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The association between cannabis use and psychiatric comorbidity in people with personality disorders: A population-based longitudinal study

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ABSTRACT

Both personality disorders (PD) and cannabis use are highly comorbid with various psychiatric disorders. While previous research indicates specific interactions between cannabis use and schizotypal PD associated with schizophrenia, research into cannabis use among individuals with other PDs and the development of several additional psychiatric disorders is scarce. We explored the prevalence and incidence of psychiatric disorders among individuals with PDs who use cannabis, and whether individuals with PDs who use cannabis are at increased risk for developing psychiatric disorders compared to cannabis users without a PD. Finally, we examined the interaction effect between cannabis use and personality disorders on comorbid psychiatric disorders. Data from 34,653 participants in waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) were analyzed. Our findings indicate that individuals with PDs who used cannabis were at increased odds for developing substance use disorders (including opioid use disorder), but not other comorbid psychiatric disorders, at 3-year follow up. No significant interaction effects were generally found between cannabis use and PD. These findings suggest that aside from specific substance use disorders, individuals with PDs are not at an increased risk for developing other psychiatric disorders following cannabis use.

1. Introduction

The association between personality disorders (PD) and other psychiatric comorbidity is firmly established (Khan et al., 2005; Tyrer et al., 2015). Different personality disorders have been shown to have variable associations with specific psychiatric comorbidities, e.g. schizotypal PD is strongly associated with bipolar disorder and several anxiety disorders (Pulay et al., 2009), while antisocial PD is strongly associated with substance use disorders and ADHD, as well as anxiety disorders (Compton et al., 2005; Goodwin and Hamilton, 2003).

The association between cannabis use and psychiatric disorders is also well-established, though causal associations were demonstrated by only a handful of studies. Nevertheless, there is substantial evidence of a statistical association between cannabis use and the development of schizophrenia or other psychoses, with the highest risk among the most frequent users, and there is moderate evidence for a statistical association between regular cannabis use and increased incidence of social anxiety disorder, depressive disorders, and increased suicidality measures (Gobbi et al., 2019; The National Academies of Sciences Engineering and Medicine, 2017)

There are consistent findings showing that substance use and substance use disorders (SUDs) are more prevalent in individuals diagnosed with a personality disorder (Hasin and Kilcoyne, 2012), and that this association is independent of sociodemographic background and psychiatric comorbidity. Several specific personality traits are associated with a higher prevalence of substance use, and these traits are variably accentuated in different personality disorders (Belcher et al., 2014).

Cannabis use is highly prevalent in the general population (UNDOC, 2018), and previous studies have shown that in several personality disorders, the odds of a Cannabis Use Disorder were up to eight-fold higher than in the general population (Hasin et al., 2016). To date, there is a paucity of data regarding the association between cannabis use and development of psychiatric disorders among individuals with PDs.

In this study we analyze data from a large, nationally representative

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sample, with a 3-year follow-up. We aim to determine the association between cannabis use and prevalence and incidence of psychiatric disorders among individuals with PDs. Given that individuals with PDs are at increased risk for comorbid psychiatric disorders and Cannabis Use Disorders, we hypothesized that cannabis use, particularly frequent use, would be associated with increased prevalence and incidence of psychiatric disorders in this population.

2. Methods

2.1. Sample

We used data from waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a survey designed by the National Institute on Alcohol Abuse and Alcoholism (Grant and Kaplan, 2005; Grant et al., 2003a, 2003b). The NESARC is a longitudinal and nationally representative survey which targets the non-institutionalized adult population of the United States, including military personnel living off-base. Interviews were conducted by experienced lay interviewers with extensive training and supervision. Wave 1 was conducted in 2001–2002 with a sample of 43,093 respondents 18 years of age and over. Wave 2 was a 3-year prospective follow-up comprising 34,653 of the Wave 1 respondents. In combination with the Wave 1 response rate of 81%, the cumulative response rate for Wave 2 was 70.2%. Extensive information regarding sampling, weighting and sociodemographic characteristics of participants in the NESARC sample has been published elsewhere (Grant et al., 2004; Stinson et al., 2006).

The US Census Bureau and the US Office of Budget and Management approved the NESARC protocol, and the Lev-Hasharon Mental Health Center IRB approved this study. NESARC data files were received from the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

2.2. Measures

The Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV Version (AUDADIS-IV) was used to assess substance use and substance use disorders (Chatterji et al., 1997; Hasin, 1997). The AUDADIS-IV has been reported to have excellent reliability and validity in the United States and internationally, with test-retest reliability ranking excellent for alcohol ($k = 0.74$) and drug ($k = 0.79$) use disorders (Chatterji et al., 1997; Cottler et al., 1997; Grant et al., 2003a, 2003b; Hasin, 1997; Pull et al., 1997; Vrasti et al., 1998). It includes an extensive list of symptom questions that separately operationalizes DSM-IV criteria for substance use disorders and additional psychiatric diagnoses.

2.2.1. Cannabis use

Respondents were given questions regarding lifetime and past-year cannabis use. Regarding frequency of past-year cannabis use, respondents were given 10 possible answers, ranging from “every day” to “once a year”. Based on previous studies (Hasin et al., 2008; Livne et al., 2018), we categorized cannabis users dichotomously according to frequency of use, with “frequent use” denoting regular use of cannabis three or more days a week, and "infrequent use" denoting cannabis use two days a week or less.

2.2.2. Personality disorders

Personality disorders were assessed by the AUDADIS-IV questionnaire, and included antisocial, avoidant, borderline, dependent, histrionic, narcissistic, obsessive-compulsive, paranoid, schizoid, and schizotypal personality disorders, as defined by the DSM-IV. The reliability of the AUDADIS-IV, assessed in test-retest studies of NESARC participants, ranged from fair (paranoid, histrionic, avoidant $\kappa = 0.40–0.45$) to very good (schizotypal, antisocial, narcissistic, borderline $\kappa = 0.67–0.71$). Convergent validity ranges from good to excellent. As various studies have shown the significant overlap of different personality disorders (Krueger, 2005; Skodol, 2012; Trull and Durrett, 2005), and due to the relatively low prevalence of several individual PDs, we grouped the different PDs according to the DSM-IV personality clusters: cluster “A” (including paranoid, schizoid, and schizotypal PD), cluster “B” (including antisocial, borderline, histrionic, and narcissistic PD), and cluster “C” (including avoidant, dependent, and obsessive-compulsive PD).

2.2.3. Analytic strategy

Cross-tabulations were conducted for exploration of sociodemographic and clinical characteristics of respondents with personality disorders. Among those with PDs, we compared cannabis users to non-users at baseline using chi-square analyses. All comparisons were repeated separately for each PD cluster.

We conducted logistic regression analyses, exploring the odds of incident, non-PD, psychiatric disorders in respondents with PDs. according to cannabis use status (frequent, infrequent, and no cannabis use). In order to analyze the potential interaction effect of PDs and cannabis use on developing any of the comorbid outcome variables, we carried out analyses using the interaction term “cannabis X personality disorder” for all combinations of level of use and PD clusters. Regression analyses were carried out in unadjusted and adjusted models – controlling for sociodemographic variables (sex, age, educational level, household income, marital status, urbanity and region), SUDs including alcohol use disorder, tobacco use disorder, other drug use disorders (including opioid use disorders, stimulant use disorders, sedative/hypnotic use disorder, inhalant/solvent use disorder, hallucinogen use disorder, and other substance use disorder), and other psychiatric disorders including any depressive disorder (MDD or dysthymia), bipolar disorder (I and II) and any anxiety disorder (specific phobia, panic disorder, agoraphobia, social anxiety disorder, and generalized anxiety disorder). Each interaction analyses provided OR of the excess, attenuated or null effect of the interaction on top of the effect of PD alone and cannabis use alone, as compared to the group of respondents with no PD and no cannabis use.

Wave 2 of the NESARC coded only 4 PDs (antisocial, borderline, schizotypal, and narcissistic), but these were not used, as personality disorders were not explored as an outcome variable.

To accurately estimate variances taking the NESARC sample design components into account, analyses were conducted using Software for Survey Data Analysis (SUDAAN) Version 11.0.1 (Research Triangle Institute), a software program that uses Taylor series linearization to adjust for the NESARC sample design characteristics.

3. Results

3.1. Personality disorders

Among 34,653 respondents, 5196 (15.0%) fulfilled diagnosis of a PD. Of these, 3455 (9.97%) were diagnosed with a cluster A PD, 4836 (14.0%) were diagnosed with a cluster B PD, and 3243 (9.36%) were diagnosed with a cluster C PD. There was a large overlap between PD cluster diagnoses, with 2099 (6.1%) of all respondents being diagnosed with PDs from two different clusters and 827 (2.4%) of all respondents being diagnosed with PDs from all three clusters.

3.2. Cannabis use

Among 5196 respondents with any PD, 470 (9.05%) reported past-year cannabis use at Wave 1, with 172 (3.3%) reporting frequent (i.e. ≥ 3 times a week) cannabis use and 298 (5.7%) reporting infrequent use. Among respondents with any PD, cannabis users were significantly more likely to be younger, unmarried and male. Regarding baseline comorbidity, cannabis users were significantly more likely to have a diagnosis of past year and lifetime major depressive disorder, mania/hypomania, alcohol use disorder, SUD (other than tobacco, cannabis or

Table 1
Socio-demographic variables by cannabis use status in different personality disorder clusters.

	Cluster A (N = 3455)			Cluster B (N = 4836)			Cluster C (N = 3243)		
	Cannabis use% (S.E) N = 298	No cannabis use % (S.E) N = 3147	P-value	Cannabis use% (S.E) N = 532	No cannabis use% (S.E) N = 4304	P-value	Cannabis use% (S.E) N = 226	No cannabis use% (S.E) N = 3017	P-value
Sex						*			**0.0012**
Male	60.92 (3.82)	44.77 (1.13)	**0.0009**	68.63 (2.39)	53.62 (1.00)		61.97 (4.48)	44.16 (0.97)	
Female	39.08 (3.82)	55.23 (1.13)		31.37 (2.39)	46.38 (1.00)		38.03 (4.48)	55.84 (0.97)	
Race			**0.016**			**0.0091**			0.16
White	67.68 (3.52)	64.28 (2.02)		66.63 (2.68)	67.36 (1.68)		72.91 (3.53)	76.04 (1.53)	
Black	13.28 (2.23)	17.82 (1.39)		11.11 (1.72)	16.02 (1.23)		10.45 (2.02)	10.19 (0.85)	
American Indian/Alaska Native	7.59 (2.06)	3.70 (0.51)		7.38 (1.54)	3.30 (0.41)		6.31 (2.01)	2.46 (0.37)	
Asian/Native Hawaiian/ Pacific Islander	0.61 (0.46)	2.64 (0.55)		2.33 (0.84)	2.87 (0.51)		1.46 (0.78)	2.79 (0.55)	
Hispanic/Latino	10.83 (2.06)	11.56 (1.42)		12.55 (1.82)	10.45 (1.17)		8.87 (2.21)	8.51 (0.99)	
Educational level			0.18			0.06			0.18
Less than highschool	21.00 (2.99)	17.49 (0.94)		21.74 (2.43)	15.48 (0.73)		17.70 (3.29)	11.99 (0.79)	
Highschool graduate	24.76 (2.82)	29.71 (1.14)		26.96 (2.16)	28.53 (0.98)		29.65 (3.74)	26.27 (1.08)	
Some college or higher	54.24 (3.89)	52.81 (1.34)		51.31 (3.09)	55.99 (1.09)		52.65 (4.68)	61.74 (1.27)	
Household Income			0.39			0.08			0.15
$0–$19,999	33.12 (3.48)	28.15 (1.02)		26.20 (2.33)	22.90 (0.85)		26.41 (3.28)	20.09 (0.95)	
$20,000–$34,999	21.62 (2.85)	20.48 (0.94)		24.76 (2.10)	20.67 (0.81)		21.00 (3.56)	18.20 (0.89)	
$35,000–$69,999	28.75 (3.18)	32.77 (1.09)		29.12 (2.39)	31.61 (0.95)		30.18 (3.89)	32.29 (1.05)	
$70,000 or greater	16.51 (3.38)	18.61 (1.02)		19.93 (2.46)	24.82 (1.15)		22.42 (3.98)	29.42 (1.26)	
Marital status			*			*			*
Married	26.43 (3.82)	52.15 (1.15)		30.97 (2.49)	54.18 (1.03)		36.42 (4.36)	63.87 (1.16)	
Widowed/divorced/ separated	19.81 (2.95)	21.66 (0.89)		15.39 (1.78)	19.33 (0.71)		18.28 (3.03)	16.77 (0.75)	
Never married	53.76 (3.59)	26.19 (1.08)		53.64 (2.67)	26.49 (0.92)		45.29 (4.11)	19.36 (0.94)	
Age			*			*			*
18–29	57.87 (3.88)	26.39 (1.04)		56.04 (2.45)	28.48 (0.96)		50.40 (4.59)	21.55 (0.92)	
30–44	32.06 (3.45)	34.43 (1.12)		32.95 (2.22)	35.20 (0.87)		39.38 (4.28)	34.53 (1.09)	
45–64	9.79 (2.31)	32.09 (1.05)		10.88 (1.62)	29.54 (0.88)		9.92 (2.52)	33.84 (1.03)	
65 +	0.28 (0.20)	7.09 (0.56)		0.13 (0.10)	6.78 (0.46)		0.30 (0.23)	10.08 (0.65)	
Urbanity			0.18			0.98			0.89
Urban	87.27 (2.25)	83.90 (1.03)		84.82 (1.98)	84.77 (0.83)		83.10 (3.19)	83.51 (1.04)	
Rural	12.73 (2.25)	16.10 (1.03)		15.18 (1.98)	15.23 (0.83)		16.90 (3.19)	16.49 (1.04)	
Region			0.34			0.34			0.13
Northeast	17.07 (2.70)	17.59 (1.48)		19.77 (2.43)	17.69 (1.38)		16.65 (3.19)	18.00 (1.38)	
Midwest	14.21 (2.64)	18.99 (1.39)		14.93 (2.02)	18.04 (1.26)		12.88 (2.69)	18.28 (1.35)	
South	40.92 (4.23)	38.49 (1.77)		39.77 (3.34)	37.85 (1.79)		47.60 (4.46)	38.61 (1.77)	
West	27.81 (3.40)	24.93 (1.32)		25.53 (2.65)	26.43 (1.27)		22.88 (3.68)	25.10 (1.36)	

* $p < 0.0001$.

alcohol), and tobacco use disorder, as well as lifetime dysthymia, past-year anxiety disorder, lifetime suicidality, and lifetime ADHD. Stratification by PD clusters demonstrated few inter-cluster distinctions. A comparison of sociodemographic and clinical variables between cannabis users and non-users among respondents with PD is provided in Tables 1 and 2.

3.3. Association of cannabis use with incident comorbid psychiatric disorders

Unadjusted logistic regression analyses exploring odds of developing comorbid, non-PD psychiatric disorders among individuals with any PD revealed that cannabis users had significantly higher odds of developing any depressive disorder, any manic disorder, alcohol use disorder, tobacco use disorder and other SUDs compared to non-users. Aside from depressive disorders, further analyses accounting for frequency of cannabis use exhibited similar findings. In fully adjusted models, any cannabis use maintained a significant association with alcohol use disorder, tobacco use disorder and substance use disorder, but not with any of the mood or anxiety disorders (Table 3). Further analysis of specific substances within the "substance use disorder" group demonstrated a significant association with opioid use disorder, stimulant use disorder and hallucinogen use disorder.

Further stratification by PD clusters generally demonstrated variable associations with different substance use disorders, and no association with incident mood or anxiety disorders in fully adjusted models (Table 3).

Analyses of interaction effects (cannabis use X PD) generally demonstrated an attenuation of the expected effect of both variables on the risk of incident psychiatric disorders, though few of these effects maintained significance in fully adjusted models. For example – the interaction between cluster B PD and any cannabis use attenuated the odds for SUD at Wave 2, with an OR of 0.47 (95% CI 0.28–0.77, $p = 0.004$). Cluster C PD had no significant interaction with any of the cannabis use variables regarding any of the outcomes examined (Table 4). Only the interactions between cluster B PD and any cannabis use or infrequent cannabis use maintained significance after Bonferroni correction for multiple comparisons.

4. Discussion

The aim of the present study was to examine the association between cannabis use and prevalence and incidence of several psychiatric comorbidities among people with personality disorders. While our findings show that among respondents diagnosed with any personality disorder, cannabis use is associated with increased odds of incident depressive, bipolar and anxiety disorders, these associations were largely due to sociodemographic and background clinical characteristics. Interestingly, cannabis use was found to have a negative moderating effect (i.e. relative attenuated risk due to interaction) on incident SUDs among groups of individuals with specific PD clusters, though after correction for multiple comparisons, this negative interaction maintained significance only among those with a cluster B PD.

Our findings indicate that, in line with previous research examining

Table 2
Clinical variables by cannabis use status in different personality disorder clusters.

	Cluster A (N = 3455)			Cluster B (N = 4836)			Cluster C (N = 3243)		
	Cannabis use% (S.E) N = 298	No cannabis use % (S.E) N = 3147	P-value	Cannabis use% (S.E) N = 532	No cannabis use% (S.E) N = 4304	P-value	Cannabis use% (S.E) N = 226	No cannabis use% (S.E) N = 3017	P-value
PY MDD	37.69 (3.11)	23.96 (1.05)	**0.0003**	27.88 (2.24)	18.34 (0.76)	**0.0002**	39.68 (3.70)	21.53 (0.94)	*
Lifetime MDD	58.31 (3.69)	43.35 (1.19)	**0.0006**	42.88 (2.77)	35.05 (1.01)	**0.0083**	63.24 (3.97)	42.98 (1.12)	*
PY dysthymia			0.11			0.20			
Yes	12.32 (2.33)	8.44 (0.66)		7.25 (1.30)	5.50 (0.43)		14.66 (2.92)	7.19 (0.59)	**0.0151**
No	87.68 (2.33)	91.56 (0.66)		92.75 (1.30)	94.50 (0.43)		85.34 (2.92)	92.81 (0.59)	
Lifetime dysthymia			0.051			0.16			
Yes	24.35 (3.53)	17.22 (0.86)		15.08 (2.11)	12.01 (0.65)		26.20 (4.00)	14.92 (0.80)	**0.0091**
No	75.65 (3.53)	82.78 (0.86)		84.92 (2.11)	87.99 (0.65)		73.80 (4.00)	85.08 (0.80)	
PY mania/hypomania			**0.0002**			**0.0011**			
Yes	24.44 (2.80)	12.31 (0.77)		17.07 (2.06)	9.44 (0.60)		28.16 (3.92)	11.05 (0.74)	**0.0001**
No	75.56 (2.80)	87.69 (0.77)		82.93 (2.06)	90.56 (0.60)		71.84 (3.92)	88.95 (0.74)	
Lifetime mania/ hypomania						*			
Yes	41.26 (3.68)	22.68 (1.05)	*	31.27 (2.43)	18.19 (0.79)		48.83 (4.62)	20.22 (0.97)	*
No	58.74 (3.68)	77.32 (1.05)		68.73 (2.43)	81.81 (0.79)		51.17 (4.62)	79.78 (0.97)	
PY anxiety disorder			**0.006**			**0.0006**			
Yes	44.50 (3.51)	33.65 (1.25)		33.50 (2.68)	23.10 (1.00)		50.95 (4.31)	34.59 (1.07)	**0.0008**
No	55.50 (3.51)	66.35 (1.25)		66.50 (2.68)	76.90 (1.00)		49.05 (4.31)	65.41 (1.07)	
Lifetime anxiety disorder			0.057						
Yes	53.95 (4.15)	45.50 (1.29)		40.99 (3.06)	33.59 (1.11)	**0.0246**	59.73 (4.37)	48.06 (1.22)	**0.0145**
No	46.05 (4.15)	54.50 (1.29)		59.01 (3.06)	66.41 (1.11)		40.27 (4.37)	51.94 (1.22)	
PY AUD			*						
Yes	55.70 (4.52)	11.16 (0.71)		54.90 (3.07)	12.92 (0.69)	*	55.78 (4.81)	10.00 (0.68)	*
No	44.30 (4.52)	88.84 (0.71)		45.10 (3.07)	87.08 (0.69)		44.22 (4.81)	90.00 (0.68)	
Lifetime AUD			*						
Yes	79.84 (2.99)	43.86 (1.37)		81.38 (2.12)	47.40 (1.18)	*	82.58 (3.26)	43.90 (1.24)	*
No	20.16 (2.99)	56.14 (1.37)		18.62 (2.12)	52.60 (1.18)		17.42 (3.26)	56.10 (1.24)	
PY SUD			*						
Yes	52.83 (3.58)	1.53 (0.25)		47.41 (2.48)	1.24 (0.20)	*	51.63 (3.98)	1.23 (0.22)	*
No	47.17 (3.58)	98.47 (0.25)		52.59 (2.48)	98.76 (0.20)		48.37 (3.98)	98.77 (0.22)	
Lifetime SUD			*						
Yes	50.78 (3.23)	11.79 (0.83)		44.85 (2.81)	13.09 (0.70)	*	48.32 (3.92)	9.99 (0.70)	*
No	49.22 (3.23)	88.21 (0.83)		55.15 (2.81)	86.91 (0.70)		51.68 (3.92)	90.01 (0.70)	
Lifetime suicidality			*						
Yes	54.51 (3.65)	35.74 (1.15)		40.75 (3.00)	29.33 (1.07)	**0.0006**	55.22 (4.05)	32.44 (1.06)	*
No	45.49 (3.65)	64.26 (1.15)		59.25 (3.00)	70.67 (1.07)		44.78 (4.05)	67.56 (1.06)	
Lifetime ADHD			**0.012**						
Yes	15.95 (2.67)	8.73 (0.63)		14.11 (1.66)	9.67 (0.59)	**0.0137**	13.40 (2.79)	6.40 (0.57)	**0.0152**
No	84.05 (2.67)	91.27 (0.63)		85.89 (1.66)	90.33 (0.59)		86.60 (2.79)	93.60 (0.57)	
Lifetime Cluster A PD			–						
Yes	–	–		43.87 (2.66)	37.32 (0.98)	**0.0227**	63.63 (4.33)	38.60 (1.19)	*
No	–	–		56.13 (2.66)	62.68 (0.98)		36.37 (4.33)	61.40 (1.19)	
Lifetime Cluster B PD			*						
Yes	81.96 (2.73)	53.19 (1.21)		–	–	–	72.33 (3.84)	35.06 (1.02)	*
No	18.04 (2.73)	46.81 (1.21)		–	–		27.67 (3.84)	64.94 (1.02)	
Lifetime Cluster C PD			**0.024**						
Yes	52.38 (4.06)	42.03 (1.09)		31.87 (2.75)	26.78 (0.92)	0.08	–	–	–
No	47.62 (4.06)	57.97 (1.09)		68.13 (2.75)	73.22 (0.92)				
PY tobacco UD			*						
Yes	64.24 (3.62)	26.18 (1.26)		57.96 (2.76)	25.50 (1.01)	*	61.57 (4.30)	22.41 (1.05)	*
No	35.76 (3.62)	73.82 (1.26)		42.04 (2.76)	74.50 (1.01)		38.43 (4.30)	77.59 (1.05)	
Lifetime tobacco UD			*						
Yes	67.44 (3.40)	31.25 (1.25)		61.19 (2.63)	31.66 (1.07)	*	65.98 (4.05)	29.58 (1.09)	*
No	32.56 (3.40)	68.75 (1.25)		38.81 (2.63)	68.34 (1.07)		34.02 (4.05)	70.42 (1.09)	
PY CUD			*						
Yes	47.80 (3.57)	0.0 (0.0)		43.14 (2.54)	0.0 (0.0)	*	48.27 (3.93)	0.0 (0.0)	*
No	52.20 (3.57)	100.0 (0.0)		56.86 (2.54)	100.0 (0.0)		51.73 (3.93)	100.0 (0.0)	
Lifetime PTSD			0.62						
Yes	17.96 (2.94)	16.46 (0.87)		15.00 (1.91)	14.24 (0.68)	0.72	16.52 (3.03)	12.74 (0.75)	0.23
No	82.04 (2.94)	83.54 (0.87)		85.00 (1.91)	85.76 (0.68)		83.48 (3.03)	87.26 (0.75)	

* $p < 0.0001$; PY – past year; MDD – major depressive disorder; AUD – alcohol use disorder; SUD – substance use disorder (other than alcohol, cannabis, and tobacco); ADHD – attention deficit/hyperactivity disorder; PD – personality disorder; UD – use disorder; CUD – cannabis use disorder; PTSD – post-traumatic stress disorder.

the association of cannabis use with psychiatric comorbidity in the general population (Blanco et al., 2016; Feingold et al., 2015), cannabis use among individuals with PDs is not associated with increased odds of incident mood or anxiety disorders but is associated with increased odds of several SUDs. These findings do not support the hypothesis that cannabis use is a specific risk factor for developing psychiatric disorders among individuals with PDs.

Examination of respondents according to clusters of personality disorders revealed similar findings regarding odds of incident mood or anxiety disorders, while associations with other SUDs did show some cluster-specific variance. For example, cannabis use among respondents with a cluster B PD was associated with increased odds for all SUDs,

Table 3
Logistic regression – OR of psychiatric disorders at Wave 2 in individuals with PD by cannabis use status at Wave 1.

	Any PD – OR (95% CI))			Cluster A – OR (95% CI			Cluster B – OR (95% CI)			Cluster C – OR (95% CI)		
	Any use	Infrequent	frequent	Any use	Infrequent	frequent	Any use	Infrequent	frequent	Any use	Infrequent	frequent
Depressive unadjusted	**1.48 (1.14–1.92)**	**1.50 (1.08–2.09)**	1.43 (0.89–2.31)	**1.43 (1.04–1.95)**	1.30 (0.85–1.99)	1.61 (0.95–2.73)	1.10 (0.86–1.41)	1.16 (0.83–1.61)	1.01 (0.65–1.56)	**1.92 (1.32–2.79)**	**1.72 (1.11–2.66)**	**2.37 (1.14–4.95)**
Depressive adjusted	1.12 (0.78–1.61)	1.19 (0.78–1.80)	0.90 (0.52–1.58)	1.17 (0.78–1.76)	1.14 (0.67–1.93)	1.22 (0.69–2.14)	0.96 (0.68–1.35)	1.03 (0.69–1.54)	0.72 (0.41–1.26)	1.13 (0.70–1.83)	1.04 (0.59–1.83)	1.02 (0.45–2.32)
Manic unadjusted	**2.28 (1.69–3.09)**	**1.85 (1.26–2.71)**	**3.05 (1.91–4.86)**	**1.98 (1.39–2.82)**	**1.76 (1.11–2.79)**	**2.31 (1.30–4.11)**	**1.44 (1.09–1.89)**	1.19 (0.84–1.68)	**1.88 (1.22–2.90)**	**3.35 (2.24–5.00)**	**2.55 (1.57–4.14)**	**5.45 (2.72–10.92)**
Manic adjusted	1.16 (0.79–1.70)	1.05 (0.65–1.70)	1.23 (0.65–2.32)	1.20 (0.76–1.91)	1.26 (0.73–2.19)	0.99 (0.50–1.97)	1.04 (0.74–1.47)	0.99 (0.65–1.52)	1.09 (0.63–1.87)	1.34 (0.77–2.34)	1.20 (0.65–2.23)	1.42 (0.51–3.92)
Anxiety unadjusted	1.26 (0.98–1.62)	1.24 (0.90–1.70)	1.29 (0.86–1.94)	1.15 (0.83–1.59)	1.12 (0.74–1.67)	1.19 (0.75–1.88)	0.97 (0.76–1.22)	1.00 (0.74–1.34)	0.91 (0.63–1.32)	**1.74 (1.19–2.54)**	1.47 (0.95–2.27)	**2.41 (1.33–4.36)**
Anxiety adjusted	1.03 (0.74–1.43)	1.02 (0.71–1.48)	0.87 (0.50–1.53)	1.02 (0.68–1.52)	0.98 (0.63–1.54)	0.94 (0.54–1.65)	0.84 (0.62–1.14)	0.87 (0.63–1.22)	0.66 (0.38–1.16)	1.02 (0.63–1.66)	0.93 (0.56–1.52)	1.02 (0.51–2.03)
AUD unadjusted	**6.21 (4.82–8.00)**	**5.54 (3.94–7.81)**	**7.38 (4.93–11.04)**	**6.26 (4.56–8.59)**	**5.79 (3.85–8.72)**	**6.83 (4.08–11.43)**	**4.72 (3.77–5.92)**	**4.32 (3.21–5.81)**	**5.42 (3.76–7.81)**	**5.71 (3.98–8.21)**	**5.76 (3.65–9.07)**	**5.54 (3.01–10.20)**
AUD adjusted	**1.81 (1.17–2.80)**	1.52 (0.91–2.53)	**2.18 (1.12–4.27)**	**1.97 (1.09–3.55)**	1.81 (0.91–3.57)	1.70 (0.78–3.74)	**1.68 (1.14–2.47)**	1.45 (0.93–2.25)	**1.97 (1.09–3.56)**	1.34 (0.67–2.71)	1.35 (0.64–2.83)	1.03 (0.39–2.68)
SUD unadjusted	**6.22 (4.35–8.90)**	**5.94 (3.80–9.28)**	**6.40 (3.86–10.59)**	**5.20 (3.45–7.84)**	**4.91 (2.91–8.29)**	**5.39 (2.92–9.98)**	**4.26 (3.08–5.89)**	**3.95 (2.65–5.88)**	**4.53 (2.82–7.26)**	**6.96 (4.19–11.57)**	**6.61 (3.54–12.32)**	**7.12 (3.17–15.98)**
SUD adjusted	**2.19 (1.09–4.40)**	1.64 (0.78–3.47)	1.39 (0.39–4.99)	1.89 (0.88–4.06)	1.61 (0.69–3.77)	1.01 (0.27–3.83)	**2.14 (1.30–3.51)**	**1.79 (1.01–3.15)**	1.68 (0.63–4.46)	1.84 (0.69–4.92)	1.69 (0.62–4.65)	0.49 (0.13–1.85)
TUD unadjusted	**3.25 (2.53–4.18)**	**2.88 (2.14–3.87)**	**3.90 (2.66–5.73)**	**3.98 (2.95–5.36)**	**3.18 (2.11–4.80)**	**5.42 (3.48–8.44)**	**2.64 (2.11–3.31)**	**2.34 (1.77–3.09)**	**3.20 (2.30–4.45)**	**4.78 (3.32–6.88)**	**4.39 (2.90–6.63)**	**5.66 (3.02–10.61)**
TUD adjusted	**1.84 (1.30–2.60)**	**1.70 (1.16–2.50)**	1.58 (0.90–2.76)	**2.21 (1.44–3.40)**	**2.15 (1.32–3.52)**	**1.92 (1.02–3.60)**	**1.80 (1.28–2.54)**	**1.66 (1.15–2.40)**	1.48 (0.84–2.63)	**1.90 (1.18–3.07)**	**2.02 (1.20–3.40)**	1.17 (0.49–2.80)

For which disorders were included in every diagnostic category – see text. AUD – alcohol use disorder; SUD – substance use disorder (other than alcohol, cannabis, and tobacco); ADHD – attention deficit/hyperactivity disorder; PD – personality disorder; TUD – tobacco use disorder; CUD – cannabis use disorder; PTSD – post-traumatic stress disorder; can – cannabis.

Table 4
Logistic regression – interaction effect of cannabis use X personality disorder at Wave 1 on OR of incident psychiatric disorders at Wave 2.

	Any PD			Cluster A			Cluster B			Cluster C		
	Any can use	Infrequent can use	Frequent can use	Any can use	Infrequent can use	Frequent can use	Any can use	Infrequent can use	Frequent can use	Any can use	Infrequent can use	Frequent can use
Depressive unadjusted	0.99 (0.69–1.42)	1.06 (0.70–1.61)	0.83 (0.42–1.65)	0.90 (0.61–1.31)	0.78 (0.48–1.28)	1.15 (0.55–2.40)	0.85 (0.60–1.21)	0.97 (0.62–1.54)	0.61 (0.30–1.22)	1.10 (0.71–1.69)	1.04 (0.62–1.73)	1.21 (0.54–2.71)
Depressive adjusted	1.11 (0.76–1.62)	1.16 (0.74–1.80)	1.04 (0.51–2.12)	0.95 (0.63–1.43)	0.81 (0.47–1.39)	1.29 (0.62–2.70)	0.94 (0.64–1.38)	1.07 (0.65–1.76)	0.72 (0.35–1.49)	1.06 (0.67–1.66)	0.98 (0.56–1.72)	1.17 (0.50–2.71)
Manic unadjusted	0.86 (0.52–1.43)	0.83 (0.46–1.50)	0.77 (0.33–1.82)	**0.64 (0.41–0.98) $p = 0.04$**	0.72 (0.40–1.31)	**0.46 (0.22–0.94) $p = 0.0345$**	**0.55 (0.32–0.94) $p = 0.03$**	0.54 (0.29–1.02)	0.47 (0.17–1.29)	1.15 (0.70–1.89)	1.11 (0.61–2.05)	1.21 (0.53–2.77)
Manic adjusted	0.89 (0.54–1.47)	0.84 (0.45–1.56)	0.92 (0.40–2.12)	0.69 (0.43–1.11)	0.80 (0.42–1.53)	0.52 (0.25–1.09)	0.63 (0.37–1.08)	0.62 (0.33–1.19)	0.62 (0.24–1.61)	1.09 (0.65–1.84)	1.08 (0.56–2.09)	1.12 (0.47–2.68)
Anxiety unadjusted	0.82 (0.57–1.19)	0.87 (0.56–1.36)	0.68 (0.35–1.30)	0.72 (0.49–1.07)	0.74 (0.46–1.19)	0.66 (0.34–1.30)	0.71 (0.49–1.02)	0.83 (0.54–1.26)	**0.48 (0.24–0.98) $p = 0.04$**	1.08 (0.68–1.72)	0.97 (0.58–1.62)	1.31 (0.63–2.76)
Anxiety adjusted	0.88 (0.60–1.28)	0.93 (0.58–1.50)	0.74 (0.39–1.39)	0.73 (0.47–1.14)	0.75 (0.44–1.27)	0.67 (0.34–1.32)	0.74 (0.50–1.10)	0.86 (0.54–1.36)	0.53 (0.26–1.08)	1.04 (0.64–1.71)	0.90 (0.51–1.58)	1.35 (0.64–2.87)
AUD unadjusted	0.84 (0.61–1.15)	1.65 (1.47–1.84)	1.10 (0.66–1.82)	0.84 (0.59–1.18)	0.78 (0.50–1.23)	0.90 (0.49–1.66)	**0.67 (0.50–0.89) $p = 0.0065$**	**0.59 (0.41–0.85) $p = 0.0051$**	0.90 (0.55–1.46)	0.72 (0.48–1.07)	0.76 (0.46–1.25)	0.63 (0.32–1.26)
AUD adjusted	0.94 (0.60–1.46)	0.76 (0.43–1.33)	1.44 (0.78–2.65)	0.87 (0.52–1.46)	0.83 (0.43–1.62)	0.91 (0.41–1.99)	0.78 (0.51–1.20)	0.67 (0.40–1.13)	1.10 (0.58–2.07)	0.63 (0.37–1.08)	0.64 (0.33–1.23)	0.60 (0.25–1.41)
SUD unadjusted	**0.57 (0.36–0.88) $p = 0.0124$**	0.63 (0.37–1.08)	**0.40 (0.20–0.80) $p = 0.0105$**	**0.45 (0.29–0.71) $p = 0.0009$**	**0.48 (0.28–0.83) $p = 0.0087$**	**0.37 (0.17–0.80) $p = 0.0124$**	**0.38 (0.24–0.61) $p = 0.0001$***	**0.40 (0.24–0.66) $p = 0.0005$***	**0.31 (0.13–0.71) $p = 0.0064$**	0.62 (0.36–1.07)	0.69 (0.35–1.38)	0.47 (0.18–1.19)
SUD adjusted	0.61 (0.37–1.01)	0.67 (0.37–1.22)	0.52 (0.24–1.12)	**0.49 (0.30–0.81) $p = 0.0064$**	0.55 (0.29–1.03)	**0.41 (0.17–0.99) $p = 0.0469$**	**0.47 (0.28–0.77) $p = 0.0037$**	**0.50 (0.28–0.90) $p = 0.0203$**	**0.40 (0.16–0.99) $p = 0.0486$**	0.63 (0.34–1.16)	0.69 (0.32–1.51)	0.51 (0.18–1.45)
TUD unadjusted	0.85 (0.62–1.18)	0.91 (0.63–1.31)	0.61 (0.36–1.04)	1.07 (0.77–1.49)	0.98 (0.63–1.54)	1.03 (0.59–1.77)	**0.73 (0.55–0.97) $p = 0.032$**	0.77 (0.55–1.10)	**0.53 (0.31–0.89) $p = 0.018$**	1.23 (0.82–1.85)	1.39 (0.86–2.25)	0.91 (0.46–1.82)
TUD adjusted	0.82 (0.58–1.16)	0.93 (0.63–1.39)	0.55 (0.30–1.03)	1.14 (0.78–1.66)	1.12 (0.68–1.84)	1.03 (0.54–1.95)	0.74 (0.54–1.03)	0.83 (0.56–1.24)	**0.51 (0.28–0.93) $p = 0.0276$**	1.11 (0.71–1.74)	1.36 (0.80–2.31)	0.70 (0.32–1.53)

For which disorders were included in every diagnostic category – see text. AUD – alcohol use disorder; SUD – substance use disorder (other than alcohol, cannabis, and tobacco); ADHD – attention deficit/hyperactivity disorder; PD – personality disorder; TUD – tobacco use disorder; CUD – cannabis use disorder; PTSD – post-traumatic stress disorder; can – cannabis.

* Significance maintained after Bonferroni correction.

while cannabis use in respondents with a cluster C diagnosis was associated with increased odds solely for tobacco use disorder.

The differences found between different PD clusters regarding incident SUDs are consistent with previous studies (Fenton et al., 2012; Hasin et al., 2011; Hasin and Kilcoyne, 2012) demonstrating that different PDs are variably associated with increased risk for different SUDs. It has been previously demonstrated that specific personality traits, such as those associated with borderline, schizotypal and antisocial PDs, explain a high part of the variance in problematic substance use (Chabrol et al., 2015), and that several cluster A and B PDs are associated with persistence of various SUDs, while obsessive-compulsive PD, a cluster C disorder, was associated with persistence of tobacco use only (Hasin et al., 2011).

Our findings fail to demonstrate a consistent dose-response relationship between frequency of cannabis use and incident comorbid psychiatric disorders among individuals diagnosed with a PD. Nevertheless, a dose-response relationship was shown among those with any PD and those with cluster B PD between cannabis use and increased odds of incident AUD. This longitudinal association between incident alcohol use disorder and frequent cannabis use has been previously demonstrated (Buu et al., 2014), though to the best of our knowledge this has not been previously reported among individuals with PDs. The reverse association found between frequency of cannabis use and tobacco use disorder may be explained by a possible "substitute-effect" where more frequent cannabis use comes in place of tobacco use, though this possibility could not be assessed directly in our study and requires further exploration.

We further examined the possibility of an interaction effect between different levels of cannabis use and different PD clusters. The interaction analyses generally show a trend for an antagonistic interaction between cannabis use and personality disorders (most notably cluster A and B PDs), but the only findings maintaining significance after correction for multiple comparisons were those in individuals with cluster B PD.

The lack of additive interaction and trend for an antagonistic interaction between cluster A and B PDs and cannabis use may be due to several, non-mutually exclusive mechanisms.

First, though both cannabis use and PDs each have an independent contribution to the incidence of SUDs, it is possible that the interaction between the two attenuates this effect through a self-medicating property of cannabis among individuals with a PD. Alternatively, there may be an additional non-measured confounder which contributed to these findings. Though adjustments were made for multiple confounders, several additional possible confounders were not accounted for, such as genetic data, specific personality traits and early life trauma, all previously found to be associated with both cannabis use and PDs (Distel et al., 2012; Dumas et al., 2002; Ersche et al., 2010; Fridberg et al., 2011; Ruiz et al., 2008; Trull et al., 2000).

The findings do not support the hypothesis that cannabis use and PDs have an additive interaction associated with an excess risk for incident psychiatric comorbidity. These negative findings may support the notion that cannabis, rather than having a causal role in the development of other SUDs, is mainly a marker of other risk factors for these conditions. Some of these risk factors may be personality traits (e.g. novelty seeking, harm avoidance), family background factors (e.g. socio-economic status, parental conflict and divorce, parental attachment) and parental adjustment factors (e.g. parental substance use, parental mental health), all of which may be shared between personality disorders and substance use (Hall and Lynskey, 2005; Kaplan et al., 1984; Osgood et al., 1988; Shedler and Block, 1990).

There are several limitations to the current study. First, the NESARC questionnaires do not directly assess schizophrenia and other psychotic disorders (comorbidities which were shown to be associated with cannabis use) (The National Academies of Sciences Engineering and Medicine, 2017), as well as some personality disorders. However, using a single question based on self-reported psychotic disorder, the association between cannabis use, schizotypal personality disorder and psychotic disorder was explored using the NESARC data in a previous paper (Davis et al., 2013), results of which indicate that the risk of both psychosis and schizotypal personality disorder increases with greater use of cannabis, in a dose- dependent manner. Second, though the study population is relatively large, some of the analyses conducted, particularly when trying to assess specific personality disorder clusters, were underpowered. This lack of statistical power is particularly relevant when discussing the findings regarding dose-response relationships, as frequent cannabis use was reported by only a small minority of cannabis users. Finally, some populations, such as individuals under 18 years of age, and those incarcerated, homeless or hospitalized during the interview periods, were not included in the sample. This is particularly of importance in the case of homeless and incarcerated people, groups with a higher prevalence of both cannabis use and PDs (Abram et al., 2003; Fazel et al., 2008; Fazel and Danesh, 2002; Jordan et al., 1996; Rasmussen et al., 2001; Rotter et al., 2002; Smith et al., 1993).

In summary, this is the first population-based epidemiologic study to examine the association of cannabis use and psychiatric comorbidity in individuals with personality disorders. Our findings support previous findings from the general population that have shown that, when adjusted for confounders, cannabis use was not associated with increased odds of incident mood or anxiety disorders, while odds of some substance use disorders were significantly increased. Our findings suggest that while cannabis use and personality disorders are both longitudinally associated with increased odds for incident psychiatric comorbidity, interaction between the two does not seem to increase odds of incident psychiatric comorbidity, and in few cases significantly decreases these odds. There is need for additional large-scale longitudinal studies focusing on the contribution of more specific variables (e.g. personality traits, early-life adversities, family background factors, neurocognitive factors) to the association of cannabis use and personality disorders with the development of other psychiatric disorders.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2019.05.041.

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