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Investigating Moderation in the Prospective Relationship of Marijuana Use to Subsequent Illicit Substance Use: Evidence from Add Health

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Abstract

Whereas socially normalized substances (e.g., marijuana) may increase the probability of subsequent progression to more harmful illicit substances, previous empirical research on the topic has yielded inconsistent results. Few studies have prospectively examined whether age of first documented current marijuana use is related to later harmful illicit substance use over multiple life course stages, or considered potential moderation of the process by age of first documented current marijuana use, gender, or race/ethnicity. To investigate this topic, data from five waves of the National Longitudinal Study of Adolescent to Adult (N=20,774), spanning ages 12-42, were used to analyze the prospective association of current marijuana use at any of the five waves to current illicit substances in early middle adulthood (i.e., Wave 5), conditional on socio-demographic controls. Moderation in the effect of first documented current marijuana use on later illicit substance use was tested for three putative moderators, gender, race/ethnicity, and age of first reported current marijuana use, using interaction effects. Multiple imputation was used to address a modest amount of missing data. Results indicate that current marijuana use at any wave was strongly associated with documented current illicit substance use in early middle adulthood (OR = 4.506, $p < .001$), conditional on socio-demographic controls. Furthermore, individuals whose first documented current marijuana use occurred in young adulthood had lower odds of using more harmful illicit substances in early middle adulthood, compared to those who first reported current marijuana use in adolescence or the transition to adulthood (OR = 0.662, $p < .05$). There was no evidence of moderation by gender or racial/ethnicity. Our results suggest that individuals who report using marijuana in adolescence and the transition to adulthood have greater likelihood of more harmful illicit substance use in early middle adulthood.

Keywords

Marijuana use, Cannabis use, Illicit substance use, Cohort study, Longitudinal data

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Abstract

Whereas socially normalized substances (e.g., marijuana) may increase the probability of subsequent progression to more harmful illicit substances, previous empirical research on the topic has yielded inconsistent results. Few studies have prospectively examined whether age of first documented current marijuana use is related to later harmful illicit substance use over multiple life course stages, or considered potential moderation of the process by age of first documented current marijuana use, gender, or race/ethnicity. To investigate this topic, data from five waves of the National Longitudinal Study of Adolescent to Adult (N=20,774), spanning ages 12-42, were used to analyze the prospective association of current marijuana use at any of the five waves to current illicit substances in early middle adulthood (i.e., Wave 5), conditional on socio-demographic controls. Moderation in the effect of first documented current marijuana use on later illicit substance use was tested for three putative moderators, gender, race/ethnicity, and age of first reported current marijuana use, using interaction effects. Multiple imputation was used to address a modest amount of missing data. Results indicate that current marijuana use at any wave was strongly associated with documented current illicit substance use in early middle adulthood (OR = 4.506, $p < .001$), conditional on socio-demographic controls. Furthermore, individuals whose first documented current marijuana use occurred in young adulthood had lower odds of using more harmful illicit substances in early middle adulthood, compared to those who first reported current marijuana use in adolescence or the transition to adulthood (OR = 0.662, $p < .05$). There was no evidence of moderation by gender or racial/ethnicity. Our results suggest that individuals who report using marijuana in adolescence and the transition to adulthood have greater likelihood of more harmful illicit substance use in early middle adulthood.

Keywords: marijuana use, cannabis use, illicit substance use, cohort study, longitudinal data

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Introduction

Marijuana is the most commonly used illicit substance in the United States (U.S.) among individuals 12 years and older. Estimates indicate that 10.1% of adolescents ages 12-17 and 34.5% of emerging adults ages 18-25 report marijuana use in the past year (Substance Abuse and Mental Health Services Administration [SAMHSA], 2020). Marijuana use in early life is linked to many adverse outcomes in early adulthood, such as poor social and behavioral adjustment, mental health issues, and lower high school graduation rates (Bagot et al., 2015; Castellanos-Ryan et al., 2017; Scholes Balog et al., 2016). However, it is less clear how the long-term health and behavioral consequences of marijuana use unfold over time. In particular, few U.S.-based

longitudinal studies have examined how first documented current marijuana use is related to more harmful illicit substance use, spanning developmental periods from adolescence to early middle adulthood.

Prior research suggests that social and biological mechanisms may shape the risk of transitioning from marijuana to more harmful illicit substances. (Cadoni et al., 2001; Panlilio et al., 2013; Pistis et al., 2004). For example, Pistis et al.'s study (2004) on animal addiction, found that early exposure to marijuana in adolescent rats increases brain sensitivity to drugs of abuse such as morphine, cocaine, and amphetamines, implying that adolescents may be particularly vulnerable to the effects of marijuana. Hall and Lynskey (2005) have indicated potential socio-environmental mechanisms, as their study suggests that adolescent marijuana users may be at a higher risk of taking on more harmful illicit substances because they could gain access through their peers. Marijuana use also may increase the acceptance level of doing substances, so young marijuana users might perceive substance use as less risky or deviant such that they become less concerned about taking on more harmful illicit substances (Wagner & Anthony 2002; Reddon et al. 2018). These mechanisms could perhaps play a salient role today given that marijuana has been legalized for medical use in more than 30 states and for recreational use for 11 states and the District of Columbia (Wu, Wen & Wilson 2021).

In addition, there are various competing theoretical frameworks and explanations as to whether exposure to marijuana increases the risk of using more harmful illicit substances. For instance, the gateway hypothesis proposed by Denise Kandel and Richard Faust (1975) has been widely used to explain adolescent substance use initiation and transition to other substances. It contends that the early onset of licit substances such as alcohol and cigarettes is typically followed by more readily available illicit substances, such as marijuana, which increases the likelihood of using more harmful illicit substances (e.g., methamphetamine, heroin, and cocaine). Several studies have confirmed this general sequence of substance use progression assumed by the gateway hypothesis (Agrawal et al., 2004; Golub & Johnson 1994; Kandel & Yamaguchi 1993; Keyes, Hamilton, Kandel, 2016; Morral et al., 2002; Secades-Villa et al., 2015).

On the other hand, many people who use marijuana may not transition to more harmful illicit substances (Attaiaa et al., 2016; Choo & Robinson 2008; Golub & Johnson 1994, Mackesy-Amiti et al., 1997; Reddon et al., 2018; Tarter et al., 2006). According to Attaiaa et al. (2016) individuals who do not use more harmful illicit substances after initiating marijuana (i.e., use hard drugs or combination of licit and illicit drugs before marijuana) may have a common liability. That is, such drug users may be predisposed to genetic and environmental risks, shaping their pattern of drug use (Kendler et al., 2007). For example, Cleveland and Wiebe (2008) used data from the National Longitudinal Study of Adolescent to Adult Health (Add Health) to examine adolescent monozygotic and dizygotic twin pairs and found that those with a genetic predisposition were more likely to try marijuana and harmful illicit substances than others, suggesting that one's substance use trajectory is genetically influenced than explained by the use of a particular substance.

Empirical discrepancies in evidence regarding whether marijuana is related to more harmful illicit substance use may result from differences in study design, analytical approach, or social context of substance use. Still, they also may reflect that this relationship is more applicable to some demographic groups than others. For example, the age of first documented current

marijuana use may be reasonably suspected to moderate the strength of this relationship. Drawing from life course perspectives, Van Gundy and Rebellon (2010) argue that changing social roles and life transitions (i.e., employment, marriage, parenting) may conflict with risky behaviors like illicit substance use later on in life. Thus, the relationship of early documented exposure of marijuana to the subsequent use of more harmful illicit substances may be more applicable to adolescents than adults (p. 246). Based on a national survey, the modal time of marijuana initiation occurs during adolescence (Azagba et al., 2020). Evidence shows that those who initiate marijuana earlier, relative to later, are more likely to use illicit substances than older first-time marijuana users (Fergusson et al., 2006; Gallegos et al., 2021). Few studies have explored age of first documented current marijuana use as a potential moderator for this relationship.

Furthermore, studies report disparities in the prevalence of marijuana and illicit substance use within race/ethnicity and gender. Whites, Native Americans, and multiracial groups report a higher prevalence of marijuana use than African Americans, Hispanics, and Asian Americans (Johnson et al., 2015; McCabe et al., 2007; Pacek et al., 2012; Wu et al., 2015; Wu et al., 2011). Another study indicates that black adolescents have the lowest prevalence of illicit substance use, whereas white adolescents report the highest prevalence (Vaughn et al., 2018). Males report higher prevalence of marijuana (Pacek et al., 2012, Wallace, 1999, Wu et al., 2015), heroin, and nonmedical prescription opioid use than females (Marsh et al., 2018). Although there are clear socio-demographic disparities in rates of substance use, it is unclear if the relationship between any reported current marijuana use and the later use of more harmful illicit substances differ by race/ethnicity or gender (Ward et al., 2019)

Using five waves of the Add Health data, spanning approximately 25 years of follow-up, we tested the prospective relationship of current marijuana use reported at any of the five waves on current documented illicit substance use in early middle adulthood (Harris, 2018). Then, we investigated whether this association varies by (1) age of first documented current marijuana use, (2) gender, and (3) race/ethnicity. Specifically, we hypothesized that there would be significant positive associations between any documented current marijuana use and current illicit substance use in early middle adulthood, but that these associations would be weaker among individuals who were first documented current marijuana users at older ages. We also expected that the association of current marijuana use at any of the five waves on subsequent current illicit substance use in early middle adulthood would differ by gender and race/ethnicity, although the directions of these moderating effects remain an empirical question**.**

Methods

Participants

In this study, we analyzed data from the National Longitudinal Study of Adolescent to Adult Health (Add Health). Add Health is a comprehensive, nationally representative longitudinal survey for adolescent health. It began with data collected from an in-school sample for grades 7-12 (Wave 1). Then, four additional waves of data collection were conducted as the participants aged through their twenties, thirties, and early forties (Wave 1: 1994-1995, Wave 2: 1996, Wave 3: 2001-2002, Wave 4: 2008, and Wave 5: 2016-2018). We used all five waves of the data in the current study; missing data were addressed through multiple imputation with chained equations (White, Royston, & Wood,

2011). Our analytical sample contained 20,774 cases.

Measures

Current Illicit Substance Use. The dependent variable for this analysis was a dichotomous variable of current illicit substance use reported at Wave 5 and was constructed based on a set of questions asking the respondent's use of illegal substances in the past 30 days. Specific substances queried included cocaine, "crack," methamphetamine, "ice," heroin, LSD, PCP, ecstasy, psilocybin mushrooms, inhalants, and other illegal drugs. Respondents who reported use of at least one of these items were coded as current illicit drug users in early middle adulthood, while those who had responded no (or legitimate skip) to all items were coded as current nonusers of illicit substance in early middle adulthood.

Age of First Documented Current Marijuana Use. The primary independent variable was current marijuana use at any of the five waves, and the primary moderated variable was the age at which current marijuana use was first reported at any wave. (Waves 1-5), The operationalization of these measures was based on the following questions asked in each wave, "During the past 30 days, how many times did you use marijuana?" If persons responded that they had used marijuana in the past 30 days in Wave 1, their age in Wave 1 was recorded as age of current marijuana use. If persons responded that they had not used marijuana in Wave 1, but had in Wave 2, their age at Wave 2 was recorded as age of current marijuana use, and so on to Wave 5. Persons who did not report using marijuana in any of the five waves were coded as "no current marijuana use at any wave." In this analysis, age of first documented current marijuana use was specified as a four-level categorical variable: no current use at any wave, first reported current use before age 25 (mean [SD] age = 18.94 [2.95]), first reported current use from ages 25-38 (mean [SD] age = 30.22 [3.67]), and first reported current use after age 38 (mean [SD] age = 39.2 [1.03]), Thus, adolescence and the transition to adulthood was defined prior to age 25, as new onset and dependence of marijuana decline significantly after 25 (Bostwick, 2012).

The cut-points were indicated by a combination of the Add Health wave structure and life course perspectives on delayed transition to adulthood (i.e., extended adolescence) in contemporary Western societies. Support for this extended adolescence perspective comes from demographic literature showing shifts in the ages of adult roles transitions (e.g., marriage, leaving the parental home, and employment) in the U.S. (Furstenberg, 2010). Furthermore, there is also neuroscience research that dovetails with this demographic data, arguing that brain maturation continues up to age 25, particularly in terms of myelination. Thus, there are multiple lines of bio-behavioral evidence suggesting that individuals may exhibit heightened vulnerability to xenobiotic exposures up to age 25 (Arain et al., 2013). Persons reporting marijuana use at any wave were coded as first documented current marijuana users in the dichotomous coding of marijuana use.

The choice of selecting current use of marijuana before 25 years of age as a reference group and the specification of the moderation variable more generally was guided by the ability to test the hypothesis of interest, i.e., that the strength of association between current marijuana use and illicit substance use varied by age at first observed current marijuana use. More specifically, the hypothesis tested is that marijuana use at the earliest developmental periods is particularly strongly associated with illicit drug use later in life, compared to individuals who first

report current marijuana use at older ages.

Socio-demographic Characteristics. Each hypothesis was tested in an unconditional and conditional model. All conditional models adjusted for a set of socio-demographic characteristics (i.e., family structure, childhood household income, parental education, adult household income (Wave 5), adult educational attainment (Wave 5), gender, age, race/ethnicity, nativity, and age) as well as for illicit substance use at Wave 1. Family structure was coded as a four-level categorical variable (i.e., (1) one biological parent, (2) biological plus stepparent, (3) other family structure, and a reference category of (4) two biological parents). Parental education included responses from all of the respondents' biological and residential mother and/or father figures. Responses were averaged if educational attainment was provided from multiple parent figures. Childhood household income (measured in thousands) was logged to reduce substantial skew (Adkins, Wang, Dupre, van den Oord, & Elder, 2009). Wave 5 household income was coded as an ascending 13-level categorical variable with level 1 corresponding to < $5000 and level 13 top coded as > $200,000. Wave 5 educational attainment was coded as an ascending 11-level categorical variable with level 1 corresponding to ≤ 8th grade and level 11 corresponding to a completed doctoral-level degree. Race/ethnicity was coded as black/African American, Hispanic American, Native American, Asian American, white (reference category), multiracial, and "other" race/ethnicity. Respondent sex was coded as female or male. Nativity status was coded as 1st (i.e., subject and parents born abroad), 2nd (i.e., subject born in U.S., parents born abroad), or 3rd (i.e., subject and parents born in the U.S.) generation.

Severe Childhood Adversity. Measures of childhood adversity comprised five dichotomous indicators: *sexual abuse, physical abuse, neglect, drugs/alcohol accessible at home, and parental incarceration,* occurring in adolescence. These five severe childhood adversities were operationalized as follows (item phrasing condensed for brevity). *Sexual abuse* was indicated by endorsement of any of the following four items: the respondent sexually interacted with a parent or other adult caregiver by grade 6; the respondent sexually interacted with a parent or other adult caregiver as a minor; or either of two items asking if the respondent had been sexually coerced as a minor, either physically, or non-physically (e.g., drugged). *Physical abuse* was indicated by endorsement of either of two items: the respondent was slapped, hit, or kicked by parents or other adult care-givers by grade 6; or as a minor. *Neglect* was indicated by endorsement of any of the following items: the respondent's parent/s or other adult caregiver/s had not taken care of basic needs, such as keeping the respondent clean or providing food or clothing by grade 6; respondent frequently felt unloved or unwanted by parent/s or caregiver/s as a minor. *Drugs/alcohol accessible at home* was indicated by endorsement of any of the following items: the respondent had easy access to illegal drugs in the home; respondent reported frequent heavy drinking in the home (e.g., open containers, intoxicated people). *Parental incarceration* was indicated by endorsement of any of the following items: the respondent's biological father, biological mother, "father figure," or "mother figure" went to jail/prison, when respondent was a minor (Alley et al., 2021).

Data Analysis

To address a moderate amount of missing data across waves, we used the multiple

imputation (MI) method, multiple imputation with chained equations (MICE) (White, Royston, & Wood, 2011). We used a conservative 50 imputations in all MI analyses (von Hippel, 2018). MI is generally superior to listwise deletion, as it performs optimally under "missing completely at random" (MCAR) conditions, as well as in scenarios in which data is "missing at random" (MAR). Thus, MI is the preferred method as it reduces possible sources of parameter estimate bias and maximizes statistical power, compared to listwise deletion (Little & Rubin, 2019; Rubin, 2004). Primary inferential analysis used logistic regression to model a dichotomous outcome variable (i.e., current illicit substance use reported at Wave 5). Sensitivity analyses using Poisson regression were used to test the robustness of results (Appendices A and B). Missingness by analysis variable is summarized in Appendix C.

Our analysis consisted of four pairs of logistic regression models, with an unconditional and conditional model testing each of the four hypotheses. The primary hypothesis was tested in the first model pair, predicting whether those who were current marijuana users at any of the five waves had greater odds of current illicit substance use reported in early middle adulthood, compared to those who did not report any current marijuana use at the five waves (referent). Then, we examined moderation of this relationship by age of first documented current marijuana use (i.e., no current marijuana use at any wave, first reported current use before age 25 (referent), first reported current use at ages 25-38, and first reported current use after age 38), race/ethnicity and gender. Moderation effects were modeled as interaction effects between current marijuana use at any wave and the dichotomous indicators for race/ethnicity and gender. To specify moderation effects for age of first documented current marijuana use, we created three dummy indicators corresponding to adolescence/transition to adulthood, young adulthood, early middle adulthood, which is equivalent to interacting a set of age of first documented current marijuana use dichotomous indicators with our primary independent variable, current marijuana use at any wave.

Results

Descriptive Statistics

Table 1 shows descriptive statistics for the analysis variables. In summary, the dependent variable, respondents who reported current illicit substance use in W5, consisted of 4% of the sample. The percentage of those who reported current marijuana use at any of the five waves (independent variable) was distributed across the sample as follows. Respondents, who first documented current marijuana use in adolescence (35%), were the modal age category of first documented current marijuana users across the age categories, and 42% of respondents reported no current marijuana use at all five waves. The frequency of first documented current marijuana use declined at older ages from adolescence (current marijuana use reported at ages 25-38: 6%; current marijuana use reported after age 38: 2%).

The mean childhood household income (measured in thousands at Wave 1) was 3.49 thousand annually, and ranged 0-99, while the mean category of parental education was 5.54 and ranged 0-9 (0 = no formal education, to 9 = graduate education). Respondents' mean category of household income (measured at Wave 5) was 8.82, which corresponds to the upper portion of the $40,000 to $49,999 interval. Last, respondent's mean category of educational attainment (measured in Wave 5) was 7.3 corresponding to "some college." As the

descriptive statistics provided in Table 1 were based on imputed data, some imputed values exceeded the non-imputed ranges described above; this is an expected and non-problematic feature of multiple imputation (Little & Rubin, 2019).

Inferential Statistics

Models 1 and 2 of Table 2 describe the unconditional and conditional tests, respectively, of our primary hypothesis that current marijuana use at any of the five waves is significantly associated with current illicit substance use reported in early middle adulthood (Wave 5). Both the unconditional and conditional models offer strong support for our primary hypothesis ($p < .001$). The

Table 1

Descriptive Statistics N = 20,774

Variable	Percentage	SD	min	max	N
Current illicit substance use reported at Wave 5	0.04	0.19	0	1	20774
Age of first documented current marijuana use					
No current marijuana use reported at any wave	0.42	0.49	0	1	20774
Current marijuana use first reported before age 25	0.35	0.48	0	1	20774
Current marijuana use first reported ages 25-38	0.06	0.23	0	1	20774
Current marijuana use first reported after age 38	0.02	0.13	0	1	20774
Socio-demographic characteristics					
Two biological parents (ref)	0.50	0.50	0	1	20774
Biological and step parent	0.08	0.27	0	1	20774
Biological parent	0.30	0.46	0	1	20774
Other family	0.12	0.33	0	1	20774
Current illicit substance use reported at Wave 1	0.12	0.32	0	1	20774
Childhood household income	3.49	0.86	-0.06	6.91	20774
Male (ref)	0.49	0.50	0	1	20774
Female	0.51	0.50	0	1	20774
Mean parental education	5.54	2.10	-2	11.52	20774
Age (Wave 5)	38.15	1.74	33.88	43.08	20774
Income (Wave 5)	8.82	2.98	-2.92	19.92	20774
Educational attainment (Wave 5)	7.30	2.41	-2.18	16.13	20774
White (ref)	0.58	0.49	0	1	20774
Hispanic American	0.17	0.38	0	1	20774
Black/African American	0.21	0.41	0	1	20774
Native American	0.01	0.11	0	1	20774
Asian American	0.07	0.25	0	1	20774
Other race/ethnicity	0.08	0.27	0	1	20774
Multiracial	0.05	0.22	0	1	20774
Immigrant generation 1	0.12	0.33	0	1	20774
Immigrant generation 2	0.06	0.23	0	1	20774
Immigrant generation 3+	0.82	0.38	0	1	20774
Sexual abuse	0.15	0.36	0	1	20774
Physical abuse	0.15	0.36	0	1	20774
Drug/alcohol accessible at home	0.10	0.30	0	1	20774
Parental incarceration	0.13	0.34	0	1	20774
Neglect	0.25	0.43	0	1	20774

Table 2

Logistic Regression Predicting Illicit Substance Use by Current Marijuana Use at Any Wave and Age of First Documented Current Marijuana Use, and Socio-demographic Factors in Add Health, Waves 1-5 (MI = 50) N = 20,774

	Model 1		Model 2		Model 3		Model 4	
	OR	t	OR	t	OR	t	OR	t
Primary hypothesis								
No current marijuana use reported at any wave (ref)	1	(.)	1	(.)	1	(.)	1	(.)
Current marijuana use at one or more waves	5.630***	(15.58)	4.506***	(13.20)				
Socio-demographic characteristics								
Two biological parents (ref)			1	(.)			1	(.)
Biological and step parent			1.060	(0.29)			1.062	(0.30)
Biological parent			1.019	(0.13)			1.018	(0.12)
Other family			1.006	(0.03)			1.011	(0.06)
Current illicit substance use (Wave 1)			1.422**	(2.68)			1.388*	(2.48)
Childhood household income			1.060	(0.73)			1.060	(0.72)
Male (ref)			1	(.)			1	(.)
Female			0.552***	(-5.58)			0.550***	(-5.61)
Mean parental education			1.049	(1.58)			1.048	(1.54)
Age (Wave 5)			0.875***	(-4.56)			0.867***	(-4.74)
Income (Wave 5)			0.892***	(-5.87)			0.892***	(-5.92)
Educational attainment (Wave 5)			0.973	(-0.99)			0.973	(-0.99)
White (ref)			1	(.)			1	(.)
Hispanic American			1.047	(0.23)			1.050	(0.24)
Black/African American			0.574**	(-3.21)			0.579**	(-3.15)
Native American			1.737	(1.61)			1.719	(1.58)
Asian American			1.391	(1.36)			1.400	(1.38)
Other race/ethnicity			1.019	(0.09)			1.013	(0.06)
Multiracial			0.975	(-0.11)			0.978	(-0.09)
1st generation American (ref)			1	(.)			1	(.)
2nd generation American			1.115	(0.41)			1.101	(0.36)
3rd generation American			0.636	(-1.76)			0.633	(-1.77)
Sexual abuse			1.442**	(2.92)			1.444**	(2.93)
Physical abuse			1.216	(1.37)			1.211	(1.34)
Drug/alcohol accessible at home			1.025	(0.17)			1.020	(0.13)
Parental incarceration			1.467*	(2.60)			1.455*	(2.54)
Neglect			0.979	(-0.17)			0.975	(-0.20)
Moderation by age at which current marijuana use was first reported								
No current marijuana use reported at any wave					0.169***	(-15.68)	0.212***	(-13.11)
Current marijuana use first reported before age 25 (ref)					1	(.)	1	(.)
Current marijuana use first reported after ages 25- 38					0.656*	(-2.36)	0.662*	(-2.24)
Current marijuana use first reported after age 38					0.954	(-0.18)	1.167	(0.57)

Note.
Exponentiated coefficients; t statistics in parentheses. *p < .05; **p < .01; ***p < .001

more conservative conditional estimates show that, adjusting for socio-demographic factors (and current illicit substance use reported in Wave 1), individuals who were current marijuana users at any wave have ~ 350% greater odds of current illicit substance use reported in early middle adulthood, relative to those who did not report any current marijuana use at any wave (reference group) ($p < .001$). Significant control variable effects from Model 2 include increased odds associated with current illicit substance use reported at Wave 1 (OR = 1.422, $p = .001$), and decreased odds associated with female gender (OR = 0.552, $p < .001$), Wave 5 age (OR = 0.875, $p < .001$), Wave 5 household income (OR = 0.892, $p < .001$), and black race/ethnicity (OR = 0.574, $p = .001$), sexual

abuse (OR = 1.442, p = .01), parental incarceration (OR = 1.467, p = .05). Model 3 and 4 of Table 2 describe the unconditional and conditional tests, respectively, of our secondary hypotheses that the effect of prospective current marijuana use at any of the five waves on current illicit substance use in early middle adulthood varies by age of first documented current marijuana use, with greater odds seen among those who first

Table 3

Logistic Regression Predicting Illicit Substance Use by Marijuana Use, Gender, Race/Ethnicity Waves 1-5 (MI = 50) N = 20,774

	Model 5		Model 6		Model 7		Model 8	
	OR	t	OR	t	OR	t	OR	t
Moderation by gender								
No current marijuana use reported at any wave	1	(.)	1	(.)	1	(.)	1	(.)
Current marijuana use at one or more waves	4.877***	(11.28)	4.213***	(9.91)	5.672***	(10.83)	4.299***	(9.13)
Female	0.522**	(-3.06)	0.483***	(-3.35)			0.553***	(-5.54)
Marijuana*Female	1.265	(0.99)	1.188	(0.72)				
Male (ref)	1	(.)	1	(.)			1	(.)
Socio-demographic characteristics								
Two biological parents (ref)			1	(.)			1	(.)
Biological and step parent			1.060	(0.29)			1.063	(0.30)
Biological parent			1.019	(0.13)			1.021	(0.14)
Other family			1.005	(0.03)			1.008	(0.04)
Current illicit substance use (Wave 1)			1.422**	(2.68)			1.435**	(2.75)
Childhood household income			1.061	(0.73)			1.060	(0.73)
Mean parental education			1.049	(1.58)			1.049	(1.57)
Age (Wave 5)			0.875***	(-4.55)			0.875***	(-4.57)
Income (Wave5)			0.892***	(-5.87)			0.892***	(-5.86)
Educational attainment (Wave 5)			0.973	(-1.00)			0.973	(-0.98)
White (ref)			1	(.)	1	(.)	1	(.)
Hispanic American			1.048	(0.23)	1.244	(0.71)	1.087	(0.25)
Black/African American			0.576**	(-3.19)	0.524	(-1.75)	0.438*	(-2.20)
Native American			1.734	(1.60)	3.363*	(2.12)	2.323	(1.46)
Asian American			1.390	(1.36)	1.639	(1.46)	1.293	(0.70)
Other race/ethnicity			1.019	(0.08)	0.967	(-0.08)	0.873	(-0.32)
Multiracial			0.974	(-0.11)	1.013	(0.02)	0.921	(-0.15)
1st generation American (ref)			1	(.)			1	(.)
2nd generation American			1.115	(0.41)			1.118	(0.42)
3rd generation American			0.636	(-1.76)			0.641	(-1.73)
Sexual abuse			1.438**	(2.89)			1.439**	(2.90)
Physical abuse			1.217	(1.37)			1.216	(1.37)
Drug/alcohol accessible at home			1.026	(0.17)			1.025	(0.16)
Parental incarceration			1.468*	(2.60)			1.469*	(2.60)
Neglect			0.980	(-0.16)			0.978	(-0.18)
Moderation by race/ethnicity								
Marijuana*Hispanic American					0.870	(-0.41)	0.943	(-0.17)
Marijuana*Black/African American					1.401	(0.85)	1.394	(0.84)
Marijuana*Native American					0.630	(-0.72)	0.661	(-0.64)
Marijuana*Asian American					0.996	(-0.01)	1.112	(0.28)
Marijuana*Other race/ethnicity					1.280	(0.52)	1.229	(0.43)
Marijuana*Multiracial					1.104	(0.17)	1.067	(0.11)

Note.

Exponentiated coefficients; t statistics in parentheses. *p < .05; **p < .01; ***p < .001

reported current marijuana use at younger ages. Both the unconditional and conditional models offer support for this hypothesis ($p < .05$). The more conservative conditional estimates show that, adjusting for socio-demographic factors (and current illicit substance use reported at Wave 1), individuals who first documented current marijuana use in young adulthood (i.e., ages 25-38) have ~ 34% lower odds of current illicit substance use reported in early middle adulthood, relative to the reference category of individuals who first reported current marijuana use in adolescence and the transition to adulthood (i.e., ages 12-24) (OR = 0.662, $p = .05$). Individuals who were first documented current marijuana users in early middle adulthood (i.e., ages 38-43) show no significant difference in odds, relative to the reference category of individuals who first reported current marijuana use in adolescence or the transition to adulthood ($p > .05$). The significance, direction, and magnitude of the control variables was unchanged from the previous conditional model.

Table 3 describes parameter estimates testing the second and third secondary hypotheses that the effect of prospective current marijuana use on current illicit substance use in early middle adulthood varies by gender (Models 5 and 6) and race/ethnicity (Models 7 and 8). Based on both unconditional and conditional models, there was no support for the gender and racial/ethnic moderation hypotheses. There were no significant gender or race/ethnic differences in odds of current illicit substance use reported in early middle adulthood after first documented current marijuana use at any wave ($p > .05$).

Discussion

Whereas prior research indicates that exposure to marijuana in adolescence is linked to a range of adverse outcomes in early adulthood, it is less clear how first documented current marijuana use across different life stages is related to more harmful illicit substance use in early middle adulthood (Bagot et al., 2015; Castellanos-Ryan et al., 2017; Scholes Balog et al., 2016). Using all five available longitudinal waves of Add Health, spanning a developmental period from early adolescence (~ age 12) to early middle adulthood (~ age 42), we examined the prospective association of current marijuana use at any of the five waves from adolescence to early middle adulthood on subsequent current illicit substance use reported in early middle adulthood. Our findings show that those who reported current marijuana use at any of the five waves were significantly associated with increased odds of current illicit substance use in early middle adulthood. We also examined the moderating effects of age of first documented current marijuana use, gender, and race/ethnicity. The results showed that participants who first documented current marijuana use in adulthood (ages 25-38) had significantly lower odds of current illicit substance use in early middle adulthood than those who first documented current marijuana use at earlier ages (i.e., ages 12-24). We found no other moderating effects.

In addition, several more studies of U.S. adolescents also have found that exposure to marijuana is linked to greater risk of using more harmful illicit substances (Keyes et al., 2016; Secades-Villa et al. 2015; Woodcock et al. 2015). However, contradictory results also have been shown (Choo et al., 2008; Mackesy-Amiti et al., 1997; Tarter et al., 2006). Jorgensen and Wells (2022) used Add Health and propensity score matching, a non-experimental causal inference approach. They considered other potential causes (i.e., peer association, victimization) that underlie the sequence from marijuana to more harmful illicit substances and concluded that marijuana use has no causal effect on more

harmful illicit substance use. Our study, on the other hand, sought to examine a slightly different research question. We were interested in whether first documented current marijuana use across different life stages is linked to current illicit substance use in early middle adulthood. We found evidence that a temporal sequence from first documented current marijuana use at any wave to current illicit substance use persists into study participants' forties. The discrepancy in our study's findings also may be due to the fact that we used a different methodological approach. We used a first documented current use at any wave specification of marijuana, whereas, Jorgensen and Wells (2022) measured infrequent and frequent marijuana use as a treatment effect within a quasi-experimental context.

A novel feature of the current study is that we examined the role of age of first documented current marijuana use as a potential moderator. Theoretically speaking, young users are more prone to the subsequent use of particular drugs than adults due to elevated risk propensity and are more susceptible to peer influence (Hall & Lynskey, 2005; Miller & Hurd 2017)**.** Little empirical work has been conducted to examine this research question. The limited available evidence is inconsistent. On the one hand, some studies show that those who first used marijuana at an early age are more likely to use more harmful illicit substances than those who are older first-time marijuana users (Fergusson et al., 2006; Gallegos et al., 2021; Miller & Hurd 2017). On the other hand, an earlier study reported that early-onset into marijuana would not lead to problematic use or rapid progression into the use of other drugs (Kandel & Chen 2000). Instead, other factors such as motivation for substance use, dysfunctional behaviors (i.e., psychopathology and delinquency), and contact with individuals engaged in illegal activities (when buying or using marijuana is illegal) were shown to be more strongly associated with further substance use than the age of initial marijuana use.

Our results add complexity to this picture. On average, in the Add Health sample, participants who first documented current marijuana use in adulthood had lower odds of current illicit substance use than those who had first documented current marijuana use in adolescence and the transition to adulthood. That said, it is important to note that the oldest first documented current marijuana users in our study (ages 38-43) did not differ from those who first reported current marijuana use during adolescence in their odds of more harmful illicit substance use in early middle adulthood. More research in independent samples is needed to clarify the implications of age of first documented current marijuana use and subsequent use of more harmful illicit substances.

As to other moderating effects, one previous study found that males were more at risk of misusing prescription opioids after initial marijuana use relative to females who first used marijuana (Fiellin et al., 2013; Becker et al., 2017; Braymiller et al., 2018). However, our results revealed no difference by gender. That is, males and females who reported current marijuana use at any wave did not differ in their odds of subsequent current illicit substance use reported in early middle adulthood. Nor did we find any moderating effect of race/ethnicity. While previous studies indicate disparities in prevalence of exposure to marijuana and illicit substances within race/ethnicity and gender (Johnson et al., 2015; Pacek et al., 2012; Wu et al., 2015; Wu et al., 2011), our evidence of no significant interaction effect within gender and race/ethnicity imply that the strength and direction of first documented current marijuana use at any wave on current illicit substance use reported in early middle adulthood are not specific to certain

subpopulations. Zhang et al. (2021) found differences within race/ethnicity in substance initiation and transition. Whereas these differences were linked to an adolescent's racial/ethnic background, overall, they suggest that different initial substances used are linked to different substance use trajectories. Thus, future research should expand its focus to include other potential substance use pathways, to improve our understanding of substance use disparities across these subpopulations. Research on this topic also should explore poly-substance use as a possible outcome, as growing evidence suggests it is a distinct risky behavior (Attaiaa et al, 2016).

Limitations and Strengths

The limitations of this study are noteworthy. Although Add Health is arguably the best source of data on adolescent-to-adult development, the study participants experienced adolescence in the 1990s – a different social environment compared to today's adolescents. Therefore, to some extent, social determinants, and behavioral consequences of adolescent experiences in the Add Health sample may not hold for the current adolescent population. Also, we used observational data and only can show associations, not causation. A major limitation of this study is that we use a "past 30 day" measure of marijuana and illicit drug use as a proxy for whether respondents have ever used these drugs. This has significant built-in measurement error, as it is possible that those who did not use marijuana and/or illicit drugs within the past 30 days have used it in their lifetime. Our operational definition of marijuana use only can determine current use by wave and not age of initial use or never use. This is perhaps why our study's findings may conflict with previous research that has used a measure that asks respondents if they have ever used marijuana, as such research is able to determine the age of initiation. In addition, our operational definition of marijuana and illicit substance use is unable to establish experimental versus heavy/frequent use. We did not control for alcohol use in our model. Alcohol is a potential gateway drug and considered as part of the causal pathway to illicit substances, so controlling for alcohol may remove part of the causal mechanism. For this reason, we did not adjust for alcohol use, but recommend future research modeling sequences of progression of alcohol, marijuana, and more harmful illicit drug use.

Strengths

Despite these limitations, our study has several strengths, particularly regarding the length of the follow-up period (~ 25 years) and the investigation of novel hypotheses. Few U.S.-based studies to date have examined the association of current marijuana use at any wave from adolescence to early middle adulthood on current illicit substances reported in early middle adulthood, prospectively. Another unique contribution of our study was that we explored the role of age of first documented current marijuana use, race/ethnicity, and gender in contributing to this relationship, an issue that few studies have examined.

Implications for Health Behavior Research

A key implication of this study for health behavior research is that prevention efforts should focus on those who are current marijuana users in adolescence and the transition to adulthood, as they were significantly associated with more harmful illicit substance use later on in life. Our study also indicates that there could be other determinants alongside age of first

documented current marijuana use, shaping progression to more harmful illicit substances. Gallegos et al. (2021) suggest that psychosocial factors such as emotional detachment from family and susceptibility to peer pressure were linked to early marijuana initiation. Future research should incorporate such contextual factors that underlie the relationship of first documented current marijuana use on subsequent illicit substance use when examining first documented marijuana use across different age groups. Such an approach may provide greater insight into the social environment of young marijuana users and guide in more targeted intervention. Furthermore, the long-term health consequences of marijuana are largely unknown and warrant investigation in future longitudinal based studies, especially now that marijuana has become more widely used than tobacco or alcohol among adolescents (SAMHSA, 2020).

Discussion Question

Our study indicates that adolescents and those transitioning to adulthood reported the highest percentage of current marijuana use and have a higher likelihood of engaging in harmful health behaviors, such as further substance use later on in life. What strategies and interventions can be used to address this issue?

Ethical Approval Statement

All participants provided written and informed consent to partake in the Add Health study in accordance with the University of North Carolina School of Public Health Institutional Review Board guidelines. This project has been approved by the University of Utah Institutional Review Board (IRB_00107767).

Potential Author Conflicts

The authors report no conflicts of interest.

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Appendix A

Poisson Regression with Sandwich Robust Standard Errors Predicting Illicit Substance Use by Marijuana Use and Age of Current Use Waves 1-5 (MI = 50) N = 20,774

	Model 1		Model 2		Model 3		Model 4	
	OR	t	OR	t	OR	t	OR	t
Primary hypothesis								
No current marijuana use reported at any wave (ref)	1	(.)	1	(.)				
Current marijuana use at one or more waves	5.302***	(15.31)	4.215***	(12.91)				
Socio-demographic characteristics								
Two biological parents (ref)			1	(.)			1	(.)
Biological and step parent			1.056	(0.29)			1.059	(0.31)
Biological parent			1.019	(0.14)			1.019	(0.14)
Other family			1.007	(0.04)			1.011	(0.07)
Illicit substance use (Wave 1)			1.373**	(2.62)			1.342*	(2.43)
Childhood household income			1.055	(0.71)			1.054	(0.70)
Male (ref)			1	(.)			1	(.)
Female			0.578***	(-5.47)			0.577***	(-5.51)
Mean parental education			1.044	(1.54)			1.044	(1.50)
Age (Wave 5)			0.885***	(-4.45)			0.877***	(-4.63)
Income (Wave 5)			0.902***	(-5.80)			0.901***	(-5.85)
Educational attainment (Wave 5)			0.975	(-0.98)			0.975	(-0.99)
White (ref)			1	(.)			1	(.)
Hispanic American			1.043	(0.23)			1.046	(0.24)
Black/African American			0.598**	(-3.13)			0.603**	(-3.08)
Native American			1.601	(1.55)			1.584	(1.52)
Asian American			1.355	(1.34)			1.363	(1.37)
Other race/ethnicity			1.016	(0.08)			1.010	(0.05)
Multiracial			0.978	(-0.10)			0.980	(-0.09)
1st generation American (ref)			1	(.)			1	(.)
2nd generation American			1.102	(0.40)			1.090	(0.35)
3rd generation American			0.658	(-1.76)			0.656	(-1.77)
Sexual abuse			1.392**	(2.84)			1.393**	(2.85)
Physical abuse			1.193	(1.34)			1.188	(1.30)
Drug/alcohol accessible at home			1.021	(0.15)			1.016	(0.11)
Parental incarceration			1.414*	(2.55)			1.402*	(2.49)
Neglect			0.981	(-0.16)			0.978	(-0.19)
Moderation by age at which current marijuana use was first reported								
No current marijuana use reported at any wave					0.180***	(-15.43)	0.227***	(-12.84)
Current marijuana use first reported before age 25 (ref)					1	(.)	1	(.)
Current marijuana use first reported after ages 25- 38					0.673*	(-2.30)	0.686*	(-2.16)
Current marijuana use first reported after age 38					0.957	(-0.18)	1.153	(0.56)

Note.
Exponentiated coefficients; t statistics in parentheses. *p < .05; **p < .01 ***p < .001

Appendix B

Poisson Regression with Sandwich Robust Standard Errors Predicting Illicit Substance Use by Marijuana Use, Gender and Race/Ethnicity Waves 1-5 (MI = 50) N = 20,774

	Model 5		Model 6		Model 7		Model 8	
	OR	t	OR	t	OR	t	OR	t
Moderation by gender								
No current marijuana use reported at any wave	1	(.)	1	(.)	1	(.)	1	(.)
Current marijuana use at one or more waves	4.557***	(11.04)	3.893***	(9.63)	5.348***	(10.66)	4.068***	(8.96)
Female	0.526**	(-3.05)	0.493**	(-3.31)			0.580***	(-5.44)
Marijuana*Female	1.290	(1.09)	1.225	(0.87)				
Male (ref)	1	(.)	1	(.)			1	(.)
Socio-demographic characteristics								
Two biological parents (ref)			1	(.)			1	(.)
Biological and step parent			1.056	(0.29)			1.059	(0.31)
Biological parent			1.019	(0.14)			1.021	(0.15)
Other family			1.006	(0.04)			1.009	(0.05)
Current illicit substance use reported at Wave 1			1.373**	(2.62)			1.385**	(2.70)
Childhood household income			1.055	(0.72)			1.054	(0.71)
Mean parental education			1.045	(1.55)			1.044	(1.53)
Age (Wave 5)			0.885***	(-4.44)			0.885***	(-4.47)
Income (Wave5)			0.901***	(-5.81)			0.902***	(-5.79)
Educational attainment (Wave 5)			0.975	(-0.99)			0.975	(-0.97)
White (ref)			1	(.)	1	(.)	1	(.)
Hispanic American			1.044	(0.23)	1.239	(0.70)	1.094	(0.28)
Black/African American			0.600**	(-3.11)	0.527	(-1.74)	0.449*	(-2.15)
Native American			1.599	(1.55)	3.242*	(2.12)	2.284	(1.49)
Asian American			1.354	(1.34)	1.625	(1.45)	1.304	(0.74)
Other race/ethnicity			1.016	(0.08)	0.967	(-0.08)	0.883	(-0.30)
Multiracial			0.977	(-0.11)	1.012	(0.02)	0.928	(-0.14)
1st generation American (ref)			1	(.)			1	(.)
2nd generation American			1.102	(0.40)			1.107	(0.41)
3rd generation American			0.659	(-1.76)			0.665	(-1.71)
Sexual abuse			1.387**	(2.80)			1.389**	(2.82)
Physical abuse			1.193	(1.34)			1.193	(1.34)
Drug/alcohol accessible at home			1.022	(0.15)			1.021	(0.15)
Parental incarceration			1.414*	(2.55)			1.415*	(2.55)
Neglect			0.982	(-0.15)			0.980	(-0.17)
Moderation by race/ethnicity								
Marijuana*Hispanic American					0.868	(-0.43)	0.933	(-0.21)
Marijuana*Black/African American					1.419	(0.90)	1.416	(0.89)
Marijuana*Native American					0.603	(-0.82)	0.622	(-0.78)
Marijuana*Asian American					0.962	(-0.10)	1.058	(0.15)
Marijuana*Other race/ethnicity					1.257	(0.49)	1.203	(0.40)
Marijuana*Multiracial					1.095	(0.16)	1.059	(0.10)

Note.
Exponentiated coefficients; t statistics in parentheses. *p < .05; **p < .01; ***p < .001

Appendix C

Percent Missingness across All Variables

Variable	Missing	Total	Percent Missing
Current illicit substance use (Wave 5)	8,516	20,774	40.99
Two biological parents	29	20,774	0.14
Biological and step parent	29	20,774	0.14
Biological parent	29	20,774	0.14
Other family	29	20,774	0.14
Illicit substance use at Wave 1	287	20,774	1.38
Childhood household income	5,423	20,774	26.1
Male (ref)	31	20,774	0.15
Female	31	20,774	0.15
Mean parental education	759	20,774	3.65
Age (Wave 1)	46	20,774	0.22
Income (Wave 5)	9,427	20,774	45.38
Educational attainment (Wave 5)	8,496	20,774	40.9
White (ref)	29	20,774	0.14
Hispanic American	91	20,774	0.44
Black/African American	29	20,774	0.14
Native American	29	20,774	0.14
Asian American	29	20,774	0.14
Other race/ethnicity	29	20,774	0.14
Multiracial	29	20,774	0.14
Immigrant generation 1	906	20,774	4.36
Immigrant generation 2	1,259	20,774	6.06
Immigrant generation 3+	4,478	20,774	21.56
Sexual abuse	5,750	20,774	28
Physical abuse	3,130	20,774	15.07
Drug/alcohol accessible at home	32	20,774	0.15
Parental incarceration	5,073	20,774	24
Neglect	5,448	20,774	26
Current marijuana use (Wave 1)	450	20,774	2.17
Current marijuana use (Wave 2)	6,289	20,774	30.27
Current marijuana use (Wave 3)	5,628	20,774	27.09
Current marijuana use (Wave 4)	5,090	20,774	24.5
Current marijuana use (Wave 5)	8,488	20,774	40.86