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Associations between DSM-IV mental disorders and subsequent non-fatal, self-reported stroke

Nicola R. Swain^{a,*}, Carmen C.W. Lim^a, Daphna Levinsonⁱ, Fabian Fiestas^e, Giovanni de Girolamo^j, Jacek Moskalewicz^o, Jean-Pierre Lepine^h, Jose Posada-Villa^c, Josep Maria Haro^l, María Elena Medina-Mora^d, Miguel Xavierⁿ, Noboru Iwata^f, Peter de Jonge^k, Ronny Bruffaerts^g, Siobhan O'Neill^m, Ron C. Kessler^b, and Kate M. Scott^a

^aDepartment of Psychological Medicine, University of Otago, Dunedin, New Zealand ^bDepartment of Health Care Policy, Harvard Medical School, Boston, MA, United States ^cColegio Mayor de Cundinamarca University, Columbia ^dNational Institute of Psychiatry Ramon de la Fuente, Mexico ^eUnit of Analysis and Generation of Evidence for Public Health, Peruvian National Institute of Health, Peru ^fDepartment of Clinical Psychology, Hiroshima International University, Japan ^gUniversity Psychiatric Centre, University of Leuven, Campus Gasthuisberg, Belgium ^hAssistance Publique Hôpitaux de Paris, Universités Paris Descartes — Paris Diderot Inserm UMR-S 1144, France ⁱMinistry of Health Israel, Mental Health Services, Israel ^jIRCCS Centro S. Giovanni di Dio Fatebenefratelli, Brescia, Italy ^kUniversity of Groningen, University Medical Center, Groningen Department of Psychiatry, Interdisciplinary Center, Psychopathology and Emotion regulation (ICPE), Groningen, The Netherlands ^lParc Sanitari Sant Joan de Déu, CIBERSAM, Universitat de Barcelona, Spain ^mSchool of Psychology, University of Ulster, Northern Ireland ⁿChronic Diseases Research Center (CEDOC), Department of Mental Health, Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Portugal ^oInstitute of Psychiatry and Neurology, Poland

Abstract

Objectives—To examine the associations between a wide range of mental disorders and subsequent onset of stroke. Lifecourse timing of stroke was examined using retrospectively reconstructed data from cross-sectional surveys.

*Corresponding author at: Department of Psychological Medicine, Otago University, PO Box 913, Dunedin, New Zealand. Nicola.swain@otago.ac.nz (N.R. Swain).

Author contributions

Dr. Scott takes full responsibility for the integrity of the data analysis and accuracy of results reported.

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Methods—Data from the World Mental Health Surveys were accessed. This data was collected from general population surveys over 17 countries of 87,250 adults. The Composite International Diagnostic Interview retrospectively assessed lifetime prevalence and age at onset of DSM-IV mental disorders. A weighted subsample (n = 45,288), was used for analysis in the present study. Survival analyses estimated associations between first onset of mental disorders and subsequent stroke onset.

Results—Bivariate models showed that 12/16 mental disorders were associated with subsequent stroke onset (ORs ranging from 1.6 to 3.8). However, after adjustment for mental disorder comorbidity and smoking, only significant relationships between depression and stroke (OR 1.3) and alcohol abuse and stroke (OR 1.5) remained. Among females, having a bipolar disorder was also associated with increased stroke incidence (OR 2.1). Increasing number of mental disorders was associated with stroke onset in a dose–response fashion (OR 3.3 for 5+ disorders).

Conclusions—Depression and alcohol abuse may have specific associations with incidence of non-fatal stroke. General severity of psychopathology may be a more important predictor of non-fatal stroke onset. Mental health treatment should be considered as part of stroke risk prevention. Limitations of retrospectively gathered cross sectional surveys design mean further research on the links between mental health and stroke incidence is warranted.

Keywords

Depression; Alcohol abuse; Stroke; Comorbidity

Introduction

Stroke is the leading cause of acquired disability in adults, and also a leading cause of death [1,2]. Despite the recent advent of improved treatment for survivors of stroke, prevention remains the best approach for reducing the burden of stroke [3,4]. Recent evidence suggests stroke rates are declining [5,6] and this has been attributed to increasing success in treating hypertension, in combination with diabetes and high cholesterol control and smoking cessation [7].

Many risk factors for stroke have been studied and quantified. Hypertension accounts for between 52% [8] and 80% of the risk [9] while smoking contributes between 12% [10] and 19% [8] of the risk of stroke. Other contributing factors are: high cholesterol [11–13], physical activity [8,9,1,12], alcohol [8,11,12], heart disease [9,13], diabetes [8,9, 12,13], obesity [9,11,13], psychosocial factors [8,9] and, diet [8,9,11].

There is also a well established relationship between depression and incident stroke [14]. Adding to that body of evidence, a recent prospective study found a two-fold increased risk of first ever stroke associated with prior depression, after controlling for confounders [15]. Another recent study reported a 70% increased risk for stroke following depression [16]. There has been limited research into the contribution of anxiety disorders and stroke incidence [17]. A recent review found that while the link between anxiety and heart disease was well established the link between anxiety and stroke was less clear with fewer studies and conflicting results [18]. A key limitation of the majority of prior studies on depression

and anxiety is that they have used symptom screening scales rather than diagnostic measures of mental disorders; a review in the area suggests that more research with diagnostic measures of mental disorders is needed [19] in order to establish whether depression and anxiety both contribute to the risk of stroke after controlling for their comorbidity, and whether other mental disorders, including substance use disorders, might also elevate stroke risk.

The rationale for a focus on mental disorders is that like hypertension, they may form a further potentially modifiable group of risk factors for stroke. American Stroke Association Guidelines in the prevention of stroke do not consider mental disorders at all [4]. Treatment of mental disorders may have a direct effect on stroke reduction, and also an indirect effect as they may influence the other known direct modifiable factors. It is possible using the present dataset to examine direct effects of mental health disorders while controlling for known mediators such as smoking, gender and hypertension. Although alcohol consumption is known to influence the risk of stroke, alcohol use disorders have not been studied as risk factors for incident stroke. Evidence regarding alcohol use and stroke suggests that low-level consumption may offer some protection from ischaemic stroke, at the same time increasing the risk of hemorrhagic stroke. Increasing consumption increases all types of stroke risk, as well as other types of cardiovascular disease [20].

The present study uses the cross-national World Mental Health (WMH) Surveys dataset to examine associations between a range of DSM-IV mental disorders and subsequent non-fatal stroke. The WMH surveys are general population surveys that retrospectively assessed lifetime history of DSM-IV mental disorders and also obtained self-report of diagnosis of selected chronic physical conditions including stroke. The surveys are cross-sectional in design, but collected information on onset timing of mental disorders and physical conditions, which allows the use of survival analysis to examine associations between temporally prior mental disorders (retrospectively reported) and the subsequent onset of non-fatal stroke, examining the influence of specific disorders as well as the cumulative influence of multiple disorders.

Method

Samples and procedures

This study uses data from 17 of the WMH surveys (see Table 1). This included all surveys that had included a question specifically on stroke. A stratified multi-stage 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 (or population register) samples while Colombia, and Mexico were based on nationally representative household samples in urbanized areas. All interviews were carried out by trained lay interviewers. 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 other respondents 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.

Analyses in this paper are based on the weighted Part 2 subsample (n = 45 288). 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 sociodemographic distributions. Measures taken to ensure data accuracy, cross-national consistency and protection of respondents are described in detail elsewhere [21,22]. All respondents provided written informed consent and procedures for protecting respondents were approved and monitored for compliance by the Institutional Review Boards in each country (see [22] for details).

Measures

Mental disorders—All surveys used the WMH survey version of the WHO Composite International Diagnostic Interview (now CIDI 3.0) [21], a fully structured interview, to assess lifetime history of mental disorders. Disorders were assessed using the definitions and criteria of the DSM-IV. The mental disorders included in this paper are: *mood disorders* (major depressive disorder/dysthymia, bipolar broad (I,II and subthreshold)); *anxiety disorders* (panic disorder, agoraphobia without panic, specific phobia, social phobia, post-traumatic stress disorder, generalized anxiety disorder, obsessive compulsive disorder); *impulse control disorders* (intermittent explosive disorder, bulimia nervosa and binge eating disorder); and, *substance use disorders* (alcohol abuse and dependence, drug abuse and dependence). 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 [23].

Stroke—In a series of questions adapted from the U.S. Health Interview Survey [24], respondents were asked about the lifetime presence of selected chronic conditions. Respondents were asked: “Have you ever had a stroke”? If respondents endorsed this question they were classified as having a history of stroke for these analyses. Respondents were also asked how old they were when their stroke first occurred. Only adult-onset stroke (onsets age 21 +) and non-fatal stroke were investigated in this paper.

Covariates—Covariates included in this analysis are current age, person-years (see below), age cohort (up to 52 years, 53–62, 63–71 and 72+, which represent quartiles of stroke onset distribution), gender, education (years) and smoking (never/ever/current).

Statistical analysis

Discrete-time survival analyses [25] with person-year as the unit of analysis were used to investigate sequential associations between first onset of mental disorders and the subsequent onset of stroke. For these analyses a person-year dataset was created in which each year in the life of each respondent up to and including the age of first stroke or their age at interview (whichever came first) was treated as a separate observational record, with the year of stroke coded 1 and earlier years coded 0 on a dichotomous outcome variable. As

stated earlier, we were interested in adults with a stroke over the age of 20, therefore the people who reported stroke onset before age 21 were excluded from the analyses ($n = 43$). 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 stroke occurred in the same year, the mental disorder would not count as a predictor. Only person-years up to the diagnosis of stroke were analyzed so that only mental disorder episodes occurring prior to the onset of stroke 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 stroke in a given year for a person with a prior history of the specific mental disorder compared to a people without that mental disorder and people without any mental disorder history at all.

A series of bivariate and multivariate models were developed including the predictor mental disorder plus control variables. All models control for person-years, countries, gender and current age. Bivariate models investigated the association of specific mental disorders with subsequent heart disease onset. The multivariate type model estimated the associations of each mental disorder with heart disease onset adjusting for mental disorder comorbidity (that is, for other mental disorders occurring at any stage prior to the onset of heart disease) as well as smoking (current/ever/never) and education (number of years). 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, smoking and education. 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 available on request).

We assessed whether associations varied by when in the life course stroke occurred by including interaction terms between person-years (coded as a continuous variable) and each type of mental disorder in the multivariate type model. Age stratified models were then run to illustrate the interaction results. Gender differences were examined by including interaction 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 these associations are generally consistent cross-nationally, despite varying prevalence of mental disorder and physical conditions [26]. 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 [27] implemented in version 10 of the SUDAAN software system [28] 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 non-fatal stroke ($n = 714$).

Type and number of mental disorders and subsequent onset of stroke

In the bivariate results presented in Table 2 it is apparent that all but four types of mental disorder were associated with subsequent onset of stroke with odds ratios (ORs) ranging between 1.6 and 3.8. When all mental disorders were taken into account in the multivariate models, the magnitude of associations diminished in all cases. The mental disorders that remained significant in the multivariate models were depression/dysthymia (OR 1.3) and alcohol abuse (OR 1.6). The global chi square test for the joint effect of all mental disorders was significant ($\chi^2_{16}=65.0$; $p < 0.001$), however the test for variation in ORs indicates that the associations do not differ significantly in magnitude ($\chi^2_{15}=13.9$, $p = 0.53$), this means that we cannot rule out the possibility that the associations between mental disorders and stroke are generalized to having any mental disorder rather than specific to one mental disorder.

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 2. This displays a clear dose–response relationship between the number of mental disorders experienced over the life course and subsequent non-fatal stroke, with ORs ranging from 1.3 for one mental disorder to 3.3 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 a more general effect where additive effects of any psychopathology may be influencing an increased stroke risk rather than specific types of mental disorders.

The additional of hypertension to this multivariate model does not change the relationship of depression and stroke (OR 1.3) but reduces alcohol abuse to (OR 1.4) a level just short of statistical significance. The dose–response relationship between the number of mental disorders and subsequent non-fatal stroke remains.

Variation across the life course (timing of stroke onset)

The first three columns of data in Table 3 shows those mental disorders for which there were significant interactions with person-year in the association with stroke onset. The interaction ORs are all negative which indicates that the associations of the mental disorders with stroke are stronger with a younger age of stroke onset. To illustrate the nature of the interaction, the person year dataset was then stratified into quartiles of the stroke onset distribution and the multivariate models re-estimated in each of these quartiles. These results, shown in the remainder of Table 3, show a general pattern of associations between these mental disorders and stroke being stronger when the stroke occurred earlier in life rather than later in life. For example, it is apparent that the association between social phobia and stroke is elevated (OR 1.8) for the younger person year groups (up to age 52) but not for those 53 years and older. Stratification of mental disorder by age of stroke onset leads to small numbers in some columns, this low statistical power may account for the few significant findings.

Gender interactions

The interaction tests between the majority (15/16) of mental disorders, stroke and gender were not significant, indicating that for these disorders gender makes little difference to the strength of association between mental disorder and stroke. For bipolar disorder, however, there was a significant gender interaction with stroke ($\chi^2 = 5.3$, $p = 0.021$). After controlling

for other mental disorders, the association between bipolar disorder and stroke onset was significant for females (2.1 OR, 95% CI 1.0–4.2) but not for males (OR 0.5, 95% CI 0.2–1.3) (See Tables 4 and 5).

Discussion

This study reports on the mental disorders associated with subsequent non-fatal stroke. After controlling for other mental disorders, age, gender, country, smoking, and education, associations remained statistically significant between depression and stroke, and between alcohol abuse and stroke. A general picture emerged that there was a strong joint effect of mental disorders on non-fatal stroke and that the number of mental disorders experienced over the life course was a stronger predictor of stroke onset than any specific type of mental disorder. Associations were also found to be stronger with strokes occurring at younger ages. The present study is unique in that it uses appropriate diagnostic criteria for mental disorders and is a general population sample from a large number of respondents from 17 countries.

The association between depression and stroke found in this study is consistent with the prior well established results on this association [19]. This replication, and the fact that the present study found this association to persist after comorbidity adjustment, suggests that depression has a specific link with increased risk of stroke. However, many clinician guidelines (e.g., *Guidelines for the Primary Prevention of Stroke*) do not consider mental disorder to be a risk factor for stroke. Thus, the present results again support the inclusion of mental disorder and/or depression as a modifiable risk factor for subsequent stroke.

The *Guidelines for the Primary Prevention of Stroke* do however, suggest that there is sufficient evidence for alcohol consumption as a modifiable risk factor [4]. Our results linking alcohol use disorders and stroke are as would be expected given the extensive prior literature on heavy alcohol consumption and cardiovascular outcomes (for review see [20,29]), but this is the first study to examine these associations after adjustment for a full range of comorbid mental disorders. Some beneficial effects of low-level alcohol consumption have been noted in previous research [20], but the present findings reinforce the finding that at levels that would constitute an alcohol use disorder there are increased risks of stroke.

These findings raise important questions about the origins of the associations between mental disorders and subsequent stroke. Broadly speaking, the literature on the topic presents some perspectives on this issue. For example, many studies indicate that depression is associated prospectively with a range of cardiometabolic outcomes including stroke [14]. The possible mechanisms listed in the meta-analysis and review by Pan et al. [14] are neuroendocrine and immunological/inflammation effects, poor health behaviors and obesity, other major co-morbidities (like diabetes or hypertension) [20], or anti-depressant use. These medical conditions may mediate (or confound) the relationship between depression and stroke. However, after controlling for hypertension the relationship between mental disorders and stroke remained significant. Nonetheless, this study cannot determine whether these associations reflect causal mechanisms between mental disorders and non-fatal stroke

and further research is recommended. A non-causal connection would be the possibility that treatment seeking for mental disorder earlier in life could result in earlier detection of stroke risk.

An interesting finding, unique to this study, was the significant association between number of mental disorders and non-fatal stroke incidence. Number of disorders is an indicator of general severity and persistence of psychopathology and the fact that this has greater influence than any specific disorder on stroke incidence may be particularly clinically important. Rather than just focusing on depression, a complete mental health history should be taken so that the full potential risk of prior and current mental health can be gauged.

These results should be considered within the context of the study limitations. This is a retrospective study and we cannot be certain of the temporal sequence or exact timing of the predictor (mental disorder) or outcome (stroke) variables in our models. The retrospective assessment of mental disorders is likely to have resulted in under-reporting of some mental disorders (mild disorders in particular) [31] and inaccuracies in the age of onset timing [32]. A second key limitation is the self-report of stroke. Under or over-report of stroke is thought to be minimal as stroke is a serious medical event which would be expected to be clearly reported to the patient. A study of self-report of medical events found although there was a slight under-reporting of stroke incidence there was a general agreement with medical records of 97.8% [33]. There is also noticeable variation in stroke incidence across countries, from 0.1% in Mexico to 2.7% in the USA. This may be because of differences in quality of treatment or rehabilitation meaning stroke survival is higher in more developed countries. Additionally, and importantly, in many cases stroke can be fatal, so those most affected by an association between mental disorder or alcohol abuse may not be in the present sample, possibly resulting in a conservative bias in these associations. Also, those with severe or debilitating strokes will not be included, as only those cognitively competent were included. The study also does not distinguish between ischemic and hemorrhagic strokes, which may have different relationships to mental disorders. Finally, this study is confined to non-fatal stroke outcomes, however, stroke morbidity is a much more common outcome and so worth investigating in its own right.

Nonetheless, within the limitations of retrospective cross-sectional data collection, the results of this study suggest associations between a range of mental disorders and subsequent non-fatal stroke, consistent with previous literature. This study offers data on the specific disorders that contribute to elevated risk of stroke after adjusting for comorbidity, and also the considerable effect of multiple mental disorders on stroke onset. These relationships were found to be stronger at younger ages and mostly independent of gender effects, from data collected in both developed and developing countries. The finding that mental disorders are associated with increased risk of subsequent stroke has wide reaching public health implications. Future research should examine the mechanisms linking mental disorders and stroke.

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Abbreviations

CIDI	Composite International Diagnostic Interview
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders
WMH	World Mental Health
OR	odds ratio

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Table 1

Characteristics of WMH samples and percent (and number) with history of stroke.

Country	Field dates	Age range	Sample size		Response rate (%)	History of stroke	
			Part 1	Part 2 sub-sample		Number unweighted (N)	Weighted (%)
Americas							
Colombia	2003	18–65	4426	2381	87.7	8	0.2
Mexico	2001–2	18–65	5782	2362	76.6	4	0.1
United States	2002–3	18+	9282	5692	70.9	140	2.7
Peru	2005–6	18–65	3930	1801	90.2	14	0.8
Asia and South Pacific							
Japan	2002–6	20+	4129	1682	55.1	29	1.8
New Zealand	2003–4	18+	12,790	7312	73.3	181	2.6
Europe							
Belgium	2001–2	18+	2419	1043	50.6	11	0.7
France	2001–2	18+	2894	1436	45.9	14	1.3
Germany	2002–3	18+	3555	1323	57.8	29	2.4
Italy	2001–2	18+	4712	1779	71.3	16	0.9
The Netherlands	2002–3	18+	2372	1094	56.4	17	1.3
Spain	2001–2	18+	5473	2121	78.6	20	0.4
Northern Ireland	2004–7	18+	4340	1986	68.4	23	1.2
Portugal	2008–9	18+	3849	2060	57.3	42	2.1
Romania	2005–6	18+	2357	2357	70.9	57	1.9
Poland	2010–11	18–64	10,081	4000	50.4	26	0.5
Middle East							
Israel	2002–4	21+	4859	4859	72.6	83	1.5
Weighted average response rate (%)					77.2		
Total sample size			87,250	45,288		714	1.5

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

Table 2

Type of disorders	Bivariate models ¹		Multivariate type model ²		Multivariate number model ³	
	OR	(95% C.I.)	OR	(95% C.I.)	OR	(95% C.I.)
I. Mood disorders						
Major depressive episode/dysthymia	1.6*	(1.3–2.1)	1.3*	(1.0–1.7)	–	–
Bipolar disorder (broad)	1.9*	(1.2–3.3)	1.1	(0.6–2.0)	–	–
II. Anxiety disorders						
Panic disorder	1.9*	(1.2–3.1)	1.3	(0.8–2.3)	–	–
Generalized anxiety disorder	1.4	(0.9–2.0)	0.8	(0.6–1.3)	–	–
Social phobia	1.9*	(1.4–2.7)	1.4	(0.9–2.0)	–	–
Specific phobia	1.7*	(1.3–2.2)	1.3	(1.0–1.7)	–	–
Agoraphobia without panic	2.1	(1.0–4.3)	1.3	(0.6–2.8)	–	–
Post-traumatic stress disorder	2.0*	(1.3–2.9)	1.4	(0.9–2.1)	–	–
Obsessive compulsive disorder	1.3	(0.5–3.8)	0.7	(0.2–2.3)	–	–
III. Impulse-control disorders						
Intermittent explosive disorder	2.1*	(1.2–3.7)	1.4	(0.8–2.6)	–	–
Binge eating disorder	1.6	(0.7–3.6)	1.0	(0.4–2.3)	–	–
Bulimia nervosa	3.8*	(1.6–9.1)	2.2	(0.9–5.5)	–	–
IV. Substance disorders						
Alcohol abuse	2.0*	(1.5–2.7)	1.5*	(1.0–2.2)	–	–
Alcohol dependence with abuse	2.4*	(1.5–3.8)	1.2	(0.7–2.0)	–	–
Drug abuse	2.6*	(1.6–4.2)	1.5	(0.9–2.6)	–	–
Drug dependence with abuse	2.4*	(1.1–5.1)	0.6	(0.3–1.5)	–	–
Joint effect of all types of disorders, χ^2_{16}						
* 65.0						
Difference between types of disorders, χ^2_{15}						
13.9						
V. Number of disorders						
Exactly 1 disorder	–	–	–	–	1.3*	(1.0–1.6)

Type of disorders	Bivariate models ¹		Multivariate type model ²		Multivariate number model ³	
	OR	(95% C.I.)	OR	(95% C.I.)	OR	(95% C.I.)
Exactly 2 disorders	-	-	-	-	1.9*	(1.4–2.4)
Exactly 3 disorders	-	-	-	-	2.2*	(1.3–3.8)
Exactly 4 disorders	-	-	-	-	3.0*	(1.9–4.8)
5+ disorders	-	-	-	-	3.3*	(2.0–5.3)
Joint effect of number of disorders, χ^2_5	49.2*					

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

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 and additionally adjusted for smoking (ever/never/current) and education (number of years).

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
Variations in associations between mental disorders and stroke by lifecourse timing of stroke onset.

Type of mental disorders	Mental disorder * person-year interaction ¹	Stratified models ²					
		Up to age 52	Age 53–62	Age 63–71	Age 72+		
	OR (95% C.I.)	χ^2	[p]	OR (95% C.I.)	OR (95% C.I.)	OR (95% C.I.)	
Major depressive episode/dysthymia	0.98 (0.97 – 1.00)	4.0*	[0.045]	1.5* (1.0–2.2)	1.2 (0.7–2.2)	1.2 (0.6–2.2)	1.4 (0.7–3.0)
Generalized anxiety disorder	0.96* (0.92 – 0.99)	6.8*	[0.009]	1.1 (0.6–2.0)	0.4 (0.1–1.3)	0.9 (0.4–2.1)	0.4 (0.1–1.2)
Social phobia	0.97* (0.96 – 0.99)	7.8*	[0.005]	1.8* (1.1–3.2)	0.9 (0.4–2.2)	0.9 (0.4–2.1)	0.7 (0.3–1.9)
Specific phobia	0.99* (0.97 – 1.00)	4.4*	[0.036]	1.5 (0.9–2.3)	1.7 (0.9–3.2)	0.7 (0.3–1.3)	1.0 (0.5–2.2)
Post-traumatic stress disorder	0.98* (0.96 – 1.00)	6.2*	[0.013]	1.4 (0.8–2.4)	2.2 (0.9–5.8)	1.4 (0.6–3.3)	0.5 (0.2–1.6)
Alcohol dependence with abuse	0.97* (0.94 – 1.00)	4.2*	[0.041]	1.4 (0.7–2.8)	2.2 (0.9–5.8)	0.0 (0.0–0.0)	0.0 (0.0–0.0)

* 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 dummy variable 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 stroke onset distribution.

Table 4

Interactions between type of mental disorder and gender in predicting the subsequent onset of stroke.

	Stroke ¹			
	Int OR	(95% C.I.)	χ^2_1	[p]
I. Mood disorders				
Major depressive episode/dysthymia	1.0	(0.6–1.6)	0.0	[0.850]
Bipolar disorder (broad)	4.5*	(1.3–16.4)	5.3*	[0.021]
II. Anxiety disorders				
Panic disorder				
Generalized anxiety disorder	0.9	(0.4–2.1)	0.1	[0.760]
Social phobia	0.6	(0.3–1.3)	1.7	[0.195]
Specific phobia	1.2	(0.6–2.3)	0.3	[0.582]
Agoraphobia without panic	1.0	(0.2–5.1)	0.0	[0.996]
Post-traumatic stress disorder	1.1	(0.5–2.5)	0.0	[0.870]
Obsessive compulsive disorder	1.9	(0.1–29.0)	0.2	[0.634]
III. Impulse-control disorders				
Intermittent explosive disorder	0.9	(0.3–2.6)	0.1	[0.829]
Binge eating disorder	1.2	(0.2–7.8)	0.1	[0.829]
Bulimia nervosa	0.5	(0.1–3.1)	0.5	[0.465]
IV. Substance disorders				
Alcohol abuse	1.1	(0.4–3.0)	0.1	[0.821]
Alcohol dependence with abuse	0.4	(0.1–1.3)	2.4	[0.118]
Drug abuse	2.0	(0.6–7.0)	1.1	[0.298]
Drug dependence with abuse	1.4	(0.2–10.1)	0.1	[0.724]

* Significant at the 0.05 level, two tailed test.

¹ Predictors are gender (female = 1, male = 0), the dummy variables for all mental disorders plus 16 cross-product terms for female and each mental disorder, plus the controls specified for earlier models.

Table 5

Multivariate type models for stroke, stratified by gender.

	<u>Male</u>		<u>Female</u>	
	OR	(95% C.I.)	OR	(95% C.I.)
Bipolar disorder (broad)	0.5	(0.2–1.3)	2.1*	(1.0–4.2)

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

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