Probability and Correlates of Dependence Among Regular Users of Alcohol, Nicotine, Cannabis, and Cocaine: Concurrent and Prospective Analyses of the National Epidemiologic Survey on Alcohol and Related Conditions

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ABSTRACT

Objective: Research on the progression from substance use to dependence typically relies on lifetime retrospective reports of dependence among ever users. We sought to evaluate probability and correlates of dependence among recent (past-year) weekly users of alcohol, nicotine, cannabis, and cocaine through cross-sectional and prospective analyses.

Methods: Data on substance use (assessed by the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV) and *DSM-IV* psychiatric disorders were assessed in 2 waves (Wave 1, N = 43,093; Wave 2, N = 34,653) through the National Epidemiologic Survey on Alcohol and Related Conditions.

Results: Conditional risk of dependence varied by frequency of substance use, although it was relatively stable for nicotine use. Among weekly past-year substance users at Wave 1, rates of dependence when rates of past-year dependence at Wave 1 were combined with new cases of dependence reported at Wave 2 were 15.6% for alcohol, 25.0% for cannabis, and 67.3% for nicotine. For past-year weekly users of cocaine at Wave 1, 49.9% met criteria for past-year dependence. Multiple demographic characteristics and past-year psychiatric disorders were correlated with past-year dependence, even among daily users. Men were generally more likely than women to be dependent on alcohol, cannabis, and cocaine, although women were more likely to be dependent on nicotine. Prospective analyses indicated that depressive disorders at Wave 1 predicted subsequent development of alcohol dependence (odds ratio [OR] = 1.40; 95% CI, 1.19–1.65; $P < .05$). Further, 33.5% of weekly tobacco smokers who were nondependent at Wave 1 developed dependence later on.

Conclusions: The present findings highlight the importance of frequency of use when determining the addictiveness of substances and suggest that certain demographic variables and psychiatric disorders are associated with substance dependence even among regular substance users.

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Alcohol, cannabis, tobacco, and cocaine represent some of the more commonly abused substances.[1–3] Among these substances, dependence estimates typically find nicotine to be the most addictive (ie, having the largest percentage of users developing dependence), with alcohol and cocaine being less addictive and cannabis being the least addictive.[1,3] Research has documented that numerous demographic and mental health variables are predictors of the transition from first use to dependence, including ethnic minority status, lower income, lower education, and psychiatric comorbidity.[1,3,4]

Research on the probability and prediction of the transition from substance use to dependence has had a few notable limitations. First, as noted elsewhere,[3] such studies often focus on specific substances or samples with little generalizability,[2,5] which makes it difficult to compare estimates of risk across substances and samples. Second, these studies often rely on lifetime retrospective reports of dependence using cross-sectional surveys.[1,3,4] Recent evidence suggests that such methods may greatly underestimate the risk of psychiatric disorders, likely due to recall difficulties and current remission status. For example, researchers examined the lifetime prevalence of psychiatric disorders using retrospective and cumulative prospective assessments and found the prevalence of disorders, including alcohol and cannabis dependence, to be doubled in prospective relative to retrospective data.[6] Studies that rely on reports of past-year dependence and risk factors for dependence are less apt to be affected by recall problems than are lifetime retrospective designs,[7,8] which may assess substance use that occurred decades ago. Additionally, estimates of the lifetime conditional risk of dependence are limited in that they do not typically consider the *duration* of use (eg, 5 years or 15 years), which most likely influences risk of dependence and may vary considerably across substances. Lastly, analysis of lifetime psychiatric disorders that correlate with lifetime dependence is often an inadequate method of identifying psychiatric disorders that may influence risk of dependence, as this method considers disorders that may have occurred long before (ie, predated) or after the occurrence of dependence. Examination of past-year dependence and past-year psychiatric disorders therefore allows researchers to identify psychiatric disorders that co-occur with dependence with greater precision.

Estimates of the conditional probability of dependence also typically focus on all individuals who have *ever* used a certain substance. However, this approach does not take into account differences in the prevalence of regular use versus experimental use that may exist across substances. Such analyses may overestimate

Clinical Points

- Research on the progression from substance use to dependence has typically relied on retrospective reports of people who have ever used the substance. This approach underestimates the addictiveness of some substances and lacks the precision for determining vulnerability factors for dependence. We examined the probability and correlates of dependence among past-year regular substance users.
- The risk of dependence among weekly (at least once a week) substance users was 15.6% for alcohol and 67.3% for nicotine. Cannabis dependence was common, occurring in 25% of weekly users.
- Depressive disorders predicted subsequent development of alcohol dependence among weekly drinkers who were not initially dependent. Additionally, one-third of weekly smokers who were not initially dependent developed nicotine dependence later on.

the addictive potential of alcohol, which is often regularly consumed, and may underestimate the addictive potential of cannabis, which is commonly used experimentally (ie, no more than a few times). For example, estimates of cannabis dependence among ever users are quite low (8.9%)[3] compared to rates of dependence that have been found among regular users (29%).[9] Examination of the progression from regular use to dependence may provide insights on the addictive potential of different substances, as well as risk factors for the progression to dependence. Additionally, existing retrospective research designs are limited in identifying vulnerability factors for dependence. Prospective analyses of nondependent regular users and risk of subsequent substance dependence would provide important information on such vulnerabilities and their role in addiction.

Together, the current investigation examined the probability and correlates of the progression from regular (at least weekly) substance use to dependence in a large, nationally representative sample, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). The study aims were to (1) examine the prevalence and correlates of past-year substance dependence among past-year ever users and regular substance users and (2) prospectively examine the prevalence and prediction of substance dependence 3 years later among regular, nondependent substance users at baseline.

METHODS

Sample and Procedures

The NESARC is a nationally representative face-to-face survey of 43,093 respondents conducted by the National Institute on Alcohol Abuse and Alcoholism from 2001–2002.[10,11] The target population of the NESARC is the noninstitutionalized civilian population residing in the entire United States. The overall survey response rate was 81.01%. Black and Hispanic households were oversampled. The NESARC sample was weighted to adjust for the probabilities of selection of a sample housing unit or equivalent from the group quarters' sampling frame, nonresponse at household and person levels, the selection of 1 person per household, and oversampling of young adults. Data were then adjusted to be representative of the US population across region, age, sex, race, and ethnicity, based on the 2000 Decennial Census.

For the prospective analyses, we examined Wave 2 of the NESARC, which was conducted from 2004 to 2005.[12] Of the 43,093 respondents interviewed at Wave 1 (age: mean = 46.40 years, SD = 18.2), 34,653 respondents were reinterviewed at Wave 2 (age: mean = 49.06 years, SD = 17.3). Sample weights in Wave 2 were recalculated to adjust for non–follow-up.[12] Subsequently, comparisons between Wave 2 data and the target population (Wave 2 respondents and eligible nonrespondents) demonstrated no significant differences between baseline (Wave 1) sociodemographic measures or the presence of any lifetime substance, mood, anxiety, or personality disorder.[12]

Measures

Diagnostic assessment. The National Institute on Alcohol Abuse and Alcoholism's Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV)[13] is a structured diagnostic interview used to assess a variety of alcohol, substance use, mood, and anxiety disorders. The AUDADIS-IV is an assessment instrument for use by trained nonclinician interviewers and was scored using computer-assisted software. The AUDADIS-IV includes an extensive list of questions covering *DSM-IV* criteria for mood, anxiety, and personality disorders, as well as substance use disorders.

AUDADIS-IV measures of alcohol and substance abuse and dependence were identical for Waves 1 and 2 of the NESARC, save for the time frames. All of the anxiety disorders were assessed at Wave 1 and Wave 2 with the exception of posttraumatic stress disorder, which was assessed only at Wave 2. Conduct disorder with and without antisocial personality disorder, avoidant personality disorder, dependent personality disorder, obsessive-compulsive personality disorder, paranoid personality disorder, schizoid personality disorder, and histrionic personality disorder were assessed at Wave 1. Only antisocial personality disorder was assessed a second time at Wave 2. Schizotypal, narcissistic, and borderline personality disorders were also assessed at Wave 2. All of the aforementioned personality disorders were explored in the current study for the Wave 1 cross-sectional analyses, although the prospective analyses of Wave 1 predictors of the onset of subsequent substance use disorder only used personality disorders assessed at Wave 1. Wave 2 diagnoses were made for 2 time periods between Waves 1 and 2: (1) the year preceding the Wave 2 interview and (2) the period of approximately 2 years following the Wave 1 interview but before the year preceding the Wave 2 interview. In this study, alcohol dependence and substance use dependence were diagnosed at Wave 2 if diagnostic criteria for new substance dependence were met since Wave 1. In the current study, only dependence diagnoses for alcohol, nicotine, cannabis, and cocaine/crack were explored as outcomes.

Table 1. Alcohol and Nicotine: Bivariate Analyses of Demographic and Psychiatric Correlates of Risk of Past-Year Substance Dependency by Past-Year Substance Use Frequency

	Alcohol			Nicotine		
Variable	Used at Least Once, OR (95% CI)	Used Weekly, OR (95% CI)	Used Daily, OR (95% CI)	Used at Least Once, OR (95% CI)	Used Weekly, OR (95% CI)	Used Daily, OR (95% CI)
Age[a]	0.94 (0.94–0.94)*	0.94 (0.93–0.94)*	0.93 (0.93–0.94)*	0.99 (0.99–0.99)*	0.99 (0.98–0.99)*	0.98 (0.98–0.99)*
Income[a]	0.96 (0.95–0.96)*	0.91 (0.90–0.92)*	0.93 (0.92–0.94)*	0.95 (0.94–0.96)*	0.96 (0.95–0.98)*	0.97 (0.96–0.99)*
Married	0.28 (0.26–0.30)*	0.29 (0.27–0.31)*	0.32 (0.28–0.37)*	0.83 (0.79–0.87)*	0.89 (0.84–0.94)*	0.88 (0.83–0.94)*
Never married	3.72 (3.51–3.95)*	3.56 (3.34–3.80)*	4.34 (3.82–4.94)*	1.13 (1.07–1.21)*	1.09 (1.02–1.17)*	1.16 (1.07–1.25)*
Divorced/separated/ widowed	1.16 (1.07–1.27)*	1.24 (1.13–1.36)*	1.20 (1.04–1.39)*	1.16 (1.09–1.24)*	1.08 (1.01–1.15)*	1.03 (0.96–1.11)
Female	0.50 (0.47–0.53)*	0.69 (0.64–0.73)*	0.59 (0.52–0.66)*	1.53 (1.45–1.61)*	1.46 (1.38–1.54)*	1.43 (1.34–1.52)*
White	0.77 (0.72–0.83)*	0.75 (0.69–0.81)*	0.60 (0.53–0.68)*	1.19 (1.14–1.24)*	1.27 (1.22–1.32)*	1.29 (1.23–1.34)*
Black	1.24 (1.14–1.35)*	1.27 (1.16–1.39)*	2.20 (1.93–2.50)*	0.83 (0.79–0.86)*	0.76 (0.73–0.79)*	0.74 (0.70–0.78)*
Asian	0.74 (0.66–0.84)*	0.74 (0.65–0.85)*	0.71 (0.34–1.47)*	0.72 (0.67–0.77)*	0.76 (0.69–0.83)*	0.75 (0.69–0.82)*
NH/PI	2.18 (1.85–2.57)*	2.59 (2.07–3.24)*	1.69 (1.58–1.79)*	1.31 (1.11–1.56)*	1.32 (1.10–1.57)*	1.44 (1.17–1.77)*
AI/AN	2.17 (1.88–2.51)*	2.41 (2.03–2.85)*	0.89 (0.67–1.18)	1.27 (1.10–1.46)*	1.25 (1.08–1.45)*	1.27 (1.08–1.49)*
Hispanic	1.16 (1.08–1.25)*	1.26 (1.17–1.36)*	1.40 (1.19–1.64)*	0.51 (0.48–0.55)*	0.52 (0.49–0.57)*	0.62 (0.57–0.67)*
Education[a]	0.91 (0.90–0.91)*	0.88 (0.87–0.89)*	0.90 (0.88–0.92)*	0.98 (0.97–0.98)*	1.02 (1.01–1.03)*	1.03 (1.02–1.04)*
Alcohol dependence	…	…	…	3.11 (2.90–3.35)*	3.63 (3.28–4.02)*	4.43 (4.00–4.89)*
Nicotine dependence	5.27 (4.95–5.62)*	5.56 (5.17–5.98)*	7.37 (6.32–8.38)*	…	…	…
Drug dependence	28.90 (24.18–34.55)*	26.66 (21.54–33.00)*	61.45 (50.59–74.63)*	9.74 (7.38–12.84)*	10.78 (8.60–13.50)*	19.42 (12.13–13.09)*
Depressive disorder	3.65 (3.35–3.97)*	4.52 (4.10–4.98)*	7.84 (6.53–9.42)*	3.13 (2.87–3.41)*	3.27 (2.99–3.58)*	3.33 (3.02–3.67)*
Bipolar disorder	5.35 (4.86–5.89)*	6.78 (6.00–7.66)*	6.15 (4.70–8.05)*	4.23 (3.68–4.88)*	4.71 (3.96–5.60)*	5.03 (4.04–6.25)*
Anxiety disorder	2.52 (2.34–2.72)*	2.96 (2.69–3.25)*	4.27 (3.70–4.94)*	3.07 (2.83–3.32)*	3.28 (3.00–3.58)*	3.29 (3.02–3.60)*
Personality disorder	3.63 (3.44–3.84)*	4.06 (3.77–4.38)*	7.36 (6.50–8.34)*	2.65 (2.52–2.79)*	2.75 (2.60–2.91)*	2.85 (2.69–3.02)*
No. of dependent/ no. of users	1,484/26,946	1,252/11,869	275/1,865	4,962/11,118	4,904/10,131	4,639/8,939
Weighted, % (SE)	5.8 (0.09)	11.0 (0.18)	15.1 (0.41)	46.1 (0.28)	50.0 (0.31)	53.4 (0.35)

[a]Age, education, and income (in logarithm scale) were entered in analyses as continuous variables.
*$P < .05$.
Abbreviations: AI/AN = American Indian or Alaskan native, NH/PI = Native Hawaiian or other Pacific Islander, OR = odds ratio, SE = standard error.
Symbol: … = not included.

Statistical Analyses

Study aims were addressed via logistic regressions conducted with Statistical Analysis Software (SAS), version 9.2. The analysis used sample weights and corrected variance estimates to allow for NESARC's complex survey design. All cross-sectional analyses relied on Wave 1 data. Bivariate tests were conducted, which were then followed by multivariable regression analyses to identify unique predictors of the progression to substance dependence (0 = not dependent on this substance, 1 = dependent on this substance). Predictors included variables representing psychopathology and demographics. The latter included gender, age, education (in years), married/cohabiting status, ethnicity, and income, which was assessed logarithmically. Because of concerns over power and the large number of variables included in multivariable analyses, only single variables reflecting marital/cohabiting status (0 = not currently married/cohabiting, 1 = currently married/cohabiting) and ethnicity (0 = nonwhite, 1 = white) were used in these analyses. Frequency of use per day for the substance under consideration (eg, number of cigarettes per day) was also entered as a predictor in prospective analyses. Variables for Wave 1 presence of drug dependence and anxiety disorders reflected any type of drug dependence or anxiety disorder being present (0 = absent, 1 = present). Bipolar I and II diagnoses were combined into 1 variable (0 = absent, 1 = present). All diagnosis variables were dichotomous (0 = absent, 1 = present). In cross-sectional analyses, only past-year ever users were examined to determine the risk of dependence in this group, while only weekly and daily users were used in weekly and daily analyses, respectively. Prospective analyses were not conducted for cocaine, given the low numbers of new dependence cases at Wave 2. Because our investigation was focused on regular substance use and for simplicity's sake, we limited our prospective analyses to only past-year weekly users at Wave 1. Regular users of the substance at Wave 1 were excluded only if they were dependent on the individual substance that was the focus of the analysis (eg, only those with Wave 1 past-year alcohol dependence were excluded from analyses of weekly alcohol use).

RESULTS

Analyses of Past-Year Substance Use and Dependence Risk at Wave 1

Rates of substance dependence by frequency of use across substance users (ie, any, weekly, daily) are presented in Tables 1 and 2. Descriptives for these analyses are presented in Supplementary eTables 1 and 2. Alcohol users included in separate analyses were past-year ever users (n = 26,946), weekly users (n = 11,869), and daily users (n = 1,865). Nicotine users included in separate analyses were past-year ever users (n = 11,118), weekly users (n = 10,131), and daily users (n = 8,939). Those considered in cannabis analyses included past-year ever users (n = 1,603), weekly users (n = 671), and daily users (n = 227), while cocaine-/crack-use analyses included past-year ever users (n = 217)

Table 2. Cannabis and Cocaine/Crack: Bivariate Analyses of Demographic and Psychiatric Correlates of Risk of Past-Year Substance Dependency by Past-Year Substance Use Frequency

	Cannabis			Cocaine/Crack	
Variable	Used at Least Once, OR (95% CI)	Used Weekly, OR (95% CI)	Used Daily, OR (95% CI)	Used at Least Once, OR (95% CI)	Used Weekly, OR (95% CI)
Age[a]	0.96 (0.95–0.97)*	0.96 (0.95–0.97)*	0.97 (0.96–0.98)*	1.03 (1.02–1.03)*	1.05 (1.03–1.07)*
Income[a]	0.93 (0.91–0.95)*	0.95 (0.93–0.96)*	0.98 (0.96–1.00)*	1.15 (1.14–1.16)*	1.82 (1.72–1.93)*
Married/cohabiting	0.69 (0.56–0.86)*	0.66 (0.52–0.83)*	0.56 (0.35–0.90)*	0.64 (0.52–0.80)*	0.69 (0.52–0.93)*
Never married	1.62 (1.33–1.98)*	1.68 (1.37–2.06)*	1.94 (1.29–2.93)*	0.98 (0.86–1.11)	0.53 (0.43–0.65)*
Divorced/separated/widowed	0.68 (0.51–0.90)*	0.71 (0.54–0.94)*	0.65 (0.42–1.02)	1.80 (1.71–1.89)*	5.23 (4.88–5.60)*
Female	0.75 (0.61–0.92)*	0.89 (0.70–1.13)	0.87 (0.63–1.20)	0.68 (0.56–0.82)*	0.95 (0.70–1.27)
White	0.91 (0.76–1.09)	1.07 (0.91–1.25)	0.59 (0.47–0.74)*	0.39 (0.35–0.44)*	0.65 (0.53–0.80)*
Black	1.16 (0.97–1.39)	1.05 (0.88–1.24)	1.62 (1.27–2.05)*	2.13 (1.87–2.44)*	1.41 (1.15–1.74)*
Asian	0.82 (0.47–1.45)	1.03 (0.59–1.82)	8.90 (7.46–10.60)*	1.05 (1.02–1.08)*	2.31 (2.20–2.42)*
NH/PI	1.19 (0.74–1.91)	1.53 (0.95–2.47)	2.36 (1.98–2.80)*	…	…
AI/AN	2.12 (1.47–3.06)*	1.24 (0.82–1.85)	1.06 (0.83–1.34)	0.82 (0.76–0.89)*	…
Hispanic	0.99 (0.82–1.21)	0.96 (0.81–1.13)	0.90 (0.75–1.09)	1.25 (1.21–1.29)*	0.80 (0.76–0.85)*
Education[a]	0.83 (0.81–0.86)*	0.90 (0.87–0.93)*	0.87 (0.82–0.92)*	0.97 (0.96–0.97)*	1.41 (1.40–1.42)*
Alcohol dependence	3.40 (2.73–4.24)*	2.54 (2.05–3.15)*	1.95 (1.51–2.53)*	3.22 (2.64–3.92)*	3.45 (2.28–5.22)*
Nicotine dependence	2.92 (2.35–3.63)*	2.11 (1.81–2.45)*	1.40 (1.11–1.75)*	4.65 (3.71–5.83)*	1.65 (1.28–2.13)*
Drug dependence	…	…	…	…	…
Depressive disorder	3.58 (2.92–4.38)*	3.39 (2.79–4.12)*	2.53 (1.63–3.93)*	4.02 (3.76–4.30)*	26.12 (24.44–27.92)*
Bipolar disorder	3.28 (2.62–4.10)*	2.73 (2.19–3.40)*	2.52 (1.66–3.83)*	3.59 (3.47–3.73)*	29.32 (27.30–31.48)*
Anxiety disorder	3.26 (2.64–4.03)*	3.05 (2.56–3.64)*	1.39 (1.01–1.91)*	2.08 (2.00–2.17)*	2.92 (2.72–3.14)*
Personality disorder	6.47 (4.90–8.54)*	5.00 (3.93–6.36)*	2.67 (1.68–4.24)*	1.72 (1.47–2.01)*	1.98 (1.49–2.62)*
No. of dependents/no. of users	133/1,603	116/671	51/227	49/217	29/58
Weighted, % (SE)	8.0 (0.36)	17.0 (0.70)	18.8 (1.3)	23.9 (0.24)	49.9 (0.58)

[a]Age, education, and income (in logarithm scale) were entered in analyses as continuous variables.
*$P < .05$.
Abbreviations: AI/AN = American Indian or Alaskan native, NH/PI = Native Hawaiian or other Pacific Islander, OR = odds ratio, SE = standard error.
Symbol: … = not included.

Table 3. Alcohol and Nicotine: Multivariable Regression Analyses of Demographic and Psychiatric Correlates of Risk of Past-Year Substance Dependence by Past-Year Frequency of Substance Use

	Alcohol			Nicotine		
Variable[a]	Used at Least Once, OR (95% CI)	Used Weekly, OR (95% CI)	Used Daily, OR (95% CI)	Used at Least Once, OR (95% CI)	Used Weekly, OR (95% CI)	Used Daily, OR (95% CI)
Age	0.96 (0.96–0.96)*	0.96 (0.95–0.96)*	0.95 (0.94–0.95)*	0.99 (0.99–1.00)*	0.99 (0.99–1.00)*	0.99 (0.99–0.99)*
Income	1.00 (0.98–1.02)	0.95 (0.94–0.97)*	0.97 (0.95–1.00)*	0.99 (0.98–1.01)	1.00 (0.98–1.01)	1.00 (0.99–1.02)
Married/cohabiting	0.48 (0.44–0.52)*	0.56 (0.51–0.61)*	0.71 (0.60–0.85)*	1.01 (0.95–1.08)	1.09 (1.02–1.16)*	1.10 (1.03–1.17)*
Female	0.45 (0.41–0.48)*	0.60 (0.55–0.64)*	0.53 (0.47–0.58)*	1.43 (1.35–1.52)*	1.39 (1.30–1.48)*	1.38 (1.28–1.48)*
White	0.96 (0.90–1.04)	1.05 (0.97–1.14)	0.89 (0.77–1.02)	1.24 (1.19–1.30)*	1.30 (1.24–1.35)*	1.31 (1.25–1.37)*
Education	0.98 (0.97–0.99)*	0.94 (0.93–0.95)*	0.97 (0.94–1.00)	0.98 (0.97–0.99)*	1.02 (1.01–1.03)*	1.03 (1.02–1.05)*
Alcohol dependence	…	…	…	2.16 (1.99–2.34)*	2.51 (2.24–2.82)*	2.95 (2.61–3.34)*
Nicotine dependence	3.05 (2.85–3.27)*	2.90 (2.68–3.15)*	3.31 (2.79–3.94)*	…	…	…
Drug dependence	5.61 (4.38–7.19)*	4.80 (3.62–6.38)*	8.62 (6.93–10.71)*	3.65 (2.67–5.00)*	3.92 (3.06–5.04)*	6.49 (3.97–10.63)*
Depressive disorder	1.57 (1.39–1.78)*	1.81 (1.54–2.12)*	3.38 (2.51–4.55)*	1.61 (1.48–1.75)*	1.66 (1.52–1.82)*	1.69 (1.52–1.87)*
Bipolar disorder	1.62 (1.44–1.82)*	1.82 (1.58–2.09)*	0.80 (0.55–1.16)	1.91 (1.63–2.24)*	2.04 (1.68–2.48)*	2.10 (1.65–2.69)*
Anxiety disorder	1.45 (1.31–1.60)*	1.57 (1.40–1.76)*	1.67 (1.34–2.09)*	1.87 (1.72–2.04)*	1.99 (1.81–2.19)*	1.99 (1.81–2.18)*
Personality disorder	1.79 (1.67–1.92)*	1.98 (1.81–2.16)*	3.04 (2.65–3.48)*	1.86 (1.75–1.96)*	1.90 (1.78–2.02)*	1.93 (1.81–2.05)*

[a]All variables were entered simultaneously in individual regression analyses associated with each column. Age, education, and income (in logarithm scale) were entered in analyses as continuous variables.
*$P < .05$.
Abbreviation: OR = odds ratio. Symbol: … = not included.

and weekly users (n = 58). Bivariate associations between past-year substance dependence across frequency of use and demographic/psychiatric variables are presented in Tables 1 and 2. Odds ratios (ORs) for each variable (eg, whites) should be considered in reference to the rest of the sample (eg, nonwhites). Multivariable associations between past-year substance dependence across frequency of use and demographic/psychiatric variables are presented in Tables 3 and 4. Being married was associated with lower conditional risk of alcohol dependence and slightly higher risk of nicotine dependence for a given frequency of use (although this effect was the opposite in multivariate analyses, suggesting a suppressor effect). Women had increased likelihood of past-year nicotine dependence. Being white was associated with increased likelihood of past-year nicotine dependence, although minorities had greater risk of cannabis dependence across frequency of use.

Psychiatric diagnosis was generally associated with substance dependence diagnosis across frequency of use. Drug dependence diagnosis predicted increased likelihood of alcohol and nicotine dependence diagnoses among weekly users, whereas alcohol and nicotine dependence did not as

Table 4. Cannabis and Cocaine/Crack: Multivariable Regression Analyses of Demographic and Psychiatric Correlates of Risk of Past-Year Substance Dependence by Past-Year Frequency of Substance Use

	Cannabis			Cocaine/Crack	
Variable[a]	Used at Least Once, OR (95% CI)	Used Weekly, OR (95% CI)	Used Daily, OR (95% CI)	Used at Least Once, OR (95% CI)	Used Weekly, OR (95% CI)
Age	0.96 (0.95–0.97)*	0.96 (0.95–0.97)*	0.98 (0.97–0.99)*	1.02 (1.01–1.04)*	1.21 (1.20–1.21)*
Income	1.00 (0.97–1.03)	1.03 (1.00–1.05)	1.10 (1.04–1.16)*	1.43 (1.37–1.50)*	1.57 (1.49–1.65)*
Married/cohabiting	0.97 (0.78–1.20)	0.85 (0.67–1.08)	0.73 (0.41–1.30)	0.79 (0.53–1.18)	0.66 (0.28–1.56)
Female	0.62 (0.49–0.80)*	0.69 (0.51–0.93)*	0.79 (0.50–1.24)	0.39 (0.29–0.52)*	0.58 (0.31–1.10)
White	0.77 (0.62–0.96)*	0.76 (0.63–0.91)*	0.43 (0.26–0.70)*	0.28 (0.22–0.35)*	2.50 (1.99–3.15)*
Education	0.95 (0.91–1.00)*	1.01 (0.96–1.06)	0.94 (0.87–1.02)	1.02 (1.00–1.05)	1.27 (1.21–1.32)*
Alcohol dependence	1.81 (1.40–2.33)*	1.36 (1.07–1.72)*	1.44 (0.89–2.31)	2.23 (1.64–3.02)*	9.67 (7.83–11.95)*
Nicotine dependence	1.67 (1.27–2.19)*	1.26 (1.02–1.55)*	0.95 (0.67–1.35)	4.89 (3.85–6.22)*	3.17 (2.72–3.69)*
Drug dependence	…	…	…	…	…[b]
Depressive disorder	1.85 (1.50–2.29)*	2.03 (1.57–2.61)*	1.79 (1.04–3.08)*	3.32 (2.21–4.99)*	
Bipolar disorder	1.25 (0.95–1.64)	1.27 (0.97–1.66)	1.63 (1.08–2.46)*	2.09 (1.33–3.27)*	205.33 (102.72–410.46)*
Anxiety disorder	1.69 (1.33–2.15)*	1.89 (1.50–2.37)*	0.91 (0.68–1.21)	1.30 (1.13–1.50)*	0.03 (0.02–0.07)*
Personality disorder	3.80 (2.83–5.10)*	3.37 (2.61–4.37)*	2.38 (1.50–3.78)*	0.79 (0.62–0.99)*	0.07 (0.03–0.13)*

[a]All variables were entered simultaneously in individual regression analyses associated with each column. Age, education, and income (in logarithm scale) were entered in analyses as continuous variables.
[b]Covariate predicts dependence perfectly for this small number of individuals.
*$P < .05$.
Abbreviation: OR = odds ratio. Symbol: … = not included.

Table 5. Prospective Analysis of Predictors of Dependence at Wave 2 Among Wave 1 Nondependent Past-Year Weekly Substance Users

	Alcohol		Nicotine		Cannabis	
Variable[a]	Bivariate OR (95% CI)	Multivariable OR (95% CI)	Bivariate OR (95% CI)	Multivariable OR (95% CI)	Bivariate OR (95% CI)	Multivariable OR (95% CI)
Age	0.96 (0.95–0.96)*	0.97 (0.96–0.97)*	0.99 (0.99–1.00)*	0.99 (0.99–0.99)*	1.00 (0.99–1.01)	1.00 (0.99–1.01)
Income	0.92 (0.89–0.95)*	0.95 (0.92–0.98)*	0.97 (0.96–0.99)*	0.99 (0.98–1.01)	0.99 (0.94–1.03)	0.98 (0.93–1.04)
Married/cohabiting	0.53 (0.48–0.59)*	0.85 (0.77–0.94)*	0.80 (0.73–0.88)*	0.83 (0.75–0.91)*	0.93 (0.67–1.29)	1.05 (0.75–1.47)
Female	0.83 (0.73–0.94)*	0.88 (0.77–1.00)*	1.32 (1.22–1.44)*	1.34 (1.22–1.46)*	1.17 (0.75–1.81)	1.23 (0.80–1.87)
White	0.68 (0.60–0.78)*	0.84 (0.74–0.95)*	0.99 (0.88–1.11)	0.92 (0.81–1.04)	0.39 (0.30–0.50)*	0.46 (0.34–0.63)*
Education	0.89 (0.88–0.90)*	0.92 (0.91–0.94)*	0.98 (0.97–1.00)*	0.99 (0.97–1.01)	1.03 (1.01–1.05)*	1.04 (1.00–1.08)*
Alcohol dependence	…	…	0.88 (0.73–1.07)	0.87 (0.70–1.08)	0.88 (0.58–1.32)	0.99 (0.58–1.69)
Nicotine dependence	2.04 (1.78–2.33)*	1.39 (1.21–1.59)*	…	…	0.77 (0.52–1.13)	0.87 (0.54–1.40)
Drug dependence	2.07 (1.66–2.57)*	0.58 (0.37–0.89)*	0.87 (0.62–1.21)	0.88 (0.52–1.49)	…	…
Depressive disorder	1.75 (1.50–2.05)*	1.40 (1.19–1.65)*	0.96 (0.80–1.14)	0.80 (0.68–0.94)*	0.89 (0.58–1.38)	1.33 (0.69–2.56)
Bipolar disorder	1.53 (1.15–2.02)*	0.76 (0.57–1.02)	1.26 (0.90–1.76)	1.14 (0.83–1.55)	0.43 (0.36–0.52)*	0.45 (0.35–0.58)*
Anxiety disorder	1.08 (0.94–1.24)	0.90 (0.77–1.04)	1.24 (1.07–1.45)*	1.17 (1.00–1.36)*	0.64 (0.40–1.03)	0.75 (0.36–1.56)
Personality disorder	1.40 (1.25–1.58)*	1.13 (0.98–1.31)	1.08 (0.95–1.23)	1.05 (0.92–1.21)	0.91 (0.62–1.34)	1.00 (0.65–1.54)
Frequency of use per day	1.18 (1.16–1.21)*	1.10 (1.07–1.12)*	1.03 (1.02–1.03)*	1.031 (1.026–1.037)*	1.08 (1.04–1.13)*	1.09 (1.03–1.15)*
No. of new dependents/no. of users	507/8,708		1,369/4,138		33/435	
% of new dependents	5.8		33.5		9.7	

[a]Age, education, and income (in logarithm scale) were entered in analyses as continuous variables. All variables were entered simultaneously in the individual multivariable regression analysis for each substance.
*Significant at $P < .05$.
Abbreviation: OR = odds ratio.

substantially increase the likelihood of cannabis dependence among weekly users. Alcohol dependence and nicotine dependence predicted increased likelihood of cocaine dependence among ever users and weekly users.

Prospective Analyses of Predictors of Dependence at Wave 2 Among Nondependent Weekly Substance Users at Wave 1

Rates of dependence for past-year weekly substance users at Wave 1 when Wave 1 past-year dependence cases were combined with new cases of dependence reported at Wave 2 were 15.6% for alcohol, 67.3% for nicotine, and 25.0% for cannabis.

To examine predictors of the progression from weekly nondependent past-year substance use at Wave 1 to dependence at Wave 2, ORs were computed and bivariate and multivariable associations are presented in Table 5. Analyses were conducted separately for users of alcohol (n = 8,708), nicotine (n = 4,138), and cannabis (n = 435).

Descriptives for these analyses are presented in Supplementary eTable 3. Multivariable analyses indicated that frequency of use was predictive of new onset of dependence across substances. Additionally, younger age and being unmarried were predictive of new dependence at Wave 2 for weekly nondependent alcohol and nicotine users at Wave 1. Men were more likely than women to progress from regular nondependent use to dependence for alcohol use, although the pattern was reversed for nicotine use. Ethnic minorities were also more likely than whites to progress from weekly nondependent use to cannabis

and alcohol dependence at Wave 2. Lower education was associated with the progression to alcohol dependence. With regard to psychiatric variables, depressive disorder and nicotine dependence were predictive of subsequent alcohol dependence, and anxiety disorders were predictive of subsequent nicotine dependence. Drug dependence was associated with lower risk of progression to alcohol dependence (although the effect was opposite in univariate analyses, suggesting a suppressor effect); depressive disorder was associated with lower risk of progression to nicotine dependence; and bipolar disorder was associated with lower risk of progression to cannabis dependence.

DISCUSSION

Many of the findings of the current study are in line with previous investigations, which generally demonstrated high rates of dependence among alcohol, nicotine, cannabis, and cocaine users.[1,3] The risk of dependence among users of alcohol, cannabis, and cocaine was approximately twice as high among past-year weekly users compared to ever users. In contrast, the risk of nicotine dependence was relatively stable across frequency of use, ranging from 46.1% among ever users to 50.0% among weekly users. These findings speak to the addictive potential of nicotine and to the fact that nicotine is much less likely to be used occasionally than these other substances. Additionally, the rates of dependence we found among weekly (17.0%) and daily (18.8%) cannabis users were lower than dependence rates previously found among "regular" (29%)[9] and "nearly daily" users (72%).[14]

Some demographic variables showed important relationships with dependence. Among all users, women were more likely than men to have nicotine dependence, whereas men were generally more likely than women to have dependence for alcohol, cannabis, and cocaine across frequency of use. Being married was generally a protective factor against alcohol dependence among drinkers of a given frequency. These findings related to gender and marital status are mostly consistent with those of Lopez-Quintero et al,[3] although they found no relationship between gender and risk of cocaine dependence among lifetime users. Our findings also contradict those of O'Brien and Anthony,[15] who found that women were at greater risk of dependence among recent cocaine users. In Lopez-Quintero and colleagues' analyses,[3] neither income nor education was correlated with dependence; however, we found that lower income was uniquely associated with dependence among weekly and daily alcohol users, and, interestingly, *greater* income was associated with cocaine dependence among ever users and weekly users. This latter finding may reflect the higher costs of cocaine and the financial resources needed for sustained use. Additionally, we found that lower education was associated with increased risk of dependence among ever and weekly alcohol users and ever nicotine and cannabis users. Greater education was associated with dependence among weekly and daily nicotine users and weekly cocaine users. Overall, these findings implicate certain demographic correlates of dependence associated with recent patterns of use that may not emerge in analyses of lifetime ever users.

Ethnic correlates of dependency among substance users also emerged. In findings consistent with Anthony et al[1] and Lopez-Quintero et al,[3] whites were more likely to develop nicotine dependence, independent of frequency of use. Further, nonwhites were generally more likely to meet criteria for dependence for cannabis and cocaine.

Cross-sectional analyses revealed multiple psychiatric disorders associated with risk for substance dependence, findings largely consistent with some previous studies.[1,3] One large cross-sectional study found that past-year alcohol dependence was associated with anxiety, bipolar, and personality disorders but not depressive disorder,[16] but we found that these disorders were all generally and uniquely associated with dependence across substances. These variables tended to correlate with dependence independent of use frequency. It was interesting to note that the strength of psychiatric disorders as predictors of dependence varied according to use for alcohol, with psychiatric disorders generally conferring greater vulnerability to dependence among daily users compared to ever and weekly users. In contrast, the relationships with psychiatric disorders and risk of dependence were relatively stable for nicotine and cannabis, across frequency of use. These differences may reflect the fact that regular alcohol use is quite common and has been linked to certain health benefits[17]; psychiatric disorders may, accordingly, play an especially prominent role in the transition to dependence in the context of regular drinking. Given that the use of nicotine and cannabis has been linked to negative mental health outcomes,[18–20] co-occurring substance use may possibly dilute the effect of psychiatric disorders in predicting the transition to dependence among more frequent users of these substances.

The prospective analyses of the progression from weekly/nondependent alcohol use to dependence indicated that being unmarried, male, and nicotine dependent and having lower age, income, and education were unique predictors of dependence. Despite the fact that depression and anxiety disorders often co-occur with alcohol dependence,[16] longitudinal research examining the direction of these relationships is surprisingly uncommon. We found that depression but not anxiety disorder was uniquely predictive of the progression to alcohol dependence, a finding that runs counter to a previous longitudinal study that found no such relationship.[21] Our findings are partially consistent with those of Swendsen et al[22] who demonstrated risk of dependence to be associated with dysthymia as well as anxiety disorders; however, they did not control for psychiatric disorders in their analyses.

Lower age, being unmarried, being female, the presence of an anxiety disorder, and the *absence* of depression were predictive of the progression from weekly/nondependent nicotine use to subsequent nicotine dependence. These findings contradict those of Breslau and colleagues,[23] who found depression but not anxiety disorder or gender to predict the progression to dependence. We also found that

the occurrence of new cases of nicotine dependence was quite common among weekly/nondependent users (33.5%). Ethnic minority status predicted subsequent cannabis dependence among weekly/nondependent users, and bipolar disorder predicted *reduced* risk of cannabis dependence in prospective analyses; yet, given the small sample used for some of these analyses, these findings should be interpreted with caution.

The present study possesses a few limitations. First, some analyses, such as those focused on cannabis and cocaine, were underpowered. Additionally, this survey was unlikely to capture some of the most severe cases of substance dependence; many such cases are likely to have been lost to attrition. The length of follow-up (3 years) was relatively short, and further examination of the long-term risk of substance dependence is needed. It is possible that certain variables we examined were vulnerability factors for dependence, only earlier in use history. Our analyses of dependence probability were limited in focus to frequency but not to quantity of use, although the latter is also obviously relevant to risk for dependence. Analyses were correlational, and causal inferences regarding relationships should not be inferred. This survey evaluated *DSM-IV* criteria for substance dependence rather than newer *DSM-5* criteria. Lastly, these data relied on a US sample and may not be generalizable to other countries.

Our investigation sought to address limitations of previous studies, which relied on lifetime retrospective reports of substance use and psychiatric disorders, unrepresentative samples, reports of ever rather than regular use, and consideration of substances in isolation. Overall, our findings suggest that the apparent addictive potential of substances depends on frequency of use. Although it has generally been found that rates of cannabis dependence are low among those who have ever used the substance, results of this study suggest that cannabis dependence is quite common among those who use the substance regularly. Additionally, the fact that certain vulnerability factors were present in the context of regular, recent use suggests that frequency and recency of use should be considered in studies of substance use disorder.

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Supplementary material: See accompanying pages.

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Supplementary material follows this article.

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Supplementary Material

Article Title: Probability and Correlates of Dependence Among Regular Users of Alcohol, Nicotine, Cannabis, and Cocaine: Concurrent and Prospective Analyses of the National Epidemiological Survey on Alcohol and Related Conditions

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List of Supplementary Material for the article

1. **eTable 1** Descriptives for Demographic and Psychiatric Correlates of Past Year Substance Dependency by Past Year Substance Use Frequency (Alcohol and Nicotine)
2. **eTable 2** Descriptives for Demographic and Psychiatric Correlates of Past Year Substance Dependency by Past Year Substance Use Frequency (Cannabis and Cocaine/Crack)
3. **eTable 3** Descriptive Statistics for Prospective Analysis of Predictors of Dependence at Wave 2 Among Wave 1 Non-Dependent Past-Year Weekly Substance Users

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Supplementary eTable 1. Descriptives for demographic and psychiatric correlates of past year substance dependency by past year substance use frequency – M(Std. Error) or N.

	Alcohol			Nicotine		
	Used at least once Non-Dep. / Dep.	Used weekly Non-Dep. / Dep.	Used daily Non-Dep. / Dep.	Used at least once Non-Dep. / Dep.	Used weekly Non-Dep. / Dep.	Used daily Non-Dep. / Dep.
Age	43.89(.10) / 32.79(.31)	45.51(.16) / 33.52(.35)	55.00(.42) / 39.14(.83)	43.94(.21) / 40.72(.21)	44.39(.23) / 40.74(.21)	45.39(.25) / 41.06(.21)
Income	9.56(.01) / 9.31(.05)	9.82(.02) / 9.35(.06)	9.78(.05) / 9.41(.12)	9.45(.03) / 9.23(.03)	9.38(.03) / 9.23(.03)	9.35(.03) / 9.23(.03)
Married	13811 / 451	5784 / 387	869 / 100	2921 / 2134	2409 / 2108	1979 / 2000
Never married	5977 / 715	2430 / 581	234 / 97	1529 / 1374	1296 / 1357	1002 / 1252
Divorced/ Separated/ Widowed	5674 / 318	2403 / 284	487 / 78	1706 / 1454	1522 / 1439	1319 / 1387
Female	13360 / 519	4253 / 399	577 / 70	2603 / 2572	2269 / 2546	1920 / 2422
White	20546 / 1157	8732 / 981	1326 / 200	4774 / 3952	3978 / 3904	3260 / 3711
Black	4142 / 259	1624 / 220	226 / 71	1207 / 872	1102 / 866	925 / 805
Asian	633 / 32	224 / 22	22 / 4	119 / 89	102 / 87	83 / 82
NH/PI	195 / 20	58 / 16	7 / 2	40 / 46	33 / 46	27 / 43
AI/AN	687 / 86	260 / 74	51 / 10	215 / 204	180 / 202	141 / 193
Hispanic	4662 / 287	1623 / 223	175 / 38	1052 / 536	847 / 527	598 / 487
Education	13.59(.02) / 12.80(.06)	13.86(.03) / 12.85(.07)	13.52(.08) / 12.63(.17)	12.59(.04) / 12.54(.03)	12.34(.04) / 12.53(.03)	12.24(.04) / 12.47(.03)
Alcohol dependence	---	---	---	280 / 634	208 / 627	138 / 575
Nicotine dependence	3236 / 634	1418 / 555	208 / 136	---	---	---
Drug dependence	91 / 131	39 / 113	3 / 29	22 / 167	16 / 166	7 / 154
Depressive disorder	2166 / 368	697 / 297	83 / 71	464 / 1030	373 / 1020	297 / 964
Bipolar disorder	724 / 204	241 / 163	33 / 29	140 / 428	108 / 422	84 / 401
Anxiety Disorder	2898 / 337	1002 / 271	133 / 71	576 / 1109	467 / 1098	377 / 1036
Personality Disorder	3796 / 593	1377 / 500	160 / 125	793 / 1557	1043 / 1535	502 / 1451
N of Non-dep. / Dep.	25462 / 1484	10617 / 1252	1590 / 275	6156 / 4962	5227 / 4904	4300 / 4639

Note: Dep. = Dependent, NH/PI = Native Hawaiians or other Pacific Islanders, AI/AN = American Indians or Alaskan Natives. Values reflect unadjusted counts and means.

Supplementary eTable 2. Descriptives for demographic and psychiatric correlates of past year substance dependency by past year substance use frequency – M(Std. Error) or N.

	Cannabis			Cocaine/Crack	
	Used at least once Non-Dep. / Dep.	Used weekly Non-Dep. / Dep.	Used daily Non-Dep. / Dep.	Used at least once Non-Dep. / Dep.	Used weekly Non-Dep. / Dep.
Age	31.25(.29) / 25.98(.82)	31.42(.49) / 26.09(.90)	29.73(.86) / 26.49(1.46)	29.80(.79) / 32.29(1.39)	34.00(2.03) / 37.17(1.47)
Income	9.27(.05) / 8.63(.19)	9.08(.09) / 8.55(.21)	8.85(.16) / 8.65(.29)	9.19(.14) / 9.31(.14)	8.81(.38) / 9.43(.18)
Married	396 / 26	155 / 22	49 / 11	45 / 9	10 / 7
Never married	805 / 93	299 / 81	99 / 35	96 / 27	14 / 13
Divorced/ Separated/ Widowed	269 / 14	101 / 13	28 / 5	27 / 13	5 / 9
Female	563 / 44	179 / 38	65 / 19	64 / 18	11 / 12
White	1144 / 97	412 / 82	133 / 33	138 / 31	19 / 16
Black	277 / 31	126 / 30	42 / 16	23 / 16	9 / 12
Asian	25 / 3	6 / 3	1 / 2	4 / 1	1 / 1
NH/PI	25 / 4	8 / 4	1 / 1	4 / 0	1 / 0
AI/AN	72 / 9	35 / 7	12 / 4	12 / 1	0 / 0
Hispanic	235 / 25	102 / 21	32 / 10	36 / 8	6 / 5
Education	13.03(.06) / 12.09(.16)	12.55(.10) / 12.01(.17)	12.18(.17) / 11.67(.24)	12.71(.17) / 12.57(.22)	12.20(.33) / 12.69(.26)
Alcohol dependence	353 / 73	158 / 62	53 / 24	73 / 34	12 / 22
Nicotine dependence	582 / 88	250 / 75	91 / 33	71 / 40	13 / 21
Drug dependence	---	---	---	---	---
Depressive disorder	290 / 61	106 / 52	31 / 21	44 / 26	6 / 19
Bipolar disorder	144 / 34	57 / 30	23 / 14	19 / 12	1 / 8
Anxiety Disorder	283 / 47	105 / 41	44 / 17	32 / 14	5 / 8
Personality Disorder	491 / 96	209 / 83	81 / 37	80 / 30	14 / 17
N of Non-dep. / Dep.	1470 / 133	555 / 116	175 / 51	168 / 49	29 / 29

Note: Dep. = Dependent, NH/PI = Native Hawaiians or other Pacific Islanders, AI/AN = American Indians or Alaskan Natives. Values reflect unadjusted counts and means.

Supplementary eTable 3. Descriptive statistics for prospective analysis of predictors of dependence at Wave 2 among Wave 1 non-dependent past-year weekly substance users – M(Std. Error) or N.

	Alcohol Non-Dep. / Dep.	**Nicotine** Non-Dep. / Dep.	**Cannabis** Non-Dep. / Dep.
Age	46.14(.18) / 37.36(.60)	44.68(.30) / 43.14(.40)	31.81(.58) / 28.85(1.82)
Income	9.90(.02) / 9.52(.09)	9.48(.04) / 9.30(.06)	9.14(.10) / 8.85(.40)
Married/Cohabiting	4665 / 222	1331 / 612	122 / 10
Female	3381 / 173	1177 / 665	139 / 12
White	6846 / 388	2135 / 1024	308 / 24
Education	14.07(.03) / 13.05(.11)	12.48(.05) / 12.34(.07)	12.61(.12) / 12.39(.37)
Alcohol dependence	---	115 / 55	124 / 9
Nicotine dependence	1024 / 118	---	187 / 15
Drug dependence	25 / 4	8 / 4	---
Depressive disorder	512 / 48	202 / 104	75 / 8
Bipolar disorder	188 / 18	63 / 30	43 / 4
Anxiety Disorder	792 / 58	247 / 140	83 / 6
Personality Disorder	1058 / 83	336 / 170	151 / 11
Frequency of Use Per Day	2.70(.02) / 4.09(.13)	11.32(.18) / 14.25(.27)	2.51(.19) / 3.33(.51)
N of Non-dep. / Dep.	8201 / 507	2769 / 1369	402 / 33

Note: Dep. = Dependent. Values reflect unadjusted counts and means.