Published in final edited form as:
JAMA Psychiatry. 2013 July ; 70(7): 718–726. doi:10.1001/jamapsychiatry.2013.1098.

A Prospective Assessment of Reports of Drinking to Self-medicate Mood Symptoms with the Incidence and Persistence of Alcohol Dependence

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Abstract

Context—Mood disorders and alcohol dependence frequently co-occur. Etiologic theories concerning the comorbidity often focus on drinking to self-medicate or cope with affective symptoms. However, there has been little to no prospective studies in population-based samples of alcohol self-medication of mood symptoms with the occurrence of alcohol dependence. Furthermore, it's not known whether these associations are effected by treatment, or symptom severity.

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The authors report no conflicts of interest.

Objective—Alcohol self-medication of mood symptoms is hypothesized to increase the probability of subsequent onset, and the persistence or chronicity of alcohol dependence.

Design—Prospective study, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

Setting—Nationally representative survey of the US population.

Participants—Drinkers at risk for alcohol dependence among the 43,093 adults surveyed in 2001-2 (wave 1); 34,653 of which were re-interviewed in 2004-5 (wave 2).

Main outcome measure—Association of alcohol self-medication of mood symptoms with incident and persistent DSM-IV alcohol dependence using logistic regression and the propensity score method of inverse probability of treatment weighting.

Results—The report of alcohol self-medication of mood symptoms was associated with an increased odds of incident alcohol dependence at follow-up (adjusted odds ratio [AOR]=3.10, 95% confidence interval [CI]=1.55-6.19, p=0.002), and persistence of dependence (AOR=3.45, CI=2.35-5.08, p<0.001). The population attributable fraction (PAF) was 11.9% (CI=6.7-16.9%) for incident dependence, and 30.6% (CI=24.8-36.0%) for persistent dependence. Stratified analyses were conducted by age, sex, raceethnicity, mood symptom severity, and treatment history for mood symptoms.

Conclusions—Individuals who drink to alleviate mood symptoms are more likely to develop alcohol dependence and to have persistent dependence once it develops. These associations occur among individuals with sub-threshold mood symptoms, with DSM-IV affective disorders, and for those who have received treatment. Drinking to self-medicate mood symptoms may be a potential target for prevention and early intervention efforts aimed at reducing the occurrence of alcohol dependence.

Introduction

Many clinical studies document the comorbid occurrence of alcohol dependence with depression.[1–3] Although there are exceptions,[4] patients with these types of co-occurring disorders tend to have a worse prognosis than those with either condition alone.[3;5–15] Data from population-based surveys also report high frequencies of comorbidity for mood and alcohol use disorders.[16–19] In a number of nationally representative surveys, the prevalence of comorbid mood and alcohol disorders is relatively high. The conditions co-occur to a greater degree than would be expected by chance alone. For example, in prior analyses of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), mood disorders, including major depression, dysthymia, mania and hypomania were found to have consistently positive associations with alcohol dependence.[19;20] Among individuals with prior year depression, 11.0% met criteria for alcohol dependence.[19] Among those with alcohol dependence in the prior year, 20.5% had concurrent depression.[19] Furthermore, there is also evidence in some studies that stronger comorbid associations are found among females.[17;18;21] Alcohol abuse also has been found to be associated with mood conditions, although in some instances, it has a weaker comorbid association with affective disorders.[17;19]

Prior studies of the comorbid relationship of mood and alcohol conditions provide evidence that there is likely a bidirectional association. Some studies have found that alcohol dependence is the primary condition and is associated with increases in the risk of depression and other mood conditions;[22;23] while others have found alcohol dependence to be secondary, whereby mood disorders are associated with an increased risk for the new development of alcohol use disorders.[24] In most instances, depression has been found to be secondary to alcohol dependence.[25] It is also plausible that there is a common etiology for both conditions that might include a genetic vulnerability, or environmental factors.[26] Etiologic theories to account for mood disorder as the primary condition often focus on the potential use of alcohol as a method of self-medicating, or coping with affective symptoms.[27] Although a frequently considered hypothesis, there is a paucity of research which has assessed this association. In particular, there is little data from prospective population-based studies, which reduce potential biases related to temporal association and sample selection. In an inpatient sample, Holahan and colleagues[28] found that drinking to cope among depressed patients was associated with an increase probability for consumption of alcohol and development of alcohol problems during a 10-year follow-up period. Yet, studies in clinical settings may not provide an adequate assessment of self-medication for mood symptoms with alcohol dependence. Although a high proportion of individuals with mood and alcohol disorders are seen in clinical settings, many if not most of the individuals affected with these conditions fail to be identified and never receive treatment.[29;30] Prior estimates indicate that only approximately 42.1 to 60.9% of those with an affective disorder[20] receive treatment for their mood symptoms. A much lower proportion of individuals with an alcohol use disorder ever receive clinical attention, and some estimate that only 4.8% to 27.9% of those with alcohol abuse or dependence receive treatment.[29]

Swendsen and colleagues[31] used experience sampling to assess self-medication of negative mood states with drinking behavior and found that nervousness, but no other affective symptom was associated with alcohol use later in the day. Studies utilizing experience sampling methods have the advantage that information is gathered as the study participant experiences the negative mood during daily activities. Any subsequent alcohol use may be monitored throughout the day and assessed in temporal relation to mood status. On the other hand, population-based studies may provide information for a large representative sample of the population, irrespective of whether they have received treatment.

Prior studies of the NESARC have examined self-medication using cross-sectional assessments of co-occurring conditions[32–34] and found strong associations of using alcohol and drugs to self-medicate mood disorders with comorbid psychopathology. Among participants with a mood disorder, a total of 24.1% of the sample reported using alcohol or drugs to self-medicate their symptoms.[32] In addition, self-medication of anxiety symptoms has been shown to be associated with an increased risk of drug use disorders.[35] Using data from the National Comorbidity Survey, it was found that between 7.9 and 35.6% of those with anxiety disorders reported self-medication with alcohol or drugs.[36] In the current analyses, we hypothesized that self-medication with alcohol for mood symptoms would be associated with an increased incidence or new onset of alcohol dependence over time. In addition, there is no population-based assessment of whether drinking to self-medicate mood symptoms alters the potential for chronicity or persistence of alcohol dependence.

Consequently, we also evaluated the hypothesis that self-medication of mood symptoms with alcohol would be associated with persistence of alcohol dependence, once it developed. Because prior findings indicate sex differences for these comorbid relationships,[31;32] we also examined whether the association of self-medication with alcohol dependence would vary by sex. We further explored these associations in race- and age-specific strata. In addition, we assessed whether these potential relationships would vary by treatment history, and by diagnosis of mood disorder as compared with sub-threshold mood symptoms. Our rationale for these latter assessments was to garner information as to whether self-medication drinking may be indicative of failure to receive treatment for an affective disorder, or the presence of refractory mood symptoms. We also aimed to assess whether individuals who met full criteria for a mood disorder, such as major depression, would be more likely to self-medicate as compared with individuals who had sub-threshold symptoms.

Methods

Sample

The sample for the current study was drawn from the National Epidemiological Survey of Alcohol and Related Conditions (NESARC) waves 1 and 2. The design and sample characteristics of NESARC have been previously described.[19;37] Briefly, the NESARC is a survey of a nationally representative sample of the population in the United States, including residents of Hawaii and Alaska, conducted by the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The interviews were conducted face-to-face with participants. To assure accurate estimates among racial and ethnic minority populations and among younger adults, the NESARC protocol included the oversampling of Blacks, Hispanics and young adults, ages 18 to 24 years. The NESARC sample was weighted to adjust for the unequal probabilities of selection and to provide nationally representative estimates.

The first wave of the NESARC was fielded between 2001 and 2002 and included 43,093 participants who were aged 18 years and older. Of these, a total of 39,959 participants were eligible for wave 2 interviews. Ineligible respondents were those who could not be interviewed because at the time of the follow-up interview they were either deceased, deported, mentally or physically impaired or on active military duty. Of the eligible wave 1 participants, 34,653 were successfully followed and re-interviewed in the wave 2 survey between 2004 and 2005. The response rates for wave 1 and eligible wave 2 surveys were 81% and 87%, respectively.

This current study sample was restricted to individuals with mood symptoms who were asked about self-medication with alcohol, reported having used alcohol in their lifetime and were re-interviewed at wave 2 (n=5,768). For the analyses that assessed incident alcohol dependence, individuals with current and lifetime alcohol dependence at baseline were excluded (n=1,547), leaving a study sample of 4,221 (12,870 person-years of follow-up). For the analyses that assessed persistence of alcohol dependence, only individuals with current or lifetime alcohol dependence at the baseline interview were included, resulting in a study sample of 1,547 (4,756 person-years of follow-up).

Measures

In this report, data from NESARC wave 1 were used to assess baseline characteristics. Mental disorders were ascertained based on DSM-IV criteria using the NIAAA's Alcohol Use Disorder and Associated Disabilities Interview Schedule–DSM-IV Version (AUDADIS-IV)[38;39] -- a structured diagnostic interview designed for use by lay interviewers to derive lifetime and 12-month substance use and mental disorders. Mood disorders included major depression, bipolar disorder and dysthymia. We focused on the experience of mood symptoms in the past year and distinguished between threshold and sub-threshold mood syndromes. Threshold mood syndromes were cases that met the full diagnostic criteria for the specific mood disorder. The sub-threshold mood syndromes were those which had some symptoms but did not meet all criteria, including the clinical significance criteria for any mood disorder. Other disorders assessed were current or lifetime alcohol abuse and dependence, drug abuse and dependence (heroin, other narcotics, cocaine, stimulants, hallucinogens, and/or marijuana), nicotine dependence, 12-month anxiety disorders (generalized anxiety, panic, and/or social anxiety), and personality disorders measured at both waves (antisocial, narcissistic, histrionic, borderline, schizoid, schizotypal, paranoid, obsessive-compulsive, dependent, and/or avoidant).

Alcohol self-medication was assessed by asking if participants had drunk alcohol in the past year to improve their mood (asked of participants reporting depression and dysthymia symptoms), or to calm down (asked of participants reporting manic or hypomanic symptoms). Treatment history for mood symptoms was assessed by asking whether participants had ever sought treatment for depressive or manic symptoms from a counselor, therapist, doctor or other professional; if they were hospitalized overnight or went to an emergency room because of mood symptoms; and if a doctor had ever prescribed medication for mood symptoms.

Other variables included in these analyses were sex, age (18-29, 30-39, 40-54 and 55+ years), race/ethnicity (non-Hispanic white, black, Hispanic and other), education (<12 years, 12 years or GED, and >12 years), family history of alcoholism, alcohol consumption patterns in the past year (every day/nearly every day vs. less than every day), and amount of alcohol used on drinking days in the past year (≥5 drinks per drinking day vs. <5 drinks). Family history of alcoholism was assessed by asking if any first-degree relatives had ever been an "alcoholic or problem drinker". Separate questions assessed participants' biological mother, father, sisters, brothers, daughters and sons.

Analyses

The two outcome variables of interest in this study were: 1) incidence of new episodes of alcohol dependence during the follow-up period, and 2) persistence of alcohol dependence through wave 2 of the study. Participants who did not meet the criteria for alcohol dependence at baseline but who did meet the criteria during the 3-year follow-up period were defined as new onset or incident cases of alcohol dependence. For the incidence analyses, individuals with a history of alcohol abuse were not excluded because many individuals first develop alcohol abuse prior to dependence. In addition, a diagnosis of alcohol abuse at the time of the baseline interview was held constant in all multivariate

analyses. In supplemental analyses examining incident alcohol abuse together with incident dependence as the outcome variable, among those that did not meet criteria at wave 1, the overall association was similar to that presented for alcohol dependence alone.

We defined persistent dependence as meeting diagnostic criteria for alcohol dependence at both waves of the study. In other words, individuals with a history of 12-month or lifetime alcohol dependence at the baseline interview who also subsequently met criteria for alcohol dependence during the 3-year follow-up interval were classified as having persistent alcohol dependence.

The analyses were conducted in three stages. First, the socio-demographic characteristics, alcohol use patterns, psychiatric and substance use comorbidity, family history and treatment for mood symptoms were compared across participants who did or did not develop alcohol dependence, as well as for those who did or did not have persistence of alcohol dependence. Second, these same characteristics were compared across participants by report of alcohol self-medication for mood symptoms at baseline separately for the study samples used to assess each outcome. These analyses were conducted to identify potential confounders and variables to be included in computation of propensity score weights described below. In the third stage of the analyses, the association of self-medication with each alcohol dependence outcome was assessed in the total sample and in strata based on socio-demographic characteristics, mood disorder diagnosis, and treatment history to examine whether the effect was more pronounced in some population subgroups than others. These analyses were conducted using both bivariate and multivariate models. The multivariate logistic regression models adjusted for socio-demographic, psychopathology, substance use, and treatment variables and whether or not the participants' symptoms met the diagnostic thresholds for mood disorder diagnoses. However, there are limitations in the use of regression adjustment, in particular model dependence when the groups are different on the observed characteristics.[40;41] Therefore, in addition to regression adjustment, we utilized the propensity score method of inverse probability of treatment weighting (IPTW)[42;43] to adjust for differences between self-medicating and non-self-medicating participants. In this technique, first propensity scores (probability of self-medication) are computed using a logistic regression model. These scores reflect each participant's likelihood of self-medicating with alcohol given their socio-demographic and clinical characteristics. Next, data are weighted by their inverse probabilities of being in their observed group (self-medicating vs. non-self-medicating).[41]

The NESARC used a complex sampling design. Analyses used the svy routines of STATA 11.0 to take into account survey weights, clustering and stratification of the data. The propensity score weights described earlier were multiplied by the survey weights and the resulting combined weights were used in analyses of the association of self-medication with alcohol dependence during follow-up. To assess the effectiveness of the IPTW in balancing the composition of the self-medicating and non-self-medicating groups, we compared the characteristics of the groups before and after applying the combined weights. Application of inverse probability of treatment weighting in these analyses was quite successful as the groups in analyses for both alcohol outcomes (incidence of alcohol dependence and persistence of alcohol dependence) were similar with respect to the observed characteristics

after using the weights.[44] Population attributable fraction (PAF) was computed using the punaf program for STATA software.[45] The program implements the method for estimating PAFs as recommended by Greenland and Drescher [46] for cohort and cross-sectional studies.

Results

Among the study participants with mood symptoms, 226 new onset cases of alcohol dependence developed during follow-up. A total of 1,708 (40.5%) of the baseline sample met the criteria for a 12-month DSM-IV mood disorder, and an additional 2,513 (59.5%) had mood symptoms without meeting full criteria for a mood disorder diagnosis. A total of 455 cases of persistent alcohol dependence were identified by the time of the wave 2 interview. The baseline characteristics associated with incidence and persistence of alcohol dependence are presented in Table 1. In the initial bivariate analyses, individuals who developed new onset alcohol dependence as well as those with persistence of alcohol dependence were more likely to report having used alcohol to self-medicate their mood symptoms. In addition, individuals with incident or persistent alcohol dependence were more likely to be male, among the youngest age group classification (18-29 years of age), to report greater quantity and frequency of consumption, and to be diagnosed with illicit drug or nicotine dependence. Furthermore, persistence of alcohol dependence tended to be more strongly associated with a mood and/or substance use disorder, family history of alcoholism, and lower education. Incident alcohol dependence was more strongly associated with minority race-ethnicity. Similar characteristics were associated with baseline alcohol self-medication in both study samples (see eTables 1A and 1B).

The findings for the multivariate IPTW logistic regression models are presented in Table 3. The analyses were completed for the entire study sample, and separately within specific strata. For example, in the sex-stratified analyses, we ran models separately for males and females. The adjusted analyses took into account the IPTW, and adjusted for sociodemographic, psychopathology, and treatment history covariates. For the total sample, self-medication of mood symptoms with alcohol was associated with an increased odds for incident alcohol dependence during follow-up (adjusted odds ratio [AOR]=3.10, 95% confidence interval [CI]=1.55-6.19, p=0.002), and for persistent alcohol dependence (AOR=3.45, CI=2.35-5.08, p<0.001). The proportion of incident alcohol dependence cases attributable to alcohol self-medication in the population, taking into account survey weights, was approximately 12% (PAF=11.9%, CI=6.7-16.9%). However, 30.6% (CI=24.8-36.0%) of persistent alcohol dependence cases can be attributable to drinking to self-medicate mood symptoms.

In the sex-, age- and race-stratified analyses, little evidence for differences among the subgroups was found as there was significant overlap in confidence intervals. Because self-medication may be less likely to occur with fewer or less severe mood symptoms, we examined the associations by whether individuals met full diagnostic criteria for mood disorders or had sub-threshold symptoms. Although odds ratios in both subgroups were elevated, self-medication drinking tended to have a stronger and statistically significant association with incident dependence among those with sub-threshold symptoms (AOR=3.88, CI=1.63-9.26, p=0.003). On the other hand, self-medication drinking was

associated with persistent alcohol dependence for those with sub-threshold symptoms, as well as those individuals who met full criteria for a mood disorder. Self-medication drinking among individuals who reported having received treatment for mood symptoms was associated with a four-fold increased odds of incident alcohol dependence in follow-up (AOR=3.94, CI=1.82-8.52, p=0.001), whereas a weaker association of self-medication with dependence was found among those without a treatment history (AOR=1.97, CI=0.50-7.76, p=0.326). Drinking to self-medicate mood symptoms was strongly associated with persistence of alcohol dependence among those with and without a treatment history (AOR=4.81, CI=2.91-7.94, p<0.001 and AOR=2.18, CI=1.27-3.74, p=0.006, respectively), but those with a treatment history had a significantly stronger association with persistent dependence (F[1, 61]=4.95, p=0.030).

In supplemental analyses we assessed the association of alcohol self-medication of mood symptoms with incident alcohol abuse as well as incident alcohol dependence at follow-up (after exclusion of all baseline cases of both alcohol abuse and alcohol dependence). In these propensity score adjusted analyses, we found a similar overall association with drinking to self-medicate mood symptoms (AOR=3.04, CI=1.43-6.47, p=0.005); however, power was attenuated to complete the proposed stratified analyses.

Discussion

Consistent with our principal hypotheses, individuals who report self-medicating their mood symptoms by drinking alcohol have a greater likelihood of developing alcohol dependence. Once the dependence has developed, self-medicating with alcohol increases the probability of its persistence. In this population-based sample, the odds for developing alcohol dependence were three times greater for those who self-medicated their symptoms relative to those who reported no self-medication. The odds for persistence were also three-fold greater for those who reported drinking to self-medicate their mood symptoms. In our study samples, approximately 12% of new cases of alcohol dependence, and 30% of persistent cases were attributable to alcohol self-medication of mood symptoms. Contrary to our initial hypotheses, the association of alcohol self-medication with incident or persistent dependence did not appreciably vary within strata by sex, age, or race-ethnicity. Furthermore, the associations were elevated among individuals who met full criteria for a mood disorder, as well as among individuals who met some but not all required criteria for an affective condition. This sub-threshold group would be less likely to receive mental health treatment because of the lower severity of their symptoms.

Although self-medication with alcohol is a commonly mentioned explanation for the comorbid occurrence of mood disorders and alcohol dependence, there is relatively little data examining whether this association potentially may increase the probability of developing dependence. There is also virtually no assessment of whether it is associated with persistence of dependence in population-based samples. Consistent with some prior cross-sectional and clinical studies,[31;47–49] utilizing different methodology and within select study samples, the current analyses provide evidence that self-medication of mood symptoms with alcohol is associated with both the new onset of dependence as well as the persistence of dependence over time. This association was found to be equally strong for

men and women, across race-ethnicity subgroups, and among older as well as young adults. Furthermore, the findings indicate that even among individuals who have some mood symptoms but who do not meet full criteria for a mood disorder, self-medication by drinking may put them at a similar potential risk for dependence as was found for those with more severe mood conditions such as bipolar disorder or major depression.

It should be kept in mind that although we found that self-medication drinking of mood symptoms is associated with an increased risk of subsequent alcohol dependence, there are other possible explanations for the comorbid associations between affective conditions and alcohol use disorders not explored here. In prior assessments of bidirectional comorbidity, most instances of comorbidity appears to result from mood disorders occurring subsequent to the alcohol use disorder.[25] There may be several physiologic mechanisms that explain the comorbidity.[36;50–52] Thus, it is likely that both causal pathways may operate.[53;54] Furthermore, there may be common underlying genetic as well as social or environmental factors which predispose to an increased risk for both disorders.[55–60]

Individuals who report a history of treatment for mood disorders had a stronger association of self-medication drinking with incident as well as persistent alcohol dependence in contrast to those without any treatment history. This finding may indicate that individuals with a treatment history have more severe mood symptoms or symptoms that are refractory to the treatment received. It also may indicate that receiving treatment for mood conditions does not necessarily mean that some individuals will not also self-medicate with alcohol. Simply addressing the mood symptoms does not necessarily mitigate the subsequent drinking behavior.[61] Once alcohol use becomes problematic, treatment modalities would need to address both the mood and substance use symptoms, as well as personal and environmental issues that may need to be considered when developing appropriate treatment plans.[62;63] Some individuals may drink in response to mood symptoms, as well as to achieve relief and separation from painful or stressful emotional experiences,[62] or as an attempt at bolstering inadequate or poorly developed coping skills. All of these may be challenging issues to address and often require a multimodal treatment strategy. In addition, it may be necessary to provide further educational efforts in treatment-seeking populations concerning the risks associated with use of alcohol as a potential coping mechanism or to alleviate symptoms.

Several limitations in these analyses are noteworthy. First, as discussed previously, the current study did not incorporate an experience sampling methodology.[64] As a consequence, we did not have the ability to evaluate mood symptoms as they might occur on a daily basis or might be linked to subsequent alcohol consumption within a limited time interval. However, this type of methodology is less feasible when attempting to link behavior changes over extended periods of time. It would also be challenging to use this methodology to establish transition to the new onset of a substance use disorder or provide evidence for the development of a chronic dependent condition in a population-based sample. Second, although using the population-based sample reduces selection biases that would likely occur within a clinical context, the potential for misclassification bias may occur due to differential reporting of self-medication. Individuals need to be aware of their behavior in order to acknowledge self-medication and to report its occurrence. Some individuals with

mood conditions may consume alcohol without the insight that their consumption may be an attempt to alleviate negative affect. We were able to take into account differences in consumption patterns by frequency and quantity, as well as differences in diagnostic history. These characteristics in our analyses did not explain the self-medication/dependence associations. Related to this potential reporting bias is the concern that adequate validation of the single survey item to assess self-medication drinking has not been completed and poses further concerns regarding potential misclassification. However, although some individuals may underreport their self-medication drinking, those who do report this behavior may be an appropriate target for prevention and early intervention efforts at reducing the occurrence of dependence. Furthermore, if a large number of individuals in the sample had mood symptoms but underreported their self-medication drinking, this would tend to weaken the hypothesized associations in our analyses. This indicates that our findings may actually underestimate the self-medication/dependence associations. Yet reporting biases may work the other way, in that individuals who drink heavily may want to use self-medication as a way of rationalizing their drinking, even if they don't have mood symptoms. We were not able to assess whether individuals without affective symptoms or depression also report self-medication drinking, as the questions concerning self-medication were only asked of individuals with mood and anxiety symptoms. Third, although we were able to hold constant a large number and range of confounding characteristics, the potential for residual confounding remains. Individual-level characteristics such as coping skills, neighborhood-level items such as poverty and availability of liquor stores, as well as medical community-level factors such as access to mental health care or substance disorder treatment may explain some of the associations found in our current study. Although we were not able to hold constant all potentially explanatory characteristics, we were able to utilize propensity score methodology to assess the causal inferences of these associations. The use of this methodology reduces confounding due to observed characteristics and any unobserved characteristics associated with the observed ones. However, non-causal explanations for the reported associations are still possible. Fourth, although this is one of the largest prospective population-based samples available with the degree of mental health and substance use measurement necessary for this complex assessment, some analyses are still limited by small subgroup sizes, such as those by specific type of treatment history, and diagnostic classification. As a consequence, power to examine these additional subgroups was inadequate.

Notwithstanding these limitations, the current analyses highlight a potentially significant risk factor for both the development and persistence of alcohol dependence that may be an appropriate target for prevention efforts. Although it's widely accepted that individuals with mood disorders should receive appropriate treatment, there is a large group of individuals with sub-threshold mood symptoms who may be at equal risk for dependence and generally do not receive treatment. Individuals with subclinical or sub-threshold symptoms are unlikely to seek out mental health treatment, but may attempt to cope with their early mood symptoms with alternate strategies. They may not be aware of the importance of avoiding alleviation of mood symptoms with alcohol. Early identification and educational efforts, particularly in clinical settings where at-risk individuals potentially are more readily

targeted, may have an impact on reducing the development and chronicity of alcohol dependence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The analyses and preparation of this project were supported by grants from the National Institute on Alcohol Abuse and Alcoholism (AA016346), and the National Institute on Drug Abuse (DA030460). Preparation of this paper also was supported by grants from the Canadian Institutes of Health Research New Investigator Award (152348), a Manitoba Health Research Council Chair award (JS), and a Johns Hopkins School of Medicine Clinician Scientist Award (AA). Dr. Rosa M. Crum had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Dr. Ramin Mojtabai performed the statistical analyses for this study.

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JAMA Psychiatry. Author manuscript; available in PMC 2014 September 02.

Table 1

Characteristics of NESARC participants with mood symptoms at the wave 1 (baseline) interview with incidence and persistence of alcohol dependence at the time of the follow-up interview (wave 2).

		***Incidence* of alcohol dependence at follow-up[a]**						***Persistence* of alcohol dependence at follow-up**					
		Absent		**Present**		**Bivariate logistic regression analyses**		**Absent**		**Present**		**Bivariate logistic regression analyses**	
Characteristics at baseline		**N**	**%**	**N**	**%**	**OR (95% CI)**	***p***	**N**	**%**	**N**	**%**	**OR (95% CI)**	***p***
Alcohol self-medication of mood:													
	Absent	3,826	96.4	187	84.6	1.00		909	85.1	236	51.5	1.00	
	Present	169	3.6	39	15.4	4.81 (3.09-7.49)	<0.001	183	14.9	219	48.5	5.39 (3.98-7.28)	<0.001
Sex:	Female	2,847	67.8	120	53.8	1.00		601	48.0	191	38.0	1.0	
	Male	1,148	32.2	106	46.2	1.81 (1.30-2.52)	0.001	491	52.0	264	62.0	1.50 (1.15-1.96)	0.003
Age (years):	18-29	826	22.1	103	54.6	1.00		318	30.5	168	43.9	1.0	
	30-39	948	22.2	47	15.8	0.29 (0.19-0.45)	<0.001	309	27.1	117	23.2	0.59 (0.42-0.84)	0.004
	40-54	1,390	35.4	56	20.8	0.24 (0.16-0.35)	<0.001	335	31.1	145	28.6	0.64 (0.47-0.88)	0.006
	55+	831	20.4	20	8.8	0.18 (0.10-0.32)	<0.001	130	11.3	25	4.3	0.26 (0.15-0.46)	<0.001
Race/ethnicity:	White	2,716	79.7	133	67.9	1.00		781	79.3	301	78.4	1.0	
	Black	526	7.2	39	14.3	2.32 (1.38-3.89)	0.002	109	5.9	58	6.6	1.47 (0.95-2.28)	0.080
	Hispanic	617	8.5	42	12.3	1.69 (1.05-2.72)	0.031	146	8.4	78	9.3	1.40 (0.91-2.16)	0.122
	Other	136	4.6	12	5.5	1.40 (0.70-2.79)	0.329	56	6.4	18	5.6	0.63 (0.31-1.28)	0.197
Education (years):	<12	438	9.9	39	13.6	1.00		116	10.7	78	16.6	1.0	
	12 or GED	1,030	25.8	57	24.9	0.70 (0.40-1.22)	0.209	274	24.6	131	30.1	0.79 (0.50-1.24)	0.295
	>12	2,527	64.3	130	61.5	0.69 (0.44-1.09)	0.112	702	64.8	246	53.4	0.53 (0.35-0.80)	0.003
Drinking pattern[b]:	<Daily	3,714	93.0	195	87.1	1.00		947	87.3	307	70.0	1.0	
	Daily/nearly daily	281	7.0	31	12.9	1.95 (1.19-3.20)	0.009	145	12.7	148	30.0	2.97 (2.16-4.08)	<0.001
Drink level[c]:	<5 on drinking days	3,766	94.2	180	81.7	1.00		865	78.2	244	53.0	1.0	
	≥5 on drinking days	222	5.8	45	18.3	3.62 (2.36-5.56)	<0.001	227	21.8	207	47.1	3.19 (2.39-4.27)	<0.001
Affective disorder[d]:	Major depression	1,257	30.6	91	37.4	1.35 (0.96-1.90)	0.078	389	33.2	200	45.7	1.69 (1.24-2.32)	0.001
	Mania/hypomania	432	10.5	38	16.6	1.68 (1.11-2.56)	0.015	199	19.0	118	26.8	1.55 (1.13-2.14)	0.008
	Dysthymia	324	7.7	19	7.8	1.00 (0.51-1.98)	0.989	97	7.5	53	11.2	1.54 (0.99-2.39)	0.054
Comorbidity[d]:	Anxiety disorders[e]												
	Personality disorders[f]	955	24.0	56	22.1	0.90 (0.59-1.36)	0.610	363	33.8	162	37.1	1.16 (0.87-1.54)	0.319
	Drug dependence[g]	1,554	38.0	130	55.6	2.04 (1.46-2.85)	<0.001	599	54.7	331	69.1	1.85 (1.41-2.43)	<0.001
	Drug abuse[h]	109	2.8	17	4.9	1.81 (0.99-3.30)	0.054	186	16.4	137	32.2	2.42 (1.77-3.30)	<0.001
	Nicotine dependence	431	11.4	43	15.2	1.40 (0.92-2.11)	0.114	375	35.2	207	45.4	1.53 (1.16-2.01)	0.003
		695	18.2	73	32.3	2.15 (1.51-3.06)	<0.001	388	36.0	247	56.1	2.27 (1.73-2.98)	<0.001
Family history of alcoholism[i]:	Absent	2,171	54.3	110	50.0	1.00		434	41.6	152	34.0	1.0	
	Present	1,821	45.7	115	50.0	1.19 (0.84-1.68)	0.316	656	58.4	301	66.0	1.39 (1.03-1.87)	0.034

Characteristics at baseline		*Incidence* of alcohol dependence at follow-up[a]						*Persistence* of alcohol dependence at follow-up					
		Absent		Present		Bivariate logistic regression analyses		Absent		Present		Bivariate logistic regression analyses	
		N	%	N	%	OR (95% CI)	*p*	N	%	N	%	OR (95% CI)	*p*
Treatment of mood symptoms[j]:	None	1,705	41.6	100	43.6	1.00		496	47.8	207	44.5	1.0	
	Any	2,290	58.4	126	56.5	0.92 (0.65-1.30)	0.645	596	52.2	248	55.5	1.14 (0.86-1.51)	0.344

[a] At baseline, all participants reported drinking alcohol in the past year but none had a lifetime history of alcohol dependence for the analyses to assess incidence of alcohol dependence. For the analyses involving persistence of dependence, all individuals had a baseline history of alcohol dependence with or without abuse.

[b] Indicates pattern of drinking in the past year.

[c] Indicates the number of alcoholic drinks consumed on drinking days in the past year. There is missing data for 8 participants for the incidence sample, and missing data for 4 participants in the persistence sample.

[d] Diagnostic categories are not mutually exclusive.

[e] Includes 12-month generalized anxiety disorder, panic disorder and social anxiety disorder.

[f] Includes antisocial, narcissistic, histrionic, borderline, schizoid, schizotypal, paranoid, obsessive-compulsive, dependent and avoidant personality disorders.

[g] Includes lifetime history of dependence on non-alcohol substances: heroin, other opioids, cocaine, cannabis, stimulants, and/or hallucinogens.

[h] Includes lifetime history of abuse on non-alcohol substances: heroin, other opioids, cocaine, cannabis, stimulants, and/or hallucinogens.

[i] There is missing data for 4 participants for both the incidence and persistence samples.

[j] Indicates any lifetime treatment history of mood symptoms including outpatient therapy, medication treatment and/or inpatient hospitalization.

Table 2

Odds ratios and 95% confidence intervals for baseline self-medication drinking with incident and persistent alcohol dependence at follow-up among the total study sample of participants with mood symptoms and among demographic and treatment related subsets.

	Association of Self-medication Drinking with Alcohol Dependence Outcomes											
	***Incident* Alcohol Dependence**						***Persistent* Alcohol Dependence**					
	Unadjusted			**Adjusted[a]**			**Unadjusted**			**Adjusted[a]**		
	OR	**95% CI**	**p**	**AOR**	**95% CI**	**p**	**OR**	**95% CI**	**p**	**AOR**	**95% CI**	**p**
Total sample	4.81	3.09-7.49	<0.001	3.10	1.55-6.19	0.002	5.39	3.98-7.28	<0.001	3.45	2.35-5.08	<0.001
Stratified samples (analyses completed separately for each subgroup)[b]												
Sex strata												
Female	4.36	2.20-8.62	<0.001	3.14	1.28-7.72	0.013	5.33	3.48-8.16	<0.001	2.68	1.55-4.61	0.001
Male	4.70	2.56-8.60	<0.001	3.01	1.40-6.45	0.005	5.30	3.53-7.96	<0.001	4.31	2.53-7.35	<0.001
Age strata (years)												
18-29	2.98	1.53-5.80	0.002	2.86	1.14-7.21	0.026	4.87	2.92-8.13	<0.001	2.52	1.46-4.35	0.001
30-39	3.72	1.38-10.01	0.010	1.78	0.48-6.64	0.385	4.02	2.15-7.52	<0.001	2.82	1.38-5.75	0.006
40-54	5.54	2.26-13.60	<0.001	3.56	1.16-10.87	0.027	7.86	4.68-13.20	<0.001	5.58	2.57-12.13	<0.001
55+[c]	13.32	3.66-48.49	<0.001	3.38	0.62-18.34	0.154	4.50	1.37-14.80	0.015	3.82	1.04-14.00	0.044
Race/ethnicity strata												
Non-Hispanic white	5.35	3.05-9.38	<0.001	2.45	1.07-5.58	0.034	5.80	4.06-8.27	<0.001	3.16	2.07-4.84	<0.001
Non-Hispanic black	2.41	0.76-7.57	0.128	2.87	0.80-10.22	0.101	5.98	2.27-15.79	0.001	6.34	2.21-18.23	0.002
Hispanic	4.41	1.35-14.46	0.016	3.44	0.78-15.20	0.099	2.11	0.80-5.59	0.124	1.97	0.39-9.92	0.392
12-month mood disorder strata[d]												
Met criteria	3.12	1.78-5.46	<0.001	1.98	0.96-4.07	0.064	5.77	3.30-10.11	<0.001	4.32	2.22-8.42	<0.001
Did not meet criteria	8.14	4.04-16.43	<0.001	3.88	1.63-9.26	0.003	5.15	3.44-7.69	<0.001	2.91	1.88-4.51	<0.001
Treatment history strata for mood symptoms[e]												
No treatment	2.01	0.84-4.78	0.113	1.97	0.50-7.76	0.326	4.46	2.76-7.21	<0.001	2.18	1.27-3.74	0.006
Any treatment	7.46	4.23-13.16	<0.001	3.94	1.82-8.53	0.001	6.23	4.23-9.16	<0.001	4.81	2.91-7.94	<0.001

[a] The estimates were adjusted by inverse probability of treatment weighting (IPTW). In addition, the regression analyses adjusted for the variables in the table. For the analyses assessing alcohol self-medication with incidence of dependence, the analyses were limited to 3,787 (221 with and 3,566 without incident alcohol dependence) whose propensity scores fell in the common support range. For the analyses assessing alcohol self-medication with persistence of dependence, the analyses were limited to 1,485 (447 with and 1,038 without persistent dependence) whose propensity scores fell in the common support range.

[b] Analyses were completed separately for each stratum or subgroup. For example, in sex-stratified analyses, models were completed separately for males and females.

[c] Odds ratios for this age range should be interpreted with caution as they are based on 18 individuals with incident dependence in this age group.

[d] The odds ratios were statistically different in the unadjusted model assessing incidence of alcohol dependence (F[1, 65]=4.55, p=0.037).

[e] The odds ratios were statistically different in the unadjusted model assessing incidence of alcohol dependence ($F[1, 65]=6.38$, $p=0.014$). The odds ratios were statistically different in the adjusted model assessing persistence of alcohol dependence ($F[1, 61]=4.95$, $p=0.030$).