



# When Marijuana Is Used before Cigarettes or Alcohol: Demographic Predictors and Associations with Heavy Use, Cannabis Use Disorder, and Other Drug-related Outcomes

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## Abstract

Recent loosening of state and federal policy restrictions on marijuana, along with changes in social norms regarding marijuana use and decreases in prevalence of other types of substance use, may lead to increases in youth initiating marijuana before other types of substances such as alcohol and tobacco. We investigated predictors and potential consequences of initiating marijuana before other drugs for youth aged 12–21-years in the USA. Nationally representative, cross-sectional survey data from the US National Survey on Drug Use and Health supplied self-reported age of first marijuana, cigarettes, alcohol, other tobacco, and other illegal drug use among 12–21-year-old samples from 2004 to 2014 ( $n = 275,559$ ). We first examined the degree to which initiating marijuana use first was associated with sex, age, race/ethnicity, and survey year. Then, we examined whether using marijuana first predicted heavy marijuana use, cannabis use disorder (CUD), alcohol use disorder (AUD), nicotine dependence (ND), or lifetime use of other illegal drugs. Among all survey youth (substance users and non-users), the proportion using marijuana first increased from 4.8 to 8.8% from 2004 to 2014. Those using marijuana first (vs. alcohol or cigarettes first) were more likely to be male and older and Black, American Indian/Alaskan Native, multiracial, or Hispanic than White or Asian. Among substance users and adjusting for age of onset and the number of substances used, using marijuana first was associated higher odds of heavy current marijuana use and CUD. In recent years, youth have been increasingly likely to use marijuana as their first drug and sequence of initiation is associated with race/ethnicity, gender, and age. Using marijuana first might increase the chance of heavy use and CUD.

**Keywords** Marijuana · Cigarettes · Alcohol · Dependence · Gateway

Initiation of tobacco and alcohol use usually precedes first of use of marijuana or other illegal drugs; this pattern has been characterized in the well-cited “gateway hypothesis” (Kandel

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and Kandel 2015; Kirby and Barry 2012; Ramo et al. 2012). Behavioral neuropharmacology research suggests that nicotine may “prime” the brain to appreciate the reinforcing effects of extrinsic substances, such as alcohol or marijuana (Kandel and Kandel 2014). Importantly, priming could work in the reverse direction; meaning marijuana use could increase sensitivity to the rewarding effects of nicotine (Ellgren et al. 2007; Panlilio et al. 2013). Therefore, whichever drug is used first could become a “gateway,” in the sense that use could lead to use of other substances. Examining adolescents’ drug sequences may enhance our understanding of factors that influence initiation of substance use, subsequent use of other substances, and drug-related outcomes.

The specific order of initiation of specific drugs used may vary based on several factors, including drug availability and legal status of drugs. Nationally representative US data show that there have been steep declines in adolescent cigarette and alcohol use, contrasted by either relatively stable or periods of

slightly increasing marijuana use (Johnson et al. 2015; Johnston et al. 2017; Nguyen et al. 2018). Nearly twice as many 12–17-year-olds report past 30-day marijuana use vs. cigarette use (respectively, 6.5 and 3.4%), whereas 9.2% report past 30-day alcohol use (Substance Abuse and Mental Health Services Administration 2017). These trends coincide with loosening of US state policies on marijuana use for adults, and implementation of multi-tiered efforts to curb underage cigarette and alcohol use (e.g., excise taxes, diversion prevention strategies) (Friend et al. 2011; Hingson and White 2014). Consequently, today's youth may have higher levels of access and exposure to marijuana than previous generations and may be more likely to initiate marijuana use prior to tobacco or alcohol. Although data are limited, changes to the drug sequence could have implications for the future risk of substance use disorders (SUDs) and other drug-related outcomes. In this study, we investigated the trends, characteristics, and potential consequences of initiating marijuana before other substances among youth aged 12–21 years in the US, from 2004 to 2014.

There are only a handful of studies that have examined factors associated with initiating marijuana first, i.e., before tobacco, alcohol, or other substances. Studies of adults have shown that 18–30-year-olds are more likely to initiate marijuana before other substances than those older than 30 (Degenhardt et al. 2009, 2010; Wells and McGee 2008). Additionally, US studies have noted higher rates of using marijuana before tobacco or alcohol among Blacks (Green et al. 2016; Kennedy et al. 2016; Sartor et al. 2013; Vaughn et al. 2008). This body of work has key limitations; most studies are based on adult (vs. adolescent) samples, were conducted outside the USA, and/or used data that are at least 10–15 years old (Degenhardt et al. 2009; Green et al. 2016). The present study builds on what is known and will provide information about drug sequencing among adolescents within the modern context.

Studies have also examined whether initiating marijuana before other substances (typically tobacco or alcohol) influences later substance-related outcomes compared to the typical initiation sequence of tobacco and/or alcohol then marijuana, and there is mixed evidence supporting that initiating substance use with marijuana first is associated with adverse outcomes. One study conducted in a US adult female twin sample reported that using marijuana before alcohol was associated with a more rapid transition to marijuana-related problems (Sartor et al. 2013). A couple of studies, one conducted among 14–15-year-olds in Australia and another in a cohort of US adolescents, found that marijuana use increased the likelihood of smoking cigarettes and becoming tobacco dependent (Patton et al. 2005; Timberlake et al. 2007). Included in the present issue, Nguyen et al. (2018) analyses of AddHealth data show that adolescent marijuana use is a risk factor for later daily cigarette smoking among women. On the other

hand, two studies conducted in the USA and New Zealand found that using marijuana before tobacco and alcohol was not associated with an increased odds of marijuana, alcohol, or tobacco dependence among users (Degenhardt et al. 2009; Wells and McGee 2008).

We build upon this literature by first identifying cross-sectional trends in the proportion of youth initiating marijuana before other substances and the demographic characteristics of such users. Next, we examined the degree to which initiating marijuana before other substances was associated with prevalent marijuana- and other drug-related outcomes: (1) daily or near daily marijuana use, (2) cannabis use disorder, (3) alcohol use disorder, (4) nicotine dependence, and (5) lifetime use of other drugs. A methodological innovation of our study allowed us to better differentiate the sequence of marijuana, cigarette, and alcohol onset when individuals self-report using two or more of these substances at the same age. In prior studies, even those based on prospective designs, the order of drug onset is based on self-reported age of first use or onset between successive follow-ups. Ties where age of first use coincide can be as high as 20–30% (Kennedy et al. 2016; Sartor et al. 2013). Studies often either exclude such ties, treat them as a separate group, or do not disclose how they are treated (Golub and Johnson 2002; Kandel and Yamaguchi 1993; Kennedy et al. 2016; Sartor et al. 2013). Pointed follow-up questions allowed for a more precise determination of the order in the drug-using sequence.

## Methods

### Data and Sample

Data were from the publicly available 2004–2014 US National Survey on Drug Use and Health (NSDUH), a nationally representative, household-based annual series of cross-sectional surveys on drug use and their correlates (United States Department of Health and Human Services 2016). A multistage area probability sampling design selected designated participants from a target population of civilian, non-institutionalized US residents aged 12 years and older ( $n = 615,701$  total sampled across survey years). Trained field staff conducted interviews using audio computer-assisted self-interview (ACASI) and computer-assisted personal interview (CAPI) methods to enhance confidentiality and accurate reporting of sensitive behaviors, such as drug use. Participants were compensated \$30 for completed interviews; the average participation level for 2004–2014 was 65%. All participants were provided with informed consent and procedures were approved by the appropriate institutional review board for the protection of human subjects. Further details of the NSDUH methodology have been published online (<http://>

[www.samhsa.gov/data/population-data-nsduh/reports?tab=38](http://www.samhsa.gov/data/population-data-nsduh/reports?tab=38); last accessed 27 02 2018).

The present study focused on a subsample of participants aged 12–21 years old ( $n = 275,559$ ; 48% of the total sampled). Excluded were adults aged 22 or older ( $n = 318,069$ ) due to concerns about accurate age of drug onset recall, and participants whose age of first drug used could not be determined due to missing data ( $n = 22,073$ ; 7.4% of 12–21-year-olds).

## Measures

### Initiation of Substance Use

Participants reported age of first use for marijuana, cigarettes, other tobacco products (i.e., cigars, snuff, chew, and smokeless tobacco), alcohol, and other drugs (i.e., inhalants, cocaine, heroin, and non-medical prescription drugs) in response to a series of questions that asked: “How old were you when you first used [drug]?” When the age of onset for cigarettes, alcohol, and marijuana coincided (i.e., ties), a series of follow-up items were asked. The first item read: “Earlier, the computer recorded that you started using [these substances] when you were [age] years old. Which did you use first?”; the second read: “After first using [first drug], which of these did you use next?” Based on responses to these items, a small value (0.1) was added to the participants’ age of onset when one drug was reported to occur after another (i.e., making them slightly older). The user-defined *rowranks* command available in Stata ranked the order of onset for each drug based on the age of onset (Cox 2009; StataCorp 2013). A variable was constructed to indicate which drug was initiated first (if at all): (1) no drug use, (2) cigarettes, (3) alcohol, (4) marijuana, (5) other tobacco products, and (6) other drugs. Seventeen percent of the sample had completed these follow-up items.

### Drug-related Outcomes

Participants were asked about the number of days they had used marijuana in the last 30 days and in the last 12 months. Heavy marijuana use was defined as reporting marijuana use on either  $\geq 20$  or more days in the past month or  $\geq 300$  days in the past year. Participants were classified as having a cannabis use disorder (CUD) or alcohol use disorder (AUD) if, within the last 12 months, they had met one or more features of abuse or three or more features of dependence based on criteria in the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (American Psychiatric Association 1994). Those whose total score on the Nicotine Dependence Syndrome Scale was  $\geq 2.75$  were classified as having nicotine dependence (ND) (Shiffman et al. 2004). Any lifetime use of other drugs was based on responses to items

about having ever used inhalants, cocaine, heroin, and non-medical prescription drugs.

### Demographic Factors

We included demographic factors as covariates, including sex, age at interview, and race/ethnicity. Race/ethnicity categories included White, Black, American Indian or Alaskan Native, Native Hawaiian or Other Pacific Islander, Asian, and Multiracial, all non-Hispanic, and a final category for Hispanic/Latino respondents of any race.

### Analyses

First, we estimated the proportion of youth who initiated substance use with marijuana, cigarettes, alcohol, other tobacco products, and other illicit drugs, and examined variation by demographic characteristics and survey year. Next, we used multinomial logistic regression to estimate the degree to which demographic characteristics and survey year were independently associated with initiating marijuana first, relative to alternative initiation sequences, including (1) marijuana vs. no drug use, (2) marijuana vs. cigarettes first, and (3) marijuana vs. alcohol first. In these models, the probability or risk of initiating marijuana first compared to one of these alternative sequences (i.e., the reference group) is expressed as a relative risk ratio (RRR), and has a similar interpretation as an odds ratio (Hilbe 2009). Finally, we explored potential two-way interactions between sex, age, and race/ethnicity.

The second series of analyses examined drug-related outcomes. We used logistic regression to estimate odds ratios (OR) associated with initiating marijuana before other substances for five dichotomous outcomes: (1) heavy cannabis use, (2) CUD, (3) AUD, (4) ND, and (5) lifetime use of other drugs. These models excluded youth who had never used drugs. Adjusted models controlled for sex, age, race/ethnicity, survey year, and the number of drugs used. Age of first marijuana use was adjusted for in models of cannabis-related outcomes, while age of first alcohol, cigarette, and other drug use was similarly adjusted for in models of AUD, ND, and lifetime other drug use, respectively. All analyses accounted for the complex survey design, sampling weights, and were conducted in Stata version 13.0 (StataCorp 2013).

## Results

For each substance, the mean age of reported first use increased over the study period. The mean age of first marijuana use increased (+0.5 years) from 14.7 years in 2004 to 15.2 years in 2014; these numbers were comparable to those for age of first use of cigarettes (13.6 vs. 15.0; +1.4 years), alcohol (14.4 vs. 15.2; +0.8 years), other tobacco (14.8 vs.

15.7; +0.9 years), and other drug use (14.4 vs. 15.0; +0.6 years).

Aggregated across survey years, 5.8% of respondents reported that they initiated marijuana before other substances, compared to 29.8% for alcohol, 14.2% for cigarettes, 3.6% for other tobacco products, and 5.9% other drugs (these data are provided in online supplemental Table S1). From 2004 to 2014, the proportion who had initiated marijuana before other substances increased from 4.4 to 8.0% (Fig. 1), declined for those having initiated cigarettes first (21.4 to 8.9%) and increased in youth having abstained from substance use (35.5 to 46.3%). Males were more likely than females to have initiated marijuana first (7.1%) or other tobacco products first (5.7%), whereas females were more likely than males to have initiated cigarettes (15.2%) or alcohol first (32.0%). Considering age, a small proportion of 12–13-year-olds (0.6%) reported initiating marijuana before other substances, but by ages 18–19 and 20–21-years, this proportion increased to 9.1 and 9.4%, respectively. American Indian/Alaskan Native (AI/AN) (11.8%) and Black youth (9.4%) had the highest proportion of initiating marijuana first; White (4.6%) and Asian youth (2.5%) has the lowest.

As shown in Table 1, males were more likely than females to have initiated marijuana first in comparison to those not using drugs (aRRR = 1.69), those initiating cigarettes first (aRRR = 1.79), or those initiating alcohol first (aRRR = 1.83). Likewise, the likelihood of initiating marijuana first relative to no drug use (aRRR = 1.69) or alcohol first (aRRR = 1.06) increased with age, but not relative to initiating cigarettes first. Compared to Whites, AI/AN youth were 3.7 times more likely to have initiated marijuana first relative to no drug use, and were 5.0 times more likely to have initiated marijuana first relative to alcohol. Notably, Black youth were the most likely to have initiated marijuana first compared to cigarettes (aRRR = 2.74). To a lesser extent, Hispanic, Native Hawaiian/Other Pacific Islander (NHOPI), and multiracial youth also had a higher likelihood of initiating marijuana before other substances compared to Whites. By contrast, Asian youth were less likely to have initiated marijuana first relative to no drug use (aRRR = 0.30) or alcohol first (aRRR = 0.59). Thus, White and Asian youth were more likely to have initiated cigarettes or alcohol first before other substances compared to other racial/ethnic groups. Even after accounting for these demographic characteristics, the likelihood of initiating marijuana before other substances increased with survey year relative to no drug use (aRRR = 1.01) or alcohol first (aRRR = 1.07), but most strongly when compared to cigarettes first (aRRR = 1.16).

In exploratory analyses, we examined subgroup interactions between sex, age, and race/ethnicity in relation to having initiated marijuana first vs. no drug use (data not in tables). We found no subgroup interactions by sex (i.e., age x sex or race/ethnicity x sex). However, there was less variation by race/

ethnicity among older age groups. For example, 20–21-year-old Black youth had a similar likelihood of initiating marijuana first relative to Whites, but 15–16-year-old Black youth had almost twice the likelihood (aRRR = 1.9).

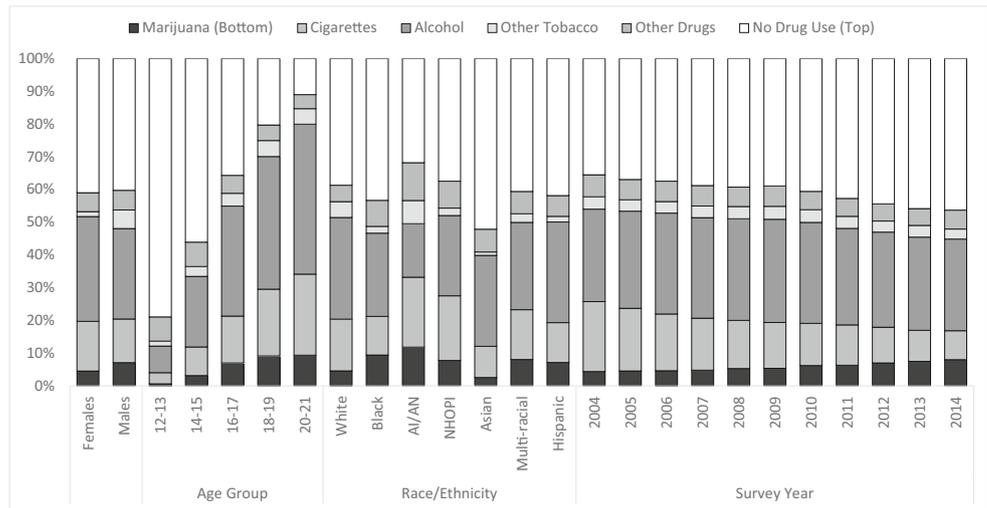
Table 2 shows the degree to which initiating marijuana before other substances is associated with the drug-related outcomes examined, after adjustment for potential confounders. Generally, those who started with a particular substance were the most like to have prevalent problematic use of that substance. For example, those who initiated marijuana before other substances were more likely currently smoking marijuana heavily and have CUD. Those who initiated alcohol before other substances were the most likely to experience prevalent AUD, and those who initiated cigarettes first were the most likely to experience prevalent ND. However, it is worth noting that those who initiated marijuana first were no less likely, statistically, to have prevalent ND as compared to those who initiated cigarettes first. Finally, youth who initiated cigarettes or other tobacco products before other substances were less likely than those starting with alcohol or marijuana to have used other drugs, such as cocaine, heroin, inhalants, and non-medical prescription drugs.

## Discussion

We found that, in 2014, 8% of US youths aged 12–21-years reported that marijuana was the first drug they used; this percentage has almost doubled since 2004. This increase could be due to a concurrent decline in those starting with cigarettes first, which dropped from about 21 to 9% over the same period. The proportion of youth initiating other tobacco products or other drugs first also declined, but to a limited extent, and there has been little change in the proportion of youth who start with alcohol first, which remained the substance youth most commonly initiate first. We also observed a significant increase in youth abstaining from substance use altogether, which rose from 36 to 46%, and therefore, it is unclear the degree to which increases in those initiating marijuana first could be due to youth abstaining or delaying cigarette smoking (Johnson et al. 2018). Higher levels of perceived risk for cigarettes compared to marijuana could be a contributing factor (Berg et al. 2015; Pacek et al. 2015). Our estimate is slightly lower than a previous estimate produced a decade ago (Gfroerer et al. 2002); however, this prior study looked only at those who started smoking marijuana within the last 12 months, which might overestimate the number who used marijuana before cigarettes or alcohol.

We found that males and older youth were more likely to start with marijuana as their first drug. Males report more opportunities to try marijuana and are less likely to perceive it as harmful than females, and therefore, lead to an increased likelihood of starting with marijuana before other substances

**Fig. 1** Percent of youth aged 12–21 years whose first drug use was marijuana, cigarettes, alcohol, other tobacco, other drugs, or no drug use by demographic characteristics and survey year. Abbreviations: American Indian/Alaska Native (AI/AN), Native Hawaiian and other Pacific Islander (NHOPI)



(Pacek et al. 2015; Van Etten and Anthony 2001). We also found that as youth aged, they were more likely to start with marijuana as their first drug compared to no drug use or using alcohol first. This could be explained by a number of age-related factors, such as greater perceived availability of marijuana and lower perceived harm relative to cigarettes and alcohol at older ages (Johnston et al. 2017). There are also important differences in the legal age of being able to purchase cigarettes (18 years) and alcohol (21 years) which may help explain why age was not significantly related to starting with marijuana first compared to cigarettes.

With the exception of Asian youth, racial/ethnic minority youth were generally more likely than White youth to start with marijuana. American Indian or Alaskan Native youth were the most likely to use marijuana first relative to no drug use or using alcohol first, but Black youth were more likely to use marijuana first compared to cigarettes first. Using data on 8th, 10th, and 12th graders in Washington state covering roughly the same time period (2004–2016), Johnson et al.

(2018) in the present issue corroborate higher rates of past 30-day marijuana among AI/AN and Black youth. American Indian youth perceive less disapproval from using marijuana by their classmates and adults compared to White youth, which might help explain our findings, is consistent with studies showing high rates of marijuana use in this group, and a greater likelihood of AI youth using marijuana before alcohol (Johnson et al. 2015; Novins et al. 2001; Stanley et al. 2014; Swaim et al. 2013).

Black youth also had a greater chance of starting with marijuana than Whites, especially compared to using cigarettes or alcohol first, which is consistent with other literature on who uses marijuana before tobacco (Golub and Johnson 2002; Kennedy et al. 2016; Vaughn et al. 2008; White et al. 2007). White youth are more likely to drink, smoke cigarettes, and start using both substances at younger ages than Blacks (Dawson 1998; Landrine et al. 1994; Roberts et al. 2016). Tolerance of situational norms and attitudes towards drinking and drunkenness are also greater among White compared to

**Table 1** Demographic and survey characteristics associated with using marijuana as the first drug used relative to no drug use, using cigarettes first, or using alcohol first ( $n = 275,559$ ), adjusted relative risk ratios (aRRR)

Variable	Marijuana vs. no drug			Marijuana vs. cigarettes			Marijuana vs. alcohol		
	aRRR	95% CI	<i>p</i> value	aRRR	95% CI	<i>p</i> value	aRRR	95% CI	<i>p</i> value
Male vs. female	1.69	(1.61, 1.78)	< 0.001	1.79	(1.71, 1.87)	< 0.001	1.83	(1.75, 1.92)	< 0.001
Age	1.69	(1.67, 1.70)	< 0.001	1.01	(1.00, 1.02)	0.249	1.06	(1.05, 1.07)	< 0.001
Race/ethnicity (vs. White)									
Black	1.69	(1.58, 1.80)	< 0.001	2.74	(2.55, 2.95)	< 0.001	2.49	(2.35, 2.64)	< 0.001
American Indian/Alaska Native	3.68	(3.03, 4.46)	< 0.001	1.91	(1.54, 2.36)	< 0.001	5.01	(4.04, 6.20)	< 0.001
Native Hawaiian or Other Pacific Islander	1.51	(1.05, 2.19)	0.027	1.28	(0.85, 1.92)	0.239	2.06	(1.42, 2.98)	< 0.001
Asian	0.30	(0.24, 0.36)	< 0.001	0.88	(0.71, 1.08)	0.210	0.59	(0.48, 0.72)	< 0.001
Multiracial	1.95	(1.71, 2.23)	< 0.001	1.59	(1.40, 1.81)	< 0.001	1.96	(1.74, 2.21)	< 0.001
Hispanic	1.39	(1.29, 1.49)	< 0.001	1.87	(1.73, 2.02)	< 0.001	1.50	(1.40, 1.61)	< 0.001
Survey year	1.01	(1.01, 1.02)	0.002	1.16	(1.15, 1.17)	< 0.001	1.07	(1.06, 1.08)	< 0.001

**Table 2** Drug used first associated with cannabis- and other drug-related outcomes among 12–21-year-olds, covariate adjusted odds ratios (aOR)

Drug used first	Heavy marijuana use among users ( <i>n</i> = 71,699)			Cannabis use disorder among users ( <i>n</i> = 71,699)			Alcohol use disorder among drinkers ( <i>n</i> = 136,399)			Nicotine dependence among smokers ( <i>n</i> = 89,202)			Other drug use <sup>c,d</sup> ( <i>n</i> = 142,630)		
	aOR	95% CI	<i>p</i> value	aOR	95% CI	<i>p</i> value	aOR	95% CI	<i>p</i> value	aOR	95% CI	<i>p</i> value	aOR	95% CI	<i>p</i> value
Models adjusted for sex, age, race/ethnicity, age of first drug use <sup>a</sup> , and number of drugs used															
Cigarettes	0.69	(0.63, 0.75)	< 0.001	0.82	(0.75, 0.90)	< 0.001	0.68	(0.64, 0.72)	< 0.001	1.00			0.62	(0.58, 0.66)	< 0.001
Alcohol	0.74	(0.68, 0.81)	< 0.001	0.89	(0.82, 0.96)	0.004	1.00			0.52	(0.49, 0.56)	< 0.001	1.00		
Marijuana	1.00			1.00			0.80	(0.74, 0.87)	< 0.001	0.92	(0.83, 1.02)	0.101	0.94	(0.86, 1.02)	0.114
Other tobacco <sup>b</sup>	0.57	(0.49, 0.66)	< 0.001	0.68	(0.59, 0.77)	< 0.001	0.89	(0.81, 0.98)	0.021	0.70	(0.59, 0.82)	< 0.001	0.42	(0.37, 0.47)	< 0.001
Other drugs <sup>c</sup>	0.60	(0.52, 0.71)	< 0.001	0.85	(0.74, 0.99)	< 0.001	0.88	(0.81, 0.95)	0.002	0.82	(0.70, 0.96)	0.013	Omitted		

<sup>a</sup> Age of first marijuana, alcohol, cigarette, or any drug use was controlled for in cannabis-related, AUD, ND, and other drug use models respectively

<sup>b</sup> Other tobacco included cigars, pipes, chew, snuff, and smokeless tobacco

<sup>c</sup> Other drugs included non-medical use of cocaine, hallucinogens, heroin, inhalants, analgesics, sedatives, stimulants, and tranquilizers

<sup>d</sup> Those having used only one drug or all five types of drugs dropped from analyses (*n* = 67,148) after controlling for number of drugs used due to no variance in the outcome

Black youth, and White peers may exert a larger influence on tobacco and alcohol behaviors compared to Black peers (Caetano and Clark 1999; Gibbons et al. 2010). Black parents are more likely than those of other races to abstain from alcohol use, and are also less likely to involve their children in family alcohol use (Peterson et al. 1994). Marijuana may be more available in Black neighborhoods and be perceived as less stigmatizing and harmful than tobacco or alcohol, which might make it a more socially acceptable alternative to tobacco and alcohol as a coping mechanism for greater victimization, discrimination, and social stress in their environment (Boardman and Alexander 2011; Furr-Holden et al. 2011; Green et al. 2016; Peterson et al. 1994; Reboussin et al. 2015; Sinclair et al. 2013; Stock et al. 2011; Storr et al. 2004). However, exploratory findings reveal that these race/ethnic differences may be more pronounced among younger adolescents (e.g., 15–16-year-olds).

Starting with marijuana first may increase the likelihood of heavy and problematic use. Even after accounting for demographics, age of marijuana onset, and the number of drug used, our results showed those who initiated marijuana first before other substances were more likely to smoke marijuana daily or near daily and currently experience CUD. In explaining these findings, it is possible that the substance youth try first might positively influence their preference and attitudes about that drug relative to others and lead them to become persistent and dependent users of that drug sooner than for substances that are tried later. Unfortunately, because our data were cross-sectional, we could not fill in the gap about youths' substance use between their first use and current experience. Nonetheless, this idea is consistent with our other findings showing that those who start with alcohol first or cigarettes first tend to be the most likely to have prevalent AUD and ND, respectively. It is also consistent with the finding by Sartor et al. (2013) that women who started with marijuana before alcohol progressed more rapidly to onset of marijuana problems than those exhibiting the reverse sequence.

However, our findings suggest that in terms of ND, there may be little difference between those who start with marijuana and later smoke cigarettes, and vice versa. Our results showed that those who started with marijuana first were statistically no less likely than those who started with cigarettes first to be nicotine dependent. High levels of co-use could be one explanation with 90% of lifetime marijuana users reporting cigarette smoking sometime in their life (Agrawal et al. 2012). Youth who start with marijuana may also have an easier and quicker time transitioning to smoking tobacco compared to other substances. Both drugs share a similar, and thus familiar, route of administration and the two drugs can be easily mixed together within a single preparation (e.g., blunts, spliffs) (Agrawal and Lynskey 2009). As shown in the paper by Nguyen and others in the present issue, adolescent

marijuana use increases the risk of daily cigarette smoking in women. Once regular cigarette smoking starts, the onset of ND symptoms can occur relatively quickly—within four weeks according to one study (DiFranza et al. 2000)—unlike for CUD and AUD, which may take several years to develop (Wagner and Anthony 2002a).

We also find that those who start with marijuana or with alcohol are equally more likely to subsequently use other drugs, such as cocaine, heroin, inhalants, or non-medical prescription drugs, compared to a lower likelihood for those who start with cigarettes or other tobacco products. Alcohol, like marijuana, has been implicated as a “gateway” drug for illegal drug use (Kandel and Kandel 2015; Kirby and Barry 2012), although critics point to alternative explanations for this relationship including the order in which youth have the opportunity to use different drugs and the role of common liability phenotypes (Morral et al. 2002; Vanyukov and Ridenour 2012). For example, youth who start with marijuana or alcohol may have more opportunities to try other illegal drugs via increased exposure to illegal markets or drug-using peers (Caulkins and Pacula 2006; Wagner and Anthony 2002b). Alcohol and marijuana may also have neurocognitive effects on adolescent brain development that impair behavioral control and lead to riskier decision-making, such as engaging in more serious drug use (Bava and Tapert 2010).

Before further discussion of this study’s implications, these findings should be viewed within the context of the following limitations. First, these data are based on retrospective self-report, and accuracy of recall for the age of substance onset could be subject to forward telescoping bias (i.e., reporting events as being closer in time than what is true) although it is unclear if this bias differs by the drug, their sequence, or the number of drugs used (Shillington et al. 2012). By restricting the sample to 12–21-year-olds, we sought to limit issues with recall, so as most youth would have initiated their first drug use within the last few years. Second, we were only able to explore prevalent outcomes associated with using marijuana first, rather than the first onset of symptoms or disordered use, which may conflate effects on incidence vs. duration. That is, we cannot account for the possibility that some who start with marijuana first may rapidly progress to heavy use, CUD, or other outcomes, but then be in remission within the year prior to interview when these outcomes were assessed. Third, analyses of potential confounders were limited to a few time-invariant demographic characteristics, since the NSDUH was not designed to assess other time-invariant or time-varying factors (e.g., parental, peer, mental health, or socioeconomic factors) present before the first drug onset, and which might help explain both using marijuana first and related outcomes.

We conclude by mentioning notable study strengths and raise future implications for research, prevention, and treatment. Strengths include the use of large, representative

samples and consistent methods across surveys that aided in promoting valid, precise, and generalizable estimates of sensitive behaviors, such as drug use. This paper demonstrates the advantage of focused follow-up questions to refine the drug onset sequence when the age of first use responses overlap. Our findings suggest important targets for public health intervention and prevention of marijuana use, especially among American Indian/Alaska Native and Black youth, who are less likely to have access to treatment or successful treatment outcomes (Peters et al. 2014; Priester et al. 2016; Vendetti et al. 2002). Specifically, drug prevention strategies may need to be better targeted to groups differently based on their risk of initiating tobacco, alcohol, or marijuana first. To the degree these trends continue and greater numbers of youth start with marijuana as their first drug, there may be an increasing need for public interventions and treatment services for marijuana-related problems.

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## Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

**Ethical Approval** The original study procedures were approved by RTI’s Institution Review Board (IRB) for the protection of human subjects. Authors had only access to the publicly available, de-identified data, and thus this research was deemed “not human subjects research” by the Johns Hopkins Bloomberg School of Public Health IRB.

**Informed Consent** All survey participants were provided informed consent.

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