Comorbidity of substance use disorders with mood and anxiety disorders: Results of the international consortium in psychiatric epidemiology

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Abstract

This article reports the results of a cross-national investigation of patterns of comorbidity between substance use and psychiatric disorders in six studies participating in the International Consortium in Psychiatric Epidemiology. In general, there was a strong association between mood and anxiety disorders as well as conduct and antisocial personality disorder with substance disorders at all sites. The results also suggest that there is a continuum in the magnitude of comorbidity as a function of the spectrum of substance use category (use, problems, dependence), as well as a direct relationship between the number of comorbid disorders and increasing levels of severity of substance use disorders (which was particularly pronounced for drugs). Finally, whereas there was no specific temporal pattern of onset for mood disorders in relation to substance disorders, the onset of anxiety disorders was more likely to precede that of substance disorders in all countries. These results illustrate the contribution of cross-national data to understanding the patterns and risk factors for psychopathology and substance use disorders.

An extensive scientific literature has amassed attesting to the strong association of substance use disorders with anxiety, depression, and antisocial personality traits (e.g., Chambless, Cherney, Caputo, & Rheinstein, 1987; Grant & Harford, 1995; Helzer & Pryzbeck, 1988; Hesselbrock, Meyer, & Keener, 1985; Kessler et al., 1997; Merikangas & Swendsen, 1997; Penick et al., 1994; Regier et al., 1990; Ross, Glaser, & Germanson, 1988; Schuckit et al., 1995; Tomasson & Vaglum, 1995; Wittchen, Nelson, & Lachner, 1998a). Individuals suffering from these forms of comorbidity also have a worsened clinical course and outcome, and are at an increased risk of suicide, impairment, and disability (see Hirschfeld, Hasin, Keller, Endicott, & Wunder, 1990; Kessler, 1995; Murphy, 1990; Merikangas & Stevens, 1998; Regier et al., 1990; Svanum & McAdoo, 1989). It is therefore not surprising that substance use comorbidity has emerged as an important clinical and public health concern, and that considerable effort is now directed at understanding the nature of these relationships.

Investigations attempting to understand the mechanisms underlying the association of substance use disorders with other psychiatric conditions have addressed both shared and causal etiologic explanations of comorbidity. However, studies of shared diathesis models over the past decade have generally not produced conclusive findings (Clifford, Hopper, & Fulker, 1984; Kendler et al., 1995; Maier, Lichtermann et al., 1994; Merikangas & Gelernter, 1990; Prescott, Neale, Corey, & Kendler, 1997). Similarly, investigations examining potential causal relationships among these conditions have been the source of considerable debate.

Some investigators have emphasized the likelihood that substance use disorders directly cause anxiety, depression, or other mental health problems (Allan, 1995; Schuckit & Hesselbrock, 1996), whereas others have demonstrated that certain psychiatric disorders may lead to substance dependence through attempts at self-medication (Cox, Swinson, Shulman, Kuch, & Reichman, 1993; Kushner et al., 1996; Kushner, Sher, Wood, & Wood, 1994). The majority of the existing literature, however, underscores the heterogeneity of these relationships as well as the possibility that causal influences (in both directions) may exist simultaneously with shared diatheses (see Kessler et al., 1997; Merikangas & Gelernter, 1990; Merikangas et al., 1996; Swendsen & Merikangas, 1998; Wittchen, Perkonigg, & Reed, 1996).

The inability of previous research to identify a single mechanism of comorbidity is due in part to the numerous subtypes of comorbid syndromes, as well as to the heterogeneity of substance use disorders themselves. For example, alcohol use can be determined by a given set of social, mood, and contextual influences that may differ greatly from the individual characteristics and risk factors associated with alcohol dependence. Furthermore alcohol dependence may differ in important ways in its association with anxiety, depression, or other conditions. In addition to the clear need to examine a spectrum of substance use problems relative to diverse comorbid disorders, research over the past three decades has also produced varied results as a function of changing diagnostic criteria and the use of samples that may not be representative of the general population.

In light of these methodological and conceptual issues, future investigations of comorbidity should advance considerably as consensus is reached about the characteristics of these relationships that can be reliably observed irrespective of culture, geographic location, and specific sample characteristics. The contribution of cross-cultural research is particularly important to this goal for its ability to elucidate contextual and environmental factors that may influence the magnitude or patterns of comorbidity. This investigation will attempt to address these concerns through the combined resources of the International Consortium in Psychiatric Epidemiology (ICPE). The major purpose of the ICPE is to facilitate cross-national comparative epidemiologic studies of psychiatric disorders through application of uniform diagnostic criteria, thereby examining topics such as diagnostic comorbidity without introducing the selection biases associated with treated samples. Using available epidemiologic data sets from Canada, Germany, Mexico, the Netherlands, and the United States, the major goals of this investigation are:

1. to investigate the magnitude of comorbidity of alcohol and drug use, problem use, and dependence in relation to mood disorders, anxiety disorders, conduct disorder, and antisocial personality disorder;
2. to examine the association between the severity of substance use and the number of comorbid psychiatric disorders; and
3. to evaluate the patterns of onset for mood and anxiety disorders across ICPE sites with respect to alcohol or drug use, problem use, and dependence.

Method

Sample

The subjects for these analyses ranged in age from 14 to 64 years derived from six epidemiologic study sites in Europe and North America. All studies used the World Health Organization's Composite International Diagnostic Interview (CIDI; World Health Organization, 1990) using criteria from the Diagnostic and Statistical Manual of Mental

Disorders, third edition, revised (DSM-III-R ; American Psychiatric Association, 1987). Information on the reliability and validity of CIDI-based diagnoses is reported by Wittchen, Robins et al. (1991) and Wittchen (1994). The characteristics of the studies that comprised the ICPE consortium are presented in Table 1. With the exception of Munich, which focused on a younger cohort, the methods and age range of the samples were nearly identical. A brief summary of each of the studies is presented below.

Fresno, USA: Mexican American Prevalence and Services Survey (MAPSS) The MAPSS interviewed a multistage, stratified probability cluster sample of persons of Mexican or Mexican-American origin residing in Fresno County, California, USA (Vega, Kolody, Aguilar-Glaxiola, Alderete, Catalano, & Caraveo-Anduaga, in press). The sample consists of 3,012 adults living in households between the ages of 18 and 59 years of age and is stratified on sex and place of residence. Only respondents up to 54 years of age were included in the ICPE analyses for a total sample size of 2,874. Categories for place of residence are: urban, town/village, and rural. The response rate among screened eligible households who were successfully contacted was 90%.

Munich, Germany: Early Developmental Stages of Psychopathology Study (EDSP) In Germany, EDSP interviewed 3,021 subjects, ages 14–24, as part of a three-wave prospective study (Wittchen et al., 1996; Wittchen, Perkonigg, Lachner, & Nelson, 1998b). This group was a stratified, simple random sample of persons in this age category, using as a sampling frame the official population registry of persons living in the greater Munich area. Persons 14 and 15 years of age were oversampled to compensate for their smaller representation in this population. The response rate in 1995 was 71.1% for complete interviews, with an additional 4% giving partial information. Data are representative of the city and surrounding areas of Munich, Germany.

Mexico City, Mexico: Epidemiology of Psychiatric Comorbidity Project (EPM) EPM administered a household survey in Mexico City to a multistage, stratified probability sample of persons aged 18 to 65 living either permanently or temporarily in households within the 16 political divisions of the city (Caraveo, Martinez, & Rivera, 1998). The sample size was 1,932, with a response rate of 60.4%, although only 8% openly refused the interview. Included in the ICPE analyses are data from respondents who were up to the age of 54 years, for a sample size of 1,734.

The Netherlands: Netherlands Mental Health Survey and Incidence Study (NEMESIS) The NEMESIS is a prospective study collecting data in three waves from a national, multistage stratified random sample of persons 18–64 years old in the Netherlands, representing households within a sample of 90 municipalities of the country (Bijl, Van Zessen, Ravelli, de Rijk, & Langendoen, in press). There was no oversampling of any groups; inclusion criteria were the respondent's age and the absence of severe language difficulties. The first wave of data collection occurred in 1996 and the sample size for complete interviews was 7,076. The response rate was 70%.

Ontario, Canada: Ontario Mental Health Supplement Survey The Ontario Mental Health Supplement Survey was administered in 1990 to a final sample size of 6,902 respondents who ranged in age from 15 to 64 years. This sample was obtained using stratified, multistage area probability sampling of the Ontario household population 15 and over who had been previously interviewed as a part of the Ontario Health Survey (Offord et al., 1994). The original response rate was 88.1%, with 76.5% participating in the mental health supplement. Persons 15–24 were oversampled; their response rate for the supplement was 77.8%.

Residents of remote areas, aboriginals living on reserves, long-term psychiatric inpatients, and prison inmates were excluded from the study.

USA: National Comorbidity Study (NCS) The NCS was administered from 1990 to 1992 to a nationally representative probability sample of persons 15–54 living in the coterminous United States (Kessler et al., 1994). A total of 8,098 respondents were interviewed with a response rate of 82.4%. A subsample of 5,877 was administered additional measures, including all respondents 15–24 plus a random sample of those 25–54. Supplemental samples of college students living in campus group housing as well as nonrespondents surveyed by telephone were also included.

Procedures

DSM-III-R lifetime diagnostic criteria were used to operationalize diagnoses in these studies. The major classes of disorders investigated include the mood disorders, anxiety disorders and behavior disorders. Alcohol and drug variables were defined according to the following three levels of severity:

1. Alcohol or Drug Use: Lifetime history of use of alcohol or illicit drugs (e.g., cannabis, opioids, stimulants, sedatives, inhalants, etc.);
2. Alcohol or Drug Problems: at least one of the DSM-III-R abuse criteria; and
3. Alcohol or Drug Dependence: meets DSM-III-R dependence criteria.

Mood disorders examined in these analyses include: bipolar disorder, major depressive disorder, and dysthymia. The anxiety disorders include the following subtypes: generalized anxiety disorder, panic disorder and phobic disorders. At the Netherlands site, drug use was based on reported use of a drug 5 or more times and alcohol/drug problems were based on abuse symptoms rather than criteria. Likewise, antisocial personality disorder and conduct disorder were defined according to the DSM-III-R Axis II and Axis I, respectively. Information on antisocial personality disorder and conduct disorder was not collected at three of the I.C.P.E. sites (i.e., Mexico, the Netherlands and Germany).

Overview of Analyses

Specific weighting variables were created for each site in order to compensate for differences in sample selection and characteristics of non-responders. Post-stratification of each weighted sample was conducted to adjust for age and sex of the corresponding survey population. Standard errors were computed using the method of jacknife repeated replication (JRR) to adjust for the differences in design introduced by clustering and weighting of observations at each site (Kish & Frankel, 1970). Odds ratios (OR) were used to measure the associations between the levels of the substance variable and other psychiatric disorders.

Results

Table 2 presents the lifetime prevalence rates for each disorder by investigation site. Despite variation in the prevalence of specific conditions, all sites reported relatively high population base rates for mood, anxiety, antisocial behavior, conduct, and substance use disorders. Furthermore, all sites reported that each substance category (use, problems, or dependence) was far more prevalent for alcohol than for drugs, and that there was a uniformly higher prevalence of substance use compared to substance-related problems or dependence diagnoses.

The frequencies and odds ratios measuring the associations between alcohol use, problems and dependence with mood, anxiety, conduct and antisocial behavior disorders by study site are presented in Table 3. In general, there was a strong association between all of the psychiatric disorders and alcohol disorders at all sites. Mood disorders were associated with alcohol use at three of the six sites, whereas anxiety disorders were generally not associated with alcohol use. In contrast, both mood and anxiety disorders were consistently associated with alcohol problems and dependence (i.e., by DSM-III-R criteria). Based on averages across sites, 20% of those persons with alcohol problems and 26% of those with alcohol dependence also had a lifetime history of any mood disorder. A somewhat stronger association was found for alcohol problems and dependence relative to anxiety disorders (whereby 25% and 32% of affected individuals, respectively, met lifetime criteria for any anxiety disorder). With the exception of Germany, there was a direct association between comorbidity magnitude and increased severity of alcohol use disorders.

Across all sites, there was a strong and consistent association between conduct disorder and alcohol disorders (range of odds ratios = 2.8–7.8), and between antisocial personality disorder and alcohol disorders (range of odds ratios = 3.5–15.4). Between one quarter and one half of those with alcohol disorders also reported a lifetime history of either conduct problems or antisocial personality. However, data were not available for conduct and antisocial personality disorder for Mexico, the Netherlands and Germany.

Table 4 presents the association between drug use disorders with affective, anxiety, conduct and antisocial behavior disorder by study site. For all sites, mood disorders were found to be significantly associated with drug use, problems, and dependence (range odds ratios = 1.9–5.3). The same pattern emerged for any anxiety disorder comorbid with drug use disorders at all levels of severity (range odds ratios = 1.8–5.2). The findings with respect to comorbidity between conduct disorder or antisocial personality with drug use disorders also revealed a consistent and potent association across sites with available data (range odds ratios = 3.2–15.2). In general, the magnitude of comorbidity with psychiatric disorders was greater for the drug disorders than for alcohol disorders. Approximately 35% of the sample with drug dependence met lifetime criteria for a mood disorder, 45% met criteria for an anxiety disorder, and 50% met criteria for either conduct or antisocial personality disorder. Moreover, the direct relationship between comorbidity and severity of substance problems was far more pronounced for drugs than for alcohol.

Not shown here, stratification of the results from Tables 3 and 4 revealed that the patterns of drug and alcohol comorbidity with other conditions were generally similar for males and females. However, the sex differences that did emerge for specific sites demonstrated that the magnitude of comorbidity tended to be greater for females, particularly at lower levels of severity of substance use.

The association between the number of mood/anxiety disorders and substance use by study sites is presented in Table 5. The results generally indicate that there is a direct relationship between the number of mood/anxiety disorders and the magnitude of comorbidity with substance disorders. Moreover, there was an association between the number of anxiety or mood disorders and the severity of drug disorders. The direct relationship between number of disorders and severity was not apparent for alcohol disorders.

The proportion of subjects with mood disorders preceding substance use problems is presented in Table 6. This table indicates that in Fresno, Mexico, Ontario, the Netherlands,

and the United States (with the exception of alcohol dependence), the onset of alcohol problems tended to occur simultaneously with or before the onset of mood disorders. In Germany, the onset of mood disorders tended to precede that of alcohol problems but not use or dependence. In contrast, no obvious patterns of onset of mood disorders with respect to drug disorders emerged. However, the most consistent finding was that, with the exception of drug dependence, the onset of mood disorders tended to postdate that of drug disorders.

Table 7 presents the proportion of subjects in whom the onset of anxiety disorders preceded that of substance use disorders. Across all sites, the onset of anxiety disorders preceded that of alcohol and drug disorders at nearly all levels of severity of substance use disorders. This temporal relationship persisted when specific phobias (which tend to begin during childhood) were excluded.

Discussion

The results presented in this investigation illustrate the significance of a cross-national approach to psychiatric epidemiology. The ICPE is one of the first large-scale collaborative efforts to combine international data using comparable methodology. The use of similar diagnostic interviews and criteria minimizes artifactual differences that may lead to misinterpretation of cultural risk factors for specific diseases. For example, the results of the landmark US-UK study revealed that greater rates of schizophrenia in the United States were attributable in part to differences in diagnostic conventions between the two countries rather than to increased urbanization in the United States (Cooper et al., 1972). Such findings underscore the need for comparability in international research, and have culminated in major advances in the development of standardized diagnostic criteria and assessment methods (DSM-IV, American Psychiatric Association, 1994; CIDI, World Health Organization, 1990; ICD-10, Robins & Helzer, 1985; World Health Organization, 1991). With respect to substance abuse, the crosscultural applicability of the diagnosis and assessment of substance use disorders across nine cultures was examined by a recent WHO study (Room et al., 1996). These methodologic advances have led to a growing body of cross-cultural studies on alcoholism (Helzer et al., 1990), as well as depression (Weissman et al., 1992; Weissman, 1996).

In addition to providing information on the comparability of disease magnitude across cultures, cross-national studies may also yield clues regarding cultural-specific disease risk factors. Systematic comparisons across diverse geographic sites with different social, cultural, political and economic conditions enable estimation of the role of contextual factors in substance abuse. If the findings are highly similar across different cultures, however, one may also conclude that such consistency may be attributable to biological or other stable human characteristics that are independent of the influence of sociocultural factors (Caetano, Hesselbrock, & Medina-Mora, 1996).

The cross-site similarity of the present findings with respect to comorbidity was quite remarkable, despite major differences in the magnitude of both substance use/ disorders and psychiatric disorders. Our earlier cross-national study also revealed similar patterns of comorbidity both in terms of the magnitude and specific subtypes of affective disorders, anxiety disorders and substance problems (Merikangas et al., 1996). The consistency in patterns of comorbidity suggests that although cultural factors may be associated with the availability and type of exposure to various substances, the links between psychopathology as risk factors and sequelae of substance disorders are not culture-specific.

Concerning the spectrum of substance use reported across sites, the direct increase in the magnitude of comorbidity according to the level of severity of substance problems suggests that there is a meaningful continuum of severity ranging from use, to problems to dependence. Furthermore, the weaker odds ratios associated with substance use (and alcohol use in particular) likely reflect increased heterogeneity of this category. That is, a greater percentage of individuals reporting alcohol use (without problems or dependence) may have tried alcohol solely due to experimentation or sporadic social contexts. These specific reasons for substance use may not be tied to other psychiatric syndromes through causal or shared etiologic mechanisms, thus leading to less stable associations and lower odds ratios. By contrast, persons meeting full criteria for alcohol dependence may be more likely to use alcohol for nonsporadic reasons (such as to assuage enduring anxiety symptoms), and therefore be more likely to continue its use over time.

In addition to a continuum of comorbidity magnitude as a function of the spectrum of substance use, there was a direct relationship between the number of comorbid disorders and increasing levels of severity of substance use. This increase was particularly pronounced for drugs as opposed to alcohol (which at low levels was rarely associated with comorbid psychopathology). These findings therefore point to the increased deviance of drug use at all levels of severity, irrespective of the normative patterns of drug and alcohol use across the world. In a study of cultural views on the use and abuse of alcohol and other drugs, Gureje, Vazquez-Barquero, and Janca (1996) reported that any use of addictive substances other than alcohol is commonly considered socially aberrant across the world, leading to a lower threshold for the identification of disorders relating to illicit substances than to alcohol. These results have been confirmed by other sources of evidence including recent family studies that implicate comorbidity as an indicator of the severity of substance-related problems, as well as increasing magnitude of familial aggregation of drug disorders as a function of deviance of the primary drug of use (Merikangas, Stolar, et al., in press).

An additional consistent ICPE finding is that the onset of anxiety disorders typically preceded that of substance use problems or dependence far more often than mood disorders. This finding is consistent (although not confirmatory) of self-medication in that anxiety is ostensibly more easily assuaged by the depressant effects of alcohol (or specific classes of drugs) on the central nervous system. Conversely, depressed states may be less readily altered by consumption of central nervous system depressants, and they are therefore less likely to be utilized as a means of self-medication. The lack of clear unidirectional patterns for mood disorders and substance use is also consistent with other clinical and epidemiologic studies showing that substances such as alcohol may be more important to the severity of depression than the reverse (see Kranzler, Del Boca, & Rounsaville, 1996; Powell, Penick, Othmer, & Bingham, 1982; Swendsen & Merikangas, 1998). However, the complex relationship between mood and anxiety states differs according to specific subtypes of these disorders as well as particular classes of drugs (Kushner et al., 1996; Mirin, Weiss et al., 1991).

Despite the similarity in the magnitude of comorbidity across sites, some site differences did emerge in these analyses. The chief site differences were found for the Mexican and German sites. The magnitude of comorbidity between mood and anxiety disorders with all levels of substance disorders was lower at the Mexico site than at the other study sites. An explanation for these differences was offered by Caetano et al. (1996) who described several cultural differences in the patterns of alcohol and drug consumption and definitions of alcohol-related problems in Mexico.

Another exception to the general trends described herein was the difference in the direction of the association between mood disorders and the severity of alcohol use disorders between the Munich and the other study sites. This difference was most likely attributable to the age composition of the Munich study sample which was far younger than that of the other ICPE sites. As this particular sample ages, the direct association observed at other sites between mood and substance use disorders may also become more evident. In addition, differences in patterns of comorbidity may be attributable to the increased frequency of normative alcohol use in Germany relative to other sites (Cockerham et al., 1989). Nevertheless, the similarity of the German findings, despite the younger age group, reveals that comorbidity between substance use disorders and psychopathology are already apparent in early adulthood. Their observation of a direct association between the severity of substance use and anxiety disorders further suggests that anxiety may play a more important role in adolescence and early adulthood comorbidity, whereas the link between depression and alcoholism may emerge later.

Several methodological considerations are noteworthy in interpreting the present findings. This cross-site investigation focused on lifetime prevalence rates in calculating the magnitude of diagnostic comorbidity across broad classes of psychiatric disorders and for the full spectrum of substance use, problems, and dependence. Future multivariate analyses will provide more detailed investigation of other risk factors or correlates relevant to substance use comorbidity such as age, sex, subtypes of disorders and different prevalence periods. For example, substance use disorders have long been observed to be more prevalent among men, and the relationship between specific disorders may also vary in important ways by gender. One possibility is that because substance use disorders are less normative for women compared to men, substance- dependent women may represent a more severe or vulnerable population and may be at greater risk for comorbid psychiatric illness. Evidence from familial transmission data also suggests a lower threshold for the development of alcoholism in women (Merikangas, Stevens, et al., in press).

Although more comprehensive analyses should be pursued, the achievement of consensus regarding consistent trends and patterns of association across diverse geographic sites provides the needed starting point for more detailed examinations of the specific mechanisms of comorbidity and, ultimately, for aiding treatment and prevention efforts. For example, the identification and treatment of common index conditions in comorbid relationships can lead to a reduction in secondary disorders, and conversely, the prevention of secondary disorders should reduce the severity of the index condition (see Kessler & Price, 1993). The current findings therefore suggest that anxiety disorders in particular should serve for many individuals as a primary target for the prevention of substance dependence, whereas a smaller portion of mood disorder cases warrant similar consideration. Future studies designed to elucidate the mechanisms for the development of comorbidity between substance and psychiatric disorders within a given cultural context will provide a stronger basis for determining the treatment and prevention implications of these findings.

Table 1. Description of participating ICPE investigations

Study site	Age range	*n*	Response rate
Fresno (USA)	18–54	2874	90.0%
Germany	14–24	3021	71.1%
Mexico	18–54	1734	60.4%
Netherlands	18–64	7076	70.0%
Ontario	15–54	6902	88.1%
United States (NCS0	15–54	8098	82.4%

Note. ICPE = International Consortium in Psychiatric Epidemiology; NCS = National Comorbidity Study.

Table 2. Lifetime prevalence rates by study site

Study site	Any mood % (SE)	Any anxiety % (SE)	Conduct % (SE)	Antisocial Behavior[a] % (SE)	Alcohol use % (SE)	Alcohol problems % (SE)	Alcohol dependence % (SE)	Drug use % (SE)	Drug problems % (SE)	Drug dependence % (SE)
Fresno (USA)	12.2 (0.7)	18.5 (0.9)	23.3 (1.4)	18.7 (0.9)	85.4 (0.9)	26.3 (1.4)	11.2 (1.0)	44.3 (1.4)	13.1 (90.8)	7.0 (0.6)
Germany	14.8 (0.8)	11.7 (0.7)	—	—	94.5 (0.3)	24.3 (1.0)	6.2 (0.6)	34.2 (1.0)	6.7 (0.6)	2.1 (0.3)
Mexico	9.2 (1.2)	9.0 (0.7)	—	—	89.1 (1.1)	16.6 (1.2)	6.7 (0.6)	10.4 (0.9)	1.5 (0.3)	0.7 (0.2)
Netherlands[b]	18.9 (0.6)	20.3 (0.7)	—	—	—	11.7 (0.5)	5.5 (0.3)	14.4 (9.5)	1.5 (0.1)	1.8 (0.2)
Ontario	9.8 (0.7)	22.3 (0.7)	11.1 (0.6)	4.9 (0.3)	93.0 (0.6)	23.7 (1.1)	9.1 (0.5)	43.2 (0.9)	8.5 (0.5)	3.2 (0.4)
USA (NCS)	19.1 (0.6)	29.7(0.9)	12.7 (0.6)	10.1 (0.5)	92.4 (0.5)	29.0 (0.9)	14.3 (0.6)	51.5 (1.0)	15.5 (0.7)	7.5 (0.4)

Note. SE = standard error; NCS = National Comorbidity Study.
[a]Corresponds to three or more antisocial personality symptoms.
[b]Alcohol/drug problems are based on abuse variables rather than criteria variables; drug use based on reported use five or more times rather than ever used.

Table 3. Comorbidity of alcohol and other psychiatric disorders among ICPE studies

	Alcohol use		Alcohol problems		Alcohol dependence	
Study site	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)
Any mood disorder						
Fresno (USA)	12.9	1.7 (0.9–3.4)	20.5	2.5 (1.7–3.8)	24.6	2.7 (1.9–4.0)
Germany	15.4	3.7 (1.8–7.6)	19.0	1.5 (1.2–1.9)	22.1	1.7 (1.0–2.7)
Mexico	9.4	1.2 (0.6–2.2)	17.0	2.5 (1.5–4.1)	18.2	2.4 (1.1–4.9)
Netherlands[a]	—	—	19.2	1.0 (0.8–1.2)	34.0	2.3 (1.9–2.8)
Ontario	10.2	2.0 (1.5–2.8)	16.2	2.3 (1.8–3.0)	23.2	3.3 (2.5–4.2)
United States	19.9	2.6 (1.7–3.9)	29.3	2.4 (2.0–2.8)	35.5	2.8 (2.3–3.4)
Any anxiety disorders						
Fresno (USA)	18.7	1.1 (0.7–1.6)	25.4	1.8 (1.3–2.4)	34.5	2.7 (2.0–3.5)
Germany	11.9	1.7 (0.9–3.1)	17.4	1.9 (1.5–2.5)	27.4	3.2 (2.0–4.9)
Mexico	8.7	0.7 (0.4–1.1)	13.4	1.7 (1.1–2.6)	14.7	2.7 (0.9–3.5)
Netherlands[a]	—	—	20.8	1.0 (0.8–1.3)	30.2	1.8 (1.3–2.3)
Ontario	23.1	2.1 (1.3–3.5)	33.5	2.2 (1.8–2.6)	39.5	2.5 (2.1–3.1)
United States	30.2	1.4 (1.0–1.8)	40.9	2.1 (1.8–2.4)	44.9	2.2 (1.9–2.5)
Conduct disorder						
Fresno (USA)	25.7	3.5 (2.5–5.8)	47.5	5.2 (4.2–6.5)	53.7	4.8 (3.4–6.7)
Germany	—	—	—	—	—	—
Mexico	—	—	—	—	—	—
Netherlands[a]	—	—	—	—	—	—
Ontario	11.7	4.6 (1.9–11.0)	26.5	5.4 (3.8–7.8)	40.7	7.8 (4.7–12.9)
United States	13.3	2.8 (1.9–4.2)	27.7	5.4 (4.6–6.4)	35.9	5.7 (4.8–6.9)
Adult antisocial behavior						
Fresno (USA)	21.3	7.5 (2.6–22.2)	47.7	10.0 (7.0–14.3)	63.6	11.6 (8.5–16.0)
Germany	—	—	—	—	—	—
Mexico	—	—	—	—	—	—
Netherlands[a]	—	—	—	—	—	—
Ontario	5.3	11.3 (3.6–35.6)	16.6	15.4 (10.9–21.9)	27.6	14.1 (8.8–22.4)
United States	10.7	3.5 (1.8–6.8)	25.7	8.8 (7.3–10.6)	37.1	9.9 (8.2–11.8)

Note. ICPE = International Consortium in Psychiatric Epidemiology; OR = odds ratio; CI = confidence interval.
[a]Alcohol/drug problems based on abuse variables rather than criteria variables; drug use based on reported use five or more times rather than ever used.

Table 4. Comorbidity of drug and other psychiatric disorders among ICPE studies

	Drug use		Drug problems		Drug dependence	
Study site	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)
Any mood disorder						
Fresno (USA)	17.7	2.6 (1.7–3.8)	33.2	5.0 (3.3–7.6)	30.0	3.5 (2.2–5.6)
Germany	21.6	2.2 (1.7–2.8)	32.7	3.1 (2.1–4.5)	32.6	2.9 (1.5–5.3)
Mexico	14.8	1.9 (1.0–3.6)	31.4	4.7 (1.7–13.1)	34.7	5.3 (1.7–16.7)
Netherlands[a]	34.8	2.7 (2.3–3.2)	41.4	3.1 (2.0–4.7)	51.1	4.6 (3.2–6.6)
Ontario	14.0	2.3 (1.7–3.0)	22.6	3.1 (1.9–5.1)	30.0	4.3 (2.2–8.4)
United States	24.1	2.0 (1.7–2.3)	34.9	2.8 (2.3–3.3)	40.6	3.3 (2.6–4.0)
Any anxiety disorders						
Fresno (USA)	24.2	2.0 (1.5–2.6)	36.8	3.1 (2.2–4.4)	44.4	4.0 (2.7–6.1)
Germany	18.4	2.5 (1.9–3.3)	33.0	4.4 (2.8–6.7)	39.3	5.2 (2.5–10.7)
Mexico	9.9	1.1 (0.7–1.7)	21.7	2.8 (1.1–7.4)	31.1	4.6 (1.4–15.1)
Netherlands[a]	32.6	2.2 (1.9–2.5)	33.2	2.0 (1.3–2.9)	56.0	5.2 (3.3–8.1)
Ontario	28.6	1.9 (1.6–2.2)	42.5	2.9 (2.4–3.5)	48.5	3.4 (2.5–4.7)
United States	35.5	1.8 (1.5–2.1)	47.6	2.5 (2.2–3.0)	55.4	3.3 (2.7–3.9)
Conduct disorder						
Fresno (USA)	39.2	5.4 (4.2–6.9)	56.1	5.7 (3.9–8.2)	59.1	5.6 (3.7–8.3)
Germany	—	—	—	—	—	—
Mexico	—	—	—	—	—	—
Netherlands[a]	—	—	—	—	—	—
Ontario	17.6	3.3 (2.4–4.4)	40.8	7.6 (4.9–11.8)	59.3	13.9 (8.1–23.7)
United States	18.4	3.2 (2.5–4.0)	33.3	5.1 (4.3–6.0)	40.0	5.6 (4.3–7.4)
Adult antisocial behavior						
Fresno (USA)	34.3	7.8 (5.0–12.1)	62.4	12.0 (8.4–17.2)	72.4	15.2 (9.2–25.3)
Germany	—	—	—	—	—	—
Mexico	—	—	—	—	—	—
Netherlands[a]	—	—	—	—	—	—
Ontario	9.6	7.8 (4.3–13.9)	27.9	13.6 (9.5–19.5)	41.1	14.1 (8.8–22.4)
United States	16.1	4.9 (3.9–6.1)	33.8	8.3 (6.7–10.3)	43.9	9.8 (7.9–12.2)

Note. ICPE = International Consortium in Psychiatric Epidemiology; OR = odds ratio; CI = confidence interval.
[a]Alcohol/drug problems based on abuse variables rather than criteria variables; drug use based on reported use five or more times rather than ever used.

Table 5. Association between number of mood/anxiety disorders and substance use disorders

Study site	Number of mood/anxiety disorders	Alcohol			Drug		
		Use OR (95% CI)	Problems OR (95% CI)	Dependence OR (95% CI)	Use OR (95% CI)	Problems OR (95% CI)	Dependence OR (95% CI)
Fresno (USA)	1	1.0 (0.6–1.5)	1.8 (1.3–2.7)	2.2 (1.5–3.3)	1.5 (1.2–2.0)	3.2 (2.0–5.1)	2.4 (1.4–3.9)
	2	1.4 (0.6–3.6)	2.2 (1.4–3.6)	3.0 (1.8–4.8)	2.5 (1.2–5.3)	3.4 (1.8–6.7)	4.3 (2.1–8.7)
	3 or more	2.7 (1.4–5.4)	2.9 (1.9–4.5)	5.0 (3.2–7.7)	3.8 (2.4–5.8)	8.2 (4.7–14.2)	7.8 (3.9–15.6)
Germany	1	3.2 (1.8–5.7)	1.3 (1.0–1.7)	1.5 (1.9–2.5)	1.9 (1.4–2.4)	2.5 (1.7–3.8)	3.9 (1.8–8.3)
	2	2.4 (0.7–8.4)	1.7 (1.1–2.6)	3.6 (1.9–6.9)	3.2 (2.1–5.0)	5.0 (2.8–9.0)	8.3 (3.0–22.5)
	3 or more	1.2 (0.4–3.9)	3.2 (1.9–5.4)	4.8 (2.1–10.9)	4.3 (2.4–7.7)	11.0 (5.7–21.4)	9.6 (3.6–25.8)
Mexico	1	0.8 (0.4–1.6)	2.1 (1.3–3.6)	1.7 (0.9–3.4)	1.6 (1.0–2.5)	1.9 (0.4–8.5)	1.8 (0.2–16.5)
	2	1.1 (0.5–2.5)	3.2 (1.6–6.7)	4.1 (1.7–10.1)	0.8 (0.3–1.9)	4.1 (1.2–13.8)	7.5 (2.0–28.3)
	3 or more	0.5 (0.3–2.0)	1.5 (0.6–3.7)	1.3 (0.3–4.9)	1.8 (0.5–6.9)	9.2 (1.8–46.7)	12.2 (1.1–134.6)
Netherlands[a]	1	—	1.1 (0.9–1.5)	1.6 (1.2–2.0)	2.0 (1.7–2.4)	2.5 (1.5–4.2)	2.2 (1.2–4.0)
	2	—	1.0 (0.7–1.4)	1.6 (1.0–2.5)	2.3 (2.0–2.7)	2.6 (1.6–4.2)	5.1 (3.0–8.8)
	3 or more	—	0.8 (0.6–1.1)	3.5 (2.6–4.9)	3.9 (3.0–5.1)	4.0 (2.2–7.5)	11.3 (6.5–19.5)
Ontario	1	2.1 (1.1–4.1)	1.9 (1.4–2.6)	2.0 (1.6–2.5)	1.6 (1.2–2.0)	2.0 (1.3–3.0)	1.9 (1.1–3.2)
	2	7.8 (2.4–24.8)	2.8 (2.0–3.8)	2.9 (2.1–4.1)	2.3 (1.8–3.0)	4.2 (2.9–6.1)	5.7 (3.3–9.7)
	3 or more	1.6 (0.7–3.9)	2.6 (1.9–3.7)	4.7 (3.1–7.2)	3.6 (2.4–5.4)	5.0 (2.7–9.4)	7.8 (3.8–16.1)
United States	1	1.3 (1.0–1.8)	1.9 (1.6–2.3)	1.8 (1.4–2.3)	1.5 (1.2–1.8)	2.2 (1.7–2.7)	2.7 (1.9–3.6)
	2	1.7 (1.1–2.7)	2.5 (2.0–3.7)	2.6 (2.1–3.4)	2.1 (1.7–2.6)	3.0 (2.3–3.7)	3.6 (2.8–4.8)
	3 or more	2.0 (1.2–3.4)	3.0 (2.5–3.7)	3.7 (3.0–4.6)	2.3 (1.8–3.0)	4.0 (3.3–4.7)	5.6 (4.5–7.1)

Note. OR = odds ratio; CI = confidence ratio.
[a]Alcohol/drug problems based on abuse variables rather than criteria variables; drug use based on use five or more times rather than ever used.

Table 6. Proportion (standard error) of subjects with onset of mood disorder prior to substance use problem[a]

Study site	Alcohol			Drug		
	Use	Problems	Dependence	Use	Problems	Dependence
Fresno (USA)	18.1 (4.6)	32.8 (4.5)	26.1 (5.3)	18.1 (4.1)	35.1 (6.5)	30.4 (7.3)
Germany	18.3 (2.0)	55.3 (4.3)	50.5 (9.6)	51.4 (3.8)	55.8 (8.3)	38.0 (12.2)
Mexico	19.8 (4.6)	34.8 (9.5)	34.3 (9.3)	22.7 (8.2)	45.0 (19.5)	35.5 (26.1)
Netherlands[b]	—	35.6 (3.9)	43.1 (5.5)	37.8 (2.2)	49.7 (6.9)	52.3 (4.8)
Ontario	14.3 (2.1)	33.0 (3.1)	46.1 (7.3)	31.2 (3.2)	46.0 (4.6)	57.3 (8.1)
United States	20.9 (1.4)	36.9 (2.3)	52.1 (3.3)	29.6 (2.0)	43.7 (3.0)	55.0 (4.0)

[a]Among those with both mood and substance use/problems.
[b]Alcohol/drug problems use abuse rather than criteria variables; drug use based on reported use five or more times rather than ever used.

Table 7. Proportion (standard error) of subjects with onset of anxiety disorder prior to substance use problem[a]

	Alcohol			Drug		
Study site	Use	Problems	Dependence	Use	Problems	Dependence
Fresno (USA)	47.4 (3.9)	57.4 (5.4)	68.6 (5.3)	48.4 (4.9)	60.2 (5.1)	72.7 (5.3)
Germany	47.7 (2.9)	61.4 (4.9)	56.7 (7.9)	64.4 (4.2)	73.8 (5.3)	67.6 (10.3)
Mexico	43.5 (5.9)	45.6 (11.0)	63.5 (13.2)	55.6 (12.9)	44.3 (21.7)	100 (—)
Netherlands[b]	—	62.8 (3.9)	75.3 (4.0)	64.1 (3.5)	73.1 (7.7)	75.5 (5.8)
Ontario	62.5 (1.8)	73.3 (2.2)	76.8 (4.5)	71.5 (1.3)	72.6 (3.3)	77.9 (5.4)
United States	56.7 (1.6)	71.0 (1.9)	79.4 (2.0)	63.4 (1.6)	74.4 (2.0)	83.4 (2.5)

[a]Among those with both anxiety and substance use/problems.
[b]Alcohol/drug problems use abuse rather than criteria variables; drug use based on reported use five or more times rather than ever used.

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