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Transitions through Stages of Alcohol Involvement: The Potential Role of Mood Disorders

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Abstract

Introduction: Although prior clinical and population-based studies have demonstrated comorbidity between mood and alcohol use disorders (AUD), there is a paucity of research assessing whether mood disorders predict transition across stages of alcohol involvement.

Method: Hypothesizing that mood disorders predict transition across sex-specific alcohol involvement stages, we used prospective data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative survey of US adults, which included male (n=14,564) and female (n=20,089) participants surveyed in 2001–2 and re-interviewed in 2004–5. Latent class (LCA) and latent transition analyses (LTA) were used to assess patterns of alcohol involvement in the US, and the association of lifetime mood disorders at baseline with transition across stages of alcohol involvement during follow-up.

Results: A three-class model of AUD criteria was identified (*No problems*, *Moderate problems* and *Severe problems*) for both males and females. Positive cross-sectional associations between mood disorder and problem classes of alcohol involvement were found among both sexes, as were positive longitudinal associations. Propensity score adjustment mitigated the associations of baseline mood disorder with progressive transition for both sexes. However, among females, baseline mood disorder was consistently associated with reduction in remission from *Severe* to *Moderate* alcohol problems (aOR=0.30, CI=0.09–0.99, p=0.048) over time.

Discussion: Our study provides evidence that mood disorders impact transition through stages of alcohol involvement, most strongly associated with hindering remission among females. Findings advance our understanding of these comorbid relationships and have clinical implications for ongoing assessment of drinking patterns among individuals with mood disorders.

Keywords

abuse; alcohol; dependence; depression; mood; risk; latent transition analysis; major depressive disorder

1. Introduction

The co-occurrence of alcohol and mood disorders is well recognized in community and clinical populations (Farell et al., 2001; Frye et al., 2003; Gilman and Abraham, 2001; Grant et al., 2004, 2015; Hasin et al., 2005; Johnson et al., 2007; Kessler et al., 1997; Lai et al., 2012; Ross, 1995; Wang and Patten, 2001). Alcohol disorders are more commonly the initial (primary) condition (Fergusson et al., 2009; Flensburg-Madsen et al., 2009), yet prospective data indicate that these associations can be bidirectional (Briere et al., 2014; Dawson et al., 2010; Flensburg-Madsen et al., 2009; Gilman and Abraham, 2001; Kuo et al., 2006; Needham, 2007; Pacek et al., 2013; Wang and Patten, 2001, 2002). Although comorbid patterns are frequently reported, there has been relatively little assessment of whether mood disorders predict transition across stages of alcohol involvement. Some studies provide evidence that mood conditions have varying associations with different classifications of alcohol outcomes (e.g., incidence as opposed to relapse) (Behrendt et al., 2011; Boschloo et al., 2012; Conway et al., 2016; Crum et al., 2001; Mattisson et al., 2007). However, most prior studies examining alcohol transitions have assessed associations across one stage and/or in one direction (e.g., no drinking to drinking initiation) (Behrendt et al., 2011; Butterworth et al., 2014; Crum et al., 2001; Martins et al., 2011; Sung et al., 2004). With relatively few exceptions (Cook et al., 2014; Windle and Davies, 1999), there has been little assessment of transitions in multiple directions across more than one stage, especially for comorbid relationships.

An individual's involvement with alcohol may progress through sequential stages, with progressively maladaptive drinking patterns. However, not everyone progresses through stages sequentially. Some individuals may remain chronically at the same stage for years. Others may undergo remission to less involved stages. Evaluating whether mood disorders impact progression to and/or remission from more severe alcohol involvement aids our understanding of possible etiologic mechanisms for this comorbidity, and may identify

potential targets for prevention or early intervention, as well as determine at which alcohol stage mood symptoms have the strongest impact.

Hypothesizing that mood disorders increase the probability of transition to more advanced alcohol involvement stages, our principal goals were to examine whether, and at what stages, baseline mood disorders impact transition through increasingly progressive stages of alcohol involvement, and to assess the possibility of progressing to advanced stages directly without passing through an intervening stage (Bucholz et al., 2000). We also sought to examine whether mood disorders were associated with inhibiting remission to less severe alcohol involvement. Our goal was to examine patterns of alcohol involvement across the entire spectrum of drinking behavior in the US, and consequently our study sample included individuals who reported no consumption and/or no alcohol-related problems. Our rationale was that these individuals may have remitted from a prior alcohol disorder, or may transition to problematic drinking, particularly in the context of mood symptomatology. Furthermore, those with more severe behavior may remit to abstinence and/or non-problematic consumption. Because prior studies have found that the impact of comorbidity may differ for males and females (Frye et al., 2003; Kessler et al., 1997; Kuo, et al., 2006; Ross, 1995; Wang and Patten, 2001), all of our analyses were stratified by sex.

2. Methods

2.1. Study sample

The study sample was drawn from waves 1 and 2 of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC), a representative survey of the US adult population. Wave 1 was fielded in 2001–2002 (n=43,093 participants, aged 18 years). Of the 39,959 wave 2 eligible participants, a total of 34,653 were re-interviewed in 2004–2005. Ineligible respondents included those deceased, deported, mentally/physically impaired, or on active military duty. Response rates for wave 1 and eligible wave 2 surveys were 81% and 87%, respectively. Additional survey and study design details are described elsewhere (Grant et al., 2004, 2009). Our study sample included 14,564 males and 20,089 females with assessments at both waves, and was weighted to adjust for unequal probabilities of selection to provide nationally representative estimates.

2.2. Measures

Baseline characteristics were assessed using wave 1 data. Mood disorders included the independent diagnoses (major depression, dysthymia, mania, hypomania), and excluded those solely due to substance-induced intoxication and/or withdrawal, or medical illnesses. Diagnoses were based on DSM-IV criteria ascertained from computerized algorithms using data from the Alcohol Use Disorder and Associated Disabilities Interview Schedule–DSM-IV Version (Grant et al., 2003; Ruan et al., 2008). Baseline lifetime mood disorder was the hypothesized predictor of alcohol involvement transition. Because each independent mood disorder, whether 12-month or lifetime, had similar associations with alcohol involvement stages, they were combined to increase precision of estimates. As we have accomplished previously (La Flair et al., 2012, 2013), alcohol involvement was captured via items assessing clinical features of DSM-IV alcohol abuse and dependence, which were

operationalized as four abuse and seven dependence criteria. Therefore, alcohol involvement refers to behaviors related to AUD criteria, and not to consumption level. Consistent with the approach adopted in DSM-V and prior latent class analyses (Ehlke et al., 2012; La Flair et al., 2012, 2013; Muthén, 2006), abuse and dependence criteria were not separated.

Potential confounders in the analyses included sex (analyses were sex-stratified), age (18–35, 36–49, 50 years; continuous in multivariable analyses), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other), education (>12 years, <12 years), lifetime illicit drug abuse and/or dependence (heroin, other narcotics, cocaine, cannabis, stimulants, hallucinogens), nicotine dependence, anxiety disorders (generalized anxiety disorder, social phobia, specific phobia, and/or panic disorder), and family history of alcoholism (any first-degree relative reported as “alcoholic or problem drinker”).

2.3. Statistical analyses

We first completed latent class analysis (LCA) on the eleven DSM-IV abuse and dependence criteria. LCA is a data-driven approach that allowed us to characterize patterns of clinical features of AUD observed in our data that may manifest prior to meeting full criteria for AUD or may represent qualitatively different subtypes (e.g., stages). The goal of LCA is to identify the smallest number of latent classes that adequately describe the associations among the clinical features. Information about the class structure is conveyed by the proportion of individuals in each class (latent class prevalences), and the probability of reporting a clinical feature within a class (item probabilities). We fit successive models with increasing numbers of latent classes to determine the most parsimonious model that provided an adequate fit to the data (Nylund et al., 2007). Model selection was based on Akaike’s information criterion (AIC), Bayesian information criterion (BIC) and the sample-size adjusted BIC (a-BIC): global fit indices that combine goodness-of-fit and parsimony. Models with lower values of AIC, BIC and a-BIC are preferred. Because of the large sample size, we have increased power to detect smaller classes, which could result in identification of spurious classes that lack substantive interpretation. Thus, in addition to global fit indices, interpretability and distinguishability of the resultant classes was considered when comparing competing latent class models. Entropy was used to measure the separation of classes, with values approaching 1.0 indicating clearer delineation of classes (Celeux and Soromenho, 1996). To avoid convergence to local maxima, which occurs frequently in LCA, results were based on 10,000 sets of random starting values, each of which was subjected to ten iterations of the estimation procedure. LCA was completed separately for waves 1 and 2 to evaluate alcohol involvement classes at each wave. Based on previous findings of sex differences for AUDs (Grucza et al., 2008; Keyes et al., 2010), models were fit separately for males and females.

Next, we estimated the probability of transitioning between the latent stages of alcohol involvement across the two waves using latent transition analysis (LTA). LTA is an extension of LCA to the longitudinal framework, which expresses change over time in terms of transition probabilities and models the impact of covariates on transitions using a multinomial regression formulation. Transition probabilities reflect the probability of transitioning from a latent stage at wave 1 to another latent stage at wave 2 (Collins and

Wugalter, 1992; Reboussin et al., 1998, 1999). Using LTA, we assessed our hypothesis that baseline mood disorder impacted the probability of progressive transition from one alcohol involvement stage to a more advanced stage. Simultaneously, we assessed whether baseline mood disorder was associated with a reduced probability of remission to a less symptomatic alcohol involvement stage.

We utilized the propensity score method of inverse probability of treatment weighting (IPTW) to address potential baseline differences between mood disordered and non-mood disordered participants, which could bias the effect estimates (Curtis et al., 2007; Rubin, 2010; Stuart, 2010). In this technique, first, propensity scores (probability of mood disorder) are computed using a logistic regression model. These scores reflect each participant's likelihood of having a mood disorder given their sociodemographic and clinical characteristics. The potential confounding baseline sociodemographic and clinical characteristics included in the propensity score model are listed in Table 1. Next, data are weighted by their inverse probability of being in their observed group (those with and without mood disorders). Because the NESARC used a complex sampling design, both LCA and LTA were carried out using *Mplus* version 7.0 (Muthén and Muthén, 1998–2010) taking into account survey weights, clustering and stratification. The propensity score weights were multiplied by the survey weights and the resulting combined weights were used in the analysis of the association of mood disorder with transitions in alcohol involvement stages (Dugoff et al., 2014). To assess the effectiveness of IPTW in balancing the composition of mood disorder and non-mood disordered groups, we compared characteristics of the group before and after applying the weights (Stuart, 2010). Application of IPTW was deemed successful as the groups were similar with respect to the observed characteristics after using the weights.

3. Results

Table 1 includes the frequency distribution of baseline characteristics for our study sample by sex. Approximately 31% of study participants were in the 18–35 year age range, 30% in the 36–49 range, and 39% were 50 years or older. Most were White with at least a high school education. Lifetime major depressive disorder was present in 21% of females and 12% of males; 9% of males and 11% of females had another mood disorder. A greater proportion of females reported family history of alcoholism, and met criteria for anxiety disorders. More males had illicit drug use disorder and nicotine dependence. Those with mood disorders were more likely to be younger, White, have an anxiety or drug use disorder, and have a family history of alcoholism. Females with mood disorders also were more likely to have less education, although the magnitude of these differences was minimal.

3.1. Latent class analyses

We chose a three-class model for each sex, based on data from the fit indices and overall interpretability of the models. As shown in Table 2, for females, the fit indices and entropy generally favored a three-class model for waves 1 and 2. For males, the fit indices and entropy initially suggested a four-class model, similar to prior LCA (Muthén, 2006). A five-class solution did not converge. In the four-class solution, prevalence of the fourth class was

relatively low (0.7% at wave 1, 0.8% at wave 2), and the two moderate/middle classes had similar profiles with no distinguishing items between them, limiting clinical interpretability. Consequently, the more parsimonious and interpretable three-class model was used in the LTA for males.

The alcohol involvement item probabilities for the three classes at waves 1 and 2 are presented in Figure 1A (males) and 1B (females). These classes reflect increasing alcohol involvement stages. Most individuals were categorized into a *No problem class*, experiencing few clinical criteria: prevalence estimates among females were 92% (wave 1) and 90% (wave 2); among males, they were 86% (wave 1) and 80% (wave 2). A second or *Moderate problem class* was also similar across the sexes and was characterized by drinking in hazardous situations, problems cutting down consumption, drinking in larger amounts and experiencing tolerance and withdrawal symptoms: estimated prevalence among females was 7% (wave 1), and 9% (wave 2), with a slightly higher prevalence among males (12% at wave 1, 17% at wave 2). The third or *Severe problem class*, again was similar for females and males, with higher item probabilities than the *Moderate class* in addition to other drinking-related criteria: role failure and social problems, giving up activities, greater time spent getting alcohol, physical and psychiatric problems. *Severe class* prevalence estimates were lowest overall, but were lower among females (1.0% (wave 1), 1.1% (wave 2)), compared with males (2.5% (wave 1), 2.8% (wave 2)). Although small differences in item probabilities existed between the waves, the overall qualitative interpretations of the three classes across waves did not change. Therefore, measurement invariance was imposed across waves to ensure that the mean of the latent classes was held constant.

In supplementary analyses, to confirm that sex-stratified analyses were appropriate, we tested whether the structure of the 3-class model varied for males and females. Measurement invariant testing suggested that pooling data for men and women would lead to a significantly worse model fit (likelihood difference test statistic=276.84, $p<0.001$, and 182.25, $p<0.001$ for waves 1 and 2, respectively). To identify the AUD criteria within a class that were driving the sex differences, we tested the invariance of each latent class indicator for each wave. We found 12 of the 33 indicators were significantly different at $p<0.05$ for wave 1, and 9 were significantly different at wave 2 (see Appendix). For example, males had significantly higher conditional probabilities for drinking in physically hazardous situations, and development of tolerance.

3.2. Latent transition analyses

We first examined the overall estimated probabilities of transitioning between the three classes across waves (Figure 2), adjusting for sampling weights. The highest stability was seen for those without problems: 93% of females and 90% of males in the *No problem* stage at baseline remained in this stage at follow-up. Notably, 65% of females and 56% of males in the *Severe stage* at baseline reported fewer alcohol criteria at follow-up (remitting to *Moderate* or *No problems* stages). A low proportion of females (0.8%) skipped an intervening stage, and transitioned from *No problems* to *Severe problems*. For males, 9% transitioned from *Moderate* to *Severe stages* compared with 1% that transitioned from *No problems* to *Severe*. Although there was greater probability for symptom improvement than

symptom progression, males were less likely to recover than females. A greater proportion of males in the *Severe* (44%) stage remained at that stage without symptom improvement compared with 35% of females. A greater proportion of females in the *Moderate stage* remitted to *No problems* compared to males (35% and 24%, respectively).

Second, we examined the cross-sectional association of lifetime mood disorder at baseline with baseline alcohol involvement stages (Table 3), with and without adjustment using the method of propensity score weighting. Findings were similar among men and women: mood disorder was significantly associated with both *Moderate* and *Severe* stages, relative to the *No problem* stage. These findings remained significant after adjustment for potential confounding except for the association of mood disorder and the *Moderate* stage among males.

Third, we assessed the longitudinal associations between mood disorders and transitioning across alcohol stages. The odds ratios presented in Table 4 correspond to the odds of transitioning between alcohol involvement stages from wave 1 to 2 relative to staying at the same stage for those with and without a mood disorder. In unadjusted analyses, we found positive progressive longitudinal associations from *Moderate* to *Severe* stages among males and *No Problems* to *Moderate* stages among females, and a negative association with remission from *Severe* to *Moderate* involvement among females. After adjustment for potential confounders using propensity score weighting, among females, mood disorder was associated with elevated odds for movement from the *No problems* to *Severe* stage at follow-up, but was not statistically significant (adjusted odds ratio (aOR)=2.16, 95% confidence interval (CI)=0.81–5.76, p=0.123). Similarly, among males in adjusted models, baseline mood disorder was associated with an almost two-fold increased odds of transitioning from *Moderate* to *Severe* stage relative to males who remained at the *Moderate* stage (aOR=1.73, CI=0.82–3.66, p=0.153), but was not statistically significant. There was no evidence that mood disorder increased the probability of progression from *No problems* to *Moderate* problems for either sex. Among females, mood disorder was negatively associated with remission. Women with a mood disorder history and *Severe* problems at baseline were significantly less likely to transition to *Moderate* problems during follow-up (aOR=0.30, CI=0.09, 0.99 p=0.048) relative to women without a mood disorder. Mood disorders had no appreciable associations with remission transitions among males.

4. Discussion

There is a relative paucity of prior studies that have examined transition patterns across stages of alcohol involvement in the general population. Bypassing the limitations inherent in defining individuals in the community as having or not having an AUD, we aimed to provide a broader understanding of the spectrum of alcohol involvement in the US, by assessing classes of criteria used to define an AUD. In addition, our goal was to provide information on transition patterns of drinking behavior among the entire national sample including those who report no drinking or no alcohol-related problems, hypothesizing that these individuals may transition to more problematic behavior, and those in more severe stages may remit to abstinence or non-problematic consumption.

Three classes of alcohol involvement were identified both for men and women. Most individuals fall within the *No problems* class, and the majority of these individuals remain in this class over time. This class structure is similar to LCA of AUD symptoms using other samples (Mancha et al., 2012; Swift et al., 2016). Consistent with our *a priori* hypotheses, having a mood disorder diagnosis at baseline, was associated with the problem classes of alcohol involvement. Mood disorder was strongly associated with the cross-sectional alcohol stages, and with some sex-specific longitudinal transitions across stages. The association of mood disorders with the progressive transition through worsening stages of alcohol involvement was mitigated once propensity score adjustment was completed. However, among women, mood disorders continued to have a strong independent association with inhibiting remission from *Severe* to *Moderate* problems even after controlling for confounding.

Associations of mood symptoms with alcohol disorders have been reported repeatedly in prior investigations (Blanco et al., 2010; Boschloo et al., 2012; Cranford et al., 2011; Edwards et al., 2011; Grant et al., 2003, 2004; Kessler et al., 1997; Marmorstein, 2009; Prisciandaro et al., 2012; Young-Wolff et al., 2009). However, with few exceptions (e.g., McBride et al., 2014), there has been relatively little assessment of mood conditions with specific transitions through alcohol involvement stages. One advantage of the methodology used in this report is the simultaneous assessment of the direction and magnitude of transitions across empirically-derived stages of alcohol involvement and our ability to examine the associations of mood disorder with stage-specific transitions. Although in cross sectional analyses, mood disorders continued to be associated with alcohol stages after controlling for confounding among both men and women, this was not found in the progressive longitudinal transitions. While an initial association was found in unadjusted models in the longitudinal transition from moderate to severe problems for men and from no problems to moderate problems for women, confounding characteristics (such as substance use involvement) explained these associations. Furthermore, it is likely that adults who initially are without drinking problems or those within a more moderate stage of alcohol involvement are more able to cope with the mood symptoms and therefore less likely to transition to more severe problematic drinking as a result of mood symptoms. Also, the cross-sectional comorbid associations well documented in prior literature may be plausibly explained by the reverse directional pathway (alcohol problems causing the development or worsening of mood symptoms) as has been found in some prior studies (Fergusson et al., 2009; Flensburg-Madsen et al., 2009). These potential etiological mechanisms need to be assessed in future investigations.

An additional important finding from the current report was the longitudinal association between baseline mood disorders and the inhibition of remission of alcohol-related problems among women. A number of prior reports indicate that individuals with comorbid disorders, compared to those with a single diagnosis, have more severe prognostic outcomes such as higher relapse rates, greater risk for treatment dropout and more severe symptoms (Britton et al., 2015; Curran et al., 2000; Driessen et al., 2001; Greenfield et al., 1998; Prisciandaro et al., 2012; van Zaane et al., 2010). This highlights the importance of recognizing maladaptive drinking behavior among patients with mood disorders, and educating patients about risks of consuming alcohol, such as might occur if used as a mechanism for self-medicating mood

symptoms (Bolton et al., 2009; Crum et al., 2013; Khantzian, 1990). In this report, the negative association of mood disorder with alcohol problem remission was only found for women. Women may be more vulnerable to the comorbid presence of mood symptoms and problematic drinking behavior. Some prior studies report stronger comorbid associations among women (Husky et al., 2008; Kessler et al., 1997; Ross, 1995). Furthermore, mood symptom severity or duration may be greater among females, given the higher prevalence of depressive disorders among women in general (Van de Velde et al., 2010; Weissman et al., 1996). Dawson and colleagues found that internalizing psychopathology was significantly more prevalent among women with lifetime alcohol dependence than was found for men (Dawson et al., 2010). Service utilization and treatment outcome also may differ by sex for those with comorbid conditions (Chen et al., 2013; Dawson et al., 2010; Farren et al., 2011), which may reflect differences in mental health care access, presence of refractory symptoms or limited response to available treatment.

The findings of this report should be considered in the context of potential limitations. First, we were unable to adjust for all possible confounding characteristics. For example, alcohol expectancies may motivate drinking behavior (Hasking et al., 2011; Jones et al., 2001; Smith, 1994), and be affected by mood state (Demmel et al., 2006; Catanzaro and Laurent, 2004). Second, although the dataset is the largest prospective population-based US survey that provides detailed alcohol and psychiatric symptom data needed for the analyses, multiple transition patterns are assessed and power is limited to evaluate some associations, including those for specific mood diagnoses. Additionally, there were relatively few transitions during the follow-up interval. Whether three years is sufficient time to assess all transitions will need further exploration in samples with longer follow-up. Third, although health services data was gathered, information on the extent and timing of service utilization related to comorbid symptoms was not available to assess potential treatment response. Furthermore, treatment utilization was limited: 34.5% of females and almost half of males (46.5%) with mood disorders reported no mood or alcohol treatment during follow-up. Inclusion of this treatment variable, as a covariate in the propensity score adjusted regression model, did not appreciably alter the estimates presented in this report. Lastly, due to limitations in prevalence, lifetime mood disorder was used. This strategy may make it more difficult to interpret the temporal relationships with the alcohol stages. However, similar associations with alcohol stages were found for both lifetime and 12-month diagnoses. Furthermore, approximately half of those with lifetime mood disorder at baseline also met criteria for 12-month mood disorder.

Notwithstanding these limitations, the current report provides new information regarding the potential impact of mood disorders on the progression and remission of alcohol-related problems. Mood disorders may have significant effects on the probability of transitioning through alcohol stages, particularly on remission from severe problems among women. The findings emphasize the importance of ongoing assessments of drinking patterns among individuals with mood disorders, the evaluation of mood symptoms among individuals with drinking problems, as well as the need to educate patients with mood disorders about the risks of maladaptive drinking behaviors and provide alternative coping strategies. Further research will be needed to explore transition patterns over longer intervals given that an interval of approximately three years may not be sufficient to reveal all transition patterns. In

addition, it will be necessary to explore the etiological mechanisms for the sex-specific findings, and the role of health service use in accelerating or diminishing the pace of transitions.

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Appendix.

Male-female invariance testing for the 3-class model of NESARC wave 1 and wave 2 alcohol use disorder criteria: conditional probabilities and p-values.

	Wave 1			Wave 2		
	Males	Females	p	Males	Females	p
No Problems Class						
Major Role Failure	0.000	0.000	1.000	0.000	0.000	1.000
Physically Hazardous	0.047	0.024	0.000	0.026	0.007	0.000
Legal Problems	0.000	0.000	0.614	0.000	0.000	0.363
Social/Interpersonal Problems	0.001	0.000	0.542	0.000	0.000	1.000
Tolerance	0.012	0.006	0.001	0.016	0.010	0.013
Unsuccessful Efforts to Cut Down	0.074	0.029	0.000	0.028	0.016	0.001
Larger Amount/Longer Periods	0.015	0.008	0.006	0.010	0.007	0.202
Withdrawal	0.007	0.007	0.711	0.022	0.020	1.000
Great Deal of Time Spent	0.000	0.000	0.198	0.000	0.000	1.000
Giving Up/Reducing Activities	0.000	0.000	0.212	0.000	0.000	1.000
Physical/Psychological Problem	0.002	0.000	0.153	0.003	0.001	0.069
Moderate Class						
Major Role Failure	0.013	0.007	0.382	0.005	0.008	1.000
Physically Hazardous	0.553	0.435	0.000	0.409	0.261	0.000
Legal Problems	0.040	0.017	0.013	0.017	0.009	0.115
Social/Interpersonal Problems	0.081	0.035	0.000	0.053	0.015	0.001
Tolerance	0.339	0.252	0.002	0.261	0.191	0.001
Unsuccessful Efforts to Cut Down	0.399	0.347	0.087	0.375	0.342	0.250
Larger Amount/Longer Periods	0.528	0.521	0.867	0.558	0.546	0.706
Withdrawal	0.378	0.451	0.026	0.457	0.541	0.002
Great Deal of Time Spent	0.081	0.055	0.111	0.065	0.053	0.322
Giving Up/Reducing Activities	0.010	0.001	0.024	0.008	0.003	0.164
Physical/Psychological Problem	0.143	0.135	0.728	0.142	0.115	0.229

No Problems Class	Wave 1			Wave 2		
	Males	Females	p	Males	Females	p
Severe Class	Males	Females	p	Males	Females	p
Major Role Failure	0.314	0.455	0.038	0.347	0.266	0.191
Physically Hazardous	0.913	0.779	0.004	0.732	0.639	0.107
Legal Problems	0.176	0.130	0.270	0.171	0.088	0.020
Social/Interpersonal Problems	0.614	0.506	0.172	0.611	0.476	1.000
Tolerance	0.753	0.737	0.810	0.667	0.601	0.333
Unsuccessful Efforts to Cut Down	0.756	0.826	0.252	0.805	0.906	0.040
Larger Amount/Longer Periods	0.909	0.891	0.666	0.906	0.889	0.658
Withdrawal	0.813	0.896	0.084	0.819	0.773	0.329
Great Deal of Time Spent	0.664	0.570	0.198	0.624	0.590	0.624
Giving Up/Reducing Activities	0.319	0.313	0.917	0.300	0.268	0.671
Physical/Psychological Problem	0.799	0.754	1.000	0.842	0.819	0.716

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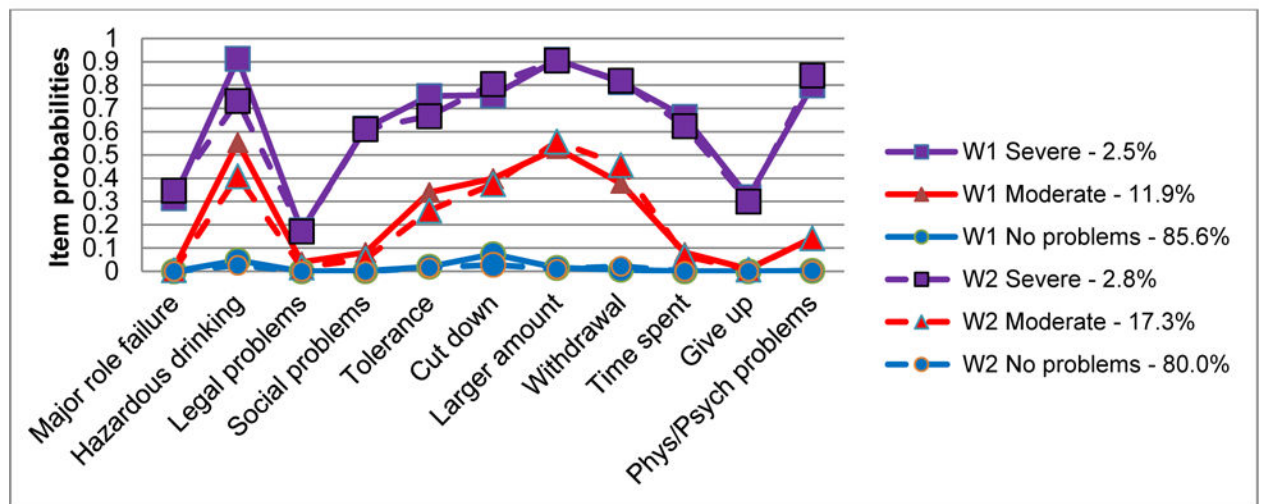
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A. Males



B. Females

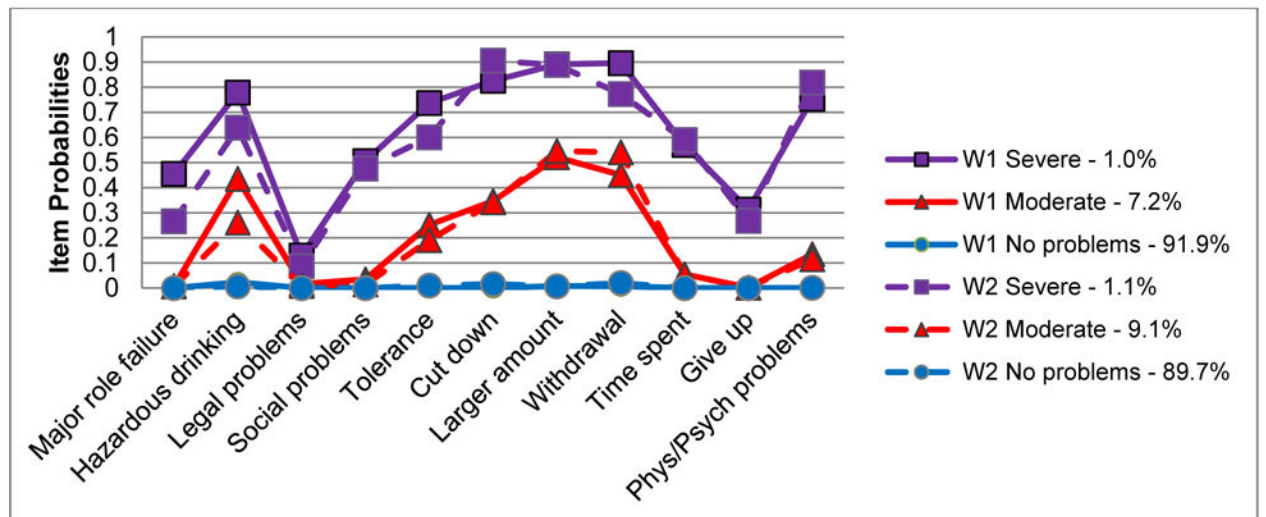


Figure 1.

Alcohol involvement item probabilities and class prevalence estimates from the three class model for **A) males** (n=14,564) and **B) females** (n=20,089) based on latent class analyses of data from the NESARC, waves 1 and 2.

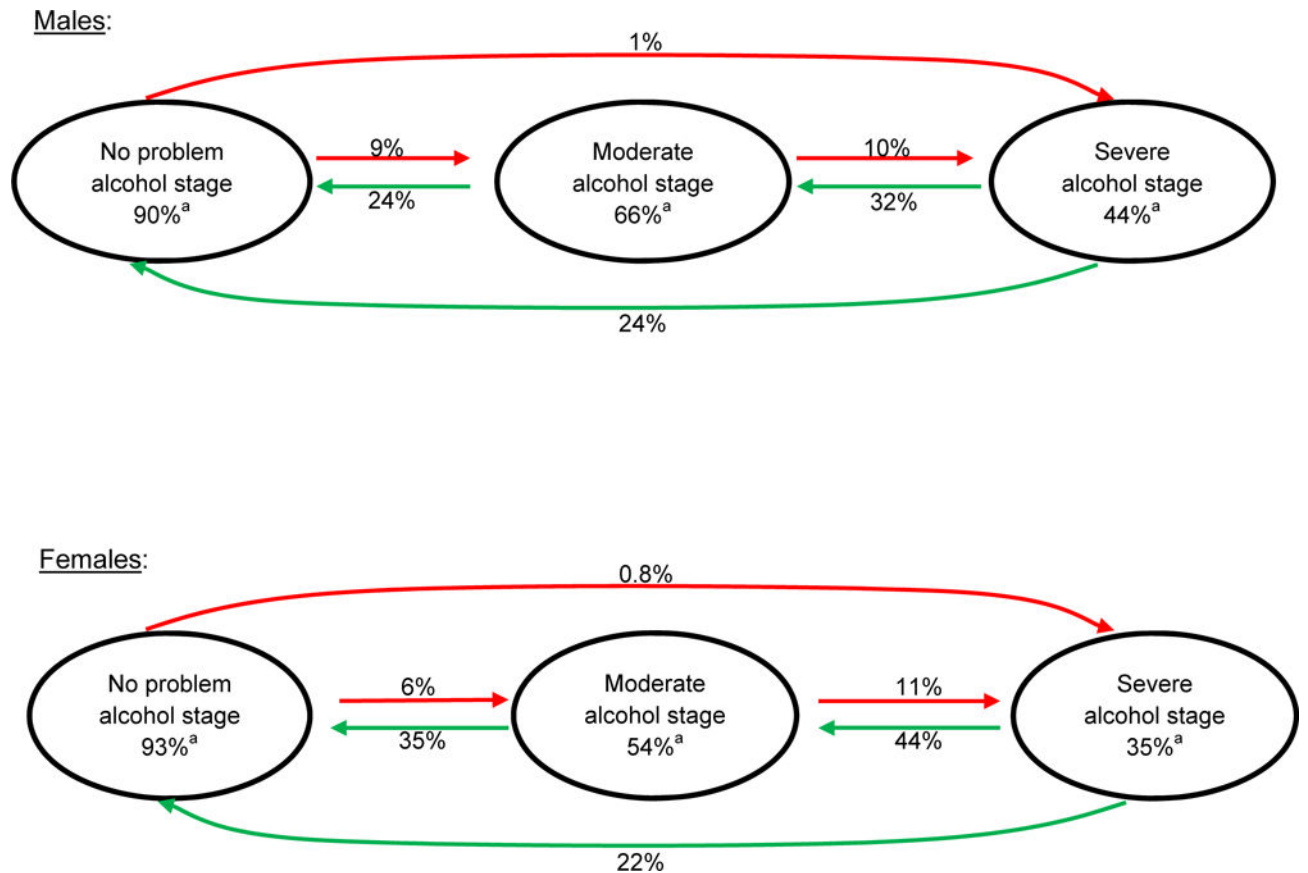


Figure 2.

Probability of transitioning across stages of alcohol involvement during follow-up for males (n=14,564) and females (n=20,089); data from NESARC, waves 1 and 2; data adjusted by sampling weights.

^a Percentages in the circles represent the proportion of individuals at a specific alcohol involvement stage at baseline that remained in the same stage at follow-up. For example, 90% of males in the *No problem stage* remained at that stage.

Characteristics of the study sample: male (n=14,564) and female (n=20,089) participants by a history of DSM-IV mood disorders at baseline; NESARC, wave 1.

Table 1.

Characteristics at baseline	Males						Females						
	Total Males			Mood disorder			Total Females			Mood disorder			
	N	%	p-value ^a	Absent	Present		Absent	Present		Absent	Present		
Age (years):													
18–35	4536	34.5		3695	33.4	841	40.8	6379	32.2	4707	31.2	1672	35.7
36–49	4533	30.0	<0.0001	3751	29.6	782	32.2	5716	28.7	4193	27.6	1523	32.3
50+	5495	35.5		4814	37.0	681	26.9	7994	39.0	6411	41.2	1583	32.0
Race/ethnicity:													
White	9090	73.1		7489	72.1	1601	78.4	11605	72.5	8489	70.6	3116	78.6
Black	2281	9.8	<0.0001	2003	10.2	278	8.0	4206	11.7	3438	12.6	768	8.8
Hispanic (any race?)	2718	12.3		2357	12.8	361	9.1	3638	10.9	2861	11.5	777	9.0
Other	475	4.8		411	4.9	64	4.5	640	4.9	523	5.3	117	3.6
Education (years):													
<12	2356	14.8		2008	14.8	348	14.9	3388	14.5	2652	14.8	736	13.6
12	12208	85.2	0.8367	10252	85.2	1956	85.1	16701	85.5	12659	85.2	4042	86.4
Mood disorder ^c :													
Major depressive disorder	1798	11.8		NA	NA	1798	77.5	4206	20.9	NA	NA	4206	89.0
Dysthymia	458	3.0		NA	NA	458	19.4	1119	5.3	NA	NA	1119	22.5
Mania	462	3.1				462	14.8	710	3.5			710	20.4
Hypomania	375	2.5				375	16.6	481	2.2			481	9.4
Anxiety disorder ^b :													
GAD ^c	418	2.8	<0.0001	105	0.9	313	13.5	1075	5.4	269	1.5	806	18.0
Panic disorder	496	3.3	<0.0001	201	1.7	295	12.4	1294	6.7	481	3.4	813	17.4

Characteristics at baseline	Males						Females							
	Total Males			Mood disorder			Total Females			Mood disorder				
	N	%	<i>p</i> -value ^a	Absent	Present	%	N	%	Absent	Present	%	N	%	<i>p</i> -value ^a
Social phobia	625	4.3	313	2.6	312	13.2	1096	5.8	410	2.8	686	15.5	<0.0001	
Specific phobia	951	6.3	582	4.5	369	16.2	2456	12.4	1365	8.7	1091	24.3	<0.0001	
Non-alcohol drug use disorder ^b														
Illicit drugs ^d	1967	13.6	1278	10.6	689	30.6	1376	7.0	672	4.4	704	15.4	<0.0001	
Nicotine	2731	19.6	1884	16.4	847	37.5	2965	15.4	1625	11.1	1340	29.6	<0.0001	
Family history of alcoholism:														
Absent	10197	70.6	8923	73.2	1274	55.6	13107	66.0	10646	70.3	2461	51.9	<0.0001	
Present	4367	29.4	3337	26.7	1030	44.4	6982	34.0	4665	29.7	2317	48.1		

^aRao-Scott chi-square tests of difference.

^bDiagnostic categories are not mutually exclusive.

^cGAD, generalized anxiety disorder.

^dIncludes lifetime history of abuse and/or dependence on non-alcohol substances: heroin, other opioids, cocaine, cannabis, stimulants, and/or hallucinogens.

Table 2. Fit statistics for latent class models of alcohol involvement by sex and NESARC wave.

	No. of Classes	AIC ^a	BIC ^b	a-BIC ^c	Entropy ^d
Males Wave 1	1	63030	63113	63078	1.00
	2	48914	49088	49015	0.94
	3	47538	47804	47692	0.90
	4	47374	47731	47582	0.88
Males Wave 2	1	68159	58243	68207	1.00
	2	53588	53762	53689	0.90
	3	51651	51916	51805	0.88
	4	51370	51726	51577	0.86
Females Wave 1	1	50097	50184	50149	1.00
	2	39013	39195	39122	0.95
	3	38002	38279	38168	0.94
	4	37957	38328	38179	0.90
Females Wave 2	1	52331	52417	52383	1.00
	2	40722	40904	40831	0.94
	3	39586	39683	39751	0.92
	4	39444	39816	39666	0.92

^a AIC: Akaike's Information Criterion. Lower values represent better fit.

^b BIC: Bayesian Information Criterion. Lower values represent better fit.

^c a-BIC: sample-size adjusted Bayesian Information Criterion. Lower values represent better fit.

^d Values closer to 1 indicated better separation of classes

Table 3.

Cross-sectional association of lifetime mood disorders at baseline with alcohol involvement stages among males and females at baseline; NESARC, wave 1.

Alcohol involvement stage	Mood disorder ^a	
	Unadjusted OR ^b (95% CI) ^c , p-value	Propensity Score Adjusted ^d OR ^b (95% CI) ^c , p-value
Males		
Severe	5.89 (4.42–7.85), <0.001	2.58 (1.75, 3.81), <0.001
Moderate	2.05 (1.72–2.45), <0.001	1.13 (0.92, 1.39), 0.250
No problems	Reference	
Females		
Severe	5.82 (4.00–8.49), <0.001	1.96 (1.27–3.06), 0.001
Moderate	2.20 (1.88–2.58), <0.001	1.32 (1.10–1.59), 0.003
No problems	Reference	

^aMood disorder includes a lifetime diagnosis of DSM-IV major depressive disorder, dysthymia, mania, or hypomania at the time of the baseline interview.

^bOR, odds ratio.

^c95% CI, confidence interval.

^dPropensity score models include age, race-ethnicity, educational level, family history of alcoholism, and the history of lifetime anxiety, nicotine, and non-alcohol drug use disorders.

Table 4.

The association of lifetime mood disorder at baseline with transitions in alcohol involvement stage at follow-up by sex; data are from the NESARC, waves 1 and 2.

Transition direction	Mood Disorders with Transitions in Alcohol Involvement Stages					
	Males			Females		
	Unadjusted OR ^a (95% CI) ^b , p-value	Propensity Score Adjusted ^c OR ^a (95% CI) ^b , p-value	Unadjusted OR ^a (95% CI) ^b , p-value	Propensity Score Adjusted ^c OR ^a (95% CI) ^b , p-value	Unadjusted OR ^a (95% CI) ^b , p-value	Propensity Score Adjusted ^c OR ^a (95% CI) ^b , p-value
Progression						
No Problems to Moderate	0.91 (0.67, 1.24) p=0.569	0.73 (0.51, 1.04) p=0.084	1.34 (1.06, 1.69) p=0.015	0.85 (0.65, 1.11) p=0.243		
No Problems to Severe	1.20 (0.52, 2.74) p=0.669	0.89 (0.26, 3.08) p=0.851	1.39 (0.67, 2.91) p=0.376	2.16 (0.81, 5.76) p=0.123		
Moderate to Severe	2.08 (1.26, 3.42) p=0.004	1.73 (0.82, 3.66) p=0.153	1.25 (0.77, 2.05) p=0.368	1.23 (0.66, 2.30) p=0.508		
Remission						
Moderate to No Problems	1.39 (0.91, 2.13) p=0.127	1.45 (0.89, 2.35) p=0.132	1.36 (0.90, 2.04) p=0.148	0.90 (0.57, 1.40) p=0.625		
Severe to No Problems	0.85 (0.45, 1.62) p=0.633	0.74 (0.27, 2.02) p=0.560	0.64 (0.28, 1.47) p=0.293	0.52 (0.12, 2.18) p=0.367		
Severe to Moderate	1.51 (0.75, 3.03) p=0.251	1.54 (0.54, 4.40) p=0.417	0.43 (0.19, 0.98) p=0.045	0.30 (0.09, 0.99) p=0.048		

^aOR, odds ratio. Odds ratios represent the odds of a mood disorder being associated with transitioning between the specific alcohol involvement stages relative to the odds of staying in the same stage.

^b95% CI, confidence interval.

^cPropensity score models include age, race-ethnicity, educational level, family history of alcoholism, and the history of lifetime anxiety, nicotine dependence, and non-alcohol drug use disorders.