Major Depression in 6050 Former Drinkers

Association With Past Alcohol Dependence

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Background: The association between alcoholism and major depression in the general population has been explained as misdiagnosed alcohol intoxication and withdrawal effects mistaken for depressive syndromes. To investigate whether this could account for the entire relationship, the association of past alcohol dependence with current major depression (ie, nonoverlapping time frames) was investigated in individuals who no longer drink or who drink very little. We conducted the study using data from the National Longitudinal Alcohol Epidemiologic Survey, a representative sample.

Methods: Former drinkers who did not use drugs or smoke in the past year (n=6050) were divided into those with and without past *DSM-IV* alcohol dependence. These 2 groups were compared for the presence of current (last 12 months) *DSM-IV* major depression. The association between prior alcohol dependence and current major depression was tested with linear logistic regression, controlling for other variables.

Results: Prior alcohol dependence increased the risk of current major depressive disorder more than 4-fold. This relationship was not attenuated by control variables. The majority of subjects with major depression last used substances 2 or more years prior to the interview, which eliminates acute intoxication or withdrawal effects as an explanation of their depressions.

Conclusions: The strong, specific association between prior alcohol dependence and current or recent major depression in a nationally representative sample of former drinkers indicates that the association is not entirely an artifact of misdiagnosed intoxication and withdrawal effects. A better understanding of the nature of the relationship between the 2 disorders should be sought and will have important public health significance.

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N ATIONAL AND international epidemiologic surveys[1-6] and reviews of the many studies of treated alcoholic subjects[7,8] consistently indicate a strong association between alcohol dependence or alcoholism and depression. However, although the association itself is well established, the reasons for it have been the subject of some debate. Given the high prevalence of each of the 2 disorders and their common co-occurrence, understanding the reasons for the association is important. It has been proposed that the association is either causal, due to shared etiology, or artifactual.[7] A directly causal relationship might arise if heavy alcohol intake pharmacologically induces major depression and its symptoms. An indirectly causal relationship between alcohol dependence and depression could arise if alcoholism causes risk factors for depression, such as job loss. A high level of association due to shared etiologic factors could arise from common underlying genetic and environmental factors, such as a disruptive family environment.

Family and adoption studies on the shared etiology hypothesis have been inconsistent.[9,10] Longitudinal studies of the effects of a lifetime diagnosis of depression on the outcome of alcoholism were also inconsistent,[11-13] possibly due to the nonspecific lifetime time frame. In contrast, with only 1 exception,[14] longitudinal studies using more clearly defined time frames showed that major depression measured at a specific point in time predicted subsequent poor outcome of alcoholism[15,16] or dependence on multiple substances including alcohol.[17] Further, changes in the status of alcoholism measured similarly predicted subsequent changes in the status of depression.[18] Numerous randomized clinical trials have investigated this issue as well through testing whether treating depression in alcoholic subjects can improve the

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course of alcoholism. Studies of antidepressant medication treatment during treatment for alcoholism[19-22] generally show that depression improves and substance abuse is modestly improved when such treatment is given. However, from an epidemiologic point of view, these studies are problematic because they rely on treated samples and thus may not fully represent the underlying population of individuals with comorbid alcohol dependence and major depression.

One factor that has persistently complicated investigation of the relationship between alcohol dependence and major depression is diagnosis. The diagnosis of major depression among actively drinking alcoholics is complicated by the fact that intoxication and withdrawal from alcohol and other substances can induce transient symptoms that mimic an independent depressive disorder.[23,24] Thus, it has been proposed that the directly causal relationship is instead artifactual, arising from diagnostic confusion.[23] To avoid such confusion between these transient symptoms and an actual diagnosis of major depressive disorder, numerous attempts have been made to define an independent depressive disorder in individuals with a history of alcohol dependence. Most of these definitions were based, in whole or in part, on the lifetime order of onset of major depression and alcoholism or alcohol dependence.[25-27] In these definitions, lifetime initial onset of major depression *before* the onset of alcohol dependence was termed "primary" major depression, and lifetime initial onset of major depression *after* the initial onset of alcohol dependence was termed "secondary." Assessing subjects retrospectively on a lifetime basis (the usual method) can present problems in recalling the order of onset for events that often occurred many years in the past. Further, the primary/secondary distinction was based on the initial occurrence of diagnosed alcoholism, but heavy drinking leading to transient depressive symptoms could precede the onset of alcohol dependence or could even occur in the absence of an alcoholism diagnosis.

The treatment of this issue in *DSM-IV* represented a substantial improvement. The *DSM-IV* differentiation between primary and substance-induced depressive disorder allows individuals with alcoholism to receive a diagnosis of primary major depressive disorder 2 ways. In the first, the syndrome is established prior to substance use leading to intoxication and/or withdrawal. In the second, the syndrome persists more than 4 weeks after the cessation of acute intoxication or withdrawal. The use of these specific time frames, especially the latter, provides a clearly defined situation for studying the association of alcoholism and later major depression that eliminates the potential diagnostic complications of acute alcohol intoxication and withdrawal.

To date, no general population study has made use of these new definitions to investigate the nature of the association between alcohol dependence and major depression. As described above, an important question in this debate concerns whether the association is entirely an artifact of intoxication or withdrawal symptoms mimicking major depression. An informative group on this question would be former drinkers who currently abstain completely or whose current drinking is so light that

it could not possibly have caused intoxication or withdrawal symptoms sufficient to mimic a full depressive disorder. In such a group of former drinkers, the prevalence of current major depression could be compared between those with a history of prior alcohol dependence and those without such a history. In studying a large representative group of former drinkers, a substantial step could be taken toward clarifying whether the relationship between alcohol dependence and major depression represents more than an artifact of misdiagnosis. Such an approach would be a fresh look at a question that has long been debated. We present such an investigation.

SUBJECTS AND METHODS

SAMPLE

Data were derived from the 1992 National Longitudinal Alcohol Epidemiologic Survey (NLAES), a nationally representative sample of the US adult population, 18 years and older (n=42 862).[28,29] The household response rate was 91.9%, and the sample person response rate was 97.4%. The NLAES featured a complex multistage design. Primary sampling units were stratified according to sociodemographic criteria and were selected with probability proportional to size. From a sampling frame of approximately 200 primary sampling units, 198 were selected for inclusion in the 1992 NLAES sample, including 52 that were self-representing, ie, selected with certainty. Within primary sampling units, geographically defined secondary sampling units, referred to as segments, were selected systematically for the sample. Oversampling of the African American population was accomplished at this stage of sample selection to secure adequate numbers for analytic purposes. Segments then were divided into clusters of approximately 4 to 8 housing units, and all occupied housing units were included in the NLAES. Within each household, one randomly selected respondent, 18 years or older, was selected to participate in the survey. Oversampling of adults aged 18 to 29 years was done at this stage of the sample selection to include a greater representation of this heavy-drinking population subgroup. This subgroup of young adults was randomly sampled at a ratio of 2.25:1.00.

In the NLAES, former drinkers were defined as those who were past but not current drinkers. More specifically, these subjects had had 1 or more years in the past during which they drank at least 12 drinks of any type of alcoholic beverage, but they did not drink at least 12 drinks during the 12 months prior to the interview. Although this cutoff can be considered conservative in identifying persons not at risk for withdrawal, we wished to use a cutoff that would not leave the issue of withdrawal in question. Of the total sample, 9264 respondents (21.6%) were classified as former drinkers. To further ensure that any current major depressions could not be attributed to the effects of drugs or smoking, all subjects who used drugs or smoked cigarettes in the 12 months prior to the interview were also excluded. The 6050 subjects remaining constituted the sample investigated in this report. This definition of former drinker was not as rigid as a requirement that no alcohol whatsoever was consumed in the 12 months prior to the interview, which might itself have produced an idiosyncratic sample. However, it eliminated the possibility that acute intoxication and/or withdrawal effects could have occurred on a persistent basis throughout the 12 months prior to the interview. Note that lifetime abstainers were not included in the analysis because they were not at risk of developing alcohol dependence.

Table 1. Demographic Characteristics of the Sample by History of Past Alcohol Dependence

Demographic Characteristics	History of *DSM-IV* Alcohol Dependence, % (SE)	
	No Past Alcohol Dependence (n = 5214)	Past Alcohol Dependence (n = 836)
Sex		
Male	47.2 (0.84)	63.2 (1.80)
Female	52.8 (0.84)	36.8 (1.80)
Age, y		
18-29	15.2 (0.58)	17.8 (1.52)
30-44	33.1 (0.79)	43.0 (2.11)
45-64	29.3 (0.76)	28.3 (1.75)
≥65	22.4 (0.69)	10.9 (1.26)
Race		
African American	9.8 (0.52)	8.5 (1.06)
All other	90.2 (0.52)	91.5 (1.06)
Education		
≥High school	81.5 (0.73)	84.8 (1.54)
<High school	18.5 (0.73)	15.2 (1.54)
Marital status		
Married	73.3 (0.67)	72.5 (1.64)
All other	26.7 (0.67)	27.5 (1.64)

DIAGNOSTIC ASSESSMENT

Diagnoses of *DSM-IV* alcohol use disorders and major depression were derived from the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS), a fully structured diagnostic interview designed to be administered by trained interviewers who were not clinicians.[29-31] The AUDADIS included an extensive list of symptom questions that operationalized the *DSM-IV* criteria for alcohol use disorders and major depression. These questions have been described in detail elsewhere.[31,32] In the AUDADIS, current disorders are defined as occurring within the 12 months prior to the interview. Past disorders are those occurring prior to the last 12 months. In an independent test-retest study conducted in the general population, AUDADIS diagnoses of alcohol use disorders and major depression were shown to be highly reliable, with κ between 0.73 and 0.76 for alcohol use disorders and 0.60 and 0.65 for major depression for the 2 time frames.[32] Several US and international studies have supported the reliability and validity of *DSM-IV* diagnoses made by the AUDADIS in various types of samples.[33-37] These diagnoses have formed the basis of an extensive series of studies of alcohol use disorders and related conditions in the general population.[29,38-41]

Consistent with the *DSM-IV*, an AUDADIS diagnosis of alcohol dependence requires that a person exhibit a maladaptive pattern of alcohol use leading to clinically significant impairment or distress, as demonstrated by at least 3 of 7 criteria of dependence in any 1-year period. The symptoms include (1) tolerance, (2) withdrawal or relief or avoidance of withdrawal, (3) persistent desire or unsuccessful attempts to cut down or stop drinking, (4) spending much time drinking or recovering from its effects, (5) giving up or reducing occupational, social, or recreational activities in favor of drinking, (6) impaired control over drinking, and (7) continuing to drink despite a physical or psychological problem caused or exacerbated by drinking. The AUDADIS is structured to confirm that symptoms cluster within a 1-year period, both for current and past dependence. An AUDADIS *DSM-IV* diagnosis of abuse requires at least 1 of the following in any 1 year: (1) continuing to drink despite a social or interpersonal problem caused or ex-

acerbated by the effects of drinking, (2) recurrent drinking in situations in which alcohol use is physically hazardous, (3) recurrent drinking resulting in a failure to fulfill major role obligations, or (4) recurrent alcohol-related legal problems. The diagnosis of abuse is precluded by a diagnosis of dependence, as required by *DSM-IV*.

Episodes of *DSM-IV* major depressive disorder were also constructed within the past year and prior to the past year time frames. Consistent with the *DSM-IV*, AUDADIS diagnoses of major depression required the presence of at least 5 depressive symptoms (1 of which must have been depressed mood or anhedonia) nearly every day for most of the day for at least a 2-week period. Social and/or occupational dysfunction must also have been present during the disturbance. Episodes of *DSM-IV* major depression due to bereavement or physical illness were ruled out. The AUDADIS diagnosis of major depression and its distribution in the entire NLAES sample has been reported in detail elsewhere.[42]

STATISTICAL ANALYSIS

A linear logistic regression analysis was used to assess the risk of past-year major depression among former drinkers. The analytic models were not conditioned on a prior history of past depression because this was not relevant to our specific research question, which focused on the occurrence of current depression in the absence of intoxication or withdrawal effects. The logistic regression analysis was conducted on weighted data using SUDAAN,[43] a software package that uses Taylor series linearization to adjust for the complex sampling design of the NLAES. The main predictor variable in the model was a past (ie, prior to the past year) diagnosis of *DSM-IV* alcohol dependence. A past diagnosis of alcohol abuse was included as well. Control variables included sex, race, age, current marital status, and education.

RESULTS

Among the sample of 6050 former drinkers who also used no drugs and did not smoke in the 12 months prior to the interview, 13.8% were classified as having a diagnosis of *DSM-IV* alcohol dependence at some point prior to the previous 12 months. The demographic characteristics of the subjects with and without a past diagnosis of *DSM-IV* alcohol dependence are shown in **Table 1**. As expected, slightly less than half the subjects without a past diagnosis of alcohol dependence were men, and a higher proportion of men had a past diagnosis of alcohol dependence. Fewer subjects with a past diagnosis of alcohol dependence were in the oldest age category. Race, education, and marital status did not differ markedly between the groups with or without a past diagnosis of alcohol dependence.

Of the subjects with past diagnoses of *DSM-IV* alcohol dependence, 7.6% had a past-year diagnosis of major depression. Among subjects with no diagnosis of past *DSM-IV* alcohol dependence, 2.0% had past-year diagnoses of major depression. Among the group with no past diagnosis of alcohol dependence, 5.1% received a diagnosis of alcohol abuse.

The results of the logistic regression analysis of past-year major depressive disorder are shown in **Table 2**. As shown, the risk of major depression during the past year was 4.2 times greater among respondents with a history of alcohol dependence than among those with no

history of alcohol dependence. This result was obtained controlling for the effects of sociodemographic characteristics. Note that the diagnosis of past *DSM-IV* alcohol abuse was not significantly related to major depression. Removing the abuse term from the model did not change the association of past alcohol dependence with current major depression among this sample of former drinkers (adjusted odds ratio, 4.12; 95% confidence interval, 2.77-6.14). Further, past alcohol abuse was not significantly related to current major depression in a model with the same covariates that did not include a term for past *DSM-IV* alcohol dependence (adjusted odds ratio, 0.94; 95% confidence interval, 0.46-1.91). These results indicate that the association with current major depression and a past alcohol use disorder was specific to alcohol dependence.

Considerable care was taken in the analyses to exclude subjects whose current use of alcohol, drugs, or cigarettes could have caused diagnostic confusion regarding intoxication or withdrawal effects. However, a concern could still be raised that the depressions were lingering intoxication or withdrawal effects among subjects who used any of these substances shortly before the beginning of the current 12-month period. To address this concern regarding drugs or cigarettes, the recency of drug and cigarette use was examined in the subjects with major depression during the current 12-month period. Among subjects with major depression in the 12 months prior to the interview who had ever used drugs, 5.1% last used drugs 13 to 23 months prior to the interview, 6.1% last used drugs 24 to 35 months prior to the interview, 6.3% last used drugs 36 to 47 months prior to the interview, and 82.5% last used drugs 48 or more months prior to the interview. The fact that the last use of drugs was more than 2 years prior to the interview in such a high proportion of the subjects with depression indicated that lingering intoxication or withdrawal effects were quite unlikely to have caused the current major depressive episodes. Similar results were found for recency of smoking. Among the subjects with major depression who ever smoked, 5.1% last smoked 13 to 23 months prior to the interview, 5.5% last smoked 24 to 35 months prior to the interview, 6.5% last smoked 36 to 47 months prior to the interview, and 82.9% last smoked 48 or more months prior to the interview. Thus, the episodes of major depression cannot be attributed to intoxication or withdrawal effects occurring among subjects who stopped smoking or using drugs shortly before the current 12-month time frame. This is because the chance that lingering withdrawal effects caused the depressions is minimal due to the extended gap between last use and the recently reported depressions in the large majority of the cases.

As described previously, we included subjects who consumed 1 to 11 drinks in the year prior to the interview in the sample because this drinking could not have been sufficient to cause ongoing intoxication or withdrawal effects. However, to address concerns about lingering alcohol intoxication or withdrawal effects, we removed all subjects who had any alcohol in the 12 months prior to the interview from the sample (n=3496) and reran the analysis. Despite removing such a large number

Table 2. Relationship of Past Alcohol Dependence to Current (Last 12 Months) Major Depression: Results of Logistic Regression Analysis*

Variable	Adjusted OR (95% CI)
Past *DSM-IV* alcohol dependence	4.21 (2.82-6.28)
Past *DSM-IV* alcohol abuse	1.39 (0.68-2.84)
Sex, male	0.44 (0.30-0.64)
Race, African American	0.32 (0.16-0.65)
Education, <high school	0.87 (0.52-1.46)
Marital status, married/living together	0.36 (0.25-0.51)
Age, y	0.96 (0.95-0.97)

*OR indicates odds ratio; CI, confidence interval.

of subjects, the association between past *DSM-IV* alcohol dependence and current major depression remained strong and significant, with an odds ratio of 3.85 (95% confidence interval, 2.05-6.83). To eliminate concerns that the depressions in subjects who abstained were due to lingering intoxication or withdrawal effects among subjects who drank shortly before the beginning of the current 12-month period, we examined recency of drinking among the abstainers. The data indicated that 9.2% of the total subjects who abstained with major depression last drank 13 to 23 months prior to the interview, 16.0% last drank 24 to 35 months prior to the interview, 11.3% last drank 36 to 47 months prior to the interview, and the rest, 63.5%, last drank 48 or more months prior to the interview. These results confirm that lingering alcohol intoxication or withdrawal effects did not cause a syndrome mimicking major depressive disorder in these subjects because all subjects who abstained last drank alcohol 13 or more months prior to the interview and more than 90% of them last drank alcohol 2 or more years prior to the interview.

COMMENT

These data from a large national epidemiological survey indicate that among former drinkers, a past diagnosis of alcohol dependence was associated with more than a 4-fold increase in risk of current or recent (last 12 months) major depressive disorder. The individuals in this study either did not drink at all or did not drink enough in the previous 12 months to experience intoxication or withdrawal effects that could mimic the 2 or more required weeks of mood and symptoms characterizing a major depressive disorder. Further, these results were found among individuals who had neither used drugs nor smoked cigarettes in the 12 months prior to the interview. Most of these subjects last drank more than 2 years prior to the interview, and, if they ever smoked or used drugs, their use of these substances was equally distal from the time of the interview. Thus, the potential confounding effects of numerous other substances were eliminated as possible explanations of the results.

Many methodological problems that characterized earlier studies examining the relationship of major depression to alcoholism were overcome in this study. First, a large group of former drinkers was identified whose current drinking levels were so low that they could not have

produced the intoxication and/or withdrawal effects that mimic the mood and symptoms of major depressive disorder. These subjects were at lifetime risk for alcohol use disorders due to their past drinking, but their recent past could be examined for depression without diagnostic confusion.

Second, this study is based on a large epidemiological survey that used state-of-the-art scientific procedures to select a nationally representative sample. This eliminated the many potential biases that can arise when samples are composed of alcoholic subjects selected from treatment settings.[44] Similarly, samples composed of relatives of patients may also be biased by selection factors, even if the relatives have never been treated themselves. This is because their method of selection, membership in families of treated alcoholic patients, is not designed to produce samples representing the general population. Research on comorbidity in samples of alcoholic patients and their relatives can obviously offer many important findings, but the findings should be confirmed in representative samples whenever possible before being accepted as definitive.

A third strength of this study is the use of 2 clearly defined and nonoverlapping time frames in measuring the episodes of alcohol dependence and major depression: past year and prior to the past year. This approach differs from the approach of the Epidemiological Catchment Area study, the National Comorbidity Survey, and other studies based on lifetime and current diagnoses. For our particular research question, reliance on lifetime or current diagnoses would not have been suitable because simultaneous occurrence of the conditions cannot be ruled in or out within these time frames. The possibility of simultaneous occurrence would not have allowed us to investigate the specific question of misdiagnosis of alcohol intoxication or withdrawal symptoms as an explanation of the depressive syndromes. Only by using sequential, *nonoverlapping* time frames could we rule out alcohol intoxication and withdrawal as constituting the entire cause of the syndromes of depression.

This approach also offered other advantages in answering our research question. It eliminated the need to determine the order of initial onset of alcohol dependence and major depression based on semistructured retrospective timelines of events, often occurring many years in the past. The approach also required the recall of depressions only during a recent period, the last 12 months, increasing the likelihood of accurate recall and reporting. Methodological research[45] suggests that recall for past psychopathological behaviors involving externalizing behavior such as substance use is better than recall for past depression. Therefore, the fact that our research design required recall of recent but not past depressions was an advantage, whereas the reports of past alcohol dependence were less likely to be problematic.

As noted, *DSM-IV* alcohol abuse did not have the same relationship to major depression as *DSM-IV* alcohol dependence. Numerous questions have been raised about the relationship of abuse to dependence, including the concern that abuse is simply a prodromal state to dependence and therefore should be subsumed under the dependence diagnosis. The results of this analysis suggest that such a course would be unwise because this would increase the heterogeneity of the dependence category and weaken or obscure the relationships found.

Neither intoxication nor withdrawal is required for *DSM-III-R*, *DSM-IV*, or other present-day diagnoses of substance use disorders. Some independent or primary depressions defined in earlier studies as occurring prior to the onset of dependence may actually have been substance-induced due to high levels of drinking or drug use that predated the onset of dependence and produced intoxication and/or withdrawal. Also, independent disorders occurring either before or after the onset of dependence but during a period of abstinence do not rule out the occurrence of a substance-induced major depression or transient self-induced depression occurring prior to the onset of dependence. The occurrence of primary disorders may actually increase the chances that a substance-induced depression or transient depressive state will occur. Regardless of etiology, when such depressive states occur in treated patients, they need to be recognized and addressed clinically to deal with the immediate impact of the symptoms.[46]

Our results differ from those of Schuckit et al,[46] who studied major depression in a large sample of treated alcoholic subjects (n=954), their alcoholic relatives who received a lifetime diagnosis of alcoholism (n=1759), and controls (n=919), recruited from medical and dental centers, advertisements, driver's license records, and questionnaires mailed to random subjects at a university. The lifetime rate of independent major depression was actually lower among subjects diagnosed with lifetime alcoholism than among controls, although lifetime rates including both independent and "concurrent" major depression were higher among the alcoholic subjects. The lack of an association between lifetime diagnoses of alcoholism and independent major depression in the Schuckit et al study may be due to several factors, including various selection and other biases among the different groups. However, a more salient difference may pertain to the assessment method. Among probands and their relatives, a lifetime "independent" major depression could only be diagnosed if it predated the initial onset of alcoholism or occurred during a period of complete abstinence. This method assumes that any drinking after the initial diagnosis of alcoholism must have been accompanied by sufficient intoxication or withdrawal effects to cause full major depressive syndromes. Although this is likely to be true for the patients, it is not as likely for the relatives, who constituted about 65% of the cases. Because most of these relatives were never treated for alcoholism, it is possible that a number of them had an early episode of developmentally limited alcoholism that remitted spontaneously without treatment,[47,48] followed by years of normal drinking. (This reasoning is consistent with known differences between treated and untreated drinkers.[49,50]) Among the relatives with this type of history, major depression could not be diagnosed during periods of normal drinking despite the absence of chronic intoxication and withdrawal effects. If there were many cases of this type, then the rates of depression among the relatives would

have been underestimated, leading to an impression that their rates were lower than they actually were. This would reduce the overall rate of independent major depression in the case group compared with controls, producing a result different from the results obtained in the present study.

Of course, having a current depressive disorder does not preclude a history of past depressions. The onset of major depression can follow the onset of alcoholism, especially in men, resulting in a diagnosis of major depression that is chronologically secondary to another disorder, such as alcoholism. We did not examine the timing of the onset of the disorders nor condition the analyses on having a prior history of depression because these steps were not relevant to the specific research question we asked, ie, whether alcohol dependence and major depression were associated even when acute intoxication or withdrawal effects were ruled out as an explanation. The fact that the association was found under these circumstances, and that it was as strong as it was, indicates that the association is not merely an artifact of misdiagnosis and suggests that the association is important to investigate further.

This study does not resolve the question of whether the relationship between *DSM-IV* alcohol dependence and major depressive disorder is indirectly causal (as defined by Swendsen and Merikangas[7]) or arises from shared etiologic factors. The findings are consistent with an indirectly causal explanation if the diagnosis of *DSM-IV* alcohol dependence caused life problems that were either ongoing themselves or that caused an ongoing successive series of difficulties eventually leading to major depression. Shared etiology also cannot be ruled out from these results because the same etiological factors may affect onset but different factors may affect the remission of each disorder, leading to cessation of one but not the other.

The results of the study should be interpreted in light of the methods used. One limitation is the cross-sectional nature of the data. Long-term prospective investigations of very large samples would be more suitable, as they are in studies of any health conditions. However, such studies are very costly and difficult. In the absence of large-scale prospective studies of representative samples, the current investigation offers information that has not been available previously. Another issue is that the information on drinking was based on self-report. Although some subjects may have minimized their levels of current drinking, numerous methodological studies of this issue[51-54] have shown that collateral reports do not necessarily indicate higher drinking levels when compared with self-report. Thus, we do not believe that the present results have been substantially altered by this factor.

Alcohol dependence and major depression are among the most prevalent mental disorders in the general population and have increased in more recent birth cohorts.[2,29,55] If the lifetime co-occurrence of these 2 disorders is not an artifact of misdiagnosis, as suggested by this study, then a better understanding of the reasons for the comorbidity may lead to better prevention and intervention efforts for each disorder. Further, these findings, in conjunction with other findings that depression during abstinence is a risk factor for relapse,[15-17] suggest that treatment for depression should not be withheld from alcoholics in stable remission on the assumption that any depressions in such individuals are due to protracted intoxication or withdrawal effects. Further clinical research is needed to help define the parameters of clinical decision-making in such cases so that the optimal treatments may be offered.

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