Associations between DSM-IV mental disorders and subsequent self-reported diagnosis of cancer

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Abstract

Objective—The associations between mental disorders and cancer remain unclear. It is also unknown whether any associations vary according to life stage or gender. This paper examines these research questions using data from the World Mental Health Survey Initiative.

Methods—The World Health Organization Composite International Diagnostic Interview retrospectively assessed the lifetime prevalence of 16 DSM-IV mental disorders in face-to-face household population surveys in nineteen countries (n = 52,095). Cancer was indicated by self-report of diagnosis. Smoking was assessed in questions about current and past tobacco use. Survival analyses estimated associations between first onset of mental disorders and subsequently reported cancer.

Results—After adjustment for comorbidity, panic disorder, specific phobia and alcohol abuse were associated with a subsequently self-reported diagnosis of cancer. There was an association between number of mental disorders and the likelihood of reporting a cancer diagnosis following the onset of the mental disorder. This suggests that the associations between mental disorders and cancer risk may be generalised, rather than specific to a particular disorder. Depression is more strongly associated with self-reported cancers diagnosed early in life and in women. PTSD is also associated with cancers diagnosed early in life.

Conclusion—This study reports the magnitude of the associations between mental disorders and a self-reported diagnosis of cancer and provides information about the relevance of comorbidity, gender and the impact at different stages of life. The findings point to a link between the two conditions and lend support to arguments for early identification and treatment of mental disorders.

Keywords

Cancer; Psychiatry; Mental disorder; Epidemiology

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Conflict of interest
The authors have no competing interests to report.

Introduction

The high prevalence of treatable mental disorders and their relatively early age of onset [1] means that any possible associations between mental disorders and cancer may merit investigation. There are several mechanisms through which mental disorder may facilitate the occurrence of cancer. The physical sequelae of stress and the symptoms of mental disorder are associated with physiological changes which can promote cancer [2]. Mental disorders are associated with poor health behaviours which increase cancer risk [3]. In addition, mental disorders may impact upon screening uptake and subsequent intervention [4].

Population studies of stress, mental disorders and subsequent cancer have yielded conflicting results. Some studies have demonstrated that stress and anxiety disorders are related [5–7]. Other studies suggest that people with diagnosed mental disorders are no more likely than the general population to have a diagnosis of cancer [5,8,9]. However, these studies focus on clinical populations and exclude people who have not received a formal psychiatric diagnosis. Additionally, in these studies mental disorders are treated as a single category, despite varying characteristics and levels of severity.

The aims of this study were to examine the association of first onset of a range of mental disorders with subsequent onset of cancer, with and without adjustment for mental disorder comorbidity using the World Mental Health (WMH) surveys dataset. Second, to assess whether an increasing number of mental disorders are associated with an increased likelihood of reporting cancer. Third, to assess whether associations vary by gender, or across the life course. These variables were examined in relation to the time of the onset of the mental disorder and the reported time of the cancer diagnosis.

Method

Samples and procedures

This study uses data from 19 World Mental Health (WMH) surveys (see Table 1). A stratified multi-stage clustered area probability sampling strategy was used to select adult respondents (18 years+) in most countries. Most of the surveys were based on nationally representative household samples whilst Colombia, Mexico and Shenzhen were based on nationally representative household samples in urbanised areas. Interviews were undertaken face-to-face by trained lay interviewers.

Internal subsampling was used to reduce burden and interview time by dividing the interview into two parts. All respondents completed Part 1 which included the core diagnostic assessment of common mental disorders. All Part 1 respondents who met the lifetime criteria for any mental disorder and a probability sample of other respondents were administered Part 2 which assessed physical conditions and other risk factors. Part 2 respondents were weighted by the inverse of their probability of selection for Part 2 adjusted for differential sampling. These analyses are based on the weighted Part 2 subsample (n = 52,095). Additional weights adjusted for differential probabilities of selection within

households, non-response, and to match population sociodemographic distributions. Quality control procedures are described in detail elsewhere [10,11]. All respondents provided informed consent and protocols were approved by the Institutional Review Boards in each country [11].

Measures

The WMH survey version of the WHO Composite International Diagnostic Interview (now CIDI 3.0) assessed lifetime history of mental disorders using the criteria of the DSM-IV. The mental disorders adjusted for in this paper include *anxiety disorders* (panic disorder, agoraphobia without panic, specific phobia, social phobia, post-traumatic stress disorder, generalised anxiety disorder, obsessive compulsive disorder); *mood disorders* (major depressive disorder/dysthymia, bipolar disorders I, II and broad); *substance use disorders* (alcohol abuse and dependence, drug abuse and dependence); and *impulse control disorders* (intermittent explosive disorder, bulimia nervosa and binge eating disorder). CIDI organic exclusion rules were applied. Clinical reappraisal studies indicate that lifetime diagnoses based on the CIDI have good concordance with diagnoses based on blinded clinical interviews [12].

Cancer status: In questions adapted from the U.S. 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….Cancer?” If respondents endorsed this item they were classified as having a history of cancer. Respondents were also asked how old they were when they were first diagnosed with cancer. This is referred to as the age of onset of cancer, although it is recognised that malignancy may develop over a period of time.

Statistical analysis

Discrete-time survival analyses [13] were used to test sequential associations between first onset of mental disorders and self-reported subsequent cancer. For these analyses a data set was created in which each year in the life of each respondent (up to and including the age of onset of cancer or their age at interview, whichever came first) was treated as a separate observational record. Year of reported cancer onset was coded 1 and earlier years coded 0. People who reported cancer onset before age 21 were excluded from analysis. Mental disorders 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 mental disorders ensured that in cases where the first onset of a mental disorder and cancer occurred in the same year, the mental disorder would not count as an independent variable predicting the reported cancer. Only person-years up to cancer diagnosis were analysed so that only mental disorder episodes occurring before the onset of cancer were included. Logistic regression was used, with the survival coefficients presented as odds ratios. The odds ratios indicated the relative odds of cancer onset in a given year for a person with a prior history of mental disorder compared to people without mental disorders.

A series of bivariate and multivariate models was developed including the independent variable, mental disorder, plus control variables. Models control for person-years, countries,

gender, current age, and in the multivariate models, other mental disorders. Bivariate models investigated associations of specific mental disorders with self-reported subsequent cancer. The next model, a multivariate model, estimated the associations of each mental disorder with reported cancer onset adjusting for mental disorder comorbidity (other mental disorders occurring at any stage prior to cancer onset). A second multivariate model included a series of independent variables for number of mental disorders (e.g., one such variable for respondents who experienced exactly one mental disorder and another for respondents who experienced two), as well as the control variables. Other more complex non-additive multivariate models were also run, for example including both type and number of mental disorders, but these did not provide a better fit for the data, so the simpler models are reported here (model fitting statistics available on request).

Our general approach was to not control for covariates that may be associated with both mental disorders and cancer. However, these variables may also confound associations so we re-estimated the multivariate model with adjustment for history of smoking (ever/never) and educational attainment. This made virtually no difference to associations (all previously significant associations remained significant and none reduced in magnitude, data available on request) so we report the results from the model unadjusted for smoking and education here.

We examined life course variation in two ways. First, we examined whether early versus late onset mental disorders differed significantly in their associations with self-reported cancer through creation of mental disorder-specific dummy variables for early onset mental disorder (< =21 years) and late onset disorder (>21 years) (see table footnotes for model specification). Second, we assessed whether associations varied by the time in the life course when cancer was diagnosed by including cross-product terms between person-years (coded as a continuous variable) and each type of mental disorder in the multivariate type model. Gender differences were examined by including cross-product terms between gender and each mental disorder in the multivariate 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. All analyses for this paper were therefore run on the pooled cross-national dataset. As the WMH data are clustered and weighted, the design-based Taylor series linearisation [13] implemented in version 10 of SUDAAN [14] was used to estimate standard errors and evaluate statistical significance.

Results

Descriptive characteristics

Characteristics of the contributing surveys and prevalence of cancer are shown in Table 1. A total of 1499 respondents reported a diagnosis of cancer.

Type and number of mental disorders as predictors of cancer diagnosis

The first column of Table 2 shows the results from bivariate models in which each mental disorder was modelled as a separate predictor of subsequent cancer, without taking mental

disorder comorbidity into account. In these models all mood disorders, panic disorder, specific phobia, PTSD, OCD, IED, binge eating disorder, alcohol abuse, alcohol dependence and drug dependence were associated with self-reported cancer. Odds ratios ranged from 1.3 to 2.2. The next column shows the results from a multivariate model adjusting for mental disorder comorbidity. This reduced the magnitude of associations but panic disorder, specific phobia and alcohol abuse remained significantly associated with self-reported cancer with ORs ranging from 1.3 to 1.5. This demonstrates the importance of comorbidity in increasing cancer risk. The global chi square value for the joint effect of all mental disorders was significant ($X^2 = 61.7$, $P < =.05$). The test for variation in the multivariate ORs approaches significance ($X^2 = 21.6$) this means that we cannot exclude the possibility that the associations between mental disorders and a self-reported diagnosis of cancer are generalised rather than specific. The ORs for PTSD and OCD are also close to significance.

The final columns of Table 2 show the association between number of mental disorders and self-reported cancer diagnosis, regardless of type of mental disorder. The odds of self-reported cancer increase from 1.3 to 1.6 from one to three disorders. The OR of 1.3 for four disorders is not significant. Finally, having five or more lifetime disorders is associated with the highest OR for self-reported cancer (2.3). The global chi square value for the joint effect of all mental disorders was significant ($X^2 = 36.6$, $P < =.05$). This again demonstrates that self reported cancer may be associated with having more than one mental disorder. This model provided a better explanation for the data than either the multivariate model or a more complex model including information about number and type (model fitting results available on request).

Timing of mental disorder onset (early versus late onset)

Table 3 presents the models examining whether mental disorders with first onset prior to age 21 were more strongly associated with a self-reported cancer diagnosis than later onset disorders. For depression, phobia, PTSD, IED, binge eating disorder, alcohol abuse, alcohol dependence, drug abuse and drug dependence with abuse early onset disorders had quantitatively larger associations with a self-reported cancer diagnosis compared to the late onset mental disorders. For panic disorder, OCD, bulimia nervosa and alcohol abuse late onset had a larger association with self-reported cancer. The magnitude of difference was significant only for depression; the OR of subsequently reporting cancer diagnosis following early onset depression was 1.7 compared with 1.2 for late onset depression. This finding may reveal an association between depression and self-reported cancer that was not apparent in Table 2, that is: depression is associated with cancer earlier in life. In the multivariate models that took other mental disorders into account, there was no association between the time of onset of disorder and self-reported cancer. The apparent effect of timing of mental disorder onset in the bivariate models is therefore due to early onset disorders being markers of comorbidity.

Variation over the life-course (timing of cancer diagnosis)

We next investigated whether associations between mental disorders and self-reported subsequent cancer diagnosis varied depending on whether the cancer was diagnosed at an early age or later in life. Table 4 shows the predictor mental disorders which demonstrated

statistically significant interactions with person-year in multivariate models. These were: depression/dysthymia, specific phobia, PTSD and drug dependence with abuse. We then stratified the person year dataset by quartiles of the timing of the reported cancer diagnosis distribution and examined the multivariate associations between each mental disorder and self-reported cancer in each of these person year subsets (Table 4). The significant interactions indicate that the effect of mental disorders varied by time of life and the stratified analyses illustrate the pattern that variation takes. For depression/dysthymia, specific phobia, PTSD and drug dependence, associations were stronger with cancer diagnosed earlier in life. This explains why associations between PTSD and self-reported cancer were not shown in the multivariate model in Table 2 as this analysis included cancer diagnosed throughout the lifetime.

Gender differences

The association between depression and self-reported cancer diagnosis was significantly stronger for women (interaction OR of 1.5; 95% CI: 1.0–2.4) (Table 5).

Again, it is important to note that the non-significant association between self-reported cancer and mental disorder in Table 2 applies only to males.

Discussion

This study has a number of limitations. The data on mental disorders is based on retrospective recall of symptoms and, for mental disorders, this is associated with underestimates and errors in estimating onset [15]. The data on cancer is also based on recall and self report rather than clinical data. The validity of self reported cancer diagnosis and the accuracy of timing of onset data may also be questioned; however data on the accuracy of self reported cancer demonstrate acceptable levels of validity [16,17]. Depression has not been found to bias the self-reporting of physical disorders [18,19]. It remains possible that the associations reported here are affected by the misclassification of either mental disorder or cancer. Due to the low prevalence of individual cancer types we have combined all forms of cancer (except non-melanoma skin cancers). This means that cancers with behavioural risk factors are combined with those with alternative aetiologies and any differences in the associations with mental disorders between these two categories are therefore not detectable. Finally, the associations between mental disorder and subsequent cancer are based on analysis of a population which only includes those who had survived and were well enough to participate. Many of those most affected are therefore missing due to illness and premature mortality. There is evidence that people with a mental disorder have a higher cancer mortality rate [6,20,21]. The associations reported here are therefore likely to be under-estimations.

This is the first epidemiological examination reporting an association between DSM mental disorders and self-reported subsequent cancer. The results conflict with earlier findings that people with mental disorders are no more likely to develop cancer [5,9]. However these are studies of clinical populations rather than general populations and this is an important distinction. People who have an undiagnosed mental disorder may have a higher risk of reporting cancer and they may have poorer lifestyle behaviours. Panic disorder, specific

phobia and alcohol abuse are associated with reporting cancer in this study, however the magnitude of the associations is reduced following adjustment for comorbidity, and the risk of reporting cancer rises if a person has more mental disorders. This leads us to conclude that the associations between mental disorders and cancer risk may be associated with features common to a range of disorders, rather than specific to a particular disorder. This finding supports the hypothesis that the stress associated with having a mental disorder increases cancer risk thus supporting findings that stress is related to cancer [5–7].

Stressful events are associated with mental disorders and having a mental disorder is itself stressful [22,23]. Anxiety disorders are accompanied by hypothalamic–pituitary–adrenal (HPA) activation which can impact upon immunological responses, thereby increasing cancer risk. Alterations in HPA functioning associated with the hyper-arousal in PTSD may explain this disorder's link with early cancers [24,25]. In this study both depression and anxiety were associated with cancer and this is difficult to explain in terms of HPA dysregulation given that these disorders are associated with opposing HPA responses [26] this suggests that anxiety–depression comorbidity is associated with a variant of HPA dysregulation [24]. Additionally, whilst adjustment for smoking and education level had no impact in this study, other behavioural risk factors, such as poor diet and lack of exercise, are associated with both stress and cancer [3]. Heavy consumption of alcohol is associated with certain cancer types [27] and stress [3]; this may explain the association between alcohol abuse and reported cancer. Finally, stress may impact upon screening and interventions; however this is likely to account for a small minority of these cancers.

Depression is more strongly associated with cancer among women than men and depression is also more strongly associated with early self-reported cancer. There is also evidence that tricyclic anti-depressants are associated with a higher risk of breast cancer [28,29]; however the effect may be removed when confounders are considered [30]. Finally, it is important to note that non-causal factors such as environmental exposure, diet, heredity and childhood adversities may also explain the associations between cancers and mental disorders and these were not considered in this study.

This is the first study to examine the associations between mental disorders and a self-reported subsequent diagnosis of cancer worldwide. The study reveals the magnitude of these associations and provides important information about the relevance of comorbidity and associations between mental disorders and cancers at different life stages. The study also reveals an association between depression and self-reported cancer for women. Further research is required to determine whether the associations are causal. Nonetheless, the associations between anxiety disorders, comorbid disorders and increasing risk for people with higher numbers of mental disorders point to the existence of a link between the two types of conditions and add further weight to arguments for the need to identify and treat mental disorders as early as possible.

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Table 1

Characteristics of WMH samples and percent (and number) with a self-reported history of cancer

Country	Field dates	Age range	Sample size		Response rate (%)	History of self-reported cancer diagnosis	
			Part 1	Part 2 sub-sample		Number unweighted (N)	Weighted (%)
Americas							
Colombia	2003	18–65	4426	2381	87.7	27	1.0
Mexico	2001–2	18–65	5782	2362	76.6	7	0.2
United States	2002–3	18+	9282	5692	70.9	361	6.9
Peru	2005–6	18–65	3930	1801	90.2	9	0.7
Asia and South Pacific							
Japan	2002–6	20+	4129	1682	55.1	57	2.9
PRC Shenzhen	2006–7	18+	7132	2475	80.0	6	0.2
New Zealand	2003–4	18+	12,790	7312	73.3	367	6.0
Europe							
Belgium	2001–2	18+	2419	1043	50.6	38	3.4
France	2001–2	18+	2894	1436	45.9	50	4.2
Germany	2002–3	18+	3555	1323	57.8	54	3.6
Italy	2001–2	18+	4712	1779	71.3	45	2.4
The Netherlands	2002–3	18+	2372	1094	56.4	47	3.6
Spain	2001–2	18+	5473	2121	78.6	40	1.0
Northern Ireland	2004–7	18+	4340	1986	68.4	43	2.5
Portugal	2008–9	18+	3849	2060	57.3	72	2.7
Romania	2005–6	18+	2357	2357	70.9	26	0.9
Poland	2010–11	18–64	10,081	4000	50.4	68	1.4
Middle East							
Israel	2002–4	21+	4859	4859	72.6	172	3.3
Iraq	2006–7	18+	4332	4332	95.2	10	0.3
Weighted average response rate (%)				78.0			
Total sample size			98,714	52,095		1499	

Table 2

Bivariate and multivariate associations (odds ratios) between DSM-IV mental disorders and the subsequent self-reported diagnosis of cancer

	Bivariate models[a]		Multivariate type model[b]		Multivariate number model[c]	
	OR	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
I. Mood disorders						
Major depressive episode/dysthymia	1.3*	(1.1–1.6)	1.2	(1.0–1.4)	–	–
Bipolar disorder (broad)	1.6*	(1.1–2.4)	1.1	(0.7–1.8)	–	–
II. Anxiety disorders						
Panic disorder	1.8*	(1.4–2.5)	1.5*	(1.1–2.0)	–	–
Generalised anxiety disorder	1.2	(0.9–1.5)	0.9	(0.7–1.2)	–	–
Social phobia	1.2	(1.0–1.5)	0.9	(0.7–1.2)	–	–
Specific phobia	1.4*	(1.2–1.7)	1.3*	(1.1–1.5)	–	–
Agoraphobia without panic	1.4	(0.9–2.3)	1.1	(0.7–1.8)	–	–
Post-traumatic stress disorder	1.5*	(1.2–1.9)	1.3	(1.0–1.6)	–	–
Obsessive compulsive disorder	2.2*	(1.2–3.8)	1.7	(1.0–3.0)	–	–
III. Impulse-control disorders						
Intermittent explosive disorder	1.6*	(1.1–2.3)	1.3	(0.9–1.9)	–	–
Binge eating disorder	1.9*	(1.0–3.4)	1.5	(0.8–2.7)	–	–
Bulimia nervosa	1.8	(1.0–3.4)	1.2	(0.6–2.4)	–	–
IV. Substance disorders						
Alcohol abuse	1.6*	(1.3–2.1)	1.5*	(1.1–2.1)	–	–
Alcohol dependence with abuse	1.5*	(1.1–2.1)	0.8	(0.5–1.3)	–	–
Drug abuse	1.5	(1.0–2.3)	0.9	(0.5–1.6)	–	–
Drug dependence with abuse	2.0*	(1.1–3.6)	1.3	(0.7–2.7)	–	–
Joint effect of all types of disorders, c^2_{16}				61.7*		
Difference between types of disorders, c^2_{15}				21.6		
V. Number of disorder						

	Bivariate models[a]		Multivariate type model[b]		Multivariate number model[c]	
	OR	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Exactly 1 disorder	–	–	–	–	1.3*	(1.1–1.6)
Exactly 2 disorders	–	–	–	–	1.4*	(1.1–1.8)
Exactly 3 disorders	–	–	–	–	1.6*	(1.2–2.2)
Exactly 4 disorders	–	–	–	–	1.3	(0.9–1.8)
5+ disorders	–	–	–	–	2.3*	(1.6–3.3)
Joint effect of number of disorders, C_5^2						36.6*

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

[a]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.

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

[c]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

Associations (odds ratios) between early vs. late mental disorder onset and the subsequent self-reported diagnosis of cancer

	Bivariate models[a]				Multivariate model[b]			
	Early	Late	Test of the difference between early and late		Early	Late	Test of the difference between early and late	
	OR (95% CI)	OR (95% CI)	c_1^2	[*P*]	OR (95% CI)	OR (95% CI)	c_1^2	[*P*]
I. Mood disorders								
Major depressive episode/dysthymia	1.7* (1.3–2.2)	1.2 (1.0–1.5)	4.2*	[.041]	1.4* (1.1–1.9)	1.1 (0.9–1.4)	2.2	[.139]
Bipolar disorder (broad)	1.7 (0.9–3.0)	1.6 (0.9–2.7)	0.0	[.890]	1.1 (0.6–2.1)	1.2 (0.7–2.1)	0.0	[.903]
II. Anxiety disorders								
Panic disorder	1.5 (0.9–2.6)	2.0* (1.4–3.0)	0.8	[.379]	1.1 (0.7–1.9)	1.7* (1.2–2.5)	1.6	[.210]
Generalised anxiety disorder	1.4 (1.0–2.0)	1.1 (0.8–1.5)	0.8	[.381]	0.9 (0.6–1.4)	0.9 (0.6–1.3)	0.0	[.852]
Social phobia	1.1 (0.9–1.4)	1.6 (0.8–3.3)	0.9	[.344]	0.9 (0.7–1.1)	1.3 (0.6–2.7)	1.2	[.280]
Specific phobia	1.5* (1.2–1.7)	1.2 (0.6–2.6)	0.2	[.633]	1.3* (1.1–1.5)	1.1 (0.5–2.3)	0.2	[.634]
Agoraphobia without panic disorder	1.6 (0.9–2.8)	1.1 (0.5–2.6)	0.4	[.523]	1.2 (0.7–2.3)	0.9 (0.4–2.2)	0.3	[.590]
Post-traumatic stress disorder	1.8* (1.3–2.6)	1.3 (0.9–1.9)	2.3	[.133]	1.4* (1.0–2.0)	1.1 (0.8–1.6)	1.3	[.253]
Obsessive compulsive disorder	1.8 (0.9–3.7)	3.0* (1.4–6.2)	1.1	[.291]	1.4 (0.7–3.0)	2.1 (1.0–4.4)	0.6	[.423]
III. Impulse-control disorders								
Intermittent explosive disorder	1.7* (1.1–2.5)	1.3 (0.5–2.9)	0.4	[.550]	1.3 (0.9–2.0)	1.0 (0.5–2.4)	0.2	[.622]
Binge eating disorder	2.3* (1.0–5.3)	1.5 (0.6–3.7)	0.5	[.471]	2.0 (0.8–4.7)	1.2 (0.5–2.8)	0.6	[.422]
Bulimia nervosa	1.3 (0.5–3.3)	2.6* (1.1–6.3)	1.0	[.310]	0.9 (0.4–2.4)	2.0 (0.8–5.0)	1.3	[.254]
IV. Substance disorders								
Alcohol abuse	1.5* (1.1–2.0)	1.7* (1.3–2.4)	0.7	[.411]	1.3 (0.9–1.9)	1.7* (1.2–2.4)	1.1	[.301]
Alcohol dependence with abuse	1.5 (0.9–2.4)	1.5 (0.9–2.5)	0.0	[.947]	0.8 (0.4–1.6)	0.9 (0.5–1.5)	0.0	[.916]
Drug abuse	1.7* (1.1–2.7)	1.3 (0.6–2.5)	0.6	[.452]	0.9 (0.5–1.6)	0.9 (0.4–2.1)	0.0	[.888]
Drug dependence with abuse	3.0* (1.6–5.7)	0.8 (0.3–2.9)	3.5	[.060]	2.1* (1.0–4.4)	0.6 (0.2–2.2)	3.3	[.069]
V. Joint effect of all early onset disorders, c_{16}^2					50.5*			

	Bivariate models[a]				Multivariate model[b]			
	Early	Late	Test of the difference between early and late		Early	Late	Test of the difference between early and late	
	OR (95% CI)	OR (95% CI)	c_1^2	[*P*]	OR (95% CI)	OR (95% CI)	c_1^2	[*P*]
VI. Joint effect of all late onset disorders, c_{16}^2						39.3 *		
VII. Joint effect of early onset disorders independent of joint effect of any disorders, c_{16}^2							20.3	

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

[a]Models include dummy variables for early onset mental disorders (=first onset <21 years of age) and for late onset disorders, plus control variables (age-cohort, person years, gender and country). A second bivariate model was estimated to test the significance of the difference between early and late onset disorders. This model included the dummy variables for the early onset disorder and the dummy variable for the disorder itself (i.e., having it at all), plus controls.

[b]Multivariate models paralleled the bivariate models in design but included dummy variables for all mental disorders entered simultaneously.

Table 4

Variations in associations between mental disorders and self-reported cancer by life course timing of cancer onset (diagnosis)

Type of mental disorders	Mental disorder* person-year interaction[a]			Stratified models[b]			
				Up to age 44	Age 45–56	Age 57–66	Age 67+
	OR (95% CI)	c_1^2	[*P*]	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Major depressive episode/dysthymia	0.98*(0.97–0.99)	22.3*	[.000]	1.6*(1.2–2.1)	1.1 (0.8–1.5)	0.9 (0.6–1.3)	1.0 (0.6–1.7)
Specific phobia	0.98*(0.98–0.99)	12.9*	[.000]	1.6*(1.2–2.1)	1.1 (0.8–1.6)	1.1 (0.6–2.0)	0.7 (0.3–1.3)
Post-traumatic stress disorder	0.97*(0.96–0.99)	16.4*	[.000]	1.5*(1.0–2.1)	1.3 (0.8–2.0)	1.2 (0.6–2.6)	0.6 (0.2–1.3)
Drug dependence with abuse	0.95*(0.92–0.99)	7.4*	[.006]	1.5 (0.7–3.2)	0.2 (0.0–1.8)	0.0*(0.0–0.0)	0.0*(0.0–0.1)

*OR significant at the 0.05 level, 2-sided test.

[a]A series of multivariate models was estimated. For example, the model for depression included the dummy variables 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.

[b]The multivariate model was estimated in the four person-year datasets corresponding to quartiles of the cancer onset distribution.

Table 5

Interactions between type of mental disorder and gender in predicting the subsequent self-reported diagnosis of cancer

	Cancer[a]			
	OR	**(95% CI)**	**Equ**	**[*P*]**
I. Mood disorders				
Major depressive episode/dysthymia	1.5*	(1.0–2.4)	3.9*	[.049]
Bipolar disorder (broad)	1.1	(0.4–2.9)	0.0	[.875]
II. Anxiety disorders				
Panic disorder	1.3	(0.6–2.7)	0.6	[.455]
Generalised anxiety disorder	0.8	(0.4–1.3)	1.1	[.303]
Social phobia	1.3	(0.8–2.2)	1.4	[.236]
Specific phobia	1.0	(0.6–1.5)	0.0	[.880]
Agoraphobia without panic	0.6	(0.2–1.7)	1.0	[.323]
Post-traumatic stress disorder	0.8	(0.4–1.6)	0.4	[.535]
Obsessive compulsive disorder	1.5	(0.3–6.4)	0.3	[.592]
III. Impulse-control disorders				
Intermittent explosive disorder	0.9	(0.4–2.0)	0.0	[.856]
Binge eating disorder	1.7	(0.3–9.8)	0.4	[.538]
Bulimia nervosa	1.4	(0.1–16.0)	0.1	[.780]
IV. Substance disorders				
Alcohol abuse	1.5	(0.8–2.8)	1.3	[.261]
Alcohol dependence with abuse	0.6	(0.3–1.3)	1.7	[.193]
Drug abuse	1.6	(0.6–4.5)	0.7	[.393]
Drug dependence with abuse	0.7	(0.2–2.5)	0.4	[.527]

*Significant at the 0.05 level, two tailed test.

[a]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, controlling for person-years, age-cohorts and country.