Cross-national Epidemiology of Panic Disorder and Panic Attacks in the World Mental Health Surveys

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In the past three years, Dr. Kessler has been a consultant for Hoffman-La Roche, Inc., Johnson & Johnson Wellness and Prevention, and Sonofi-Aventis Groupe. Dr. Kessler has served on advisory boards for Mensante Corporation, Plus One Health Management, Lake Nona Institute, and U.S. Preventive Medicine. Dr. Kessler is a co-owner of DataStat, Inc. Dr. Demyttenaere is on the speaker bureau for Astra Zeneca, Eli Lilly, Lundbeck and Servier and has received research grants from Eli Lilly, from the foundation 'Ga voor Geluk' and from the Flemish Research Council. In the past three years, Dr. Stein has received research grants and/or consultancy honoraria from AMBRF, Biocodex, Cipla, Lundbeck, National Responsible Gambling Foundation, Novartis, Servier and Sun. The other authors report no disclosures.

Abstract

Context: The scarcity of cross-national reports and the changes in DSM-5 regarding panic disorder (PD) and panic attacks (PAs) call for new epidemiological data on PD and PAs and its subtypes in the general population.

Objective: To present representative data about the cross-national epidemiology of PD and PAs in accordance with DSM-5 definitions.

Design and Setting: Nationally representative cross-sectional surveys using the World Health Organization Composite International Diagnostic Interview version 3.0.

Participants: Respondents (n=142,949) from 25 high, middle and lower-middle income countries across the world aged 18 years or older.

Main Outcome Measures: PD and presence of single and recurrent PAs.

Results: Lifetime prevalence of PAs was 13.2% (s.e. 0.1%). Among persons that ever had a PA, the majority had recurrent PAs (66.5%; s.e. 0.5%), while only 12.8% fulfilled DSM-5 criteria for PD. Recurrent PAs were associated with a subsequent onset of a variety of mental disorders (OR 2.0; 95% CI 1.8-2.2) and their course (OR 1.3; 95% CI 1.2-2.4) whereas single PAs were not (OR 1.1; 95% CI 0.9-1.3 and OR 0.7; 95% CI 0.6-0.8). Cross-national lifetime prevalence estimates were 1.7% (s.e. 0.0%) for PD with a median age of onset of 32 (IQR 20-47). Some 80.4% of persons with lifetime PD had a lifetime comorbid mental disorder.

Conclusions: We extended previous epidemiological data to a cross-national context. The presence of recurrent PAs in particular is associated with subsequent onset and course of mental disorders beyond agoraphobia and PD, and might serve as a generic risk marker for psychopathology.

Introduction

Anxiety disorders are among the major contributors to the worldwide burden of disease (1,2). Among the anxiety disorders, panic disorder (PD) defined by the presence of recurrent, unexpected panic attacks (PAs) is of specific interest. However, epidemiological data regarding PD and PAs is limited and only few available studies have distinguished between PAs and PD, and within PAs, between single versus recurrent attacks (3,4). Also, most of the available epidemiological data comes from studies performed solely in the US (5-9), but it is especially important to study the characteristics of PD and PA cross-nationally given the evidence that the prevalence of PD differs substantially across cultures (10). In the only cross-national account, that took place more than 20 years ago, only PD (using DSM-III criteria) and not PAs were studied (10).

In a review of the literature by Craske et al (4), several recommendations were made regarding the diagnostic criteria for PAs and PD, which were followed to a large extent in the Diagnostic and Statistical Manual version 5 (DSM-5). Importantly, the diagnosis of PD became no longer linked to the presence or absence of agoraphobia (AGO) as was done in DSM-IV. Also, the presence of PAs in DSM-5 was reframed as a generic symptom specifier that can be added to each of the diagnoses in DSM-5 and thus became no longer restricted to PD or AGO (3). This change was based among others on a series of studies suggesting PAs being associated with many mental disorders (e.g. anxiety and mood disorders, psychosis and substance abuse) and not with PD or AGO alone (4,12). Also, the presence of PAs was found to increase symptom severity, comorbidity rates and suicide, while negatively impacting treatment response in a number of disorders (4).

These changes regarding PD and PAs in DSM-5 call for new epidemiological data. In the present study we report on data regarding the epidemiology of PD from 25 lower-middle, middle, and high income countries. In addition, we report on data regarding PAs and their association with onset and course of mental disorders as this will further inform us about the utility of PAs as a risk marker for psychopathology. We specifically distinguished between single and recurrent PAs in this context as only very few studies are available on this issue. Given the importance of worrying about next PAs, we expected that particularly recurrent PAs would be associated with onset and course of mental disorders, in line with the DSM-IV field trial by Horwath et al (12). We used data from the World Mental Health Surveys (13).

Method

Samples

The WMH surveys included data from the low/lower-middle income countries of Colombia, Iraq, Nigeria, Peru, the People's Republic of China – Beijing and Shanghai, and Ukraine, the upper-middle income countries of Brazil, Bulgaria, Colombia (Medellin), Lebanon, Mexico, and Romania, and the high income countries of Australia, Belgium, France, Germany, Israel, Italy, Japan, New Zealand, Northern Ireland, Poland, Portugal, Spain, Spain – Murcia, the Netherlands, and the United States. Most surveys used stratified multistage clustered area probability household sampling with no substitution for non-participants. Data collection took place between 2001 and 2012, and response rates ranged from 45.9 to 97.2%, with an average of 69.0% (Table 1). Classification of countries into income categories (low-lower, upper-middle, high) was based on World Bank criteria (14).

INSERT TABLE 1

Assessment of mental disorders

All WMH surveys were conducted face-to-face by lay interviewers who had received standardized training. Standardized translation, back-translation, harmonization and quality control procedures were applied for each of the participating surveys (13,15). Informed consent was obtained according to protocols endorsed by local Institutional Review Boards. The presence of mental disorders was assessed using the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) version 3.0. All respondents completed Part 1 of the WHO CIDI (13) which assesses lifetime mood disorders (major depressive episode and/or dysthymia, bipolar disorder), anxiety disorders (panic disorder, agoraphobia, specific phobia, social phobia, generalized anxiety disorder, post-traumatic stress disorder), substance use disorders (alcohol and drug abuse with or without dependence) and impulse control disorder (intermittent explosive disorder, binge-eating disorder and bulimia nervosa). Diagnostic hierarchy and organic exclusion rules were applied for all diagnoses other than substance abuse (with or without dependence). A probing strategy was used to assess age

of onset for each of the disorders (15). A blinded clinical reappraisal study using the Structured Clinical Interview for DSM-IV (SCID) (16) found good diagnostic concordance between CIDI and SCID diagnoses. For panic disorder, this was indicated by an area under the curve of 0.72 (17).

Part I data were weighted to adjust for the differential probability of being selected and the socio-demographic and geographic structure of each sample. Respondents with a Part I disorder and an additional probability sub-sample were administered Part II of the survey, which assessed a number of other disorders and correlates. Further weightings were applied to the Part II data to adjust for the differential selection procedure and to match base population distributions on socio-demographic and geographic data.

Panic attacks in DSM-IV and DSM-5

In DSM-IV (18), criteria for PA consisted of a discrete period of intense fear or discomfort, in which four (or more) of the following symptoms develop abruptly and reach a peak within 10 minutes: 1) palpitations, pounding heart, or accelerated heart rate, 2) sweating, 3) trembling or shaking, 4) sensations of shortness of breath or smothering, 5) feeling of choking, 6) chest pain or discomfort, 7) nausea or abdominal distress, 8) feeling dizzy, unsteady, lightheaded, or faint, 9) derealization (feelings of unreality) or depersonalization (being detached from oneself), 10) fear of losing control or going crazy, 11) fear of dying, 12) paresthesias (numbness or tingling sensations), 13) chills or hot flushes. PAs were not distinguished as a codable disorder, but only coded in the specific diagnosis in which the PA occurred (e.g. panic disorder with agoraphobia).

In DSM-5, the essential features of the PA specifier remained unchanged, although the DSM-IV terminology for describing different types of PAs (i.e., situationally bound/cued, situationally predisposed, and unexpected/uncued) was replaced with the terms unexpected (out of the blue) and expected PA. PAs function as a specifier and prognostic factor for severity of diagnosis, course, and comorbidity across an array of disorders, including but not limited to anxiety disorders. Hence, PAs can be listed as a specifier applicable to any of the DSM-5 disorders. In the CIDI 3.0, the presence of panic attacks was probed before the diagnosis of PD, as was information on whether the attacks were single or recurrent, expected or unexpected, therefore PAs could be unlinked from PD.

Panic Disorder in DSM-IV and DSM-5

In DSM-IV, diagnostic criteria for Panic Disorder With or Without Agoraphobia include (1) recurrent, unexpected PAs and (2) at least one of the attacks has been followed by 1 month (or more) of one (or more) of the following: (a) persistent concern about having additional attacks, (b) worry about the implications of the attack or its consequences (e.g., losing control, having a heart attack, "going crazy"), (c) a significant change in behavior related to the attacks. In addition, it is coded whether PD occurred in the presence or absence of agoraphobia. Finally, it is checked that PAs are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism), and whether PAs are not better accounted for by another mental disorder, such as social phobia (e.g., occurring on exposure to feared social situations), specific phobia (e.g., on exposure to a specific phobic situation), obsessive-compulsive disorder (e.g., on exposure to dirt in someone with an obsession about contamination), posttraumatic stress disorder (e.g., in response to stimuli associated with a severe stressor), or separation anxiety disorder (e.g., in response to being away from home or close relatives).

In DSM-5, diagnostic criteria were changed in that PD and agoraphobia are unlinked. Essentially, the former DSM-IV diagnoses of PD with agoraphobia, PD without agoraphobia, and agoraphobia without history of PD have been replaced by two diagnoses, PD and agoraphobia, each with separate criteria. DSM-5 PD consists of the presence of recurrent unexpected panic attacks, as defined previously. The additional criteria regarding concerns, maladaptive behaviors and exclusion criteria (due to physiological effects or better explained by other mental disorders) were somewhat reworded but largely kept in line with DSM-IV. In CIDI 3.0, since the criteria regarding PD and agoraphobia were scored first and the specific diagnoses were made later, PD could be unlinked from agoraphobia to arrive at DSM-5 compatible PD diagnosis.

Socio-demographic variables

Socio-demographic variables included age at interview, ages of onset of PA and PD, sex, education, employment status, marital status, and household income based on country-specific quartiles of gross household earnings in the past 12 months (19).

Statistical analysis

We determined rates of lifetime PAs split into persons with and without lifetime PD. Among persons with lifetime PAs without lifetime PD, we distinguished between persons with single and recurrent PAs. Of persons with lifetime diagnosis of PD and of those with a lifetime presence of PAs, we determined the proportion of persons with 12-month prevalence of PD and PAs, as an indicator of the chronicity of PD and PAs. Similarly, persons with 12-month prevalent PD and PAs were split into persons with and without 30-day prevalence of PD and PAs.

Prevalence rates were compared across countries, World Bank income groups, and WHO regions using the Chi-square test of homogeneity. In addition, the estimated proportion of the population who will have the disorder at age 75 (projected risk) was calculated using survival analysis on the basis of age of onset data (except for four of the surveys where age was restricted to 18-65). Specific analyses comparing single versus recurrent PAs in their association with other (phobic) disorders were done. For analyses examining whether PAs predict onset and course of psychiatric disorders, we used PAs *in the absence of PD*, as otherwise they would count as being part of a comorbid psychiatric disorder (PD).

Logistic regression and survival analyses were used to examine sociodemographic correlates. Survival analysis was used to estimate age of onset (AOO) and projected lifetime risk. The actuarial method implemented in SAS 9.4 was used to generate the AOO curves. Significance was calculated using Wald and McNemar's Chi-square tests. Because the data were weighted and clustered, the Taylor series linearization method (20) implemented in the SUDAAN software package (11.0) (21) was used to estimate design-based standard errors. Statistical significance was consistently evaluated using two-sided tests, with $P < 0.05$ considered significant.

Results

Prevalence, age of onset, and lifetime risk of PA and PD

Lifetime prevalence of PAs for all countries combined was 13.2% (se. 0.1%) (Table 2). Of the persons with lifetime PA, 12.8% had lifetime PD, for a population-level lifetime prevalence of PD of 1.7% (se. 0.0%) (i.e., 12.8% x 13.2%). Of persons with lifetime PA without PD, about two thirds (66.5%; se. 0.5%) had recurrent PAs.

Significant differences in prevalence rates of PAs and PD were observed between country groups based on income level and on WHO regions, with higher prevalence rates in high income countries and countries in the region of the Americas, Western Pacific and Western Europe. Twelve month prevalence rates of PAs and PD were 4.9% (se. 0.1%) and 1.0% (se. 0.0%) respectively (appendix Table 1). Some 34.5% (se. 0.5%) of persons with lifetime PAs without lifetime PD had PAs in the last twelve months. For PD, this figure was 57.1% (se. 1.3%). Prevalence rates for last 30 days PAs and PD were 1.6% (se. 0.0%) and 0.4% (se. 0.0%) respectively. Of persons with past 12 months prevalence of PAs without PD, 29.2% (se. 0.7%) had PAs in the last 30 days. For PD, this figure was 40.6% (se. 1.7%) (Appendix Table 2). Median age of onset of PAs was 34 years (IQR 20-51) and for PAs without PD this was 35 years (IQR 20-52), resulting in a projected risk at age 75 of 23.0% (se. 0.4) for PAs and 20.6% (se. 0.4) for PAs without PD. Median age-of-onset of PD was 32 years (IQR 20-47). The age-of-onset distribution resulted in a projected risk of PD at age 75 of 2.7% (se. 0.1%).

INSERT TABLE 2 ABOUT HERE

Lifetime co-morbidity with other mental disorders in persons with lifetime PD was 80.4% (se. 1.1%) (Appendix table 3). Co-morbidity levels were particularly high for other anxiety disorders (63.1%, se 1.3%) and mood disorders (53.7%, se 1.4%), and considerably lower for substance abuse disorders (26.2% se 1.4%) and impulse controls disorders (10.4%, se 0.7%). In persons with lifetime co-

morbidity, onset of PD preceded the onset of the other disorders in a minority of cases (15.4%, se. 0.9%).

Socio-demographic correlates of PA and PD

Belonging to groups below 60, early age of onset, female gender, other employment status (largely unemployed), being divorced/separated/widowed, lower education, and having a low household income were associated with both PAs without PD and with PD (Appendix Tables 4 and 5). These correlates were largely comparable for the different income level country groups. Few differences were found when comparing risk factors for 30-day, lifetime, 12-month prevalence among lifetime, and 30-days prevalence among 12 months cases, suggesting that largely the same risk factors may operate for onset and course of PAs and PD. However, as an exception, gender was found to be related to onset of PAs and PD, but not to 30-day prevalence among those with a 12-month prevalent disorder.

PAs as a predictor of subsequent mental disorder onset and disorder course

In Table 3, we distinguished between single and recurrent PAs. Single PAs were generally not associated with subsequent mental disorders, with only some exceptions. In contrast, recurrent PAs were associated with increased odds of all included mental disorders. A comparable pattern of results, though less pronounced, emerged when predicting the rates of 12-month cases among lifetime cases per disorder in order to estimate the associations of PAs with course of disorder. Here we found that single PAs appear generally slightly protective while recurrent PAs were associated with a worsened course.

INSERT TABLE 3 ABOUT HERE

Discussion

The goal of this study was to present the cross-national epidemiology of PAs and PD. The general findings were that DSM-5 lifetime prevalence for PD is 1.7% and its projected lifetime risk at age 75 is 2.7%. These findings are in line with previous cross-national estimates of 1.4-2.9% (11), while estimates based on American data alone were slightly higher than ours: 4.8%, 3.4% and 2.2% (7-9). The present study extends these findings to 25 countries spread over several regions in the world and income groups. Significant variation in prevalence between countries was observed and this seemed to be both related to income differences and to regional differences. Consistent with previous reports (6,22,23), high levels of comorbidity were found for persons with PD. In the present study, as many as 80.4% of persons with lifetime PD had a lifetime comorbid other mental disorder, particularly mood or anxiety disorder, and in only a minority of persons did PD precede the onset of any other disorder (15.4%). Previous reports have found panic as a comorbid disorder to be related to an adverse course of other mental disorders (24).

The lifetime prevalence of PAs was 13.2% in our sample, with a projected risk at age 75 of 23.0%, making the presence of PAs a common phenomenon in the general population, as observed earlier (25,26). Still, these figures are lower than a previous report based on American data alone (7) (28.3%). Consistent with these findings however, in our cross-national sample, highest lifetime prevalence rates were found for the United States (27.3%) and New Zealand (27.4%). Comparable to the previous report on US data, most PAs occur in the absence of PD: 20.6% out of 23.0%.

Among persons that ever had a PA, the majority had recurrent PAs. Of interest, recurrent PAs were associated with a subsequent onset of a variety of mental disorders whereas single PAs were not. Also, only recurrent PAs were associated with higher rates of past 12 month disorders among persons with lifetime disorders. This pattern was seen for all mental disorders combined, and specifically for major depression/dysthymia and drug dependence. These findings seem to suggest that particularly the presence of recurrent PAs may be seen as a risk marker for general psychopathology – a suggestion made earlier with respect to PAs in general (12). This finding is of interest as in the review by Craske et al (2010), which served as the evidence base for the suggestion to use PAs as a generic specifier in DSM-5, it was stated that the issue is whether the presence of PAs would “predict

treatment response, comorbidity or course of mental disorder”. In this study, we were able to address the latter two points and found that this seems to hold only for recurrent PAs.

The results of this study should be considered within the context of the following limitations and strengths. The WMH Surveys are essentially cross-sectional in nature and the retrospective assessment of mental disorders and their age of onset is likely to have resulted in inaccuracies in the prevalence of PAs and PD and the age of their onset. Although probing of age of onset was performed on the basis of validated techniques that facilitate accurate recall (27), some bias may have been introduced, probably in the form of underestimation (28). This may particularly be true for PAs which do not have the status of mental disorders and as such are not as extensively probed by multiple items, and their associated disability and treatment status was not scored. In this study, of the persons that ever experienced a PA, 9.1% were not able to remember if they had single or recurrent PAs. We could therefore not address the point that would be the optimal cut-off for the number of PAs to predict later onset of mental disorders. Also, we could not address other subtypes of PAs to refine the PA specifier in DSM-5, such as symptom-based (29) or age of onset-based subtypes (30). Future research could address the utility of distinguishing between single versus recurrent PAs, and expected versus unexpected PAs, and symptom-based subtypes of PAs in terms of their associated disability and treatment status. Among the strengths of this study, the WMH surveys consist of cross-national samples whereas most reports have been based on a single, national study. This offered the possibility to look into differences between countries, and between groups of countries based on income levels and regions in the world. This strategy has resulted in a large sample of respondents that enabled us to explore in more detail specific subgroups of persons, such as those having PAs in the absence of PD and further dissection into the kind of PAs, without encountering power issues.

In sum, in this study we provided cross-national epidemiological data on DSM-5 PD and PAs, and found a cross-national lifetime prevalence of PD of 1.7% and an estimated risk at age 75 of 2.7%. For PAs, these figures were 13.2% and 23.0% respectively. We found that about two thirds of PAs were recurrent and that only recurrent PAs are associated with onset and course of a variety of mental disorders.

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Table 1. World Mental Health sample characteristics by World Bank Income categories^a.

Country	Survey ^b	Sample characteristics ^c	Field dates	Age range ^d	Sample Size		Response rate (%) ^e
					Part 1	Part 2 sub-sample	
Low - lower middle income countries							
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.	2006-7	18+	4332	4332	95,2
Nigeria	NSMHW	21 of the 36 states in the country, representing 57% of the national population. The surveys were conducted in Yoruba, Igbo, Hausa and Efik languages.	2002-3	18+	6752	2143	79,3
Peru	EMSMP	Nationally representative.	2004-5	18-65	3930	1801	90,2
PRC ^f Beijing/Shanghai	B-WMH S-WMH	Beijing and Shanghai metropolitan areas.	2002-3	18+	5201	1628	74,7
PRC ^f Shen Zhen	Shenzhen	Shenzhen metropolitan area. Included temporary residents as well as household residents.	2006-7	18+	7132	2475	80,0
Ukraine	CMDPSD	Nationally representative.	2002	18+	4725	1719	78,3

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Total					32568	14679	81,4
Upper-middle income countries							
Brazil	São Paulo Megacity	São Paulo metropolitan area.	2005-7	18+	5037	2942	81,3
Bulgaria	NSHS	Nationally representative.	2003-7	18+	5318	2233	72,0
Colombia (Medellin) ^s	MMHHS	Medellin metropolitan area	2011-2	18-65	3261	1673	97,2
Lebanon	LEBANON	Nationally representative.	2002-3	18+	2857	1031	70,0
Mexico	M-NCS	All urban areas of the country (approximately 75% of the total national population).	2001-2	18-65	5782	2362	76,6
Romania	RMHS	Nationally representative.	2005-6	18+	2357	2357	70,9
Total					24612	12598	77,2
High-income countries							
Australia	SMHWB	Nationally representative.	2007	18+	8463	8463	60,0
Belgium	ESEMeD	Nationally representative.	2001-2	18+	2419	1043	50,6
France	ESEMeD	Nationally representative.	2001-2	18+	2894	1436	45,9
Germany	ESEMeD	Nationally representative.	2002-3	18+	3555	1323	57,8
Israel	NHS	Nationally representative.	2002-4	21+	4859	4859	72,6
Italy	ESEMeD	Nationally representative.	2001-2	18+	4712	1779	71,3
Japan	WMHJ	Eleven metropolitan areas.	2002-6	20+	4129	1682	55,1
New Zealand	NZMHS	Nationally representative.	2003-4	18+	12790	7312	73,3

Northern Ireland	NISHS	Nationally representative.	2004-7	18+	4340	1986	68,4
Poland	EZOP	Nationally representative.	2010-11	18-64	10081	4000	50,4
Portugal	NMHS	Nationally representative.	2008-9	18+	3849	2060	57,3
Spain	ESEMeD	Nationally representative.	2001-2	18+	5473	2121	78,6
Spain (Murcia)	PEGASUS-Murcia	Murcia region	2010-2	18+	2621	1459	67,4
The Netherlands	ESEMeD	Nationally representative.	2002-3	18+	2372	1094	56,4
The United States	NCS-R	Nationally representative.	2002-3	18+	9282	5692	70,9
Total					81839	46309	62,3
Total					142949	75386	
Weighted average response rate (%)							68,6

^a The World Bank. (2008). Data and Statistics. Accessed May 12, 2009 at: <http://go.worldbank.org/D7SN0B8YU0>

^b NSMH (The Colombian National Study of Mental Health); IMHS (Iraq Mental Health Survey); NSMHW (The Nigerian Survey of Mental Health and Wellbeing); EMSMP (La Encuesta Mundial de Salud Mental en el Peru); B-WMH (The Beijing World Mental Health Survey); S-WMH (The Shanghai World Mental Health Survey); CMDPSD (Comorbid Mental Disorders during Periods of Social Disruption); NSHS (Bulgaria National Survey of Health and Stress); MMHHS (Medellín Mental Health Household Study); LEBANON (Lebanese Evaluation of the Burden of Ailments and Needs of the Nation); M-NCS (The Mexico National Comorbidity Survey); RMHS (Romania Mental Health Survey); NSMHWB (National Survey of Mental Health and Wellbeing); ESEMeD (The European Study Of The Epidemiology Of Mental Disorders); NHS (Israel National Health Survey); WMHJ2002-2006 (World Mental Health Japan Survey); NZMHS (New Zealand Mental Health Survey); NISHS (Northern Ireland Study of Health and Stress); EZOP (Epidemiology of Mental Disorders and Access to Care Survey); NMHS (Portugal National Mental Health Survey); PEGASUS-Murcia (Psychiatric Enquiry to General Population in Southeast Spain-Murcia); NCS-R (The US National Comorbidity Survey Replication).

^cMost WMH surveys are based on stratified multistage clustered area probability household samples in which samples of areas equivalent to counties or municipalities in the US were selected in the first stage followed by one or more subsequent stages of geographic sampling (e.g., towns within counties, blocks within towns, households within blocks) to arrive at a sample of households, in each of which a listing of household members was created and one or two people were selected from this listing to be interviewed. No substitution was allowed when the originally sampled household resident could not be interviewed. These household samples were selected from Census area data in all countries other than France (where telephone directories were used to select households) and the Netherlands (where postal registries were used to select households). Several WMH surveys (Belgium, Germany, Italy) used municipal resident registries to select respondents without listing households. The Japanese sample is the only totally un-clustered sample, with households randomly selected in each of the 11 metropolitan areas and one random respondent selected in each sample household. 19 of the 28 surveys are based on nationally representative household samples.

^dFor the purposes of cross-national comparisons we limit the sample to those 18+.

^eThe response rate is calculated as the ratio of the number of households in which an interview was completed to the number of households originally sampled, excluding from the denominator households known not to be eligible either because of being vacant at the time of initial contact or because the residents were unable to speak the designated languages of the survey. The weighted average response rate is 68,6%.

^fPeople's Republic of China

^gThe newer Colombian survey in Medellin was classified as upper-middle income country (due to a change of classification by The World Bank) although the original survey Colombia was classified as a low-lower middle income country.

Table 2. Lifetime prevalence of panic attack (PA) and panic disorder (PD) in the World Mental Health Surveys.

Country	Among total population						Among lifetime PA without lifetime PD cases				Part 1 sample sizes	Sample size used ^b
	Lifetime PA		Lifetime PA without lifetime PD cases		Lifetime PD		proportion of single attack		proportion of recurrent attacks ^a			
	%	SE	%	SE	%	SE	%	SE	%	SE		
Low-Lower middle income countries	6,9	0,2	6,1	0,2	0,8	0,1	29,8	1,4	61,5	1,4	36498	36395
Colombia	18,5	0,7	17,2	0,8	1,3	0,2	43,4	2,6	52,8	2,5	4426	4422
Iraq	7,5	0,6	6,2	0,6	1,4	0,3	27,6	4,8	47,4	5,5	4332	4295
Nigeria	2,6	0,3	2,4	0,3	0,2	0,1	25,0	4,9	67,3	5,3	6752	6713
Peru	7,1	0,4	6,7	0,4	0,5	0,1	31,2	2,9	62,7	2,6	3930	3929
PRC China	2,1	0,3	1,7	0,2	0,4	0,1	17,2	4,5	79,5	4,9	5201	5197
PRC Shen Zhen	2,5	0,3	2,2	0,3	0,3	0,1	20,9	5,0	79,1	5,0	7132	7129
Ukraine	13,4	0,6	11,2	0,6	2,2	0,3	16,8	1,7	70,4	2,0	4725	4710
Upper-middle income countries	11,1	0,3	10,0	0,3	1,1	0,1	28,7	1,1	57,1	1,2	24612	24565

Brazil	11,7	0,6	10,0	0,6	1,7	0,2	26,1	1,7	56,8	2,2	5037	5023
Bulgaria	6,0	0,3	5,0	0,3	1,1	0,1	14,7	2,4	53,5	3,9	5318	5301
Colombia (Medellin)	20,1	1,3	18,8	1,2	1,3	0,3	39,5	2,4	48,7	2,5	3261	3260
Lebanon	13,9	0,9	13,4	0,9	0,5	0,1	32,2	2,9	55,9	2,6	2857	2851
Mexico	7,8	0,5	6,8	0,5	1,0	0,2	28,8	3,0	69,5	2,9	5782	5781
Romania	13,9	0,8	13,3	0,8	0,7	0,2	19,2	2,9	63,1	3,2	2357	2349
High income countries	16,6	0,2	14,4	0,2	2,2	0,1	22,5	0,5	69,4	0,5	81839	81754
Australia	21,5	0,6	17,9	0,6	3,7	0,3	25,6	1,5	71,9	1,7	8463	8461
Belgium	10,1	1,0	8,5	0,8	1,6	0,3	27,6	3,2	58,2	3,2	2419	2417
France	11,1	0,9	9,0	0,8	2,1	0,3	37,5	3,5	58,9	3,6	2894	2894
Germany	10,1	0,6	8,5	0,6	1,6	0,2	29,5	3,9	66,5	3,9	3555	3555
Israel	10,0	0,5	9,1	0,5	0,9	0,1	24,3	2,2	55,6	2,5	4859	4853
Italy	8,0	0,5	6,4	0,4	1,6	0,2	14,9	2,2	70,0	2,7	4712	4708
Japan	6,6	0,4	5,9	0,4	0,8	0,1	28,2	3,2	65,8	3,7	4129	4126
New Zealand	27,4	0,6	24,7	0,5	2,8	0,2	22,8	1,0	74,3	1,0	12790	12781
Northern Ireland	24,4	0,8	21,1	0,7	3,3	0,3	23,1	1,8	70,6	2,0	4340	4335
Poland	5,9	0,2	5,6	0,2	0,3	0,1	11,3	1,1	47,1	2,1	10081	10049

Portugal	19,6	0,7	17,9	0,6	1,7	0,3	21,9	1,9	64,4	2,1	3849	3841
Spain	9,6	0,5	8,4	0,5	1,2	0,2	33,5	3,0	54,1	3,2	5473	5472
Spain (Murcia)	16,3	1,0	14,7	1,0	1,6	0,4	27,1	2,3	54,5	4,1	2621	2617
The Netherlands	14,0	0,8	11,0	0,7	3,0	0,4	24,3	3,7	72,3	3,7	2372	2370
The United States	27,3	0,7	22,6	0,7	4,7	0,2	16,0	0,8	79,2	0,8	9282	9275
All countries combined	13,2	0,1	11,5	0,1	1,7	0,0	24,4	0,4	66,5	0,5	147264	142714
WHO regions^c												
Region of the Americas	16,8	0,4	14,6	0,4	2,2	0,1	26,7	0,9	66,6	0,9	31718	31690
African Region	2,6	0,3	2,4	0,3	0,2	0,1	25,0	4,9	67,3	5,3	11067	6713
Western Pacific Region	15,6	0,3	13,7	0,2	2,0	0,1	23,7	0,8	73,4	0,8	37715	37694
Eastern Mediterranean Region	10,0	0,4	9,1	0,4	1,0	0,1	27,9	1,8	53,7	1,9	12048	11999
Western European Region	13,6	0,2	11,7	0,2	1,9	0,1	25,7	0,9	64,1	1,0	32235	32209
Eastern European Region	8,4	0,2	7,4	0,2	0,9	0,1	15,0	0,9	58,4	1,3	22481	22409
Comparison between countries^d	$\chi^2_{27} = 164.6^*$, P <.001		$\chi^2_{27} = 143.0^*$, P <.001		$\chi^2_{27} = 32.4^*$, P <.001		$\chi^2_{27} = 12.7^*$, P <.001		$\chi^2_{27} = 16.9^*$, P <.001			

Comparison between low, middle and high income country groups^d	$\chi^2_2 = 638.7^*$, P < .001	$\chi^2_2 = 529.7^*$, P < .001	$\chi^2_2 = 130.8^*$, P < .001	$\chi^2_2 = 22.5^*$, P < .001	$\chi^2_2 = 50.5^*$, P < .001
Comparison between WHO regions^d	$\chi^2_5 = 320.6^*$, P < .001	$\chi^2_5 = 275.2^*$, P < .001	$\chi^2_5 = 85.8^*$, P < .001	$\chi^2_5 = 20.3^*$, P < .001	$\chi^2_5 = 30.8^*$, P < .001

^aRecurrent panic attacks is more than one panic attack. Percentages do not count up to 100% as 9.1% of those with PAs did not recall how many PAs they had.

^bSample size used after excluding lifetime panic attack cases with missing age of onset.

^c**Region of the Americas** (Colombia, Mexico, Brazil, Peru, The United States, Medellin); **African region** (Nigeria); **Western Pacific region** (PRC Shen Zhen, PRC Beijing and Shanghai, Japan, Australia, New Zealand); **Eastern Mediterranean region** (Israel, Iraq, Lebanon); **Western European region** (Belgium, France, Germany, Italy, The Netherlands, Spain, Northern Ireland, Portugal, Murcia); **Eastern European region** (Romania, Bulgaria, Poland, Ukraine).

^dChi-square test of homogeneity to determine if there is variation in prevalence estimates across countries.

Table 3. Comorbidity of single and recurrent panic attacks in the absence of panic disorder with mental disorders.

Type of disorder	Panic attack without panic disorder as a predictor of disorder onset				Panic attack without panic disorder as a predictor of disorder course			
	Single attack		Recurrent attacks		Single attack		Recurrent attacks	
	% with lifetime single PA onset prior to onset of lifetime disorder	Lifetime single PA predicting lifetime disorder ^a	% with lifetime recurrent PA onset prior to onset of lifetime disorder	Lifetime recurrent PA predicting lifetime disorder ^a	% with lifetime single PA prior to 12-month disorder episode among lifetime disorder cases ^b	Lifetime single PA predicting 12-month disorder episode among lifetime disorder cases ^c	% with lifetime recurrent PA prior to 12-month disorder episode among lifetime disorder cases ^b	Lifetime recurrent PA predicting 12-month disorder episode among lifetime disorder cases ^c
	(S E)	OR (95% C.I.)	(S E)	OR (95% C.I.)	(S E)	OR (95% C.I.)	(S E)	OR (95% C.I.)
Mood disorders								
Major depressive episode/Dysthymia	1 7,8 (1.5)	1 (0.9-1.3)	3 (1.0)	2.0 (1.9-2.2)*	3 (0.2)	0 (0.4-.5)* (0.6)	2 (0.6)	1 (1.1-.2)* (1.3)
Bipolar disorder (broad)	2 1,0 (4.1)	0 (0.6-1.3)	5 (2.4)	2.9 (2.5-3.4)*	2 (0.4)	0 (0.2-.4)* (0.7)	2 (1.4)	1 (0.8-.1) (1.3)
Any mood disorder	1 8,0 (1.4)	1 (0.9-1.3)	3 (1.0)	2.1 (2.0-2.2)*	2 (0.2)	0 (0.4-.5)* (0.6)	2 (0.6)	1 (1.1-.2)* (1.3)
Anxiety disorders								
Generalized anxiety disorder	1 7,3 (2.4)	0 (0.6-1.2)	4 (1.6)	2.3 (2.0-2.6)*	3 (0.4)	0 (0.5-.6)* (0.9)	2 (1.1)	0 (0.8-.9) (1.1)
Social phobia	5 (1.6)	0 (0.4-	1 (1.	2.1 (1.8-	3 (0.	0 (0.6-	2 (1.	1 (0.8-

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	,9	,6 (1.1)	9,5 (3)	* (2.4)	,4 (4)	,9 (1.2)	7,9 (0)	,0 (1.1)
Specific phobia	1 ,9 (0.7)	0 (0.2- ,5* 1.0)	7 (0. ,5 7)	1.3 (1.1- * 1.6)	3 (0. ,5 3)	0 (0.7- ,9 1.2)	2 (0. 1,5 6)	1 (0.8- ,0 1.1)
Agoraphobia without panic	9 ,9 (5.6)	0 (0.3- ,8 2.7)	2 (2. 5,3 3)	2.9 (2.3- * 3.7)	4 (1. ,2 0)	1 (0.4- ,0 2.4)	3 (2. 7,1 3)	1 (0.8- ,2 1.6)
Post-traumatic stress disorder	1 2,0 (2.3)	0 (0.5- ,7 1.0)	4 (1. 1,0 8)	2.4 (2.1- * 2.7)	4 (0. ,0 6)	0 (0.4- ,6* 1.0)	3 (1. 1,0 4)	1 (0.9- ,2 1.4)
Any anxiety disorder	6 ,1 (1.0)	0 (0.5- ,7* 1.0)	1 (0. 8,1 8)	1.9 (1.7- * 2.1)	3 (0. ,5 2)	0 (0.5- ,7* 0.9)	2 (0. 4,2 6)	1 (0.9- ,0 1.2)
Impulse-control disorders								
Intermittent explosive disorder	1 5,6 (3.0)	1 (0.9- ,3 1.9)	3 (2. 6,9 1)	2.7 (2.3- * 3.2)	2 (0. ,7 5)	0 (0.5- ,8 1.4)	2 (1. 0,9 2)	1 (0.8- ,1 1.4)
Binge eating disorder	3 5,1 (9.4)	1 (0.7- ,5 3.1)	6 (4. 2,8 2)	2.8 (2.1- * 3.6)	3 (1. ,8 1)	1 (0.4- ,2 3.4)	2 (2. 4,1 7)	0 (0.6- ,9 1.4)
Bulimia nervosa	2 (10. 8,7 6)	1 (0.6- ,5 3.6)	5 (5. 0,0 0)	2.4 (1.7- * 3.5)	6 (2. ,0 2)	2 (0.9- ,3 6.1)	2 (4. 4,8 4)	1 (0.6- ,0 1.8)
Any impulse-control disorder	2 3,1 (3.9)	1 (1.0- ,5* 2.2)	4 (2. 1,5 1)	2.5 (2.1- * 2.9)	3 (0. ,2 5)	1 (0.6- ,0 1.6)	2 (1. 2,2 2)	1 (0.8- ,0 1.3)
Substance-use disorders								
Alcohol abuse	2 5,1 (2.8)	1 (1.0- ,3* 1.8)	5 (1. 5,6 6)	2.3 (2.1- * 2.6)	3 (0. ,2 6)	1 (0.7- ,0 1.5)	1 (1. 6,6 1)	1 (0.9- ,1 1.3)
Alcohol dependence	2 0,0 (4.3)	0 (0.6- ,9 1.4)	5 (2. 6,9 4)	2.7 (2.3- * 3.2)	3 (1. ,0 0)	0 (0.3- ,7 1.7)	2 (2. 1,0 0)	1 (0.8- ,0 1.3)
Drug abuse	2 2,9 (4.0)	1 (0.9- ,3 1.9)	5 (2. 3,1 4)	2.6 (2.2- * 3.0)	3 (1. ,3 0)	0 (0.3- ,6 1.1)	2 (2. 5,6 5)	1 (0.9- ,2 1.7)
Drug dependence	2 3,8 (6.3)	1 (0.6- ,1 2.1)	5 (3. 7,0 3)	3.0 (2.4- * 3.8)	3 (1. ,3 3)	0 (0.2- ,5 1.3)	3 (4. 5,8 3)	1 (1.1- ,8* 2.8)
Any substance-use disorder	2 0,8 (2.4)	1 (0.9- ,2 1.6)	5 (1. 1,1 5)	2.3 (2.0- * 2.5)	3 (0. ,4 6)	1 (0.6- ,0 1.6)	1 (1. 8,3 0)	1 (1.0- ,2 1.4)
Any mental disorder	1 0,9 (0.9)	1 (0.9- ,1 1.3)	2 (0. 3,3 7)	2.0 (1.8- * 2.2)	3 (0. ,4 2)	0 (0.6- ,7* 0.8)	2 (0. 1,2 4)	1 (1.2- ,3* 1.4)

*Significant at the .05 level, 2 sided test.

^aEach model was estimated using lifetime panic attack as predictor of lifetime comorbid disorder onset in separate discrete-time survival model controlling for country, person-years, gender, age-cohort. Person-years were restricted up to and including the first onset of lifetime comorbid disorder.

^bRespondents with lifetime PA onset that occurs 12 month of the age of interview were not included in the numerator.

^cEach model was estimated using lifetime panic attack as predictor of 12 month comorbid episode among lifetime comorbid disorder cases in separate logistic regression model controlling for country, gender, age-cohort, time since comorbid disorder onset and age of comorbid disorder onset. Respondents with lifetime PA onset that occurs 12 month of the age of interview were not counted as a predictor.

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Appendix Table 1. 12-month prevalence of panic attack (PA) and panic disorder (PD) in the World Mental Health surveys.

Country	Among the total population										Part 1 sample sizes	Sample size used ^a
							12-month PA among lifetime PA cases without lifetime PD	12-month PD among lifetime PD				
	12-month PA with or without lifetime PD		12-month PA without lifetime PD cases		12-month PD							
	%	SE	%	SE	%	SE						
Low-Lower middle income countries	2.9	0.1	2.4	0.1	0.5	0.1	38.4	1.3	64.4	3.6	36498	36395
Colombia	6.1	0.4	5.4	0.4	0.7	0.1	31.2	2.2	53.7	9.0	4426	4422
Iraq	3.7	0.5	2.7	0.4	1.0	0.3	43.5	4.6	71.5	6.5	4332	4295
Nigeria	1.3	0.2	1.1	0.2	0.1	0.1	46.7	5.3	76.2	16.1	6752	6713
Peru	3.0	0.2	2.7	0.2	0.3	0.1	40.3	2.1	70.5	6.4	3930	3929
PRC China	1.0	0.2	0.8	0.2	0.2	0.1	47.6	8.4	50.1	13.0	5201	5197
PRC Shen Zhen	0.9	0.1	0.7	0.1	0.2	0.1	33.4	4.1	78.9	7.7	7132	7129
Ukraine	6.2	0.4	4.8	0.3	1.4	0.3	42.6	2.4	64.4	6.2	4725	4710
Upper-middle income countries	4.3	0.2	3.7	0.2	0.7	0.1	36.4	1.2	62.1	3.5	28927	24565
Brazil	5.1	0.3	4.0	0.3	1.0	0.2	40.2	2.2	61.8	8.2	5037	5023
Bulgaria	2.7	0.3	2.2	0.3	0.6	0.1	43.7	4.4	53.5	5.4	5318	5301
Colombia (Medellin)	7.1	0.7	6.1	0.6	0.9	0.2	32.6	2.4	73.8	7.2	3261	3260
Lebanon	4.8	0.5	4.6	0.5	0.3	0.1	34.1	2.7	49.2	10.3	2857	2851
Mexico	3.3	0.4	2.6	0.3	0.7	0.1	38.6	3.1	65.3	7.1	5782	5781
Romania	4.7	0.4	4.2	0.4	0.4	0.1	32.0	3.3	63.3	12.1	2357	2349
High income countries	6.0	0.1	4.8	0.1	1.2	0.1	33.3	0.5	55.2	1.4	81839	81754
Australia	7.3	0.4	5.5	0.4	1.8	0.2	30.8	1.7	50.0	3.9	8463	8461
Belgium	3.5	0.7	2.7	0.5	0.9	0.3	31.4	4.0	54.6	11.4	2419	2417
France	3.2	0.4	2.3	0.2	1.0	0.3	25.2	2.3	46.0	9.7	2894	2894
Germany	3.2	0.4	2.5	0.4	0.7	0.2	28.9	3.3	46.9	7.2	3555	3555
Israel	5.0	0.3	4.4	0.3	0.6	0.1	48.7	2.5	62.6	7.5	4859	4853

Italy	2.7	0.3	2.1	0.3	0.7	0.1	32.1	3.4	42.5	5.8	4712	4708
Japan	2.0	0.3	1.7	0.2	0.3	0.1	28.8	3.1	45.0	10.6	4129	4126
New Zealand	9.2	0.3	7.5	0.3	1.7	0.1	30.5	1.1	60.3	3.2	12790	12781
Northern Ireland	9.5	0.5	7.2	0.5	2.3	0.2	34.1	1.8	70.7	3.6	4340	4335
Poland	2.5	0.1	2.3	0.1	0.2	0.1	41.4	2.1	62.8	8.5	10081	10049
Portugal	6.9	0.4	6.0	0.4	0.9	0.2	33.3	1.9	52.9	6.9	3849	3841
Spain	3.7	0.3	3.1	0.3	0.6	0.1	36.9	2.7	49.2	6.8	5473	5472
Spain (Murcia)	6.0	0.5	5.3	0.6	0.7	0.1	36.3	2.7	45.7	6.5	2621	2617
The Netherlands	4.5	0.4	3.2	0.4	1.3	0.3	29.1	3.1	41.5	6.2	2372	2370
The United States	10.7	0.4	8.0	0.4	2.7	0.2	35.2	1.2	57.9	3.0	9282	9275
All countries combined	4.9	0.1	4.0	0.1	1.0	0.0	34.5	0.5	57.1	1.3	147264	142714
WHO regions^b												
Region of the Americas	6.5	0.2	5.2	0.2	1.3	0.1	35.3	0.8	60.0	2.4	31718	31690
African Region	1.3	0.2	1.1	0.2	0.1	0.1	46.7	5.3	76.2	16.1	11067	6713
Western Pacific Region	5.3	0.2	4.2	0.1	1.1	0.1	30.9	0.9	55.4	2.4	37715	37694
Eastern Mediterranean Region	4.5	0.3	3.8	0.2	0.6	0.1	42.3	1.8	65.3	4.9	12048	11999
Western European Region	4.9	0.1	3.9	0.1	1.0	0.1	32.8	0.9	52.5	2.2	32235	32209
Eastern European Region	3.6	0.1	3.0	0.1	0.6	0.1	40.4	1.4	61.1	3.8	22481	22409
Comparison between countries^c	$\chi^2_{27} = 55.3^*$, P < .001		$\chi^2_{27} = 43.8^*$, P < .001		$\chi^2_{27} = 15.9^*$, P < .001		$\chi^2_{27} = 4.7^*$, P < .001		$\chi^2_{27} = 2.1^*$, P = 0.001			
Comparison between low, middle and high income country groups^c	$\chi^2_2 = 183.1^*$, P < .001		$\chi^2_2 = 147.3^*$, P < .001		$\chi^2_2 = 50.8^*$, P < .001		$\chi^2_2 = 8.4^*$, P < .001		$\chi^2_2 = 3.8^*$, P = 0.024			
Comparison between WHO regions^c	$\chi^2_5 = 71.7^*$, P < .001		$\chi^2_5 = 52.8^*$, P < .001		$\chi^2_5 = 35.7^*$, P < .001		$\chi^2_5 = 12.4^*$, P < .001		$\chi^2_5 = 2.1$, P = 0.063			

^aSample size used after excluding lifetime panic attack cases with missing age of onset.

^b**Region of the Americas** (Colombia, Mexico, Brazil, Peru, The United States, Medellin); **African region** (Nigeria); **Western Pacific region** (PRC Shen Zhen, PRC Beijing and Shanghai, Japan, Australia, New Zealand); **Eastern Mediterranean region** (Israel, Iraq, Lebanon); **Western European region** (Belgium, France, Germany, Italy, The Netherlands, Spain, Northern Ireland, Portugal, Murcia); **Eastern European region** (Romania, Bulgaria, Poland, Ukraine).

^cChi-square test of homogeneity to determine if there is variation in prevalence estimates across countries.

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Appendix Table 2. 30-day prevalence of panic attack (PA) and panic disorder (PD) in the World Mental Health surveys.

Country	Among the total population										Part 1 sample sizes	Sample size used ^a
							30-day PA among 12-month PA cases without lifetime PD	30-day PD among 12-month PD				
	30-day PA		30-day PA without lifetime PD cases		30-day PD							
	%	SE	%	SE	%	SE						
Low-Lower middle income countries	1.0	0.1	0.8	0.1	0.3	0.0	32.4	1.9	50.4	4.7	36498	36395
Colombia	1.6	0.2	1.3	0.2	0.3	0.1	24.9	3.2	44.8	10.6	4426	4422
Iraq	1.9	0.3	1.2	0.3	0.7	0.3	45.1	7.0	71.4	10.3	4332	4295
Nigeria	0.3	0.1	0.3	0.1	0.0	0.0	24.6	7.2	17.2	14.0	6752	6713
Peru	0.9	0.1	0.8	0.1	0.1	0.0	30.8	4.8	35.6	13.1	3930	3929
PRC China	0.3	0.1	0.3	0.1	0.1	0.1	30.4	7.6	36.3	22.4	5201	5197
PRC Shen Zhen	0.3	0.1	0.3	0.1	0.1	0.0	34.6	9.3	36.1	14.6	7132	7129
Ukraine	2.5	0.3	1.8	0.2	0.7	0.2	37.1	2.9	52.4	6.3	4725	4710
Upper-middle income countries	1.4	0.1	1.2	0.1	0.3	0.0	31.7	1.9	38.9	4.8	28927	24565
Brazil	1.7	0.2	1.3	0.2	0.4	0.1	32.9	3.6	37.0	8.8	5037	5023
Bulgaria	1.2	0.2	0.9	0.2	0.3	0.1	41.0	5.6	49.4	11.4	5318	5301
Colombia (Medellin)	1.7	0.3	1.4	0.2	0.3	0.1	22.9	3.6	34.1	11.1	3261	3260
Lebanon	1.5	0.3	1.4	0.3	0.1	0.1	31.0	5.0	33.0	16.4	2857	2851
Mexico	1.0	0.2	0.7	0.1	0.2	0.1	28.5	4.4	30.9	8.9	5782	5781
Romania	2.1	0.3	1.8	0.3	0.3	0.1	42.2	5.9	67.6	21.2	2357	2349
High income countries	1.8	0.1	1.3	0.1	0.5	0.0	27.9	0.8	39.1	2.0	81839	81754
Australia	1.9	0.2	1.3	0.2	0.6	0.1	24.3	2.6	33.0	4.9	8463	8461
Belgium	1.2	0.5	0.8	0.3	0.5	0.3	28.9	8.3	50.8	15.8	2419	2417
France	0.8	0.2	0.5	0.1	0.2	0.1	24.3	5.2	22.6	10.3	2894	2894
Germany	1.0	0.2	0.6	0.1	0.4	0.2	23.3	4.5	53.1	12.0	3555	3555
Israel	1.4	0.2	1.3	0.2	0.2	0.1	28.3	3.2	32.8	8.8	4859	4853

Italy	1.0	0.2	0.7	0.2	0.3	0.1	31.8	5.9	46.5	9.8	4712	4708
Japan	0.5	0.1	0.3	0.1	0.2	0.1	20.3	5.7	46.2	14.1	4129	4126
New Zealand	2.9	0.2	2.2	0.2	0.7	0.1	29.3	1.7	41.3	3.8	12790	12781
Northern Ireland	3.3	0.3	2.2	0.2	1.1	0.2	30.9	3.0	45.8	4.8	4340	4335
Poland	0.7	0.1	0.6	0.1	0.0	0.0	26.7	3.0	19.4	9.4	10081	10049
Portugal	2.0	0.2	1.7	0.2	0.4	0.1	27.8	2.8	39.0	10.7	3849	3841
Spain	1.2	0.2	1.0	0.2	0.3	0.1	30.9	4.9	47.1	7.8	5473	5472
Spain (Murcia)	1.6	0.4	1.4	0.3	0.2	0.1	27.0	5.0	28.2	14.3	2621	2617
The Netherlands	1.3	0.4	0.7	0.3	0.5	0.2	23.0	7.2	43.2	11.4	2372	2370
The United States	3.3	0.2	2.2	0.2	1.0	0.1	28.0	1.9	38.1	4.6	9282	9275
All countries combined	1.6	0.0	1.2	0.0	0.4	0.0	29.2	0.7	40.6	1.7	147264	142714
WHO regions^b												
Region of the Americas	1.9	0.1	1.4	0.1	0.5	0.1	27.8	1.3	37.4	3.4	31718	31690
African Region	0.3	0.1	0.3	0.1	0.0	0.0	24.6	7.2	17.2	14.0	11067	6713
Western Pacific Region	1.6	0.1	1.2	0.1	0.4	0.0	27.7	1.4	38.0	2.9	37715	37694
Eastern Mediterranean Region	1.6	0.2	1.3	0.1	0.4	0.1	33.3	2.8	53.8	7.9	12048	11999
Western European Region	1.5	0.1	1.1	0.1	0.4	0.0	28.5	1.5	43.0	3.2	32235	32209
Eastern European Region	1.3	0.1	1.1	0.1	0.3	0.1	34.9	1.9	47.6	5.2	22481	22409
Comparison between countries^c	$\chi^2_{27} = 22.7^*$, P < .001		$\chi^2_{27} = 15.1^*$, P < .001		$\chi^2_{27} = 10.2^*$, P < .001		$\chi^2_{27} = 1.4$, P = 0.095		$\chi^2_{27} = 1.0$, P = 0.537			
Comparison between low, middle and high income country groups^c	$\chi^2_2 = 40.9^*$, P < .001		$\chi^2_2 = 29.4^*$, P < .001		$\chi^2_2 = 14.7^*$, P < .001		$\chi^2_2 = 3.6^*$, P = 0.028		$\chi^2_2 = 2.1$, P = 0.119			
Comparison between WHO regions^c	$\chi^2_5 = 37.8^*$, P < .001		$\chi^2_5 = 19.8^*$, P < .001		$\chi^2_5 = 38.3^*$, P < .001		$\chi^2_5 = 2.7^*$, P = 0.021		$\chi^2_5 = 1.5$, P = 0.193			

^aSample size used after excluding lifetime panic attack cases with missing age of onset.

^b**Region of the Americas** (Colombia, Mexico, Brazil, Peru, The United States, Medellin); **African region** (Nigeria); **Western Pacific region** (PRC Shen Zhen, PRC Beijing and Shanghai, Japan, Australia, New Zealand); **Eastern Mediterranean region** (Israel, Iraq, Lebanon); **Western European region** (Belgium, France, Germany, Italy, The Netherlands, Spain, Northern Ireland, Portugal, Murcia); **Eastern European region** (Romania, Bulgaria, Poland, Ukraine).

^cChi-square test of homogeneity to determine if there is variation in prevalence estimates across countries.

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Appendix Table 3 . Comorbidity of panic disorder with other mental disorders.

	Panic disorder cases with comorbid disorders									
	Mood disorder		Anxiety disorder		Impulse-control disorder		Substance-use disorder		Any mental disorder	
	%	SE	%	SE	%	SE	%	SE	%	SE
Lifetime comorbidity^a										
Lifetime	53.7	1.4	63.1	1.3	10.4	0.7	26.2	1.4	80.4	1.1
12-month	55.4	1.7	64.9	1.7	12.2	1.1	28.1	1.7	81.8	1.5
12-month comorbidity^b										
12-month	43.6	1.8	57.6	1.8	8.1	0.8	11.2	1.3	71.7	1.6
Temporal priority of panic disorder^c										
Lifetime	33.0	1.8	15.2	1.4	36.9	3.1	45.8	3.2	15.4	0.9
12-month	35.1	2.2	17.3	2.0	34.4	3.4	51.1	3.8	15.7	1.3

^aPercentage of respondents with either lifetime or 12 month panic disorder who also meet lifetime criteria for at least one of the other DSM-IV disorders.

^bPercentage of respondents with 12 month panic disorder who also meet 12 month criteria for at least one of the other disorders.

^cPercentage of respondents with either lifetime or 12 month panic disorder and at least 1 of the other disorders, whose age of onset of panic disorder is reported to be younger than the age of onset of all comorbid disorders under consideration (ie, either mood, anxiety, substance use, impulse control or any disorder).

Appendix Table 4. Bivariate associations between socio-demographics correlates and panic disorder.

Correlates	30-day Panic Disorder ^a		Lifetime Panic Disorder ^b		12-month Panic Disorder among lifetime cases ^c		30-day Panic Disorder among 12-month cases ^c	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Age-cohort								
18-29	1.7*	(1.2-2.4)	6.4*	(5.2-7.7)				
30-44	2.0*	(1.5-2.6)	5.0*	(4.2-5.8)				
45-59	1.6*	(1.2-2.1)	3.0*	(2.6-3.6)				
60+	1.0		1.0					
Age-cohort difference ^d	$\chi^2_3 = 24.5^*$, P <.001		$\chi^2_3 = 455.2^*$, P <.001		□		□	
			□		□		□	
Age of onset								
Early					2.2*	(1.6-3.0)	1.2	(0.8-1.7)
Early-average					1.3	(0.9-1.7)	1.2	(0.8-1.8)
Late-average					0.9	(0.7-1.1)	0.9	(0.6-1.3)
Late					1.0		1.0	
Age of onset difference ^d					$\chi^2_3 = 34.7^*$, P <.001		$\chi^2_3 = 3.0$, P = 0.387	
Time since onset (Continuous)								
					0.98*	(0.97-0.99)	1.00	(0.99-1.01)
					$\chi^2_1 = 23.6^*$, P <.001		$\chi^2_1 = 0.2$, P = 0.655	
			□		□		□	
Gender								
Female	2.0*	(1.6-2.5)	1.8*	(1.6-2.0)	1.2	(1.0-1.5)	1.0	(0.7-1.3)
Male	1.0		1.0		1.0		1.0	
Gender difference ^d	$\chi^2_1 = 35.0^*$, P <.001		$\chi^2_1 = 109.0^*$, P <.001		$\chi^2_1 = 3.4$, P = 0.064		$\chi^2_1 = 0.0$, P = 0.956	
Employment status								
Student	1.1	(0.6-2.0)	1.3	(0.9-1.8)	1.8	(0.9-3.8)	1.0	(0.4-2.1)

Homemaker	1.4*	(1.0-2.0)	1.4*	(1.2-1.6)	1.5*	(1.1-2.0)	0.8	(0.5-1.2)
Retired	1.1	(0.8-1.6)	1.3*	(1.0-1.6)	1.5*	(1.0-2.2)	1.1	(0.7-1.8)
Other	3.0*	(2.3-4.1)	2.0*	(1.7-2.4)	2.2*	(1.6-3.2)	1.5*	(1.0-2.1)
Employed	1.0		1.0		1.0		1.0	
Employment status difference ^d	$\chi^2_4 = 57.5^*$, P <.001		$\chi^2_4 = 84.2^*$, P <.001		$\chi^2_4 = 25.4^*$, P <.001		$\chi^2_4 = 6.3$, P = 0.182	
Marital status								
Never married	1.1	(0.8-1.4)	1.3*	(1.2-1.5)	1.2	(0.9-1.6)	1.2	(0.8-1.7)
Divorced/separated/widowed	2.6*	(2.0-3.4)	1.7*	(1.5-1.9)	1.6*	(1.2-2.1)	1.5*	(1.1-2.1)
Currently married	1.0		1.0		1.0		1.0	
Marital status difference ^d	$\chi^2_2 = 48.8^*$, P <.001		$\chi^2_2 = 77.4^*$, P <.001		$\chi^2_2 = 12.9^*$, P = 0.002		$\chi^2_2 = 6.2^*$, P= 0.044	
Education level								
No education	3.8*	(1.3-11.4)	1.6	(0.9-2.6)	4.2*	(1.8-10.2)	2.3	(0.8-6.9)
Some primary	5.7*	(3.6-8.9)	1.8*	(1.4-2.2)	2.9*	(1.7-5.0)	4.0*	(2.2-7.5)
Finished primary	5.0*	(2.9-8.6)	2.2*	(1.8-2.8)	1.7*	(1.1-2.6)	2.6*	(1.5-4.7)
Some secondary	2.9*	(2.0-4.1)	1.8*	(1.5-2.1)	1.5*	(1.0-2.1)	2.0*	(1.3-3.0)
Finished secondary	2.6*	(1.8-3.8)	1.7*	(1.4-1.9)	1.3	(0.9-1.8)	1.8*	(1.2-2.8)
Some college	2.0*	(1.4-2.8)	1.5*	(1.3-1.8)	0.9	(0.7-1.3)	1.8*	(1.2-2.8)
Finished college	1.0		1.0		1.0		1.0	
Education level difference ^d	$\chi^2_6 = 66.4^*$, P <.001		$\chi^2_6 = 65.0^*$, P <.001		$\chi^2_6 = 28.7^*$, P <.001		$\chi^2_6 = 23.4^*$, P = 0.001	
Household income								
Low	1.8*	(1.3-2.4)	1.5*	(1.3-1.7)	1.5*	(1.1-2.1)	1.2	(0.8-1.8)
Low-average	1.3	(1.0-1.8)	1.2*	(1.1-1.4)	1.3	(0.9-1.7)	1.0	(0.7-1.5)
High-average	1.1	(0.8-1.5)	1.1	(1.0-1.3)	0.9	(0.7-1.3)	1.0	(0.7-1.5)
High	1.0		1.0		1.0		1.0	
Household income difference ^d	$\chi^2_3 = 21.7^*$, P <.001		$\chi^2_3 = 38.7^*$, P <.001		$\chi^2_3 = 11.3^*$, P = 0.010		$\chi^2_3 = 2.1$, P = 0.554	

N ^e	142949	6250338	2563	1465

*Significant at the .05 level, 2 sided test.

^aThese estimates are based on logistic regression models adjusted for age, gender and country.

^bThese estimates are based on survival models adjusted for age-cohorts, gender, person-years and country.

^cThese estimates are based on logistic regression models adjusted for time since panic disorder onset, age of panic disorder onset, gender and country.

^dChi square test of significant differences between blocks of sociodemographic variables.

^eDenominator N: 142,949 = total sample; 6,250,338 = number of person-years in the survival models; 2,563 = number of lifetime cases of panic disorder; 1,465 = number of 12-month cases of panic disorder.

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Appendix Table 5. Bivariate associations between socio-demographics correlates and recurrent panic attacks.

Correlates	30-day Panic Attack without Lifetime Panic Disorder ^a		Lifetime Panic Attack without lifetime Panic Disorder ^b		12-month Panic Attack among lifetime Panic attack without lifetime Panic Disorder ^c		30-day Panic Attack among 12-month Panic Attack without Lifetime Panic disorder ^c	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Age-cohort								
18-29	1.5*	(1.2-1.8)	5.1*	(4.7-5.6)				
30-44	1.6*	(1.3-1.9)	3.2*	(2.9-3.4)				
45-59	1.5*	(1.2-1.8)	2.1*	(2.0-2.3)				
60+	1.0		1.0					
Age-cohort difference ^d	χ ² ₃ = 27.4*, P <.001		χ ² ₃ = 1435.3*, P <.001		□		□	
			□		□		□	
Age of onset								
Early					1.5*	(1.3-1.7)	0.9	(0.7-1.2)
Early-average					1.1	(1.0-1.3)	0.7*	(0.6-0.9)
Late-average					0.9	(0.8-1.0)	0.9	(0.7-1.1)
Late					1.0		1.0	
Age of onset difference ^d					χ ² ₃ = 51.4*, P <.001		χ ² ₃ = 6.8, P = 0.080	
Time since onset (Continuous)					0.98*	(0.97-0.98)	1.01*	(1.00-1.01)
					χ ² ₁ = 183.6*, P <.001		χ ² ₁ = 8.8*, P = 0.003	
			□		□		□	
Gender								
Female	2.0*	(1.7-2.3)	1.6*	(1.5-1.7)	1.4*	(1.2-1.5)	1.0	(0.9-1.2)
Male	1.0		1.0		1.0		1.0	
Gender difference ^d	χ ² ₁ = 97.5*, P <.001		χ ² ₁ = 406.1*, P <.001		χ ² ₁ = 41.8*, P <.001		χ ² ₁ = 0.0, P = 0.926	

Employment status								
Student	1.1	(0.8-1.5)	1.1	(1.0-1.3)	1.2	(0.9-1.5)	1.0	(0.7-1.5)
Homemaker	1.3*	(1.1-1.6)	1.1	(1.0-1.1)	1.2	(1.0-1.3)	1.2	(0.9-1.5)
Retired	1.0	(0.8-1.3)	1.0	(0.9-1.1)	1.4*	(1.2-1.6)	0.8	(0.6-1.1)
Other	1.9*	(1.6-2.3)	1.4*	(1.3-1.5)	1.7*	(1.5-2.0)	1.1	(0.9-1.3)
Employed	1.0		1.0		1.0		1.0	
Employment status difference ^d	$\chi^2_4 = 45.5^*$, P <.001		$\chi^2_4 = 86.7^*$, P <.001		$\chi^2_4 = 56.0^*$, P <.001		$\chi^2_4 = 4.5$, P = 0.340	
Marital status								
Never married	1.1	(0.9-1.3)	1.1*	(1.0-1.2)	1.1*	(1.0-1.3)	1.2*	(1.0-1.5)
Divorced/separated/widowed	1.4*	(1.2-1.7)	1.2*	(1.1-1.3)	1.2*	(1.1-1.3)	1.1	(0.9-1.3)
Currently married	1.0		1.0		1.0		1.0	
Marital status difference ^d	$\chi^2_2 = 18.4^*$, P <.001		$\chi^2_2 = 37.6^*$, P <.001		$\chi^2_2 = 10.9^*$, P = 0.004		$\chi^2_2 = 4.1$, P = 0.129	
Education level								
No education	2.5*	(1.5-4.2)	1.7*	(1.4-2.0)	1.7*	(1.1-2.5)	1.3	(0.7-2.3)
Some primary	1.9*	(1.5-2.5)	1.5*	(1.4-1.7)	2.0*	(1.6-2.5)	0.8	(0.6-1.2)
Finished primary	2.0*	(1.5-2.6)	1.4*	(1.3-1.6)	1.8*	(1.5-2.2)	1.0	(0.7-1.4)
Some secondary	1.5*	(1.2-1.9)	1.2*	(1.1-1.3)	1.4*	(1.2-1.6)	1.0	(0.8-1.3)
Finished secondary	1.3*	(1.1-1.6)	1.2*	(1.1-1.3)	1.3*	(1.1-1.4)	1.0	(0.8-1.2)
Some college	1.2	(1.0-1.6)	1.2*	(1.1-1.3)	1.2*	(1.0-1.4)	1.0	(0.8-1.3)
Finished college	1.0		1.0		1.0		1.0	
Education level difference ^d	$\chi^2_6 = 42.4^*$, P <.001		$\chi^2_6 = 100.7^*$, P <.001		$\chi^2_6 = 55.5^*$, P <.001		$\chi^2_6 = 3.1$, P = 0.800	
Household income								
Low	1.6*	(1.3-2.0)	1.1*	(1.0-1.2)	1.5*	(1.3-1.7)	1.4*	(1.1-1.7)
Low-average	1.4*	(1.1-1.7)	1.1*	(1.0-1.2)	1.2*	(1.1-1.4)	1.2	(0.9-1.5)
High-average	1.4*	(1.1-1.7)	1.0	(1.0-1.1)	1.2*	(1.0-1.3)	1.3	(1.0-1.6)

High	1.0	1.0	1.0	1.0
Household income difference ^d	$\chi^2_3 = 20.4^*$, P < .001	$\chi^2_3 = 7.7$, P = 0.053	$\chi^2_3 = 31.7^*$, P < .001	$\chi^2_3 = 6.6$, P = 0.087
N ^e	138281	5843592	12730	4971

*Significant at the .05 level, 2 sided test.

^aThese estimates are based on logistic regression models adjusted for age, gender and country.

^bThese estimates are based on survival models adjusted for age-cohorts, gender, person-years and country.

^cThese estimates are based on logistic regression models adjusted for time since panic attack onset, age of panic attack onset, gender and country.

^dChi square test of significant differences between blocks of sociodemographic variables.

^eDenominator N: 138,281 = total sample; 5,843,592 = number of person-years in the survival models; 12,730 = number of lifetime panic attack without lifetime panic disorder cases; 4,971 = number of 12-month panic attack without lifetime panic disorder cases.

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