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Towards a comprehensive developmental model of cannabis use disorders

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Abstract

Aims—To develop a comprehensive risk-factor model of cannabis use disorders (CUD) based on Kendler's development model for major depression.

Design—Risk factors were divided into five developmental tiers based on Kendler's model of depression (childhood, early adolescence, late adolescence, adulthood, past-year). Hierarchical logistic regression models were used to examine the independent contribution of each risk factor. Separate models were built to predict the lifetime risk of cannabis use and the risk of CUD among those with a history of lifetime risk of cannabis use.

Setting—Data were drawn from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) in the United States.

Participants—Participants consisted of Wave 2 of the NESARC (n= 34653).

Measurements—Odds ratios (OR), Adjusted OR (AOR) and confidence intervals (95% CI) were used to determine the risk factors in each tier and with multiple models.

Findings—After mutually adjusting for the effect of other risk factors, lifetime history of drug use disorder (AOR=4.78, 95% CI=1.53–14.91), past-year alcohol use disorders (AOR=6.55, 95% CI=2.54—16.89) and independent (AOR=1.57, 95% CI=1.15–2.14) and dependent (AOR=1.25, 95% CI=1.01–1.55) stressful life events predicted lifetime cannabis use. Impulsivity (AOR=2.18, 95% CI=1.34–3.53), past-year alcohol use disorders (AOR=4.09, 95% CI=2.29–7.31), greater number of axis I disorders (AOR=1.56, 95% CI=1.01–2.40) and social deviance (AOR=1.19, 95% CI=1.08–1.32) independently increased the risk of the development of CUD, whereas religious service attendance (AOR=0.50, 95% CI=0.30–0.85) decreased this risk. In both models, the effect of earlier development tiers was mediated by more proximal ones. There were few gender differences in both models.

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Declarations of interest
None of the authors report competing interests.

Conclusions—A modification of Kendler's risk factor model for major depression which stratifies risk factors into five groups (childhood, early adolescence, late adolescence, adulthood, past-year) provides a useful foundation for a comprehensive developmental model of cannabis use and cannabis use disorders.

Keywords

Cannabis use disorders; epidemiology; risk factors; development

INTRODUCTION

Cannabis is the most commonly used and abused illicit drug. In 2010, the prevalence of cannabis use disorders, i.e. abuse and dependence, among persons aged 12 and over in the US was estimated to be 1.8%, representing 4.5 million individuals and constituting by far the most common substance use disorder (SUD) consequent to use of an illegal drug in the US [1]. A better understanding of the etiology of cannabis use disorders (CUD) is essential to develop more effective prevention and treatment programs.

A substantial body of research has identified a number of risk factors for CUD, including childhood sexual abuse [2, 3], vulnerable family environment [4], antisocial behavior [5], early-onset anxiety disorders and substance use [6–8], impulsivity [9, 10], and genetic factors [11, 12] among others. However, risk factors are unlikely to act in isolation [13]. For instance, sexual abuse during childhood and violence are related to mood and anxiety disorders [14, 15], and these disorders may mediate the effect of the prior on SUD [16]. Thus, a natural next step is the development of conceptual models that integrate several risk factors and examine their joint and independent effects to elucidate pathways in the etiology of CUD.

A few studies have started to develop these models by focusing on a single set of variables such as personality traits [17] or behavioral disinhibition [18, 19]. We sought to build on that work by examining whether a promising alternative, Kendler's model for major depression disorder (MDD), could be adapted to advance our understanding of CUD, since both MDD and CUD appear to have multifactorial etiology and many of the risk factors for CUD are also risk factors for MDD [20, 21].

Kendler's model, which is based on over two decades of work on the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders and over 3,000 twin pairs, is highly predictive of the risk for 12-month MDD. It posits that: 1) the etiology of MDD is multifactorial; 2) contemporary risk factors tend to influence each other; and, 3) the effect of earlier risk factors such as childhood sexual abuse is partially mediated through later risk factors such as childhood-onset anxiety and psychiatric comorbidity.

Kendler's model, organizes predictors into tiers roughly approximating five developmental periods: childhood, early adolescence, late adolescence, adulthood, and the last year. The model seeks to be comprehensive and parsimonious, rather than exhaustive, and recognizes that several variables can have effects beyond their tier and possibly exert different effects by gender and across individuals.

Prior to our analyses, we modified Kendler's model to incorporate aspects more important in the etiology and course of SUD than of MDD. First, we substituted impulsivity, which plays an important role in SUD [18, 19] for neuroticism which plays a larger role in internalizing disorders. Second, we included a measure of early-onset substance use (defined as onset prior to age 14), which appears to increase the risk of SUD [22, 23]. Third, we included low

social support in the last-year tier, given its prominent role in drug use maintenance and relapse [24, 25]. Fourth, we added religious service attendance to the last-year tier, given its inverse association with SUD [26, 27]. Furthermore, because the predictors of use may differ from those of use disorders [28], we examined predictors of cannabis use in the full population, and examined predictors of CUD only among those with a history of cannabis use.

METHODS

Sample and procedures

The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) [29, 30] was the source of data. The NESARC target population at Wave 1 was the civilian non-institutionalized population 18 years and older residing in households and group quarters. Blacks, Hispanics, and adults 18 to 24 years were oversampled, with data adjusted for oversampling and household and person-level non-response. Interviews were conducted with 43,093 participants by experienced lay interviewers [29, 30]. All procedures, including informed consent, received full ethical review and approval from the US Census Bureau and the US Office of Management and Budget. The Wave 2 interview was conducted approximately 3 years later (mean interval, 36.6 months). Excluding ineligible respondents (e.g., deceased), the Wave 2 response rate was 86.7% reflecting 34,653 completed interviews [30].The cumulative response rate at Wave 2 was the product of the Wave 1 and Wave 2 response rates, or 70.2. Wave 2 NESARC weights include a component that adjusts for non-response, demographic factors, and psychiatric diagnoses to ensure that the Wave 2 sample approximated the target population, that is, the original sample minus attrition between the two waves. As described previously [30], adjustment for non-response was successful, as the Wave 2 respondents and the original target population did not differ on age, race/ethnicity, gender, socioeconomic status, or the presence of any substance, mood, anxiety, or personality disorder [30]. Participants included in this analysis were those with Wave 2 data and the primary outcome was Wave 2 diagnoses of current (i.e., 12-month) DSM-IV cannabis abuse and dependence (n= 491).

Data collection

Data were collected with the Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV) [31–33], a structured diagnostic interview that includes computer algorithms to generate DSM-IV diagnoses. Diagnoses assessed by the AUDADIS-IV include substance use disorders (nicotine dependence, alcohol use disorders, cannabis use disorders, and other drug use disorders), mood disorders (dysthymic disorder, major depressive disorder), anxiety disorders (simple phobia, social anxiety disorder, panic disorder, generalized anxiety disorder and posttraumatic stress disorders) and all ten DSM-IV personality disorders.

Measures

Based on Kendler's original model, we divided the potential risk factors for past year CUD into 5 developmental tiers: childhood, early adolescence, late adolescence, adulthood, and past year.

Childhood tier including family history of SUD (lifetime history of alcohol or drug use disorders [AUD or DUD, respectively] in the biological parents or siblings), any sexual abuse, vulnerable family environment (assessed using the childhood emotional neglect scale of the Childhood Trauma Questionnaire; CTQ), and parental loss (parent's divorce or death of at least one parent before the participant was 18 years old).

Early adolescence tier including impulsivity (dichotomous, scored 1 if the respondents considered that they had often done things impulsively), low self-esteem (dichotomous, scored 1 if respondents believed they were not as good, smart, or attractive as most other people), age of onset of anxiety disorders (with childhood onset before age 18), age of cannabis use onset (with early onset defined as before age 14) [8, 22, 23], and social deviance (assessed as the number of conduct disorder or antisocial personality disorder (ASPD) behaviors in which the respondent engaged before age 15, range 0 to 33).

Late adolescence tier including educational attainment (in years), any history of trauma out of the list of 23 traumatic events that measure post-traumatic stress disorder (PTSD), number of personality disorders and number of axis I disorders with onset before age 18.

Adulthood tier including history of divorce, history of SUD (AUD, nicotine dependence, CUD, and other DUD), and social deviance (measured as the number of ASPD behaviors in which the individual engaged after age 15 but prior to the Wave 1 assessment).

Past year tier including social support (assessed with the Interpersonal Social Support Evaluation List; ISEL-12, a 12-item likert scale), past year AUD, nicotine dependence, comorbidity with psychiatric disorders other than SUD, current religious service attendance, marital problems (whether the respondent got separated, divorced or broke off a steady relationship in the last 12 months), number of stressful life events divided into independent (those the respondent is unlikely to have caused such as a death of a family member, range: 0–9) and dependent (those in which the respondent is likely to play an active role such as serious problems with a neighbor, range 0–5), and social deviance (measured as the number of ASPD behaviors in which the respondent engaged between Waves 1 and 2).

Statistical analyses

To obtain a thorough understanding of the relative importance of each variable and group of variables in the final model, we conducted our analysis in two stages, first identifying predictors of lifetime cannabis use and then predictors of 12-month CUD among cannabis users. To identify predictors of lifetime cannabis use, we compared data from respondents with lifetime cannabis use versus those with no lifetime cannabis use. We used odds ratios (ORs) to examine the bivariate relationships between each predictor and lifetime cannabis use (Table 1; Model 1). We then examined the interactions of each predictor with sex (using men as the reference group), by constructing one logistic regression model for each tier, and including age and ethnicity as covariates in each model (Table 2; Model 2). Following established procedures for model building [34], in the last step we constructed one logistic regression model with the variables that were significant in the prior step (Model 3).

The second stage in our model development was to identify predictors of 12-month CUD from the subsample with lifetime cannabis use. To do that, we followed procedures similar to those used to construct our cannabis use model and built successive models starting from bivariate associations, followed by within-tier logistic regressions and finally logistic regressions with predictors across tiers (Table 3; Model 4, Table 4; Model 5, and Model 6 respectively). Because we predicted that past CUD would be a strong predictor of last-year CUD, we built an additional model that included CUD in adulthood but not in the past-year (Model 7). Predictive accuracy of lifetime cannabis use and 12-month CUD across the different models was assessed with the c-index [35]. The c-index is a measure of concordance between the predicted and the observed outcome and equals the area under the receiver operating characteristic curve such that values of 0.50 represent prediction no better than chance and values of 1.0 represent perfect prediction.

All analyses, including ORs and 95% confidence intervals (95% CI) were estimated using SUDAAN [36] to adjust for the design effects of the NESARC.

RESULTS

Lifetime cannabis use

Table 1 presents the bivariate analyses of the variables included in our theoretical model in the sample with and without lifetime history of cannabis use (Model 1). The results indicate that most variables were significantly associated with increased odds of lifetime cannabis use. However, being Black, Asian or Hispanic, having higher educational attainment, past history of nicotine dependence, and religious service attendance significantly decreased the odds of lifetime use.

In Model 2 (Table 2), which examined the effect of each variable adjusted for age, race/ethnicity and all other variables within the same tier as well as gender by variable interactions, 16 out of 26 variables had significant main effects. The strongest association of cannabis use was with past-year AUD (AOR= 9.41; 95% CI = 4.25–20.81), whereas the AOR of the other significant associations ranged from ranged between 1.05 (vulnerable family environment) and 5.05 (ever divorced). Low educational attainment and history of nicotine dependence significantly decreased the odds of lifetime cannabis use in this model. Furthermore, in this model, there were significant gender interactions with impulsivity, educational attainment, psychiatric comorbidity during late adolescence, AUD in adulthood and past-year marital problems. The interactions indicated that the association of those variables with cannabis use was stronger in women then in men in all cases, except for educational attainment, for which the opposite was true.

In Model 3 (Table 2), which consisted of all significant predictors from Model 2, only lifetime DUD, past-year AUD and stressful life events had significant main effects. Nicotine dependence and independent stressful life events had a significant gender interaction, indicating that there is stronger effect of these variables in women than in men for lifetime risk of cannabis use.

12-month cannabis use disorders

As in the bivariate models of cannabis use, 12-month CUD among individuals with lifetime cannabis use was significantly associated to most predictors in the model (Model 4; Table 3). Prior history of CUD (OR=15.53; 95% CI= 10.99–21.99) and past-year AUD (OR= 6.11; 95% CI = 4.77–7.82) were the variables with the strongest association with last year CUD. The ORs of the other significant variables ranged from 1.07 (adult social deviance) and 2.96 (past-year nicotine dependence). Older age, higher educational attainment, a history of divorce, greater past-year social support, and religious service attendance decreased odds of last year CUD. Furthermore, the only childhood tier variable associated with increased risk of last year CUD was parental loss (OR= 1.25; 95% CI = 1.02–1.55), which was not significantly associated to the odds of lifetime cannabis use. Childhood-onset of anxiety, which also increased the odds of lifetime cannabis use, did not predict 12-month CUD.

Because of the strong effect of history of CUD in the bivariate analysis and its role as a potential mediator, we excluded it from Model 5 (Table 4), the within-tier analysis. In Model 5, which adjusted for age and race/ethnicity and examined variables within their tier, sexual abuse, impulsivity, history of trauma, greater number personality disorders, prior history of other drug use disorders, past-year AUD, past-year nicotine dependence, past-year psychiatric disorders, greater number of independent stressful life events and social deviance were significant predictors of past-year CUD. Sexual abuse, impulsivity and history of AUD

were more strongly associated to 12-month CUD among women than men. Religious service attendance was the only protective factor of 12-month CUD.

Predictors in models 6 and 7, the models that included predictors that were significant in the within-tier analysis, were quite similar (Table 4). Impulsivity was the only significant predictor with onset before adulthood. Prior history of other drug use disorder (in adulthood) also increased the risk of 12-month CUD, with all other significant predictors included in the last-year tier. With the exception of past history of CUD (in Model 7), past-year AUD was the strongest predictor of 12-month CUD, followed by impulsivity, past-year nicotine dependence (in Model 6 only), past-year psychiatric comorbidity, and social deviance. Religious service attendance was a significant protective factor of 12-month CUD among lifetime cannabis users. Prior history of AUD decreased the risk of 12-month, probably due to its collinearity with past history of other drug use disorder with past-year history of AUD. In both models 6 and 7, there was a significant gender interaction with impulsivity and history of AUD, indicating that these two variables were more strongly associated to CUD in women than in men.

DISCUSSION

In a nationally representative sample of US adults, a broad range of variables in several developmental tiers individually predicted lifetime cannabis use and 12-month CUD. However, after mutually adjusting for the effect of other covariates, the number of significant predictors was reduced for both outcomes. The predictive power of the models for lifetime use and for 12-month CUD was high, but the predictors for lifetime use and 12-month CUD did not completely overlap. Furthermore, there were few gender differences in the models for lifetime cannabis use and 12-month CUD.

In accord with prior studies [37, 38], we found that when examined individually, a broad range of variables increased the likelihood of cannabis use. However, after adjusting for the effect of other covariates, a more restricted set of variables independently contributed to the probability of use. Specifically, variables in the later tiers (i.e., adulthood and past year) were more likely to remain significant than those in earlier tiers, suggesting that the effect of earlier risk factors is largely mediated by the effect of later ones, as hypothesized by the model. The c-index was of the final model was 0.843, suggesting good predictive power.

Consistent with the results for lifetime use in this study and the findings of Kendler and coworkers on the etiology of MDD [39, 40] and more recently AUD [41], we also found that although multiple variables predicted 12-month CUD in the bivariate and within-tier analyses, more distal predictors were no longer significant after taken into account the effect of more proximal ones. Other studies have also found that earlier adverse experiences can lead to more distal negative outcomes. For example, childhood sexual abuse has been linked to risk for a broad range of psychopathology [14, 42] and to marital problems [43], both of which increase the risk of CUD. Similarly, parental loss has been associated with social deviance [44], and family history of substance use disorders with increased impulsivity [45]. Overall, our findings highlight the utility of integrated etiological models, particularly those that emphasize their developmental aspects, and support the applicability of Kendler's model beyond MDD. An intriguing avenue for future research will be to examine whether earlier risk factors convey a general level of liability for psychopathology that is later shaped by more proximal risk factors [46], or whether different psychiatric disorders are the result of similar risk factors combined in different proportions or experienced at different developmental periods.

Not surprisingly, we found that lifetime history of CUD was the single most important predictor for 12-month CUD. Substance use disorders are probably best conceptualized as chronic conditions [47], which often follow an episodic course. Therefore, the genetic predisposition [26], developmental influences [48, 49], and environmental cues that make individuals vulnerable to CUD at some point in their lives are also likely to increase the risk of current CUD. Despite the large proportion of variance explained by having a lifetime history of CUD, we found other risk factors such as impulsivity, last-year AUD, other psychiatric disorders, and social deviance also independently increased the risk of 12-month CUD. Our findings emphasize the multifactorial nature of the etiology of CUD, and offer some opportunities to develop and implement effective interventions. For instance, despite the efficacy of treatment of comorbid depression in improving the outcome of SUD [50], treatment of psychiatric comorbidity among individuals with SUD is rare [51, 52]. For some individuals, religiosity may also have a protective effect against risk of CUD [27].

We found substantial differences in the models for lifetime cannabis use versus those for 12-month CUD. For example, history of drug use disorders and stressful life events predicted lifetime cannabis use but not 12-month CUD. By contrast, impulsivity, past-year AUD, comorbid psychiatric disorders and social deviance predicted past-year CUD but not lifetime cannabis use. These findings are consistent with prior genetic studies documenting that the risk factors for drug initiation and dependence differ [12]. Similar findings were recently reported for pathological gambling [53], a disorder often considered a behavioral addiction.

By looking at the sex interactions we were also able to identify some variables where the models differed by gender. For example, nicotine dependence and independent stressful life events were significantly more strongly associated with lifetime cannabis use among females than males. Similarly, impulsivity and past history of AUD were significantly more strongly associated to the risk of 12-month CUD among females than males. However, most interactions were not significant, indicating that overall, the models for both lifetime cannabis use and 12-month CUD did not differ much by gender. Similar findings of few gender differences have been previously reported regarding comprehensive developmental models of the etiology of major depressive disorder [39, 40].

Our results have preventive and treatment implications. From the preventive perspective, by indicating that the etiology of CUD is multifactorial, our model suggests that interventions that act on several risk factors are likely to be more effective than those acting on a single risk factor. By identifying risk factors in different tiers, our model also suggests the possibility of developing interventions targeted towards individuals at different stages of development. From the treatment perspective, the model suggests that successful treatment programs may need to address predisposing (i.e., distal) factors as well as more proximal risk factors. There is a need to develop medications and psychological interventions that might modify the effect of those factors. Furthermore, treating CUD as a chronic condition (e.g., monitoring onset of symptoms, initiating treatment during early stages of relapse) has the potential to improve harm reduction and reduce the overall amount of treatment needed per patient.

Limitations

Despite its potential contributions, this study is not without limitations. First, information on substance use is based on self-report and not validated with biological tests, which would be extremely difficult to obtain in such a large sample. Second, information on several variables was collected retrospectively, and thus subject to recall bias. Collection of prospective information on such a large cohort does not appear feasible with currently existing methods. Furthermore, some variables such as impulsivity and self-esteem are dichotomous, which may have limited their statistical power. Third, the sample is limited to

individuals 18 and older. Our models may not hold for younger individuals. Fourth, although for clarity we organized the predictors into five discrete developmental periods, there is clear overlap and considerable between-subject variability across those periods. Nevertheless, we believe that the use of those periods provide some structure, however imperfect, to organize these diverse set of variables. Furthermore, although our model is comprehensive, it is not exhaustive. In order to be parsimonious, we limited the number of variables in our model. Even with a limited number of variables, our models were highly accurate. Nevertheless, alternative models could be built to examine specific aspects that were not included in our study.

Conclusions

A modification of Kendler's model for MDD provided a useful foundation for the development of a comprehensive developmental model of CUD. The model included five developmental tiers in which the effect of more distal tiers was mediated by more proximal ones in both male and females, with few differences across genders. Future studies should examine whether Kendler's modified model can be used to examine the etiology of other substance use disorders.

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Table 1

Bivariate associations of risk factors and prevalence of lifetime cannabis use in the general population. NESARC Wave 2 (n=34463).

	No use (n=27025)			Cannabis Use (n=7438)			Model 1[a]
	%/mean	CI		%/mean	CI		OR (CI 95%)
Age[b]							
18–29	14.29	13.62	14.98	43.04	41.63	44.46	Ref
30–39	17.18	16.47	17.92	4.06	3.61	4.57	**0.08 (0.07–0.09)**
40–49	18.93	18.29	19.59	1.99	1.65	2.41	**0.03 (0.03–0.04)**
>50	49.60	48.51	50.69	0.89	0.67	1.18	**0.01 (<0.01–0.01)**
Race/ethnicity							
White, non-Hispanic	69.29	65.80	72.58	76.51	74.11	78.76	Ref
Black, non-Hispanic	11.32	10.02	12.76	10.07	8.66	11.68	**0.81 (0.72–0.91)**
Native American	1.92	1.59	2.31	3.15	2.57	3.85	**1.49 (1.18–1.88)**
Asian	4.93	3.86	6.28	2.05	1.48	2.82	**0.38 (0.30–0.48)**
Hispanic	12.55	10.14	15.43	8.22	6.68	10.07	**0.59 (0.51–0.69)**
Childhood							
Family history of SUD	35.39	34.20	36.59	54.51	52.97	56.04	**2.19 (2.06–2.33)**
Sexual abuse	8.39	7.91	8.89	16.35	15.32	17.43	**2.13 (1.96–2.33)**
Vulnerable family environment (mean)	3.11	3.02	3.20	3.69	3.56	3.82	**1.03 (1.02–1.04)**
Parental loss	20.82	20.11	21.55	30.71	29.14	32.33	**1.69 (1.55–1.83)**
Early adolescence							
Impulsivity	14.28	13.69	14.89	26.30	24.98	27.66	**2.14 (1.97–2.32)**
Low self-esteem	11.39	10.73	12.08	14.80	13.73	15.94	**1.35 (1.23–1.48)**
Childhood-onset anxiety[b]	8.44	7.84	9.09	14.20	12.97	15.53	**1.79 (1.62–1.99)**
Social deviance[c] (mean)	0.33	0.31	0.35	1.31	1.23	1.39	**1.56 (1.51–1.61)**
Late adolescence							
Education years (mean)[b]	13.76	13.66	13.87	11.21	11.12	11.31	**0.79 (0.78–0.81)**
History of trauma	39.95	38.76	41.15	58.28	56.66	59.88	**2.10 (1.96–2.25)**
Number of Axis I disorders excluding SUD (mean)[b]	0.19	0.18	0.20	0.39	0.36	0.42	**1.58 (1.50–1.67)**
Number of personality disorders (mean)	0.30	0.28	0.31	0.76	0.71	0.80	**1.51 (1.46–1.56)**

	No use (n=27025)			Cannabis Use (n=7438)			Model 1[a]
	%/mean	CI		%/mean	CI		OR (CI 95%)
Adulthood[d]							
Ever divorced[b]	33.92	32.97	34.89	34.43	32.86	36.04	1.02 (0.96–1.09)
History of SUD							
Alcohol[b]	22.80	21.53	24.13	21.99	20.69	23.34	0.95 (0.87–1.05)
Other drugs[b]	1.16	0.98	1.36	5.09	4.44	5.82	**4.58 (3.76–5.59)**
Nicotine[b]	13.66	12.88	14.47	7.48	6.67	8.37	**0.51 (0.45–0.58)**
Social deviance (mean)[b,c]	1.14	1.09	1.20	4.07	3.90	4.24	**1.42 (1.40–1.45)**
Past year							
Social support (mean)	42.52	42.39	42.65	42.57	42.41	42.72	1.00 (1.00–1.01)
Alcohol use disorders[b]	5.85	5.46	6.27	43.40	31.16	56.50	**12.34 (7.31–20.82)**
Nicotine dependence[b]	10.28	9.66	10.93	26.83	16.89	39.81	**3.20 (1.77–5.77)**
Any Axis I disorder (no SUD)[b]	17.36	16.66	18.09	46.63	34.31	59.37	**4.16 (2.49–6.95)**
Religious service attendance[b]	57.60	56.49	58.71	31.49	21.59	43.42	**0.34 (0.20–0.57)**
Marital problems[b]	3.66	3.40	3.93	18.80	9.42	34.01	**6.10 (2.72–13.67)**
Stressful life events (mean)[b]	1.27	1.23	1.31	2.16	2.09	2.23	**1.33 (1.31–1.36)**
Independent (mean)[b]	0.61	0.59	0.63	1.31	1.00	1.63	**1.94 (1.60–2.36)**
Dependent (mean)[b]	0.62	0.60	0.64	1.79	1.32	2.25	**1.92 (1.65–2.25)**
Social deviance (mean)[b,c]	0.22	0.21	0.24	1.79	1.50	2.08	**1.84 (1.68–2.00)**

[a] Bivariate model;

[b] for individuals with lifetime CU, variables provide information for age at first use whereas for those drug naïve, the information reflects the value at the time of the interview;

[c] in early adolescence antisocial behavior before age 15; in adulthood since age 15; and past year between Wave 1 and Wave 2;

[d] lifetime but before 12 month. Significant results are bolded ($p<0.05$).

Table 2

Multivariable associations of risk factors and lifetime cannabis use. NESARC Wave 2 (n=34653).

	Model 2[a]		Model 3[b]	
	Main effect	**Sex Interaction**	**Main effect**	**Sex Interaction**
	AOR (CI 95%)	**AOR (CI 95%)**	**AOR (CI 95%)**	**AOR (CI 95%)**
Childhood				
Family history of SUD	**2.47 (2.10–2.90)**	0.96 (0.76–1.23)	1.39 (0.64–3.00)	1.28 (0.41–3.95)
Sexual abuse	**2.23 (1.80–2.75)**	1.09 (0.75–1.59)	2.00 (0.96–4.15)	
Vulnerable family environment	**1.05 (1.03–1.07)**	1.02 (0.99–1.05)	1.02 (0.97–1.07)	0.94 (0.87–1.02)
Parental loss	0.87 (0.74–1.03)	1.16 (0.92–1.47)		
Childhood c index= 0.963				
Early adolescence				
Impulsivity	**2.22 (1.79–2.76)**	**1.75 (1.32–2.38)**	2.01 (0.93–4.36)	1.38 (0.42–4.51)
Low self-esteem	0.89 (0.71–1.12)	1.00 (0.70–1.41)		
Childhood-onset anxiety	**1.34 (1.07–1.67)**	1.11 (0.79–1.56)	1.09 (0.32–3.79)	0.44 (0.07–2.89)
Social deviance[c]	**1.20 (1.12–1.27)**	1.08 (0.98–1.18)	1.05 (0.78–1.42)	1.00 (0.65–1.52)
Early Adolescence c index= 0.961				
Late adolescence				
Education years	**0.88 (0.85–0.92)**	**0.94 (0.90–0.99)**	1.11 (0.99–1.23)	1.07 (0.94–1.23)
History of trauma	**1.35 (1.16–1.56)**	0.96 (0.76–1.22)	0.86 (0.36–2.04)	0.50 (0.17–1.54)
Number of Axis I disorders excluding SUD (mean)[b]	1.07 (0.95–1.19)	**1.23 (1.03–1.49)**	0.97 (0.59–1.61)	1.14 (0.48–2.72)
Number of personality disorders (mean)	**1.18 (1.09–1.28)**	0.98 (0.86–1.12)	1.13 (0.89–1.45)	1.38 (0.71–2.69)
Late Adolescence c index= 0.96				
Adulthood[d]				
Ever divorced	**5.05 (4.16–6.14)**	0.97 (0.73–1.29)	1.25 (0.56–2.77)	0.84 (0.27–2.68)
History of SUD				
Alcohol	**1.92 (1.51–2.45)**	**1.55 (1.15–2.09)**	1.93 (0.75–4.97)	1.05 (0.28–3.95)
Other drugs	**2.14 (1.18–3.88)**	0.48 (0.21–1.11)	**4.78 (1.53–14.91)**	0.72 (0.11–4.75)
Nicotine	**0.53 (0.39–0.71)**	0.90 (0.59–1.37)	2.07 (0.98–4.39)	**6.31 (1.41–28.34)**
Social deviance[c]	**1.20 (1.15–1.24)**	1.04 (0.99–1.08)	0.85 (0.71–1.03)	0.81 (0.64–1.02)
Adulthood c index= 0.967				
Past year				
Social support	0.98 (0.94–1.02)	0.98 (0.91–1.05)		
Alcohol use disorders	**9.41 (4.25–20.81)**	2.17 (0.69–6.67)	**6.55 (2.54–16.89)**	2.14 (0.61–7.48)
Nicotine dependence	1.25 (0.57–2.74)	1.15 (0.33–4.00)		
Any Axis I disorder (no SUD)	1.92 (0.96–3.84)	0.79 (0.28–2.27)		
Religious service attendance	0.46 (0.21–1.01)	0.80 (0.29–2.22)		
Marital problems	2.04 (0.84–4.98)	**5.56 (1.11–25.00)**	2.09 (0.91–4.82)	3.91 (0.72–21.25)
Stressful life events				
Independent	0.94 (0.66–1.36)	1.54 (0.97–2.44)	**1.57 (1.15–2.14)**	**1.90 (1.21–3.00)**
Dependent	1.08 (0.66–1.78)	1.22 (0.69–2.13)	**1.25 (1.01–1.55)**	1.15 (0.65–2.06)

	Model 2[a]		Model 3[b]	
	Main effect	**Sex Interaction**	**Main effect**	**Sex Interaction**
	AOR (CI 95%)	**AOR (CI 95%)**	**AOR (CI 95%)**	**AOR (CI 95%)**
Social deviance[c]	**1.22 (1.01–1.47)**	0.96 (0.75–1.25)	1.11 (0.91–1.35)	0.82 (0.60–1.12)
	Past year c index= 0.805		Model 3 c index= 0.835	

[a] Controlling for age, ethnicity and other variables with the same tier;

[b] controlling for age, ethnicity and significant variables in Model 2. CUD is not included in this model;

[c] in early adolescence antisocial behavior before age 15; in adulthood since age 15; and past year between Wave 1 and Wave 2;

[d] lifetime but before 12 month. AOR= adjusted odds ratio; SUD= substance use disorders; significant variables are bolded ($p<0.05$). Reference group= no cannabis use. Reference group for sex interactions= males.

Table 3

Bivariate associations of risk factors and prevalence of 12-month cannabis use disorders CUD among individuals with lifetime cannabis use. NESARC Wave 2 (n=7438).

	CU with no CUD (n=6947)			CUD (n=491)			Model 4[a]
	%/mean	CI		%/mean	CI		OR (CI 95%)
Age							
18–29	21.51	20.22	22.87	48.99	42.89	55.13	Ref
30–39	24.12	22.93	25.35	21.61	17.10	26.92	**0.39 (0.28–0.54)**
40–49	30.92	29.56	32.30	19.21	15.36	23.76	**0.27 (0.20–0.37)**
>50	23.45	22.31	24.63	10.19	7.05	14.51	**0.19 (0.12–0.29)**
Race/ethnicity							
White, non-Hispanic	76.96	74.54	79.22	70.62	64.96	75.71	Ref
Black, non-Hispanic	9.75	8.36	11.35	14.19	10.51	18.89	**1.59 (1.12–2.24)**
Native American	3.04	2.47	3.74	4.59	2.56	8.11	1.65 (0.89–3.06)
Asian	1.99	1.42	2.77	2.89	1.22	6.66	1.59 (0.64–3.94)
Hispanic	8.26	6.72	10.12	7.70	5.26	11.16	1.02 (0.72–1.44)
Childhood							
Family history of SUD	54.65	53.10	56.19	52.71	47.05	58.30	0.93 (0.74–1.16)
Sexual abuse	16.16	15.11	17.27	18.78	15.02	23.24	1.20 (0.91–1.59)
Vulnerable family environment (mean)	3.69	3.56	3.82	3.68	3.26	4.10	1.00 (0.98–1.02)
Parental loss	30.36	28.75	32.02	35.32	30.80	40.11	**1.25 (1.02–1.55)**
Early adolescence							
Impulsivity	24.71	23.39	26.08	46.96	41.74	52.25	**2.70 (2.17–3.36)**
Low self-esteem	14.40	13.34	15.52	20.07	15.16	26.09	**1.49 (1.06–2.11)**
Childhood-onset anxiety	15.49	14.21	16.85	17.57	12.84	23.56	1.16 (0.82–1.65)
Early-onset cannabis use	13.20	12.33	14.14	22.45	18.32	27.20	**1.90 (1.46–2.47)**
Social deviance[b] (mean)	1.25	1.18	1.33	2.00	1.70	2.31	**1.10 (1.07–1.14)**
Late adolescence							
Education years (mean)	14.54	14.39	14.69	13.46	13.15	13.78	**0.88 (0.83–0.92)**
History of trauma	60.59	58.96	62.20	75.31	70.56	79.52	**1.98 (1.57–2.51)**
Number of Axis I disorders excluding SUD (mean)[b]	0.75	0.71	0.79	1.14	0.94	1.33	**1.23 (1.14–1.34)**

	CU with no CUD (n=6947)			CUD (n=491)			Model 4[a]
	%/mean	CI		%/mean	CI		OR (CI 95%)
Number of personality disorders (mean)	0.71	0.67	0.75	1.38	1.16	1.60	**1.30 (1.23–1.38)**
Adulthood[c]							
Ever divorced	35.09	33.49	36.72	25.89	20.97	31.49	**0.65 (0.49–0.85)**
History of SUD							
Cannabis	38.56	36.91	40.23	90.69	87.32	93.24	**15.53 (10.96–21.99)**
Alcohol	69.60	67.87	71.27	75.22	69.46	80.21	**1.33 (1.00–1.76)**
Other drugs	21.74	20.34	23.20	39.36	34.02	44.96	**2.34 (1.84–2.97)**
Nicotine	39.40	37.42	41.42	49.57	43.52	55.63	**1.51 (1.18–1.94)**
Social deviance[b] (mean)	4.14	3.97	4.31	5.70	5.08	6.31	**1.07 (1.05–1.09)**
Past year							
Social support	42.65	42.50	42.80	41.46	40.86	42.06	**0.96 (0.95–0.98)**
Alcohol use disorders	19.85	18.63	21.13	60.20	54.54	65.61	**6.11 (4.77–7.82)**
Nicotine dependence	24.57	22.81	26.41	49.11	43.04	55.21	**2.96 (2.25–3.90)**
Any Axis I disorder (no SUD)	26.75	25.54	27.99	45.11	40.08	50.23	**2.25 (1.82–2.79)**
Religious service attendance	40.42	38.65	42.22	23.83	19.69	28.52	**0.46 (0.36–0.59)**
Marital problems	7.97	7.26	8.74	18.00	14.06	22.76	**2.54 (1.87–3.44)**
Stressful life events (mean)	2.05	1.98	2.11	3.63	3.35	3.91	**1.34 (1.28–1.39)**
Independent (mean)	0.86	0.83	0.89	1.55	1.42	1.69	**1.63 (1.50–1.77)**
Dependent (mean)	1.11	1.06	1.15	1.90	1.71	2.08	**1.48 (1.38–1.59)**
Social deviance[b] (mean)	0.71	0.66	0.76	2.72	2.36	3.08	**1.38 (1.32–1.45)**

[a] Bivariate model;

[b] in early adolescence antisocial behavior before age 15; in adulthood since age 15; and past year between Wave 1 and Wave 2;

[c] lifetime but before 12 month; significant variables are bolded (p<0.05).

Table 4

Mulivariable associations of risk factors and 12-month cannabis use disorders among individuals with lifetime cannabis use. NESARC wave 2 (n=7438).

	Model 5[a]		Model 6[b]		Model 7[c]	
	Main effect	**Sex Interaction**	**Main effect**	**Sex Interaction**	**Main effect**	**Sex Interaction**
	AOR (CI 95%)	**AOR (CI 95%)**	**AOR (CI 95%)**	**AOR (CI 95%)**	**AOR (CI 95%)**	**AOR (CI 95%)**
Childhood						
Family history of SUD	0.92 (0.58–1.46)	0.83 (0.46–1.52)				
Sexual abuse	**2.31 (1.44–3.72)**	**1.92 (1.01–3.57)**	1.18 (0.72–1.96)	1.35 (0.69–2.63)	1.12 (0.64–1.94)	1.27 (0.61–2.63)
Vulnerable family environment	1.02 (0.97–1.07)	1.02 (0.96–1.08)				
Parental loss	0.85 (0.55–1.31)	0.73 (0.43–1.25)				
	Childhood c index= 0.726					
Early adolescence						
Impulsivity	**3.81 (2.36–6.15)**	**2.22 (1.25–3.85)**	**2.18 (1.34–3.53)**	**2.08 (1.18–3.70)**	**2.29 (1.37–3.80)**	**2.38 (1.30–4.35)**
Low self-esteem	1.55 (0.90–2.66)	1.33 (0.71–2.50)				
Childhood-onset anxiety	1.14 (0.66–1.97)	1.23 (0.62–2.44)				
Early-onset of cannabis use	1.27 (0.76–2.09)	0.89 (0.50–1.61)				
Social deviance[d]	1.05 (0.99–1.12)	1.02 (0.94–1.10)				
	Early Adolescence c index= 0.760					
Late adolescence						
Education years	0.95 (0.87–1.03)	1.03 (0.93–1.15)				
History of trauma	**2.56 (1.51–4.34)**	1.59 (0.88–2.86)	1.62 (0.89–2.93)	1.27 (0.65–2.50)	1.60 (0.88–2.91)	1.37 (0.69–2.70)
Number of Axis I disorders excluding SUD (mean)[b]	0.94 (0.80–1.10)	0.93 (0.76–1.15)				
Number of personality disorders (mean)	**1.33 (1.18–1.50)**	1.15 (0.98–1.35)	1.00 (0.88–1.14)	1.04 (0.87–1.25)	1.00 (0.88–1.13)	1.09 (0.92–1.28)
	Late Adolescence c index= 0.752					
Adulthood[e]						
Ever divorced	0.94 (0.62–1.43)	1.49 (0.93–2.39)				
History of SUD						
Cannabis					**15.73 (9.7–25.1)**	0.63 (0.29–1.37)
Alcohol	0.75 (0.50–1.14)	**2.17 (1.18–4.00)**	**0.39 (0.26–0.60)**	**2.33 (1.18–4.55)**	**0.27 (0.17–0.43)**	**2.38 (1.19–5.00)**
Other drugs	**2.08 (1.45–3.00)**	1.08 (0.56–2.08)	**1.62 (1.11–2.35)**	0.89 (0.45–1.79)		
Nicotine	1.17 (0.84–1.63)	1.03 (0.64–1.67)				

	Model 5[a]		Model 6[b]		Model 7[c]	
	Main effect	**Sex Interaction**	**Main effect**	**Sex Interaction**	**Main effect**	**Sex Interaction**
	AOR (CI 95%)	**AOR (CI 95%)**	**AOR (CI 95%)**	**AOR (CI 95%)**	**AOR (CI 95%)**	**AOR (CI 95%)**
Social deviance[d]	1.03 (0.98–1.08)	1.01 (0.95–1.08)				
	Adulthood c index= 0.746					
Past year						
Social support	1.00 (0.96–1.04)	1.01 (0.96–1.06)				
Alcohol use disorders	**4.08 (2.48–6.71)**	1.30 (0.70–2.44)	**4.09 (2.29–7.31)**	0.94 (0.47–1.89)	**4.16 (2.27–7.60)**	0.96 (0.48–1.96)
Nicotine dependence	**1.82 (1.11–2.99)**	1.28 (0.71–2.33)	**1.73 (1.03–2.89)**	1.16 (0.65–2.08)	1.39 (0.82–2.36)	0.96 (0.54–1.69)
Any Axis I disorder (no SUD)	**1.93 (1.20–3.12)**	1.47 (0.79–2.78)	**1.56 (1.01–2.40)**	1.14 (0.65–2.00)	**1.72 (1.10–2.68)**	1.23 (0.71–2.13)
Religious service attendance	**0.51 (0.30–0.85)**	0.81 (0.42–1.56)	**0.50 (0.30–0.85)**	0.78 (0.40–1.49)	**0.46 (0.26–0.80)**	0.71 (0.36–1.39)
Marital problems	1.29 (0.64–2.60)	1.22 (0.52–2.86)				
Stressful life events						
Independent	**1.25 (1.08–1.44)**	0.89 (0.71–1.12)				
Dependent	1.00 (0.89–1.13)	0.95 (0.76–1.19)				
Social deviance[d]	**1.25 (1.12–1.39)**	1.09 (0.96–1.22)	**1.19 (1.08–1.32)**	1.01 (0.90–1.14)	**1.18 (1.05–1.34)**	1.01 (0.88–1.16)
	Past year c index= 0.842		Model 6 c index= 0.843		Model 7 c index= 0.901	

[a] Controlling for age, ethnicity and other variables within the same tier,;

[b] controlling age, ethnicity and all significant variables in Model 5, but excluding CUD;

[c] controlling for age, ethnicity and all significant variables in Model 5, including CUD;

[d] in early adolescence antisocial behavior before age 15; in adulthood since age 15; and past year between Wave 1 and Wave 2;

[e] lifetime but before 12 month AOR= adjusted odds ratio; SUD= substance use disorders; significant variables are bolded ($p<0.05$). Reference group= cannabis use without abuse or dependence. Reference group for sex interactions= males.