Published in final edited form as:
Drug Alcohol Depend. 2010 November 1; 112(1-2): 9–17. doi:10.1016/j.drugalcdep.2010.04.019.

Gender Differences in the Relationship of Internalizing and Externalizing Psychopathology to Alcohol Dependence: Likelihood, Expression and Course

Deborah A. Dawson[a], **Risë B. Goldstein**[a], **Howard B. Moss**[b], **Ting-Kai Li**[c], and **Bridget F. Grant**[a]

[a] Laboratory of Epidemiology and Biometry, Division of Clinical and Biological Research, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda, MD, 20892 USA

[b] Office of the Director, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda, MD, 20892 USA

[c] Duke University School of Medicine, Durham, NC, 27710 USA

Abstract

Objective—To determine whether internalizing and externalizing psychopathology were differentially associated with alcohol dependence in men and women.

Methods—Four categories of lifetime psychopathology were examined: neither internalizing nor externalizing (NINE), internalizing only (IO), externalizing only (EO) and both internalizing and externalizing (BIE). Multivariate models assessed gender differences in the adjusted associations of these categories with the odds of lifetime alcohol dependence in a representative sample of 43,093 U.S. adults 18 and older and with clinical course and expression in a subsample of 4,781 lifetime alcoholics.

Results—The excess odds of lifetime alcohol dependence associated with IO, EO and BIE were significantly greater for women than men, OR = 2.6, 8.8 and 10.7 versus 1.9, 4.0 and 6.5, respectively. Regardless of gender, the ORs were significantly higher for EO than IO and for BIE than EO. Gender differences in the expression and course of alcoholism were most pronounced for the categories of NINE and IO, with men having greater consumption, dependence severity and treatment but less familial alcoholism. Gender variation in the association of psychopathology with the expression and course of alcoholism most evident in the BIE category, where the associations were stronger for women. Lifetime externalizing psychopathology was associated with an increased likelihood of treatment utilization, especially among women.

Conclusions—Findings highlight the need to increase alcoholism screening, prevention and intervention among women with psychopathology, especially externalizing. The greater numbers of

Please send all correspondence to: Deborah A. Dawson, Ph.D., NIAAA/LEB, Room 3071, 5635 Fishers Lane, MSC9304, Bethesda, MD 20892-9304, Telephone: 301-435-2255, Fax: 301-443-1400, ddawson@mail.nih.gov.

The views and opinions expressed in this paper are those of the authors and should not be construed to represent the views of any of the sponsoring organizations, agencies or the U.S. government.

An abbreviated version of this paper was presented at the 2009 Annual Meeting of the Research Society on Alcoholism.

internalizing than externalizing alcoholics emphasizes the need to treat symptoms of depression and anxiety in alcohol treatment settings.

Keywords

alcohol dependence; psychopathology; gender; externalizing; internalizing

1. Introduction

1.1 Comorbidity of alcohol dependence with internalizing and externalizing psychopathology

Numerous studies in general population samples have demonstrated that alcohol dependence is highly comorbid with internalizing and externalizing psychopathology. These broad psychiatric dimensions are generally construed to represent fear and distress domains for the internalizing spectrum and substance abuse and aggression domains for the externalizing spectrum (Kramer et al., 2008; Krueger et al., 2005; Krueger and South, 2009; Slade, 2007). Given that alcohol dependence lies along the continuum of externalizing psychopathology (Krueger et al., 2005; Markon and Krueger, 2004), it is not surprising that its associations with other externalizing disorders exceed its associations with internalizing disorders. According to the 2001–2002 NESARC, the odds of past-year alcohol dependence were increased seven-fold among individuals with antisocial personality disorder (ASPD) (Grant et al., 2004b) and nearly ten-fold among individuals with past-year drug dependence (Stinson et al, 2005). Associations with past-year mood and anxiety disorders were considerably lower, with OR of 4.1 and 2.6 respectively (Grant et al., 2004a). All of these associations were adjusted for sociodemographic characteristics and the other comorbid disorders. Earlier studies of lifetime comorbidity based on the National Comorbidity Survey (NCS) and the Epidemiologic Catchment Area Study (ECA) similarly showed higher OR for disorders characterized by externalizing than internalizing behaviors (Kessler et al., 1997; Regier et al., 1990).

Longitudinal studies of adolescents have provided rich data on the substantial impact of externalizing symptomatology on the likelihood of early initiation of drinking, heavy drinking and alcohol problems within a developmental framework (Englund et al., 2008; King and Chassin, 2007; Merline et al., 2008; Maggs et al., 2008; Sartor et al., 2007). Some adolescent and twin studies have shown a common genetic liability to traits underlying the spectrum of externalizing psychopathology (Dick et al., 2008, 2009; Esposito-Smythers et al., 2009; Hicks et al., 2007a; Iacono and McGue, 2006). Other, though, suggest that some genetic linkages are specific to alcohol dependence (Kendler et al., 2006) and that nongenetic factors may be as important as genetic factors in accounting for co-occurrence of alcohol problems and other externalizing behaviors, at least among women (Hicks et al., 2007b; Knopik et al., 2009).

Although associations during youth and adolescence between alcohol problems and internalizing symptoms generally appear weaker than those with externalizing symptoms (King et al., 2004), a recent review of adolescent studies (Saraceno et al., 2009) identified numerous studies in which alcohol problems preceded the development of internalizing symptomatology and vice versa (e.g., Hahesy et al., 2002; Kuo et al., 2006; Trim et al., 2007; White et al., 2001). As is the case with externalizing symptomatology, the co-occurrence of alcohol problems and interlizing symptomatology shows evidence of both shared genetic and nongenetic factors (Kendler et al., 2003; Middlethorp et al., 2005; Windle and Davies, 1999; see also review in Hopfer et al., 2003).

1.2 Gender differences in the comorbidity of alcohol dependence with internalizing and externalizing psychopathology

Past studies have reported gender differences in alcoholic subtypes, including an excess of women in internalizing subtypes and an excess of men in antisocial/externalizing subtypes (Epstein et al., 2002; Moss et al., 2007; Carpenter and Hasin, 2001; Pombo and Lesch, 2009). These differences correspond to gender differences in the prevalence of internalizing and externalizing disorders in the total population (Grant et al., 20041, 2004b, Stinson et al., 2005). The few studies that have examined gender differences in the comorbidity of alcohol dependence have reported disparate findings. Data from the NCS revealed that lifetime associations of alcohol dependence with prior drug use disorder and ASPD (externalizing psychopathology) were twice as great for women as for men, although the difference was significant only for drug use disorder. There were no significant gender differences in the NCS lifetime associations of alcohol dependence with prior mood and anxiety disorders (Kessler et al., 1997). Data on 12-month disorders from the European Study of the Epidemiology of Mental Disorders (ESEMeD) showed alcohol dependence was more strongly associated with GAD among men but more strongly associated with major depression among women (Alonso et al., 2004). Neither the NCS nor the ESEMeD associations were adjusted for confounding effects of sociodemographic characteristics or other comorbidity. A factor analysis of the overall dimensions of internalizing and externalizing psychopathology (the latter including alcohol dependence), using a twin study design that eliminated many potential sources of confounding, found that the best fitting model reflected gender invariance in comorbidity of the two dimensions (Kramer et al., 2008).

1.3 Associations of internalizing and externalizing psychopathology with expression and course of alcohol dependence

Studies in treatment and population samples have confirmed that alcoholic subtypes marked by psychopathology are more severely dependent. Epstein et al.(2002) found that Type B alcoholic patients, with higher rates of psychopathology as per Babor et al. (1992), consumed more alcohol, had higher dependence screening scores and had more medical, physical and social consequences than Type A patients. Windle and Scheidt (2004) reported increased levels of consumption, physical and social consequences and lifetime severity in subtypes characterized by externalizing and internalizing psychopathology. In another treatment sample, the odds of poor psychological quality of life at intake were more than quadrupled by psychiatric comorbidity, independent of severity of dependence (Lahmek et al., 2009). In the general population, Moss et al. (2007) reported the highest levels of consumption in the young antisocial and severe chronic alcoholic subtypes. Both subtypes were characterized by high levels of externalizing disorder, the latter also by high levels of internalizing disorder. In another general population sample, Carpenter and Hasin (2001) reported higher levels of consumption, severity, treatment utilization and dependence among Dionysian than Apollonian problem drinkers, with the former characterized by higher levels of psychopathology, especially externalizing.

1.4 Gender differences in associations of internalizing and externalizing psychopathology with expression and course of alcohol dependence

Few studies have examined gender variation in the association of internalizing and externalizing psychopathology with the *expression* of alcohol dependence. Among alcohol dependent individuals participating in the Collaborative Studies on the Genetics of Alcoholism, Schuckit et al. (1995) found no gender differences in the multiple clinical dimensions used to classify Type A-Type B alcoholics or in other clinical characteristics. However, they did not formally test for interactions between gender and subtype; nor was this done in the initial study defining the Type A-Type B typology (Babor et al., 1992).

1.5 Limitations of existing research and goals of present analysis

Much remains to be clarified about the associations of internalizing and externalizing psychopathology with the likelihood, expression and course of alcohol dependence and how they vary by gender. The few studies that have directly addressed gender differences did not adjust for potential confounders, e.g., other comorbid conditions, which could increase the risk of spurious associations (Grant et al., 2009). Moreover, gender differences in the association of alcohol dependence with other specific disorders cannot be presumed to extend to the broader categories of internalizing and externalizing psychopathology. The mediating roles of drinking *per se* and consumption level have received little if any attention, despite the literature linking externalizing behavior with early onset and heavy drinking. Studies of the expression and course of alcoholism based on treatment samples cannot be extrapolated to the general population. Treatment samples are over-representative of individuals with multiple disorders (Carroll et al., 2006), and any gender differences in treatment utilization could affect interactions between gender and psychopathology. Given that only about one quarter of alcoholics access any type of alcohol treatment (Dawson et al., 2006), data from alcohol treatment samples cannot be assumed to reflect the experience of the majority of alcohol-dependent individuals.

To address these gaps in the literature, this paper uses data from a nationally representative sample of U.S. adults to examine the associations of internalizing and externalizing psychopathology with the likelihood, expression and course of DSM-IV alcohol dependence and to determine whether these associations differ for men and women. The specific aims of the paper are to determine, in a nationally representative sample of U.S. adults: 1) whether the distribution of internalizing and externalizing psychopathology in lifetime alcoholics varies by gender; 2) whether men and women differ in the extent to which lifetime alcohol dependence is associated with lifetime internalizing and externalizing psychopathology, other factors held constant; 3) whether the potentially mediating effects of being a drinker and volume of consumption affect gender differences in comorbidity; 4) whether the expression and course of alcoholism among individuals with different types of psychopathology vary by gender, and 5) whether the associations of internalizing and externalizing psychopathology with the expression and course of alcoholism vary by gender after controlling for potential confounders.

2. Methods

2.1 Sample

The data used in this analysis came from Wave 1 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), designed by the National Institute on Alcohol Abuse and Alcoholism. The 2001–2002 Wave 1 NESARC sample (n = 43,093 including 18,518 men and 24,575 women, response rate = 81.0%) represented U.S. adults 18 years or older residing in households and noninstitutional group quarters in all 50 states and the District of Columbia. Some analyses were restricted to lifetime drinkers (n=34,827 including 16,274 men and 18,553 women) or individuals with lifetime alcohol dependence (n=4,781 including 2,974 men and 1,807 women). The NESARC data were weighted to reflect design characteristics, including oversampling of Blacks, Hispanics and young adults, and nonresponse relative to sociodemographic characteristics (Grant et al., 2001a). Weighted data were further adjusted to match the civilian, noninstitutionalized population of the United States on socioeconomic variables based on the 2000 Decennial Census. Data were collected in personal interviews, using a computer-assisted survey instrument administered by lay interviewers. All potential respondents were informed in writing about the nature of the survey, the statistical uses of the survey data, the voluntary aspect of their participation and the Federal laws that rigorously provide for the confidentiality of identifiable survey information. Only respondents consenting to participate after receiving this information were interviewed. The

research protocol, including informed consent procedures, received full ethical review and approval from the U.S. Census and the U.S. Office of Management and Budget.

2.2 Measurement of DSM-IV alcohol dependence

DSM-IV alcohol dependence (American Psychiatric Association, 1994) was measured using the Alcohol Use Disorders and Associated Disabilities Interview Schedule - DSM-IV Version (AUDADIS-IV) (Grant et al., 2001b). To be classified with lifetime alcohol dependence, respondents had to endorse one or more symptoms of at least three of the seven dependence criteria (tolerance, withdrawal, persistent desire or attempts to reduce or stop drinking, much time spent drinking or recovering from drinking, reduction/cessation of important activities in favor of drinking, impaired control over drinking, and continued use despite physical or psychological problems), and some of these experiences had to happen within the same 1-year period (Grant et al., 2004a).

2.3 Measurement of externalizing and internalizing psychopathology

Four categories of lifetime psychopathology were considered in this analysis: 1) neither internalizing nor externalizing (NINE); 2) internalizing only (IO); 3) externalizing only (EO); and 4) both internalizing and externalizing (BIE). This categorization corresponds to one of the most strongly validated alcohol typologies considered in a study by Penick et al.(1999). In this study, internalizing psychopathology comprised lifetime major depression, bipolar I and II disorders, dysthymia, panic disorder with or without agoraphobia, specific or social phobia and generalized anxiety disorder. Externalizing psychopathology comprised antisocial personality disorder (ASPD) and lifetime illicit drug dependence.

All psychiatric disorders were defined in accordance with DSM-IV criteria. Mood and anxiety disorders ruled out substance- or illness-induced disorders, and major depression also ruled out bereavement. ASPD and other personality disorders were defined to reflect pervasive, lifelong patterns of functioning, excluding behavior during periods of depression, mania, anxiety, heavy drinking, drug use, alcohol or drug withdrawal, or physical illness. Drug dependence was defined using algorithms similar to those for alcohol dependence and reflected dependence on any of 10 types of drugs. Full details of the derivation of NESARC diagnoses of mood, anxiety, substance use and personality disorders have been published elsewhere (Grant et al., 2004a, 2004b; Stinson et al., 2005).

2.4 Measurement of clinical presentation and course of alcohol dependence

All measures were based on self-report. Consumption measures reflected self-identified period of heaviest drinking. Average daily volume of ethanol intake was estimated on the basis of overall frequency of drinking, usual and largest quantities of drinks consumed, and frequencies of drinking the largest quantity and 5+ drinks for all types of alcoholic beverage combined. Frequencies were coded from categories into days per year; largest quantity of drinks consumed in a single day was asked in open-ended format. Age at first drink excluded small tastes and sips, and onset of dependence was the age when symptoms began to co-occur. Density of familial alcoholism (Stoltenberg et al., 1998) was calculated by adding a value of 0.5 for each alcoholic parent and 0.25 for each alcoholic grandparent reported by the respondent (range = 0 to 2). Episodes of dependence required an interval of one year without any symptoms between episodes. Wave 1 remission was defined as no symptoms of abuse or dependence in the year preceding the Wave 1 interview. Lifetime treatment comprised 13 different sources, including 12-step or other mutual help programs.

2.5 Reliability and validity of measures

AUDADIS-IV alcohol diagnoses have demonstrated good reliability and validity in test-retest and other studies, including clinical reappraisals (Grant et al., 2003; Canino et al., 1999; Cottler et al., 1997; Hasin et al., 1997; Muthen et al., 1993; Nelson et al., 1999; Pull et al., 1997). Test-retest reliability for family history, alcohol consumption, use of tobacco, marijuana and cocaine, drug use disorders, and other Axis I disorders have been good to excellent, and personality disorders have demonstrated levels of reliability comparable to those reported in the clinical literature (Cottler, 1997; Grant et al., 1995, 2003; Ruan et al., 2008).

2.6 Analysis

Statistical analyses employed SUDAAN software (Research Triangle Institute, 2001) to account for complex design characteristics. Gender differences in unadjusted proportions and means were assessed using t-tests. Multivariate logistic regression models assessed the odds of lifetime alcohol dependence with respect to lifetime psychopathology, controlling for sociodemographic characteristics, lifetime drug abuse and nicotine dependence, personality disorders other than ASPD, and any significant interactions between gender and these covariates. Gender interactions were tested within a single model containing men and women; gender-specific odds ratios (OR) were presented regardless of whether significantly different or not. The same approach was followed in multivariate linear and logistic regression models examining the associations between psychopathology and clinical presentation and course indicators among lifetime alcoholics (n=4,781). Some variables were topcoded to reduce skew: volume of ethanol intake to 14.4 ounces, largest quantity of drinks to 36, age at onset of dependence to 45 years and interval to onset of dependence to 25 years. This involved the uppermost 3% to 5% of reported values for these variables. Post-hoc t-tests were conducted to assess the significance of differences in ORs and beta parameters across type of psychopathology and different populations.

3. Results

3.1 Unadjusted associations of lifetime internalizing and externalizing psychopathology with alcohol dependence

Most U.S. adults -- three quarters of men and nearly two thirds of women -- had no history of either internalizing or externalizing psychopathology, the latter excluding alcohol dependence (top panel of Table 1). Among those with some psychopathology, the vast majority had internalizing only (IO), 17.7% of men and 31.3% of women, compared to 3.1% and 0.7%, respectively, for externalizing only (EO) and 4.5% and 2.6% for both internalizing and externalizing (BIE). IO was almost twice as common among women as among men, whereas EO was about four times as common and BIE about twice as common among men (all $p<.001$). All types of lifetime psychopathology were considerably more prevalent ($p<.001$) among individuals with DSM-IV lifetime alcohol dependence (middle panel of Table 1) than in the total population. Among lifetime alcoholics, IO continued to be more prevalent among women and EO more prevalent among men ($p<.001$), but male and female lifetime alcoholics were equally likely to have BIE.

For both men and women, the prevalence of lifetime alcohol dependence was lowest among individuals with neither internalizing nor externalizing psychopathology (NINE), higher for those with IO, higher still for those with EO and highest for those with BIE (bottom panel of Table 1). All pair-wise differences by type of psychopathology were statistically significant ($p<.05$) for both men and women. Within all categories of psychopathology other than EO, the prevalence of lifetime alcohol dependence was significantly higher among men than women ($p<.001$).

3.2 Adjusted associations of lifetime internalizing and externalizing psychopathology with alcohol dependence

Following adjustment for sociodemographic factors and other comorbid conditions, the odds of lifetime alcoholism were increased among men by a factor of 1.9 in association with IO, by a factor of 4.0 in association with EO and by a factor of 6.5 in association with BIE (Table 2). Among women, the comparable ORs were 2.6, 8.8 and 10.7, respectively, all significantly higher than the comparable ORs for men (p = .002 to .006). The magnitudes of the ORs were not significantly different for lifetime drinkers than in the total population, but the significance of the gender differences was weaker (p = .023 to .099). After controlling for volume of consumption, the ORs for externalizing (but not internalizing) psychopathology were generally reduced in magnitude, as was the significance of most of the gender differences (p = .015 to . 259). However, even holding constant volume of consumption, men and women with internalizing and/or externalizing psychopathology were at two- to five-fold increased risk of lifetime alcohol dependence, and the increase in risk was generally greater for women than men (the exception being in the BIE category).

3.3 Unadjusted associations of lifetime internalizing and externalizing psychopathology with clinical course and presentation of alcohol dependence

There were numerous gender differences (p<.05) in the expression and course of alcohol dependence among individuals with NINE or with IO (Table 3). Men had a greater volume of alcohol consumption, frequency of overall and heavy drinking and largest quantity of drinks consumed in a single day. Men in these categories also had more lifetime AUD symptoms and were more likely to have received alcohol treatment (including 12-step participation), but they reported a lower density of familial alcoholism. Among lifetime alcoholics with EO, the only significant gender differences were a greater volume of ethanol intake, frequency of heavy drinking and largest quantity of drinks among men. Among alcoholics with BIE, frequency of heavy drinking and largest quantity of drinks (but not volume of consumption) were greater among men, whereas women had a greater density of familial alcoholism and a shorter interval from first drink to onset of dependence. Irrespective of psychopathology, there were no gender differences among lifetime alcoholics in age at onset of dependence, early initiation of drinking, multiple episodes of dependence and remission from dependence.

In general, men and women with EO and BIE had higher levels of consumption, familial alcoholism, dependence severity and alcohol treatment than those with IO or NINE (p<.05). Individuals with IO had a higher density of familial alcoholism and greater number of AUD symptoms than those with NINE (p<.05), but they did not demonstrate any excess consumption. Interestingly, the presence of psychopathology was not associated with the likelihood of remission.

3.4 Adjusted associations of lifetime internalizing and externalizing psychopathology with clinical course and presentation of alcohol dependence

After adjusting for sociodemographics and other comorbidity, the associations of internalizing and externalizing psychopathology with the expression and course of alcoholism showed very few gender differences for the categories of IO and EO (Table 4). IO had a negative association with largest quantity of drinks that was limited to males, and EO more strongly increased the odds of alcohol treatment among women than men (OR of 5.5 versus 2.1, p=.009). In contrast, BIE showed stronger positive associations (p<.05) for women than men with most measures of alcohol consumption, as well as with early and rapid onset of alcoholism and the likelihood of alcohol treatment (OR of 4.2 versus 2.4, p=.024).

Men and women with IO showed almost no significant adjusted differences in expression and course of alcohol dependence compared to those with NINE (Table 4). Those with EO or BIE

demonstrated many more significant differences relative to those with NINE, including greater consumption, earlier onset of dependence, more familial alcoholism and AUD symptoms, more early initiation of drinking and increased treatment utilization ($p<.05$). Among men with EO, there was a modest increase in the likelihood of remission. The magnitude of the OR was similar for women with EO (1.4 versus 1.6 for men), but it fell short of significance ($p>.05$).

4. Discussion

4.1 Differences by gender

This study provided the first nationally representative U.S. estimates of gender differences in the lifetime comorbidity and clinical expression of alcohol dependence as a function of internalizing and externalizing psychopathology. Consistent with clinical and general population data (Epstein et al., 2002; Carpenter and Hasin, 2001; Pombo and Lesch, 2009; Baumeister and Harter, 2007; Kessler et al., 2005), this study found that men were overrepresented among individuals with externalizing psychopathology and that women were overrepresented among individuals with internalizing psychopathology. The male excess prevalence of externalizing psychopathology was reduced among lifetime alcoholics; in fact, male and female alcoholics were equally likely to have combined internalizing and externalizing psychopathology. Consistent with this reduction and in line with Kessler et al. (1997), we confirmed a stronger association between externalizing psychopathology and alcohol dependence among women compared to men. Unlike Kessler et al., we also found a stronger association between internalizing psychopathology and alcohol dependence among women. This disparity likely reflects the larger sample size and greater statistical power of the NESARC sample, as Kessler et al. did find nonsignificantly higher OR for the associations of alcohol dependence with all affective and all anxiety disorders among women. Although the higher OR among women for the association of alcohol dependence with I) could be seen as contradictory of the gender invariant associations between the overall internalizing and externalizing dimensions reported by (Kramer et al., 2008), this discrepancy might be explained by genetic linkages specific to alcohol dependence rather than to the entire externalizing spectrum (Kendler et al., 2006).

The gender differential in adjusted associations of alcohol dependence was largest for individuals with externalizing psychopathology only (EO), with an OR of 8.8 for women versus 4.0 for men. This may reflect gender differences in the composition of externalizing psychopathology. Among individuals with EO, the prevalence of ASPD was higher among men (75% versus 48% for women), whereas the prevalence of drug dependence was higher among women (58% versus 32% for men). As adjusted comorbidity rates for alcohol dependence are higher for drug dependence than ASPD (Hasin et al., 2007), this may account for the higher OR for women than men with EO and suggests that a common genetic liability for addiction may more strongly increase the risk for alcohol dependence than do the excessive adolescent drinking and any shared genetic risk associated with ASPD.

This study found gender differences in both the unadjusted and adjusted associations of psychopathology with the expression and course of alcoholism. In absolute terms, male alcoholics drank more heavily than female alcoholics, irrespective of psychopathology, just as they do in the total population (Dawson, 2000). In contrast, female alcoholics tended to report a greater density of familial alcoholism, again reflecting differentials observed in the total population (Dawson and Grant, 1998). Other differences observed primarily among alcoholics with NINE or IO included more lifetime AUD symptoms and a greater likelihood of lifetime alcohol treatment among males.

In contrast, gender differences in the adjusted associations of psychopathology with the expression and course of alcoholism were primarily restricted to the category of BIE, which

was more strongly associated with heavy drinking and early- and rapid-onset dependence among women. The ORs for women with BIE were generally higher (though not always significantly so) than those for women with EO, but this was not the case for men. It is not clear from this study whether this reflects a greater sensitivity among women to the total number of comorbid disorders (by definition at least two among individuals with BIE compared to only one required for IO and EO) or to something specific about the combination of internalizing and externalizing. One gender difference that extended to all externalizing alcoholics, both EO and BIE, was a stronger association with alcohol treatment among women. This may again reflect gender differences in type of externalizing psychopathology, i.e., women's greater prevalence of drug dependence having led to increased likelihood of combined alcohol and drug treatment.

4.2 Differences with respect to type of psychopathology

Confirming prior findings (Carpenter and Hasin, 2001; Epstein et al., 2002; Grant et al., 2004a, 2004b; Kesslet et al., 1997; Moss et al., 2007; Pombo and Lesch, 2009; Penick et al., 1999; Regier et al., 1990; Windle and Scheidt, 2004), we found that the adjusted associations with lifetime alcohol dependence were lowest for IO, higher for EO and highest for BIE. The associations between psychopathology and dependence were not significantly reduced among lifetime drinkers, indicating that the increased risk of dependence associated with internalizing and externalizing psychopathology does not solely reflect an increased probability of being a drinker. The reduction in the ORs for externalizing psychopathology after controlling for volume of consumption suggests that the early and heavy drinking associated with externalizing symptomatology (Englund et al., 2008; King and Chassin, 2007; Merline et al., 2008; Maggs et al., 2008; Sartor et al., 2007) mediates some of the increased risk of alcohol dependence. However, the positive associations that remained even after controlling for volume of consumption suggest possible roles of shared genetic liability or residual associations between externalizing psychopathology and drinking pattern, drinking motivation, drinking expectancies and/or behavioral response to drinking (Hicks et al., 2007b, Kendler et al., 2006; Klopnik et al., 2009).

Alcoholic phenotypes based on psychopathology differed in terms of expression and course, primarily reflecting the presence or absence of externalizing psychopathology. The greatly increased consumption levels among alcoholics with externalizing psychopathology are consistent with numerous adolescent, general population and clinical studies (King and Chassin, 2007; Merline et al., 2008; Maggs et al., 2008; Sartor et al., 2007; Epstein et al., 2002; Windle and Scheidt, 2004; Carpenter and Hasin, 2001) and corresponded to a substantial increase in the number of AUD symptoms. Surprisingly, externalizing alcoholics were no less likely to have achieved remission by the time they were interviewed than those without externalizing psychopathology; in fact, male alcoholics with EO were 60% *more* likely to be in remission than those with NINE. This seemingly anomalous finding is consistent with Zucker's (1986) developmentally limited alcoholic subtype, which is characterized by maturing out of heavy drinking and drinking problems with the adoption of adult role responsibilities but may also reflect the fact that externalizing alcoholics were more likely than those with NINE or IO to have received alcohol treatment.

4.3 Study limitations and clinical implications

A number of limitations indicate caution in interpreting this study's results. First, all self-report data are subject to unintentional (e.g., through recall error) or intentional misreporting. If the ability or willingness to report AUD symptoms were positively correlated with recall or reporting of other mental disorders, this could upwardly bias estimates of their associations. Despite evidence that social desirability bias is inversely related to reporting of both substance abuse (Cox et al., 1994; Davis et al., 2010; Johnson and Fendrich, 2005; Welte and Russell,

1993) and other psychopathology (Kuentzel et al., 2008; Logan et al., 2008; McEwan et al., 2009), we are unaware of any evidence that this form of bias contributes to exaggerated associations between the two. However, several recent studies have reported slightly increased OR between psychological and somatic conditions/symptoms resulting from social desirability bias (Baumeister et al., 2010; Horn et al., 2010; Ladwig et al., 2010). Fortunately, social desirability bias and its associations with reporting alcohol use and problems do not appear to vary by sex (Welte and Russell, 1993; Kolarcik et al., 2009); accordingly, there is no evidence to suggest that gender differences in associations between alcohol dependence and psychopathology would be affected by this form of reporting bias.

Second, the lifetime time frame entails the risk that comorbid conditions may not have occurred during the same time period. The onset internalizing and externalizing disorders may have occurred after the onset – or even after remission – of alcohol dependence. Thus, their associations with alcohol dependence reflect an increased likelihood of having ever been dependent rather than an increased risk of becoming dependent as a function of antecedent or concurrent psychopathology. This limits the usefulness of the study results for delimiting the role of comorbid psychopathology in the etiology of alcohol dependence and, perhaps even more importantly, for making clinical recommendations related to screening and treatment.

This study also may be limited by our definitions of internalizing and externalizing psychopathology. Many studies have included the milder disorders of drug abuse, conduct disorder and adult antisocial behavior in the externalizing spectrum (Krueger et al., 2005); others (Farmer et al., 2009) have included attention-deficit/hyperactivity disorder (ADHD). Moreover, some studies have post-traumatic stress disorder (PTSD) in the internalizing spectrum but have excluded bipolar disorders (Kramer et al., 2008; Slade, 2007). To determine the impact of our definitions, we examined the effect of alternative definitions on the associations of internalizing and externalizing psychopathology with lifetime alcohol dependence. Because the NESARC did not measure PTSD and ADHD until the 2004–2005 Wave 2 follow up interview, we conducted the reanalysis with the Wave 2 sample (n=34,653 representing 86.7% of Wave 1 respondents eligible for reinterview, see Grant et al., 2007). After first verifying that the original definitions produced equivalent results in the Wave 2 sample, we added drug abuse, conduct disorder, adult antisocial behavior not preceded by conduct disorder (Goldstein et al., 2007) and ADHD into the externalizing dimension. We added PTSD into the internalizing dimension but removed bipolar disorder. The resulting ORs for IO, EO and BIO (1.8, 4.6 and 6.1 for men, 2.3, 6.4 and 9.3 for women) all lay within the 95% confidence intervals of our original estimates and all gender differences remained statistically significant ($p<.05$). Thus, the results of this study appear to be fairly robust with respect to the definitions of internalizing and externalizing psychopathology.

Despite its limitations, this study provided confirmation at the general population level of the importance of internalizing and externalizing psychopathology in discriminating among alcoholic phenotypes, and it revealed significant gender differences in phenotypes defined by type of disorder. It showed that whereas alcohol dependence and externalizing psychopathology are more common among men than women, their association is greater among women. Bearing in mind the uncertainties imposed by studying lifetime comorbidity, these findings suggest the need to increase alcoholism screening, prevention and intervention among women with externalizing psychopathology, a highly vulnerable group with high rates of alcohol dependence nearly comparable to those of their male counterparts. Despite externalizing psychopathology having the stronger association with alcohol dependence among both men and women, internalizing psychopathology was far more prevalent among lifetime alcoholics. Thus, the emphasis on the externalizing psychopathology in the alcohol literature should not obscure the importance of addressing symptoms of mood and anxiety disorders in alcoholism treatment settings. Finally, among alcoholics with no psychopathology

or internalizing psychopathology only, especially women, our data indicate the need for more active screening and referral in various treatment/primary care settings to match the alcohol treatment levels of alcoholics with externalizing psychopathology.

References

Alonso J, Angermeyer MC, Berbert S, Bruffearts R, Brugha TS, Bryson H, deGirolamo G, de graaf R, Demyttenaere K, Gasquet I, Haro JM, Katz SJ, Kessler RCk, Kovess V, Lépine JP, Ormel G, Polidori G, Russo LJ, Vilagut G. 12-month comorbidity patterns and associated factors in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. Acta Psychiatr Scand 2004;109:28–37.

American Psychiatric Association. The Diagnostic and Statistical Manual of Mental Disorders. 4. American Psychiatric Association; Washington, DC: 1994.

Babor TF, Hofmann M, DelBoca FK, Hesselbrock V, Meyer RE, Dolinsky ZS, Rounsaville B. Types of alcoholics, I. Evidence for an empirically derived typology based on indicators of vulnerability and severity. Arch Gen Psychiatry 1992;49:599–608. [PubMed: 1637250]

Baumeister H, Kriston L, Bengel J, Härter M. High agreement of self-report and physician-diagnosed somatic conditions yields limited bias in examining mental-physical comorbidity. J Clin Epidemiol 2010;63:558–565. [PubMed: 19959329]

Baumeister H, Härter M. Prevalence of mental disorders based on general population surveys. Soc Sci Paychiatr Epidemiol 2007;42:537–546.

Canino GJ, Bravo M, Ramirez R, Febo V, Fernandez R, Hasin DS. The Spanish Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability and concordance with clinical diagnoses in a Hispanic population. J Stud Alcohol 1999;60:790–799. [PubMed: 10606491]

Carpenter KM, Hasin DS. Reliability and discriminant validity of the TypeI/II and Type A/B alcoholic subtype classifications in untreated problem drinkers: a test of the Apollonian – Dionysian hypothesis. Drug Alcohol Depend 2001;63:51–67. [PubMed: 11297831]

Carroll, RJ.; Ruppert, D.; Stefanski, LA.; Crainiceanus, CM. Measurement Error in Nonlinear Models. A Modern Perspective. 2. Chapman and Hall; Boca Raton, FL: 2006.

Cottler LB, Grant BF, Blaine J, Mavreas V, Pull CB, Hasin DS, Compton WM, Rubio-Stipec M, Mager D. Concordance of DSM-IV alcohol and drug use disorder criteria and diagnoses as measured by the AUDADIS-ADR, CIDI and SCAN. Drug Alcohol Depend 1997;47:195–205. [PubMed: 9306045]

Cox BJ, Swinson RP, Direnfeld DM, Bourdeau D. Social desirability and self-reports of alcohol abuse in anxiety disorder patients. Behav Res Ther 1994;32:173–178.

Davis CG, Thake J, Vilhena N. Social desirability biases in self-reported alcohol consumption and harms. Addict Behav 2010;35:302–311. [PubMed: 19932936]

Dawson DA. Drinking patterns among individuals with and without DSM-IV alcohol use disorders. J Stud Alcohol 2000;61:111–120. [PubMed: 10627104]

Dawson DA, Grant BF. Family history of alcoholism and gender: their combined effects on DSM-IV alcohol dependence and major depression. J Stud Alcohol 1998;59:97–106. [PubMed: 9498321]

Dawson DA, Grant BF, Stinson FS, Chou PS, Huang B, Ruan WJ. Recovery from DSM-IV alcohol dependence: United States, 2001–2002. Addiction 2006;100:281–292. [PubMed: 15733237]

Dick DM, Aliev F, Wang JC, Grucza RA, Schuckit M, Kuperman S, Kramer J, Hinrichs A, Bertelsen S, Budde JP, Hesselbrock V, Porjesz B, Edenberg HJ, Beirut LJ, Goate A. Using dimensional models of externalizing psychopathology to aid in gene identification. Arch Gen Psychiatry 2008;65:310–318. [PubMed: 18316677]

Dick DM, Latendresse SJ, Lansford JE, Budde JP, Goate A, Dodge AK, Petit GS, Bates JE. Role of GABRA2 in trajectories of externalizing behavior across development and evidence of monitoring by parental monitoring. Arch Gen Psychiatry 2009;66:649–657. [PubMed: 19487630]

Englund MM, Egeland B, Oliva EM, Collins WA. Childhood and adolescent predictors of heavy drinking and alcohol use disorders in early adulthood: a longitudinal developmental analysis. Addiction 2008;103 (Suppl):23–25. [PubMed: 18426538]

Epstein EE, Labouvie E, McCrady BS, Jensen NK, Hayaki J. A multi-site study of alcohol subtypes: classification and overlap of unidimensional and multidimensional typologies. Addiction 2002;97:1041–1053. [PubMed: 12144607]

Esposito-Smythers C, Spirito A, Rizzo C, McGeary JE, Knopik VS. Pharmacol Biochem Behav 2009;93:306–312. [PubMed: 19344737]

Goldstein RB, Dawson DA, Saha TD, Ruan WJ, Compton WM, Grant BF. Antisocial behavioral syndromes and DSM-IV alcohol use disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Alcohol Clin Exp Res 2007;31:814–828. [PubMed: 17391341]

Grant BF, Dawson DA, Stinson FS, Chou PS, Kay W, Pickering RP. The Alcohol Use Disorder and Associated Disabilities Schedule-IV (AUDADIS-IV): Reliability of alcohol consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. Drug Alcohol Depend 2003;71:7–16. [PubMed: 12821201]

Grant, BF.; Dawson, DA.; Hasin, DS. The Alcohol Use Disorders and Associated Disabilities Interview Schedule - Version for DSM-IV (AUDADIS-IV). National Institute on Alcohol Abuse and Alcoholism; Bethesda, MD: 2001b.

Grant BF, Goldstein RB, Chou SP, Huang B, Stinson FS, Dawson DA, Saha TD, Smith SM, Pulay AJ, Pickering RP, Ruan WJ, Compton WM. Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. Molec Psychiatr 2009;14:1051–1066.

Grant BF, Harford TC, Dawson DA, Chou PS, Pickering RP. The alcohol use disorder and associated disabilities schedule (AUDADIS): reliability of alcohol and drug modules in a general population sample. Drug Alcohol Depend 1995;39:37–44. [PubMed: 7587973]

Grant, BF.; Kaplan, K.; Shepard, J.; Moore, T. Source and Accuracy Statement for Wave 1 of the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions. National Institute on Alcohol Abuse and Alcoholism; Bethesda, MD: 2001a.

Grant BF, Stinson FS, Dawson DA, Chou P, Dufour MC, Compton W, Pickering RP, Kaplan KS. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders. Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2004a;61:807–816. [PubMed: 15289279]

Grant BF, Stinson FS, Dawson DA, Chou SP, Ruan WJ, Pickering RP. Co-occurrence of 12-month alcohol and drug use disorders and personality disorders in the United States. Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2004b; 61:361–368. [PubMed: 15066894]

Grant, BF.; Kaplan, KK.; Stinson, FS. Source and Accuracy Statement: The Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. National Institute on Alcohol Abuse and Alcoholism; Bethesda, MD: 2007.

Hahesy AL, Wilens TE, Biederman J, Van Patten SL, Spencer T. Temporal associations between childhood psychopathology and substance use disorders: findings from a sample of adults with opioid or alcohol dependency. Psychiatry Res 2002;109:245–253. [PubMed: 11959361]

Hasin, DS.; Muthen, B.; Grant, BF. The dimensionality of DSM-IV alcohol abuse and dependence: Factor analysis in a clinical sample. In: Vrasti, R., editor. Alcoholism: New Research Perspectives. Hogrefe and Hubner; Gottingen, Germany: 1997. p. 27-39.

Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability and comorbidity of alcohol abuse and dependence in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2007;64:830–842. [PubMed: 17606817]

Hicks BM, Bernat E, Malone SM, Iacono WG, Patrick CJ, Krueger RF, McGue M. Genes mediate the association between P3 amplitude and externalizing disorders. Psychophysiology 2007a;44:98–105. [PubMed: 17241145]

Hicks BM, Blonigen DM, Kramer MD, Kreuger RF, Patrick CJ, Iacono WG, McGue M. Gender differences and developmental change in externalizing disorder from late adolescence to early adulthood: A longitudinal twin study. J Abnorm Psychol 2007b;116:433–447. [PubMed: 17696699]

Hopfer CJ, Crowley TJ, Hewitt JK. Review of twin and adoption studies of adolescent substance use. J Am Acad Child Adolesc, Psychiatry 2003;42:710–719. [PubMed: 12921479]

Horn O, Sloggett A, Ploubidis GB, Hull L, Hotopf M, Wessely S, Rona RJ. Upward trends in symptom reporting in the US Armed Forces. Eur J Epidemiol 2010;25:87–94. [PubMed: 20024604]

Iacono WG, McGue M. Association between P3 event-related potential amplitude and adolescent problem behavior. Psychophysiology 2006;43:365–469.

Johnson T, Fendrich M. Modeling sources of self-report bias in a survey of drug use epidemiology. Ann Epidemiol 2005;15:381–389. [PubMed: 15840552]

Kendler KS, Prescott CA, Myers J, Neale MC. The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. Arch Gen Psychiatry 2003;60:929–937. [PubMed: 12963675]

Kendler KS, Kuo PH, Webb BT, Kalsi G, Neale MC, Sullivan PF, Walsh D, Patterson DG, Riley B, Prescott CA. A joint genomewide linkage analysis of symptoms of alcohol dependence and conduct disorder. Alcohol Clin Exp Res 2006;30:1972–1977. [PubMed: 17117961]

Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62:617–627. [PubMed: 15939839]

Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC. Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. Arch Gen Psychiatry 1997;54:313–321. [PubMed: 9107147]

King KM, Chassin L. A prospective study of the effects of age of initiation of alcohol and drug use on young adult substance dependence. J Stud Alcohol Drugs 2007;68:256–265. [PubMed: 17286344]

King SM, Iacono WG, McGue M. Childhood externalizing and internalizing psychopathology in the prediction of early substance use. Addiction 2004;99:1548–1559. [PubMed: 15585046]

Knopik VS, Heath AC, Bucholz KK, Madden PAF, Waldron M. Genetic and environmental influences on externalizing behavior and alcohol problems in adolescence: A female twin study. Pharmacol Biochem Behav 2009;93:313–321. [PubMed: 19341765]

Kolarcik P, Madarascova, Geckova A, Orosova O, van Dijk JP, Reijneveld SA. Predictors of health-endangering behavior among Roma and non-Roma adolescents in Slovakia by gender. J Epidimiol Community Health. 2009 E-pub ahead of print Nov 12.

Kramer MD, Krueger RF, Hicks BM. The role of internalizing and externalizing liability factors in accounting for gender differences in the prevalence of common psychopathological syndromes. Psych Med 2008;38:51–61.

Krueger RF, Markon KE, Patrick CJ, Iacono WG. Externalizing psychopathology in adulthood: A dimensional-spectrum conceptualization and its implications for DSM-V. J Abnorm Psychology 2005;114:537–550.

Krueger RF, South SC. Externalizing disorders: Cluster 5 of the proposed meta-structure for DSM-V and ICD-11. Psychol Med 2009;39:2061–2070. [PubMed: 19796431]

Kuentzel JG, Henderson MJ, Melville CL. The impact of social desirability biases on self-report among college student and problem gamblers. J Gamb Stud 2008;24:307–319.

Kuo PH, Gardner CO, Kendler KS, Prescott CA. The temporal relationship of the onsets of alcohol dependence and major depression: using a genetically informative study design. Psychol Med 2006;36:1153–1162. [PubMed: 16734951]

Ladwig KH, Marten-Mittag B, Lacruz ME, Henningsen P, Creed F. for the MONIC KORA Investigators. Screening for multiple somatic complaints in a population-based survey: Does excessive symptom reporting capture the concept of somatic symptom disorders: Findings from the MONICA-KORA Cohort Study. J Psychosom Res 2010;68:427–437. [PubMed: 20403501]

Lahmek P, Berlin I, Michel L, Berghout C, Meunier N, Aubin HJ. Determinants of improvement in quality of life of alcohol-dependent patients during an inpatient withdrawal programme. Int J Med Sci 2009;6:160–167. [PubMed: 19461935]

Logan DE, Claar RL, Scharff L. Social desirability response bias and self-report of psychological distress in pediatric chronic pain patients. Pain 2008;136:366–372. [PubMed: 17822848]

Maggs J, Patrick, Feinstein L. Childhood and adolescent predictors of alcohol use and problems in adolescence and adulthood in the National Child Development Study. Addiction 2008;103(Suppl): 7–22. [PubMed: 18426537]

Markon KE, Krueger RF. Categorical and continuous models of liability to externalizing disorders. A direct comparison in NESARC. Arch Gen Psychiatry 2005;62:1352–1359. [PubMed: 16330723]

McEwan TE, Davis MR, MacKenzie R, Mullen PE. The effects of social desirability bias on STAXI-2 profiles in a clinical forensic sample. Br J Clin Psychol 2009;48:431–436. [PubMed: 19555524]

Merline A, Jager J, Schulenberg JE. Adolescent risk factors for adult alcohol use and abuse: stability and change of predictive value across early and middle adulthood. Addiction 2008;103(Suppl):84–89. [PubMed: 18426542]

Middlethorp CM, Cath DC, Van Dyck R, Boomsma DI. The co-morbidity of anxiety and depression in the perspective of genetic epidemiology. A review of twin and family studies. Psychol Med 2005;35:611–624. [PubMed: 15918338]

Moss HB, Chen CM, Yi H. Subtypes of alcohol dependence in a nationally representative sample. Drug Alcohol Depend 2007;91:149–158. [PubMed: 17597309]

Muthen B, Grant BF, Hasin DS. The dimensionality of alcohol abuse and dependence: Factor analysis of DSM-III-R and proposed DSM-IV criteria in the 1988 National Health Interview Survey. Addiction 1993;88:1079–1090. [PubMed: 8401162]

Nelson CB, Rehm J, Ustun B, Grant BF, Chatterji S. Factor structure of DSM-IV substance disorder criteria endorsed by alcohol, cannabis, cocaine and opiate users: Results from the World Health Organization Reliability and Validity Study. Addiction 1999;94:843–855. [PubMed: 10665074]

Penick EC, Nickel EJ, Powell BJ, Liskow BI, Campbell J, Dale TM, Hassanein RE, Noble E. The comparative validity of eleven alcoholism typologies. J Stud Alcohol 1999;60:188–202. [PubMed: 10091957]

Pombo S, Lesch OM. The alcoholic phenotypes among different multidimensional typologies: Similarities and their classification procedures. Alcohol Alcohol 2009;44:46–54. [PubMed: 18832138]

Pull CB, Saunders JB, Mavreas V, Cottler LB, Grant BF, Hasin DS, Blaine J, Mager D, Ustun B. Concordance between ICD-10 alcohol and drug use disorder criteria and diagnoses as measured by the AUDADIS-ADR, CIDI and SCAN: Results of a cross-national study. Drug Alcohol Depend 1997;47:207–216. [PubMed: 9306046]

Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK. Comorbidity of mental disorders with alcohol and other drug abuse: Results from the Epidemiologic Catchment Area (ECA) Study. JAMA 1990;264:2511–2518. [PubMed: 2232018]

Ruan WJ, Goldstein RB, Chou SP, Smith SM, Saha TD, Pickering RP, Dawson DA, Huang B, Stinson FS, Grant BF. The Alcohol Use Disorder and Associated Disabilities Schedule-IV (AUDADIS-IV): Reliability of new psychiatric diagnostic modules and risk factors in a general population sample. Drug Alcohol Depend 2008;92:27–36. [PubMed: 17706375]

Research Triangle Institute. SUDAAN User's Manual. Research Triangle Institute; Research Triangle Park, NC: 2001.

Saraceno L, Munafó M, Heron J, Craddock N, van den Bree MBM. Genetic and non-genetic influences on the development of co-occurring alcohol problem use and internalizing symptomatology in adolescence: a review. Addiction 2009;104:1100–1121. [PubMed: 19438423]

Sartor CE, Lynskey MT, Heath AC, Jacob T, True W. The role of childhood risk factors in initiation of alcohol use and progression to alcohol dependence. Addiction 2007;102:216–225. [PubMed: 17222275]

Schuckit MA, Tipp JE, Smith TL, Shapiro E, Hesselbrock VM, Bucholz KK, Reich T, Nurnberger JI Jr. An evaluation of Type A and Type B alcoholics. Addiction 1995;90:1189–1203. [PubMed: 7580817]

Slade T. The descriptive epidemiology of internalizing and externalizing psychiatric dimensions. Soc Psychiatry Psychiatr Epidemiol 2007;42:554–560. [PubMed: 17516015]

Stinson FS, Grant BF, Dawson DA, Ruan WJ, Huang B, Saha T. Comorbidity between DSM-IV alcohol and specific drug use disorders in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Drug Alcohol Depend 2005;80:105–116. [PubMed: 16157233]

Stoltenberg SF, Mudd SA, Blow FC, Hill EM. Evaluating measures of family history of alcoholism: density versus dichotomy. Addiction 1998;93:1511–1520. [PubMed: 9926555]

Trim RS, Meehan BT, King KK, Chassin L. The relation between adolescent substance use and young adult internalizing symptoms: Findings from a high-risk longitudinal sample. Psych Addict Behav 2007;21:97–107.

Welte JW, Russell M. Influence of socially desirable responding in a study of stress and substance abuse. Alcohol Clin Exp Res 1993;17:758–761. [PubMed: 8214409]

White HR, Xie M, Thompson W, Loeber R, Southammer-Loeber M. Psychopathology as a predicter of adolescent drug use trajectories. Psychol Addict Behav 2001;15:210–215. [PubMed: 11563798]

Windle M, Scheidt DM. Alcoholics subtypes: are two sufficient? Addiction 2004;99:1508–1519. [PubMed: 15585042]

Zucker, RA. The four alcoholisms: A developmental account of the etiologic process. In: Dienstbier, RA.; Rivers, PC., editors. Alcohol and Addictive Behavior. Vol. 34. University of Nebraska; Lincoln, NE: 1986. p. 27-83.

Table 1

Covariation of lifetime psychopathology[a] and lifetime alcohol dependence: U.S. adults 18 years of age and older, by sex

	Type of lifetime psychopathology[a]			
	Neither internalizing nor externalizing (NINE) (n=30,189)	**Internalizing only (IO) (n=10,771)**	**Externalizing only (EO) (n=737)**	**Both internalizing and externalizing (BIE) (n=1,396)**
	% SE	**% SE**	**% SE**	**% SE**
Prevalence of selected types of psychopathology in the total population				
Male (n=18,518)	74.7 (0.6)	17.7 (0.4)	3.1 (0.2)	4.5 (0.2)
Female (n=24,575)	65.4 (0.7)	31.3 (0.7)	0.7 (0.1)	2.6 (0.1)
p-value gender diff.	*<.001*	*<.001*	*<.001*	*<.001*
Prevalence of selected types of psychopathology among lifetime alcoholics				
Male (n=2,974)	47.6 (1.1) [b]	27.1 (0.9) [b]	8.6 (0.6) [b]	16.7 (0.9) [b]
Female (n=1,807)	29.0 (1.3) [b]	50.8 (1.4) [b]	3.5 (0.5) [b]	16.7 (1.0) [b]
p-value gender diff.	*<.001*	*<.001*	*<.001*	*.966*
Prevalence of lifetime alcohol dependence by type of psychopathology				
Male	11.1 (0.4)	26.5 (1.0)	48.1 (2.4)	64.2 (2.1)
Female	3.5 (0.2)	12.9 (0.5)	39.5 (4.6)	51.4 (2.6)
p-value gender diff.	*<.001*	*<.001*	*.109*	*<.001*

Note: Figures in parentheses are standard errors of percentages. Shaded cells indicate percentages that are significantly different (p<.05) for males and females.

[a] Internalizing = major depressive disorder, bipolar 1 or 2 disorder, dysthymia, panic disorder with or without agoraphobia, specific and social phobia, generalized anxiety disorder; externalizing = illicit drug dependence, ASPD

[b] Significantly different (p<.001) than comparable percentage in the total population

Table 2

Adjusted* odds ratios and 95% confidence intervals for associations between lifetime alcohol dependence and other lifetime psychopathology[a]: U.S. adults 18 years of age and older

Type of lifetime psychopathology	Total population (n=43,093)	Lifetime drinkers (n=34,827)	Lifetime drinkers, adjusted for volume of consumption[c] (n=32,756)
Neither internalizing nor externalizing (NINE)			
Male	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Female	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Internalizing only (IO)			
Male	1.9 (1.7–2.2)	1.9 (1.7–2.2)	1.9 (1.6–2.2)
Female	2.6 (2.2–3.1)	2.3 (2.0–2.7)	2.4 (2.0–2.8)
p-value gender diff.	*.002*	*.048*	*.031*
Externalizing only (EO)			
Male	4.0 (3.1–5.1)[c]	3.9 (3.0–5.0)[c]	2.3 (1.7–3.1)[e,f]
Female	8.8 (5.3–14.6)[c]	7.4 (4.5–12.2)[c]	4.9 (2.8–8.6)[c]
p-value gender diff.	*.006*	*.023*	*.015*
Both internalizing and externalizing (BIE)			
Male	6.5 (5.2–8.1)[c,d]	6.7 (5.2–8.5)[c,d]	4.3 (3.3–5.7)[c,d,e,f]
Female	10.7 (8.2–13.8)[c]	8.9 (6.8–11.6)[c]	5.4 (3.9–7.4)[c,e,f]
p-value gender diff.	*.003*	*.099*	*.259*

Note: Figures in parentheses are 95% confidence intervals. Shaded cells indicate OR that are significantly different (p<.05) for males and females.

*Adjusted for age, gender, race-ethnicity, whether ever married, whether ever had children, whether ever attended/completed college, lifetime drug abuse, lifetime nicotine dependence, other personality disorders and any other significant (p<.05) gender interactions.

[a]Internalizing = major depressive disorder, bipolar 1 or 2 disorder, dysthymia, panic disorder with or without agoraphobia, specific and social phobia, generalized anxiety disorder; externalizing = illicit drug dependence, ASPD

[b]Average daily volume of ethanol intake during period of heaviest consumption, logged to improve model fit

[c]Significantly different (p<.05) than OR for internalizing only

[d]Significantly different (p<.05) than OR for externalizing only

[e]Significantly different (p<.05) than OR for the total population

[f]Significantly different (p<.05) than OR for lifetime drinkers unadjusted for consumption

Table 3

Mean values for selected aspects of expression and course of alcoholism: U.S. adults 18 years of age and older with lifetime DSM-IV alcohol dependence, by type of lifetime psychopathology[a]

Aspects of clinical presentation/course	Type of lifetime psychopathology[a]							
	Neither internalizing nor externalizing (NINE)		Internalizing only (IO)		Externalizing only (EO)		Both internalizing and externalizing (BIE)	
	Male (n=1,422)	Female (n=514)	Male (n=814)	Female (n=921)	Male (n=252)	Female (n=67)	Male (n=486)	Female (n=305)
Average daily volume of ethanol intake (oz.)[b]	4.6 (0.2)	2.3 (0.2)	4.8 (0.3)	2.7 (0.2)	10.3 (1.8) [c,d]	3.2 (0.5)	8.2 (0.8) [c,d]	6.5 (1.0) [c,d,e]
Overall freq. drinking [b]	231.8 (4.3)	192.7 (6.7)	243.4 (5.5)	200.8 (4.8)	276.2 (8.0) [c,d]	252.7 (19.5) [c,d]	262.3 (6.9) [c,d]	249.5 (8.8) [c,d]
Freq. drinking 5+ drinks [b]	186.5 (4.7)	119.2 (6.7)	197.0 (6.5)	126.1 (5.6)	249.4 (9.2) [c,d]	172.9 (21.4) [c,d]	229.2 (7.5) [c,d]	196.5 (10.3) [c,d]
Largest quantity of drinks consumed in a single day[b]	16.0 (0.3)	8.9 (0.3)	14.7 (0.5) [c]	9.3 (0.3)	20.5 (1.2) [c,d]	10.1 (0.7)	19.6 (0.7) [c,d]	13.8 (0.7) [c,d,e]
Mean age at onset of dependence	24.5 (0.3)	24.8 (0.5)	24.5 (0.3)	25.1 (0.4)	21.3 (0.5) [c,d]	22.7 (1.1) [d]	22.5 (0.4) [c,d]	21.6 (0.5) [c,d]
Mean years from initiation of drinking to onset of dependence	7.6 (0.3)	7.1 (0.4)	7.3 (0.3)	7.2 (0.3)	6.3 (0.5) [c]	6.8 (1.1)	7.0 (0.4)	5.7 (0.4) [c,d],
Density of familial alcoholism	0.26 (0.01)	0.32 (0.02)	0.31 (0.02) [c]	0.44 (0.02) [c]	0.45 (0.03) [c,d]	0.59 (0.07) [c,d]	0.51 (0.03) [c,d]	0.64 (0.04) [c,d]
# lifetime AUD symptoms	11.6 (0.2)	10.1 (0.3)	13.3 (0.3) [c]	11.1 (0.3) [c]	16.0 (0.6) [c,d]	16.4 (1.5) [c,d]	17.0 (0.4) [c,d]	16.9 (0.5) [c,d]
% initiating drinking <15	12.8 (1.1)	13.3 (1.9)	13.9 (1.4)	13.9 (1.6)	37.3 (4.1) [c,d]	33.1 (7.0) [c,d]	34.6 (2.5) [c,d]	40.3 (3.3) [c,d]
% with multiple episodes of dependence	23.8 (1.6)	21.0 (2.4)	29.2 (1.9) [c]	25.7 (1.8)	32.3 (4.5)	41.6 (7.2) [c,d]	39.8 (2.5) [c,d]	36.2 (3.5) [c,d]
% in full remission from dependence at Wave 1	43.3 (1.6)	40.6 (2.8)	46.7 (2.1)	47.0 (2.0)	47.2 (3.9)	50.1 (8.1)	41.4 (2.6)	41.1 (3.6)
% ever treated/ participated in 12-step program	21.9 (1.3)	11.9 (1.5)	22.5 (1.6)	16.5 (1.5) [c]	36.4 (3.9) [c,d]	44.5 (6.7) [c,d]	39.6 (2.7) [c,d]	38.8 (3.4) [c,d]

Note: Figures in parentheses are standard errors of percentages. Shaded cells indicate mean values that are significantly different ($p<.05$) for males and females.

[a] Internalizing = major depressive disorder, bipolar 1 or 2 disorder, dysthymia, panic disorder with or without agoraphobia, specific and social phobia, generalized anxiety disorder; externalizing = illicit drug dependence, ASPD

[b] During period of heaviest consumption

[c] Significantly different (p<.05) than value for neither internalizing nor externalizing

[d] Significantly different (p<.05) than value for internalizing only

[e] Significantly different (p<.05) than value for externalizing only

Table 4

Adjusted* associations of lifetime psychopathology[a] with selected aspects of expression and course of alcoholism: U.S. adults 18 years of age and older with lifetime DSM-IV alcohol dependence (n=4,781)

Aspects of clinical presentation/course	Type of lifetime psychopathology[a] (Referent = individuals with neither internalizing nor externalizing psychopathology)					
	Internalizing only (IO)		Externalizing only (EO)		Both internalizing and externalizing (BIE)	
	Male	Female	Male	Female	Male	Female
Average daily volume of ethanol intake (oz.)[b]	β = − 0.11 (0.21)	β = 0.13 (.20)	β = 1.94 (.40) [c,d]	β = 0.84 (.57)	β = 1.46 (.28) [c,d]	β = 2.22 (.34) [c,d,e]
Overall freq. drinking [b]	β = 2.1 (6.4)	β = −3.2 (7.6)	β = 45.2 (8.6) [c,d]	β = 51.9 (24.5) [c,d]	β = 25.8 (7.3) [c,d]	β = 56.0 (11.7) [c,d]
Freq. drinking 5+ drinks [b]	β = 0.8 (7.7)	β= 4.2 (7.5)	β = 57.1 (9.7) [c,d]	β = 42.3 (24.8)	β = 34.2 (7.5) [c,d]	β = 66.9 (13.0) [c,d]
Largest quantity of drinks consumed in a single day [b]	β =−1.7 (0.4) c	β= −0.3 (0.4)	β = 2.4 (0.8) [c,d]	β = 0.7 (0.9)	β = 1.7 (0.6) [c,d]	β = 3.3 (0.7) [c,d]
Mean age at onset of dependence	β =−0.1 (0.4)	β= −0.4 (0.5)	β = −2.2 (0.5) [c,d]	β = −3.1 (1.1) [c,d]	β = −1.0 (0.5) [c]	β = −2.6 (0.6) [c,d]
Mean years from initiation of drinking to onset of dependence	β =−0.4 (0.4)	β= −0.5 (0.5)	β = −0.4 (0.5)	β = −1.0 (1.2)	β = 0.2 (0.4)	β = −1.4 (0.5) [c]
Density of familial alcoholism	β =0.03 (0.02)	β= 0.08 (.03) [c]	β = 0.16 (.03) [c,d]	β = 0.26 (.07) [c,d]	β = 0.20 (.03) [c,d]	β = 0.24 (.04) [c,d]
# lifetime AUD symptoms	β =1.2 (0.4) [c]	β= 0.2 (0.3)	β = 4.1 (0.6) [c,d]	β = 5.7 (1.5) [c,d]	β = 4.8 (0.4) [c,d]	β = 5.7 (0.6) [c,d]
% initiating drinking <15	OR=1.0 (0.7–1.3)	OR=0.9 (0.6–1.4)	OR=3.5 (2.3–5.3) [c,d]	OR=3.2 (1.5–6.5) [c,d]	OR=2.9 (2.1–4.0) [c,d]	OR=3.1 (2.0–4.9) [c,d]
% with multiple episodes of dependence	OR=1.2 (0.9–1.5)	OR=1.2 (0.8–1.6)	OR=1.5 (1.0–2.4)	OR=2.6 (1.4–5.0) [c,d]	OR=1.9 (1.4–2.5) [c]	OR=1.8 (1.2–2.8) [c]
% in full remission from dependence at Wave 1	OR=1.1 (0.9–1.4)	OR=1.2 (0.8–1.6)	OR=1.6 (1.1–2.3) [c]	OR=1.4 (0.7–2.9)	OR=1.2 (0.9–1.6)	OR=1.2 (0.7–1.7)
% ever treated/participated in 12-step program	OR=0.9 (0.7–1.2)	OR=1.2 (0.8–1.8)	OR=2.1 (1.4–3.1) [c,d]	OR=5.5 (2.8–10.8) [c,d]	OR=2.4 (1.8–3.2) [c,d]	OR=4.2 (2.7–6.7) [c,d]

Note: Shaded cells indicate effects that are significantly different (p<.05) for males and females. Figures in parentheses are standard errors of beta coefficients (β) and 95% confidence intervals for odds ratios (OR).

*Adjusted for age, gender, race-ethnicity, whether ever married, whether ever had children, whether ever attended/completed college, lifetime drug abuse, lifetime nicotine dependence, other personality disorders and any other significant (p<.05) gender interactions. Beta coefficients reflect adjusted difference in absolute value of continuous outcomes; ORs reflect excess odds of dichotomous outcomes.

[a]Internalizing = major depressive disorder, bipolar 1 or 2 disorder, dysthymia, panic disorder with or without agoraphobia, specific and social phobia, generalized anxiety disorder; externalizing = illicit drug dependence, ASPD

[b]During period of heaviest consumption

[c]Significantly different (p<.005) than value for neither internalizing nor externalizing

[d]Significantly different (p<.005) than value for internalizing only

[e] Significantly different ($p<.005$) than value for externalizing only