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12-Month comorbidity patterns and associated factors in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project

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Objective: Comorbidity patterns of 12-month mood, anxiety and alcohol disorders and socio-demographic factors associated with comorbidity were studied among the general population of six European countries.
Method: Data were derived from the European Study of the Epidemiology of Mental Disorders (ESEMeD), a cross-sectional psychiatric epidemiological study in a representative sample of adults aged 18 years or older in Belgium, France, Germany, Italy, the Netherlands and Spain. The diagnostic instrument used was the Composite International Diagnostic Interview (WMH-CIDI). Data are based on 21 425 completed interviews.
Results: In general, high associations were found within the separate anxiety disorders and between mood and anxiety disorders. Lowest comorbidity associations were found for specific phobia and alcohol abuse—the disorders with the least functional disabilities. Comorbidity patterns were consistent cross-nationally. Associated factors for comorbidity of mood and anxiety disorders were female gender, younger age, lower educational level, higher degree of urbanicity, not living with a partner and unemployment. Only younger people were at greater risk for comorbidity of alcohol disorder with mood, anxiety disorders or both.
Conclusion: High levels of comorbidity are found in the general population. Comorbidity is more common in specific groups. To reduce psychiatric burden, early intervention in populations with a primary disorder is important to prevent comorbidity.

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Key words: comorbidity; mental disorders; associated factors

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Introduction

Since the adoption of classification systems for psychiatric disorders in the early 1980s, research on the co-occurrence of psychiatric disorders ('comorbidity') has proliferated (1). The explicit diagnostic criteria defined by these systems has made it possible to study comorbidity in a systematic way.

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Comorbidity is not only substantial in clinical samples, but also in the general population. For example, the National Comorbidity Study in the USA found that 56% of all adults aged 15–54 years with a lifetime history of at least one DSM-III-R disorder had also experienced other mental disorders (2, 3). Comorbidity is related to increased severity (4–7), longer duration of the disorder (3, 8) and greater functional disability (4, 9, 10), and increases the use of healthcare services (3, 11). Comorbid disorders have different risk-factor profiles compared with pure disorders (12, 13).

In view of the consequences of psychiatric comorbidity, it is important to promote prevention and treatment in the general population and provide information about the probability of mental disorders co-occurring and the associated factors of comorbidity.

This study is based the European Study of the Epidemiology of Mental Disorders/Mental Health Disability: a European Assessment in year 2000 (ESEMeD/MHEDEA 2000), here after referred to as the ESEMeD project, a population survey carried out in six European countries and is part of the WHO World Mental Health (WMH) Survey Initiative (14).

Aims of the study

The aim of this paper is to present data on comorbidity of 12-month mood, anxiety and alcohol disorders, with a focus on the proportion of individuals with a mental disorder who also had at least one other disorder, the patterns of associations between the different types of mental disorders, the prevalence of pure and comorbid disorders, and the socio-demographic factors associated with pure and comorbid disorders. Patterns of comorbidity can differ dramatically by gender (15), therefore most results will be stratified by gender.

Material and methods

Sample

The study was cross-sectional in nature and individuals were assessed in person at their homes using computer-assisted interview (CAPI) techniques. The target population is the non-institutionalized adult population aged 18 years or older of Belgium, France, Germany, Italy, the Netherlands and Spain—a total of 212 000 000 Europeans. A stratified, multistage, clustered area, probability sample design was used. A description of the methods, the sampling frame and selection, and the participants is provided in another paper in this supplement (16).

The diagnostic instrument was a new version of the Composite International Diagnostic Interview, the WMH-CIDI, which was developed and adapted by the Coordinating Committee of the WHO World Mental Health (WMH) Survey Initiative. In total, 21 425 respondents between January 2001 and August 2003 provided data for the project. The overall response rate in the six countries investigated was 61.2%, with the highest rates in Spain (78.6%) and Italy (71.2%), and the lowest rates in Germany (57.8%), Belgium (50.6%), France (45.9%) and the Netherlands (56.4%). Estimated prevalences were weighted to account for the known probability of selection as well as to restore the distribution of the population within each country. In addition, overall estimates were weighted to restore the relative dimension of the population across countries (e.g. German totals represented the highest share, followed by French and Italian, with Belgium representing the least, proportional to the total adult population in each country).

12-month comorbidity associations

Data presented here are limited to 12-month mood, anxiety and alcohol disorders. The proportion of individuals diagnosed according to DSM-IV criteria, who had an additional mental disorder, and comorbidity associations (odds ratios [ORs]), were studied. The mental disorders included mood disorders (major depression and dysthymia), anxiety disorders (generalized anxiety disorder [GAD], social phobia, specific phobia, post-traumatic stress disorder [PTSD], agoraphobia and panic disorder), and alcohol disorders (alcohol abuse, alcohol dependence). Other disorders included in the WMH-CIDI questionnaire, such as obsessive-compulsive disorder, eating disorders, drug use, childhood disorder and psychotic disorders have not been evaluated in this issue because they were only assessed in a small subsample of respondents.

Pure and comorbid 12-month disorders and its associated factors

Associated factors for pure and comorbid disorders were assessed in the broad diagnostic groupings mood, anxiety and alcohol disorder. A pure 12-month mood disorder was defined as any mood disorder present in a specified 12-month period in a person who did not meet full criteria for any anxiety and alcohol disorder within the same period. A comorbid 12-month mood disorder was

defined as the presence of a mood disorder within the same 12-month period an individual also met full criteria for any anxiety disorder (anxiety-comorbid mood disorder), any alcohol disorder (alcohol-comorbid mood disorder), or both an anxiety and alcohol disorder. Pure anxiety and pure alcohol disorder were defined similarly. In addition to the comorbid conditions mentioned above, alcohol-comorbid anxiety disorder could also be distinguished. We confined ourselves to the main diagnostic groupings, therefore comorbidity between separate disorders within one of the groups did not influence the definitions.

In the risk-factor analyses, the dependent variables were the presence of mood, anxiety or alcohol disorder, either pure or comorbid, at any time within the 12 months prior to the interview (0 = absence; 1 = presence). The following socio-demographic variables were used as potential determinants of pure and comorbid disorders: gender, age (five categories: 18–24, 25–34, 35–49, 50–64, ≥65 years), educational attainment (four categories: 0–4, 5–8, 9–12, ≥13 years of education), urbanicity (three categories: rural, mid-sized urban, large urban), cohabitation status (two categories: living with a partner or not, irrespective of children) and employment status (two categories: paid employment or not).

Statistical analysis

The proportion of respondents in the general population with a specific 12-month mood, anxiety or alcohol disorder who also had at least one additional disorder were assessed. Cross-tabulations were used to calculate bivariate odds ratios (ORs) and 95% confidence intervals (CIs) to gauge the strength of comorbidity between pairs of 12-month mood, anxiety and alcohol disorders. The prevalence of the broad categories of 12-month pure and comorbid mood, anxiety and alcohol disorders were then assessed. Determinants of these 12-month pure and comorbid mood, anxiety and alcohol disorder were investigated by means of univariate logistic regression analysis. To test for linear trends (Cochran test), the potential determinants age, education and urbanicity were modelled as continuous variables. In all analyses, gender and country differences were assessed by means of the Chi-squared test. In the majority of analyses, results were significant if $P < 0.05$. However, because of the high number of comparisons between genders and countries for the strength of comorbidity between pairs of disorders, a stricter *P*-value was adopted using the Hochberg method.

Comorbidity was studied, therefore disorders were defined without applying DSM-IV diagnostic hierarchy rules. In order to ensure that the sample data represented the general population of interest, weights were developed and applied to adjust for the probability of selection, non-response and for undercoverage of the sampling frame (16).

Results

Socio-demographic characteristics

The characteristics of the study sample are shown in Table 1. Mean age was 47 years (95% CI 46.7–47.4), with the majority of the respondents (28%) being between 35 and 49 years old. Males represented 48% of the sample. Some 67% was married or living with a partner, 39% lived in mid-sized urban areas and 35% of the sample had been in full-time education for more than 13 years. The majority were in paid employment at the time of the interview (54%).

How often are 12-month disorders comorbid?

Table 2 shows the proportion of individuals in the general population with a mood, anxiety or alcohol disorder in the past 12 months, who also met criteria for at least one other disorder in that same period. For the three broad categories (mood, anxiety and alcohol disorders), the percentages of people who also had at least one disorder from another broad category are shown. In the case of the various separate disorders within each broad category, the percentages refer to individuals who also had at least one additional mood, anxiety or alcohol disorder.

Of all respondents with a mood disorder, 41.7% also had an anxiety or alcohol disorder. Among those with an anxiety disorder, 28.3% also had a disorder from another broad category, whereas for alcohol disorder this figure was 22.8%. Thus, mood disorder is the broad category most likely to be comorbid with another broad category.

Of the separate mood disorders, dysthymia had higher rates of comorbidity than major depression (73.3% vs. 53.1%). In general, anxiety disorders were highly comorbid. Agoraphobia (81.0%), GAD (69.4%) and panic disorder (63.8%) were the most comorbid anxiety disorders; specific phobia (28.6%) and social phobia (49.1%) were the least. Alcohol dependence was more frequently comorbid with other disorders (27.7%) than alcohol abuse (20.8%). Alcohol abuse was the least comorbid of all the separate disorders.

Table 1. Description of the ESEMeD study sample (raw numbers and weighted proportions)

	Total sample	
	$n = (21\ 425)$	%
Age (mean)	47.0	
18–24	1790	11.0
25–34	3798	18.3
35–49	6450	28.2
50–64	4986	21.9
65+	4401	20.7
Gender:		
Male	9953	48.0
Female	11 472	52.0
Education categories*:		
0–4	1153	5.1
5–8	4697	27.0
9–12	5194	32.6
13+ years	6639	35.0
Missing	68	0.3
Marital status categories:		
Married or living with someone	14 552	67.1
Previously married	2802	11.5
Never married	4071	21.5
Living arrangement:		
Not living with someone	3554	15.1
Living with someone	17 871	84.9
Geographical area:		
Rural (<10 000)	6269	33.2
Mid-size urban (10 000–100 000)	9292	38.9
Large urban (>100 000)	5864	28.0
Missing	16	0.1
Employment:		
Paid employment	11 471	54.1
Unemployed	1299	6.6
Retired	4854	23.2
Homemaker	2358	9.1
Student	516	3.1
Maternity leave	130	0.9
Illness leave	170	0.7
Disabled	454	1.5
Other	87	0.5
Don't know or refused	86	0.3
Country†		
Belgium	2419	3.8
France	2894	20.5
Germany	3555	31.5
Italy	4712	22.4
the Netherlands	2372	6.1
Spain	5473	15.6

*Education information for France and for the French speaking respondents from Belgium are not included in the overall sample description due to differences in the questionnaire items.
†Country; weighted percentages.

There were no significant country differences in these data (data not shown). Two significant gender differences were found: GAD and alcohol dependence were significantly more often comorbid in women.

Association between 12-month disorders

Table 3 shows the pairwise associations between 12-month mental disorders. Among the broad categories, the association between any mood and any anxiety disorders was higher (OR 13.4; 95% CI 11.0–16.3) than those between any mood and any alcohol disorders (OR 4.0; 95% CI 2.4–6.6) and between any anxiety and alcohol disorders (OR 3.2; 95% CI 2.0–5.0).

Table 2. Proportion of comorbid disorders among individuals with a 12-month mental disorder in six European countries in the ESEMeD project

	Total population % (95% CI)	Male % (95% CI)	Female % (95% CI)
	$n = 21\ 425$	$n = 9953$	$n = 11\ 472$
Any mood disorder	41.7 (37.5–45.9)	36.4 (28.4–44.4)	44.2 (39.2–49.1)
Any anxiety disorder	28.3 (25.1–31.5)	27.3 (21.0–33.7)	28.7 (25.0–32.4)
Any alcohol disorder	22.8 (15.3–30.2)	18.7* (11.1–26.4)	45.3 (24.4–66.1)
Major depression	53.1 (48.6–57.6)	48.8 (40.1–57.5)	55.2 (49.9–60.4)
Dysthymia	73.3 (66.4–80.2)	74.4 (62.5–86.3)	72.8 (64.2–81.3)
GAD	69.4 (60.6–78.1)	51.6* (32.4–70.8)	75.7 (66.9–84.6)
Social phobia	49.1 (40.6–57.6)	42.9 (29.0–56.9)	52.5 (42.0–63.0)
Specific phobia	28.6 (24.3–33.0)	28.2 (19.8–36.5)	28.8 (23.7–33.9)
PTSD	57.9 (48.3–67.4)	68.3 (49.3–87.2)	54.9 (44.1–65.8)
Agoraphobia	81.0 (71.2–90.9)	83.2 (62.1-104.3)	80.2 (69.2–91.2)
Panic disorder	63.8 (55.1–72.5)	60.2 (45.1–75.3)	65.6 (55.0–76.2)
Alcohol abuse	20.8 (11.9–29.7)	19.0 (9.9–28.1)	34.5 (4.2–64.8)
Alcohol dependence	27.7 (13.6–41.7)	18.0* (4.2–31.8)	58.2 (25.4–91.1)

GAD; Generalized Anxiety Disorder: PTSD; Post Traumatic Stress Disorder.
*$P < 0.05$: statistically significant overall gender difference.

For the separate disorders, major depression was highly correlated with dysthymia (OR > 99.9; 95% CI > 99.9– > 99.9). Major depression was significantly linked to all anxiety disorders, with high correlations with GAD (OR 33.7; 95% CI 23.2–49.1), PTSD (OR 20.7; 95% CI 13.8–30.9), agoraphobia (OR 25.8; 95% CI 14.8–45.0) and panic disorder (OR 29.4; 95% CI 19.9–43.4). Furthermore, major depression was associated with alcohol abuse (OR 2.6; 95% CI 1.8–3.9) and alcohol dependence (OR 6.7; 95% CI 3.1–14.3). In general, dysthymia was less correlated with other disorders than major depression; thus the data in Table 2 reporting high comorbidity of dysthymia with any other disorder, was largely due to its comorbidity with major depression. The strongest comorbidity of dysthymia with any anxiety or alcohol disorders was with agoraphobia (OR 29.4; 95% CI 14.1–61.3).

In general, anxiety disorders were strongly interrelated. GAD was highly correlated to social phobia (OR 13.5; 95% CI 7.7–23.5), PTSD (OR 15.1; 95% CI 8.1–28.3), agoraphobia (OR 25.7; 95% CI 12.9–51.0) and panic disorder (OR 20.3; 95% CI 11.4–36.0). Social phobia showed strong associations with agoraphobia (OR 21.6; 95% CI 10.5–44.5). Specific phobia was generally less correlated with other anxiety disorders, with the exception of agoraphobia (OR 24.2; 95% CI 13.9–42.3). PTSD was most strongly correlated to panic

Table 3. Associations (OR and 95% CI) between 12-month mental disorders in the general population of the European countries in the ESEMeD project

	Major depression	Dysthymia	GAD	Social phobia	Specific phobia	PTSD	Agoraphobia	Panic disorder	Alcohol abuse	Alcohol dependence
Major depression										
Dysthymia	> 99.9* (> 99.9–> 99.9)									
GAD	33.7* (23.2–49.1)	17.6 (10.4–29.7)								
Social phobia	10.2* (6.9–15.1)	5.4 (2.6–11.5)	13.5* (7.7–23.5)							
Specific phobia	6.2* (4.7–8.1)	3.5 (2.1–5.8)	6.7* (4.2–10.7)	9.7 (6.3–15.1)						
PTSD	20.7* (13.8–30.9)	18.4 (10.6–31.9)	15.1* (8.1–28.3)	9.6 (5.1–18.0)	3.5* (2.1–5.9)					
Agoraphobia	25.8* (14.8–45.0)	29.4 (14.1–61.3)	25.7* (12.9–51.0)	21.6 (10.5–44.5)	24.2* (13.9–42.3)	12.5* (5.1–30.3)				
Panic disorder	29.4* (19.9–43.4)	10.0 (5.5–18.2)	20.3* (11.4–36.0)	11.6 (5.7–23.5)	7.8* (4.7–12.9)	17.6* (8.8–34.9)	25.8 (11.5–57.9)			
Alcohol abuse	2.6* (1.8–3.9)	1.7 (0.7–4.5)	2.5* (1.3–5.1)	2.7 (1.5–4.7)	2.0* (1.3–3.2)	1.9* (1.0–3.6)	2.9 (1.2–6.6)	3.3 (1.8–5.8)		
Alcohol dependence	6.7* (3.1–14.3)	2.2 (0.6–8.3)	11.2* (3.8–32.9)	2.7 (0.6–12.3)	3.3* (1.3–8.4)	3.1* (1.0–9.5)	10.7 (3.0–38.5)	6.8 (2.2–21.1)	–	–

*Significant gender difference was found after adjusting the raw *P*-value to the number of comparisons performed by Hochberg method at $P < 0.0002$.

disorder (OR 17.6; 95% CI 8.8–34.9). The highest anxiety disorder intercorrelation was between agoraphobia and panic disorder (OR 25.8; 95% CI 11.5–57.9). All, except one, anxiety disorders were correlated with alcohol dependence, but only two anxiety disorders were correlated with alcohol abuse.

Of the alcohol disorders, alcohol abuse was only associated with panic disorder (OR 3.3; 95% CI 1.8–5.8), agoraphobia (OR 2.9; 95% CI 1.2–6.6), social phobia (OR 2.7; 95% CI 1.5–4.7), major depression (OR 2.6; 95% CI 1.8–3.9), GAD (OR 2.5; 95% CI 1.3–5.1), and specific phobia (OR 2.0; 95% CI 1.3–3.2), but with relatively low ORs. Alcohol dependence was correlated to most mood and anxiety disorders, with high associations with GAD (OR 11.2; 95% CI 3.8–32.9) and agoraphobia (OR 10.7; 95% CI 3.0–38.5).

No country differences were observed for the association between the broad categories, or for the separate disorders.

Gender differences were observed between the broad categories. Females more often reported comorbidity between mood and anxiety disorders. Men more frequently reported comorbidity between mood and alcohol disorders, whereas comorbidity between anxiety and alcohol disorders was more common in men. Many gender differences were found for the separate disorders. All associations between major depression and the anxiety and alcohol disorders were higher in men, with the exception of agoraphobia and alcohol dependence, which were higher in women. The ORs between GAD on the one hand and social phobia, specific phobia, PTSD, panic disorder, alcohol abuse and dependence on the other hand were higher in men, but the OR between GAD and agoraphobia was higher in women. Comorbidity of specific phobia with PTSD, agoraphobia and panic disorder was more common in men, whereas alcohol abuse and dependence were more common in women. The ORs of PTSD with agoraphobia and panic disorder were higher in women, whereas alcohol abuse and dependence were higher in men.

Prevalence rate of pure and comorbid 12-month disorders

Table 4 shows the prevalence of pure and comorbid 12-month broad categories of mood, anxiety and alcohol disorder in the general population. Pure anxiety disorder was the most prevalent pure disorder (4.6%). Anxiety-comorbid mood disorder was the most prevalent comorbid condition of all (1.6%). Comorbidity of mood and alcohol disorder (0.1%), of anxiety and alcohol disorder (0.1%),

Table 4. Prevalence of pure and comorbid 12-month mood, anxiety and alcohol disorder in the general population of six European countries in the ESEMeD project

	Total population % (95% CI)	Male % (95% CI)	Female % (95% CI)
	$n = 21\ 425$	$n = 9953$	$n = 11\ 472$
Pure disorders			
Mood	2.5 (2.2–2.7)	1.8* (1.4–2.1)	3.1 (2.7–3.7)
Anxiety	4.6 (4.2–4.9)	2.8* (2.3–3.2)	6.2 (5.6–6.8)
Alcohol	0.7 (0.6–0.9)	1.4* (1.1–1.7)	0.2 (0.1–0.2)
Comorbid disorders			
Mood & anxiety	1.6 (1.4–1.9)	0.8* (0.6–1.1)	2.4 (2.0–2.7)
Mood & alcohol	0.1 (0.0–0.1)	0.1* (0.0–0.2)	0.0 (0.0–0.0)
Anxiety & alcohol	0.1 (0.0–0.1)	0.1 (0.0–0.2)	0.0 (0.0–0.1)
Mood & anxiety & alcohol	0.1 (0.0–0.1)	0.1 (0.0–0.2)	0.1 (0.0–0.1)

*$P < 0.05$: statistically significant overall gender difference.

and of mood, anxiety and alcohol disorders (0.1%), was much less prevalent.

Clear country differences were found for all pure disorders. Italy and Spain showed low prevalences of pure mood, anxiety and alcohol disorders, whereas Belgium, France, Germany and the Netherlands showed higher prevalences, with the exception of a low prevalence of pure mood disorder in Germany. For the comorbid disorders, alcohol-comorbid anxiety disorder was more prevalent in Belgium and Germany, and comorbidity of all three broad categories were more prevalent in France, Germany and the Netherlands (data not shown).

Pure mood and pure anxiety disorder were significantly more prevalent in women and pure alcohol disorder more prevalent in men. Among the comorbid conditions, significant gender differences were found for anxiety-comorbid mood disorder, which was more common among women, and for alcohol-comorbid mood disorder, which was more common among men.

Predictors of pure and comorbid 12-month disorders

Table 5 shows the univariate socio-demographic risk-factor profiles of pure and comorbid 12-month mood, anxiety and alcohol disorder. Because of the low number of subjects, comorbidity of mood and alcohol disorder, of anxiety and alcohol disorder, and of mood, anxiety and alcohol disorder, were combined into one category: comorbid alcohol disorder.

Gender differences were associated with all types of disorders, with the exception of comorbid alcohol disorder. As mentioned previously, women were more likely to have pure mood, pure anxiety and anxiety-comorbid mood disorder, whereas men were more likely to have pure alcohol disorder. The gender difference was greatest for anxiety-comorbid mood disorder (OR 2.9; 95% CI 2.1–4.2) and pure alcohol disorder (OR 0.1; 95% CI 0.1–0.2). There was a trend towards a reduced risk with increasing age for pure anxiety disorder, pure alcohol disorder and comorbid alcohol disorder. Higher educational level was associated with a greater risk for pure anxiety disorder, pure alcohol disorder and a lower risk for anxiety-comorbid mood disorder. Living without a steady partner increased the risk for almost all disorders. Unemployed people were more at risk for pure mood disorder and anxiety-comorbid mood disorder. This last finding can be explained by the higher average age of unemployed people within the study.

Discussion

Key findings

Twelve-month comorbidity of disorders seemed to be substantial. High pairwise associations were found within the anxiety disorders; the highest was between agoraphobia and panic disorder. Affective and anxiety disorders were also strongly associated, with high correlations found between major depression and panic disorder and between major depression and GAD. The associations between GAD and mood disorders are relatively strong, furthermore other studies have shown that mood disorders and GAD cluster together in analyses of dimensions of diagnoses (17, 18).

Previous investigators point to the importance of comorbidity between substance use disorders and both mood and anxiety disorders ('dual diagnoses') (19). Although comorbidity of drug disorders was not assessed here, we found evidence for this for alcohol dependence, but not for alcohol abuse. The very weak association between alcohol abuse and other disorders has been found in other studies (19, 20). One explanation for this might be that the CIDI diagnosis of alcohol abuse does not necessarily reflect a form of psychopathology (21). Young men are more likely to be diagnosed with alcohol abuse (22), a behaviour more associated with a particular phase of young male adulthood and not with psychopathology.

The lowest comorbidity rates within the three broad classes of disorders were for specific phobia and alcohol abuse. These are generally considered to be the least severe anxiety and substance use disorders in terms of functional disabilities (8). Furthermore, other studies have found that, generally, the least severe disorders of each broad

Table 5. Sociodemographic associations of 12-month pure and comorbid mood, anxiety and alcohol disorder in the general population of six European countries in the ESEMeD project

Characteristic	Pure mood disorder OR (95% CI)	Pure anxiety disorder OR (95% CI)	Pure alcohol disorder OR (95% CI)	Comorbid mood & anxiety OR (95% CI)	Comorbid alcohol OR (95% CI)
Number in model	21 353	21 353	21 353	21 353	21 353
Number with diagnosis	575	926	159	358	21
Gender					
Male	1.0	1.0	1.0	1.0	1.0
Female	1.8 (1.4–2.3)	2.3 (1.9–2.8)	0.1 (0.1–0.2)	2.9 (2.1–4.2)	0.8 (0.3–2.1)
Age					
18–24 years	1.0	1.0	1.0	1.0	1.0
25–34 years	1.1 (0.8–1.5)	1.1 (0.9–1.4)	2.5 (1.6–3.9)	1.0 (0.7–1.4)	1.6 (0.5–5.4)
35–49 years	0.9 (0.7–1.2)	1.1 (0.9–1.3)	0.9 (0.6–1.4)	0.9 (0.7–1.2)	1.0 (0.3–2.9)
50–64 years	1.1 (0.8–1.4)	1.1 (0.9–1.3)	0.5 (0.3–0.8)	1.2 (0.9–1.6)	0.3 (0.1–1.1)
>65 years	0.9 (0.6–1.1)	0.5 (0.4–0.6)	0.1 (0.0–0.3)	0.5 (0.3–0.9)	0.0 (0.0–0.0)
Trend test (z, *P* -value)	0.60, 0.55	6.70, 0.00	8.02, 0.00	2.69, 0.01	3.61, 0.00
Education*					
0–4 Years	1.4 (0.9–2.0)	0.7 (0.5–1.1)	0.3 (0.0–2.1)	2.0 (1.3–3.3)	0.0 (0.0–0.0)†
5–8 Years	1.0 (0.7–1.3)	0.7 (0.5–0.8)	0.5 (0.2–0.9)†	1.0 (0.7–1.5)	0.6 (0.1–2.7)†
9–12 Years	1.0 (0.8–1.3)	1.3 (1.0–1.6)	1.0 (0.6–1.8)†	0.9 (0.6–1.3)	1.8 (0.5–6.7)†
13 Years or more	1.0	1.0	1.0	1.0	1.0
Trend test (z, *P* -value)	1.13, 0.26	–3.86, 0.00	–5.54, 0.00	2.44, 0.01	–1.67, 0.09
Urbanicity					
Rural	1.0	1.0	1.0	1.0	1.0
Mid-sized urban	1.2 (0.9–1.5)	1.0 (0.8–1.2)	1.0 (0.7–1.6)	1.1 (0.8–1.4)	1.5 (0.5–4.1)†
Large urban	1.1 (0.9–1.5)	1.1 (0.9–1.3)	1.4 (0.9–2.2)	1.1 (0.8–1.5)	0.7 (0.2–2.3)
Trend test (z, *P* -value)	–4.14, 0.00	–1.59, 0.11	–2.53, 0.01	–1.96, 0.05	–0.40, 0.69
Marital status					
Married/LWS	1.0	1.0	1.0	1.0	1.0
Unmarried/Others	1.5 (1.2–1.9)	1.0 (0.8–1.2)	1.8 (1.2–2.7)	1.7 (1.3–2.3)	4.4 (1.6–12.5)†
Employment					
Paid employed	1.0	1.0	1.0	1.0	1.0
Unemployed/Others	1.5 (1.2–1.9)	0.9 (0.7–1.0)	0.8 (0.5–1.2)	1.7 (1.3–2.3)	0.8 (0.3–2.2)

* Exclude education data from France and those from Belgium who were administered the French questionnaire. LWS; living with someone.
† Less than five observations.

category are associated with the lowest comorbidity (2, 23).

Comorbidity of mental disorders seemed consistent cross-nationally, irrespective of differences in prevalence rates of these disorders (with higher prevalence rates in northern European countries) (22). There were no significant country differences for the broad categories or the separate disorders, with regard to the proportion of disorders that were comorbid. Also, the associations between disorders did not show between-country differences.

Our findings show that comorbidity is more common in several demographic subgroups. Women had a threefold greater risk of anxiety-comorbid mood disorder than men. Other categories at risk for comorbidity between mood and anxiety disorders were younger people, people with a lower educational level, those not living with a partner and unemployed people. Only younger people were at greater risk for comorbidity of alcohol disorder with mood, anxiety disorders, or both. It should be noted that the number of cases with comorbid alcohol disorder was small, thus the likelihood of achieving statistical significance was low.

The odds ratio patterns of comorbid disorders differed from those of pure disorders. One other study, the Netherlands Mental Health Survey and Incidence Study (NEMESIS) (13), has also assessed risk-factor profiles for 12-month pure and comorbid mood, anxiety and substance use disorders. Using DSM-IV and DSM-III-R in ESEMeD and NEMESIS, respectively, the disorders measured among the respondents differed slightly. ESEMeD also included PTSD and NEMESIS included OCD, bipolar disorder and drug disorders. These differences should be borne in mind when comparing the results of both studies. In both ESEMeD and NEMESIS, gender differences were associated with all pure disorders (pure mood disorder was baseline significant in NEMESIS) and with anxiety-comorbid mood disorder, whereas in NEMESIS this association also existed for comorbid substance use disorders, with men being more likely to have this disorder.

Individuals in the NEMESIS sample were younger (18–64 years) than those in ESEMeD (>18 years). Both studies found a diminishing risk of pure alcohol or substance use disorder and all comorbid conditions with increasing age; ESEMeD also found this pattern for pure anxiety disorder. A trend toward a reduced risk for pure anxiety and anxiety-comorbid mood disorder with higher levels of education was found in NEMESIS, whereas in ESEMeD this trend was reversed for pure anxiety disorder. This might be explained by differences in the measurement of educational level: ESEMeD measured number of years in education, whereas NEMESIS asked for type of highest educational level. In NEMESIS and ESEMeD, people not living with a steady partner had a greater probability for all pure disorders (except for pure anxiety disorder) and of anxiety-comorbid-mood disorder than people who did cohabit. In both studies, unemployment was associated with a greater risk of anxiety-comorbid-mood disorder.

Strengths and limitations

The ESEMeD/MHEDEA project is the largest and most comprehensive population-based epidemiological study conducted in Europe to date. It is the first study to assess comorbidity patterns and prevalence of comorbid 12-month mental disorders and their associated factors across the general population of several different countries in a single continental region, using the same diagnostic instrument. The use of fully structured computer-assisted diagnostic interviews to standardize data collection procedures and employment of rigorous quality control procedures have provided a robust database.

When interpreting the results of this study, one should be aware of its limitations. Diagnoses were made using fully structured computer-assisted diagnostic interviews administered by lay interviewers. CIDI diagnoses have shown acceptable reliability and validity (24–28), but have shown some variance with diagnoses made by clinicians.

Second, the data were based on retrospective recall. Although there can be considerable recall bias in recording lifetime disorders (29), this is less likely for the 12-month disorders dealt with here.

Third, we do not know whether non-responders differ from responders in having a pure or comorbid disorder. If people with comorbid disorders refuse participation more often than people with pure or no disorders (30, 31), the reported proportion of disorders that were comorbid, the prevalence of comorbid disorders and the associations between disorders are underestimated. Particular groups (homeless individuals, people not sufficiently fluent in the national language(s) and long-term institutionalized patients) have not been sampled in the ESEMeD/MHEDEA project. It might be that the comorbidity patterns in these groups diverge from the individuals described here. However, because such groups are relatively small, we believe that their exclusion does not alter the general pattern.

A fourth limitation is that our predictors of pure and comorbid disorders were recorded at baseline, whereas the onset of the disorders could have occurred long before that. Thus, because of the cross-sectional nature of the data, the direction of causality cannot be assessed.

Implications

Although clinical trials often focus on pure disorders, this is not typical of the real world where comorbid disorders are more prevalent. In particular disorders with high functional disability are more often comorbid. This finding has major implications for assessment and treatment. To achieve full remission, treatment may need to be designed for each of the concomitant disorders (32).

The importance of primary prevention of secondary disorders has been emphasized (32–34). Pure disorders are usually mild in severity and introduce the interesting notion that prevention of serious mental disorders is, to some extent, the same as prevention of comorbidity. This means that early intervention of pure disorders (e.g. simple phobia, alcohol abuse, dysthymia) to prevent progression to more serious disorders in the class and comorbidity might be a useful strategy. To do this, however, we need greater insight into which of these disorders are the most powerful predictors of comorbidity, when in the life course these disorders occur and how much time elapses from the onset of the primary disorder to the onset of the secondary disorder (21). This difference in onset times is the 'window of opportunity' for primary prevention of secondary disorders.

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