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Association between cannabis use, psychosis, and schizotypal personality disorder: findings from the National Epidemiologic Survey of Alcohol and Related Conditions

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Abstract

Background—Studies to date showing an association between cannabis use and schizophrenia-spectrum disorders are of relatively small sample sizes with limitations in generalizability. The present study addresses this gap by examining the relationship between cannabis use and psychotic-like symptoms in a large representative community sample.

Method—Data were derived from the 2004 – 2005 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC, Wave 2), a large, nationally representative sample of 34 653 adults from the United States population. We evaluated the association between lifetime cannabis use, psychosis, and schizotypal personality features.

Results—The prevalence of psychosis and schizotypal personality disorder increased significantly with greater cannabis use in a dose-dependent manner. The association between cannabis use and psychosis was 1.27 (95% CI 1.03–1.57) for lifetime cannabis use, 1.79 (95% CI 1.35–2.38) for lifetime cannabis abuse, and 3.69 (95% CI 2.49–5.47) for lifetime cannabis dependence. There was a similar dose-response relationship between the extent of cannabis use and schizotypal personality disorder (OR = 2.02 for lifetime cannabis use, 95% CI 1.69–2.42; OR = 2.83 for lifetime cannabis abuse, 95% CI 2.33–2.43; OR = 7.32 for lifetime cannabis

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Contributors

GD and CB were extensively involved in the conception and planning of the focus and content of this manuscript. GD undertook the literature search and completed the first draft of the paper. SW conducted the statistical analysis for this study. GD worked closely with CB in subsequent revisions of the manuscript. MC and FL provided feedback and provided additional content to the body of the report. All authors contributed to and have approved the final manuscript.

Conflict of Interest

The authors have no conflicts of interest to declare.

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dependence, 95% CI 5.51–9.72). Likelihood of individual schizotypal features increased significantly with increased extent of cannabis use in a dose-dependent manner.

Conclusion—This is the first population-based study to examine the association between lifetime cannabis use, psychosis, and schizotypal personality traits. These results add to evidence that cannabis use may be a risk factor for psychosis liability.

Keywords

cannabis; epidemiology; psychosis; schizotypal; NESARC

1. INTRODUCTION

Cannabis is the most widely used illicit substance in the United States (Substance Abuse and Mental Health Services Administration, 2010) and the most commonly used illicit drug among patients with schizophrenia. Accumulating evidence from longitudinal epidemiologic studies also suggests that cannabis use may increase the risk of schizophrenia (Andreasson et al., 1987; Arseneault et al., 2002; Degenhardt et al., 2001; Fergusson et al., 2003; Henquet et al., 2005; Tien and Anthony, 1990; van Os et al., 2002; Zammit et al., 2002), serving as a component cause of the disorder, meaning one of a constellation of complex factors that may hasten the development of psychotic symptoms while neither necessary nor sufficient to do so alone (Compton et al., 2009).

One approach to explore the relationship between cannabis use and psychotic symptoms is to examine cannabis use as a correlate of schizotypal personality disorder (SPD), characterized by a set of dimensional traits that are thought to contribute to risk for psychosis. SPD traits have been reported to be more prevalent in relatives of patients with schizophrenia (Appels et al., 2004; Kendler et al., 1995) and may share some of the same genetic underpinnings as schizophrenia (Fanous et al., 2007). Individuals with SPD also exhibit social deficits similar to, but less prominent than, those found in schizophrenia (Dickey et al., 2005).

An emerging body of research suggests an association between schizotypy and cannabis use. Several small studies of university students have found associations between cannabis use and positive schizotypal features (Bailey and Swallow, 2004; Barkus and Lewis, 2008; Dumas et al., 2002; Esterberg et al., 2009; Mass et al., 2001; Najolia et al., 2012; Nunn et al., 2001; Schiffman et al., 2005; Skosnik et al., 2001; Williams et al., 1996). One study of 40 college undergraduates found a significant positive correlation between schizotypy scores and cannabis use (Skosnik et al., 2001). Another study (Bailey and Swallow, 2004) found an association between cannabis use and the presence of positive, negative, and disorganized schizotypal traits among 60 undergraduates. However, other studies have shown that cannabis users have lower negative schizotypal traits than non-users (Nunn et al., 2001; Schiffman et al., 2005).

Understanding the relationship between cannabis use and SPD is important for enhancing our understanding of cannabis use as a risk factor for schizophrenia-spectrum disorders and has implications for prevention and treatment, especially in light of evidence showing that interventions targeting personality factors can significantly reduce substance use (Conrod et al., 2008). While studies to date provide a foundation for establishing an association between cannabis use and schizotypy, previous studies have shown both positive and negative associations between cannabis use and domains of schizotypy, as described above. Discrepancy in previous research challenges our understanding of the relationship between cannabis use and schizotypy. One possible explanation for the discrepancy in previous studies is that all of them are limited by relatively sample sizes and limited statistical power,

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as well as limitations in generalizability. None has examined whether the extent of cannabis use is associated with likelihood of having SPD features. We aim to clarify the discrepancy in previous research on cannabis use and schizotypy using an epidemiologic approach that extends current evidence based on small survey samples. The present study examines – in a large, representative U.S. sample – the relationship between cannabis use and both psychosis and SPD, and whether there is a dose-response relationship between the extent of cannabis use and psychosis and specific schizotypal personality traits.

2. METHODS

2.1 Sample and procedures

Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) was used as the source of data. The NESARC is a large, nationally representative survey of people living in the 50 states of the U.S. and the District of Columbia, including citizens and noncitizens, aged 18 years and older (Grant, 2003; Grant et al., 2005; Grant et al., 2004). Wave 1 of the NESARC was conducted in 2001 and 2002 with households and non-institutional group quarters, with a total of 43 093 respondents and response rate of 81.2%. The Wave 1 NESARC assessed Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) alcohol and specific drug use disorders, mood and anxiety disorders, and some personality disorders (avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic, and antisocial). In Wave 2, conducted in 2004 – 2005, attempts were made to interview all 43 093 respondents from Wave 1. After excluding individuals ineligible for Wave 2 (e.g., deceased), the Wave 2 response rate was 86.7%, reflecting 34,653 completed Wave 2 interviews. The Wave 2 interview assessed DSM-IV alcohol and specific drug use disorders and mood/anxiety disorders assessed in Wave 1, in addition to schizotypal, borderline, and narcissistic personality disorders, posttraumatic stress disorder and attention-deficit/hyperactivity disorder. The current study is an analysis of Wave 2 NESARC data (SPD was not assessed in Wave 1).

The weighted data were adjusted to represent the U.S. civilian population based on the 2000 Census. All of the potential respondents were informed about the nature of the survey, the statistical uses of data, the voluntary nature of their participation, and federal laws regarding the confidentiality of the identifiable survey information. Additional details about the NESARC methodology can be found elsewhere (Grant, 2003).

2.2 Diagnostic assessment

The Alcohol Use Disorder and Associated Disabilities Interview Schedule, DSM-IV Version (AUDADIS-IV) (Grant et al., 2003), a structured diagnostic interview designed for administration by professional interviewers, was used to assess lifetime and past-year DSM-IV disorders. In addition to questions to diagnose mood, anxiety, psychotic, and personality disorders, the AUDADIS-IV included questions on an extensive list of symptoms that separately operationalized DSM-IV criteria for substance use disorders, including drug-specific abuse and dependence for cannabis and nine other classes of drugs. Information on the reliability and validity of the AUDADIS-IV has been previously published (Grant et al., 2003; Ruan et al., 2008). Due to concerns about the feasibility of assessing psychotic diagnoses in general population surveys (Kendler et al., 1996; Kessler et al., 2005) as well as the length of the interview, a diagnosis of lifetime schizophrenia or a psychotic illness or episode (SPIE) was given to any person who answered yes to the question, “Did a doctor or other health professional ever diagnose you with schizophrenia or a psychotic illness or episode?” This method, which was validated in a prior study (Supina and Patten, 2006), provides prevalence rates of schizophrenia similar to those estimated in the North American population (Jablensky, 1997).

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The diagnosis of personality disorders requires evaluation of long-term patterns of functioning (American Psychiatric Association, 1994). Diagnoses of SPD in the AUDADISIV were made accordingly. All NESARC respondents were asked a series of SPD symptom questions about how they felt or acted most of the time throughout their lives, regardless of the situation or whom they were with at the time. They were instructed not to include symptoms occurring only when they were depressed, manic, anxious, drinking heavily, using medicines or drugs, experiencing withdrawal symptoms (defined earlier in the interview), or physically ill.

Multiple symptom items were used to operationalize the criteria for DSM-IV personality disorders, including SPD. Personality disorder symptom items (Grant et al., 2003) were similar to those appearing in the Structured Clinical Interview for DSM-IV Axis II Disorders (First et al., 1997), the International Personality Disorder Examination (Loranger, 1999), and the Diagnostic Interview for DSM-IV Personality Disorders (Zanari et al., 1996).

The reliability of AUDADIS-IV personality disorder diagnoses and symptoms scales was assessed in large test-retest studies conducted as part of the Wave 1 and Wave 2 NESARC surveys. The test-retest reliability of the SPD section of the measure has been reported as .67 in smaller samples, with average test and retest interval of 5.9 weeks (Ruan et al., 2008). The internal consistency of the SPD section of the NESARC data is .83, which supports the reliability of the measure in the NESARC (Ahmed et al, 2013). The test-retest reliabilities ranged from fair to good (κ = 0.40 to 0.71) for other personality disorders and from 0.79 to 0.83 for schizophrenia or psychotic episode (Grant et al., 2003), with little variability in test and retest intervals between sites, ranging from 3 to 20 weeks with average of approximately 10.2 weeks.

2.3 Statistical Analyses

Among Wave 2 respondents, we compared demographic characteristics (sex, age, and race) of lifetime cannabis users (defined as at least one episode of cannabis use during a person's lifetime) and non-users. We also determined the percentage of participants with lifetime cannabis use, SPIE, and SPD in all Wave 2 respondents. Logistic regression analyses were used to obtain odds ratios (ORs) measuring the association between lifetime cannabis use, abuse, and dependence (using no lifetime cannabis use as the reference group) with psychosis and SPD. Logistic regression analyses also yielded ORs measuring the association between lifetime cannabis use, abuse, and dependence and likelihood of individual symptoms of SPD to examine whether the strength of association varied by symptom.

Standard errors and 95% confidence intervals for all analyses were estimated using SUDAAN (Research Triangle Park, 2008) to account for design effects of the NESARC. In examining associations between lifetime cannabis use and SPIE and SPD, adjustments were made for sociodemographic characteristics (sex, age, and race).

To be comprehensive in our analyses, we conducted the same analyses with individuals with lifetime cannabis use and individuals with past-year cannabis use. The pattern of results was the same for both sets of analyses, although due to the smaller sample size, some of the analyses using past-year users had lower power. Therefore, we present the results of the lifetime analyses. The results of the past-year analyses are available upon request.

3. RESULTS

Table 1 shows the descriptive sample characteristics of lifetime cannabis users and nonusers. Compared to non-users (n = 27 025), lifetime cannabis users (n = 7 438) were significantly more likely to be male. There were also significant differences with regard to age and race.

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Lifetime cannabis users were more likely to be younger (30–44 years old), and they were more likely to be white compared to cannabis non-users.

Table 2 shows the percentage of lifetime cannabis users in the entire sample (n = 34,653) categorized as: no use, 77.53%; use, 12.82%; abuse, 7.91%; or dependence, 1.74%). SPIE was reported in 3.12% of the sample, and SPD was diagnosed in 3.93%.

There was a dose-response relationship between the level of cannabis use and SPIE (Table 3). Compared to individuals without lifetime cannabis use, the OR for SPIE was 1.10 for lifetime cannabis use, 1.45 for lifetime cannabis abuse, and 2.72 for lifetime cannabis dependence. The association between cannabis use and SPIE remained significant after adjusting for sociodemographic characteristics (OR = 1.27 for lifetime cannabis use, 1.79 for lifetime cannabis abuse, and 3.69 for lifetime cannabis dependence).

There was also a dose-response relationship between the level of cannabis use and SPD (Table 3) that was stronger than that between level of cannabis use and SPIE. After adjusting for sociodemographic characteristics, the OR for SPD was 2.02 for lifetime cannabis use, 2.83 for lifetime cannabis abuse, and 7.32 for lifetime cannabis dependence.

In the analysis of individual SPD symptoms (Table 4), cannabis use predicted a significantly greater prevalence of almost all domains of schizotypy, increasing with severity of use, even after controlling for sociodemographic characteristics. In Figure 1, the symptoms more strongly associated with severity of cannabis use (categorized as use, abuse, or dependence) were: suspicious or paranoid ideation (AOR = 1.75, 2.69, and 5.62, respectively); inappropriate or constricted affect (AOR = 1.70, 2.42, 3.76, respectively); and behavior or appearance that is odd, eccentric, or peculiar (AOR = 2.54, 3.59, and 8.04, respectively). Cannabis use also predicted a significantly greater likelihood of other SPD features (ideas of reference, odd beliefs or magical thinking, unusual perceptual disturbances, lack of close friends or confidants other than first-degree relatives, and excessive social anxiety). A dose-response relationship was apparent for each of the nine SPD features.

4. DISCUSSION

This is the first population-based study to examine the association between lifetime cannabis use, self-reported history of psychotic illness or episode (SPIE), schizotypal personality disorder (SPD), and schizotypal features, further implicating cannabis use as a possible risk factor for psychosis liability. The results indicate that the risk of both psychosis and SPD increases with greater use of cannabis, in a dose-dependent manner. Compared to non-users, greater cannabis use showed significantly elevated risk of having been diagnosed with SPIE and elevated risk of all SPD symptoms, even after adjusting for sociodemographic characteristics. Although the cross-sectional design of the study limits inferences about causality, together with previous studies (Andreasson et al., 1987; Arseneault et al., 2002; Degenhardt et al., 2001; Fergusson et al., 2003; Henquet et al., 2005; Tien and Anthony, 1990; van Os et al., 2002; Zammit et al., 2002) our findings suggest that cannabis use may contribute to the etiopathogenesis of psychotic features.

The association between cannabis use and SPIE and SPD found in this study could be explained by three mechanisms: (1) Direct pharmacological effects of cannabis lead to psychosis or schizotypal traits; (2) Psychosis or schizotypal traits lead to cannabis use as a means for individuals to cope with these symptoms; or (3) Another associative factor influences both tendency toward psychosis or schizotypal traits and cannabis use. Concerning the first potential mechanism, it has been well established that cannabis use can increase positive symptoms in individuals with psychosis (D'Souza et al., 2005; Henquet et al., 2005; Negrete et al., 1986), a relationship that could be mediated by dopaminergic

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hyperactivity. Cannabinoids increase the activity of dopaminergic neurons in the ventral tegmental area within the mesolimbic pathway (Ameri, 1999). While there is limited support for a separate clinical diagnosis of “cannabis psychosis” (Thornicroft, 1990), the ability of cannabis to increase activity of the mesolimbic dopaminergic system could explain the short-term persistence of psychotic-like effects after cannabis intoxication (D'Souza et al., 2009).

An alterative explanation to the pharmacological effects of cannabis is that individuals with SPIE or SPD may use cannabis in an attempt to alleviate their symptoms. Case reports have suggested that cannabidiol, a component of cannabis, might exert antipsychotic effects in individuals with psychosis (Zuardi et al., 2006; Zuardi et al., 1995), and experimental studies suggest that cannabidiol may reduce psychosis-like effects of Δ^9-tetrahydrocannabinol and synthetic analogs (Bhattacharyya et al., 2010; Leweke et al., 2000). Evoking the “self-medication” hypothesis in schizophrenia (Peralta and Cuesta, 1992), individuals with SPIE or SPD could therefore attempt to reduce psychotic-like symptoms (or other illness features) by using cannabis (Khantzian, 1997; Schneier and Siris, 1987).

A third potential explanation for the observed association between psychosis, schizotypal traits, and cannabis use could be a co-occurrence without any causal link but with a common etiopathological factor. Based on the cannabinoid hypothesis of schizophrenia (Leweke et al., 1999; Schneider et al., 1998), perturbations in the endogenous cannabinoid system could lead to both a vulnerability for schizophrenia-spectrum symptoms and to a vulnerability for cannabis use. Each of these hypotheses appears viable, and they are not mutually exclusive.

In addition to showing an association between cannabis use and higher scores of measures of schizotypy (Bailey and Swallow, 2004; Barkus and Lewis, 2008; Dumas et al., 2002; Esterberg et al., 2009; Najolia et al., 2012; Nunn et al., 2001; Schiffman et al., 2005; Skosnik et al., 2001; Williams et al., 1996), the current study suggests a broader association between cannabis use and SPD across all domains of schizotypy. The nine features of SPD appear to belong to three broad psychopathological domains (Raine, 2006): positive/cognitive-perceptual (paranoid ideation, magical thinking, unusual perceptual disturbances, ideas of reference), negative/interpersonal (constricted affect, lack of close friends, excessive social anxiety), and disorganized features (odd/eccentric behavior, odd speech). Among non-clinical young adult populations, cannabis use has previously been associated with higher rates of positive and disorganized, but not negative/interpersonal, schizotypy traits (Bailey and Swallow, 2004; Cohen et al., 2011; Earleywine, 2006; Mass et al., 2001; Schiffman et al., 2005; Williams et al., 1996). The current study shows that cannabis use is associated with schizotypy across all three SPD symptoms clusters, including negative/interpersonal traits (constricted affect, lack of close friends, excessive social anxiety). In fact, excessive social anxiety was a SPD symptom found in this study to be strongly associated with the extent of cannabis use (cannabis use AOR = 2.04, 95% CI = 1.48–2.82; abuse AOR = 2.62, 95% CI = 1.90–3.60; and dependence AOR = 9.32, 95% CI = 5.99–14.49). This finding is clinically significant in light of studies showing that there is a positive relationship between social anxiety and cannabis use disorder (Agosti et al., 2002; Buckner et al., 2012; Buckner and Schmidt, 2008) and cannabis-related problems (Buckner et al., 2011; Buckner et al., 2006a; Buckner and Schmidt, 2008, 2009; Buckner et al., 2006b; Marmorstein et al., 2010) in the general population.

As noted, the current study cannot determine if schizotypal traits predispose subjects to use cannabis or if cannabis use increases schizotypal traits. One previous study used a longitudinal design to explore the temporal relationship between cannabis use and the development of SPD symptoms (Anglin et al., 2012). Prospective data from 804 participants

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in that study showed that the initiation of cannabis use prior to age 14 strongly predicted SPD symptoms in adulthood, independent of early adolescent SPD symptoms, major depression, anxiety disorder, other drug use, and cigarette use. The sample size in that study did not provide adequate statistical power to make firm conclusions regarding specific SPD features. However, those data, together with the findings of the present cross-sectional analysis, suggest the need to investigate in a developmental context the mechanisms that underlie the association of cannabis use and SPD symptoms.

Methodological limitations inherent to the current study design should be considered. First, the diagnosis of SPIE was based on individuals' self-report by asking them if a physician or other health professional had ever diagnosed them with schizophrenia or psychotic disorder. It should be acknowledged that self-report of these diagnoses is questionably reliable. Yet self-report method described above has been used in previous studies, and results are consistent with accepted prevalence rates of psychotic disorders in the North American population (McMillan et al., 2009; Supina and Patten, 2006). These reports have shown similar rates of self-reported schizophrenia in population-based samples as those found in several studies relying on clinical diagnoses, with similar age and sex distribution.

A second methodological is that it is possible that some aspects of schizotypy may not be fully recognized by those who have such traits. Fourth, the cross-sectional nature of the study limits inferences about causality. Finally, although the NESARC sampling frame included group quarters, some special 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.

In summary, this is the first population-based epidemiologic study to examine the association of cannabis use, psychosis, and schizotypy, showing that prevalence of both psychosis and SPD increases with greater severity of cannabis use in a dose-dependent manner. Compared to non-users, cannabis users had a significantly elevated prevalence of SPD symptoms across all domains (positive/cognitive-perceptual, negative/interpersonal, and disorganized), adding to evidence that cannabis use may contribute to the etiopathogenesis of schizophrenia-related symptoms. There is a need to examine the biological underpinnings of the relationship between cannabis use and the development of schizophrenia-spectrum symptoms, which may ultimately inform the development of more effective interventions for individuals with cannabis use and schizophrenia-spectrum disorders.

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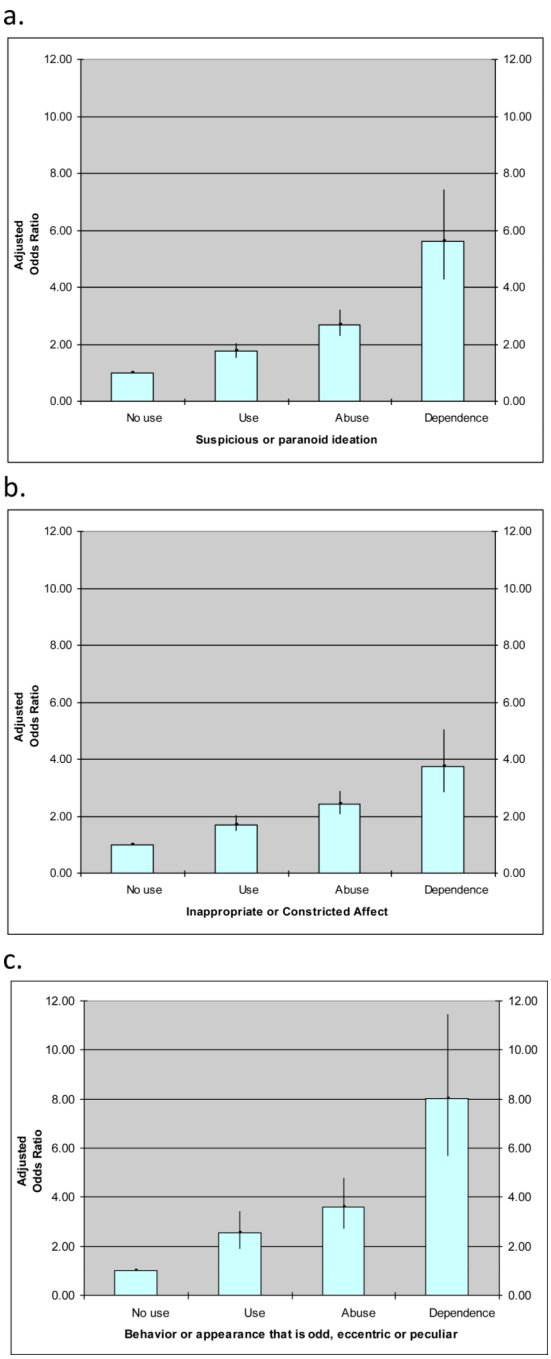

Figure 1.

Relationship between cannabis use, abuse, and dependence and three of nine features of schizotypal personality disorder in NESARC Wave 2 (n = 34,653). (a) Suspicious or paranoid ideation; (b) Inappropriate or constricted affect; (c) Behavior or appearance that is odd, eccentric, or peculiar.

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Table 1

Descriptive Sample Characteristics of Cannabis Users and Nonusers

	Lifetime Cannabis Users (N=7,438)			Nonusers (N=27,025)					
Characteristics	**%**	**95% CI**		**%**	**95% CI**		**OR**	**95% CI**	
Sex									
Male	58.51	57.12	59.89	44.83	44.06	45.61	1.74	1.63	1.85
Female	41.49	40.11	42.88	55.17	54.39	55.94	1.00	1.00	1.00
Age									
18–29 years old	23.47	22.13	24.87	14.29	13.62	14.98	1.00	1.00	1.00
30–44 years old	39.33	37.94	40.74	26.90	26.03	27.79	0.89	0.80	0.99
45+ years old	37.20	35.79	38.63	58.81	57.78	59.84	0.39	0.35	0.42
Race									
White	76.51	74.11	78.76	69.29	65.80	72.58	1.00	1.00	1.00
Non-White	23.49	21.24	25.89	30.71	27.42	34.20	0.69	0.63	0.77

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Table 2

Descriptive Sample Characteristics of Cannabis Users and Nonusers

	All Subjects (N=34,653)		
Characteristics	**%**	**95% CI**	
Cannabis use (lifetime)			
No use	77.53	76.46	78.58
Use	12.82	12.15	13.52
Abuse	7.91	7.42	8.42
Dependence	1.74	1.53	1.97
Cannabis use (past-year)			
No use	95.43	95.05	95.78
Use	2.97	2.71	3.25
Abuse	1.23	1.07	1.40
Dependence	0.37	0.29	0.49
Schizophrenia or a psychotic illness or episode	3.12	2.80	3.47
Schizotypal personality disorder	3.93	3.63	4.26

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Table 3

Associations between Cannabis Use, Psychosis, and SPD

	All Subjects					
Comparison	**OR**	**95% CI**		**AOR***	**95% CI**	
Cannabis use (lifetime) vs. likelihood of psychosis						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	1.10	0.89	1.35	1.27	1.03	1.57
Abuse	1.45	1.09	1.92	1.79	1.35	2.38
Dependence	2.72	1.83	4.05	3.69	2.49	5.47
	All Subjects					
Comparison	**OR**	**95% CI**		**AOR***	**95% CI**	
Cannabis use (lifetime) vs. likelihood of schizotypal personality disorder						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	2.03	1.70	2.42	2.02	1.69	2.42
Abuse	2.88	2.38	3.48	2.83	2.33	3.43
Dependence	7.97	6.00	10.60	7.32	5.51	9.72

*adjusted for sociodemographic characteristics

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Table 4

Associations between Cannabis Use and Features of Schizotypal Personality Disorder (SPD)

	All Subjects					
Comparison	**OR**	**95% CI**		**AOR***	**95% CI**	
Cannabis use (lifetime) vs. Symptoms of SPD						
Ideas of reference						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	0.93	0.63	1.38	0.95	0.63	1.43
Abuse	2.13	1.44	3.15	2.26	1.51	3.38
Dependence	5.20	3.12	8.66	5.15	3.04	8.75
Odd beliefs or magical thinking						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	2.08	1.63	2.65	2.21	1.73	2.82
Abuse	2.38	1.83	3.10	2.55	1.94	3.36
Dependence	6.36	4.42	9.15	6.66	4.60	9.65
Unusual perceptual experiences						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	2.07	1.47	2.92	2.16	1.53	3.06
Abuse	2.21	1.43	3.40	2.39	1.52	3.77
Dependence	6.55	3.96	10.85	6.47	3.86	10.85
Odd thinking and speech						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	2.58	1.88	3.52	2.62	1.91	3.60
Abuse	3.69	2.63	5.18	3.79	2.66	5.39
Dependence	8.26	5.47	12.49	8.47	5.53	12.97
Suspicious or paranoid ideation						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	1.81	1.56	2.10	1.75	1.50	2.03
Abuse	2.72	2.31	3.20	2.69	2.27	3.18

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	All Subjects					
Comparison	**OR**	**95% CI**		**AOR***	**95% CI**	
Dependence	6.12	4.64	8.08	5.62	4.27	7.40
Inappropriate or constricted affect						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	1.80	1.53	2.12	1.70	1.45	2.01
Abuse	2.71	2.29	3.20	2.42	2.04	2.87
Dependence	4.35	3.25	5.81	3.76	2.81	5.02
Behavior or appearance that is odd, eccentric or peculiar						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	2.48	1.86	3.31	2.54	1.89	3.40
Abuse	3.51	2.68	4.60	3.59	2.71	4.76
Dependence	7.94	5.61	11.25	8.04	5.66	11.42
Lack of close friends or confidants other than first degree relatives						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	2.48	1.90	3.24	2.42	1.83	3.20
Abuse	2.73	1.93	3.85	2.76	1.93	3.96
Dependence	5.40	3.09	9.42	5.33	3.06	9.31
Excessive social anxiety						
No use	1.00	1.00	1.00	1.00	1.00	1.00
Use	2.03	1.49	2.78	2.04	1.48	2.82
Abuse	2.49	1.81	3.42	2.62	1.90	3.60
Dependence	9.18	5.91	14.26	9.32	5.99	14.49

*adjusted for sociodemographic characteristics