

between lifetime asthma and specific mental disorders and between lifetime asthma and mental disorder groups (any depressive disorder, any anxiety disorder or any alcohol use disorder) were calculated in each survey with at least 25 respondents who reported to have asthma. The ORs were calculated in logistic regression equations that adjusted for age and sex. Associations were not further adjusted for socioeconomic status, as some research suggests that socioeconomic status may be part of the background vulnerability giving rise to asthma–mental disorder comorbidity [16]. For countries in which the cross-classification of mental disorder and asthma status was null, the OR was not calculated. Ninety-five percent confidence intervals for prevalence estimates and ORs were estimated using the Taylor series method [26] with SUDAAN software [27] to adjust for clustering and weighting. Pooled estimates of mental disorder prevalence rates were not reported due to significant variations in the prevalence rates of mental disorders across surveys.

Using meta-analytical methods to summarize results across surveys, pooled estimates of ORs describing the association of each mental disorder and mental disorder groups with asthma across surveys were developed. The pooled estimate of ORs was weighted by the inverse of the variance of the estimate for each survey with a reported OR. The confidence intervals for the pooled estimates of ORs were estimated using methods described by DerSimonian and Laird [28]. For each association of a specific mental

disorder with asthma, we assessed whether the heterogeneity of OR estimates across surveys was greater than expected by chance [28], using a conservative  $\alpha$  value of  $<.05$ .

Funnel graphs plot the OR for each survey on a log scale ( $y$ -axis) against the precision of the estimate of each OR ( $x$ -axis). Precision is the reciprocal of the standard error of the OR estimate. The “funnel” in these graphs shows the 95% confidence intervals (95% CIs) around the pooled estimate of the OR at varying levels of precision. Each survey’s estimate was plotted on the funnel graph, showing whether it falls within the 95% CI of the pooled estimate given the estimated precision of the individual survey estimate. Less precise estimates are located to the left (where the funnel is wider); more precise estimates are located to the right (where the funnel is narrower). These graphs provide a visual summary both of the overall (pooled) relationship between asthma and depressive disorders, anxiety disorders and alcohol use disorders and of the extent to which individual country estimates cluster around the pooled estimate.

### 3. Results

#### 3.1. Sample characteristics

The proportion of the sample aged  $\geq 60$  years was higher in developed countries than in developing countries, and the percentage with  $\geq 12$  years of education was also generally higher in developed countries (Table 1). The sample size

Table 1  
Sample characteristics and asthma prevalence

Country	Part 1 sample ( $n$ )	Part 2 subsample ( $n$ )	Mean age <sup>a</sup>	Aged $\geq$ 60 years (%)	Female (%)	$\geq$ Secondary education (%)	Asthma prevalence <sup>b</sup>	
							$n$	Weighted prevalence (%)
<b>Americas</b>								
Colombia	4426	2381	36.6	5.3	54.5	46.4	93	3.0
Mexico	5782	2362	35.2	5.2	52.3	31.4	63	2.2
United States	9282	5692	45.0	21.2	53.0	83.2	751	11.6
<b>Asia and South Pacific</b>								
Japan	2436	887	51.4	34.9	53.7	70.0	57	5.4
Beijing, PRC	2633	914	39.8	15.6	47.5	61.4	37	2.3
Shanghai, PRC	2568	714	42.9	18.7	48.1	46.8	28	5.1
New Zealand	12992	7312	44.6	20.7	52.2	60.4	1357	17.2
<b>Europe</b>								
Belgium	2419	1043	46.9	27.3	51.7	69.7	61	5.8
France	2894	1436	46.3	26.5	52.2	NA	111	7.5
Germany	3555	1323	48.2	30.6	51.7	96.4	63	4.5
Italy	4712	1779	47.7	29.2	52.0	39.5	86	4.6
The Netherlands	2372	1094	45.0	22.7	50.9	69.7	102	8.5
Spain	5473	2121	45.5	25.5	51.4	41.7	130	5.7
Ukraine	4725	1720	46.1	27.3	55.1	79.5	54	1.8
<b>Middle East and Africa</b>								
Lebanon	2857	602	40.3	15.3	48.1	40.5	9	1.2
Nigeria	6752	2143	35.8	9.7	51.0	35.6	17	0.6
Israel	4859	4859	44.4	20.3	51.9	78.3	353	7.2
South Africa	4315	4315	37.1	8.8	53.6	38.9	256	5.8

<sup>a</sup> Age range  $\geq 18$  years, except for Colombia, Mexico (18–65 years), Japan ( $\geq 20$  years) and Israel ( $\geq 21$  years).

<sup>b</sup> Lifetime diagnosis of asthma.

Table 2  
Prevalence (%) of depressive disorders among persons with asthma versus persons without asthma, and age-adjusted and sex-adjusted odds of association

Country	Major depression			Dysthymia		
	Without asthma (%)	With asthma (%)	OR (CI) (adjusted for age and sex)	Without asthma (%)	With asthma (%)	OR (CI) (adjusted for age and sex)
Colombia	5.7	19.7	3.8 (1.8, 8.3)*	0.9	6.7	7.5 (1.6, 34.7)*
Mexico	4.1	5.0	1.2 (0.4, 3.0)	0.9	0.7	0.7 (0.1, 3.5)
United States	7.9	11.3	1.4 (1.1, 1.7)*	2.1	3.7	1.7 (1.1, 2.6)*
Japan	2.2	2.8	1.2 (0.3, 4.3)	0.8	0.6	0.9 (0.1, 7.1)
Beijing	2.3	4.0	2.5 (0.8, 8.1)	0.3	1.3	2.8 (0.3, 26.9)
Shanghai	1.7	2.2	1.4 (0.2, 7.8)	0.4	0.0	-
New Zealand	6.0	9.5	1.5 (1.2, 1.8)*	1.7	2.6	1.5 (1.0, 2.1)*
Belgium	5.5	6.5	1.2 (0.4, 3.2)	1.4	0.3	0.2 (0.0, 2.2)
France	5.8	9.3	1.5 (0.7, 3.2)	1.5	3.2	2.6 (0.7, 9.9)
Germany	2.9	5.6	2.1 (0.5, 9.4)	0.8	4.3	5.4 (0.8, 37.3)
Italy	3.0	5.9	2.2 (1.1, 4.4)*	1.0	1.6	1.6 (0.4, 5.9)
The Netherlands	5.1	7.2	1.4 (0.6, 3.5)	1.7	2.6	1.6 (0.6, 4.4)
Spain	3.8	8.8	2.7 (1.6, 4.5)*	1.3	2.7	2.5 (1.1, 6.0)*
Ukraine	9.2	25.5	2.7 (1.4, 5.2)*	3.9	16.7	3.6 (1.5, 8.6)*
Lebanon	1.8	3.8	-	0.7	0.0	-
Nigeria	1.1	8.8	-	0.2	0.0	-
Israel	5.9	8.1	1.4 (0.9, 2.1)	1.2	1.4	1.1 (0.5, 2.7)
South Africa	4.6	9.5	2.1 (1.1, 4.0)*	0.1	0.0	-
Pooled OR	-	-	1.6 (1.4, 1.8)*	-	-	1.7 (1.4, 2.1)*

OR is not listed and the percentage of those with asthma is shown as 0.0 if fewer than 25 respondents have asthma or if the cross-classification of mental disorder and asthma is null.

\*  $P < .05$ .

numbers provided in Table 1 are the numbers of respondents completing Part 2 of the interview, including the question concerning the presence of asthma. Consistent with the multicountry ECRHS [24,29], the prevalence of lifetime asthma was highest in two English-speaking developed countries: New Zealand and the United States (Table 1). Also consistent with ECRHS findings, age and sex patterns

in asthma prevalence were not consistent across countries (data not shown).

### 3.2. Depressive disorders and asthma

Prevalence estimates for major depression among persons with asthma varied from 2% to 26% across the surveys (Table 2), but generally fell in the 5–10% range. The

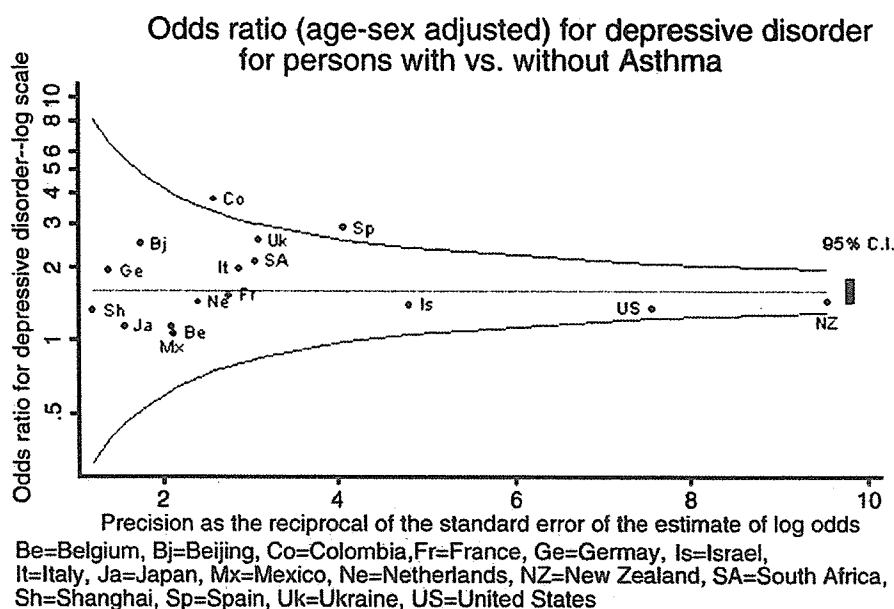


Fig. 1. Pooled OR (95% CI) of the association between any depressive disorder and asthma, with survey-specific ORs plotted as a function of the precision of the estimate.

prevalence of dysthymia among those with asthma was typically lower. Age-adjusted and sex-adjusted ORs measuring the association of major depression with asthma were significant for 7 of 16 surveys for which ORs were calculated and for 5 of 14 surveys in the case of dysthymia. Variability in OR estimates across the surveys was not found to be greater than expected by chance for either major depression ( $P=.26$ ) or dysthymia ( $P=.25$ ). Pooled ORs indicate that

both major depression (OR=1.6) and dysthymia (OR=1.7) are significantly associated with asthma.

Fig. 1 shows the funnel graph of age-adjusted and sex-adjusted ORs for depressive disorders for all surveys. The central line indicates the pooled estimate of the association between asthma and depressive disorders (OR=1.6; 95% CI=1.4, 1.8). Curved funnel lines show the 95% CI around the pooled estimate for a given level of precision. Two

Table 3  
Prevalence (%) of anxiety disorders among persons with asthma versus persons without asthma, and age-adjusted and sex-adjusted odds of association

Country	Generalized anxiety			Agoraphobia or panic disorder		
	Without asthma (%)	With asthma (%)	OR (CI) (adjusted for age and sex)	Without asthma (%)	With asthma (%)	OR (CI) (adjusted for age and sex)
Colombia	1.0	0.7	0.6 (0.1, 5.9)	2.1	4.5	2.0 (0.8, 5.2)
Mexico	0.6	0.0		1.3	1.1	0.7 (0.2, 3.4)
United States	3.7	6.7	1.7 (1.2, 2.5)*	3.5	4.7	1.3 (0.9, 1.8)
Japan	1.5	2.2	1.7 (0.4, 7.8)	0.7	0.7	0.8 (0.1, 6.7)
Beijing	1.1	3.6	2.9 (0.5, 17.2)	0.4	0.0	–
Shanghai	0.8	0.0	–	0.1	0.0	–
New Zealand	2.7	4.7	1.7 (1.2, 2.2)*	2.0	3.2	1.5 (1.0, 2.1)*
Belgium	0.9	3.5	4.0 (0.8, 19.6)	1.6	0.0	–
France	1.8	5.3	2.8 (1.0, 7.7)*	1.4	1.2	0.8 (0.1, 4.1)
Germany	0.5	0.0	–	1.0	3.2	4.1 (1.4, 12.0)*
Italy	0.5	0.0	–	1.0	0.4	0.4 (0.1, 3.3)
The Netherlands	1.1	0.6	0.6 (0.1, 3.3)	1.5	4.1	3.0 (0.7, 12.9)
Spain	0.9	2.2	2.8 (0.8, 10.0)	0.8	1.2	1.6 (0.5, 5.7)
Ukraine	2.3	3.4	1.2 (0.2, 6.1)	1.7	10.6	6.0 (2.1, 16.8)*
Lebanon	0.2	0.0	–	0.2	0.0	–
Nigeria	0.0	0.0	–	0.3	0.0	–
Israel	2.6	3.2	1.2 (0.6, 2.3)	0.9	1.5	1.7 (0.7, 4.1)
South Africa	1.7	5.1	2.7 (1.1, 6.5)*	5.1	12.5	2.6 (1.5, 4.3)*
Pooled OR	–	–	1.7 (1.4, 2.1)*	–	–	1.7 (1.4, 2.0)*

Country	Social phobia			Posttraumatic stress disorder		
	Without asthma (%)	With asthma (%)	OR (CI) (adjusted for age and sex)	Without asthma (%)	With asthma (%)	OR (CI) (adjusted for age and sex)
Colombia	2.8	3.3	1.1 (0.3, 3.6)	0.6	0.0	–
Mexico	1.9	5.7	2.9 (1.1, 7.5)*	0.5	2.1	3.6 (0.9, 15.1)
United States	6.8	7.5	1.0 (0.8, 1.3)	3.4	4.9	1.3 (0.8, 1.9)
Japan	0.5	1.9	3.8 (0.7, 22.1)	0.3	1.6	4.3 (1.0, 19.6)
Beijing	0.3	0.9	5.0 (0.8, 29.4)	0.3	0.0	–
Shanghai	0.0	0.0	–	0.1	0.0	–
New Zealand	4.9	6.0	1.1 (0.9, 1.4)	2.6	5.1	1.8 (1.3, 2.6)*
Belgium	1.1	1.1	0.9 (0.1, 6.8)	0.7	0.3	0.5 (0.1, 4.4)
France	2.4	5.6	2.1 (0.7, 6.9)	2.0	6.6	3.3 (0.9, 12.3)
Germany	1.8	1.5	1.0 (0.2, 4.5)	0.7	0.0	–
Italy	1.0	2.8	3.2 (0.5, 20.6)	0.7	1.7	2.8 (0.5, 14.5)
The Netherlands	1.2	1.8	1.4 (0.5, 4.1)	1.9	9.1	5.5 (1.5, 20.8)*
Spain	0.5	3.7	8.1 (1.8, 35.8)*	0.4	1.7	3.8 (1.2, 12.7)*
Ukraine	2.1	1.1	0.8 (0.1, 5.2)	2.6	13.0	4.1 (1.0, 17.8)
Lebanon	0.6	0.0	–	1.7	1.1	–
Nigeria	0.3	0.0	–	0.0	0.0	–
Israel	–	–	–	0.6	0.3	0.6 (0.1, 4.2)
South Africa	1.7	5.0	3.1 (1.5, 6.5)*	0.6	0.5	0.8 (0.1, 6.2)
Pooled OR	–	–	1.3 (1.1, 1.5)*	–	–	1.8 (1.4, 2.3)*

OR is not listed and the percentage of those with asthma is shown as 0.0 if fewer than 25 respondents have asthma or if the cross-classification of mental disorder and asthma is null.

\*  $P < .05$ .

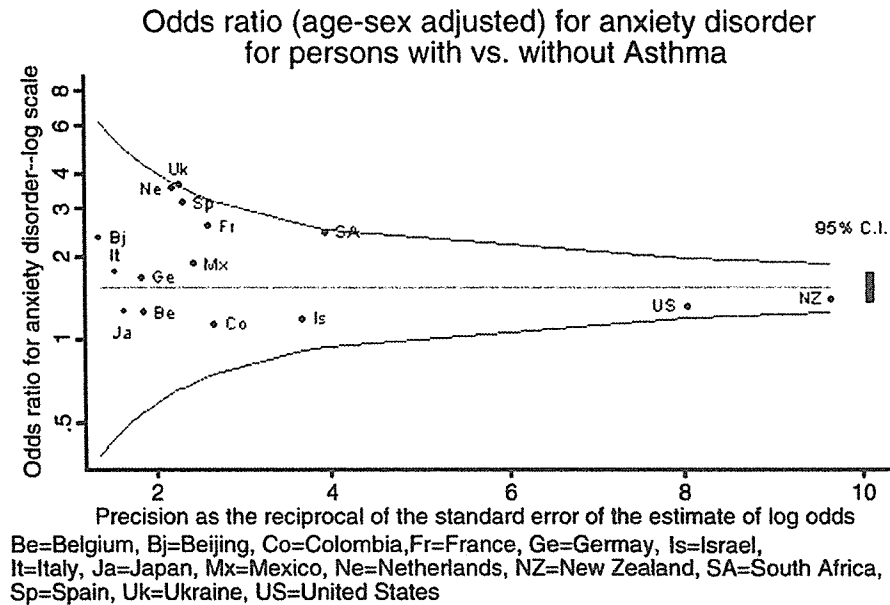


Fig. 2. Pooled OR (95% CI) of the association between any anxiety disorder and asthma, with survey-specific ORs plotted as a function of the precision of the estimate.

important observations can be made from this graph: first, that all estimates, except those for Spain and Columbia, fell within the 95% CIs of the pooled estimate; and, second, that the estimates of those countries within the funnel cluster in fairly close proximity to the pooled estimate. These observations support the conclusion that persons with lifetime asthma are more likely to experience

depressive disorders than otherwise comparable persons without lifetime asthma.

### 3.3. Anxiety disorders and asthma

The prevalences of specific anxiety disorders among people with and without asthma are reported in Table 3A and B. Because specific anxiety disorders were less

Table 4  
Prevalence (%) of alcohol use disorders among persons with asthma versus persons without asthma, and age-adjusted and sex-adjusted odds of association

Country	Alcohol abuse or dependence		
	Without asthma	With asthma	OR (CI) (adjusted for age and sex)
Colombia	2.2	12.5	8.9 (3.0, 26.5)*
Mexico	2.2	2.7	1.6 (0.3, 9.4)
United States	2.8	5.1	1.8 (1.2, 2.7)*
Japan	1.1	1.6	1.6 (0.2, 14.9)
Beijing	2.5	1.0	0.9 (0.2, 5.0)
Shanghai	0.5	0.2	0.8 (0.1, 8.0)
New Zealand	2.5	4.1	1.5 (1.0, 2.1)
Belgium	1.3	1.2	0.9 (0.1, 11.3)
France	0.8	0.5	0.6 (0.1, 5.4)
Germany	1.2	1.7	1.8 (0.2, 19.5)
Italy	0.1	0.0	–
The Netherlands	1.6	3.0	2.0 (0.4, 10.3)
Spain	0.3	1.0	2.9 (0.2, 34.6)
Ukraine	6.0	13.2	5.4 (0.6, 50.1)
Lebanon	1.1	0.0	–
Nigeria	0.7	0.0	–
Israel	1.1	1.7	1.7 (0.7, 4.0)
South Africa	4.9	5.9	1.4 (0.6, 2.9)
Pooled OR	–	–	1.7 (1.4, 2.1)*

OR is not listed and the percentage of those with asthma is shown as 0.0 if fewer than 25 respondents have asthma or if the cross-classification of mental disorder and asthma is null.

\*  $P < .05$ .

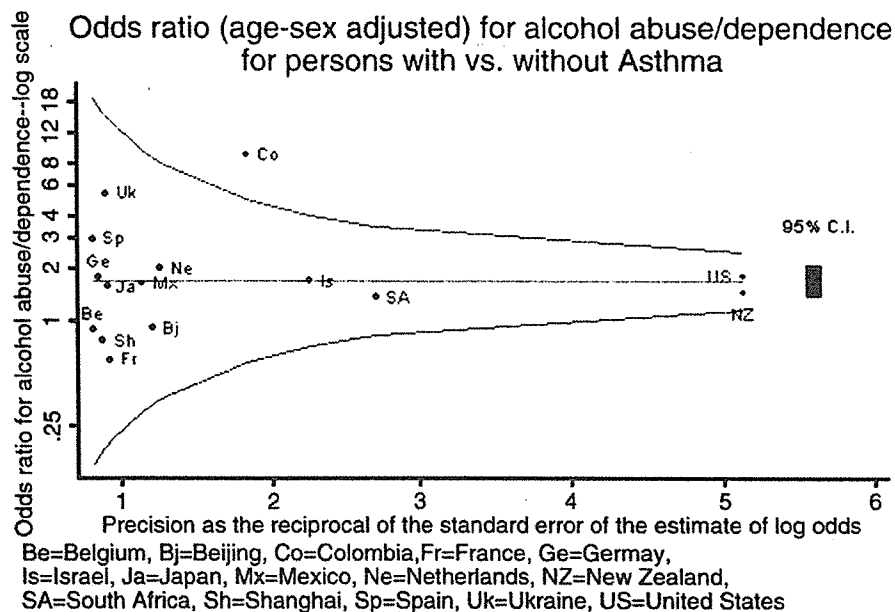


Fig. 3. Pooled OR (95% CI) of the association between any alcohol use disorder and asthma, with survey-specific ORs plotted as a function of the precision of the estimate.

common than depressive disorders, it was not possible to estimate ORs for many of the participating surveys. Given the relatively small sample sizes, it is not surprising that OR estimates were significant for some surveys but not for others, even when the confidence intervals of OR estimates included the pooled estimate. The heterogeneity test for variability among the ORs was nonsignificant for generalized anxiety disorder ( $P=.71$ ), agoraphobia/panic ( $P=.07$ ) and posttraumatic stress disorder ( $P=.14$ ), although it was significant for social phobia ( $P=.02$ ). Given the limited number of cases available in each survey, the pooled estimate of the OR provides a more precise estimate of the association of anxiety disorder with asthma. Across the four anxiety disorders, pooled ORs were all significantly greater than 1 and fell within the 1.3–1.8 range.

The association of any anxiety disorder with asthma (Fig. 2) showed a pattern similar to that observed for any depressive disorder. The pooled estimate of the OR was 1.5 (95% CI=1.4, 1.7). Among survey-specific estimates, all but one (Ukraine) fell within the 95% CI of the pooled estimate. These results indicate that the strength of the association of anxiety disorders, as a class, with asthma is comparable to that observed for depressive disorders.

#### 3.4. Alcohol use disorders and asthma

The prevalence of alcohol abuse or dependence among those with asthma was highly variable across countries (Table 4). ORs for the association of alcohol abuse or dependence with asthma were significantly greater than 1 in only 2 of 15 surveys with estimable ORs, but the estimates

were not found to be heterogeneous across surveys ( $P=.45$ ). The pooled estimate for the association of alcohol abuse or dependence and asthma was 1.7 (95% CI=1.4, 2.1), with 14 of 15 survey estimates falling within the 95% CI of the pooled estimate (Fig. 3). These results suggest that alcohol abuse or dependence tends to occur with greater frequency among persons with asthma.

#### 4. Discussion

This report provides the first cross-national population-based assessment of the association of lifetime asthma with a range of common mental disorders among adults. Although the prevalence of 12-month mental disorders and asthma varies greatly across individual surveys, the association of the two shows much less cross-national variability, with survey estimates of the association between asthma and mental disorder groups (depressive, anxiety and alcohol use) in the vast majority of countries clustering around pooled estimates. This consistency of results across surveys is notable in light of the fact that the participating surveys included countries that differ markedly in culture, language and level of socioeconomic development. Key findings are that depressive, anxiety and alcohol use disorders are all significantly, albeit modestly, associated with asthma and that the degree of association is fairly similar across mental disorder groups.

Previous research on the adult general population has been suggestive of a relationship between asthma and both anxiety and mood disorders, but in the most comprehensive population study investigating a range of *DSM-IV* disorders,

the relationship was more consistently observed for anxiety disorders than for mood disorders and was not observed at all for substance use disorders [11]. The current study replicates the finding for anxiety disorders, confirms a similar-magnitude relationship with depressive disorders and demonstrates for the first time a relationship with alcohol use disorders. The magnitude of the associations observed here is similar to those of previous population studies, with associations between asthma and the any-depressive-disorder and any-anxiety-disorder groups in this study being 1.5 and 1.6, respectively, compared with 1.5–2.1 in other population studies, which have used diagnostic measures of mental disorders [11,16,17].

A strength of this study is that the estimates are pooled across a large number of consistently conducted surveys. Individual surveys might appear to yield disparate results if examined individually, yet whether country-specific ORs are statistically significant varies largely as a function of variation in sample or cell size. More important is the fact that country-specific ORs do not typically differ significantly from each other, allowing confidence in pooled estimates, and that estimates from most individual surveys fall within the 95% CIs of the pooled estimates. This result reflects the usefulness of a meta-analytical approach when investigating the co-occurrence of mental and physical problems (where the smaller number of people with both disorders reduces power in an individual survey).

These results need to be interpreted in light of the limited assessment of asthma. There are two main aspects to this limitation. First, it is a lifetime measure, not a measure of current symptoms; second, although it is a measure of asthma diagnosis, it is self-reported diagnosis. With regard to the issue of time period (lifetime vs. current), the study by Goodwin et al. [11] found that associations between any severe mental disorder were virtually identical for lifetime severe versus current severe asthma (although only significant in the former) and were somewhat stronger for current nonsevere asthma versus lifetime nonsevere asthma. Other research by Goodwin and Eaton [15] found that panic attacks were associated with current asthma under treatment, but not with remitted asthma, which suggests that the lifetime measure used here could have resulted in somewhat attenuated estimates of the association between asthma and mental disorders. However, as noted above, the estimates obtained in this study are in line with other population studies using diagnostic measures of mental disorders. Additionally, our measure of reported diagnosis rather than symptoms means that the associations observed are not likely to be an artifact of the known relationship between symptoms of anxiety and depression and self-reports of asthma symptoms [13], since this bias is not observed with self-reported diagnoses of asthma [13,30].

With regard to the second issue relating to asthma ascertainment, it is not clear how much discrepancy there might be between self-reported diagnosis and physician-confirmed diagnosis of lifetime asthma. Goodwin et al. [11]

report the proportion of physician-confirmed lifetime asthma from among those who endorsed a screening question about current asthma, so this is not directly comparable to the current study. While acknowledging this limitation, it is reassuring to note that the estimates of asthma prevalence for the German population across the two studies are fairly comparable (with the present study being the more conservative of the two), as are the associations obtained between lifetime asthma and mental disorders.

Lastly, on the limitations of asthma ascertainment, it should be noted that there were neither measures of asthma severity nor measures of asthma medication use. The associations reported are therefore averaged across the full spectrum of asthma severity and, as such, are likely to underestimate the magnitude of the relationship between mental disorders and severe asthma.

Due to the cross-sectional nature of the surveys, the observed associations do not provide information with regard to the direction of the relationship between asthma and mental disorders. Other research suggests that, in contrast to earlier thinking on the role of psychological factors in asthma, mental disorders are probably not etiologic; atopic and immunologic factors are more probably the prime causal candidates for the development of asthma [1]. A study by Goodwin et al. [16] on a longitudinal sample of 18- to 21-year-olds in New Zealand found that the associations between asthma and mental disorders disappeared altogether when adverse childhood conditions and other unspecified correlates were controlled for, allowing the possibility that asthma and mental disorders are associated through other common factors. Adverse childhood conditions may well explain the association observed here between asthma and alcohol use disorders. It does not, however, mean that the link between asthma and mental disorders is spurious. By whatever mechanisms they come to be associated, the interplay of mental disorders with asthma may be mutually self-perpetuating. Katon et al. [31] have developed a model of the possible cognitive and behavioral mechanisms that link anxiety and depressive symptoms with asthma, each serving to maintain the other. Other research, too, confirms the important clinical consequences of the co-occurrence of depressive and anxiety disorders with asthma. Anxiety and depression have been found to influence the perception of asthma symptoms and the response to asthma symptoms [3,32], reduce treatment adherence and increase hospitalization [32–35], and reduce quality of life [9,14,32,35,36].

Given these clinical ramifications, the results of this study confirm the importance of awareness among clinicians, in whichever setting they work, of the significant overlap of asthma with mental disorders.

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## Research report

## Depression–anxiety relationships with chronic physical conditions: Results from the World Mental Health surveys<sup>☆</sup>

K.M. Scott<sup>a,\*</sup>, R. Bruffaerts<sup>b</sup>, A. Tsang<sup>c</sup>, J. Ormel<sup>d</sup>, J. Alonso<sup>e</sup>, M.C. Angermeyer<sup>f</sup>,  
C. Benjet<sup>g</sup>, E. Bromet<sup>h</sup>, G. de Girolamo<sup>i</sup>, R. de Graaf<sup>j</sup>, I. Gasquet<sup>k</sup>, O. Gureye<sup>l</sup>,  
J.M. Haro<sup>m</sup>, Y. He<sup>n</sup>, R.C. Kessler<sup>o</sup>, D. Levinson<sup>p</sup>, Z.N. Mneimneh<sup>q</sup>,  
M.A. Oakley Browne<sup>r</sup>, J. Posada-Villa<sup>s</sup>, D.J. Stein<sup>t</sup>,  
T. Takeshima<sup>u</sup>, M. Von Korff<sup>v</sup>

<sup>a</sup> Department of Psychological Medicine, Wellington School of Medicine and Health Sciences, PO Box 7343 Wellington South, New Zealand

<sup>b</sup> University Hospital Gasthuisberg, Herestraat 49, Leuven B-300, Belgium

<sup>c</sup> Hong Kong Mood Disorders Centre, The Chinese University of Hong Kong, Shatin, Hong Kong, China

<sup>d</sup> Department of Psychiatry, University Medical Center Groningen, PO Box 30001, 9700RB Groningen, The Netherlands

<sup>e</sup> Health Services Research Unit, Institut Municipal d'Investigació Mèdica (IMIM), Doctor Aiguader, 80, Barcelona 08003, Spain

<sup>f</sup> Department of Psychiatry, University of Leipzig, Johannisallee 20, 04317 Leipzig, Germany

<sup>g</sup> National Institute of Psychiatry, Calzada Mexico Xochimilco, No 101, Col. San Lorenzo Huipulco, Tlalpan, Mexico City, DF 14370, Mexico

<sup>h</sup> Department of Psychiatry, SUNY Stony Brook, Punam Hall-South Campus, Stony Brook, NY 11794 8790, United States

<sup>i</sup> Department of Mental Health, AUSL di Bologna, Viale Pepoli 5, Bologna 40123, Italy

<sup>j</sup> Trimbos Institute, Da Costakade 45, Utrecht 3521VS, The Netherlands

<sup>k</sup> U669, INSERM, Paris, France-75679; AP-HP, Villejuif, 94804, France

<sup>l</sup> Department of Psychiatry, University College Hospital, Ibadan PMB 5116, Nigeria

<sup>m</sup> Sant Joan de Deu-SSM, Dr. Antoni Pujades, 42, Sant Boi de Llobregat, Barcelona 08830, Spain

<sup>n</sup> Shanghai Mental Health Center, 600 Wan Ping Nan Lu, Shanghai 200030, China

<sup>o</sup> Department of Health Care Policy, Harvard Medical School, 180 Longwood Avenue, Boston, MA 02115, United States

<sup>p</sup> Ministry of Health, Mental Health Services, 2 Ben Tabai St, Jerusalem 91010, Israel

<sup>q</sup> IDRAAC, 166227 Achrafieh, Beirut 1100 2110, Lebanon

<sup>r</sup> Department of Rural and Indigenous Health, School of Rural Health, P.O. Box 973, Moe Victoria 3825, Australia

<sup>s</sup> Development Rehabilitation System FSC, Saldurriaga Concha Foundation, Cra 11 No. 94–02 of. 5–02, Bogotá 57, Colombia

<sup>t</sup> Department of Psychiatry and Mental Health, J-Block Groote Schuur Hospital Observatory, 07505 Cape Town, South Africa

<sup>u</sup> Mental Health Administration, National Institute of Mental Health, NCNP, 4-1-1 Ogawahigashi-machi Kodaira-shi, Tokyo 187–8502, Japan

<sup>v</sup> Group Health Cooperative, Centre for Health Studies, 1730 Minor Ave, Suite 1600, Seattle, WA 98101, United States

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### Abstract

**Background:** Prior research on the association between affective disorders and physical conditions has been carried out in developed countries, usually in clinical populations, on a limited range of mental disorders and physical conditions, and has seldom taken into account the comorbidity between depressive and anxiety disorders.

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\* Corresponding author. Tel.: +64 4 3855999x6584; fax: +64 4 3895725.

E-mail address: kate.scott@otago.ac.nz (K.M. Scott).

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**Methods:** Eighteen general population surveys were carried out among adults in 17 countries as part of the World Mental Health Surveys initiative ( $N=42,249$ ). DSM-IV depressive and anxiety disorders were assessed using face-to-face interviews with the Composite International Diagnostic Interview (CIDI 3.0). Chronic physical conditions were ascertained via a standard checklist. The relationship between mental disorders and physical conditions was assessed by considering depressive and anxiety disorders independently (depression without anxiety; anxiety without depression) and conjointly (depression plus anxiety).

**Results:** All physical conditions were significantly associated with depressive and/or anxiety disorders but there was variation in the strength of association (ORs 1.2–4.5). Non-comorbid depressive and anxiety disorders were associated in equal degree with physical conditions. Comorbid depressive–anxiety disorder was more strongly associated with several physical conditions than were single mental disorders.

**Limitations:** Physical conditions were ascertained via self report, though for a number of conditions this was self-report of diagnosis by a physician.

**Conclusions:** Given the prevalence and clinical consequences of the co-occurrence of mental and physical disorders, attention to their comorbidity should remain a clinical and research priority.

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**Keywords:** Anxiety; Depression; Cross-sectional; Chronic conditions

## 1. Introduction

It is now well established that there is significant comorbidity (co-occurrence) of mental disorders, particularly mood disorders, with chronic physical conditions (Wells et al., 1989a,b; Dew, 1998; Katon and Ciechanowski, 2002; Harter et al., 2003; McWilliams et al., 2003; Buist-Bouwman et al., 2005; Simon et al., 2006; Ortega et al., 2006). These associations have considerable individual and public health significance in their impact on role impairment (Sullivan et al., 1997; Kessler et al., 2003), treatment costs and adherence (Simon et al., 1995; Ciechanowski et al., 2000) and premature mortality risk (Harris and Barraclough, 1998; van Melle et al., 2004; Zhang et al., 2005). However, prior research on the strength of the association between mental disorders and physical conditions has been limited by a preponderance of clinical relative to general population studies, a restricted range of mental or physical conditions explored and an absence of information from developing countries.

There is a further limitation to the earlier research on this topic. Anxiety and depressive disorders often co-occur. Population surveys have found that about half those with a current mood disorder also have a comorbid anxiety disorder (Kessler et al., 1996; Scott et al., 2006). Since prior research has not usually taken this depression–anxiety comorbidity into account, it is not known whether the association of anxiety disorders with chronic physical conditions might be due to comorbid mood disorder, or conversely, whether the association of mood disorders with chronic physical conditions might be due to comorbid anxiety disorder. Additionally, comorbid depression–anxiety is believed to be a more severe and chronic form of psychological disorder than

non-comorbid depressive or anxiety disorders (Angst, 1997), so it is of interest to determine if comorbid depressive–anxiety disorder is associated with increased risks of chronic physical conditions. Lastly, since prior research has typically studied single or small numbers of chronic physical conditions, it is not clear whether there are substantial differences in mental–physical comorbidity patterns across different chronic physical conditions.

This paper addresses these issues by using data from 18 surveys participating in the World Mental Health Surveys to investigate the association of 10 chronic physical conditions with depressive and anxiety disorders, taking the comorbidity between depressive and anxiety disorders into account. The objectives of this paper are: 1) to determine whether non-comorbid depressive disorder and/or non-comorbid anxiety disorder are associated with specific physical conditions; 2) to determine whether comorbid depressive–anxiety disorder is more strongly associated than is non-comorbid depressive or anxiety disorder with physical conditions; and 3) to contrast the strength of association of different chronic physical conditions with depressive and anxiety disorders.

## 2. Methods

The methods employed in the World Mental Health surveys relevant to this report have been described in detail in prior reports (Kessler et al., 2004). Here we provide a brief overview of the key methodologic features.

### 2.1. Samples

Eighteen surveys were carried out in 17 countries in the Americas (Colombia, Mexico, United States), Europe (Belgium, France, Germany, Italy, Netherlands,

Spain, Ukraine), the Middle East (Israel, Lebanon), Africa (Nigeria, South Africa), Asia (Japan, People's Republic of China: Beijing, Shanghai), and New Zealand. An effort was made to recruit as many countries as possible in the initiative. The final set of countries was determined by availability of collaborators in the country who were able to obtain funding for the survey. All surveys were based on multi-stage, clustered area probability household samples. All interviews were carried out face-to-face by trained lay interviewers. The combined total sample size was 85,052. Survey response rate varied, with a weighted average response rate across surveys of 71%.

Internal sub-sampling was used to reduce respondent burden by dividing the interview into two parts. Part 1 included the core diagnostic assessment of mental disorders. Part 2 included additional information relevant to a wide range of survey aims, including assessment of chronic physical conditions. All respondents completed Part 1. All Part-1 respondents who met criteria for any mental disorder and a probability sample of other respondents were administered Part 2. 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 article were based on the weighted Part-2 sample ( $N=42,249$ ). Additional weights were used to adjust for differential probabilities of selection within households and to match the samples to population socio-demographic distributions.

## 2.2. Training and field procedures

The central World Mental Health (WMH) staff trained bilingual supervisors in each country. Consistent interviewer training documents and standardized translation protocols were used across surveys. The institutional review board of the organization that coordinated the survey in each country approved and monitored compliance with procedures for obtaining informed consent and protecting human subjects.

## 2.3. Mental disorder status

All surveys assessed mental disorders with the World Mental Health version of the WHO Composite International Diagnostic Interview (WMH-CIDI, now CIDI 3.0) (Kessler and Ustun, 2004), a fully structured diagnostic interview. Disorders considered in this paper include 12-month anxiety disorders (generalized anxiety disorder, panic disorder and/or agoraphobia, posttraumatic stress disorder, and/or social phobia) and 12-month depressive

disorders (dysthymia and/or major depressive disorder). Disorders were assessed using the definitions and criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* (APA, 1994). CIDI organic exclusion rules were imposed in making all diagnoses. Methodological evidence collected in the WHO-CIDI Field Trials and later clinical calibration studies showed that all the disorders considered herein were assessed with acceptable reliability and validity in the WMH-CIDI (Kessler et al., 2004).

## 2.4. Mental disorder comorbidity status

The analyses in this paper consider persons in three mutually exclusive groups, those with: 1) a depressive disorder in the absence of comorbid anxiety disorder; 2) an anxiety disorder in the absence of comorbid depressive disorder; and 3) comorbid depressive and anxiety disorder.

## 2.5. Chronic physical conditions

Physical conditions were assessed with a standard chronic disorder checklist, of the kind commonly used in national health surveys (NCHS, 1994). For the conditions reported here respondents were asked if they had ever had arthritis, chronic back or neck problems, frequent or severe headaches (referred to here as 'chronic headaches'), other chronic pain, stroke, heart attack, or whether they had ever been told by a doctor they had heart disease, high blood pressure, asthma, diabetes or ulcer. The category 'multiple pains' includes two or more of arthritis, chronic back or neck problems, chronic headaches, or other chronic pain. Prior research has demonstrated reasonable correspondence between self-reported chronic conditions such as diabetes, heart disease and asthma, and general practitioner records (Kriegsman et al., 1996). Obesity was defined as a body mass index (BMI) of 30 kg/m<sup>2</sup> or greater. Height and weight were self-reported.

## 2.6. Analytic methods

Analyses were run for all ten physical conditions on a country-by-country basis (data available on request). Odds ratios for the association of the three mental disorder groups with each of the physical conditions were estimated for each survey adjusting for age and sex. Associations were not further adjusted for socioeconomic status as this may be part of the vulnerability for mental–physical comorbidity and the purpose of this paper was descriptive rather than explanatory. Countries

were included in a particular analysis if they had at least 25 respondents with the physical condition. Some countries did not collect obesity data. Ninety-five percent confidence intervals for the odds ratios were estimated using the Taylor Series method (Wolter, 1985) with SUDAAN software (SUDAAN, 2002) to adjust for clustering and weighting.

Using meta-analytic methods to summarise results across surveys, pooled estimates of the odds ratios were developed describing the association of each of the mental disorder groups with the specific physical condition across surveys. The pooled estimate of the odds ratio was weighted by the inverse of the variance of the estimate for each survey (DerSimonian and Laird, 1986). Tests were carried out to assess whether heterogeneity among the country-specific odds of association between each of the mental disorder status groups and a given physical condition was greater than that expected by chance (DerSimonian and Laird, 1986), using a conservative alpha value of  $p < 0.05$ .

Table 1  
Sample characteristics

Country	Part-2 subsample (N)	Mean age <sup>a</sup>	% (60 years or older)	% (women)	Education (secondary or greater)
<i>Americas</i>					
Colombia	2381	36.6	5.3	54.5	46.4
Mexico	2362	35.2	5.2	52.3	31.4
United States	5692	45.0	21.2	53.0	83.2
<i>Asia and South Pacific</i>					
Japan	887	51.4	34.9	53.7	70.0
PRC	914	39.8	15.6	47.5	61.4
Beijing					
PRC	714	42.9	18.7	48.1	46.8
Shanghai					
New Zealand	7312	44.6	20.7	52.2	60.4
<i>Europe</i>					
Belgium	1043	46.9	27.3	51.7	69.7
France	1436	46.3	26.5	52.2	NA
Germany	1323	48.2	30.6	51.7	96.4
Italy	1779	47.7	29.2	52.0	39.5
Netherlands	1094	45.0	22.7	50.9	69.7
Spain	2121	45.5	25.5	51.4	41.7
Ukraine	1720	46.1	27.3	55.1	79.5
<i>Middle East and Africa</i>					
Lebanon	602	40.3	15.3	48.1	40.5
Nigeria	2143	35.8	9.7	51.0	35.6
Israel	4859	44.4	20.3	51.9	78.3
South Africa	4315	37.1	8.8	53.6	38.9

<sup>a</sup> Age range  $\geq 18$ , except for Colombia, Mexico (18–65), Japan ( $\geq 20$ ) and Israel ( $\geq 21$ ).

Table 2

Association of mental disorders with chronic physical conditions-- odds ratios pooled across 17 countries, adjusted for age and sex (95% confidence intervals)

Type of physical condition	Type of mental disorder		
	Non-comorbid depressive disorder	Non-comorbid anxiety disorder	Comorbid depression-anxiety
Obesity	1.1 (0.9, 1.2)	1.2 (1.1, 1.4)*	1.2 (1.0, 1.4)*
Diabetes	1.3 (1.1, 1.6)*	1.3 (1.1, 1.5)*	1.4 (1.1, 1.8)*
Asthma	1.7 (1.4, 2.0)*	1.6 (1.4, 1.8)*	1.6 (1.4, 1.9)*
Hypertension	1.5 (1.4, 1.8)*	1.7 (1.5, 1.9)*	1.8 (1.5, 2.1)*
Arthritis	1.6 (1.4, 1.8)*	1.7 (1.5, 1.9)*	2.5 (2.2, 2.9)*
Ulcer	1.8 (1.6, 2.2)*	1.9 (1.7, 2.3)*	2.7 (2.3, 3.2)*
Heart disease	2.0 (1.7, 2.3)*	1.9 (1.6, 2.3)*	2.8 (2.3, 3.4)*
Back/neck problems	2.2 (1.9, 2.4)*	2.0 (1.8, 2.3)*	2.9 (2.5, 3.3)*
Chronic Headache	2.5 (2.2, 2.8)*	2.3 (2.1, 2.5)*	4.0 (3.5, 4.7)*
Multiple pains	2.5 (2.2, 2.9)*	2.3 (2.1, 2.6)*	4.5 (4.0, 5.1)*

Reference group: persons with neither a depressive nor an anxiety disorder.

\*  $p < 0.05$ .

The first set of analyses (shown in Table 2) determined the association of physical conditions with non-comorbid depressive or anxiety disorder and with comorbid depressive-anxiety disorder, where the reference group was those with neither a depressive nor an anxiety disorder. The second set of analyses (shown in Table 3) determined the association of physical conditions with comorbid depressive-anxiety disorder, and also with no mental disorder, where the reference group was persons with a non-comorbid depressive or anxiety disorder. This second set of analyses established whether the association between physical conditions and comorbid depressive-anxiety disorder was significantly greater than the association between physical conditions and non-comorbid depressive or anxiety disorder.

### 3. Results

Information on sample characteristics is provided in Table 1. The sample size numbers refer to the Part-2 subsample that completed the section of the interview containing the physical condition checklist. The proportion of the sample that was age 60 or greater was higher in the developed countries than the developing countries, and the percent with 12 or more years of education was also generally higher in the developed countries.

The majority of heterogeneity tests assessing whether the variability in odds ratio estimates across surveys was

greater than chance were non-significant (data available on request). Where they were significant this was due to obviously outlying estimates from one or two countries with very small numbers with the comorbid conditions. Such extreme estimates do not make a significant contribution to the pooled estimate as this is weighted by the inverse of the variance of the estimate for each survey. The pooled results across countries for the association between the mental disorder groups (non-comorbid depression or anxiety and comorbid depressive–anxiety disorder) and the ten physical conditions are presented in Table 2.

Considerable variability in the strength of association between specific physical conditions and mental disorders is apparent. The chronic pain conditions (back/neck problems, chronic headache and multiple pains) show the strongest associations with depressive and anxiety disorders. Non-comorbid depressive and anxiety disorders are remarkably similar to each other in their strength of association with the ten physical conditions examined. They are both independently related to each physical disorder, with the one exception that non-comorbid depressive disorder was not significantly associated with obesity. For the physical conditions with generally weaker associations with mental disorder (e.g., obesity, diabetes, asthma), the association with comorbid depressive–anxiety disorder is roughly equal to the strength of association of the physical condition with non-comorbid depression or anxiety. For those physical conditions with stronger overall relationships with mental disorder (e.g., chronic

pain conditions, ulcer, heart disease), their relationship with comorbid depressive–anxiety disorder appears stronger than with depression or anxiety alone, though the formal test for that is presented in Table 3.

The results in Table 3 confirm that for six of the ten physical conditions (arthritis, ulcer, heart disease, back/neck problems, chronic headache and multiple pains), their association with comorbid depressive–anxiety disorder is significantly stronger than with depression or anxiety alone. This table also confirms that having neither a depressive nor an anxiety disorder is protective in terms of the likelihood of experiencing any of the ten physical conditions, relative to those with a single mental disorder.

#### 4. Discussion

Despite great diversity in demographic, socioeconomic and health patterns among the 17 countries surveyed, the pooled cross-national results consistently showed that depressive and anxiety disorders were independently and comparably related to a wide range of chronic physical conditions. Comorbid depressive–anxiety disorder was more strongly associated with several physical conditions than was non-comorbid depression and anxiety. There was considerable variability between physical conditions in their strength of association with mental disorders. The findings observed here that heart disease and the chronic pain conditions, among the physical conditions studied, showed the strongest associations with depressive and anxiety disorders is consistent with research highlighting the robust links between these physical conditions and major depressive disorder (Evans et al., 2005). The particular contributions of this report are two-fold. First, it confirms that both anxiety and depressive disorders are independently associated with chronic physical conditions: comorbidity research has often focused on one (Harter et al., 2003) or the other (Evans et al., 2005). Second, this research produces the novel finding that having both depression and anxiety further increases the risk of a number of physical conditions co-occurring.

A limitation of this study is that physical conditions were ascertained by a standard checklist, rather than physician's examination. A distinction may be drawn between those conditions which were ascertained via self-report of symptoms (the pain conditions) and those ascertained via self-report of a physician's diagnosis (asthma, heart disease, high blood pressure, diabetes, ulcer). Self-report of chronic pain conditions has reasonable validity given that these are largely self-defined. For the other conditions, while acknowledging the limitation of self-report, methods research indicates

Table 3

Association of no depressive or anxiety disorder, and of comorbid depressive anxiety disorder, with physical conditions— odds ratios pooled across 17 countries, adjusted for age and sex (95% confidence intervals)

Type of physical condition	Type of mental disorder	
	Neither depression nor anxiety	Both depression and anxiety
Obesity	0.9 (0.8, 1.0) *	1.0 (0.8, 1.2)
Diabetes	0.8 (0.7, 0.9) *	1.1 (0.9, 1.4)
Asthma	0.6 (0.5, 0.7) *	1.1 (0.9, 1.4)
Hypertension	0.6 (0.6, 0.7) *	1.0 (0.9, 1.2)
Arthritis	0.6 (0.6, 0.7) *	1.6 (1.3, 1.8) *
Ulcer	0.5 (0.5, 0.6) *	1.4 (1.1, 1.7) *
Heart disease	0.5 (0.5, 0.6) *	1.5 (1.2, 1.8) *
Back/neck problems	0.5 (0.4, 0.5) *	1.4 (1.2, 1.6) *
Chronic headache	0.4 (0.4, 0.5) *	1.7 (1.5, 2.0) *
Multiple pains	0.4 (0.4, 0.4) *	1.9 (1.6, 2.1) *

Reference group: persons with non-comorbid depressive or anxiety disorder.

\*  $p < 0.05$ .

that self-report of diagnosis generally shows good agreement with medical records data (Kehoe et al., 1994; NCHS, 1994; Kriegsman et al., 1996), and importantly, the presence of depressive or anxiety symptoms has not been found to bias or inflate the self-report of diagnosed physical conditions (Kolk et al., 2002). A further limitation is that there were no measures of the severity of the chronic conditions. The associations reported are therefore averaged across the full spectrum of physical condition severity.

A strength of this study is that the estimates are pooled across a large number of consistently conducted surveys. For a given physical condition, whether or not the country-specific odds ratios were statistically significant varied (data available on request), largely as a function of variation in sample or cell size. But the heterogeneity tests indicated that the majority of the country-specific odds ratios did not differ significantly from each other, allowing confidence in the pooled estimates. This reflects the usefulness of a meta-analytical approach when investigating the co-occurrence of mental and physical problems (where the smaller number of people with both disorders reduces power in an individual survey).

The cross-sectional nature of this study limits conclusions about the direction or causal nature of the relationships between mental disorder and physical conditions. Other research suggests that for many of the physical conditions studied here the relationship with mental disorder may be bi-directional, involving a combination of biological and psychosocial mechanisms (Cohen and Rodriguez, 1995; Dew, 1998; Kiecolt-Glaser et al., 2002). However, with regard to our finding that the association between mental disorder and many physical conditions is strengthened in the presence of both anxiety and depression relative to either alone, the following observation may be made. This finding seems more comprehensible within a framework of mental disorder leading to physical condition (whereby the odds of a physical condition are increased with the experience of more mental disorders), than within a framework of physical condition leading to mental disorder (which would imply that a physical condition is more likely to result in both depression and anxiety than either alone). Another possible interpretation is that the combination of factors (both internal and external to the individual) that is conducive to the experience of multiple mental disorders is also conducive to the occurrence of a number of physical conditions. Further research is required to test these possibilities.

What is clear is that mental–physical comorbidity is clinically consequential; it has been shown to complicate treatment, alter disease course, contribute to disability and

increase mortality risks (Harris and Barraclough, 1998; Cassano and Fava, 2002; Evans et al., 2005). From this clinical standpoint, the concurrent presentation of mental with physical disorder may be the critical issue, rather than the question of which disorder came first. However, many countries manage the delivery of mental health services separately from that of general medical services, which is not optimal for the adequate recognition and treatment of mental–physical comorbidity (Kathol and Clarke, 2005). Even where depressive and anxiety disorders are predominantly treated within general practice settings, they are typically under-detected there (Ormel et al., 1991; Cassano and Fava, 2002). Moreover, while many primary care clinicians may be aware of the associations between depression and physical conditions, they may be less aware of the connections observed in this study between anxiety disorders and physical conditions, despite the greater prevalence of anxiety disorders relative to depressive disorders (Demyttenaere et al. 2004). Given the increasing prevalence of chronic conditions (Popkin, 1998) and possibly also of anxiety and depressive disorders (Kessler et al., 2005), improved understanding of the determinants, consequences and management of their comorbidity remains a research priority.

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