 4.0 (2.5-6.5) with chronic lung disease. For all physical conditions (except cancer), a dose-response pattern was evident; even for cancer, the association (OR; 95% CI) with 5 or more disorders was stronger (1.9; 1.4-2.7) than the association with 1 disorder (1.3; 1.0-1.5).

Variation of Associations by Age at Physical Condition Onset or Diagnosis

For mood disorders (eTable 4 in the Supplement), the ORs for the mood disorder × person-year interactions were all less than 1.0, with 8 of 10 of the ORs being significant. This finding indicates that the association between mood disorder and the physical condition outcomes was stronger among people with younger (relative to older) age at onset or diagnosis of the physical condition. This finding could be a substantive effect (such that the potential for mental health to affect physical health diminishes as the deleterious effects of aging increase) or an artifact of survival bias in these samples. This same pattern was evident for a few of the physical outcomes in associations with the other 3 classes of mental disorders.

PARP Associations

We calculated population-level associations of mental disorders (unadjusted for comorbidity) with physical outcomes.

Table 2. Bivariate Associations Between *DSM-IV* Mental Disorders and the Subsequent Onset or Diagnosis of Chronic Physical Conditions

Mental Disorder[a]	Chronic Physical Condition, OR (95% CI)									
	Arthritis	Any Chronic Pain[b]	Heart Disease	Stroke	Hypertension	Diabetes Mellitus	Asthma	Chronic Lung Disease	Peptic Ulcer	Cancer
Mood disorder										
Major depressive episode/dysthymia	1.6 (1.5-1.8)[c]	1.7 (1.6-1.8)[c]	1.5 (1.3-1.8)[c]	1.6 (1.3-2.1)[c]	1.4 (1.2-1.5)[c]	1.4 (1.2-1.6)[c]	1.5 (1.3-1.8)[c]	2.1 (1.6-2.8)[c]	1.7 (1.5-1.9)[c]	1.2 (1.0-1.5)[c]
Bipolar disorder (broad)	1.7 (1.4-2.0)[c]	1.8 (1.6-2.1)[c]	1.6 (1.1-2.4)[c]	1.9 (1.1-3.1)[c]	1.4 (1.1-1.8)[c]	1.7 (1.2-2.3)[c]	2.4 (1.7-3.3)[c]	2.3 (1.5-3.7)[c]	1.8 (1.4-2.3)[c]	1.5 (1.0-2.2)
Anxiety disorder										
Panic disorder	1.5 (1.3-1.8)[c]	1.9 (1.6-2.1)[c]	2.1 (1.6-2.7)[c]	1.9 (1.1-3.1)[c]	1.7 (1.4-2.0)[c]	1.8 (1.3-2.4)[c]	1.9 (1.3-2.7)[c]	2.2 (1.4-3.3)[c]	1.9 (1.4-2.4)[c]	1.6 (1.2-2.1)[c]
Generalized anxiety disorder	1.8 (1.6-2.0)[c]	1.9 (1.8-2.2)[c]	1.4 (1.1-1.7)[c]	1.5 (1.0-2.3)[c]	1.4 (1.2-1.5)[c]	1.3 (1.0-1.6)[c]	1.7 (1.4-2.2)[c]	2.5 (1.8-3.5)[c]	1.5 (1.3-1.8)[c]	1.0 (0.8-1.3)
Social phobia	1.5 (1.4-1.7)[c]	1.8 (1.7-2.0)[c]	1.5 (1.2-1.9)[c]	1.8 (1.3-2.5)[c]	1.5 (1.3-1.6)[c]	1.3 (1.1-1.6)[c]	1.4 (1.1-1.7)[c]	1.9 (1.4-2.6)[c]	1.8 (1.6-2.2)[c]	1.1 (0.9-1.3)[c]
Specific phobia	1.5 (1.4-1.7)[c]	1.8 (1.7-1.9)[c]	1.8 (1.5-2.1)[c]	1.6 (1.3-2.1)[c]	1.5 (1.3-1.6)[c]	1.4 (1.1-1.6)[c]	1.5 (1.3-1.8)[c]	1.6 (1.2-2.1)[c]	1.8 (1.6-2.1)[c]	1.4 (1.2-1.6)[c]
Agoraphobia without panic	1.4 (1.1-1.8)	1.8 (1.4-2.2)	1.3 (0.8-2.0)	2.2 (1.0-4.5)	1.6 (1.2-2.0)	1.6 (1.2-2.4)	1.3 (0.9-2.1)	2.0 (1.1-3.6)	1.6 (1.1-2.4)	1.3 (0.8-2.1)
Posttraumatic stress disorder	1.8 (1.6-2.1)[c]	1.9 (1.7-2.2)[c]	2.1 (1.6-2.7)[c]	1.7 (1.1-2.6)[c]	1.3 (1.1-1.6)[c]	1.4 (1.0-1.9)[c]	1.9 (1.4-2.5)[c]	1.6 (1.1-2.3)[c]	2.3 (1.9-2.9)[c]	1.3 (1.0-1.8)[c]
Obsessive-compulsive disorder	1.4 (1.0-1.9)[c]	2.1 (1.7-2.6)[c]	1.6 (1.1-2.5)[c]	1.5 (0.6-3.8)	1.3 (0.9-1.8)	1.2 (0.6-2.3)	0.7 (0.4-1.5)	1.9 (0.8-4.5)	2.0 (1.2-3.6)[c]	1.8 (1.0-3.2)
Impulse control disorder										
Intermittent explosive disorder	1.6 (1.4-2.0)[c]	2.3 (2.0-2.6)[c]	1.6 (1.1-2.4)[c]	1.9 (1.1-3.3)[c]	1.5 (1.2-1.8)[c]	1.8 (1.3-2.5)[c]	1.3 (0.9-2.0)	3.0 (2.0-4.7)[c]	2.0 (1.5-2.5)[c]	1.5 (1.0-2.2)[c]
Bulimia nervosa	1.5 (1.0-2.2)[c]	2.1 (1.6-2.7)[c]	1.9 (0.9-3.9)	3.3 (1.4-8.0)[c]	2.3 (1.7-3.2)[c]	3.6 (2.0-6.6)[c]	1.3 (0.8-2.4)	0.7 (0.2-2.3)	1.6 (0.9-2.9)	1.6 (0.8-3.0)
Binge-eating disorder	1.7 (1.3-2.3)[c]	2.0 (1.5-2.6)[c]	1.4 (0.8-2.6)	1.5 (0.7-3.4)	2.0 (1.4-2.7)[c]	3.4 (2.0-5.9)[c]	2.1 (1.4-3.2)[c]	1.4 (0.7-2.5)	1.6 (1.0-2.5)[c]	1.6 (0.9-3.0)
Substance use disorder										
Alcohol abuse	1.6 (1.4-1.8)[c]	1.4 (1.3-1.6)[c]	1.7 (1.4-2.1)[c]	2.1 (1.5-3.0)[c]	1.6 (1.4-1.8)[c]	1.3 (1.1-1.6)[c]	1.6 (1.3-2.0)[c]	2.4 (1.8-3.2)[c]	1.6 (1.4-1.9)[c]	1.4 (1.1-1.8)[c]
Alcohol dependence	1.7 (1.4-2.0)[c]	1.6 (1.4-1.9)[c]	2.3 (1.8-3.0)[c]	2.8 (1.5-5.0)[c]	1.8 (1.5-2.1)[c]	1.5 (1.1-2.1)[c]	2.1 (1.5-2.8)[c]	2.0 (1.3-3.2)[c]	1.9 (1.5-2.4)[c]	1.4 (1.0-2.0)
Drug abuse	1.9 (1.6-2.2)[c]	1.6 (1.4-1.9)[c]	2.2 (1.6-3.0)[c]	1.9 (1.1-3.3)[c]	1.9 (1.6-2.2)[c]	1.8 (1.2-2.5)[c]	1.4 (1.0-2.0)	1.9 (1.3-2.8)[c]	2.0 (1.6-2.5)[c]	1.3 (0.9-2.1)
Drug dependence	2.1 (1.7-2.7)[c]	1.8 (1.4-2.3)[c]	1.7 (1.1-2.6)[c]	1.9 (0.9-3.9)	2.1 (1.6-2.8)[c]	2.5 (1.5-4.1)[c]	1.2 (0.7-2.0)	1.7 (0.9-3.3)	2.3 (1.8-3.1)[c]	1.4 (0.8-2.7)

Abbreviation: OR, odds ratio.

[a] Each mental disorder was estimated as a predictor of the physical condition onset in a separate discrete time survival model controlling for age cohorts, sex, person-years, country, smoking (current, ever, or never), and respondent's educational level.

[b] Respondent reported any of the following: chronic back or neck pain, frequent or severe headaches, and other chronic pain condition.

[c] Significant at $P < .05$, 2-sided test.

Table 3. Bivariate and Multivariate Associations Between *DSM-IV* Mental Disorder Classes and the Subsequent Onset or Diagnosis of Chronic Physical Conditions

Mental Disorder	Chronic Physical Condition, OR (95% CI)										
	Arthritis	Any Chronic Pain[a]	Heart Disease	Stroke	Hypertension	Diabetes Mellitus	Asthma	Chronic Lung Disease	Peptic Ulcer	Cancer
Bivariate model[b]										
Any mood disorder	1.6 (1.5-1.8)[c]	1.7 (1.6-1.8)[c]	1.5 (1.3-1.7)[c]	1.6 (1.3-2.1)[c]	1.4 (1.2-1.5)[c]	1.4 (1.2-1.6)[c]	1.6 (1.3-1.8)[c]	2.1 (1.7-2.7)[c]	1.7 (1.5-1.9)[c]	1.2 (1.0-1.5)[c]
Any anxiety disorder	1.5 (1.4-1.7)[c]	1.9 (1.8-2.0)[c]	1.8 (1.6-2.0)[c]	1.6 (1.2-2.0)[c]	1.5 (1.4-1.6)[c]	1.3 (1.1-1.5)[c]	1.5 (1.3-1.8)[c]	1.7 (1.3-2.3)[c]	1.8 (1.6-2.1)[c]	1.2 (1.0-1.4)[c]
Any impulse control disorder	1.6 (1.4-1.9)[c]	2.2 (2.0-2.4)[c]	1.6 (1.2-2.2)[c]	2.0 (1.3-3.1)[c]	1.7 (1.4-1.9)[c]	2.1 (1.6-2.7)[c]	1.5 (1.1-2.1)[c]	2.6 (1.7-3.8)[c]	1.9 (1.5-2.4)[c]	1.6 (1.2-2.1)[c]
Any substance use disorder	1.6 (1.4-1.8)[c]	1.5 (1.4-1.6)[c]	1.7 (1.4-2.0)[c]	2.2 (1.6-3.1)[c]	1.6 (1.5-1.8)[c]	1.4 (1.1-1.7)[c]	1.7 (1.4-2.0)[c]	2.4 (1.8-3.2)[c]	1.6 (1.4-1.9)[c]	1.4 (1.1-1.8)[c]
Any disorder	1.6 (1.5-1.7)[c]	1.9 (1.8-2.0)[c]	1.7 (1.5-1.9)[c]	1.7 (1.4-2.0)[c]	1.5 (1.4-1.6)[c]	1.3 (1.1-1.5)[c]	1.5 (1.3-1.8)[c]	2.1 (1.6-2.6)[c]	1.9 (1.7-2.1)[c]	1.3 (1.1-1.5)[c]
Multivariate model[d]										
Any mood disorder	1.4 (1.3-1.5)[c]	1.3 (1.2-1.4)[c]	1.2 (1.0-1.4)[c]	1.3 (1.0-1.7)	1.1 (1.0-1.3)[c]	1.3 (1.1-1.5)[c]	1.3 (1.1-1.6)[c]	1.7 (1.3-2.1)[c]	1.3 (1.2-1.5)[c]	1.1 (1.0-1.3)
Any anxiety disorder	1.4 (1.3-1.5)[c]	1.8 (1.7-1.8)[c]	1.6 (1.4-1.9)[c]	1.4 (1.1-1.7)[c]	1.3 (1.2-1.5)[c]	1.2 (1.0-1.4)	1.3 (1.1-1.6)[c]	1.3 (1.0-1.7)	1.6 (1.4-1.9)[c]	1.1 (1.0-1.3)
Any impulse-control disorder	1.3 (1.1-1.5)[c]	1.7 (1.5-1.9)[c]	1.2 (0.8-1.7)	1.4 (0.9-2.3)	1.4 (1.2-1.6)[c]	1.8 (1.4-2.4)[c]	1.2 (0.9-1.6)	1.8 (1.2-2.6)[c]	1.4 (1.2-1.8)[c]	1.4 (1.0-1.9)[c]
Any substance use disorder	1.4 (1.2-1.6)[c]	1.2 (1.1-1.3)[c]	1.5 (1.2-1.8)[c]	2.0 (1.4-2.8)[c]	1.5 (1.3-1.6)[c]	1.2 (1.0-1.5)[c]	1.5 (1.2-1.8)[c]	1.9 (1.5-2.6)[c]	1.4 (1.2-1.6)[c]	1.3 (1.0-1.7)[c]
Global, χ^2_4	210.4[c]	814.0[c]	112.4[c]	43.5[c]	191.4[c]	47.4[c]	51.1[c]	69.9[c]	174.1[c]	19.6[c]
No. of disorders[e]										
1	1.4 (1.3-1.5)[c]	1.8 (1.7-1.9)[c]	1.5 (1.3-1.7)[c]	1.2 (1.0-1.6)	1.4 (1.2-1.5)[c]	1.2 (1.0-1.4)	1.3 (1.1-1.6)[c]	1.8 (1.4-2.2)[c]	1.6 (1.4-1.8)[c]	1.3 (1.0-1.5)[c]
2	1.6 (1.4-1.8)[c]	2.2 (2.0-2.3)[c]	1.8 (1.5-2.1)[c]	2.2 (1.5-3.1)[c]	1.6 (1.5-1.8)[c]	1.3 (1.0-1.6)[c]	1.5 (1.2-1.8)[c]	1.8 (1.3-2.7)[c]	2.0 (1.7-2.4)[c]	1.3 (1.0-1.6)[c]
3	2.0 (1.7-2.3)[c]	2.2 (2.0-2.5)[c]	2.3 (1.8-3.0)[c]	2.3 (1.3-3.9)[c]	1.7 (1.4-2.0)[c]	1.7 (1.3-2.1)[c]	1.9 (1.4-2.5)[c]	3.7 (2.5-5.5)[c]	2.5 (2.0-3.1)[c]	1.4 (1.0-1.9)[c]
4	2.2 (1.9-2.6)[c]	2.2 (1.9-2.6)[c]	2.4 (1.7-3.2)[c]	2.9 (1.8-4.6)[c]	1.6 (1.3-1.9)[c]	1.8 (1.2-2.5)[c]	2.7 (1.9-3.9)[c]	2.9 (1.7-5.0)[c]	2.9 (2.1-4.1)[c]	1.2 (0.8-1.6)
≥5	2.7 (2.2-3.2)[c]	2.8 (2.4-3.2)[c]	2.7 (1.9-3.9)[c]	3.2 (2.0-5.1)[c]	2.4 (2.0-2.9)[c]	2.7 (2.0-3.7)[c]	2.4 (1.8-3.4)[c]	4.0 (2.5-6.5)[c]	3.0 (2.3-3.9)[c]	1.9 (1.4-2.7)[c]
Global, χ^2_5	220.7[c]	821.7[c]	111.9[c]	47.8[c]	178.1[c]	52.3[c]	45.5[c]	55.2[c]	169.9[c]	19.5[c]

Abbreviation: OR, odds ratio.

[a] Respondent reported any of the following: chronic back or neck pain, frequent or severe headaches, and other chronic pain condition.

[b] Each mental disorder class was estimated as a predictor of the physical condition onset in a separate discrete time survival model controlling for age cohorts, sex, person-years, country, smoking (current, ever, or never), and respondent's educational level.

[c] Significant at $P < .05$, 2-sided test.

[d] This type of model was estimated with dummy variables for all mental disorder classes entered simultaneously, including the controls.

[e] This type of model was estimated with dummy variables for the number of mental disorders without any information about type of mental disorders, including the controls.

Table 4. PARPs of Physical Outcomes Associated With Mental Disorders in Bivariate Models

	Chronic Physical Condition, %									
PARP[a]	Arthritis	Any Chronic Pain[b]	Heart Disease	Stroke	Hypertension	Diabetes Mellitus	Asthma	Chronic Lung Disease	Peptic Ulcer	Cancer
Any mood disorder	6.4	5.2	6.2	7.6	3.9	4.9	6.7	13.3	8.3	3.0
Any anxiety disorder	7.1	7.9	11.1	9.6	6.2	4.4	7.6	11.0	11.6	3.2
Any impulse-control disorder	1.5	1.7	1.7	3.0	1.6	3.1	1.6	4.6	2.6	1.7
Any substance use disorder	4.0	2.2	5.3	9.3	4.1	3.0	5.2	10.7	4.8	3.1

Abbreviation: PARPs, population-attributable risk proportions.

[a] More information on PARP estimates is presented in eTable 1 in the Supplement.

[b] Respondent reported any of the following: chronic back or neck pain, frequent or severe headaches, and other chronic pain condition.

Mood disorders were predictors of 3.0% to 13.3% of physical condition onsets, with corresponding ranges of 3.2% to 11.6% for anxiety disorders, 1.5% to 4.6% for impulse control disorders, and 2.2% to 10.7% for substance use disorders (**Table 4**). The variation in magnitude of these PARPs reflects, in part, the variation in the prevalence of mental disorders (highest for anxiety disorders and lowest for impulse control disorders).

Discussion

This investigation of mental-physical sequential associations in multiple countries yielded 4 main findings. First, most of the matrix of possible associations between 16 mental disorders and subsequent onset or diagnosis of 10 physical conditions were statistically significant after controlling for covariates. Second, associations were reduced in magnitude after controlling for mental disorder comorbidity, but all mental disorder classes (mood, anxiety, impulse control, and substance use) remained associated with between 7 and 10 of the physical condition outcomes. Third, increasing numbers of mental disorders experienced over the life course were associated with increasing odds of subsequent onset or diagnosis of all 10 physical conditions. Fourth, specific mental disorders were associated with between 1.5% and 13.3% of chronic physical condition onsets. To put the PARPS in context, high body mass index, which has similarities to mental disorders in being a prevalent risk factor associated with multiple outcomes, is associated with 13% to 15% of cardiometabolic deaths.[20] The PARPs in the present study were modest, but they were based on specific types of mental disorders in the general population, including both remitted and unremitted disorders, and so may substantially underestimate the effect of the more severe and comorbid disorders typically seen in treatment settings.

The study design limitations need to be considered. Retrospective recall of age at onset of mental disorders is subject to bias, and, although the probing strategy used in the WMH surveys has been shown to reduce some types of bias (telescoping), it is likely that some inaccuracy in onset timing remains. Recall of age at onset of physical conditions may be more reliable,[21] but the retrospective recall of event timing for both mental and physical conditions remains a significant limitation of this study. The cross-sectional design also raises the possibility of spurious or inflated associations through mental disorders at the time of interview affecting self-report of physical conditions; however, sensitivity analyses excluding individuals with mental disorders at the time of the interview found no meaningful alteration in associations.[9]

Retrospective assessment is known to lead to underreporting of mental disorders and, to a lesser extent, of physical conditions.[22] The assessment of physical conditions in the present study was less rigorous than the assessment of mental disorders, and self-report of physician-assigned diagnoses will miss some conditions that are asymptomatic in the early stages. These limitations will undoubtedly have resulted in some individuals with a history of mental disorder and/or physical condition being misclassified as noncases; this kind of misclassification tends to bias associations toward the null, making the results conservative. Survival bias may also contribute to the conservative nature of these findings. In addition, the associations were based on disorders ranging in severity and across remitted and unremitted disorders; therefore, the strength of associations is probably understimated in individuals with severe or recurrent disorders.

Although observational studies cannot determine whether these mental-physical sequential associations reflect causal links, we note that the dose-response pattern in the association of number of mental disorders with risk of physical condition onset is consistent with a causal interpretation. Moreover, many plausible causal mechanisms have been identified including biological,[23,24] behavioral,[25] effects of psychotropic medications,[26] and inequities in health care provision.[27] However, some potential common underlying determinants of comorbid mental and physical ill health in adulthood have not yet been fully explored, such as genetics, diet, low birth weight, and predicators of early adverse circumstances.[28]

Even with the limitations of the retrospective method, the findings of this study are worthy of note. Although evidence for specific mental-physical associations will gradually accumulate from prospective studies, the resulting piecemeal perspective may obscure our study's broader message that mental disorders of all types are associated with increased odds of a wide range of chronic physical conditions. Current efforts to address health inequalities among the mentally ill are almost

entirely focused on those with severe mental illness, who make up a very small proportion of those with mental disorders.

Conclusions

The study findings need to be confirmed in prospective designs, but they suggest that the deleterious effects of mental disorders on physical health (if causal) accumulate over the life course and increase with mental disorder comorbidity. If this is the case, then given the early onset of most mental disorders and the similarly early etiopathogenesis of many chronic physical conditions,[29] treatment of all mental disorders should optimally incorporate attention to physical health and health behaviors, with this parallel focus on physical health beginning as early in the course of the mental disorder as possible. Disappointing outcomes from depression treatment trials in patients with heart disease[30] may indicate that mental-physical comorbidity could be better addressed by an early focus on the physical health of those with mental disorders rather than a later focus on the mental health of those with chronic physical conditions. Existing programs have proved effective in improving health behaviors of individuals with mental disorders.[31] Psychological interventions could be augmented to include a focus on health behaviors. In addition, much could be done in primary care to optimize chronic disease prevention approaches for individuals with mental disorders so that these approaches are more effective than they are at the present time.[32] Movement toward the primary prevention of chronic physical conditions among people with mental disorders would do much to enhance their quality and quantity of life.

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Study concept and design: Scott.
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