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Associations between DSM-IV mental disorders and diabetes mellitus: a role for impulse control disorders and depression

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Abstract

Aims/hypothesis—No studies have evaluated whether the frequently observed associations between depression and diabetes could reflect the presence of comorbid psychiatric conditions and their associations with diabetes. We therefore examined the associations between a wide range of pre-existing Diagnostic Statistical Manual, 4th edition (DSM-IV) mental disorders with self-reported diagnosis of diabetes.

Methods—We performed a series of cross-sectional face-to-face household surveys of community-dwelling adults (*n*=52,095) in 19 countries. The World Health Organization Composite International Diagnostic Interview retrospectively assessed lifetime prevalence and age at onset of 16 DSM-IV mental disorders. Diabetes was indicated by self-report of physician's diagnosis together with its timing. We analysed the associations between all mental disorders and diabetes, without and with comorbidity adjustment.

Results—We identified 2,580 cases of adult-onset diabetes mellitus (21 years +). Although all 16 DSM-IV disorders were associated with diabetes diagnosis in bivariate models, only depression (OR 1.3; 95% CI 1.1, 1.5), intermittent explosive disorder (OR 1.6; 95% CI 1.1, 2.1), binge eating disorder (OR 2.6; 95% CI 1.7, 4.0) and bulimia nervosa (OR 2.1; 95% CI 1.3, 3.4) remained after comorbidity adjustment.

Conclusions/interpretation—Depression and impulse control disorders (eating disorders in particular) were significantly associated with diabetes diagnosis after comorbidity adjustment. These findings support the focus on depression as having a role in diabetes onset, but suggest that this focus may be extended towards impulse control disorders. Acknowledging the comorbidity of mental disorders is important in determining the associations between mental disorders and subsequent diabetes.

Keywords

Comorbidity; Depression; Epidemiology; Impulse control disorders; Mental disorders

Introduction

Many studies have reported sequential associations between mood disorders and diabetes mellitus and these have been summarised in a series of meta-analyses [1–4]. These analyses have clarified several points: (1) depression and diabetes frequently co-occur; (2) the presence of depression increases the risk of future diabetes and (3) diabetes increases the risk of subsequent depression. Moreover, the comorbidity of depression and diabetes has been found to be particularly harmful in terms of cardiovascular events, cardiac mortality and mortality in general [5–8].

Most attention in this body of literature has been directed to the possibility that depression serves as a risk factor for diabetes, as depression is potentially modifiable and its treatment might translate into a decreased risk of diabetes onset [9]. This is theoretically plausible as the typical age of onset of depression is considerably lower than the typical age of diabetes onset. A recent report of the World Mental Health (WMH) surveys concluded that the mean age of depression onset is about 25 years [10], while for type 2 diabetes mellitus—by far the most common form of diabetes—mean age of onset is >45 years [11]. Moreover, several physiological and behavioural mechanisms have been proposed to explain this possible link [12–14].

Most of the available evidence has been derived from observational studies. However, two limitations of the existing observational studies significantly hamper progress in our understanding of the depression–diabetes association. First, although some recent studies were performed in Asia (e.g. [14]), the literature is dominated by study samples from the USA and Europe [15–17]. This poses a problem as prevalence rates of depression and diabetes vary substantially across nations and level of national development [14]. Second, and more importantly, it is unclear whether the depression–diabetes association may be explained by the presence of other mental disorders. Depression frequently co-occurs not only with anxiety disorders but also with many of the other Diagnostic Statistical Manual, 4th edition (DSM-IV) mental disorders such as eating disorders and alcohol abuse [18–20]. For instance, the lifetime rate of major depressive disorder in individuals with eating disorders is as high as 50–75% [21], although some heterogeneity in findings has been reported [22]. As the literature has focused exclusively on depression, it remains possible for a person to develop an eating disorder, become depressed later on, and in the end develop diabetes mellitus. Targeting the eating disorder in this case will theoretically be a far more promising approach than focusing solely on depression.

Previous studies were unable to address these problems as they were mostly based on a single country, and in particular did not collect reliable data on the presence of mental disorders other than depression. We therefore conducted the present study within the framework of the WMH surveys [23, 24] to examine the associations between a wide range of DSM-IV mental disorders and diabetes diagnosis. This approach enabled us to investigate the association between first onset of mood, anxiety, impulse control (including eating disorders) and substance use disorders with diabetes diagnosis in a large international sample. Moreover by conducting analyses without and with adjustment for mental disorder comorbidity we evaluated whether the exclusive focus on depression as a risk factor for diabetes onset is warranted.

Methods

Samples and procedures

This study uses data from 19 of the WMH surveys: Colombia, Mexico, Peru, USA, Shenzhen (China), Japan, New Zealand, Belgium, France, Germany, Italy, the Netherlands, Romania, Spain, Portugal, Israel, Iraq, Northern Ireland and Poland (see Table 1). Using stratified multi-stage clustered area probability sampling we selected adult respondents (18 years +) in most WMH survey countries. Most of the surveys were based on nationally

representative household samples except for those from Colombia, Mexico and Shenzhen, which were based on nationally representative household samples in urbanised areas.

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, including the core diagnostic assessment of most mental disorders. Part 2, which assessed physical conditions and a range of other information related to the aims of the survey, was administered to all part 1 respondents who met lifetime criteria for any mental disorder and also to a probability sample of other respondents. 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=52,095). Additional weights were used to adjust for differential probabilities of selection within households, adjusting for non-response, and matching the samples to population sociodemographic distributions. Measures taken to ensure interviewer and data accuracy and cross-national consistency are described elsewhere [22, 23] All respondents provided informed consent and procedures for protecting respondents were approved and monitored for compliance by the Institutional Review Boards in each country (see [22] for details).

Data collection: mental disorders

All surveys used the WMH version of the WHO Composite International Diagnostic Interview (CIDI 3.0) [23], a fully structured interview conducted by trained laypersons, to assess lifetime history of most of the mental disorders. All interviewers were trained in the use of the CIDI by a WHO-authorised training and reference centre. It should be noted, however, that not all disorders were assessed (e.g. the CIDI interview does not include schizophrenia). Disorders covered by the CIDI were assessed using the definitions and criteria of the DSM-IV. A total of 16 mental disorders were used for the present analyses. Anorexia nervosa was excluded due to too low prevalence in the data set to warrant reliable analyses. The mental disorders evaluated in this paper include anxiety disorders (panic disorder, generalised anxiety disorder, social phobia, specific phobia, agoraphobia without panic, post-traumatic stress disorder, obsessive–compulsive disorder); mood disorders (major depressive disorder/dysthymia, bipolar disorder [broad]); impulse control disorders (intermittent explosive disorder, bulimia nervosa, binge eating disorder) and substance use disorders (alcohol abuse and dependence, drug abuse and dependence). Depression and dysthymia were analysed together as CIDI validation studies indicated that a clinical diagnosis of dysthymia was not well-captured by the CIDI interview.

CIDI organic exclusion rules were applied in making diagnoses, while no hierarchical rules were used except with respect to the two eating disorders. Clinical reappraisal studies conducted in some of the WMH survey 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 [25].

Data collection: diabetes mellitus

In a series of questions adapted from the US Health Interview Survey, respondents were asked about the lifetime presence of selected chronic conditions. Respondents were asked:

"Did a doctor or other health professional ever tell you that you had any of the following illnesses….diabetes?" If respondents endorsed this question they were classified as having a history of diabetes for these analyses. Respondents were also asked how old they were when they were first diagnosed with diabetes. This year is referred to herein as the age of onset of diabetes, although it is recognised that the underlying pathology develops over many years and that it is possible to have diabetes before it is detected. Only adult-onset diabetes (onset age 21+ years) was investigated in this paper. As a sensitivity analysis, we restricted the age of onset to a minimum of 30 years to further reduce the risk of including individuals with type I diabetes.

Statistical analysis

Although the data collection was cross-sectional, there was a time element in the data as we asked for the time of onset of diabetes and mental disorders. Essentially, we analysed the associations between mental disorder and diabetes by using this time-related information. We only wanted to consider associations between temporally pre-existing mental disorders and diabetes, excluding episodes of mental disorders that occurred in the same year as diabetes diagnosis, or following diabetes. It is only by using survival analysis that we are able to exclude such episodes from the predictor set because the data are organised in person-year files. Comparable with previous studies using these data [26, 27], we used discrete-time survival analyses [28] with person-year as the unit of analysis to test associations between first onset of mental disorders and diabetes diagnosis. 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 onset of diabetes or their age at interview (whichever came first) was treated as a separate observational record, with the year of diabetes onset coded 1 and earlier years coded 0 on a dichotomous outcome variable. Persons who reported diabetes onset before age 21 years (n=192) were excluded from analysis. 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 diabetes occurred in the same year, the mental disorder would not count as a predictor. Only person-years up to the diagnosis of diabetes were analysed so that only mental disorder episodes occurring before the onset of diabetes were included in the predictor set. Logistic regression analysis was used to analyse these data with the survival coefficients presented as ORs, indicating the relative odds of diabetes diagnosis in a given year for a person with a history of mental disorder compared with a person without that mental disorder (for details, see electronic supplementary material [ESM] Methods).

A series of bivariate and multivariable models were developed including the predictor mental disorder plus control variables. Models control for person-years, country, sex, current age and, in the multivariable models, other mental disorders. Bivariate models investigated the association of specific mental disorders with subsequent diabetes onset. The next model, a multivariable model, estimated the association of each mental disorder with diabetes onset adjusting for mental disorder comorbidity. Our approach was to not control for covariates that could be on the causal pathway between mental disorders and subsequent diabetes as our design does not allow us to distinguish between confounders, mediators and

consequences. We did not split results for men and women as we did not find significant interaction effects between sex and most of the psychiatric disorders. The proportionality assumption was checked by including time-dependent covariates in the model (i.e. interactions of each of the predictors [mental disorders] with time [person-year] in predicting diabetes diagnosis). We did this for each predictor individually. Only three of the 16 predictors showed significant interactions with person-years (depression, social phobia and generalised anxiety disorder). The interactions were further explored and interpreted as chance findings.

Our earlier studies of concurrent mental–physical comorbidity in the WMH surveys found that these associations were generally consistent across nations, despite varying prevalence of mental disorders and physical conditions [15, 29]. 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 linearisation [30] implemented in version 10 of the SUDAAN software system (RTI International, Research Triangle Park, NC, USA) was used to estimate standard errors and evaluate the statistical significance of coefficients. Given the number of tests, we set statistical significance at $p<0.01$.

Results

Descriptives

The survey characteristics are shown in Table 1, together with information about the number of survey respondents reporting a history of diabetes (n=2,580), representing a total of 2,161,945 person-years. The mean age of adult diabetes onset was 50.3 years (median 49.8). There were 395 cases with a reported diagnosis of diabetes under 30 years of age and 2,377 at or after 30 years of age.

Mental disorders as predictors of diabetes onset

Table 2 shows the prevalence rates of mental disorders for the total sample (n=52,095) and persons reporting diabetes (n=2,580). Within this subsample we identified those mental disorders with an onset before diabetes. The highest prevalence rates were found for major depression (11.3%), specific phobia (7.0%) and alcohol abuse (5.8%). The mean age of onset of mental disorders ranged from 9.3 to 31.6 years, with the lowest mean onset age for specific phobia (9.3 years), social phobia (13.7 years), and bulimia nervosa (15.6 years).

The associations between individual mental disorders and diabetes diagnosis were first investigated in a series of bivariate models (i.e. only one mental disorder considered at a time). The data presented in Table 3 show that all mental disorders were associated with diabetes except for obsessive–compulsive disorder, with ORs in the range 1.3–3.9. The two eating disorders, binge eating disorder and bulimia nervosa, stand out as having a particularly strong association with diabetes (OR 3.8 and 3.9, respectively).

To investigate the possibility that comorbidity among mental disorders plays a role in the associations with diabetes onset, we first examined the levels of comorbidity in individuals that would develop diabetes (Table 4). All mental disorders were significantly associated with each other, with some exceptions: agoraphobia and panic, alcohol abuse and alcohol

dependence, drug abuse and drug dependence. These disorders are by definition mutually exclusive, explaining the lack of correlations. In addition, no significant associations were found between obsessive–compulsive disorder and alcohol and drug abuse. For the rest, all mental disorders were substantially associated, with ORs as high as 66.4 for alcohol dependence and drug dependence and 37.8 for binge eating disorder and bulimia nervosa. Most of the remaining ORs were in the range of 5–10, indicating high levels of comorbidity.

When lifetime comorbidity until the age of diabetes onset was taken into account in the multivariable models, the magnitude of associations diminished substantially for most of the disorders, rendering the associations significant only for 4 out of 16: major depressive episode/dysthymia, intermittent explosive disorder, binge eating disorder and bulimia nervosa (Table 5).

The test of the global null hypothesis—as to whether any of the set of predictors coefficients is not equal to zero—was significant (χ^2=114.7, p≤0.01) and the test for significant difference between ORs indicates that we can reject the hypothesis that the ORs are the same for all mental disorders (χ^2=32.2, p≤0.01). The sensitivity analysis, in which we restricted age of onset of diabetes to a minimum of 30 years, resulted in highly similar findings (see ESM Tables 1 and 2).

Discussion

This is the first study evaluating the associations of a wide range of DSM-IV mental disorders with diabetes diagnosis in an international sample. The inclusion of a wide range of disorders and the large sample size enabled us to reliably adjust for mental disorder comorbidity and thus estimate the unique association of each of the mental disorders with diabetes. Our main findings were that in unadjusted models virtually all included mental disorders were associated with diabetes and that controlling for mental comorbidity resulted in significant associations only for depression and impulse control disorders (intermittent explosive disorder and eating disorders in particular). The magnitude of the association between depression and diabetes diagnosis was about 40% increased risk in unadjusted analyses and 30% in adjusted analyses. These findings are in concordance with results from previous meta-analyses (37–56% unadjusted) [9, 31] and a recent report using insurance claims data (43% unadjusted) [32], and suggest that the association between depression and diabetes is relatively independent from other psychiatric disorders. The association between impulse disorders and diabetes diagnosis has not been reported before. By far the strongest prospective associations were found with respect to eating disorders and diabetes. From a mechanistic point of view, this association seems to point to the importance of glucose dys-regulation and obesity-associated eating disorders, which may eventually result in later diabetes [33, 34]. However, based on the associations between impulse control disorders, including intermittent explosive disorders, and diabetes, at least two other candidate mechanisms may be suggested, namely low levels of HDL-cholesterol and decreased serotonin functioning, both of which have been associated with aggression and diabetes [35, 36]. It should be noted that these processes may be already present early in life and may manifest differently during the life course. For instance, a child with disturbed serotonin functioning may be characterised by poor impulse control and problematical eating

behaviour early in life and by obesity and diabetes later in life, perhaps accompanied by depression. Unfortunately with the present data, we are not able to evaluate this in more detail and can only speculate.

The vast majority of studies investigating the associations of mental disorders with diabetes has been restricted to depression. Our current findings stress that depression indeed seems to have an independent association with diabetes onset, as controlling for mental comorbidity only moderately affected the association between depression and diabetes. However, our analyses did signal that impulse control disorders are also important. It should be kept in mind, however, that their prevalence rates are considerably lower than that of depression (i.e. 0.9% for binge eating disorder, 0.5% for bulimia nervosa and 1.8% for intermittent explosive disorder compared with 11.3% for depression). Of interest, impulse control disorders have a typical age of onset at around 20 years of age, which is generally earlier than the age of onset for most of the other mental disorders that were considered in this study, including depression. Indeed, in our sample we found that specifically bulimia nervosa had a relatively early age of onset (15.6 years). Perhaps further studies could evaluate the possibility that impulse control disorders, including eating disorders and intermittent explosive disorder, may serve as risk factors for depression and diabetes, or that these disorders are expressions of an underlying pathology that might lead to diabetes. The fact that in particular these four disorders remained associated with diabetes is also compatible with a hypothesis in which these disorders represent relatively independent risk factors for diabetes.

The results of this study should be considered within the context of the following strengths and limitations. The retrospective assessment of mental disorders is likely to have resulted in under-reporting of some mental disorders and inaccuracies in the age of onset timing. A second key limitation is the self-report of diabetes. Although self-reports of medically diagnosed diabetes have been shown to have good validity [37, 38], it is possible that we have missed cases of diabetes (particularly undetected type 2 diabetes), which may have differed across the included countries. Both limitations will probably have resulted in largely non-differential misclassification of individuals with regard to the predictor and outcome in this study. This will have the effect of weakening the strength of the reported associations between mental disorders and diabetes, making the results we report here conservative. However, there may also be forms of differential misclassification leading to biased estimates of variables. For instance, it is possible that persons with a mental disorder have a decreased access to healthcare, which would reduce the risk of diabetes being diagnosed. A further limitation is that as this study was only conducted among diabetes (and mental disorder) survivors some of those most affected by an association between mental disorder and diabetes are not included in the sample due to premature mortality. In addition, it should be noted that although we used a large international sample of respondents, we did not stratify per country or culture. Stratifying by country would have led to insufficient numbers of subjects with which to conduct the multivariable models, while stratifying for culture would result in rather arbitrary decisions in classifying countries. We did control for country as a confounder, which we think is an advantage over the existing literature, which largely focuses on single country-based studies. A further limitation of the present study is that we were not able to differentiate between type 1 and type 2 diabetes. Although the majority of

cases will be type 2 diabetes, and this is strengthened by the fact that we included only diabetes cases with an adult onset and found similar results when heightening the age of onset to a minimum of 30 years, some of the cases might be type 1 diabetes. In addition, it should be noted that although the aetiology of type 1 and type 2 diabetes is markedly different, the associations with depression appear to be rather comparable. In a recent meta-analysis [39] it was concluded that the risk of depression associated with diabetes mainly depends on whether diabetes is detected or remains undiagnosed. However, it remains unclear whether the same argument would hold with respect to eating disorders and diabetes onset. Further studies should therefore try to clarify whether our present findings are different for patients with type 1 and type 2 diabetes. We were not able to include all mental disorders in our analyses and therefore were not able to present a complete picture. Specifically, in a large-scale population-based study such as the WMH surveys it is not possible to include the diagnosis of schizophrenia because the interviewer would require specific clinical skills to rule out false-positive cases. The CIDI interview is conducted by trained laypersons, and therefore does not cover schizophrenia. This is unfortunate as the literature suggests a role for several metabolism-related hormones in schizophrenia that are also be related to diabetes [40, 41]. Furthermore, there are indications that shared susceptibility genes may link the two [42], and there are also potential effects of antipsychotic medication that are relevant to diabetes onset [43]. As a final limitation, we can only speculate regarding the mechanisms that may be involved in the associations found. This study did not aim to explain the associations but rather documented them in a large population-based sample that was less biased than the existing registry studies.

In conclusion, we found that in bivariate analyses almost all mental disorders had associations with diabetes. Most of these associations were attributable to psychiatric comorbidity and specific associations of depression and eating disorders with diabetes. Our findings thus suggest that the focus on depression in the context of diabetes prediction is warranted, but may be extended to impulse control disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

CIDI	Composite International Diagnostic Interview
DSM-IV	Diagnostic Statistical Manual, 4th edition
WMH	World Mental Health

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Table 1

Characteristics of WMH survey samples and number of persons with diabetes

Country	Field date	Age range (years)	Mean age (years)	% Women	Part 1 (*n*)	Part 2 (*n*)	Response rate (%)	Diabetes (*n*)	Diabetes (%)
Americas									
Colombia	2003	18–65	36.7	62.8	4,426	2,381	87.7	54	2.9
Mexico	2001–2002	18–65	36.0	63.9	5,782	2,362	76.6	125	4.8
USA	2002–2003	18+	43.4	58.2	9,282	5,692	70.9	373	7.3
Peru	2005–2006	18–65	36.8	55.8	3,930	1,801	90.2	32	2.0
Asia and South Pacific									
Japan	2002–2006	20+	52.5	56.4	4,129	1,682	55.1	99	5.0
Shenzhen (People's Republic of China)	2006–2007	18+	31.6	49.3	7,132	2,475	80.0	33	0.8
New Zealand	2003–2004	18+	43.8	59.6	12,790	7,312	73.3	401	4.8
Europe									
Belgium	2001–2002	18+	47.6	55.3	2,419	1,043	50.6	40	3.7
France	2001–2002	18+	46.1	59.3	2,894	1,436	45.9	52	4.1
Germany	2002–2003	18+	47.7	57.6	3,555	1,323	57.8	63	4.8
Italy	2001–2002	18+	47.0	54.5	4,712	1,779	71.3	59	3.4
The Netherlands	2002–2003	18+	47.3	58.9	2,372	1,094	56.4	61	7.2
Spain	2001–2002	18+	49.6	61.4	5,473	2,121	78.6	140	5.8
Northern Ireland	2004–2007	18+	47.6	58.6	4,340	1,986	68.4	68	3.3
Portugal	2008–2009	18+	45.3	63.2	3,849	2,060	57.3	145	7.2
Romania	2005–2006	18+	50.5	53.7	2,357	2,357	70.9	101	3.6
Poland	2010–2011	18–64	40.6	55.0	10,081	4,000	50.4	159	3.6
Middle East									
Israel	2002–2004	21+	45.8	51.0	4,859	4,859	72.6	410	7.8
Iraq	2006–2007	18+	37.4	51.7	4,332	4,332	95.2	165	4.0
Weighted average response rate (%)							78.0		
Total sample size (*n*)					98,714	52,095		2,580	

Table 2

Lifetime prevalence and age of onset of the 16 mental disorders

	Total sample (*N*=52,095)		Subjects with adult-onset diabetes (*n*=2,580)		Subjects with adult-onset diabetes (*n*=2,580) and mental disorders with onset prior to diabetes			
	Prevalence		Prevalence		Prevalence		Age of onset	
	%	SE	%	SE	%	SE	Mean	SE
Major depressive episode/dysthymia	12.6	0.2	14.8	0.7	11.3	0.7	31.6	0.8
Bipolar disorder (broad)	1.9	0.1	1.7	0.2	1.2	0.2	25.0	1.9
Panic disorder	1.8	0.1	2.3	0.3	1.8	0.3	25.6	2.0
Generalised anxiety disorder	4.2	0.1	5.8	0.5	3.9	0.4	28.7	1.3
Social phobia	4.4	0.1	4.2	0.4	4.1	0.4	13.7	1.0
Specific phobia	7.3	0.1	7.3	0.6	7.0	0.6	9.3	0.6
Agoraphobia without panic	0.9	0.0	1.0	0.2	0.9	0.2	18.7	1.9
Post-traumatic stress disorder	3.3	0.1	4.5	0.5	3.3	0.5	28.7	1.9
Obsessive–compulsive disorder	1.3	0.1	0.7	0.2	0.6	0.2	17.1	2.5
Intermittent explosive disorder	2.1	0.1	1.9	0.3	1.8	0.3	19.7	1.7
Binge eating disorder	0.7	0.0	1.0	0.2	0.9	0.2	25.8	2.9
Bulimia nervosa	0.4	0.0	0.6	0.2	0.5	0.2	15.6	1.9
Alcohol abuse	7.4	0.1	6.2	0.5	5.8	0.5	24.1	0.8
Alcohol dependence with abuse	2.1	0.1	2.2	0.3	2.1	0.3	24.6	1.5
Drug abuse	2.5	0.1	1.8	0.3	1.8	0.3	21.0	0.7
Drug dependence with abuse	0.9	0.0	0.9	0.2	0.9	0.2	21.7	1.0

Table 3

Bivariate associations (ORs) between DSM-IV mental disorders and the subsequent diagnosis of diabetes[a]

Disorder	OR (95% CI)	*p* value
Major depressive episode/dysthymia	1.4 (1.3, 1.7)	<0.001
Bipolar disorder (broad)	1.7 (1.2, 2.3)	0.001
Panic disorder	1.6 (1.2, 2.2)	0.002
Generalised anxiety disorder	1.3 (1.1, 1.7)	0.009
Social phobia	1.4 (1.1, 1.7)	0.008
Specific phobia	1.4 (1.1, 1.6)	0.001
Agoraphobia without panic	1.5 (1.0, 2.1)	0.043
Post-traumatic stress disorder	1.5 (1.1, 2.0)	0.012
Obsessive–compulsive disorder	1.4 (0.7, 2.6)	0.388
Intermittent explosive disorder	1.9 (1.4, 2.6)	<0.001
Binge eating disorder	3.8 (2.2, 6.5)	<0.001
Bulimia nervosa	3.9 (2.2, 7.1)	<0.001
Alcohol abuse	1.3 (1.1, 1.6)	0.008
Alcohol dependence with abuse	1.6 (1.2, 2.2)	0.001
Drug abuse	2.0 (1.4, 2.8)	<0.001
Drug dependence with abuse	2.9 (1.8, 4.7)	<0.001

[a]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, sex, person-year and country

Table 4

Bivariate associations (odds ratios) of DSM-IV Lifetime mental disorders, with hierarchy

Disorder	MD	BD	PD	GAD	SocP	SpecP	Ago	PTSD	OCD	IED	BED	BN	AA	AD	DA	DD
Major depression episode/dysthymia (MD)																
Bipolar disorders (BD)	8.5*** (7.5, 9.7)															
Panic disorder (PD)	9.0*** (7.9, 10.3)	8.0*** (6.5, 9.7)														
Generalised anxiety disorder (GAD)	8.1*** (7.3, 9.1)	6.0*** (4.9, 7.3)	8.9*** (7.4, 10.7)													
Social phobia (SocP)	6.9*** (6.3, 7.6)	7.9*** (6.8, 9.1)	9.3*** (8.0, 10.8)	8.4*** (7.3, 9.5)												
Specific phobia (SpecP)	4.2*** (3.9, 4.6)	5.0*** (4.4, 5.8)	7.6*** (6.6, 8.7)	4.0*** (3.5, 4.6)	8.3*** (7.5,9.2)											
Agoraphobia without panic (Ago)	6.5*** (5.3, 7.9)	7.8*** (5.9, 10.2)	–	6.7*** (5.1, 8.7)	18.7*** (15.1,23.2)	12.6*** (10.3,15.5)										
Post-traumatic stress disorder (PTSD)	9.9*** (8.8, 11.1)	7.7*** (6.5, 9.3)	8.3*** (7.0, 9.9)	7.9*** (6.8, 9.2)	7.7*** (6.9,8.7)	5.7*** (5.0, 6.4)	6.2*** (4.7, 8.2)									
Obsessive compulsive disorder (OCD)	3.0*** (2.4, 3.8)	5.5*** (4.2, 7.2)	4.6*** (3.2, 6.6)	3.7*** (2.7, 5.3)	3.8*** (2.9,5.0)	3.9*** (3.0, 5.2)	6.4*** (4.0, 10.5)	3.0*** (2.2, 4.1)								
Intermittent explosive disorder (IED)	3.6*** (3.2, 4.1)	7.3*** (6.0, 9.0)	4.9*** (3.9, 6.1)	5.1*** (4.0, 6.5)	5.5*** (4.7,6.3)	3.5*** (3.0, 4.0)	5.0*** (3.5, 7.0)	4.3*** (3.6, 5.2)	4.6*** (3.3, 6.5)							
Binge eating disorder (BED)	5.6*** (4.5, 6.9)	7.2*** (5.1, 10.0)	6.3*** (4.4, 8.9)	4.5*** (3.2, 6.3)	6.7*** (5.2,8.7)	4.9*** (3.9, 6.3)	6.7*** (4.1, 10.9)	6.1*** (4.6, 8.2)	3.6*** (2.3, 5.7)	3.5*** (2.4, 5.3)						
Bulimia nervosa (BN)	8.8*** (6.7, 11.6)	10.3*** (7.2, 14.7)	7.2*** (4.8, 10.9)	9.0*** (6.4, 12.6)	11.1*** (8.4,14.7)	5.5*** (4.1, 7.5)	7.1*** (4.4, 11.6)	12.1*** (8.6, 16.9)	7.5*** (4.4, 12.6)	3.1*** (1.8, 5.4)	37.8*** (24.6,58.0)					
Alcohol abuse (AA)	2.0*** (1.8, 2.3)	3.8*** (3.2, 4.5)	2.2*** (1.8, 2.8)	2.1*** (1.8, 2.6)	2.5*** (2.2,2.9)	1.8*** (1.6, 2.1)	2.2*** (1.7, 3.0)	2.6*** (2.2, 3.1)	0.7 (0.5, 1.1)	3.0*** (2.4, 3.6)	2.2*** (1.5, 3.1)	2.8*** (1.8, 4.4)				
Alcohol dependence (AD)	4.9*** (4.3, 5.5)	11.0*** (9.2, 13.1)	7.4*** (5.9, 9.2)	4.6*** (3.7, 5.6)	6.8*** (5.9,7.9)	3.9*** (3.4, 4.5)	4.7*** (3.3, 6.5)	6.7*** (5.5, 8.1)	2.7*** (1.9, 3.7)	6.7*** (5.3, 8.3)	7.1*** (4.8, 10.3)	8.6*** (5.9, 12.6)	–			
Drug abuse (DA)	4.1*** (3.5, 4.7)	5.5*** (4.3, 7.1)	4.3*** (3.4, 5.6)	4.6*** (3.6, 5.9)	4.4*** (3.7,5.2)	2.4*** (2.0, 2.9)	2.6*** (1.7, 4.0)	4.0*** (3.2, 5.1)	1.4 (0.9, 2.2)	4.5*** (3.5, 5.8)	4.8*** (3.3, 7.0)	7.0*** (4.2, 11.7)	18.9*** (16.2,22.1)	14.6*** (12.2,17.4)		
Drug dependence (DD)	8.0*** (6.8, 9.6)	14.4*** (11.3,18.2)	11.4*** (8.5, 15.3)	5.4*** (4.0, 7.2)	11.4*** (9.4,14.0)	5.8*** (4.7, 7.2)	5.8*** (3.9, 8.6)	12.0*** (9.7, 14.8)	4.3*** (2.9, 6.4)	7.1*** (5.3, 9.6)	11.6*** (7.7, 17.6)	15.1*** (9.2, 24.6)	7.8*** (6.0, 10.1)	66.4*** (53.0,83.2)	–	

Data are shown as OR (95% CI)

The disorders with hierarchy in this table were generalised anxiety disorder, intermittent explosive disorder, binge eating disorder, bulimia nervosa, alcohol abuse and drug abuse

*** $p<0.001$

Table 5

Multivariable associations (ORs) between DSM-IV mental disorders and the subsequent diagnosis of diabetes[a]

Disorder	OR (95% C.I.)	*p* value
Major depressive episode/dysthymia	1.3 (1.1, 1.5)	0.002
Bipolar disorder (broad)	1.2 (0.8, 1.6)	0.392
Panic disorder	1.2 (0.9, 1.7)	0.174
Generalised anxiety disorder	1.0 (0.8, 1.3)	0.971
Social phobia	1.1 (0.8, 1.3)	0.714
Specific phobia	1.2 (1.0, 1.4)	0.104
Agoraphobia without panic	1.1 (0.8, 1.7)	0.532
Post-traumatic stress disorder	1.1 (0.8, 1.6)	0.445
Obsessive–compulsive disorder	1.1 (0.6, 2.1)	0.785
Intermittent explosive disorder	1.6 (1.1, 2.1)	0.007
Binge eating disorder	2.6 (1.7, 4.0)	<0.001
Bulimia nervosa	2.1 (1.3, 3.4)	0.003
Alcohol abuse	1.0 (0.8, 1.4)	0.760
Alcohol dependence with abuse	1.1 (0.8, 1.6)	0.583
Drug abuse	1.2 (0.8, 1.8)	0.294
Drug dependence with abuse	1.5 (0.9, 2.5)	0.167

[a]The model was estimated with dummy variables for all mental disorders entered simultaneously, including adjustment for age cohorts, sex, person-year and country