Age at First Drink and the First Incidence of Adult-Onset DSM-IV Alcohol Use Disorders

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Background: Existing studies of the association between age at first drink (AFD) and the risk of alcohol use disorders (AUD) suffer from inconsistent levels of control and designs that may inflate associations by failure to control for duration of exposure to risk.

Methods: This study examined associations between AFD (ages < 15 and 15–17 vs. 18 + years) and first incidence of DSM-IV alcohol dependence, abuse, and specific AUD criteria over a 3-year follow-up in a longitudinal study of U.S. drinkers 18 years of age and older at baseline (n = 22,316), controlling for duration of exposure, family history, and a wide range of baseline and childhood risk factors.

Results: After adjusting for all risk factors, the incidence of dependence was increased for AFD < 15 years (OR = 1.38) and for women only with AFD at ages 15 to 17 (OR = 1.54). The incidence of abuse was increased at AFD < 15 and 15 to 17 years (OR = 1.52 and 1.30, respectively). Most dependence criteria showed significant associations with AFD, but hazardous drinking and continued drinking despite interpersonal problems were the only abuse criteria to do so. All associations were nonsignificant after controlling for volume of consumption, except that AFD at all ages < 18 combined was associated with a reduced likelihood of impaired control, and AFD at ages 15 to 17 was associated with lower odds of drinking more/longer than intended among heavy-volume drinkers. In a population of low-risk drinkers that excluded those with positive family histories, personality disorders, and childhood risk factors, there were strong associations between early AFD (< 18) and the incidence of dependence (OR = 3.79) and continued drinking despite physical/psychological problems (OR = 2.71), but no association with incidence of abuse.

Conclusions: There is a robust association between AFD and the risk of AUD that appears to reflect willful rather than uncontrolled heavy drinking, consistent with misuse governed by poor decision-making and/or reward-processing skills associated with impaired executive cognitive function (ECF). Additional research is needed to determine causality in the role of impaired ECF, including longitudinal studies with samples of low-risk adolescents.

Key Words: Age at First Drink, Incidence of AUD.

THE QUESTION OF whether early initiation of drinking increases the risk of alcohol use disorders (AUD) has been debated in numerous studies. Among the studies that have supported an association between early age at first drink (AFD) and subsequent alcohol problems, cross-sectional data from 2 representative samples of U.S. adults revealed an inverse association between AFD and the lifetime prevalence of AUD after controlling for sociodemographic factors (Chou and Pickering, 1992; Grant and Dawson, 1997), and this difference was maintained in a separate study that additionally adjusted for family history of alcoholism (Grant, 1998). Hingson et al. (2006) replicated this finding in survival analysis of a third U.S. population sample, adding controls for other substance use and childhood antisocial behavior and depression. Perhaps the most robust cross-sectional evidence of an association between early drinking and AUD risk came from a survival analysis of a representative Canadian population sample (DeWit et al., 2000), which adjusted for the effects of childhood conduct problems, parental separation, parental substance abuse and mental health problems, childhood abuse, and other adverse childhood events. This study found that individuals who started drinking before age 15 had a 2- to 3-fold increased risk of developing alcohol abuse and alcohol dependence compared with individuals who started drinking at age 19 or older.

Prospective and twin studies have also provided evidence of an association between early AFD and increased risk of AUD. A study that followed a sample of Norwegian adolescents for 6 years and took into account parental and peer substance use patterns and norms (Pedersen and Skrondal, 1998) found that AFD was independently associated with alcohol

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consumption and alcohol problems. Likewise, a study that followed Finnish youth from age 8 to 42 (Pitkänen et al., 2005) found that AFD was inversely related to alcohol problem screening scores; however, this study did not control for potential confounders. McGue et al. (2001a), who studied a sample of twin families from the Minnesota Twin Family Study, found that early onset drinking was positively associated with an increased risk of lifetime DSM-III-R alcohol dependence and reduced P3 amplitude, a highly heritable marker of alcoholism risk.

Other studies, though, have indicated that early AFD was associated with some but not all measures of AUD or that the association was not statistically significant after adjusting for other risk factors. A telephone survey of a representative U.S. adult sample, with few controls, found that AFD was associated with lifetime but not past-year AUD (York et al., 2004). A longitudinal study of U.S. youth originally interviewed at 14 to 21 years of age found an inverse relationship between AFD and the odds of past-year alcohol dependence 8 and 12 years later. There was an inverse association with the odds of alcohol abuse after 8 years, but not after 12 years. This study adjusted for family history of alcoholism, lifetime marijuana use, and number of antisocial behaviors (Grant et al., 2001b). In a prospective study of a community sample followed from age 12, the association between AFD and problem drinking at ages 30 to 31 lost statistical significance after adjusting for the significant effects of family history of alcoholism and delinquency (Warner and White, 2003). Similarly, King and Chassin (2007), who studied 395 children of alcoholics and matched controls from adolescence through two 5-year follow-up interviews, reported that the association between early AFD and subsequent alcohol dependence lost statistical significance after adjusting for externalizing symptoms, family conflict and parental alcoholism, and antisocial personality disorder.

In another study of that assigned offspring of male twins into genetic and environmental risk groups, individuals who started drinking before 15 years of age had the greatest likelihood of lifetime alcohol dependence, but neither AFD nor risk group was significantly associated with the hazard of developing alcohol dependence after accounting for nicotine dependence, generalized anxiety disorder, and conduct disorder (Sartor et al., 2006). Prescott and Kendler (1999), using data from the Virginia Twin Registry, found that early drinking had a strong association with lifetime alcohol dependence and a weaker but still significant association with alcohol abuse. However, because co-twin AFD also was associated with respondent risk of alcohol dependence, they concluded that these associations were due to genetic and shared environmental factors and that early initiation of drinking was a marker of an inherent liability for AUD rather than a modifiable risk factor.

In summary, results of prior studies suggest that early initiation of drinking has a fairly robust association with an increased likelihood of developing an AUD, but that this association may be accounted for by pre-existing risk factors consistent with an overall liability to addiction rather than a specific risk for AUD caused by early drinking. Although deficits in executive cognitive processing associated with disadvantageous reward processing and decision-making skills have been particularly implicated among causal mechanisms that might link early heavy drinking and the development of AUD, it is unclear from existing developmental and brain imaging studies whether dysmaturation of the prefrontal cortex and associated impairment in executive cognitive function (ECF) are the cause or result of adolescent heavy drinking (Clark and Tapert, 2008; Giancola and Moss, 1998; Goudriaan et al., 2007; Johnson et al., 2008).

Further contributing to the uncertainty are the uneven levels of adjustment for potential confounders across studies. Developmental studies have revealed correlates of early AFD that include many factors also associated with the risk of AUD, e.g., parental alcoholism and AFD, male gender, parental divorce, childhood sexual abuse, and behavioral disinhibition as manifested in extraversion, oppositionality, conduct disorder, attention-deficit/hyperactivity disorder (ADHD), and impulsivity (Fisher et al., 2007; Hill et al., 2000; Kuperman et al., 2005; McGue et al., 2001b; Sartor et al., 2006, 2007). Insufficient control for these factors may result in spurious associations between AFD and the risk of AUD and inappropriate attribution of the association to direct causal mechanisms, e.g., permanent or long-lasting alcohol-induced effects on reward, decision-making, and other cognitive processes that might result in habitual heavy drinking, thus increasing the risk for developing tolerance, withdrawal, and AUD. We are unaware of any studies that have examined the relationship of early initiation of drinking and AUD among low-risk individuals, i.e., those without the other AUD risk factors listed above, despite the potential of this approach for identifying effects of AFD that are independent of these risk factors.

In addition, many studies have examined the lifetime incidence of AUD, often without adjusting for duration of exposure to risk or considering whether its association with AFD remains significant over the life course. Importantly, these studies do not rule out the possibility that the increased risk of AUD associated with early AFD is driven solely by excess rates of adolescent-onset AUD, for which individuals who delay drinking until ages 18 or older are not at risk. There has been little testing for gender-specific associations, despite gender differences in maturation rates and recent evidence that early drinking may have different effects on the brain functioning of boys and girls (see review in Clark and Tapert, 2008). Moreover, only a few studies have contrasted the associations of AFD with alcohol abuse versus alcohol dependence, and none to our knowledge has examined specific AUD criteria, even though these may provide useful clues as to the mechanisms underlying the association of AFD with AUD. For example, increased rates of hazardous drinking or other indicators of repeated heavy drinking (e.g., withdrawal symptoms, time spent drinking) among individuals with early AFD might connote support for the importance of impaired ECF; higher rates of tolerance might implicate lower initial

and/or continuing levels of response to alcohol leading to heavy drinking and increased AUD risk; increased rates of impaired control might indicate a role of craving mediated by the endocannabinoid or other neurotransmitter systems, etc.

While positive associations of early AFD and various consumption measures have been reported (e.g., Pedersen and Skrondal, 1998; Pitkänen et al., 2005; York et al., 2004), consumption generally has not been controlled in studies of AUD risk, nor have interactions between consumption and AFD been considered. Thus, it is unclear whether the association between early AFD and AUD is driven by differential levels of consumption or whether differential response to ethanol, as might correspond to low levels of response that have been noted in samples of adolescent alcoholics or individuals with familial alcoholism, plays a role.

To address these issues, this analysis examined the association of AFD with the first incidence of DSM-IV alcohol dependence and alcohol abuse, among individuals at risk, over the course of a 3-year follow-up interval between 2 waves of a national survey of U.S. adults. The short length of the follow-up interval reduced the likelihood of recall error for AUD symptoms and duration of exposure to risk, i.e., the number of months between the Wave 1 and Wave 2 interviews during which the respondents consumed alcohol. The age of the sample (18 or older at the baseline Wave 1 interview) ruled out associations based on adolescent-onset AUD, for which individuals with later AFD were not at risk, and the large sample permitted control for many family history, childhood and adult risk factors, and examination of interactions with age and gender. In addition, it permitted identification of a low-risk subsample of respondents who did not have any of the family history of childhood risk factors that might predispose to both early AFD and the risk of AUD.

Thus, the goals of this study were to determine: (1) whether there remained an association between early initiation of drinking and adult-onset AUD after controlling for all pertinent risk factors including those thought to predispose to adolescent drinking, both through multivariate models of the total population at risk and by means of a sensitivity analysis in the low-risk subsample; (2) whether the risk extended to all AUD criteria; (3) whether the risk varied by age (i.e., over the life course) or gender; and (4) whether the association was accounted for or modified by consumption level.

METHODS

Sample

The data used in this analysis came from Waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), designed by the National Institute on Alcohol Abuse and Alcoholism. The 2001 to 2002 Wave 1 NESARC sample represented U.S. adults 18 years or older residing in households and noninstitutional group quarters in all 50 states and the District of Columbia (n = 43,093, response rate = 81.0%). In Wave 2, the re-interview rate among eligibles (those who had not died, become incapacitated or institutionalized, or left the country and were not in the military for the duration of the Wave 2 interviewing) was 86.7%, yielding a Wave 2 sample of 34,653 adults and a cumulative response rate of 70.2%. Wave 2 data were weighted to reflect design characteristics, including oversampling of Blacks, Hispanics and young adults, and nonresponse relative to sociodemographic characteristics as well as Wave 1 lifetime substance use, and other psychiatric disorders. Weighted data were then adjusted to match the civilian, noninstitutionalized population of the United States on socioeconomic variables based on the 2000 Decennial Census. Data were collected in personal interviews. All potential respondents were informed in writing about the nature of the survey, the statistical uses of the survey data, the voluntary aspect of their participation and the Federal laws that rigorously provide for the confidentiality of identifiable survey information. Only respondents consenting to participate after receiving this information were interviewed. The research protocol, including informed consent procedures, received full ethical review and approval from the U.S. Census Bureau and the U.S. Office of Management and Budget.

This analysis is based on a subsample of respondents who had consumed at least 1 drink between the Wave 1 and Wave 2 interviews and who reported their AFD (n = 22,316). Analyses of the incidence of AUD and specific AUD criteria were restricted to individuals who were at risk for first incidence of those disorders or criteria. The risk groups for alcohol abuse and dependence comprised individuals who had not met the criteria for those disorders prior to the Wave 1 interview. Similarly, the risk groups for specific AUD criteria comprised individuals who had not endorsed the specific criteria in question prior to Wave 1. Incidence for specific dependence criteria did not require a positive diagnosis for dependence.

Measures

AFD. AFD was determined by asking respondents how old they were when they first started drinking, not counting small tastes or sips. Because it was highly skewed, AFD was examined as a categorical variable, with ages <15 and 15 to 17 years compared with ages 18 years or older.

Incidence of AUDs. Using the Alcohol Use Disorder and Associated Disabilities Interview Schedule—DSM-IV Version (AUDADIS-IV, Grant et al., 2001a), AUDs were defined for past year, i.e., the year preceding the Wave 2 interview, and the period since the Wave 1 interview but prior to the past year. To be classified with alcohol dependence during either period, respondents had to report symptoms of at least 3 of the 7 DSM-IV dependence criteria (American Psychiatric Association, 1994). For the period prior to the past year, they also had to report that some of these symptoms occurred within the same 1-year period. To be classified with abuse, respondents had to report the occurrence of at least 1 symptom of any of the 4 DSM-IV abuse criteria in either of the 2 time periods. Individuals were counted as positive for the incidence of dependence and abuse if they met the criteria for these disorders *for the first time* in either of the 2 time periods between Wave 1 and Wave 2. Because of evidence that individuals with dependence can develop abuse without dependence, and vice versa (Grant et al., 2008; Hasin et al., 1990; Schuckit et al., 2001), we chose not to impose the DSM-IV hierarchy of these disorders in which a diagnosis of dependence preempts abuse. Thus, individuals were eligible for the incidence of abuse even if classified with dependence during the same or an earlier time period.

Duration of Exposure to Risk. Duration of exposure to risk was set to the number of months between the Wave 1 and Wave 2 interviews minus the number of months since last drink. For individuals who did not start drinking until after the Wave 1 interview, this duration was further reduced by the number of months between the Wave 1 interview and the first drink, assumed to be

6 months if age at Wave 2 interview was equal to AFD, 12 months if they were 1 year apart, etc.

Model Covariates. In addition to sociodemographic measures in the year preceding the Wave 1 interview (age, sex, race/ethnicity, marital status, attended/completed college, and presence of children under 18 years in the home), other baseline and childhood risk factors are included.

Baseline Risk Factors. Family history measures for alcohol, drug, depressive, and behavioral problems were constructed based on questions for 14 different types of first- and second-degree relatives, and asked during the Wave 1 interview following introductory statements that summarized the types of problems to be considered (e.g., the criteria for AUDs, major depression, etc.). These questions asked whether the relative(s) had ever experienced problems of the sort described. For alcohol problems, a family history density variable was constructed using the algorithm proposed by Stoltenberg et al. (1998). Dichotomous variables were constructed to reflect any versus no family history of depressive, behavioral, and drug problems. Baseline past-year smokers were defined as individuals who reported use of cigarettes, cigars, pipe tobacco, snuff or chewing tobacco in the year preceding the Wave 1 interview. Baseline past-year illicit drug users were defined as those who reported nonprescription use of sedatives, tranquilizers, painkillers or stimulants or any use of marijuana, cocaine/crack, hallucinogens, inhalants/solvents, heroin or other illicit drugs in the year preceding the Wave 1 interview. Individuals were classified with baseline past-year nicotine or drug dependence if they had met the criteria for DSM-IV dependence on nicotine or any illicit drug in the year preceding the Wave 1 interview, using algorithms comparable to those described above for alcohol dependence.

Baseline past-year mood disorders included past-year major depressive disorder (MDD), dysthymia, bipolar disorders and hypomania, and baseline past-year anxiety disorders included past-year panic disorder (with or without agoraphobia), specific and social phobias, and generalized anxiety disorder. All reflected diagnoses for the year preceding the Wave 1 interview, and all ruled out cases that were exclusively illness- or substance-induced. MDD diagnoses also ruled out bereavement. The NESARC measured 10 personality disorders (PD): antisocial (measured at Wave 1 and updated at Wave 2), avoidant, paranoid, dependent, schizoid, obsessive-compulsive and histrionic (measured exclusively at Wave 1), and borderline narcissistic and schizotypal (measured exclusively at Wave 2). As all are considered to be lifetime disorders reflecting pervasive behavioral patterns, all were treated as baseline risk factors, even those not measured until the Wave 2 interview. Because of their strong links with AUD in the literature, borderline PD and antisocial PD were considered separately from the other 8 PD, which were combined into a single category.

Childhood Risk Factors. Unless otherwise specified, all childhood risk factors reflected the period prior to 18 years of age. Family structure distinguished individuals who never lived with their biological fathers and those whose parents divorced from those with intact families. Parental mental health problems reflected whether a parent or other adult living in the home was ever treated or hospitalized for mental illness or attempted/committed suicide, and parental behavioral problems reflected whether a parent or other adult living in the home went to jail or prison. Parental alcohol and drug use problems were based on direct questions, e.g., "Before you were 18 years old, was a parent or other adult living in your home a problem drinker or alcoholic?" History of juvenile delinquency reflected self-report of having been in jail or a juvenile detention facility before age 18. Childhood ADHD was assessed through 20 symptom items that operationalized the DSM-IV criteria for this disorder. Childhood physical and sexual abuse scores were constructed based on scales that measured the frequency with which specific indicators of abuse occurred. Because these scales were highly skewed, they were recoded (values >5 recoded to 5 for both scales) to improve model fit. Number of childhood conduct problems was measured using 31 symptom items asked with respect to the period prior to age 15. Public assistance reflected the number of years before age 18 during which the respondent's family received money from a government assistance program.

Alcohol Consumption. Volume of ethanol intake during the period of heaviest consumption between the Wave 1 and Wave 2 interviews (the only period for which data were available for all drinkers, including those who started drinking after the Wave 1 interview) was estimated on the basis of a series of questions that determined frequency of drinking, usual and largest quantities of drinks consumed, and frequencies of drinking the largest quantity and 5+ drinks, for all alcoholic beverages.

Reliability and Validity. Test–retest reliability of the AFD measure used in this analysis was good, kappa = 0.72 (Grant et al., 1995). Likewise, AUDADIS-IV alcohol diagnoses have demonstrated good reliability and validity in test–retest and other studies, including clinical reappraisals (Canino et al., 1999; Cottler et al., 1997; Grant et al., 1995, 2003; Hasin et al., 1997; Muthen et al., 1993; Nelson et al., 1999; Pull et al., 1997). Test–retest reliability for family history, childhood risk factors, alcohol consumption, use of tobacco, marijuana and cocaine, drug use disorders, and other Axis I disorders have been good to excellent, and PDs have demonstrated levels of reliability comparable to those reported in the clinical literature (Grant et al., 1995, 2003; Ruan et al., 2008).

Analysis

Statistical analyses were conducted using SUDAAN software (Research Triangle Institute, 2001) to adjust variance estimates for design characteristics. Multivariate logistic regression models assessed the odds of incident AUD and AUD criteria among individuals at risk, comparing AFD <15 and 15 to 17 with 18 or older. Covariates were entered sequentially: sociodemographic factors first, followed by adult risk factors, and then by childhood risk factors. At each stage, factors not significant at the $p < 0.05$ level were removed before proceeding to the next stage. Duration of exposure was included at all stages to avoid possible bias resulting from differential exposure to risk. Tests for interactions with age and gender were added to the fully reduced models, as were consumption and its interactions with AFD. As an additional sensitivity analysis, reduced models for incidence of AUD and specific AUD criteria were estimated in a low-risk population of drinkers for whom early initiation of drinking was unlikely to have been a manifestation of pre-existing psychopathology or genetic risk. This low-risk population consisted of drinkers who did not report any family history of substance use or mental disorder and who were negative for all PDs and childhood risk factors ($n = 1{,}867$).

RESULTS

As is evident in Table 1, AFD varied with baseline characteristics, childhood risk factors, alcohol consumption, and the unadjusted incidence of AUD. Individuals who started drinking at ages 18 or later were older; less likely to be male, never have married, and have children under age 18 in the home; and more likely to be Black than those who started drinking at earlier ages. The proportion of individuals who attended/completed college increased steadily with AFD. There were strong inverse relationships between AFD and

Table 1. Selected Baseline and Childhood Characteristics, Baseline Alcohol Consumption, and Incidence of Alcohol Use Disorders, by Age at First Drink: Individuals Who Drank Between Wave 1 and Wave 2 Interviews

	Age at first drink		
	<15 (*n* = 1,552)	15–17 (*n* = 5,362)	18+ (*n* = 15,402)
Sociodemographic characteristics			
Mean age	38.4 (0.5)	37.9 (0.2)	44.0 (0.2)[a,b]
% Male	61.3 (1.6)	59.6 (0.9)	48.2 (0.5)[a,b]
% Black	6.9 (0.9)	6.8 (0.5)	10.3 (0.7)[a,b]
% Hispanic	11.8 (1.4)	9.8 (1.0)	10.8 (1.2)
% Never married	27.3 (1.5)	27.2 (0.9)	21.3 (0.6)[a,b]
% Widowed/divorced/separated	14.7 (1.0)	12.6 (0.5)	14.6 (0.3)[b]
% who attended/completed college	55.8 (1.8)	62.1 (0.9)[a]	65.6 (0.7)[a,b]
% with children <18 years of age in home	47.1 (1.6)	46.8 (0.9)	41.1 (0.6)[a,b]
Mean family history of alcoholism density	0.4 (<0.1)	0.3 (<0.1)[a]	0.2 (<0.1)[a,b]
% with family history of depression	50.8 (1.5)	46.4 (1.0)[a]	37.7 (0.7)[a,b]
% with family history of behavior problems	40.2 (1.7)	30.1 (0.9)[a]	21.3 (0.5)[a,b]
% with family history of drug problems	37.0 (1.6)	28.7 (0.8)[a]	20.9 (0.5)[a,b]
Baseline adult risk factors			
% past-year smokers	50.8 (1.7)	41.2 (0.9)[a]	25.5 (0.6)[a,b]
% past-year illicit drug users	22.8 (1.3)	13.1 (0.6)[a]	4.8 (0.2)[a,b]
% with past-year nicotine or drug dependence	29.6 (1.6)	21.1 (0.9)[a]	10.7 (0.4)[a,b]
% with past-year mood or anxiety disorder	27.6 (1.4)	20.5 (0.7)[a]	15.6 (0.4)[a,b]
% with antisocial PD	20.9 (1.3)	6.8 (0.5)[a]	2.0 (0.2)[a,b]
% with borderline PD	15.0 (1.0)	7.7 (0.5)[a]	5.2 (0.2)[a,b]
% with other PD	34.0 (1.4)	23.0 (0.8)[a]	16.3 (0.4)[a,b]
Childhood risk factors (*before age 18*)			
% w. father never present	13.5 (1.1)	11.2 (0.5)[a]	10.9 (0.3)[a]
% whose parents divorced	29.6 (1.5)	21.1 (0.7)[a]	15.1 (0.4)[a,b]
% with parental mental health problems	12.2 (1.1)	8.5 (0.5)[a]	6.6 (0.2)[a,b]
% with parental behavioral problems	14.8 (1.3)	8.6 (0.5)[a]	6.3 (0.3)[a,b]
% with parental substance use problems	37.4 (1.6)	26.8 (0.8)[a]	21.6 (0.4)[a,b]
% with juvenile detention history	14.2 (1.1)	5.6 (0.4)[a]	2.2 (0.2)[a,b]
% with ADHD	6.9 (0.9)	3.2 (0.3)[a]	2.0 (0.1)[a,b]
% with any physical abuse	57.9 (1.6)	47.8 (0.8)[a]	41.6 (0.6)[a,b]
% with any sexual abuse	18.5 (1.2)	11.1 (0.5)[a]	9.6 (0.3)[a,b]
% who used tobacco	67.7 (1.5)	56.9 (0.8)[a]	32.9 (0.7)[a,b]
% who used illicit drugs	49.7 (1.6)	36.0 (0.8)[a]	10.2 (0.3)[a,b]
Mean years on welfare	1.3 (0.1)	0.8 (<0.1)[a]	0.7 (<0.1)[a,b]
Mean no. conduct problems before age 15	2.2 (0.1)	0.8 (<0.1)[a]	0.4 (<0.1)[a,b]
Wave 1–2 alcohol consumption			
Mean daily ethanol intake (oz.)[c]	1.3 (0.1)	0.8 (<0.1)[a]	0.5 (<0.1)[a,b]
Mean duration of drinking (months)	34.2 (0.2)	34.6 (0.1)[a]	33.8 (0.1)[b]
Incidence of alcohol use disorders			
DSM-IV alcohol dependence	9.0 (1.2)	6.8 (0.5)	4.1 (0.2)[a,b]
DSM-IV alcohol abuse	15.4 (2.0)	13.0 (0.9)	6.9 (0.4)[a,b]

[a]Significantly different than estimate for individuals who started drinking at ages <15 ($p < 0.05$).
[b]Significantly different than estimate for individuals who started drinking at ages 15–17 ($p < 0.05$).
[c]The period of heaviest drinking between Wave 1 and Wave 2 interviews.

family history of psychopathology, baseline substance use, baseline psychiatric disorders, lifetime PDs, childhood risk factors, and volume of alcohol consumption. The unadjusted incidence of alcohol abuse and dependence was lower among individuals who started drinking at ages 18 or older, but did not differ among those who initiated drinking before age 15 and at ages 15 to 17.

For individuals with incident dependence, the mean age at onset was 34.8 (range = 18 to 87), and the mean number of lifetime AUD symptoms prior to the Wave 1 baseline interview was 3.5 (range = 0 to 30, with rare large symptom counts reflecting individuals who did not satisfy the clustering criterion for the dependence symptoms, i.e., who did not report that some of these symptoms occurred within the same 1-year period) (data not shown). Mean age at onset was higher for individuals who started drinking at ages 18 and older (35.9) than for those who initiated drinking at ages 15 to 17 (32.4), and individuals who started drinking at 18 or older had fewer baseline lifetime AUD symptoms than those who started drinking at ages < 15 or 15 to 17 (2.7 vs. 5.7 and 4.5, respectively). Among individuals with incident abuse, similar patterns were observed with respect to age at onset (mean = 35.6, range = 19 to 87) and number of baseline AUD symptoms (mean = 1.8, range = 0 to 15) (data not shown).

Associations Between AFD and AUD Diagnoses and Criteria

Adjusting solely for duration of exposure to risk (Table 2), the odds of developing alcohol dependence were significantly increased for individuals who initiated drinking before age 15

Table 2. Odds Ratios (OR) and 95% Confidence Intervals for Associations Between Age at First Drink (AFD) and Incidence of Alcohol Use Disorders, With Successive Levels of Adjustment for Potential Confounders

	OR (95% CI) for first drink at	
	<15 versus age 18+	15–17 versus 18+
Incidence of alcohol dependence		
Adjusted only for duration of exposure (n = 19,036)	**2.33 (1.74–3.13)**	**1.70 (1.40–2.06)**[a]
Additionally adjusted for significant sociodemographics (n = 19,036)	**2.01 (1.47–2.75)**	**1.31 (1.07–1.61)**[a]
Additionally adjusted for significant baseline risk factors (n = 19,036)	**1.45 (1.05–2.00)**	1.16 (0.94–1.42)
Additionally adjusted for significant childhood risk factors[a] (n = 18,694)	**1.38 (1.00–1.90)**	1.15 (0.94–1.42)[b]
Incidence of dependence criteria (*fully adjusted*)		
Tolerance (need more alcohol to achieve same effect) (n = 16,077)	1.23 (0.89–1.71)	1.04 (0.86–1.25)
Withdrawal syndrome/substance use to relieve withdrawal (n = 17,085)	**1.54 (1.11–2.15)**	**1.25 (1.04–1.50)**
Drank more or for longer than intended (n = 15,254)	**1.31 (1.01–1.69)**	**1.17 (1.01–1.36)**
Desire or unsuccessful attempts to stop drinking (n = 16,521)	1.06 (0.80–1.41)	1.10 (0.93–1.29)
Much time spent drinking/getting over effects of drinking (n = 19,255)	1.50 (1.00–2.26)	**1.31 (1.01–1.68)**
Important activities given up because of drinking (n = 21,600)	**1.85 (1.08–3.18)**	0.84 (0.54–1.30)[a]
Continued drinking despite physical/psychological effects (n = 19,683)	1.33 (0.89–1.97)	**1.25 (1.03–1.52)**
Incidence of alcohol abuse		
Adjusted only for duration of exposure (n = 14,732)	**2.45 (1.76–3.43)**	**1.97 (1.65–2.36)**
Additionally adjusted for significant sociodemographics (n = 14,732)	**2.04 (1.44–2.89)**	**1.44 (1.18–1.75)**
Additionally adjusted for significant baseline risk factors (n = 14,732)	**1.71 (1.20–2.46)**	**1.35 (1.11–1.64)**
Additionally adjusted for significant childhood risk factors (n = 14,689)	**1.52 (1.05–2.21)**	**1.30 (1.07–1.59)**
Incidence of abuse criteria (*fully adjusted*)		
Failure to fulfill major role obligations because of drinking (n = 21,367)	1.31 (0.77–2.23)	1.22 (0.84–1.77)
Recurrent drinking in hazardous conditions (n = 15,336)	**1.47 (1.03–2.09)**	**1.28 (1.06–1.55)**[c]
Recurrent alcohol-related legal problems (n = 20,591)	1.67 (0.93–2.99)	0.89 (0.57–1.38)[a]
Continued drinking despite alcohol-related interpersonal problems (n = 19,824)	**1.95 (1.25–3.04)**	1.32 (0.97–1.78)

Values in bold font are statistically significant ($p < 0.05$). Other significant risk factors in fully reduced models are summarized in Table A1.
[a]OR for ages 15–17 at first drink is significantly different from OR for ages <15 at first drink ($p < 0.05$).
[b]A significant interaction between AFD and gender indicated that the OR for AFD at ages 15–17 was 0.97 (0.75–1.25) for men compared with 1.54 (1.12–2.11) for women.
[c]A significant interaction between AFD and gender indicated that the OR for AFD at ages 15–17 was 1.10 (0.87–1.40) for men compared with 1.63 (1.23–2.13) for women.

or at ages 15 to 17 and showed a clear linear trend with AFD. These differences remained significant after adjusting for sociodemographic characteristics, but the OR for AFD at ages 15 to 17 fell short of significance after controlling for baseline and childhood risk factors. Individuals who started drinking at ages younger than 15 did remain at increased risk of the incidence of alcohol dependence after controlling for all significant risk factors (OR = 1.38, p = 0.047).

The associations between AFD and most dependence criteria remained significant after adjustment for all covariates. AFD showed a significant linear trend with withdrawal and drinking more/longer than intended. The associations with time spent drinking and continued drinking despite adverse physical/psychological effects were significant for individuals who started drinking at ages 15 to 17 but not for those who started drinking at ages <15. However, when all AFD <18 were combined, the associations with these 2 criteria were significant relative to initiation of drinking at ages 18 or older (OR = 1.34 and 1.27, data not shown) and no meaningful differences were lost by combining the 2 categories. In the case of activities given up because of drinking, there was a strong and significant association limited to initiation of drinking at <15 years of age (OR = 1.85).

The association between AFD and the incidence of alcohol abuse retained its significance even after adjusting for all significant covariates (OR = 1.52 and 1.30 for AFD at ages <15 and 15 to 17). The only abuse criterion that showed a significant linear trend with AFD was recurrent drinking in hazardous situations; however, individuals who started drinking before age 15 were almost twice as likely as those who started drinking at 18 or older to have experienced the incidence of continued drinking despite alcohol-related interpersonal problems.

As indicated in Table A1, other significant risk factors for the AUD diagnoses and criteria varied; however, longer duration of exposure to risk, younger age at baseline, male gender, never having been married, parental substance problems when the respondent was growing up, borderline PD, and baseline smoking increased the likelihood of most of these outcomes. In contrast, the presence of children under 18 years in the home reduced the likelihood of most of the incident outcomes.

Sensitivity Analysis

As an additional test of the association between AFD and the incidence of AUD, reduced models were estimated for a population of low-risk drinkers (data not shown). Because this population consisted of small numbers of individuals who initiated drinking at ages <15 (n = 45) and ages 15 to 17 (n = 185), these 2 groups were combined to reflect initiation of drinking before age 18. Relative to initiation of drinking at 18 or older, the resulting OR for incidence of dependence (OR = 3.79, p = 0.001) was far greater than the

comparable OR for the total population, and it no longer demonstrated a significant interaction with gender. In contrast, the OR for incidence of alcohol abuse in the population of low-risk drinkers was reduced in magnitude and no longer statistically significant (OR = 1.11, $p = 0.835$). Reflecting the nature of the low-risk population, some of the more severe AUD criteria had incidence rates too low to estimate their associations with AFD. Of those criteria that could be examined, the only one for which there was an increased risk associated with AFD <18 was continued drinking despite physical/psychological problems caused by drinking (OR = 2.71, $p = 0.021$).

Interaction of AFD With Age and Gender

The associations of AFD with the incidence of alcohol dependence and specific dependence criteria did not demonstrate any significant modification by age at baseline. There was, however, an interaction between gender and initiation of drinking at ages 15 to 17 ($p = 0.037$), which indicated no increased risk of dependence for males who commenced drinking at those ages but a significantly increased risk for females (OR = 1.54, data not shown). This interaction did not extend to any of the individual criteria for alcohol dependence, although it fell just short of significance for continued drinking despite adverse physical/psychological effects ($p = 0.064$).

The association of AFD with the incidence of alcohol abuse was not modified by either age or gender. Neither were the associations of AFD with the incidence of individual abuse criteria modified by age; however, there was a significant interaction ($p = 0.034$) between gender and initiation of drinking at ages 15 to 17 for recurrent drinking in hazardous situations (OR = 1.65 for females but nonsignificant for males, data not shown).

Consumption as a Mediator and Moderator of Associations With AFD

As shown in Table 3, all of the associations between AFD and the incidence AUD and specific AUD criteria lost statistical significance after adjusting for average daily volume of ethanol consumption. Interestingly, early initiation of drinking showed a *negative* association with the incidence of impaired control (desire or unsuccessful attempts to stop or cut down on drinking) after adjusting for consumption, and this association was statistically significant when the AFD categories of <15 and 15 to 17 were combined (OR = 0.85, $p = 0.044$, data not shown).

Reflecting a negative interaction between volume of consumption and AFD, the incidence of drinking more/longer than intended was significantly reduced among individuals with AFD at ages15 to 17 who consumed the equivalent of 2 or more standard drinks per day. A similar interaction was observed for the incidence of withdrawal, but the reduction in risk at heavy volumes of consumption failed to reach statistical significance.

DISCUSSION

This study found that individuals who started drinking before 15 years of age were significantly more likely to experience the incidence of alcohol dependence and alcohol abuse in adulthood than those who delayed initiation of drinking until 18 or older. Among individuals who started drinking at ages 15 to 17, there was an increased adult incidence of

Table 3. Odds Ratios (OR) and 95% Confidence Intervals for Associations Between Age at First Drink and Incidence of Alcohol Use Disorders, Fully Adjusted for All Risk Factors and Including Adjustment for Volume of Alcohol Consumed

	OR (95% CI) for first drink at	
	<15 versus ages 18+	15–17 versus 18+
Incidence of alcohol dependence (*n* = 18,881)	1.02 (0.70–1.48)	0.89 (0.70–1.12)
Incidence of dependence criteria		
Tolerance (need more alcohol to achieve same effect) (*n* = 15,993)	1.03 (0.72–1.46)	0.87 (0.71–1.05)
Withdrawal syndrome/substance use to relieve withdrawal[a] (*n* = 17,710)	1.34 (0.94–1.91)	1.09 (0.90–1.32)
Drank more or for longer than intended[b] (*n* = 15,182)	1.12 (0.85–1.48)	0.94 (0.80–1.11)
Desire or unsuccessful attempts to stop drinking (*n* = 16,440)	0.81 (0.58–1.13)	0.85 (0.72–1.01)
Much time spent drinking/getting over effects of drinking (*n* = 19,154)	1.19 (0.74–1.90)	0.99 (0.75–1.31)
Important activities given up because of drinking (*n* = 21,475)	1.49 (0.86–2.60)	0.67 (0.42–1.08)
Continued drinking despite physical/psychological effects (*n* = 19,580)	1.03 (0.67–1.58)	1.02 (0.83–1.25)
Incidence of alcohol abuse (*n* = 14,614)	1.26 (0.82–1.93)	1.07 (0.84–1.35)
Incidence of abuse criteria		
Failure to fulfill major role obligations because of drinking (*n* = 21,247)	1.12 (0.65–1.95)	1.02 (0.69–1.51)
Recurrent drinking in hazardous conditions (*n* = 15,255)	1.17 (0.78–1.74)	1.06 (0.86–1.31)
Recurrent alcohol-related legal problems (*n* = 20,266)	1.29 (0.72–2.33)	0.76 (0.48–1.20)
Continued drinking despite alcohol-related interpersonal problems (*n* = 19,720)	1.46 (0.89–2.40)	1.03 (0.74–1.44)

[a]A significant interaction between volume of consumption and age at first drink indicated that the OR for first drink at ages 15 to 17 declined from positive but nonsignificant at volumes of less than 1 standard drink per day to negative but nonsignificant at higher average daily volume of ethanol intake in ounces (ADV).

[b]A significant interaction between volume of consumption and age at first drink indicated that the OR for first drink at ages 15 to 17 declined from positive but nonsignificant at ADV of less than 2 standard drinks per week to negative at higher volumes, significantly so at volumes of 2 or more standard drinks per day.

alcohol abuse for both men and women and an increased incidence of dependence that was limited to women. These results demonstrate that the association between early AFD and increased risks of lifetime AUD cannot be solely attributed to adolescent-onset disorders—disorders that may reflect unique, age-specific vulnerabilities related to level of maturation and drinking patterns and context and for which individuals with later AFD are not at risk.

The magnitude of excess risk reported in this study was smaller than that reported in an earlier analysis of a Canadian sample (DeWit et al., 2000), which controlled for a nearly identical range of childhood factors. Several factors may account for the discrepancy. First, the Canadian study used a slightly older reference category of AFD, ages 19 or older. Second, it examined lifetime prevalence of AUD, whereas the current study ruled out cases of abuse or dependence that began prior to the Wave 1 NESARC, including adolescent-onset disorders. Finally, the Canadian study did not control for family history or for mood, anxiety, and PDs. In this study, the OR for early AFD declined sharply after these controls were added. The fact that we found a significant association between AFD and the incidence of AUD even after adjusting for these additional risk factors speaks to the robustness of this association.

This study found that early AFD was as strongly associated with abuse as with dependence. This finding, coupled with the specific AUD criteria for which significant associations were noted, suggests that the increased risk of adult-onset AUD among individuals with early AFD derives in large part from a greater likelihood of their engaging in heavy and/or hazardous patterns of drinking in adulthood. This interpretation, consistent with studies that have examined the direct association of AFD and consumption in adolescence or adulthood (Pedersen and Skrondal, 1998; Pitkänen et al., 2005; York et al., 2004), is further supported by total attenuation of AFD and AUD associations that resulted from adjusting for volume of consumption. Additional support is provided by the lack of association between AFD and abuse in a low-risk population that excluded individuals with characteristics reflecting impulsivity or impaired ability to make choices based on perceived consequences of their drinking behavior—characteristics that would predispose to adverse drinking patterns. There was no indication that early AFD was associated with impaired control, the hallmark of addiction. Indeed, at comparable levels of alcohol intake, individuals who started drinking before age 18 were somewhat *less* likely to report the incidence of desire/unsuccessful attempts to stop or cut down on their drinking, and at higher volumes of intake they were less likely to report drinking more/longer than intended. Both of these findings are more consistent with a willful misuse of alcohol, possibly reflecting poor decision-making and/or reward-processing skills, than with either an inability to control drinking or a greater level of physical dependence (tolerance or withdrawal) in relation to a given level of ethanol intake.

The fact that AFD at ages 15 to 17 was associated with an increased risk of incident dependence for women only (as well as a greater risk of hazardous drinking among women) lends itself to various interpretations. First, drinking at those ages might reflect a more deviant behavior among girls than boys, thus one more likely to be associated with increased risk of psychopathology, including AUD. The proportion of women who started drinking at ages 15 to 17 was lower than the proportion of men (21% vs. 29%). Although this analysis controlled for the factors thought most likely to contribute to any selectivity in terms of deviance-proneness, the dichotomous measures used for some risk factors may not have accounted for gender differences in the *severity* of psychiatric disorder among individuals with AFD at ages 15 to 17. Moreover, interpreting the gender interaction with AFD at ages 15 to 17 as a reflection of greater severity of psychopathology among women would be consistent with the lack of a comparable gender interaction in the low-risk population of individuals that excluded individuals with predisposing psychopathology. The lack of a comparable interaction between gender and initiation of drinking at ages < 15 could reflect either the smaller gender difference in the prevalence of AFD before age 15 (8% of men vs. 6% of women) or the possibility that drinking at such extremely early ages is sufficiently deviant for both boys and girls as to obviate the importance of that difference.

Alternatively, at comparable levels of predisposing factors, women who initiated drinking at 15 to 17 years of age might have been at increased risk for the incidence of dependence relative to men because older romantic partners exposed some of them to more regular drinking occasions on which greater amounts of alcohol were consumed, setting in motion a process of heavier drinking that culminated in a greater incidence of dependence in adulthood. This explanation is consistent with the near-significant increased risk of the incidence of drinking despite adverse physical/psychological consequences among women, consequences that might result from a greater volume of ethanol intake, as well as with the fact that there was no gender interaction with AFD after adjusting for consumption level. Indirect support for this interpretation was found by Castillo Mezzich et al. (1999), who reported more adult male sexual partners among adolescent girls with substance use disorders.

Although this study did not formally test for mediation (Baron and Kenny, 1986) of the association between AFD and AUD, the results permit cautious inferences as to the potential mediating roles of a number of possible causal mechanisms, and they suggest promising avenues for additional research. Of primary interest from a policy point of view is whether the associations found in this study are more consistent with (1) direct neurotoxic and/or pharmacological effects of early drinking, (2) habituation of heavy drinking arising from the contexts in which adolescent drinking often occurs, or (3) selectivity of early drinkers. Any causal role of impaired neuromaturation or executive cognitive dysfunction resulting from neurotoxicity would appear to be ruled out by the fact that women, who experience neuromaturation at

earlier ages than men, were at greater risk of the incidence of dependence among those who initiated drinking at ages 15 to 17. However, a recent brain imaging study reported a reduced volume of prefrontal white matter in association with AUD among 15- to 17-year-old girls but not boys (Medina et al., 2008), a finding that did support the gender-specific association found in this study. A better understanding of any possible neurotoxic effects of adolescent drinking clearly requires much additional research, including studies with samples large enough to reliably test for gender differences. Any direct pharmacological effect specific to early alcohol use also appears unlikely, because similar risks associated with early use have been reported for tobacco and cannabis (Kandel et al., 2007; Lynskey et al., 2006) and because early initiation of drinking was shown to increase the odds of drug rather than alcohol dependence in 1 prospective study (King and Chassin, 2007).

Habituation of heavy drinking and associated alcohol-related expectancies resulting from the uncontrolled context in which adolescent drinking usually occurs—a context that is arguably more conducive to excessive drinking than contexts in which adults and more extensive social controls are present—cannot be either confirmed or ruled out as a causal mechanism because of the lack of data in the NESARC on patterns and contexts of drinking during adolescence. At the same time, the argument that both early initiation of drinking and risk for AUD might be manifestations of a more general deviance syndrome (Jessor and Jessor, 1977; Newcomb and McGee, 1991) or of pre-existing impairment of executive skills regulating decision making (Goudriaan et al., 2007; Johnson et al., 2008) was countered by the strong associations between the 2 in the low-risk sample, which excluded individuals with other indicators of deviance and/or poor ECF. Nevertheless, before we can reject a mediating role of selectivity it will be critical to determine whether the rare low-risk sample members who initiated drinking before age 18 were characterized by AUD risk factors beyond the typical indicators of deviancy. Potential candidates might include early-onset mood and anxiety disorders, positive expectancies related to the effects of alcohol, peer alcohol use, parental approval of drinking, and so forth. Pending additional investigation, it would be premature to rule out either selectivity, habituation of heavy drinking or direct neurotoxic effects of adolescent drinking as causal mechanisms mediating the association between early AFD and risk of adult-onset AUD, although it might be argued that the persistence of increased AUD risk over the lifespan, as indicated by the lack of interactions between AFD and age at interview, are more supportive of underlying vulnerabilities than of direct effects.

Any mediating role of other psychopathology seems unlikely given the continued association of AFD and AUD after controlling for most Axis I and II disorders (although the reduction in the magnitude of the association is consistent with partial mediation). However, this study did not test for a moderating role of other psychopathology, as could be done in future studies. The stronger association of AFD and AUD in the low-risk population suggests the possibility of unmeasured negative interactions between early AFD and the factors that were used to exclude individuals from the low-risk population. That is, early-onset drinking might have more potential for an independent association with the risk of AUD when that risk has not already been increased by predisposing family history, baseline, and childhood risk factors.

This study has a number of limitations that must be considered in interpreting its findings. First, the reliability of self-reported AFD may have been poorer for older respondents, leading to telescoping, i.e., recall of AFD at older/more recent ages. This possibility would be consistent with the older mean age of respondents who started drinking at ages 18 and older, although the possibility of a genuine cohort effect cannot be ruled out. Given that the incidence of AUD decreased with age, any such telescoping might have upwardly biased the positive association of early AFD and AUD incidence. In addition, the validity of the sensitivity analysis may have been somewhat compromised by our inability to ascertain the timing of AFD relative to the onsets of the events and PD used as exclusionary criteria for the low-risk population. Another limitation is the absence of data that would permit testing for mediating effects of low initial level of response to ethanol (Schuckit et al., 1997) and social modeling of drinking behavior. Finally, our family history measures, though highly reliable, were based on respondent report rather than direct ascertainment in family members. Respondents may not have known the full extent of their family history, and birth cohort and cultural factors may have influenced recognition or willingness to report positive family histories. Moreover, reporting of family history may have been greater among respondents with manifestations of the same disorders (Kendler et al., 1991; Rice et al., 1995).

The fact that the diagnostic and criterion outcomes in this study were examined in different populations, i.e., those at risk for each outcome, could arguably cast doubt on inferences regarding causal mechanisms based on the relative magnitudes of the associations of early AFD with various AUD criteria. To examine the impact of having used outcome-specific risk groups, we repeated the models in Table 2 within a common risk group of individuals who had not satisfied *any* AUD criteria as of the baseline Wave 1 interview (n = 10,708). The significant positive associations between AFD <15 and the incidence of dependence, withdrawal, important activities given up, abuse, and recurrent drinking in hazardous conditions remained significant and were generally somewhat increased in magnitude, but the significant positive associations between AFD <15 and drinking more or longer than intended and continued drinking despite alcohol-related interpersonal problems were no longer significant. Of the significant associations between AFD at ages 15 to 17 and the various outcomes, only 1—drinking more or longer than intended—remained significant, with the others both losing significance and being slightly reduced in magnitude. Although this pattern of results suggests that only the earliest ages at first drink are clearly associated with an increased risk

of the incidence of *any* alcohol problems, such a conclusion must be made with caution, as none of the OR derived from the common risk group were significantly different from their counterparts in Table 2, and loss of significance may have resulted from the reduced sample size upon which the models using the common risk group were based. The results of this experiment do not rule out any of the previous inferences regarding causal mechanisms.

However, it is critical to note that most possible causal mechanisms linking early AFD and increased risk of AUD entail the assumption that early drinking leads to heavy drinking during adolescence, with heavy exposure to ethanol during a period of physical and neurological maturation constituting the primary direct risk factor and/or marker of risk. Clearly, not all early drinkers engage in heavy adolescent drinking, and the link between the 2 behaviors may be particularly tenuous in cultures where early drinking is the norm. Consequently, the lack of data on volume and pattern of consumption and drinking context during adolescence constitutes a serious limitation of this analysis, both for understanding the etiology and assessing the policy implications of the association between early drinking and subsequent risk for AUD (Rossow, 2006).

This study, by design, did not measure the association of AFD with lifetime incidence of AUD. By focusing on individuals who were still at risk of AUD at the time of the Wave 1 interview, it investigated the impact of AFD in what might be termed a resilient population, one that had remained free of AUD until at least 18 years of age—and until much older than that in most cases. That an association between early AFD and incidence of AUD was found in such a resilient population, and that it did not diminish with age at baseline, provides more evidence that this is an extremely robust, though modest, association. Because AUDs are so common and have such devastating consequences for affected individuals and their families, even an association of modest magnitude has major clinical and public health implications. Given that this study was unable to rule out the possibility of direct adverse effects of adolescent drinking or to identify consumption thresholds at which any such effects might occur, there is a clear need for more longitudinal research based on samples large enough to evaluate gender differences and distinguish low-risk and high-risk individuals, ideally utilizing multiple sources of information on familial risk factors and collecting detailed data on adolescent drinking patterns and contexts.

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APPENDIX

Table A1. Summary of Significant Associations With Incidence of DSM-IV Alcohol Use Disorders and Criteria in Fully Adjusted, Reduced Models

	DSM-IV alcohol dependence								DSM-IV alcohol abuse (nonhierarchical)				
	Dx.	Cr. 1	Cr. 2	Cr. 3	Cr. 4	Cr. 5	Cr. 6	Cr. 7	Dx.	Cr. 1	Cr. 2	Cr. 3	Cr. 4
Duration of exposure to risk	+	+	+	+	+	+	+	+	+		+	+	
Sociodemographic risk factors													
Age	−	−	−	−	−	−	−	−	−	−	−	−	−
Male	+	+	+	+	+	+	+	+	+	+	+	+	+
Black	+	+			+								
Hispanic	+	+			+		+	+	−		−		
College education		−			−							−	
Widowed/divorced/separated					+	+	+	+		+			+
Never married	+	+		+	+		+	+	+	+			+
Children under 18 in home	−	−	−	−	−	−	−	−	−		−	−	
Childhood risk factors													
Father never present									+				
Parents divorced													+
Years on welfare		+	+										
No. conduct problems			−		−		−	−					
Juvenile jail/detention		+	+							+	+	+	
Parental substance problems	+	+	+	+	+	+	+	+	+	+	+	+	
Parental behavioral problems													
Parental depression problems	−												
ADHD	+		+			+							
Physical abuse			+	+	+	+	+	+			+		+
Sex abuse													
Adolescent tobacco use		+					+	+					
Adolescent drug use									+		+		
Baseline risk factors													
Family history: alcoholism (density)					+								
Mood or anxiety disorder										+			
Antisocial personality disorder													
Borderline PD	+	+	+	+	+	+	+	+	+	+	+	+	+
Other PD	+	+	+				+	+					
Smoker	+		+	+	+	+	+	+	+	+	+		+
Illicit drug user			+	+		+	+	+				+	
Other substance dependence												+	
Family history: drug problems													
Family history: behavioral problems													
Family history: mental problems		−			−				−		−	−	