ORIGINAL ARTICLE

Depressed Mood in Childhood and Subsequent Alcohol Use Through Adolescence and Young Adulthood

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Context: Despite prior evidence supporting cross-sectional associations of depression and alcohol use disorders, there is relatively little prospective data on the temporal association between depressed mood and maladaptive drinking, particularly across extended intervals.

Objective: To assess the association between depressed mood in childhood and alcohol use during adolescence and young adulthood by mood level and sex and race/ethnicity subgroups.

Design: Cohort study of individuals observed during late childhood, early adolescence, and young adulthood.

Setting: Urban mid-Atlantic region of the United States.

Participants: Two successive cohorts of students from 19 elementary schools have been followed up since entry into first grade (1985, cohort I [n=1196]; 1986, cohort II [n=1115]). The students were roughly equally divided by sex (48% female) and were predominantly African American (70%). Between 1989 and 1994, annual assessments were performed on students remaining in the public school system, and between 2000 and 2001, approximately 75% participated in an interview at young adulthood (n=1692).

Main Outcome Measures: Among participants who reported having used alcohol, Cox and multinomial regression analyses were used to assess the association of childhood mood level, as measured by a depression symptom screener, with each alcohol outcome (incident alcohol intoxication, incident alcohol-related problems, and *DSM-IV* alcohol abuse and dependence).

Results: In adjusted regression analyses among those who drank alcohol, a high level of childhood depressed mood was associated with an earlier onset and increased risk of alcohol intoxication, alcohol-related problems during late childhood and early adolescence, and development of *DSM-IV* alcohol dependence in young adulthood.

Conclusions: Early manifestations associated with possible depressive conditions in childhood helped predict and account for subsequent alcohol involvement extending across life stages from childhood through young adulthood.

Arch Gen Psychiatry. 2008;65(6):702-712

DEPRESSION AND ALCOHOL use disorders have been found to co-occur in cross-sectional studies of adults and adolescents. This confluence has been well recognized in clinical samples.[1-4] Although there are exceptions,[5] patients with comorbid diagnoses of depression and an alcohol use disorder tend to have worse prognoses than those with either diagnosis alone, as evidenced by heavier drinking[6-13] and greater depressive symptom severity.[14-16] However, some prior investigators have not found these comorbid associations. For example, Harrington et al[17] completed a case-control study of child and adolescent psychiatric patients and found no association with nondepressive psychiatric disorders in adulthood.

Data from population-based surveys have also documented the co-occurrence of depression and alcohol use disorders.[18-20] Despite evidence from cross-sectional data, there is relatively little information available from prospective studies that might aid in improving our understanding of the temporal association between these conditions. Findings differ depending on the measurement and methodology used as well as the timing of the longitudinal assessments.[21-25] For example, in a meta-analysis, Hartka et al[23] suggested that over the short term, depression was followed by decreased alcohol use; yet, over the long term, in women but not men, depression was a positive predictor of alcohol consumption. In addition to inconsistencies in clinical and population-based studies, there is also a paucity of prospective data that ex-

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tend across life stages.[26-28] Using a birth cohort of youth from New Zealand, Fergusson and Woodward[28] assessed outcomes during young adulthood associated with adolescent depression and found that the association with alcohol use disorders was explained by social, personal, and familial characteristics. Rao and colleagues[29] observed a sample of female adolescents into early adulthood and reported that substance use disorders predicted depression, but not the reverse.

Psychological theories used to help explain these associations include the general concept of using alcohol for self-medicating depressive symptoms or general tension reduction[30] and the stress-response dampening model.[31] Social learning theory[32] might explain roles played by alcohol expectancies, coping skills, and self-efficacy in the regulation of drinking,[33-35] especially in the presence of stress or mood symptoms.[36-38] Life-course developmental models[39,40] suggest that both social adaptational status (the interaction between social task demands and how one's responses are judged) and psychological well-being form a foundation for mental health and predict subsequent behavioral patterns, such as alcohol consumption.[39,41] Furthermore, there may be common underlying genetic as well as social or environmental factors that are associated with increased risk of both disorders.[42-46] Family history of alcoholism as well as depression may be influential.[47,48] Other conditions may explain familial associations. In a male twin sample, evidence indicated that antisocial personality disorder may account for the genetic association found between depression and alcohol dependence.[49] Chassin et al[50] found that externalizing but not internalizing symptoms mediated the effects of a parental history of alcohol disorders.

In the current study, we used data gathered from 2 cohorts originally assessed in the first grade and subsequently followed up through adolescence and young adulthood. Prior analyses of these cohorts have shown that depressed mood in childhood is associated with alcohol initiation without parental permission.[51] Our objective here was to extend these findings among alcohol drinkers to improve our understanding of the temporal association of depressed mood with subsequent risk associated with several alcohol outcomes. Using a depression symptom screener, we examined varying levels of nondiagnostic depressed mood to assess whether alcohol involvement might covary with these levels. Specifically, we hypothesized that any level of depressed mood in childhood would be associated with an increased risk of alcohol intoxication and the development of alcohol-related problems during adolescence and that this association would extend into young adulthood, possibly accounting for the occurrence of alcohol abuse or dependence. Because prior evidence indicates that these associations may differ for some subgroups,[21,23,52-55] we completed separate analyses by sex and race/ethnicity.

METHODS

STUDY POPULATION

The data for these analyses were derived from a prospective study, which began in 1985-1986, conducted within the context of a randomized trial of 2 primary school interventions directed toward academic achievement and classroom behavior. A total of 2311 students were sampled during 2 successive school years in first grade classrooms of 19 elementary schools in an urban mid-Atlantic region of the United States (1985, cohort I [n=1196]; 1986, cohort II [n=1115]). Parental consent was obtained from 95% of the original cohort. Additional details on the study design and data collection are available elsewhere.[39,56-58]

Between 1989 and 1994, trained interviewers administered face-to-face assessments annually in private locations at each school. Interviewers were young adults of both sexes from predominantly minority racial/ethnic backgrounds, similar to the racial/ethnic composition of the study sample. The interviews conducted in 1990 are considered the baseline interviews for this current study, because 1990 was the first year that depressed mood was assessed by face-to-face interviews. Of this baseline sample, 92.8% were interviewed again in 1991 (90.7% of cohort I and 94.9% of cohort II), 84.7% were interviewed again in 1992 (83.1% of cohort I and 86.3% of cohort II), and 75.7% were interviewed again in 1993 (74.6% of cohort I and 76.7% of cohort II). In 1994, limited resources were focused on following up youths in cohort II so that they would be followed up to a similar mean age as the first cohort (30.7% of cohort I and 69.0% of cohort II). A total of 77.0% of the baseline sample had at least 3 years of follow-up between 1991 and 1994. Child assent was obtained at the time of each interview. A certificate of confidentiality was secured, and the study was approved by the Johns Hopkins Bloomberg School of Public Health Committee on Human Research.

Funding for follow-up was not available during the high school years of these 2 cohorts. Nevertheless, it was possible to start the follow-up and tracing processes again so that between 2000 and 2001, approximately 75% of the pupils surviving from the original sample of 2311 participants, including 154 incarcerated individuals, could be traced and interviewed in face-to-face assessments in young adulthood (n=1692). An additional 12% were successfully located but either chose not to be interviewed (n=142) or were not available (eg, they lived out of state with no telephone number or had military postings overseas [n=133]). The mean age for young adulthood follow-up was 21.0 years.

We assessed individuals at 2 separate life stages, defined here by length of follow-up (**Figure 1**): (1) during late childhood/early adolescence (age range, 10-16 years [n=1392]) and (2) during young adulthood (age range, 19-24 years [n=1920]). The analysis for the late childhood/early adolescence follow-up involved exclusion of 919 youths from the original list of 2311 students enrolled in first grade (526 youths who did not have ≥1 interviews subsequent to 1990 as well as 393 youths who had not initiated alcohol use and therefore were not at risk of transitioning to the alcohol outcomes). The analyses for the young adulthood follow-up included all the individuals who reported alcohol use (1392 individuals who reported alcohol use during late childhood/early adolescence and an additional 528 individuals who reported ever having used alcohol when interviewed during young adulthood). Excluded from the young adulthood analysis were the 61 individuals who never used alcohol (as reported on the young adulthood interview), 245 individuals who were not followed up either during adolescence or young adulthood, and 85 individuals who had not begun drinking at their last late childhood/early adolescence contact. Participants with missing follow-up information were more likely to be white and to have paid for lunch as opposed to receiving reduced or free lunch during first grade. In the young adulthood assessment, men were also more likely to be missing than women (32% vs 23%).

MEASURES

Four facets of depressed mood were assessed, based on 4 questions that asked about being in a bad mood, feeling sad, feel-

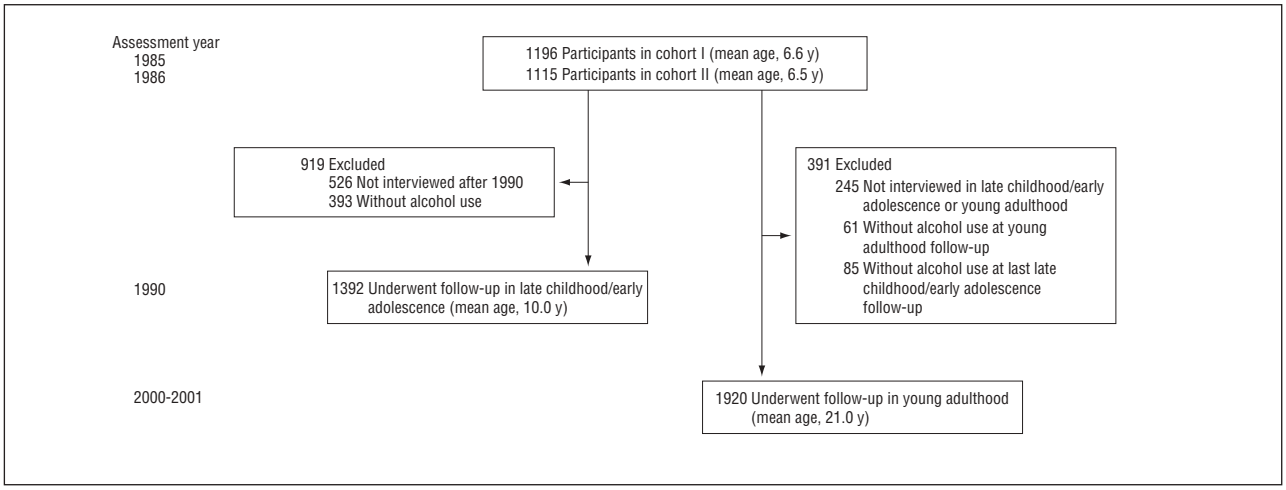

Figure 1. Flowchart of cohorts and sample used for data analyses. Data are from an epidemiologic sample originally recruited at entry into first grade in 1985-1986 from an urban mid-Atlantic public school system (N=2311).

ing crabby or cranky, and feeling like crying "all the time or almost all of the time." Four items queried whether each feeling had ever occurred every day or almost every day for 2 weeks or for the prior 2 weeks if the mood problem was described as current.[59,60] We refer to a high level of depressed mood only if (1) at least 3 of the 4 feelings had been experienced all of the time or almost all of the time or (2) at least 2 of the 4 feelings were described as being current (within the prior 2 weeks) as well as having occurred for at least 2 weeks in the past. Low depressed mood refers to mood in youths who (1) had expressed no more than 1 of the feelings at any time or (2) had experienced 2 of the 4 feelings (current or in the past but not both). The reference category for the high- and low-level depressed mood classifications were youth who did not report any of these mood features at the time of the 1990 assessment. Our reason for the mood categories was to distinguish those with multiple features or evidence for chronicity in the high-level group from those in the low-level group with only 1 feeling and little evidence of persistence of depressed mood. We hypothesized that those with greater burdens of depressed mood, as evidenced by the greater number of features and recurrence or persistence of these feelings, would be associated with the highest risk for alcohol involvement. This measure of depressed mood has adequate internal consistency (Cronbach $\alpha=0.7$) and predictive validity with respect to an adapted version of the Composite International Diagnostic Interview, University of Michigan version (CIDI-UM),[61] module of major depression (relative to those without depressed mood by the time of the 1990 interview, high–depressed mood level is associated with CIDI-UM major depression assessed during the 1993-1994 interview [odds ratio, 3.17; 95% confidence interval, 1.68-5.95; $P<.001$]). However, the measure is a screener questionnaire and is not intended to be used to diagnose depression. Furthermore, the features measured may indicate a range of psychopathology.

Information on alcohol use was based on responses to the question asked each year (1989-1994) regarding whether the student had "ever drunk beer, wine, wine coolers, or any other drink with alcohol in it, even just a sip or taste." Alcohol intoxication was assessed yearly by the question, "How old were you the first time you got drunk or high on alcohol?" Individuals with intoxication before or at the 1990 interview were excluded to assess new-onset intoxication. Data on the occurrence and age at onset of alcohol-related problems were also assessed through 1994. The alcohol-related problem construct was represented by 2 groups of indicators[25]: (1) having social difficulties because of drinking, such as trouble in school, at home, or with the police, or (2) having health or physical problems related to using alcohol, such as a "sick stomach," feeling "panicky," or feeling a "hunger to use" alcohol. Individuals with alcohol-related problems before or at baseline were removed to focus this inquiry on incident problem drinking.

The interview assessment for the *DSM-IV*[62] classifications of lifetime alcohol abuse and dependence in the young adulthood follow-up was an amended version of the approach used in the United States National Comorbidity Survey Replication and in the World Mental Health Surveys Initiative. The amendment involved the addition of this global alcohol problems screening question: "Was there ever a time in your life when people told you they thought you drank too much or when you thought you might have a drinking problem?" This was added in an effort to increase sensitivity for clinically significant alcohol dependence. Reed et al[58] provide more detail on this approach (Web-only Appendix available at http://www.archgenpsychiatry.com). Because of the relatively short developmental interval for these new dependence cases (during late adolescence to young adulthood), we included the entire group of individuals who met 3 or more dependence criteria in our definition (70.5% also self-reported 12-month symptom clustering). When we excluded those without self-reported clustering, substantive conclusions were unchanged.

Covariates included in the analyses were sex and race/ethnicity (where applicable in stratified analyses, African American individuals vs all other races/ethnicities [>90% white]), caregiver history of heavy drinking and/or illegal drug use (yes=1, no=0), youth report of peer alcohol use (yes=1, no=0), age at baseline (continuous variable), level of conduct problems, and neighborhood disadvantage. Caregiver history of heavy drinking and/or illegal drug use was self-reported by the adult participants. Peer drinking was assessed with 1 question asking whether participants had any friends who drank alcohol. The presence of conduct problems was assessed using the 11-item Baltimore Conduct Problems and Delinquency Scale, which assesses delinquent and antisocial behavior. This measure was previously described[63] and is an adaptation of a self-report measure developed by Elliott et al[64] for the National Survey of Delinquency and Drug Use. In our work, the number of items was increased to provide full coverage of the *DSM* criteria for conduct disorder. Responses from the 4-point Likert scale (not at all to ≥3 times in the prior year) were summed, and high and low categories were characterized (above and below the median scale score for this sample). Psychometric analyses suggest good to excellent

internal consistency (Cronbach $\alpha = 0.74$-0.86, during middle school). A 1-year test-retest analysis using a subsample of youths in middle school yielded an intraclass correlation coefficient of 0.63. With respect to concurrent validity, sixth graders in the top quartile of the Baltimore Conduct Problems and Delinquency Scale were nearly 3 times more likely than youths below the 75th percentile to be suspended or expelled from school and to be referred for mental health services for antisocial behavior. In terms of predictive validity, for every unit of increase on the Baltimore Conduct Problems and Delinquency Scale in sixth grade, there was a 3-fold increased odds of antisocial personality disorder at ages 19 to 20 years (odds ratio, 3.31; 95% confidence interval, 2.42-4.51). Level of neighborhood disadvantage was assessed using an 18-item scale adapted from one initially developed for use in the National Youth Survey.[65] The scale is a self-report measure of neighborhood characteristics, including items that address concepts such as church and religious involvement, whether neighbors take care of each other, and whether neighbors damage or steal property.[65,66] Score tertiles were used in the analyses to be consistent with prior use of this scale.[66] The data for these potential confounding covariates were gathered during the 1990 interview, except for the Baltimore Conduct Problems and Delinquency Scale, which was first assessed in 1991, and caregiver alcohol and drug use history, which was reported in adulthood. The rationale for including these covariates was based on prior studies, which have shown that these characteristics may influence the occurrence of alcohol involvement.[60,66-72]

STATISTICAL ANALYSIS

After exploratory data analyses, we completed initial and multiple regression models to assess the strength of the associations between depressed mood levels and the risk of each of the subsequent alcohol-related outcomes. Cox proportional hazard ratios were calculated for time to first alcohol-related problem and first episode of alcohol intoxication at the late childhood/early adolescence follow-up. Multinomial regression was used to examine the association of childhood depressed mood with the occurrence of *DSM-IV* alcohol use disorders at the young adulthood follow-up. In lieu of survival analysis with the young adulthood outcomes, we used multinomial regression because of a violation of the proportionality assumption of the Cox model for these outcomes, with too few cases to stratify by age groups. A single multinomial regression model was used, with the outcome having 4 levels: alcohol abuse, alcohol dependence, no alcohol disorder (reference category), and a category for those with missing information for the diagnostic criteria. For all regression models, stratified analyses were completed by sex and race/ethnicity.

Potential confounding was constrained in these analyses via statistical adjustment. To take into account various occurrences of missing information and to keep the representativeness of the original sample intact, we created dummy-coded covariate categories to denote subgroups with missing covariate data. This approach stabilizes the number of participants contributing information to the regression analyses. An alternative approach to handling missing values (multiple imputation)[73] did not alter the results. We also included a covariate for receipt of subsidized lunch during first grade in the multiple regression analyses because this characteristic was associated with attrition. To hold constant the participants' first grade intervention status, this covariate was also included in the adjusted analyses. Lastly, a variant of the Huber-White sandwich estimator of variance was used to obtain robust SEs and variance estimates in all regression analyses to accommodate the initial sample design and clustering of students within schools.[74]

RESULTS

Among the 2311 first graders, a total of 1785 completed at least 1 follow-up interview after 1990. Because those followed up in late childhood/early adolescence and young adulthood come from the same original study population, the distributions are similar (**Table 1**). Half of the participants are female and most are African American. At the time of the baseline interview for these analyses, the students were aged a mean of 10.0 years (SD, 0.8 years). Forty percent had a caregiver history of either heavy drinking or drug use. Most had received free or subsidized lunches in first grade.

In **Table 2**, we present the distribution of depressed mood level at baseline, stratified by sex and race/ethnicity. Among those followed up in late childhood/early adolescence, 20% had been in the low–depressed mood category at baseline in 1990, and 12% were at the high level. Among those followed up in young adulthood, 16% and 10% had been in the low and high baseline categories of depressed mood, respectively. Contrary to our prior hypotheses, there was no appreciable association of sex or race/ethnicity with the baseline assessment of depressed mood.

As presented in **Table 3**, by the time of the late childhood/early adolescence follow-up, 16% of the youths had experienced at least 1 episode of alcohol intoxication and 22% had experienced alcohol-related problems for the first time. These frequency differences may occur because some underage drinking problems do not require drinking to intoxication. Similar drinking outcome proportions were found for each of the sex and race/ethnicity subgroups. By young adulthood, 12% had developed alcohol abuse, with a greater cumulative incidence proportion of abuse occurring among the male (16%) and other race/ethnicity (18%) subgroups. A total of 9.5% had developed alcohol dependence, with a greater cumulative incidence proportion for males (14%) and for individuals in the other race/ethnicity category (13%). For reasons discussed by Degenhardt et al,[75] this estimate for *DSM-IV* alcohol dependence should be regarded as possibly conservative, as the clinical significance criterion was in place. Drinkers without evidence of maladaptive or hazardous alcohol problems were not counted in the numerators for these estimates.

Kaplan-Meier survival curves were estimated for each of the alcohol-related outcomes by depressed mood. Age at first intoxication was earliest for those with high depressed mood at baseline (log-rank test, $\chi^2_2 = 18.21$, $P < .001$) (**Figure 2**). The smoothed hazard estimates indicate proportionality, which helped motivate use of the Cox model. Similar findings were found for Kaplan-Meier curves assessing age at first alcohol problem (log-rank test, $\chi^2_2 = 10.91$, $P = .004$). With respect to the young adulthood follow-up outcomes, no appreciable association was found for age at first clinical feature of alcohol abuse in relation to baseline depressed mood level (log-rank test, $\chi^2_2 = 2.55$, $P = .28$). However, with respect to the first alcohol dependence criterion, individuals with high baseline depressed mood started the process earlier (log-rank test, $\chi^2_2 = 10.24$, $P = .006$) (**Figure 3**).

Table 1. Baseline Characteristics of Sample Observed at Late Childhood/Early Adolescence and Young Adulthood Follow-ups

Characteristic[a]	No. (%)	
	Late Childhood/ Early Adolescence Follow-up (n=1392)	Young Adulthood Follow-up (n=1920)
Age, y		
9	404 (29.0)	603 (31.4)
10	641 (46.0)	889 (46.3)
11	312 (22.4)	388 (20.2)
12	33 (2.4)	37 (1.9)
13	2 (0.1)	3 (0.2)
Sex		
F	671 (48.2)	968 (50.4)
M	721 (51.8)	952 (49.6)
Race/ethnicity[b]		
African American	1010 (72.6)	1317 (68.6)
Other	382 (27.4)	603 (31.4)
Peer alcohol use		
Yes	201 (14.4)	222 (11.6)
No	802 (57.6)	937 (48.8)
Missing[c]	389 (28.0)	761 (39.6)
Caregiver history of heavy drinking and/or illegal drug use		
Yes	563 (40.5)	767 (39.9)
No	524 (37.6)	760 (39.6)
Missing[c]	305 (21.9)	393 (20.5)
Neighborhood disadvantage tertiles		
Low	353 (25.4)	407 (21.2)
Middle	334 (24.0)	383 (19.9)
High	304 (21.8)	353 (18.4)
Missing[c]	401 (28.8)	777 (40.5)
Subsidized lunch[d]		
Yes	805 (57.8)	1046 (54.5)
No	586 (42.1)	870 (45.3)
Missing[e]	1 (0.1)	4 (0.2)
Conduct problems[f]		
Low	581 (41.7)	726 (37.8)
High	686 (49.3)	753 (39.2)
Missing[c]	125 (9.0)	441 (23.0)

[a] Information on all of the characteristics listed was gathered at the baseline interview for these analyses (1990), except for subsidized lunch, which was gathered from school records in first grade (1985-1986), conduct problems, which were assessed in 1991, and household history of heavy drinking and/or illegal drug use, which was assessed in young adulthood.

[b] In the late childhood/early adolescence and young adulthood follow-ups, respectively, a total of 361 (94.5%) and 579 (96.0%) participants in the other race/ethnicity group were white.

[c] Individuals did not provide this information at the late childhood/early adolescence or young adulthood follow-ups.

[d] Receipt of free or subsidized lunch in first grade.

[e] This information was not available from school records for these individuals.

[f] The categories represent scores above and below the median score for this sample.

In **Table 4**, we present the unadjusted and adjusted hazard ratios based on a comparison of the subgroups' onset of alcohol intoxication and alcohol-related problems as assessed during the late childhood/early adolescence follow-up. **Table 5** presents odds ratios for the occurrence of alcohol abuse and dependence observed at the young adulthood follow-up. Based on covariate-adjusted Cox models, the estimated hazards for alcohol intoxication at the late childhood/early adolescence follow-up among individuals with high childhood depressed mood were roughly 2-fold greater than values observed for youths without depressed mood. High–depressed mood level at baseline was also associated with the onset of alcohol-related problems among the male and other race/ethnicity subgroups. An estimated 2-fold increased risk of alcohol dependence was associated with those who had high childhood depressed mood relative to those without (Table 5); for individuals in the other race/ethnicity subgroup, this association was attenuated with wider confidence intervals. Childhood depressed mood was not associated with risk of developing alcohol abuse by the time of the young adulthood follow-up. Because our analyses were restricted to those who drank alcohol, which theoretically could introduce bias, we also repeated these regression analyses including the nondrinkers as part of the reference group in the Cox models and as a separate outcome in the multinomial regression analyses. These supplemental analyses did not lead to any differences in substantive conclusions.

COMMENT

Consistent with our hypotheses in this prospective study, depressed mood as assessed in childhood helped to predict and may account for increased risk of several manifestations of alcohol involvement. For predictive associations, the strength of the associations increased with greater severity of depressed mood, but the risk estimates for the subgroup at a lower level of baseline depressed mood were not statistically different from estimates for children without depressed mood. Higher depressed mood in childhood also signaled earlier onset of alcohol involvement, and in general congruent risk ratios were observed for the sex and race/ethnicity subgroups we studied. For the assessment of mood level with first report of alcohol-related problems, males and participants in the other race/ethnicity category had the strongest associations. The vulnerability to increased risk for alcohol involvement extended across both life stages studied and was independent of potential causal determinants of maladaptive drinking, such as family income in childhood, heavy drinking among caregivers, peer alcohol use, level of conduct problems, and neighborhood disadvantage. Possible explanations for these findings include motives to use alcohol for stress reduction.[31,76] Children with early mood symptoms may be more likely to subsequently use alcohol as a method for coping with negative affect.[36,77] In addition, the association of childhood depressed mood with later alcohol involvement may be mediated or moderated by alcohol-related expectancies.[33,78-82] Familial factors or processes, with both genetic and/or environmental substrates, may influence the development of affective symptoms as well as the occurrence of maladaptive drinking patterns.[38,71,83-86] These processes may be specific for alcohol involvement relatively early in life.[87-89]

Our findings are consistent with clinical and population-based cross-sectional data and extend findings from prior prospective analyses.[27,90-95] However, our findings

Table 2. Childhood Depressed Mood in Those Reporting Alcohol Use at Late Childhood/Early Adolescence and Young Adulthood Follow-ups

	No. (%)									
	Late Childhood/Early Adolescence Follow-up					Young Adulthood Follow-up				
Childhood Depressed Mood	Total (n=1392)	Boys (n=721)	Girls (n=671)	African American Participants (n=1010)	Participants of Other Race/ Ethnicity (n=382)[a,b]	Total (n=1920)	Men (n=952)	Women (n=968)	African American Participants (n=1317)	Participants of Other Race/ Ethnicity (n=603)[a,c]
None	557 (40.0)	287 (39.8)	270 (40.2)	397 (39.3)	160 (41.9)	649 (33.8)	322 (33.8)	327 (33.8)	474 (36.0)	175 (29.0)
Low	274 (19.7)	138 (19.1)	136 (20.3)	215 (21.3)	59 (15.4)	309 (16.1)	160 (16.8)	149 (15.4)	243 (18.5)	66 (11.0)
High	170 (12.2)	78 (10.8)	92 (13.7)	133 (13.2)	37 (9.7)	199 (10.4)	87 (9.1)	112 (11.6)	155 (11.8)	44 (7.3)
Missing	391 (28.1)	218 (30.2)	173 (25.8)	265 (26.2)	265 (33.0)	763 (39.7)	383 (40.2)	380 (39.3)	445 (33.8)	318 (52.7)

[a] In the late childhood/early adolescence and young adulthood follow-ups, respectively, a total of 361 (94.5%) and 579 (96.0%) participants from the other race/ethnicity group were white.
[b] African American participants compared with the other race/ethnicity group, $\chi^2_3 = 12.51$, $P < .001$.
[c] African American participants compared with the other race/ethnicity group, $\chi^2_3 = 65.77$, $P < .001$.

Table 3. Incident Cases of Alcohol Involvement Among Those Reporting Alcohol Use During Late Childhood/Early Adolescence and Young Adulthood

	Incident Cases of Alcohol Involvement, No. (%)				
Alcohol Involvement	Total (n=1392)	Boys (n=721)	Girls (n=671)	African American Participants (n=1010)	Participants of Other Race/Ethnicity (n=1382)
	Late Childhood/Early Adolescence Follow-up				
Alcohol intoxication[a]					
Yes	218 (15.7)	105 (14.6)	113 (16.8)	166 (16.4)	52 (13.6)
No	1039 (74.6)	535 (74.2)	504 (75.1)	784 (77.6)	255 (66.8)
Missing	135 (9.7)	81 (11.2)	54 (8.1)	60 (5.9)	75 (19.6)
Alcohol-related problem					
Yes	309 (22.2)	163 (22.6)	146 (21.8)	229 (22.7)	80 (20.9)
No	1076 (77.3)	555 (77.0)	521 (77.6)	778 (77.0)	298 (78.0)
Missing	7 (0.5)	3 (0.4)	4 (0.6)	3 (0.3)	4 (1.1)
Alcohol Involvement	Total (n=1920)	Men (n=952)	Women (n=968)	African American Participants (n=1317)	Participants of Other Race/Ethnicity (n=603)
	Young Adulthood Follow-up				
Alcohol abuse[b]					
Yes	237 (12.3)	154 (16.2)	83 (8.6)	126 (9.6)	111 (18.4)
No	1384 (72.1)	609 (64.0)	775 (80.1)	1018 (77.3)	366 (60.7)
Missing	299 (15.6)	189 (19.8)	110 (11.4)	173 (13.1)	126 (20.9)
Alcohol dependence[c]					
Yes	183 (9.5)	132 (13.9)	51 (5.3)	103 (7.8)	80 (13.3)
No	529 (27.6)	304 (31.9)	225 (23.2)	295 (22.4)	234 (38.8)
Other alcohol drinkers	909 (47.3)	327 (34.3)	582 (60.1)	746 (56.6)	163 (27.0)
Missing	299 (15.6)	189 (19.9)	110 (11.4)	173 (13.1)	126 (20.9)

[a] African American participants compared with the other race/ethnicity group, $\chi^2_2 = 59.38$, $P < .001$.
[b] Men compared with women, $\chi^2_2 = 61.92$, $P < .001$; African American participants compared with the other race/ethnicity group, $\chi^2_2 = 57.99$, $P < .001$.
[c] Clinically significant alcohol dependence syndromes. Men compared with women, $\chi^2_3 = 138.84$, $P < .001$; African American participants compared with the other race/ethnicity group, $\chi^2_3 = 146.56$, $P < .001$.

differ from prior reports that indicate that adolescent depression predicts alcohol disorders only in the presence of conduct disorder symptoms (data for this interaction are not shown).[27] Our results may differ because we examined mood at an earlier life stage (in childhood as opposed to adolescence). In our analyses, early depressed mood level predicted all but 1 of the alcohol involvement outcomes. We found no association with alcohol abuse. Early depressed mood appears to predict the transition from high-risk drinking to alcohol dependence but not to the occurrence of alcohol abuse without dependence. Similar findings have been documented in some prior data. In analyses of the National Comorbidity Survey, using retrospective reports from cross-sectional data,

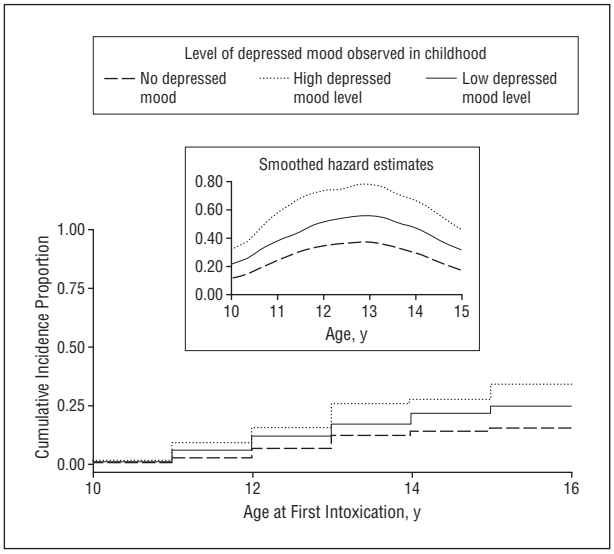

Figure 2. Kaplan-Meier survival estimates for the age at first alcohol intoxication by level of childhood depressed mood among youth reporting alcohol use (log-rank test, χ^2_2=18.21, P<.001). The insert graph provides the smoothed hazard estimates by depressed mood level.

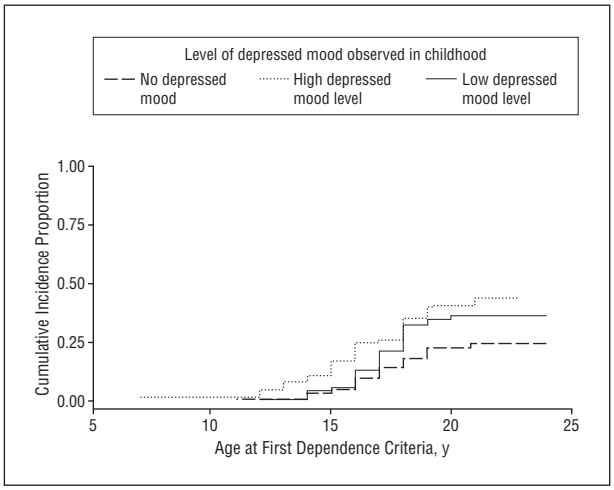

Figure 3. Kaplan-Meier survival estimates for the age at first experience with *DSM-IV* criteria for alcohol dependence by level of childhood depressed mood among those reporting alcohol use observed at the young adult follow-up (log-rank test, χ^2_2=10.24, P=.006).

mood disorders were positively associated with alcohol dependence but negatively associated with alcohol abuse among men.[95] In the European Study of the Epidemiology of Mental Disorders project, alcohol abuse had the weakest association with depression among all the comorbid patterns assessed.[96] Some investigators speculate that field research assessments of the *DSM* alcohol abuse construct may reflect nonpathologic drinking patterns that occur inextricably with adolescent or young adult drinking experiences, particularly for young male drinkers.[96,97]

One of the issues to consider in understanding these associations is the role of concurrence and persistence of depressed mood and drinking. These study estimates may challenge the idea that depressed mood must take place concurrently with drinking behaviors to affect the development of some alcohol-related outcomes. Furthermore, depressive conditions that occur in childhood may increase vulnerability for maladaptive drinking outcomes, whereas similar conditions that occur later in life may not be as strongly associated. This window of vulnerability may be in place for some but not all comorbid associations. Childhood mood disturbances occur at a significant stage for neurobiological development.[98] During this critical period, mood disturbances may inhibit the normal progression of a child's ability to develop mechanisms to cope with stress and negative expectations and may increase the likelihood that skills to handle stress-related occurrences are poorly developed or remain immature. Early manifestations of depressive conditions can also be difficult to recognize by families and health care providers. It is typically quite a challenge to determine whether these features are clinically relevant. Our assessment of depressed mood queried about "being crabby," having "frequent crying spells," and "being sad." These feelings are common to many children, and it may be difficult for families and clinicians to recognize when they may indicate a psychiatric disturbance or when further evaluation is warranted. Although early depressive feelings may be a potential predictor of alcohol involvement, other psychopathologic conditions are also associated with risk for alcohol disorders, including disruptive behaviors, other substance use, anxiety, and affective disorders.[99-104]

There are several limitations in our analyses that should be mentioned. First, residual confounding may be present (eg, familial history of psychopathology [depression, anxiety, alcohol dependence, or antisocial personality] or participant history of childhood trauma). For example, family history may be associated with early occurrence of depressive conditions and increased vulnerability for alcohol involvement[84,85,105,106] owing to genetic predispositions as well as familial influences, such as modeling behavior, provision of support, and parental monitoring.[67,70,71,107] However, we were able to include information on report of illicit drug use and heavy drinking in the caregiver, which might help to hold constant these potential confounding characteristics. Second, our assessment of depressed mood in childhood did not include a structured psychiatric interview and thus cannot be regarded as diagnostic of depression. In addition, the measure used identified features that may be present in a range of psychopathology. However, as we discussed previously, this measure had adequate internal consistency and was associated with major depression (evidence of predictive validity) assessed by CIDI-UM. Third, as mentioned previously, our assessment of alcohol dependence focused on clinically significant dependence syndrome. As discussed by Degenhardt et al,[75] this use of clinical significance criteria may miss some individuals who developed a milder form of alcohol dependence. Fourth, as with any prospective study, particularly one extending across long intervals, there was participant attrition and missing information. We have addressed these concerns by using 2 statistical strategies: including covariates for missing data in the regression models and multiple imputation. Yet, the potential for bias remains. Fifth, generalizability of the findings from this sample of school-attending youths rests on replication of the findings elsewhere.

Table 4. Risk of Alcohol Intoxication and Alcohol-Related Problems During Late Childhood/Early Adolescence by Level of Childhood Depressed Mood Among Youth Reporting Alcohol Use Based on Cox Regression Analyses

Childhood Depressed Mood	Total		Boys		Girls		African American Participants		Participants of Other Race/Ethnicity	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Alcohol Intoxication										
Unadjusted										
None	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Low	1.65 (1.15-2.37)	.007	1.79 (1.05-3.06)	.03	1.53 (0.93-2.54)	.10	1.42 (0.94-2.15)	.10	2.95 (1.37-6.34)	.006
High	2.28 (1.55-3.37)	<.001	2.33 (1.29-4.23)	.005	2.16 (1.28-3.66)	.004	2.13 (1.39-3.28)	.001	3.03 (1.21-7.54)	.02
Adjusted[a]										
None	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Low	1.59 (1.10-2.29)	.01	1.73 (1.00-2.99)	.05	1.51 (0.91-2.52)	.12	1.33 (0.87-2.03)	.18	2.90 (1.33-6.29)	.007
High	1.99 (1.33-2.97)	.001	2.06 (1.10-3.87)	.02	1.99 (1.16-3.42)	.01	1.77 (1.14-2.76)	.01	2.78 (1.04-7.40)	.04
Alcohol Problems										
Unadjusted										
None	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Low	1.44 (1.06-1.95)	.02	1.63 (1.06-2.50)	.03	1.25 (0.80-1.95)	.32	1.47 (1.04-2.08)	.03	1.31 (0.66-2.60)	.43
High	1.68 (1.20-2.35)	.003	2.23 (1.39-3.58)	.001	1.29 (0.78-2.11)	.32	1.50 (1.02-2.22)	.04	2.33 (1.18-4.58)	.01
Adjusted[a]										
None	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Low	1.35 (0.99-1.84)	.06	1.48 (0.95-2.30)	.09	1.21 (0.77-1.92)	.40	1.29 (0.91-1.84)	.15	1.41 (0.71-2.80)	.32
High	1.47 (1.04-2.08)	.03	1.97 (1.21-3.23)	.007	1.15 (0.69-1.91)	.60	1.27 (0.85-1.91)	.24	2.19 (1.07-4.46)	.03

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] Adjusted for sex and race (when applicable), age, caregiver history of heavy drinking and/or illegal drug use, peer drinking, neighborhood disadvantage, conduct problems, intervention status, subsidized lunch, and clustering within schools. To avoid biases resulting from nonrandom deletion of participants within our prospective study cohorts and to keep the representativeness of the original sample intact, thereby stabilizing the number of participants contributing information to the regression analyses, we created separate categories for subgroups with missing information for each covariate included in each multivariate model.

Table 5. Estimated Risk of Alcohol Abuse and Alcohol Dependence in Young Adulthood by Level of Childhood Depressed Mood Among Youth Reporting Alcohol Use Based on Multinomial Regression Analyses[a]

Childhood Depressed Mood	Total		Males		Females		African American Participants		Participants of Other Race/Ethnicity	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Alcohol Abuse										
Unadjusted										
None	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Low	0.96 (0.61-1.52)	.86	0.89 (0.47-1.69)	.72	0.98 (0.47-2.04)	.95	0.90 (0.47-1.73)	.75	1.56 (0.93-2.62)	.09
High	0.53 (0.25-1.16)	.11	0.62 (0.24-1.60)	.32	0.63 (0.21-1.95)	.42	0.52 (0.18-1.53)	.24	0.62 (0.23-1.65)	.34
Adjusted[b]										
None	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Low	0.94 (0.57-1.53)	.79	0.86 (0.47-1.60)	.64	1.01 (0.53-1.93)	.98	0.78 (0.40-1.53)	.48	1.51 (0.88-2.57)	.13
High	0.58 (0.27-1.22)	.15	0.60 (0.29-1.25)	.17	0.58 (0.19-1.74)	.33	0.53 (0.20-1.45)	.22	0.70 (0.24-2.08)	.53
Alcohol Dependence[c]										
Unadjusted										
None	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Low	1.56 (1.01-2.43)	.047	1.29 (0.73-2.27)	.38	2.26 (1.07-4.78)	.03	1.60 (0.95-2.69)	.08	2.23 (0.79-6.26)	.13
High	1.82 (1.20-2.76)	.005	2.00 (1.23-3.23)	.005	2.56 (1.32-4.96)	.005	2.21 (1.49-3.29)	<.001	1.42 (0.58-3.47)	.45
Adjusted[b]										
None	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Low	1.50 (0.89-2.52)	.13	1.29 (0.67-2.47)	.45	2.27 (1.04-4.95)	.04	1.35 (0.75-2.42)	.32	2.14 (0.71-6.48)	.18
High	2.07 (1.31-3.26)	.002	2.20 (1.37-3.52)	.001	2.55 (1.16-5.62)	.02	2.46 (1.68-3.61)	<.001	1.38 (0.47-4.09)	.56

Abbreviations: CI, confidence interval; OR, odds ratio.

[a] One multinomial regression model was used to assess alcohol abuse and alcohol dependence as separate outcomes, with alcohol drinkers without either disorder as references.

[b] Adjusted for sex and race (when applicable), age, caregiver history of heavy drinking and/or illegal drug use, peer drinking, neighborhood disadvantage, conduct problems, intervention status, subsidized lunch, and clustering within schools. To avoid biases resulting from nonrandom deletion of participants within our prospective study cohorts and to keep the representativeness of the original sample intact, thereby stabilizing the number of participants contributing information to the regression analyses, we created separate categories for missing information for all variables in the model.

[c] Clinically significant alcohol dependence syndrome.

Notwithstanding these limitations, the study contributes new information about childhood depressed mood and subsequent alcohol outcomes as well as possible childhood predictors of alcohol involvement that may extend across adolescence into young adulthood. The effects of internalizing symptoms on transitional and sequential stages of drinking will need to be explored in future research. In addition, this research can be extended from this initial platform of evidence in an exploration of the potential moderating and mediating influences attributable to other drug use, externalizing behaviors, and expectancies associated with drinking alcohol. Whether and how the observed mood manifestations change, persist, or progress through one's life stages deserves scrutiny. Co-occurring transitions in drinking behavior may have important implications for identifying and targeting high-risk groups for prevention and early intervention efforts.

Submitted for Publication: July 6, 2007; final revision received December 3, 2007; accepted January 9, 2008.
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Financial Disclosure: None reported.
Funding/Support: The analyses for this work were supported by grant AA014869 from the National Institute on Alcohol Abuse and Alcoholism. Data gathering for the study was supported by grants DA04392 and DA09897 and career development award K05DA015799 (J.C.A.) from the National Institute on Drug Abuse.
Additional Information: The Appendix is available online at http://www.archgenpsychiatry.com.

REFERENCES

1. Salokangas RK, Poutanen O. Risk factors for depression in primary care: findings of the TADEP project. *J Affect Disord*. 1998;48(2-3):171-180.
2. Brown RA, Monti PM, Myers MG, Martin RA, Rivinus T, Dubreuil ME, Rohsenow DJ. Depression among cocaine abusers in treatment: relation to cocaine and alcohol use and treatment outcome. *Am J Psychiatry*. 1998;155(2):220-225.
3. Miller NS, Klamen D, Hoffmann NG, Flaherty JA. Prevalence of depression and alcohol and other drug dependence in addictions treatment populations. *J Psychoactive Drugs*. 1996;28(2):111-124.
4. Davidson KM. Diagnosis of depression in alcohol dependence: changes in prevalence with drinking status. *Br J Psychiatry*. 1995;166(2):199-204.
5. Davidson KM, Blackburn IM. Co-morbid depression and drinking outcome in those with alcohol dependence. *Alcohol Alcohol*. 1998;33(5):482-487.
6. Curran GM, Flynn HA, Kirchner J, Booth BM. Depression after alcohol treatment as a risk factor for relapse among male veterans. *J Subst Abuse Treat*. 2000;19(3):259-265.
7. Bobo JK, McIlvain HE, Leed-Kelly A. Depression screening scores during residential drug treatment and risk of drug use after discharge [erratum published in *Psychiatr Serv*. 1998;49(6):828]. *Psychiatr Serv*. 1998;49(5):693-695.
8. Greenfield SF, Weiss RD, Muenz LR, Vagge LM, Kelly JF, Bello LR. The effect of depression on return to drinking: a prospective study. *Arch Gen Psychiatry*. 1998;55(3):259-265.
9. Pettinati HM, Pierce JD Jr, Wolf AL, Rukstalis MR, O'Brien CP. Gender differences in comorbidly depressed alcohol-dependent outpatients. *Alcohol Clin Exp Res*. 1997;21(9):1742-1746.
10. Donohue B, Acierno R, Kogan E. Relationship of depression with measures of social functioning in adult drug abusers. *Addict Behav*. 1996;21(2):211-216.
11. Driessen M, Meier S, Hill A, Wetterling T, Lange W, Junghanns K. The course of anxiety, depression and drinking behaviours after completed detoxification in alcoholics with and without comorbid anxiety and depressive disorders. *Alcohol Alcohol*. 2001;36(3):249-255.
12. Röggla H, Uhl A. Depression and relapses in treated chronic alcoholics. *Int J Addict*. 1995;30(3):337-349.
13. Brown SA, Inaba RK, Gillin JC, Schuckit MA, Stewart MA, Irwin MR. Alcoholism and affective disorder: clinical course of depressive symptoms. *Am J Psychiatry*. 1995;152(1):45-52.
14. Salloum IM, Mezzich JE, Cornelius J, Day NL, Daley D, Kirisci L. Clinical profile of comorbid major depression and alcohol use disorders in an initial psychiatric evaluation. *Compr Psychiatry*. 1995;36(4):260-266.
15. Cornelius JR, Salloum IM, Mezzich J, Cornelius MD, Fabrega H, Ehler JG, Ulrich RF, Thase ME, Mann JJ. Disproportionate suicidality in patients with comorbid major depression and alcoholism. *Am J Psychiatry*. 1995;152(3):358-364.
16. Worthington J, Fava M, Agustin C, Alpert J, Nierenberg AA, Pava JA, Rosenbaum JF. Consumption of alcohol, nicotine, and caffeine among depressed outpatients: relationship with response to treatment. *Psychosomatics*. 1996;37(6):518-522.
17. Harrington R, Fudge H, Rutter M, Pickles A, Hill J. Adult outcomes of childhood and adolescent depression, I: psychiatric status. *Arch Gen Psychiatry*. 1990;47(5):465-473.
18. Grant BF, Stinson FS, Dawson DA, Chou SP, Dufour MC, Compton W, Pickering RP, Kaplan K. 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*. 2004;61(8):807-816.
19. Weissman MM, Myers JK. Clinical depression in alcoholism. *Am J Psychiatry*. 1980;137(3):372-373.
20. 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(19):2511-2518.
21. Moscato BS, Russell M, Zielezny M, Bromet E, Egri G, Mudar P, Marshall JR. Gender differences in the relation between depressive symptoms and alcohol problems: a longitudinal perspective. *Am J Epidemiol*. 1997;146(11):966-974.
22. Aneshensel CS, Huba GJ. Depression, alcohol use, and smoking over one year: a four-wave longitudinal causal model. *J Abnorm Psychol*. 1983;92(2):134-150.
23. Hartka E, Johnstone B, Leino EV, Motoyoshi M, Temple MT, Fillmore KM. The Collaborative Alcohol-Related Longitudinal Project: a meta-analysis of depressive symptomatology and alcohol consumption over time. *Br J Addict*. 1991;86(10):1283-1298.
24. Dixit AR, Crum RM. Depression and the risk of heavy alcohol use in women: a prospective study. *Am J Psychiatry*. 2000;157(5):751-758.
25. Crum RM, Storr CL, Chan YF. Depression syndromes with risk of alcohol dependence in adulthood: a latent class analysis. *Drug Alcohol Depend*. 2005;79(1):71-81.
26. Costello EJ, Sung M, Worthman C, Angold A. Pubertal maturation and the development of alcohol use and abuse [published online ahead of print February 1, 2007]. *Drug Alcohol Depend*. 2007;88(suppl 1):S50-S59. doi:10.1016/j.drugalcdep.2006.12.009.
27. Pardini D, White HR, Stouthamer-Loeber M. Early adolescent psychopathology as a predictor of alcohol use disorders by young adulthood [published online ahead of print January 25, 2007]. *Drug Alcohol Depend*. 2007;88(suppl 1):S38-S49. doi:10.1016/j.drugalcdep.2006.12.014.

28. Fergusson DM, Woodward LJ. Mental health, educational, and social role outcomes of adolescents with depression. *Arch Gen Psychiatry*. 2002;59(3):225-231.
29. Rao U, Daley SE, Hammen C. Relationship between depression and substance use disorders in adolescent women during the transition to adulthood. *J Am Acad Child Adolesc Psychiatry*. 2000;39(2):215-222.
30. Greeley J, Oei T. Alcohol and tension reduction. In: Leonard KE, Blane HT, eds. *Psychological Theories of Drinking and Alcoholism*. 2nd ed. New York, NY: The Guilford Press; 1999:14-53.
31. Sher KJ, Levenson RW. Risk for alcoholism and individual differences in the stress-response-dampening effect of alcohol. *J Abnorm Psychol*. 1982;91(5):350-367.
32. Bandura A. *Social Learning Theory*. Englewood Cliffs, NJ: Prentice Hall; 1977.
33. Evans DM, Dunn NJ. Alcohol expectancies, coping responses and self-efficacy judgments: a replication and extension of Copper et al's 1988 study in a college sample. *J Stud Alcohol*. 1995;56(2):186-193.
34. Maisto SA, Connors GJ, Zywiak WH. Alcohol treatment, changes in coping skills, self-efficacy, and levels of alcohol use and related problems 1 year following treatment initiation. *Psychol Addict Behav*. 2000;14(3):257-266.
35. Christiansen BA, Goldman MS, Brown SA. The differential development of adolescent alcohol expectancies may predict adult alcoholism. *Addict Behav*. 1985;10(3):299-306.
36. Kassel JD, Jackson SI, Unrod M. Generalized expectancies for negative mood regulation and problem drinking among college students. *J Stud Alcohol*. 2000;61(2):332-340.
37. Goldstein AL, Wall AM, McKee SA, Hinson RE. Accessibility of alcohol expectancies from memory: impact of mood and motives in college student drinkers. *J Stud Alcohol*. 2004;65(1):95-104.
38. Catanzaro SJ, Laurent J. Perceived family support, negative mood regulation expectancies, coping, and adolescent alcohol use: evidence of mediation and moderation effects. *Addict Behav*. 2004;29(9):1779-1797.
39. Kellam SG, Wethamer-Larsson L, Dolan LJ, Brown CH, Mayer LS, Rebok GW, Anthony JC, Laudolff J, Edelsohn G, Wheeler L. Developmental epidemiologically based preventive trials: baseline modeling of early target behaviors and depressive symptoms. *Am J Community Psychol*. 1991;19(4):563-584.
40. Mrazek PG, Haggerty RJ, eds. *Reducing Risks for Mental Disorders: Frontiers for Preventive Intervention Research*. Washington, DC: National Academy Press; 1994.
41. Kellam SG, Brown CH, Rubin BR, Ensminger ME. Paths leading to teenage psychiatric symptoms and substance use: developmental epidemiological studies in Woodlawn. In: Guze SB, Earls FJ, Barrett JE, eds. *Childhood Psychopathology and Development*. New York, NY: Raven Press; 1983.
42. Nellissery M, Feinn RS, Covault J, Gelernter J, Anton RF, Pettinati H, Moak D, Mueller T, Kranzler HR. Alleles of a functional serotonin transporter promoter polymorphism are associated with major depression in alcoholics. *Alcohol Clin Exp Res*. 2003;27(9):1402-1408.
43. Kendler KS, Health AC, Neale MC, Kessler RC, Eaves LJ. Alcoholism and major depression in women: a twin study of the causes of comorbidity. *Arch Gen Psychiatry*. 1993;50(9):690-698.
44. Dohrenwend BP, Levav I, Shrout PE, Schwartz S, Naveh G, Link BG, Skodol AE, Stueve A. Socioeconomic status and psychiatric disorders: the causation-selection issue. *Science*. 1992;255(5047):946-952.
45. Maier W, Merikangas K. Co-occurrence and cotransmission of affective disorders and alcoholism in families. *Br J Psychiatry Suppl*. June 1996;(30):93-100.
46. Clark DB, De Bellis MD, Lynch KG, Cornelius JR, Martin CS. Physical and sexual abuse, depression and alcohol use disorders in adolescents: onsets and outcomes. *Drug Alcohol Depend*. 2003;69(1):51-60.
47. Merikangas KR, Risch NJ, Weissman MM. Comorbidity and co-transmission of alcoholism, anxiety and depression. *Psychol Med*. 1994;24(1):69-80.
48. Schuckit MA, Smith TL, Danko GP, Pierson J, Trim R, Nurnberger JI, Kramer J, Kuperman S, Bierut LJ, Hesselbrock V. A comparison of factors associated with substance-induced versus independent depressions. *J Stud Alcohol Drugs*. 2007;68(6):805-812.
49. Fu Q, Health AC, Bucholz KK, Nelson E, Goldberg J, Lyons MJ, True WR, Jacob T, Tsuang MT, Eisen SA. Shared genetic risk of major depression, alcohol dependence, and marijuana dependence: contribution of antisocial personality disorder in men. *Arch Gen Psychiatry*. 2002;59(12):1125-1132.
50. Chassin L, Pitts SC, DeLucia C, Todd M. A longitudinal study of children of alcoholics: predicting young adult substance use disorders, anxiety, and depression. *J Abnorm Psychol*. 1999;108(1):106-119.
51. Crum RM, Storr CL, Ialongo N, Anthony JC. Is depressed mood in childhood associated with an increased risk for initiation of alcohol use during early adolescence? *Addict Behav*. 2008;33(1):24-40.
52. Gilman SE, Abraham HD. A longitudinal study of the order of onset of alcohol dependence and major depression. *Drug Alcohol Depend*. 2001;63(3):277-286.
53. Wang J, Patten SB. A prospective study of sex-specific effects of major depression on alcohol consumption. *Can J Psychiatry*. 2001;46(5):422-425.
54. King AC, Bernardy NC, Hauner K. Stressful events, personality, and mood disturbance: gender differences in alcoholics and problem drinkers. *Addict Behav*. 2003;28(1):171-187.
55. Maag JW, Irvin DM. Alcohol use and depression among African-American and Caucasian adolescents. *Adolescence*. 2005;40(157):87-101.
56. Kellam SG, Anthony JC. Targeting antecedents to prevent tobacco smoking: findings from an epidemiologically based randomized field trial. *Am J Public Health*. 1998;88(10):1490-1495.
57. Storr CL, Reboussin BA, Anthony JC. Early childhood misbehavior and the estimated risk of becoming tobacco-dependent. *Am J Epidemiol*. 2004;160(2):126-130.
58. Reed PL, Storr CL, Anthony JC. Drug dependence enviromics: job strain in the work environment and risk of becoming drug-dependent. *Am J Epidemiol*. 2006;163(5):404-411.
59. Wu LT, Anthony JC. Tobacco smoking and depressed mood in late childhood and early adolescence. *Am J Public Health*. 1999;89(12):1837-1840.
60. Chen LS, Anthony JC, Crum RM. Perceived cognitive competence, depressive symptoms and the incidence of alcohol-related problems in urban school children. *J Child Adolesc Subst Abuse*. 1999;8(4):37-53.
61. World Health Organization. *World Health Organization, Composite International Diagnostic Interview*. Geneva, Switzerland: World Health Organization; 1990.
62. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 1994.
63. Johnson EO, Arria AM, Borges G, Ialongo N, Anthony JC. The growth of conduct problem behaviors from middle childhood to early adolescence: sex differences and the suspected influence of early alcohol use. *J Stud Alcohol*. 1995;56(6):661-671.
64. Elliott DS, Huizinga D, Ageton SS. *Explaining Delinquency and Drug Use*. Beverly Hills, CA: Sage Publications; 1985.
65. Elliott DS, Huizinga D, Menard S. *Multiple Problem Youth: Delinquency, Substance Use, and Mental Health Problems*. New York, NY: Springer Verlag; 1989.
66. Crum RM, Lillie-Blanton M, Anthony JC. Neighborhood environment and opportunity to use cocaine and other drugs in late childhood and early adolescence. *Drug Alcohol Depend*. 1996;43(3):155-161.
67. Duncan TE, Duncan SC, Hops H. The effects of family cohesiveness and peer encouragement on the development of adolescent alcohol use: a cohort-sequential approach to the analysis of longitudinal data. *J Stud Alcohol*. 1994;55(5):588-599.
68. Moss HB, Kirisci L. Aggressivity in adolescent alcohol abusers: relationship with conduct disorder. *Alcohol Clin Exp Res*. 1995;19(3):642-646.
69. Curran PJ, Stice E, Chassin L. The relation between adolescent alcohol use and peer alcohol use: a longitudinal random coefficients model. *J Consult Clin Psychol*. 1997;65(1):130-140.
70. Mason WA, Windle M. Family, religious, school and peer influences on adolescent alcohol use: a longitudinal study. *J Stud Alcohol*. 2001;62(1):44-53.
71. Nash SG, McQueen A, Bray JH. Pathways to adolescent alcohol use: family environment, peer influence, and parental expectations. *J Adolesc Health*. 2005;37(1):19-28.
72. Fite PJ, Colder CR, O'Connor RM. Childhood behavior problems and peer selection and socialization: risk for adolescent alcohol use. *Addict Behav*. 2006;31(8):1454-1459.
73. Rubin DB. *Multiple Imputation for Nonresponse in Surveys*. New York, NY: John Wiley and Sons; 1987.
74. Corp STATA. *STATA Statistical Software, Release 7.0, Reference Manual*. College Station, TX: STATA Press; 2000.
75. Degenhardt L, Bohnert KM, Anthony JC. Case ascertainment of alcohol dependence in general population surveys: "gated" versus "ungated" approaches. *Int J Methods Psychiatr Res*. 2007;16(3):111-123.
76. Rutledge PC, Sher KJ. Heavy drinking from the freshman year into early young adulthood: the roles of stress, tension-reduction drinking motives, gender and personality. *J Stud Alcohol*. 2001;62(4):457-466.
77. Catanzaro SJ, Wasch HH, Kirsch I, Mearns J. Coping-related expectancies and dispositions as prospective predictors of coping responses and symptoms. *J Pers*. 2000;68(4):757-788.
78. Cooper ML, Russel M, Skinner JB, Frone MR, Mudar P. Stress and alcohol use: moderating effects of gender, coping, and alcohol expectancies. *J Abnorm Psychol*. 1992;101(1):139-152.
79. Laurent J, Catanzaro SJ, Callan MK. Stress, alcohol-related expectancies and coping preferences: a replication with adolescents of the Cooper et al (1992) model. *J Stud Alcohol*. 1997;58(6):644-651.

80. Simons-Morton B, Haynie DL, Crump AD, Saylor KE, Eitel P, Yu K. Expectancies and other psychosocial factors associated with alcohol use among early adolescent boys and girls. *Addict Behav*. 1999;24(2):229-238.
81. Cable N, Sacker A. The role of adolescent social disinhibition expectancies in moderating the relationship between psychological distress and alcohol use and misuse. *Addict Behav*. 2007;32(2):282-295.
82. Christiansen BA, Smith GT, Roehling PV, Goldman MS. Using alcohol expectancies to predict adolescent drinking behavior after one year. *J Consult Clin Psychol*. 1989;57(1):93-99.
83. Maher BS, Marazita ML, Zubenko WN, Kaplan BB, Zubenko GS. Genetic segregation analysis of alcohol and other substance-use disorders in families with recurrent, early-onset major depression. *Am J Drug Alcohol Abuse*. 2002; 28(4):711-731.
84. Tambs K, Harris JR, Magnus P. Genetic and environmental contributions to the correlation between alcohol consumption and symptoms of anxiety and depression: results from a bivariate analysis of Norwegian twin data. *Behav Genet*. 1997;27(3):241-250.
85. Hill EM, Blow FC, Young JP, Singer KM. Family history of alcoholism and childhood adversity: joint effects on alcohol consumption and dependence. *Alcohol Clin Exp Res*. 1994;18(5):1083-1090.
86. Poulton R, Caspi A, Milne BJ, Thomson WM, Taylor A, Sears MR, Moffitt TE. Association between children's experience of socioeconomic disadvantage and adult health: a life-course study. *Lancet*. 2002;360(9346):1640-1645.
87. Lieb R, Isensee B, Hofler M, Pfister H, Wittchen HU. Parental major depression and the risk of depression and other mental disorders in offspring: a prospective-longitudinal community study. *Arch Gen Psychiatry*. 2002;59(4):365-374.
88. Puig-Antich J, Goetz D, Davies M, Kaplan T, Davies S, Ostrow L, Asnis L, Twomey J, Iyengar S, Ryan ND. A controlled family history study of prepubertal major depressive disorder. *Arch Gen Psychiatry*. 1989;46(5):406-418.
89. Kovacs M, Devlin B, Pollock M, Richards C, Mukerji P. A controlled family history study of childhood-onset depressive disorder. *Arch Gen Psychiatry*. 1997; 54(7):613-623.
90. Swendsen JD, Merikangas KR, Canino GJ, Kessler RC, Rubio-Stipec M, Angst J. The comorbidity of alcoholism with anxiety and depressive disorders in four geographic communities. *Compr Psychiatry*. 1998;39(4):176-184.
91. Henry B, Feehan M, McGee R, Stanton W, Moffitt TE, Silva P. The importance of conduct problems and depressive symptoms in predicting adolescent substance use. *J Abnorm Child Psychol*. 1993;21(5):469-480.
92. Costello EJ, Erkanli A, Federman E, Angold A. Development of psychiatric comorbidity with substance abuse in adolescents: effects of timing and sex. *J Clin Child Psychol*. 1999;28(3):298-311.
93. King SM, Iacono WG, McGue M. Childhood externalizing and internalizing psychopathology in the prediction of early substance use. *Addiction*. 2004;99(12): 1548-1559.
94. Holahan CJ, Moos RH, Holahan CK, Cronkite RC, Randall PK. Drinking to cope and alcohol use and abuse in unipolar depression: a 10-year model. *J Abnorm Psychol*. 2003;112(1):159-165.
95. 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(4):313-321.
96. Alonso J, Angermeyer MC, Bernert S, Bruffaerts R, Brugha TS, Bryson H, de Girolamo G, Graaf R, Demyttenaere K, Gasquet I, Haro JM, Katz SJ, Kessler RC, Kovess V, Lepine JP, Ormel J, Polidori G, Russo LJ, Vilagut G, Almansa J, Arbabzadeh-Bouchez S, Autonell J, Bernal M, Buist-Bouwman MA, Codony M, Domingo-Salvany A, Ferrer M, Joo SS, Martinez-Alonso M, Matschinger H, Mazzi F, Morgan Z, Morosini P, Palacin C, Romera B, Taub N, Vollebergh WA; ESEMeD/MHEDEA 2000 Investigators, European Study of the Epidemiology of Mental Disorders (ESEMeD) Project. 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 Suppl*. 2004;(420): 28-37.
97. de Graaf R, Bijl RV, Spijker J, Beekman AT, Vollebergh WA. Temporal sequencing of lifetime mood disorders in relation to comorbid anxiety and substance use disorders: findings from the Netherlands Mental Health Survey and Incidence Study. *Soc Psychiatry Psychiatr Epidemiol*. 2003;38(1):1-11.
98. Nolan CL, Moore GJ, Madden R, Farchione T, Bartoi M, Lorch E, Stewart CM, Rosenberg DR. Prefrontal cortical volume in childhood-onset major depression. *Arch Gen Psychiatry*. 2002;59(2):173-179.
99. Elkins IJ, McGue M, Iacono WG. Prospective effects of attention-deficit/hyperactivity disorder, conduct disorder, and sex on adolescent substance use and abuse. *Arch Gen Psychiatry*. 2007;64(10):1145-1152.
100. 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(5):814-828.
101. Kuperman S, Schlosser SS, Kramer JR, Bucholz K, Hesselbrock V, Reich T, Reich W. Developmental sequence from disruptive behavior diagnosis to adolescent alcohol dependence. *Am J Psychiatry*. 2001;158(12):2022-2026.
102. Kushner MG, Sher KJ, Erickson DJ. Prospective analysis of the relation between DSM-III anxiety disorders and alcohol use disorders. *Am J Psychiatry*. 1999;156(5):723-732.
103. Goodwin RD, Lieb R, Hoefler M, Pfister H, Bittner A, Beesdo K, Wittchen HU. Panic attack as a risk factor for severe psychopathology. *Am J Psychiatry*. 2004; 161(12):2207-2214.
104. Frye MA, Altshuler LL, McElroy SL, Suppes T, Keck PE, Denicoff K, Nolen WA, Kupka R, Leverich GS, Pollio C, Grunze H, Walden J, Post RM. Gender differences in prevalence, risk, and clinical correlates of alcoholism comorbidity in bipolar disorder. *Am J Psychiatry*. 2003;160(5):883-889.
105. Conway KP, Swendsen JD, Merikangas KR. Alcohol expectancies, alcohol consumption, and problem drinking: the moderating role of family history. *Addict Behav*. 2003;28(5):823-836.
106. Warner LA, White HR, Johnson V. Alcohol initiation experiences and family history of alcoholism as predictors of problem-drinking trajectories. *J Stud Alcohol Drugs*. 2007;68(1):56-65.
107. Ary DV, Tildesley E, Hops H, Andrews J. The influence of parent, sibling, and peer modeling and attitudes on adolescent use of alcohol. *Int J Addict*. 1993; 28(9):853-880.