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## Predictive validity of cannabis consumption measures: Results from a national longitudinal study

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#### Abstract

**Background**—Validating the utility of cannabis consumption measures for predicting later cannabis related symptomatology or progression to cannabis use disorder (CUD) is crucial for prevention and intervention work that may use consumption measures for quick screening. This study examined whether cannabis use quantity and frequency predicted CUD symptom counts, progression to onset of CUD, and persistence of CUD.

**Methods**—Data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) at Wave 1 (2001–2002) and Wave 2 (2004–2005) were used to identify three risk samples: (1) current cannabis users at Wave 1 who were at risk for having CUD symptoms at Wave 2; (2) current users without lifetime CUD who were at risk for incident CUD; and (3) current users with past-year CUD who were at risk for persistent CUD. Logistic regression and zero-inflated Poisson models were used to examine the longitudinal effect of cannabis consumption on CUD outcomes.

**Results**—Higher frequency of cannabis use predicted lower likelihood of being symptom-free but it did not predict the severity of CUD symptomatology. Higher frequency of cannabis use also predicted higher likelihood of progression to onset of CUD and persistence of CUD. Cannabis use

Conflict of Interest The authors declare no conflicts of interest.

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**Contributors** Buu and Lin conceived the study. Buu provided leadership for the team and completed the manuscript. Hu and Lin conducted statistical analysis and drafted the method section. Pampati and Arterberry conducted literature review and drafted the introduction section. All authors contributed to and approved the final manuscript.

quantity, however, did not predict any of the developmental stages of CUD symptomatology examined in this study.

**Conclusions**—This study has provided a new piece of evidence to support the predictive validity of cannabis use frequency based on national longitudinal data. The result supports the common practice of including frequency items in cannabis screening tools.

#### Keywords

cannabis use disorder; consumption; onset; persistence

#### 1. Introduction

Measures of substance consumption have not been included as part of the commonly adopted diagnostic criteria for substance use disorders such as the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994) and Fifth Edition (DSM-5; APA, 2013). Yet, a paper based on the first wave of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) has shown that among individuals with past-year use of cannabis, the frequency and quantity of cannabis use differed by the DSM-IV cannabis use disorder (CUD) status (Moss et al., 2012). Another NESARC study (Compton et al., 2009) aggregated the frequency and quantity items into a dichotomous consumption variable (smoking at least one joint per week) and included it with the DSM-IV CUD criteria in an item response theory analysis, with findings suggesting that this consumption criterion had excellent psychometric properties and represented the mild end of the CUD continuum. Furthermore, other crosssectional studies found an association between cannabis use quantity or frequency and the risk for cannabis dependence (Chen et al., 1997; Coffey et al., 2002; Grant & Pickering, 1998). Longitudinal studies, however, were sparse and generated mixed results (Coffey et al., 2003; van der Pol et al., 2013).

Validating the utility of cannabis consumption measures for *predicting* later cannabis related symptomatology or progression to CUD (i.e. predictive validity) is crucial for prevention and intervention work that may use consumption measures for quick screening, because in many clinical settings, it is not feasible to routinely conduct a diagnostic interview. A handful of cannabis screeners have been developed: some did not include any quantity or frequency items (Legleye et al., 2007), whereas the others only had frequency items that were worded very differently across measures (Adamson et al., 2010; Adamson & Sellman, 2003; Alexander & Leung, 2004; Bashford et al., 2010). Although these screeners were validated with diagnostic gold standards, they were mostly developed and tested among clinical or community samples with homogeneous ethnic/cultural background (Bashford et al., 2010). Most importantly, they were all based on cross-sectional data except for one study (Bashford et al., 2010).

This study aims to fill in the current knowledge gap about the predictive validity of cannabis consumption measures by conducting secondary analysis on the NESARC data from Waves 1 and 2. The study's longitudinal design and diagnostic interviews conducted at both waves have provided an invaluable opportunity to validate the utility of cannabis use quantity and

frequency at Wave 1 for predicting CUD symptomatology and progression to CUD at Wave 2. This set of analysis provides new information to the literature because the study followed a representative sample of the U.S. general population for a longer period than existing studies and assessed both quantity and frequency.

#### 2. Material and Methods

#### 2.1. Data and Study Sample

This study conducted secondary analysis on data from the NESARC (Grant et al., 2004) at Wave 1 (2001–2002) and Wave 2 (2004–2005). A representative sample of the non-institutionalized adult population in the U.S was surveyed on substance use and related disorders. Among the 43,093 respondents that were interviewed at Wave 1, 34,653 were followed up 3 years later at Wave 2. Because of this study's focus on the progression of CUD from Wave 1 to Wave 2, we used data from the participants who completed both waves to identify risk samples. Statistical comparisons between cannabis users at Wave 1 who completed Wave 2 (n = 1,279) and those who did not (n = 324) did not find significant differences in CUD symptom counts or cannabis use frequency.

Due to the longitudinal design of the NESARC and diagnostic interviews conducted at both waves, we were able to identify three risk samples based on their cannabis use in the past 12 months and DSM-IV CUD diagnosis at Wave 1: (1) participants using cannabis in the past 12 months (defined as current users) at Wave 1 were at risk for having any past-year CUD symptoms at Wave 2 (n = 1,279); (2) the current users with no lifetime CUD at Wave 1 were at risk for meeting past-year CUD diagnosis (defined as *incident CUD*) at Wave 2 (n = 525); and (3) the current users with past-year CUD at Wave 1 were at risk for meeting past-year CUD diagnosis again (defined as *persistent CUD*) at Wave 2 (n = 444).

#### 2.2. Measures

**2.2.1. Outcome Variables**—This study has three outcome variables based on Wave 2 data: past-year CUD symptom count (out of the 11 symptoms of DSM IV cannabis abuse and dependence), incident CUD (dichotomous), and persistent CUD (dichotomous). They correspond to the three risk samples described in Section 2.1, respectively. The symptoms and diagnosis of CUD and other psychiatric disorders were derived from the Alcohol Use Disorders and Associated Disabilities Interview Schedule-DSM-IV version (AUDADIS-IV; Grant et al., 2003).

**2.2.2. Quantity and Frequency of Cannabis Use**—We used both the quantity and frequency items to capture cannabis consumption at Wave 1. The quantity question was: "On the days that you used marijuana in the last 12 months, about how many joints did you usually smoke in a single day?" The frequency question was: "During the last 12 months, about how often did you use marijuana?" Participants responded to the frequency question on a 0–10 scale (e.g., 0 = never, 5 = once a month; 10 = everyday). Both variables were standardized to facilitate interpretation of the fitted models.

**2.2.3. Lifetime Psychiatric Disorders**—Because CUD tends to occur with other psychiatric disorders including other substance use disorders, major depression, anxiety disorders, and antisocial personality disorder (Center for Behavioral Health Statistics and Quality, 2015), we included participants' lifetime DSM-IV diagnosis (dichotomous) on these comorbid disorders at Wave 1 as covariates in the models to adjust for potential confounding effects.

**2.2.4. Sociodemographic Variables**—In addition to psychiatric disorders, sociodemographic variables at Wave 1 (see Table 1) potentially associated with CUD (Agrawal & Lynskey, 2009; Compton et al., 2004; Hasin et al., 2015; Khan et al., 2013) were used as control variables in the statistical models and were dummy coded to facilitate interpretation.

#### 2.3. Statistical Analysis

A regression model was fit on the data from each of the three risk samples described in Section 2.1 based on the corresponding outcome measure. For the CUD symptom count at Wave 2, the zero-inflated Poisson (ZIP) model was adopted because the symptom count data had excess zero values (72%) and over-dispersion was not evident (Buu et al., 2012). The ZIP model had two submodels: the logistic submodel examining the relationship between predictors and the likelihood of being symptom-free; and the Poisson submodel examining the relationship between predictors and the severity of CUD symptomatology (assuming more symptoms indicated higher severity). Furthermore, the logistic regression was adopted for the two binary outcomes: incident CUD and persistent CUD at Wave 2. In all the three models fitted by using Stata 14 SE (StataCorp, 2015), cannabis consumption measures were the primary predictors, while sociodemographic variables and lifetime psychiatric disorders were included as control variables.

#### 3. Results

#### 3.1. Descriptive Statistics

Table 1 shows descriptive statistics by the three risk samples. Among current cannabis users at Wave 1 (n=1,279), 41% had no lifetime CUD of whom 10% had incident CUD at Wave 2; and 35% had past-year CUD of whom 34% had persistent CUD at Wave 2. About 72% of the current users did not develop any CUD symptoms at Wave 2, while among those who had symptoms, the median symptom count was 2. On average, the current users with past-year CUD reported higher quantity and frequency of cannabis use and had higher rates of lifetime substance use disorder (other than CUD), major depression, and antisocial personality disorder (p<.01).

#### 3.2. Predictive Validity of Cannabis Consumption

Table 2 shows the odds ratio or incident risk ratio which are exponential transformation of the estimated regression coefficients of the three fitted models. The logistic submodel of ZIP indicated that higher frequency of cannabis use at Wave 1 decreased the odds for CUD symptom free at Wave 2, whereas the effect of quantity was not significant. Additionally, the Poisson submodel of ZIP did not find either consumption variable to be predictive for the

severity of symptomatology. Further, the logistic regression models showed that higher frequency of cannabis use increased the odds for both incident CUD and persistent CUD. The quantity of cannabis use, however, did not predict the odds for incident CUD or persistent CUD.

#### 4. Discussion

The results of this study indicate that among cannabis users, higher frequency of cannabis use predicted lower likelihood of being free of any CUD symptoms but it did not predict the severity of CUD symptomatology. Higher frequency of cannabis use also predicted higher likelihood of progression to onset of CUD and persistence of CUD. Cannabis use quantity, however, did not predict any of the outcomes. A possible reason why neither consumption variable predicted severity of symptomatology is that we used the symptom count to indicate severity. Since each DSM-IV CUD symptom has a different prevalence rate with different standing of the *latent* severity continuum (Compton et al., 2009), the same symptom count with different combinations of symptoms may indicate different severity.

The insignificant finding on cannabis use quantity may result from the over-simplified quantity measure used in NESARC: the number of joints. Unlike alcohol and cigarettes, quantifying cannabis use has been a difficult issue because it is consumed in a variety of ways including joints, blunts, pipes, bongs, and vaporizers, each of which potentially contains a different amount of cannabis per unit; the issue is further complicated by the high prevalence of sharing among users and variation in potency (Gray et al., 2009). A more sophisticated measure that provides an estimated total number of puffs per unit for each consumption method with adjustment by potency and sharing has been proposed (Gray et al., 2009). Moreover, other studies have incorporated number of grams noting this unit as being commonly used in the purchase and selling of marijuana (Van Dam et al., 2012; Walden and Earlywine, 2008). Alternatively, surrogate substances (Mariani et al., 2011; Norberg et al., 2012) have been used in timeline followback interviews to facilitate participants' estimation of quantity. Nevertheless, these new self-report quantity measures are only approximations of cannabis exposure (Temple, 2014); whether they could be adopted in national surveys or screening tools is an open research question.

The finding that cannabis use frequency predicted both incident and persistent CUD reopens a debate about whether consumption should be included in the CUD diagnostic criteria. Indeed, weekly cannabis use was considered for inclusion in DSM-5 but the Work Group decided to add craving instead (Hasin et al., 2013). Nevertheless, a study using a sample of the adolescent general population in France showed that the psychometric model adding three criteria (daily use, use before midday, and use when alone) to DSM-IV criteria exhibited higher levels of information, especially in the mild and moderate ranges of the CUD continuum (Piontek et al., 2011). More research is needed in this area.

Although the NESARC data collected in 2001–2005 may be considered dated, they are still highly valuable for studying predictive validity of cannabis consumption measures in a nationally representative sample. Other more recent national surveys are not sufficient because they did not collect either longitudinal or diagnostic data. Other limitations of this

study include using DSM-IV criteria, self-report data, and results not generalizable beyond the US adult population. Because adolescence is a critical period for brain development that is particularly vulnerable to cannabinoids (Rubino, 2008), we expect the adverse effects observed in this study to be stronger in an adolescent sample.

In summary, this study has offered a new piece of evidence to support the predictive validity of cannabis use frequency using national longitudinal data. The result supports the common practice of including frequency items in cannabis screening tools. Furthermore, the insignificant result of cannabis use quantity may call for better quantity measures in future national surveys or screening tools.

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#### Highlights

- Higher frequency of cannabis use predicted higher likelihood of incident CUD.
- Higher frequency of cannabis use predicted higher likelihood of persistent CUD.
- Frequency of cannabis use may be included in future screening tools.

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## Table 1

Descriptive statistics of the relevant variables of National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

			n (%), n	nean (SD), or median (S	(D)		
	Current canna (n	bis users at Wave 1 =1,279)	Cannabis users v at Wave 1 4	with no lifetime CUD 41.05% (n=525)	Cannabis users w Wave 1 34	ith past year CUD at 71% ( <i>n</i> =444)	<i>p</i> -value <sup>a</sup>
1. Major outcomes at Wave 2							
Symptom counts of Cannabis Use Disorder (CUD)							
Number of zero symptom cases	918	(71.77%)	I	I	Ι	I	I
Count for people with symptoms $(n=725)$ b	2	(1.82)	I	I	I	I	I
Cannabis Use Disorder							
Incidence	I	I	54	(10.29%)	I	I	I
Persistence	I	I	I	I	153	(34.46%)	I
2. Sociodemographics							
Age $^{\mathcal{C}}$	31.22	(11.15)	31.47	(11.25)	28.77	(10.45)	<0.01
<29	665	(51.99%)	270	(51.43%)	272	(61.26%)	<0.01
30-49	524	(40.97%)	216	(41.14%)	152	(34.23%)	
>50	06	(7.04%)	39	(7.43%)	20	(4.5%)	
Male	<i>TT</i> 2	(60.36%)	291	(55.43%)	298	(67.12%)	<0.01
Race/Ethnicity							
Non-Hispanic white	66L	(62.47%)	309	(58.86%)	275	(61.94%)	0.32
Non-Hispanic black	215	(16.81%)	108	(20.57%)	71	(15.99%)	
Hispanic	199	(15.56%)	80	(15.24%)	75	(16.89%)	
Other	99	(5.16%)	28	(5.33%)	23	(5.18%)	
Education							
Less than high school	216	(16.89%)	79	(15.05%)	88	(19.82%)	<0.01
High school	726	(56.76%)	285	(54.29%)	268	(60.36%)	
College	278	(21.74%)	125	(23.81%)	77	(17.34%)	
Graduate school	59	(4.61%)	36	(6.86%)	11	(2.48%)	
Marital status							
Single	357	(27.91%)	156	(29.71%)	109	(24.55%)	0.18
Married	12	(0.94%)	3	(0.57%)	4	(0.9%)	

			n (%), n	nean (SD), or median (S	(D)		
	Current canna (n:	bis users at Wave 1 =1,279)	Cannabis users	with no lifetime CUD 41.05% (n=525)	Cannabis users w Wave 1 34,	ith past year CUD at 71% (n=444)	<i>p</i> -value <sup>a</sup>
Widowed	910	(71.15%)	366	(69.71%)	331	(74.55%)	
Employed	897	(70.13%)	374	(71.24%)	300	(67.57%)	0.22
Region							
Northeast	249	(19.47%)	116	(22.10%)	85	(19.14%)	0.40
Midwest	307	(24.00%)	119	(22.67%)	114	(25.68%)	
South	312	(24.39%)	136	(25.90%)	104	(23.42%)	
West	411	(32.13%)	154	(29.33%)	141	(31.76%)	
3. Cannabis use in past 12 month							
Quantity (# of joints) at Wave 1 $^{\mathcal{C}}$	1.91	(2.09)	1.40	(1.18)	2.67	(2.84)	<0.01 **
Frequency at Wave 1 b d	9	(2.93)	4	(2.79)	7	(2.35)	<0.01 **
Quantity (# of joints) at Wave 2 $^{c}$	0.87	(1.56)	0.61	(1.30)	1.18	(1.77)	<0.01 **
Frequency at Wave 2 b d	0	(3.63)	0	(3.20)	4	(3.95)	<0.01 **
4. Lifetime psychiatric disorders (Wave 1)							
Substance use disorder $^{\mathcal{C}}$	1,055	(82.49%)	379	(72.19%)	396	(89.19%)	<0.01 **
Major depression	417	(32.60%)	132	(25.14%)	164	(36.94%)	<0.01 **
Anxiety disorders $f$	351	(27.44%)	123	(23.43%)	125	(28.15%)	0.09
Antisocial personality disorder	250	(19.55%)	51	(9.71%)	125	(28.15%)	<0.01
* p<0.05;							

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\*\* p<0.01

<sup>a</sup>Based on independent sample t tests for continuous variables (i.e., age and quantity of cannabis use), Wilcoxon-Mann Whitney test for ordinal categorical variable (i.e., frequency of cannabis use), and chisquare tests for all other nominal categorical variables between the group without lifetime CUD and the group with past year CUD at Wave 1.

bData presented as median and standard deviation (SD).

cData presented as mean and SD.

 $d_{The}$  frequency of cannabis use was measured as an ordinal scale with 11 levels (0 = *never*; 1 = *once a year*; 2 = 2 *times a year*; 3 = 3-6 *times a year*; 4 = 7-11 *times a year*; 5 = *once a month*; 6 = 2-3 *times* a month; 7 = 1-2 times a week; 8 = 3-4 times a week; 9 = nearly every day; 10 = every day).

e Positive diagnosis with at least one of the following substances: alcohol, nicotine, sedatives, tranquilizers, opioids, heroin, amphetamines, cocaine, hallucinogens, inhalants/solvents, or other drugs.

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fPositive diagnosis with at least one of the following conditions: generalized anxiety disorder, panic disorder with or w/o agoraphobia, agoraphobia with no history of panic disorder, social phobia, or specific phobia.

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## Table 2

The effects of Wave 1 cannabis use quantity/frequency on cannabis use disorder (CUD) symptom counts, incident CUD, and persistent CUD at Wave 2, adjusting for the effects of sociodemographic variables and lifetime psychiatric disorders at Wave 1.

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	ZIP model (lo CID Symmetry	ogistic submodel) n Counts n=1.246	ZIP model (F CTID Symnto	oisson submodel) m Counts n=1.246	Logistic mod	lel Incident CUD =505	Logistic mode	el Persistent CUD
	OR	95%CI	IRR	95%CI	OR	95%CI	OR	95%CI
1. Sociodemographic (W1):								
Age:								
<29 (ref)	I	I	I	I	I	I	I	I
30–49	0.99	0.69, 1.42	0.85	0.65, 1.11	0.76	0.38, 1.51	0.93	0.58, 1.49
>50	0.80	0.25, 2.60	0.67	0.36, 1.22	0.70	0.21, 2.29	06.0	0.32, 2.57
Male	0.48 **	0.34, 0.69	0.86	0.66, 1.13	1.61	0.84, 3.09	$1.67^{*}$	1.04, 2.68
Race/Ethnicity:								
Non-Hispanic white (ref)	I	I	I	I	I	I	I	I
Non-Hispanic black	1.30	0.81, 2.10	1.15	0.80, 1.65	0.39	0.16, 1.00	1.27	0.69, 2.34
Hispanic	1.59	0.97, 2.61	1.13	0.75, 1.71	0.41	0.16, 1.04	06.0	0.50, 1.63
Other	1.37	0.65, 2.90	1.20	0.70, 2.05	0.29	0.05, 1.72	0.92	0.36, 2.37
Education:								
Less than high school (ref)	I	I	I	I	I	I	I	I
High school	0.78	0.49, 1.23	0.96	0.70, 1.30	1.08	0.45, 2.64	1.83	1.02, 3.26
College	0.76	0.43, 1.34	0.95	0.63, 1.44	1.17	0.40, 3.39	2.37 *	1.14, 4.93
Graduate school	1.34	0.46, 3.90	0.95	0.41, 2.23	0.76	0.15, 3.97	2.16	0.55, 8.48
Marital status:								
Single (ref)	I	I	I	I	I	I	I	I
Married	0.91	0.62, 1.34	0.97	0.75, 1.25	0.71	0.35, 1.47	0.94	0.57, 1.53
Widowed	2.56	0.36, 18.16	0.98	0.42, 2.30	0.66	0.02, 21.55	0.30	0.01, 6.61
Employed:	$1.57^{*}$	1.06, 2.33	1.23	0.95, 1.58	0.67	0.35, 1.27	1.08	0.69, 1.71
Region:								
Northeast (ref)	I	I	I	I	I	I	I	I
Midwest	1.12	0.70, 1.78	1.09	0.77, 1.54	0.63	0.22, 1.84	1.08	0.59, 1.97
South	0.94	0.58, 1.52	0.89	0.63, 1.26	1.67	0.69, 4.06	0.80	0.42, 1.51

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OR         55%CI         IRR         55%CI         OR         55%CI         OR         55%CI         OR         55%CI         95%CI         95%CI	OR         95%CI         IR         95%CI         OR         95%CI         OR         95%CI         OR         95%CI         OR         95%CI         OR         95%CI         OR         95%CI         95%CI <th< th=""><th></th><th>ZIP model (lc CUD Symptor</th><th>gistic submodel) n Counts n=1,246</th><th>ZIP model (P CUD Symptor</th><th>'oisson submodel) m Counts n=1,246</th><th>Logistic mod n</th><th>el Incident CUD =505</th><th>Logistic mode n</th><th>I Persistent CUD =434</th></th<>		ZIP model (lc CUD Symptor	gistic submodel) n Counts n=1,246	ZIP model (P CUD Symptor	'oisson submodel) m Counts n=1,246	Logistic mod n	el Incident CUD =505	Logistic mode n	I Persistent CUD =434
West $0.57^*$ $0.34, 0.97$ $0.78$ $0.53, 1.13$ $2.02$ $0.87, 4.71$ $1.02$ $0.56, 1.84$ <b>2. Cannabis use (W1):</b> Frequency (0-10 scale) $^{a}$ $0.51^*^*$ $0.42, 0.62$ $1.13$ $0.95, 1.35$ $2.08^{**}$ $1.49, 2.90$ $1.35^{**}$ $1.07, 1.70$ Frequency (0-10 scale) $^{a}$ $0.96$ $0.82, 1.13$ $1.03$ $0.94, 1.13$ $0.98$ $0.74, 1.30$ $1.08$ $0.87, 1.35$ Quantity (joint) $^{a}$ $0.96$ $0.82, 1.13$ $1.03$ $0.94, 1.13$ $0.98$ $0.74, 1.30$ $1.08$ $0.87, 1.35$ Apprintic disorders $0.16$ $0.82, 1.13$ $1.03$ $0.94, 1.13$ $0.74, 1.30$ $1.08$ $0.87, 1.35$ Ansior depression $0.76$ $0.47, 1.24$ $0.85$ $0.51, 2.16$ $0.71, 3.16$ $0.71, 3.16$ $0.79, 3.45$ Ansior depression $0.74, 1.32$ $1.05, 1.25$ $0.74, 1.32$ $0.51, 2.14$ $1.65$ $0.79, 3.45$ Ansior depression $0.74, 1.32$ $0.54$ $0.23, 1.28$ $0.74, 1.16$	West $0.57^{*}$ $0.34, 0.97$ $0.78$ $0.53, 1.13$ $2.02$ $0.87, 4.71$ $1.02$ $0.56, 1.84$ <b>2. Cannabis use (W1):</b>		OR	95%CI	IRR	95%CI	OR	95%CI	OR	95%CI
<b>. Cannabis use (W1):</b> Frequency (0-10 scale) $^a$ 0.51 **       0.42, 0.62       1.13       0.95, 1.35 $2.08^{***}$ 1.49, 2.90       1.35 **       1.07, 1.70         Quantity (joint) $^a$ 0.96       0.82, 1.13       1.03       0.94, 1.13       0.98       0.74, 1.30       1.08       0.87, 1.35 <b>Specialative disorders (lifetime at W1):</b> Substance use disorder $b$ 0.76       0.47, 1.24       0.85       0.57, 1.25       1.05       0.51, 2.14       1.65       0.79, 3.45         Major depression       0.76       0.47, 1.24       0.85       0.57, 1.25       1.05       0.51, 2.14       1.65       0.79, 3.45         Anxiety disorder $b$ 0.76       0.47, 1.24       0.85       0.57, 1.25       1.05       0.71, 3.16       0.79, 3.45         Anxiety disorder $c$ 1.11       0.76, 1.62       1.11       0.84, 1.46       0.51, 2.16       0.75, 1.26       0.71, 3.16       0.91, 2.36         Antisocial personality disorder       1.11       0.72, 1.69 $_{123}^{*}$ 1.021, 1.32       0.31, 2.16       0.72, 1.06       0.91, 2.36       0.41, 1.16	<b>. Cannabis use (W1):</b> Frequency (0-10 scale) <sup><i>A</i></sup> $0.51^{**}$ $0.42, 0.62$ $1.13$ $0.95, 1.35$ $2.08^{**}$ $1.49, 2.90$ $1.35^{**}$ $1.07, 1.70$ Prequency (0-10 scale) <sup><i>A</i></sup> $0.51^{**}$ $0.42, 0.62$ $1.13$ $0.95, 1.35$ $2.08^{**}$ $1.49, 2.90$ $1.35^{**}$ $1.07, 1.70$ Quantity (joint) <sup><i>A</i></sup> $0.96$ $0.82, 1.13$ $1.03$ $0.94, 1.13$ $0.98$ $0.74, 1.30$ $1.08$ $0.87, 1.35$ Appendiate law VI): $0.76$ $0.82, 1.13$ $0.94, 1.13$ $0.98$ $0.74, 1.30$ $1.05$ $0.71, 1.30$ $1.07, 1.36$ Substance use disorder b $0.76$ $0.71, 1.24$ $0.88$ $0.57, 1.25$ $1.05$ $0.71, 3.16$ $1.65$ $0.75, 1.86$ Major depression $0.73$ $0.71, 1.24$ $0.84, 1.46$ $0.54$ $0.23, 1.28$ $1.47$ $0.91, 2.36$ Anxiety disorders c $1.10$ $0.72, 1.69$ $1.33^{*}$ $1.02, 1.73$ $0.31, 2.16$ $0.71, 2.31$ $0.71, 2.36$ $0.91, 2.36$ Anxiety disorders c $1.10$ $0.72, 1.69$ $1.33^{*}$	West	$0.57^{*}$	0.34, 0.97	0.78	0.53, 1.13	2.02	0.87, 4.71	1.02	0.56, 1.84
Frequency (0-10 scale) $^a$ 0.51 **       0.42, 0.62       1.13       0.95, 1.35 $2.08^{**}$ 1.49, 2.90 $1.35^{**}$ 1.07, 1.70         Quantity (joint) $^a$ 0.96       0.82, 1.13       1.03       0.94, 1.13       0.98       0.74, 1.30       1.08       0.87, 1.35         Argeniatric disorders       (lifetime at W1):       0.76       0.47, 1.24       0.85       0.57, 1.25       1.05       0.51, 2.14       1.65       0.79, 3.45         Major depression       0.73       0.51, 1.06       0.99       0.74, 1.32       1.50       0.71, 3.16       1.18       0.75, 1.86         Antisocial personality disorder       1.11       0.76, 1.62       1.11       0.84, 1.46       0.54       0.23, 1.28       1.47       0.91, 2.36         Antisocial personality disorder       1.10       0.72, 1.69 $_{123}^{**}$ 1.02, 1.73       0.82       0.31, 2.16       0.44, 1.16	Fequency (0-10 scale) a $0.51$ ** $0.42$ , $0.62$ $1.13$ $0.95$ , $1.35$ $1.49, 2.90$ $1.35$ ** $1.07, 1.70$ Quantity (join) a $0.96$ $0.82, 1.13$ $1.03$ $0.94, 1.13$ $0.98$ $0.74, 1.30$ $1.08$ $0.87, 1.35$ Aryotiatic disorder b $0.76$ $0.87, 1.12$ $0.82$ $0.57, 1.25$ $1.05$ $0.74, 1.30$ $1.08$ $0.87, 1.35$ Aryotiatic disorder b $0.76$ $0.77, 1.24$ $0.85$ $0.57, 1.25$ $1.05$ $0.71, 2.16$ $1.65$ $0.79, 3.45$ Major depression $0.73$ $0.73$ $0.51, 1.06$ $0.99$ $0.74, 1.32$ $1.05$ $1.16$ $1.05, 1.36$ Major depression $0.73$ $0.73, 1.26$ $0.74, 1.32$ $1.05, 1.73$ $0.71, 3.16$ $1.18$ $0.75, 1.86$ Anxiety disorders c $1.11$ $0.76, 1.62$ $1.11$ $0.84, 1.46$ $0.54$ $0.23, 1.28$ $1.47$ $0.91, 2.36$ Anxiety disorder b $1.10$ $0.72, 1.69$ $1.33^*$ $1.02, 1.73$ $0.82$ $0.31, 2.16$ $0.74, 1.30$ $0.71, 2.16$ $0.91, 2.36$	2. Cannabis use (W1):								
Quantity (joint) $^{a}$ 0.96       0.82, 1.13       1.03       0.94, 1.13       0.98       0.74, 1.30       1.08       0.87, 1.35 <b>3. Psychiatric disorders</b> (lifetime at W1):       0.76       0.47, 1.24       0.85       0.57, 1.25       1.05       0.74, 1.30       1.08       0.87, 1.35         Substance use disorder $b$ 0.76       0.47, 1.24       0.85       0.57, 1.25       1.05       0.51, 2.14       1.65       0.79, 3.45         Major depression       0.73       0.51, 1.06       0.99       0.74, 1.32       1.50       0.71, 3.16       1.18       0.75, 1.86         Anxiety disorders $c$ 1.11       0.76, 1.62       1.11       0.84, 1.46       0.54       0.23, 1.28       1.47       0.91, 2.36         Antisocial personality disorder       1.10       0.72, 1.69 $_{1.23}$ *       1.02, 1.73       0.82       0.31, 2.16       0.44, 1.16	Quantity (join) $^{a}$ 0.960.82, 1.131.030.94, 1.130.980.74, 1.301.080.87, 1.35 <b>3. Psychiatric disorders</b> (lifetime at W):Substance use disorder $^{b}$ 0.760.47, 1.240.850.57, 1.251.050.51, 2.141.650.79, 3.45Major depression0.730.51, 1.060.990.74, 1.321.500.71, 3.161.180.75, 1.86Anxiety disorders $^{c}$ 1.110.76, 1.621.110.84, 1.460.540.23, 1.281.470.91, 2.36Anxiety disorders $^{c}$ 1.100.72, 1.691.33*1.02, 1.730.820.31, 2.160.91, 2.36Anxiety disorders $^{c}$ 1.100.72, 1.691.33*1.02, 1.730.820.31, 2.160.91, 2.36Antisocial personality disorder1.100.72, 1.691.33*1.02, 1.730.820.31, 2.160.91, 2.36 $^{*}$ 0.050.330.820.31, 2.160.94, 1.160.34, 2.160.44, 1.16Antisocial personality disorder1.100.72, 1.691.33*1.02, 1.730.820.31, 2.160.44, 1.16 $^{*}$ 0.050.33*0.820.31, 2.160.91, 2.360.44, 1.160.44, 1.16 $^{*}$ 0.050.35*0.31, 2.160.31, 2.160.31, 2.160.31, 2.160.44, 1.16 $^{*}$ 0.050.35*0.32, 1.280.31, 2.160.31, 2.160.31, 2.160.44, 1.16 $^{*}$ 0.050.35*0.31, 3.160.31, 3	Frequency $(0-10 \text{ scale})^{2}$	$0.51^{**}$	0.42, 0.62	1.13	0.95, 1.35	2.08	1.49, 2.90	1.35 **	1.07, 1.70
<b>3. Psychiatric disorders</b> (lifetime at W1):         Substance use disorder $b$ $0.76$ $0.47, 1.24$ $0.85$ $0.57, 1.25$ $1.05$ $0.51, 2.14$ $1.65$ $0.79, 3.45$ Major depression $0.73$ $0.51, 1.06$ $0.99$ $0.74, 1.32$ $1.50$ $0.71, 3.16$ $1.18$ $0.75, 1.86$ Anxiety disorders $c$ $1.11$ $0.76, 1.62$ $1.11$ $0.84, 1.46$ $0.54$ $0.23, 1.28$ $1.47$ $0.91, 2.36$ Antisocial personality disorder $1.10$ $0.72, 1.69$ $_{1.23}*$ $1.02, 1.73$ $0.82$ $0.31, 2.16$ $0.44, 1.16$	<b>3. Psychiatric disorders</b> (lifetime at W1:         Substance use disorder $b$ 0.76       0.47, 1.24       0.85       0.57, 1.25       1.05       0.51, 2.14       1.65       0.79, 3.45         Major depression       0.73       0.51, 1.06       0.99       0.74, 1.32       1.50       0.71, 3.16       1.18       0.75, 1.86         Anxiety disorders $c$ 1.11       0.76, 1.62       1.11       0.84, 1.46       0.53, 1.28       1.47       0.91, 2.36         Antisocial personality disorder       1.10       0.72, 1.69       1.33*       1.02, 1.73       0.82       0.31, 2.16       0.91, 2.36	Quantity (joint) <sup>a</sup>	0.96	0.82, 1.13	1.03	0.94, 1.13	0.98	0.74, 1.30	1.08	0.87, 1.35
Substance use disorder $b$ 0.76         0.47, 1.24         0.85         0.57, 1.25         1.05         0.51, 2.14         1.65         0.79, 3.45           Major depression         0.73         0.51, 1.06         0.99         0.74, 1.32         1.50         0.71, 3.16         1.18         0.75, 1.86           Anxiety disorders $c$ 1.11         0.76, 1.62         1.11         0.84, 1.46         0.54         0.23, 1.28         1.47         0.91, 2.36           Antisocial personality disorder         1.10         0.72, 1.69 $_{123}^{**}$ 1.02, 1.73         0.82         0.31, 2.16         0.74, 1.16	Substance use disorder b $0.76$ $0.47, 1.24$ $0.85$ $0.57, 1.25$ $1.05$ $0.51, 2.14$ $1.65$ $0.79, 3.45$ Major depression $0.73$ $0.51, 1.06$ $0.99$ $0.74, 1.32$ $1.50$ $0.71, 3.16$ $1.18$ $0.75, 1.86$ Anxiety disorders c $1.11$ $0.76, 1.62$ $1.11$ $0.84, 1.46$ $0.54$ $0.23, 1.28$ $1.47$ $0.91, 2.36$ Antisocial personality disorder $1.10$ $0.72, 1.69$ $1.33^*$ $1.02, 1.73$ $0.81, 2.16$ $0.71, 2.16$ $0.74, 1.16$ ** $\rho^{-0.05};$	3. Psychiatric disorders (lifetime at W1):								
Major depression $0.73$ $0.51, 1.06$ $0.99$ $0.74, 1.32$ $1.50$ $0.71, 3.16$ $1.18$ $0.75, 1.86$ Anxiety disorders $c$ $1.11$ $0.76, 1.62$ $1.11$ $0.84, 1.46$ $0.54$ $0.23, 1.28$ $1.47$ $0.91, 2.36$ Antisocial personality disorder $1.10$ $0.72, 1.69$ $_{1.32}^{*}$ $1.02, 1.73$ $0.82$ $0.31, 2.16$ $0.72$ $0.44, 1.16$	Major depression $0.73$ $0.51, 1.06$ $0.99$ $0.74, 1.32$ $1.50$ $0.71, 3.16$ $1.18$ $0.75, 1.86$ Anxiety disorders $c$ $1.11$ $0.76, 1.62$ $1.11$ $0.84, 1.46$ $0.54$ $0.23, 1.28$ $1.47$ $0.91, 2.36$ Antisocial personality disorder $1.10$ $0.72, 1.69$ $1.33^*$ $1.02, 1.73$ $0.82$ $0.31, 2.16$ $0.74, 1.16$ ******	Substance use disorder b	0.76	0.47, 1.24	0.85	0.57, 1.25	1.05	0.51, 2.14	1.65	0.79, 3.45
Anxiety disorders $c$ 1.11         0.76, 1.62         1.11         0.84, 1.46         0.54         0.23, 1.28         1.47         0.91, 2.36           Antisocial personality disorder         1.10         0.72, 1.69         1.32*         1.02, 1.73         0.82         0.31, 2.16         0.72         0.44, 1.16	Anxiety disorders $c$ 1.11         0.76, 1.62         1.11         0.84, 1.46         0.54         0.23, 1.28         1.47         0.91, 2.36           Antisocial personality disorder         1.10         0.72, 1.69 $1.33^*$ 1.02, 1.73         0.82         0.31, 2.16         0.74, 1.16           * $\rho^{-0.05}$ ;	Major depression	0.73	0.51, 1.06	0.99	0.74, 1.32	1.50	0.71, 3.16	1.18	0.75, 1.86
Antisocial personality disorder $1.10$ $0.72, 1.69$ $1, 33^{*}$ $1.02, 1.73$ $0.82$ $0.31, 2.16$ $0.72$ $0.44, 1.16$	Antisocial personality disorder         1.10 $0.72, 1.69$ $1.33^*$ $1.02, 1.73$ $0.82$ $0.31, 2.16$ $0.72$ $0.44, 1.16$ * $p^{<0.05}$ ; $p^{<0.05$	Anxiety disorders $^{\mathcal{C}}$	1.11	0.76, 1.62	1.11	0.84, 1.46	0.54	0.23, 1.28	1.47	0.91, 2.36
	* p<0.05;	Antisocial personality disorder	1.10	0.72, 1.69	1.33	1.02, 1.73	0.82	0.31, 2.16	0.72	0.44, 1.16
		p<0.05;								

*p*<0.01

Note: Data are from the National Epidemiologic Survey on Alcohol and Related Conditions (Waves 1 and 2). IRR = incident risk ratio; OR = odds ratio; CI = confidence interval.

<sup>a</sup>Cannabis use frequency and quantity have been standardized by their standard deviations to facilitate interpretation of IRR and OR.

<sup>C</sup>Positive diagnosis with at least one of the following conditions: generalized anxiety, panic disorder with or w/o agoraphobia, agoraphobia, with no history of panic disorder, social phobia, or specific b Positive diagnosis with at least one of the following substances: alcohol, nicotine, sedatives, tranquilizers, opioids, heroin, amphetamines, cocaine, hallucinogens, inhalants/solvents, or other drugs.

phobia.