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Probability and predictors of the cannabis gateway effect: A national study

Roberto Secades-Villa, Ph.D.^{a,b}, Olaya Garcia-Rodríguez, Ph.D.^{a,b}, Chelsea, J. Jin, M.A., M.S.^b, Shuai Wang, Ph.D., and Carlos Blanco, M.D., Ph.D.^b

^aDepartment of Psychology. University of Oviedo. Plaza Feijoo, s/n, 33003 Oviedo, Spain

^bNew York State Psychiatric Institute, Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY 10032

Abstract

Background—While several studies have shown a high association between cannabis use and use of other illicit drugs, the predictors of progression from cannabis to other illicit drugs remain largely unknown. This study aims to estimate the cumulative probability of progression to illicit drug use among individuals with lifetime history of cannabis use, and to identify predictors of progression from cannabis use to other illicit drugs use.

Methods—Analyses were conducted on the sub-sample of participants in Wave 1 of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) who started cannabis use before using any other drug (n= 6,624). Estimated projections of the cumulative probability of progression from cannabis use to use of any other illegal drug use in the general population were obtained by the standard actuarial method. Univariate and multivariable survival analyses with time-varying covariates were implemented to identify predictors of progression to any drug use.

Results—Lifetime cumulative probability estimates indicated that 44.7% of individuals with lifetime cannabis use progressed to other illicit drug use at some time in their lives. Several sociodemographic characteristics, internalizing and externalizing psychiatric disorders and indicators of substance use severity predicted progression from cannabis use to other illicit drugs use.

Conclusion—A large proportion of individuals who use cannabis go on to use other illegal drugs. The increased risk of progression from cannabis use to other illicit drugs use among individuals with mental disorders underscores the importance of considering the benefits and adverse effects of changes in cannabis regulations and of developing prevention and treatment strategies directed at curtailing cannabis use in these populations.

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*Corresponding author: Roberto Secades-Villa Facultad de Psicología – Universidad de Oviedo Plaza Feijoo s/n 33003 – Oviedo – Spain Phone: +34-98-5104139 Fax: +34-98-5104144 secades@uniovi.es.

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Keywords

gateway; progression; cannabis; other illicit drugs

1. INTRODUCTION

The gateway hypothesis holds that substance use progresses in sequential stages beginning with alcohol and tobacco use, followed by cannabis use and, later, the use of other illicit drugs (Kandel, 1975, 2003; Kandel, Yamaguchi, & Chen, 1992; Kandel, Yamaguchi, & Klein, 2006). According to the gateway hypothesis, individuals rarely use certain substances, such as heroin or cocaine, without having first used “gateway” substances, such as legal drugs or cannabis. The validity of the gateway hypothesis has been the topic of intense debate since the early 1970s. Although some studies have found that use of legal drugs or cannabis are not a requirement for the progression to other illicit drugs (Golub & Johnson, 1994; Mackesy-Amiti, Fendrich, & Goldstein, 1997; Malone, Lamis, Masyn, & Northrup, 2010; Morral, McCaffrey, & Paddock, 2002; Tarter et al., 2012; Tarter, Vanyukov, Kirisci, Reynolds, & Clark, 2006), most studies have supported the “gateway sequence” (Degenhardt et al., 2009; Fergusson, Boden, & Horwood, 2006; Fergusson & Horwood, 2000; Grau et al., 2007; Makanjuola, Oladeji, & Gureje, 2010; Mayet, Legleye, Falissard, & Chau, 2012; Rebellon & Van Gundy, 2006; Van Ours, 2003; Yamaguchi & Kandel, 1984).

In recent years there has been a growing interest in the effects of cannabis on mental health and psychosocial functioning (Blanco et al., 2014; Copeland, Rooke, & Swift, 2013; Moore et al., 2007; van Gastel et al., 2013; Van Ours & Williams, 2012), including the extent to which cannabis acts as a ‘gateway drug’ (Fergusson et al., 2006; Vanyukov et al., 2012). Cannabis would meet the conditions for gateway drug if (a) its use was initiated prior to the onset of other illicit drug use; and, (b) cannabis use increased the likelihood of using other illicit drugs (Fergusson et al., 2006).

While most of the studies have shown a high degree of association between cannabis use and use of other illicit drugs (Agrawal, Neale, Prescott, & Kendler, 2004; Fergusson & Horwood, 2000; Khan et al., 2013; Lynskey et al., 2003; O’Donnell & Clayton, 1982; Van Ours, 2003), the predictors of progression from cannabis to other illicit drugs remain largely unknown (Kandel et al., 2006; Van Gundy & Rebellon, 2010). Identification of those predictors is a crucial step in understanding the etiology of substance use disorders that could help in the development of more effective treatment and preventive interventions.

Prior research has indicated that genetic predisposition (Agrawal et al., 2004), higher frequency of cannabis use (Fergusson & Horwood, 2000; Mayet et al., 2012) and early onset of cannabis use (Fergusson et al., 2006; Van Gundy & Rebellon, 2010) are associated with increased risk of progression to other illicit drug use. Presence of depressive symptoms (Yamaguchi & Kandel, 1984), stress and unemployment (Van Gundy & Rebellon, 2010), peer influence (Wagner & Anthony, 2002) or drug availability (Degenhardt et al., 2010) have also been linked to increased risk of progression to other illicit drug use. Despite this body of knowledge, important questions remain regarding predictors of progression from

cannabis use to use of other drugs (Kandel et al., 2006). For example, several sociodemographic, psychopathologic and substance use related predictors previously reported for other types of drug use transitions (Florez-Salamanca et al., 2013; Lopez-Quintero, Perez de los Cobos, et al., 2011; Ridenour, Maldonado-Molina, Compton, Spitznagel, & Cottler, 2005) have not been examined. With the exception of one study that examined depression, no published study has investigated the effect of psychiatric comorbidity (i.e., anxiety, conduct or personality disorders) on progression from cannabis use to use of other drugs.

We sought to build on prior work by drawing on data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a large nationally representative study of the United States (US) adult population (Grant & Kaplan, 2005). The main goals of this study were to: 1) estimate the cumulative probability of progression to illicit drug use among individuals with lifetime history of cannabis use; and, 2) assess the association between several sociodemographic characteristics, psychiatric comorbidity and substance use-related variables and the risk of progression from cannabis use to other illicit drugs use.

2. METHODS

2.1. Sample

The NESARC target population at Wave 1 (2001-2002) was the civilian non-institutionalized population 18 years and older residing in households and group quarters. The final sample included 43,093 respondents. Blacks, Hispanics, and adults 18-24 were oversampled, with data adjusted for oversampling, household- and person-level non-response. The overall survey response rate was 81%. Data were adjusted using the 2000 Decennial Census, to be representative of the US civilian population for a variety of sociodemographic variables. Interviews were conducted by experienced lay interviewers with extensive training and supervision (Grant et al., 2009; Grant, Hasin, et al., 2004). All procedures, including informed consent, received full human subjects review and approval from the US Census Bureau and US Office of Management and Budget. This study examined data of the sub-sample of individuals who started cannabis use at Wave 1 before using any other drug (n= 6,624). Those who used other illicit drug before cannabis (n= 484) and those who only used other illicit drug (n=964) were not included in the current analyses.

Data were collected using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV (AUDADIS-IV) (Grant et al., 2003). The AUDADIS-IV is a structured diagnostic interview, developed to advance measurement of substance use and mental disorders in large-scale surveys (Grant, Stinson, et al., 2004). Computer algorithms produced DSM-IV diagnoses based on AUDADIS-IV data.

2.2. Measures

2.2.1. Sociodemographic variables—Sociodemographic factors included gender, self-reported age, race/ethnicity (Whites, Blacks, Hispanics, Asians and Native Americans), urbanicity (urban vs. rural), nativity (U.S.-born vs. foreign-born), educational attainment, marital status and employment status. Family history of substance use disorders (SUD) was

defined as any alcohol or drug use disorder among first degree relatives (Heiman, Ogburn, Gorroochurn, Keyes, & Hasin, 2008).

2.2.2. Substance use, abuse and dependence—Extensive AUDADIS-IV questions covered DSM-IV criteria for nicotine, alcohol and cannabis use disorders. For nicotine and alcohol dependence, 3 or more of 7 criteria within a 12-month period are required. The diagnosis of cannabis dependence required that at least 3 criteria from a list of six during a 12-month period be met. Because DSM-IV does not describe a withdrawal syndrome for cannabis, the AUDADIS-IV withdrawal criterion was not included in the diagnosis of cannabis dependence. For alcohol and cannabis abuse, participants had to meet 1 or more of 4 criteria within a 12-month period and not meet the criteria for dependence (American Psychiatric Association, 1994). Age of substance use onset was determined by asking respondents about the age at which they first used: cannabis, sedatives, tranquilizers, analgesics, stimulants, cocaine or crack, hallucinogens, inhalants/solvents, heroin, and other. Consistent with prior reports (Blanco et al., 2007; Blanco et al., 2013; Martins et al., 2012) non-medical use of a prescription drug was defined to respondents as using a prescription drug (sedatives, tranquilizers, analgesics, and stimulants) “without a prescription, in greater amounts, more often, or longer than prescribed, or for a reason other than a doctor said you should use them”. After the initial probe item, the respondent was given an extensive list of examples of prescription drugs and asked if s/he used any of the prescription drugs on the list or similar drugs ‘nonmedically’. The good to excellent test-retest reliability and validity of AUDADIS-IV SUD diagnoses is well documented in clinical and general population samples (Grant et al., 2003; Ruan et al., 2008).

2.2.3. Psychiatric disorders—Mood disorders included DSM-IV primary major depressive disorder, dysthymia, and bipolar I and II disorders. Anxiety disorders included DSM-IV panic disorder, social anxiety disorder, specific phobia and generalized anxiety disorder. AUDADIS-IV methods to diagnose these disorders are described in detail elsewhere (Grant, Hasin, et al., 2004; Grant et al., 2005; Hasin, Goodwin, Stinson, & Grant, 2005; Stinson et al., 2007). Avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic and antisocial personality disorders were assessed on a lifetime basis at Wave 1 and described in detail elsewhere (Grant, Hasin, et al., 2004).

Test-retest reliabilities for AUDADIS-IV mood, anxiety and personality disorders diagnoses in the general population and clinical settings were fair to good ($\kappa=0.40-0.77$) (Canino et al., 1999; Grant et al., 2003; Ruan et al., 2008). Convergent validity was good to excellent for all affective, anxiety, and personality disorders diagnoses (Grant, Hasin, et al., 2004; Hasin et al., 2005) and selected diagnoses showed good agreement ($\kappa=0.64-0.68$) with psychiatrist reappraisals (Canino et al., 1999).

2.3. Statistical Analyses

Weighted frequencies and their respective 95% confidence intervals (95% CI) were computed to characterize the sample. Estimated projections of the cumulative probability of progression from cannabis use to any drug use in the general population were obtained by the standard actuarial method (Machin, Cheung, & Parmar, 2006) as implemented in PROC

LIFETEST in SAS version 9.1.3 (SAS Institute, Cary, N.C.). This method, which is often used in the analysis of cross-sectional data (Lopez-Quintero, Hasin, et al., 2011; Lopez-Quintero, Perez de los Cobos, et al., 2011; Wang et al., 2005), allows to estimate retrospectively the time of events (in this case onset of cannabis use) and use that information to project future cumulative rates (Hosmer, Lemehsow, & May, 2008). Individuals who started using other drugs prior to using cannabis (18.9% of lifetime cannabis users) were not included in these analyses.

Univariate and multivariable survival analyses with time-varying variables (with person-year as the unit of analysis) (Jenkins, 1995) were implemented using SUDAAN version 9.1, (Research Triangle Institute, Research Triangle Park). In accord with established recommendations (Hosmer et al., 2008), only variables that were significant in the bivariate analyses at $p < 0.20$ were included in the multivariable model. These unadjusted and adjusted models aimed at assessing the association between sociodemographic, psychiatric comorbidity and substance use-related covariates and the hazards of progression from cannabis use to use of any other drug. The person-year variable was defined as the number of years from cannabis use onset to any drug use onset or age at Wave 1 interview (for censored cases). Educational attainment, marital status, and presence of DSM-IV mood, anxiety, and nicotine, alcohol and cannabis disorders were included as time-dependent variables. Modeling psychiatric disorders as time-varying variables ensured that the disorders always preceded the transition from cannabis use to use of other illicit drugs and thus could be considered predictors and not consequences of the use of those drugs.

3. RESULTS

3.1. Probability of progression from cannabis use to any other illicit drug use

Lifetime cumulative probability estimates indicated that 44.7% of individuals with lifetime cannabis use progressed to other illicit drug use at some time in their lives. During the second year after first cannabis use, the probability of other illicit drug initiation was 8.7%. The estimated cumulative probability of other illicit drug initiation a decade after the onset of cannabis use was 36% (Figure 1).

3.2. Sociodemographic characteristics

Sociodemographic characteristics of the study sample are presented in Table 1. Despite similar percentage and CI between 18-29 and 30-44 age groups, we found statistical significant differences between both groups ($p < 0.005$). The majority of respondents who progressed to other illicit drug use were male, between 30 and 44 years old, US-born, urban people, and had less than high school education.

3.3. Psychiatric and substance use comorbid disorders

Psychiatric comorbid disorders and other substance use-related characteristics of the study sample are presented in Table 2. Among individuals with any drug use who had Axis I disorder, a mood disorder, an anxiety disorder, a lifetime history of conduct disorder, a personality disorder, nicotine dependence, alcohol use disorder, or cannabis use disorder, about 50% started cannabis use before using any other drug. Of those with a family history

of SUD, almost 45% progress to use another illicit drug. The mean age of first use of cannabis was 16.1 years (SD=3.52; range: 5-45) and the mean age of first use of other illicit drugs was 20.61 (SD=6.34; range: 8-58).

3.4. Predictors of progression from cannabis use to any other illicit drug use

In univariate (Table 3) and multivariable (Table 4) survival models, several sociodemographic, psychopathological and substance use-related variables predicted progression from cannabis use to other illicit drug use.

3.4.1. Sociodemographic predictors—As shown in the adjusted models (Table 4) males were more likely than females to progress from cannabis use to other illicit drug use (HR=1.23, 95% CI = 1.09-1.36). Compared to White cannabis users, Blacks were less likely to progress to other illicit drug use (HR=0.46, 95% CI =0.39-0.55). Individuals living in urban areas were more likely than individuals living in rural areas to report progression to other illicit drug use (HR=1.19, 95% CI =1.02-1.36). Compared to cannabis married users, those divorced or separated (HR=1.94, 95% CI =1.49-2.54) and those never married (HR=2.15, 95% CI =1.79-2.58) were more likely to report progression to other illicit drug use.

3.4.2. Psychiatric and substance use-related predictors—In the adjusted models (Table 4) cannabis users with mood disorder (HR=1.33, 95% CI =1.12-1.57), anxiety disorder (HR=1.17, 95% CI =1.01-1.36), personality disorder (HR=1.34, 95% CI =1.17-1.53), nicotine dependence (HR=1.58, 95% CI =1.35-1.86), alcohol use disorder (AUD) (HR=1.53, 95% CI =1.36-1.72), or cannabis use disorder (CUD) (HR=2.33, 95% CI =2.06-2.62) were more likely to progress to other illicit drug use than individuals without these disorders. Family history of SUD (HR=1.28, 95% CI =1.15-1.43) and early use onset of cannabis (HR=0.94, 95% CI =0.92-0.97) also increased the risk of progression from cannabis use to other illicit drug use.

4. DISCUSSION

To our knowledge, this is the first study to identify subgroups of the population at increased risk for progression from cannabis use to use of other illicit drugs in a large, nationally representative sample of U.S. adults. The cumulative probability of transition from cannabis use to other illicit drug use was 44.7%. Several sociodemographic and psychiatric variables and indicators of substance use severity predicted progression, including being male, urban residence, being never married, separated or divorced, having a broad range of psychiatric disorders or a family history of SUD, and early onset of cannabis use.

Our results, in line with previous findings (Agrawal et al., 2004; Fergusson et al., 2006; Fergusson & Horwood, 2000; Lynskey et al., 2003; Van Gundy & Rebellon, 2010) suggest that a large proportion, but not all, of individuals who use cannabis go on to use other illegal drugs. Moreover, in agreement with the predictions of the GH, a minority of the total NESARC sample reported used other illicit drug before cannabis or only used other illicit drug.

Several complementary pathways involving biochemical, social learning and environmental factors may contribute to explain the progression from cannabis use to other illicit drug use. Cannabis users are often more exposed to opportunities to use other illicit drugs because the environment and distribution channels for cannabis and other illegal drugs frequently overlap (Dishion & Owen, 2002; Fergusson & Horwood, 1997; Wagner & Anthony, 2002). Cannabis use also provides the individual with learning experiences (e.g., pleasurable effects) that can encourage experimentation with other illicit drugs (Fergusson, Horwood, Lynskey, & Madden, 2003). Furthermore, the pharmacological effects of cannabis appear to lead to neuroadaptations that render the brain more sensitive to the euphoric effects of other illicit drugs (Ellgren, Spano, & Hurd, 2007; Schenk, 2002). Being intoxicated with one drug may also lower reservations about using other drugs.

An important, novel finding of the current study was the identification of subgroups of the population at risk for progression to other illicit drug use, i.e., individuals for which cannabis use constitute a gateway to other drug use. Mental disorders (both internalizing and externalizing) predicted progression from cannabis use to other illicit drug use. Several mechanisms may contribute to explain this association. First, individuals with mental disorders may use drugs in a maladaptive attempt to relieve their psychiatric symptoms, which may lead to further escalation (Compton, Dawson, Conway, Brodsky, & Grant, 2013; Glassman, 1993). Second, in accord with the sensitization hypothesis, cannabis use may potentiate the effect of other drugs, increasing their abuse liability (Huang, Kandel, Kandel, & Levine, 2013; Klein, 2001; Levine et al., 2011; Schenk, 2002). Similarly, drug interactions resulting in decreased adverse effects and synergism of drug effects may favor the simultaneous use of different substances (Desai, Barber, & Terry, 1999; Leri, Bruneau, & Stewart, 2003) and consumption of more than one drug may lead to faster neuroadaptations (Leri et al., 2003). Alcohol, nicotine or cannabis disorders may also trigger the use of other illegal substances through associated environmental factors such as cues and opportunities under peer influence (Mayet et al., 2012). There are also genetic factors that increase the risk of most substances of abuse (Kendler, Jacobson, Prescott, & Neale, 2003).

In accord with prior findings (Degenhardt, Hall, & Lynskey, 2001b), males were more likely than women to progress to other illicit drug use, consistent with previous research indicating that, in the general population, the prevalence of SUD is higher among men (Compton, Thomas, Stinson, & Grant, 2007; Degenhardt, Hall, & Lynskey, 2001a; Hasin, Stinson, Ogburn, & Grant, 2007; Regier et al., 1990). Biological (Nolen-Hoeksema & Hilt, 2006) and cultural factors such as peer behavior and socialization into traditional gender roles (Schulte, Ramo, & Brown, 2009; Swendsen et al., 2009) could explain this difference in rates of progression (Khan et al., 2013). Our study also found that the probability of progression to other illicit drug use was higher for individuals living in urban settings and for those divorced, separated or never married, while it was lower for Blacks compared to Whites. Higher availability of drugs, lower family cohesion or more diffuse social networks may help explain the higher risk of progression to illicit drug use among individuals in urban settings (Martino, Ellickson, & McCaffrey, 2008). Previous research has documented a consistent association between SUD and lower social support (Boden, Fergusson, & Horwood, 2013). Genetic protective factors (Scott & Taylor, 2007) and cultural/environmental (Gibbs et al., 2013; Giger, Appel, Davidhizar, & Davis, 2008; McLaughlin,

Hatzenbuehler, & Keyes, 2010; Primm et al., 2010) variables such as role modeling and interpersonal influence may decrease the risk for progression to use of other illicit drugs among Blacks compared to Whites (Griesler & Kandel, 1998). Furthermore, consistent with prior work (Agrawal et al., 2004; Fergusson et al., 2006; Kandel, 1984; Morral et al., 2002), earlier age at first cannabis use, increased the probability of other illegal drug use. Given the strong association between early use of cannabis, cannabis use disorder and progression to other illicit drug use, delaying cannabis use could reduce the probability of use of other illicit drugs among individuals who start cannabis use before using any other illicit drug.

Taken together, these results suggest that the strength associations between cannabis use and other illicit drug use may be driven by individual characteristics rather than being wholly explained by causal mechanisms. This pattern of transition is compatible with a common liability model of vulnerability to addictions (Morral et al., 2002). One potential policy implication is that preventive strategies that target this underlying common liability may be overall more effective than those focused on individual drugs. Nevertheless, because cannabis is the most commonly used drug, policies that contribute to decrease cannabis use may be useful in reducing involvement in other illicit drugs use particularly among individuals with psychiatric comorbidity.

These results should be considered in the light of some methodological limitations. First, information on substance use and SUD was based on self-report and not confirmed by objective methods which may have led to an underestimate due to the stigma associated with mental health problems (Pickles et al., 1998). Second, diagnoses may be subject to recall bias and to cognitive impairment associated with the use of drugs. Third, the cross-sectional nature of the study limits our ability to draw causal inferences. Therefore, while we are able to describe associations, we are not able to ascribe causality. Fourth, by design, we focused on individuals who started using cannabis before use of any other illicit drug. Our results may not generalize to those whose use of other illicit drugs preceded use of cannabis. The study of determinants of other illicit drugs use among subjects who followed alternative sequences should be made to complete the present study. It also has some important strengths, including its large sample size, generalizability (except for individuals just mentioned), careful methodology and the inclusion of predictors that have not been examined in previous studies.

In conclusion, our study indicates that about 40% of individuals with lifetime cannabis use progressed to other illicit drug use, highlighting the potential dangers of policies that may increase the availability of cannabis, at least for the fraction of individuals at risk for other illicit drug use. Furthermore, psychiatric comorbidity is a strong predictor of the association between cannabis use and progression to other illicit drug use. There is a need to consider the health benefits and adverse effects of changes in cannabis regulation that expand access to this substance, and for the development of prevention and intervention efforts targeted at cannabis users with co-occurring mental disorders.

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Highlights

We examined progression from cannabis use to other illicit drugs use in the NESARC.

44.7% of individuals with lifetime cannabis use progressed to other illicit drug use.

Mental disorders predicted progression from cannabis use to other illicit drug use.

This study can help guide interventions for drug use and cannabis regulations.

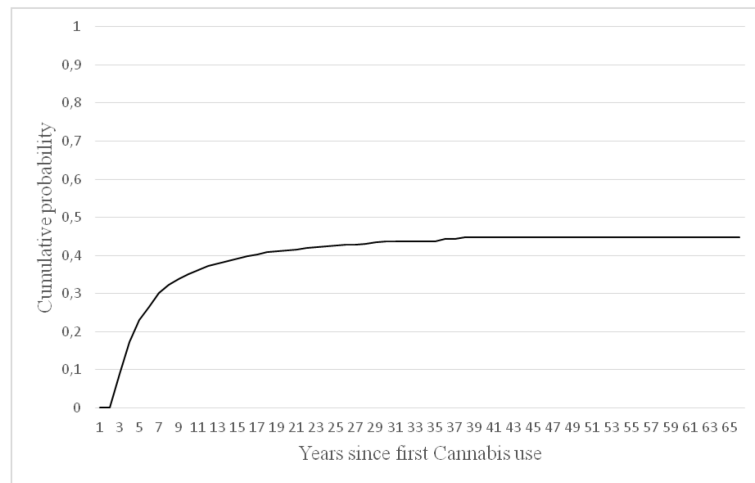


Figure 1. Cumulative probability of other illicit drug use initiation among individuals with lifetime history of cannabis use

Table 1

Proportion of individuals with lifetime cannabis used who progressed to the use of other illicit drugs, by sociodemographic characteristics

| Characteristics | Any Drug Use ^a (n=2572) | | |
|-----------------------------|------------------------------------|--------------------|-------|
| | % | 95%CI ^b | |
| Gender | | | |
| Male | 42.71 | 40.65 | 44.80 |
| Female | 34.98 | 32.82 | 37.20 |
| Age group | | | |
| 18-29 | 38.53 | 35.56 | 41.60 |
| 30-44 | 43.75 | 41.49 | 46.04 |
| 45 | 33.25 | 30.53 | 36.08 |
| Race/ethnicity | | | |
| Whites | 40.54 | 38.82 | 42.28 |
| Blacks | 25.17 | 22.02 | 28.60 |
| Hispanics | 43.07 | 38.64 | 47.61 |
| Asians | 43.68 | 34.74 | 53.06 |
| Native American | 47.87 | 39.25 | 56.62 |
| Urbanicity | | | |
| Rural | 36.11 | 32.67 | 39.69 |
| Urban | 40.05 | 38.28 | 41.85 |
| US Born | | | |
| Yes | 39.76 | 38.12 | 41.41 |
| No | 32.36 | 27.06 | 38.16 |
| Education | | | |
| < High school | 43.25 | 38.64 | 47.97 |
| High school | 39.58 | 36.42 | 42.84 |
| College | 38.70 | 36.89 | 40.55 |
| Marital Status | | | |
| Married/living with someone | 37.57 | 35.57 | 39.62 |
| Divorced/separated | 43.10 | 39.41 | 46.87 |
| Widowed | 33.51 | 22.24 | 47.04 |
| Never married | 41.63 | 38.66 | 44.66 |
| Employment status | | | |
| Ever employed | 39.93 | 38.17 | 41.73 |
| Never employed | 37.40 | 34.40 | 40.50 |

^a Sedatives, tranquilizers, painkillers, stimulants, cocaine or crack, hallucinogens, inhalants/solvents, heroin, and other,

^b 95% confidence interval.

Table 2

Proportion of individuals with life cannabis who progressed to the use of other illicit drugs, by presence of psychiatric disorders

| Characteristics | <u>Any Drug Use^a (n=2572)</u> | | |
|--|--|--------------------|-------|
| | % | 95%CI ^b | |
| Any Axis I disorder | | | |
| Yes | 43.22 | 41.54 | 44.93 |
| No | 16.82 | 13.87 | 20.26 |
| Any mood disorder | | | |
| Yes | 48.76 | 45.97 | 51.56 |
| No | 35.61 | 33.73 | 37.54 |
| Any anxiety disorder | | | |
| Yes | 47.44 | 44.23 | 50.67 |
| No | 36.72 | 34.99 | 38.49 |
| Any conduct disorder | | | |
| Yes | 40.34 | 29.58 | 52.12 |
| No | 39.37 | 37.77 | 41.00 |
| Any personality disorder | | | |
| Yes | 50.68 | 47.87 | 53.48 |
| No | 34.08 | 32.28 | 35.92 |
| Family history of SUD | | | |
| Yes | 44.68 | 42.58 | 46.79 |
| No | 33.18 | 31.03 | 35.39 |
| Nicotine Dependence | | | |
| Yes | 51.97 | 49.35 | 54.58 |
| No | 31.98 | 30.12 | 33.90 |
| Alcohol Use Disorder | | | |
| Yes | 47.08 | 45.07 | 49.11 |
| No | 24.83 | 22.56 | 27.26 |
| Cannabis Use Disorder | | | |
| Yes | 56.35 | 53.74 | 58.93 |
| No | 28.92 | 27.20 | 30.71 |
| Age first used cannabis (continuous, mean) | 16.15 | 15.97 | 16.33 |
| Age first used OID^c (continuous, mean) | 20.61 | 20.29 | 20.94 |

^aSedatives, tranquilizers, painkillers, stimulants, cocaine or crack, hallucinogens, inhalants/solvents, heroin, and other,

^b95% confidence interval,

^cother illicit drugs.

Table 3

Predictors of progression from cannabis use to other drug use among individuals with lifetime cannabis use preceding lifetime use of other drugs at NESARC wave 1. Univariate results of survival analyses

| Characteristics | Any Drug Use ^a (n=2572) | | | p |
|--------------------------|------------------------------------|--------------------|------|-------|
| | HR ^b | 95%CI ^c | | |
| Gender | | | | |
| Female | 1.00 | 1.00 | 1.00 | |
| Male | 1.28 | 1.17 | 1.40 | 0.000 |
| Age group | | | | |
| 18-29 | 1.00 | 1.00 | 1.00 | |
| 30-44 | 0.86 | 0.77 | 0.96 | 0.098 |
| 45 | 0.90 | 0.78 | 1.04 | 0.155 |
| Race/ethnicity | | | | |
| White | 1.00 | 1.00 | 1.00 | |
| Black | 0.54 | 0.47 | 0.63 | 0.000 |
| Hispanic | 1.00 | 0.86 | 1.16 | 1.000 |
| Asian | 1.14 | 0.82 | 1.58 | 0.451 |
| Native American | 1.19 | 0.90 | 1.57 | 0.229 |
| Urbanicity | | | | |
| Rural | 1.00 | 1.00 | 1.00 | 0.075 |
| Urban | 1.12 | 0.99 | 1.28 | |
| US Born | | | | |
| Yes | 1.20 | 0.94 | 1.53 | 0.136 |
| No | 1.00 | 1.00 | 1.00 | |
| Education | | | | |
| < High school | 0.94 | 0.75 | 1.17 | 0.575 |
| High school | 0.94 | 0.80 | 1.10 | 0.446 |
| College | 1.00 | 1.00 | 1.00 | |
| Marital Status | | | | |
| Married | 1.00 | 1.00 | 1.00 | |
| Divorced/separated | 2.06 | 1.59 | 2.67 | 0.000 |
| Widowed | 2.11 | 0.57 | 7.78 | 0.262 |
| Never married | 2.19 | 1.84 | 2.60 | 0.000 |
| Employment status | | | | |
| Ever employed | 1.00 | 1.00 | 1.00 | |
| Never employed | 1.00 | 0.89 | 1.12 | 0.953 |

| Characteristics | Any Drug Use ^a (n=2572) | | | |
|---|------------------------------------|--------------------|------|-------|
| | HR ^b | 95%CI ^c | | p |
| Any Axis I disorder | | | | |
| Yes | 2.30 | 2.07 | 2.57 | 0.000 |
| No | 1.00 | 1.00 | 1.00 | |
| Mood disorder | | | | |
| Yes | 1.67 | 1.45 | 1.93 | 0.000 |
| No | 1.00 | 1.00 | 1.00 | |
| Anxiety disorder | | | | |
| Yes | 1.29 | 1.13 | 1.46 | 0.000 |
| No | 1.00 | 1.00 | 1.00 | |
| Conduct disorder | | | | |
| Yes | 0.98 | 0.67 | 1.43 | 0.905 |
| No | 1.00 | 1.00 | 1.00 | |
| Personality disorder | | | | |
| Yes | 1.55 | 1.38 | 1.74 | 0.000 |
| No | 1.00 | 1.00 | 1.00 | |
| Family history of SUD | | | | |
| Yes | 1.33 | 1.21 | 1.47 | 0.000 |
| No | 1.00 | 1.00 | 1.00 | |
| Nicotine Dependence | | | | |
| Yes | 2.01 | 1.75 | 2.32 | 0.000 |
| No | 1.00 | 1.00 | 1.00 | |
| Alcohol Use Disorder | | | | |
| Yes | 1.97 | 1.78 | 2.19 | 0.000 |
| No | 1.00 | 1.00 | 1.00 | |
| Cannabis Use Disorder | | | | |
| Yes | 2.74 | 2.46 | 3.05 | 0.000 |
| No | 1.00 | 1.00 | 1.00 | |
| Age first used cannabis (continuous) | | | | |
| | 0.94 | 0.92 | 0.96 | 0.000 |

^a Sedatives, tranquilizers, analgesics, stimulants, cocaine/crack, hallucinogens, inhalants/solvents, heroin, and other,

^b hazard ratio,

^c 95% confidence interval.

Predictors included as time-dependent variables: Education, marital status, mood disorder, anxiety disorder, nicotine dependence, alcohol use disorder and cannabis use disorder.

Table 4

Predictors of progression from cannabis use to other drug use among individuals with lifetime cannabis use preceding lifetime use of other drugs in the NESARC wave 1. Multivariate results of survival analyses

| Characteristic | Any Drug Use ^a (n=2572) | | |
|---|------------------------------------|--------------------|-------------|
| | HR ^b | 95%CI ^c | |
| Gender | | | |
| Female | 1.00 | 1.00 | 1.00 |
| Male | 1.23 | 1.09 | 1.36 |
| Race/ethnicity | | | |
| White | 1.00 | 1.00 | 1.00 |
| Black | 0.46 | 0.39 | 0.55 |
| Hispanic | 0.95 | 0.80 | 1.13 |
| Asian | 1.20 | 0.81 | 1.77 |
| Native American | 0.96 | 0.70 | 1.31 |
| Urbanicity | | | |
| Rural | 1.00 | 1.00 | 1.00 |
| Urban | 1.19 | 1.02 | 1.36 |
| Marital Status | | | |
| Married | 1.00 | 1.00 | 1.00 |
| Divorced/separated | 1.94 | 1.49 | 2.54 |
| Widowed | 1.97 | 0.46 | 8.41 |
| Never married | 2.15 | 1.79 | 2.58 |
| Mood disorder | | | |
| | 1.33 | 1.12 | 1.57 |
| Anxiety disorder | | | |
| | 1.17 | 1.01 | 1.36 |
| Personality disorder | | | |
| | 1.34 | 1.17 | 1.53 |
| Family history of SUD | | | |
| | 1.28 | 1.15 | 1.43 |
| Nicotine Dependence | | | |
| | 1.58 | 1.35 | 1.86 |
| Alcohol Use Disorder | | | |
| | 1.53 | 1.36 | 1.72 |
| Cannabis Use Disorder | | | |
| | 2.33 | 2.06 | 2.62 |
| Age first used cannabis (continuous) | | | |
| | 0.94 | 0.92 | 0.97 |

^aSedatives, tranquilizers, analgesics, stimulants, cocaine or crack, hallucinogens, inhalants/solvents, heroin, and other,

^bhazard ratio,

^c95% confidence interval.

Predictors included as time-dependent variables: Education, marital status, mood disorder, anxiety disorder, nicotine dependence, alcohol use disorder and cannabis use disorder.