Association of Cannabis Use–Related Predictor Variables and Self-Reported Psychotic Disorders: U.S. Adults, 2001–2002 and 2012–2013

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Objective: The authors sought to determine the association of cannabis indicators with self-reported psychotic disorders in the U.S. general population.

Methods: Participants were from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; 2001–2002; N=43,093) and NESARC-III (2012–2013; N=36,309). Logistic regression was used to estimate standardized prevalences of past-year self-reported psychotic disorders within each survey and to evaluate the association of past-year self-reported psychotic disorders with indicators of nonmedical cannabis use (any use; frequent use [at least three times/week], daily/near-daily use, and DSM-IV cannabis use disorder) compared with those with no past-year nonmedical cannabis use. Whether the strength of associations differed between surveys was indicated by difference-in-difference tests (between-survey contrasts) and ratios of odds ratios between surveys.

Results: Self-reported psychotic disorders were significantly more prevalent among participants with any nonmedical cannabis use than those without (2001–2002: 1.65% compared with 0.27%; 2012–2013: 1.89% compared with 0.68%). In 2001–2002, self-reported psychotic disorders were unrelated to either frequent use or daily/near-daily use. However, in 2012 – 2013, compared with nonusers, self-reported psychotic disorders were more common among participants with frequent use and those with daily/near-daily nonmedical cannabis use (2012–2013: 2.79% and 2.52%, respectively, compared with 0.68% among nonusers). Self-reported psychotic disorders were significantly more prevalent among participants with cannabis use disorder than nonusers in both surveys (2001–2002: 2.55% compared with 0.27%; 2012 – 2013: 3.38% compared with 0.68%). The strength of these associations did not change over time.

Conclusions: Data from the U.S. general population, especially more recent data, suggest associations between self-reported psychotic disorder and frequent nonmedical cannabis use and cannabis use disorder. Clinicians and policy makers should consider these relationships when monitoring patients and formulating programs.

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Schizophrenia spectrum and other psychotic disorders are a heterogeneous group of serious mental disorders that involve impairment in thinking, perception, and emotion (1, 2). Despite being relatively uncommon in the general population, psychotic disorders result in substantial social, economic, and health-related burdens (1, 3–5), are leading causes of disability-adjusted life-years in the United States and worldwide (6–8), and increase the risk of suicide and early mortality (9–11). Information on change over time in the prevalence of psychotic disorders can help gauge need for services and identify changes in potentially modifiable risk factors. However, many methodological issues make determining time trends in the prevalence of psychotic disorders challenging. While meta-analyses (12, 13) have not found evidence of change in the incidence or prevalence of psychotic disorders over time, considerable heterogeneity in study designs and the resulting prevalence estimates could have obscured changes in prevalence. Further, most of the meta-analyzed data originated outside the United States. Studies utilizing large-scale national data are needed to begin to understand time trends in rates of psychotic disorders in the United States and factors that may be associated with change.

One such factor may be cannabis use. Cannabis is one of the most widely used psychoactive substances in the United States and worldwide (14). The prevalences of adult nonmedical cannabis use, frequent use, and cannabis use disorder have increased in the U.S. general population and in large-sample studies of patient populations (15–18). In addition, the THC potency of illicit plant cannabis increased more than threefold since 1995, and the THC potency of legal cannabis products is often substantially higher (19–21).

Findings from several prospective and cross-sectional studies indicate a dose-response relationship between frequency of cannabis use and risk for psychosis, as illustrated in a 2016 meta-analysis (22). Further, there is increasing evidence of strong associations between high-potency cannabis use and psychosis (23, 24).

While fewer studies have addressed the relationship of cannabis use disorder to psychosis, longitudinal studies suggest that cannabis use disorder is prospectively associated with increased risk for development of psychotic disorders (25, 26). Although the nature of the relationship of cannabis to psychosis has been debated—that is, whether the relationship is causal or due to shared genetic risk factors (27, 28)—a prudent conclusion appears to be that some part of the relationship is causal (27, 28), and therefore that further study of the relationship is warranted.

Lengthy, detailed symptom-based measures of psychotic disorders have not been feasible in recent U.S. national surveys, leading to a gap in knowledge about psychosis and potential risk factors among U.S. adults. An alternative survey approach is to ask respondents to self-report on schizophrenia or psychotic illness that has been diagnosed by a doctor or other health professional (self-reported psychosis). This approach was used in the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (29). One study of NESARC data (30) showed associations between lifetime self-reported psychosis and a combined substance use disorder category, but provided little information specific to cannabis. Other NESARC studies showed associations of lifetime self-reported psychosis with cannabis use and cannabis use disorder (31, 32), but these studies did not address current (past-year) disorders, and also reported on data collected before the substantial increases in adult cannabis use, cannabis potency, and cannabis use disorder since the mid-2000s (15, 33). These changes in the U.S. cannabis landscape warrant examination of whether the prevalence of self-reported psychosis and its association with cannabis use or cannabis use disorder has changed over time.

We therefore used data from two U.S. nationally representative adult surveys, the 2001–2002 NESARC and the 2012–2013 NESARC-III, to examine three questions: 1) Did the prevalence of current self-reported psychosis (self-reported psychotic episode in the past year) change over time? 2) Were cannabis use indicators (any nonmedical use, frequent nonmedical use, daily/near-daily nonmedical use, or cannabis use disorder) associated with current self-reported psychosis in either survey? 3) Did the relationships of cannabis indicators and current self-reported psychosis change between 2001–2002 and 2012–2013?

METHODS

Samples and Procedures

The NESARC (29) and NESARC-III surveys (34) used multistage designs to sample adults (age ≥18 years) in households and group quarters. Sample weights adjusted for nonresponse and probability of selection. The total sample analyzed was 79,402 (43,093 in NESARC, 36,309 in NESARC-III). Across surveys, rigorous field procedures were similar (16, 35), including structured in-class training and home study for interviewers, random callbacks to verify interview data, and expert supervision. The examination of trends over time in important health outcomes was possible because of the methodological similarities between the two surveys (16, 36–38). For the 2001 − 2002 NESARC, the U.S. Bureau of the Census and the Office of Management and Budget institutional review boards approved the protocol and written consent procedures. The response rate for NESARC was 81.0%. For NESARC-III, the institutional review boards at the National Institutes of Health and Westat approved the protocol and verbal (recorded electronically) consent procedures. The response rate for NESARC-III was 60.1%, similar to other U.S. representative surveys conducted in similar years (39, 40).

Measures

In both surveys, substance use and substance use disorders were assessed using a structured computer-assisted interview, the Alcohol Use Disorder and Associated Disabilities Interview Schedule.

The outcome, self-reported psychotic disorders in the past year, was measured in NESARC and NESARC-III with nearly identical questions, asking if a doctor or other health professional told the respondent that they had schizophrenia or psychotic illness or episode. This brief survey measure has previously been validated (41).

Predictors included four past-year cannabis use-related variables: any nonmedical use, frequent nonmedical use, daily/near-daily nonmedical use, and DSM-IV cannabis use disorder. In both surveys, identical questions were used to assess nonmedical cannabis use, defined as use without a prescription or other than prescribed, for example, to get high (35). Any use was assessed using a two-level variable: "yes" for use at least one time in the past year and "no" otherwise. Frequent use was assessed using a three-level variable: use at least 3 days per week; any use but less than 3 days per week; and no past-year use. Similarly, daily/near-daily use was assessed using a three-level variable: use 5–7 days per week; any use but less than 5–7 days per week; and no past-year use. Cannabis use disorder was assessed using a three-level variable: DSM-IV abuse or dependence, that is, at least three of six DSM-IV dependence criteria (cannabis withdrawal was not included in DSM-IV) or at least one of four DSM-IV abuse criteria; any use but no cannabis use disorder; and no past-year use. Abuse and dependence were combined because an extensive review of studies conducted in preparation for the publication of DSM-5 showed that the criteria for cannabis abuse and dependence were unidimensional, reflecting a single cannabis use disorder diagnosis (42). Consistent with this, such a DSM-IV cannabis use disorder variable remains widely used in large-scale studies

(35, 43–47). In both surveys, the 22 cannabis use disorder symptom items were mostly identical; the large differences in cannabis use disorder prevalence across the two surveys could not be accounted for by the few slight differences in item wording (16, 35). For sensitivity analyses, we redefined cannabis use disorder, adding a cannabis withdrawal criterion and requiring three of seven dependence criteria to be positive for cannabis use disorder. Cannabis withdrawal was assessed identically in NESARC and NESARC-III, as three or more of five withdrawal symptoms: nervousness/anxiety, sleep difficulty, depressed mood, restlessness, or physical symptoms (one or more of headache, shakiness, sweating, abdominal pain, and fever); or use to avoid or relieve withdrawal symptoms. This was done because DSM-5 includes withdrawal as a cannabis use disorder criterion, given evidence showing its validity and relatedness to the other cannabis use disorder criteria (42). For consistency across predictors and clarity of interpretation, the reference group for all four predictors was no past-year nonmedical use.

Control covariates included gender; age (18–29, 30–44, 45–64, ≥65 years); race/ethnicity (Hispanic; non-Hispanic: White, Black; and other [Native American, Asian, Pacific Islander]); education (less than high school, high school graduate or GED, at least some college); and urbanicity (urban, rural). Dichotomous variables were constructed for alcohol, tobacco, and stimulant use, indicating past-year use (yes/no), as these substances are potential confounders of the examined associations (48, 49). In sensitivity analyses, we included a covariate indicating whether respondents' state of residence had medical cannabis laws, as determined by economic and legal experts as in previous studies (35, 44, 50). The medical cannabis law variable was defined with three levels: never medical cannabis law; medical cannabis law enacted by 2001 (NESARC); and medical cannabis law enacted between 2002 and 2012 (NESARC-III). Seven states (California, Colorado, Hawaii, Maine, Nevada, Oregon, Washington) had medical cannabis laws by 2001. Nine more states (Arizona, Connecticut, Maryland, Massachusetts, Michigan, Montana, New Jersey, New Mexico, Vermont) had medical cannabis laws by 2012.

Statistical Analysis

As in other studies evaluating trends between the two surveys (16, 35–37), the NESARC and NESARC-III data sets were concatenated, adding a survey variable. To determine the change in self-reported psychosis over time, we used logistic regression to model self-reported psychosis as a function of survey (time) and sociodemographic control variables (age, race/ethnicity, gender, education, and urbanicity). A second model also controlled for past-year alcohol, tobacco, and stimulant use. Model-predicted standardized prevalence of self-reported psychosis (i.e., back-transformed from the log scale with sociodemographic characteristics averaged between the surveys) was estimated for each of the two surveys, and the difference between the two prevalence estimates indicated the change over time.

Logistic regression was then used to evaluate the association of each cannabis-related predictor variable with self-reported psychosis, modeling self-reported psychosis as a function of the cannabis-related predictor, survey, cannabis-related predictor-by-survey interactions, and sociodemographic control variables. Model-predicted standardized prevalence of self-reported psychosis was estimated in each survey by the cannabis-related predictors, compared to those with no nonmedical cannabis use. The difference in these prevalence estimates indicated association of the cannabis-related predictor with self-reported psychosis within each survey. Whether the associations differed between the surveys (i.e., changed over time) was indicated by contrasts between these prevalence differences (difference-in-difference tests). Additive effects and interactions were evaluated because they are considered most appropriate from the public health perspective (51–53), since additive effects can indicate groups with the greatest population-level risk (44). For readers more familiar with odds ratios, we also evaluated effects and interactions on the multiplicative scale. Using the logistic regression models described above, ratios of the odds of self-reported psychosis among those with the cannabis predictor divided by the odds among those without nonmedical use was estimated within each survey. Multiplicative interaction was evaluated as the ratio of odds ratios, that is, the odds ratio for 2012–2013 divided by the odds ratio for 2001–2002, given by the exponentiated regression coefficient for the multiplicative interaction term.

For all analyses, SUDAAN, version 11.0.1 (54) was used, incorporating survey weights to adjust for the complex sampling design, to yield U.S. adult population-representative estimates. Statistical tests were two-tailed, with significance based on $p<0.05$, as indicated by 95% confidence intervals. Interpretation of the confidence intervals differs for difference (additive) and relative (multiplicative) effects. For difference effects, a value of 0.0 indicates no difference, so an estimate with a 95% confidence interval not including 0.0 is statistically significant at $p<0.05$. For relative effects, a value of 1.0 indicates no difference, so an estimate whose 95% confidence interval does not include 1.0 is statistically significant at $p<0.05$.

Two sensitivity analyses were conducted. First, to reflect the addition of cannabis withdrawal in DSM-5, we added cannabis withdrawal to the dependence criteria and reran the models for cannabis use disorder. Second, we added a covariate indicating state medical cannabis law status at the time of each survey and reran the models. Participants from the 42 states included in both surveys were included in this analysis (41,706 from NESARC; 36,309 from NESARC-III; total=78,015), as in previous studies (35).

RESULTS

Trend in Self-Reported Psychotic Disorders

The standardized prevalence of past-year self-reported psychosis among U.S. adults was 0.33% in 2001–2002 and

TABLE 1. Prevalence of self-reported psychotic disorder by survey and past-year cannabis-related variables[a]

	NESARC, 2001–2002				NESARC-III, 2012–2013			
		Self-Reported Psychotic Disorder				Self-Reported Psychotic Disorder		
Category	N of Total Sample	N	Standardized Prevalence[b]	SE	N of total Sample	N	Standardized Prevalence[b]	SE
Total sample	43,093	178	0.33	0.03	36,309	337	0.80	0.06
Past-year nonmedical cannabis use groups								
No cannabis use	41,490	151	0.27	0.03	32,608	271	0.68	0.06
Any cannabis use	1,603	27	1.65	0.47	3,701	66	1.89	0.33
Frequent cannabis use	464	6	1.00	0.46	1,527	39	2.79	0.62
Daily/near-daily cannabis use	348	5	0.88	0.43	1,161	28	2.52	0.66
Cannabis use disorder	560	11	2.55	1.08	1,086	29	3.38	0.85
Proxy for DSM-5 cannabis use disorder[c]	565	12	2.80	1.11	1,104	29	3.33	0.84

[a] Data are from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) survey and the 2012–2013 NESARC-III survey. Nonmedical cannabis use is defined as use without a prescription or other than prescribed, for example, to get high.
[b] Standardized prevalence is the model-predicted prevalence of self-reported psychotic disorders, adjusted for sociodemographic covariates (age, gender, race/ethnicity, education level, and urbanicity), from logistic regression.
[c] Includes six DSM-IV cannabis use disorder criteria plus proxy for cannabis withdrawal syndrome (three or more of five symptoms: nervousness/anxiety; sleep disturbances; restlessness; depressed mood; and any physical symptoms: sweating/fast heartbeat; fever; shaking; nausea, vomiting, stomach pain; or headache), or using cannabis to avoid withdrawal symptoms.

0.80% in 2012–2013, a significant increase on the additive scale (prevalence difference=0.47%, 95% CI=0.33, 0.61) and on the relative scale (odds ratio=2.46, 95% CI=1.89, 3.22). In an adjusted model further controlling for past-year alcohol, tobacco, and stimulant use, the results were essentially the same as in the original model. The adjusted prevalence of self-reported psychosis in 2001–2002 was 0.32%, and in 2012–2013 it was 0.79%, with a prevalence difference of 0.47 (95% CI=0.32, 0.62), suggesting that the change observed was not primarily driven by alcohol, tobacco, or stimulant use.

Within-Survey Association of Cannabis Predictors With Self-Reported Psychotic Disorders

Any past-year nonmedical cannabis use. Self-reported psychotic disorders were more prevalent among participants with any nonmedical cannabis use compared with nonusers in 2001–2002 (1.65% compared with 0.27%; prevalence difference=1.38, 95% CI=0.47, 2.29) and in 2012–2013 (1.89% compared with 0.68%; prevalence difference=1.21, 95% CI=0.56, 1.86) (Tables 1, 2).

Frequent nonmedical cannabis use. Self-reported psychotic disorders were more prevalent among participants with frequent nonmedical cannabis use compared with nonusers in 2012–2013 (2.79% compared with 0.68%; prevalence difference=2.11, 95% CI=0.89, 3.33), but not in 2001–2002 (Tables 1, 2).

Daily/near-daily nonmedical cannabis use. Self-reported psychotic disorders were more prevalent among participants with daily/near-daily nonmedical cannabis use compared

TABLE 2. Within-survey associations of past-year cannabis-related indicators with self-reported psychotic disorders[a]

	NESARC, 2001–2002				NESARC-III, 2012–2013			
Cannabis Indicator	Prevalence Difference[b]	95% CI	Odds Ratio[c]	95% CI	Prevalence Difference[b]	95% CI	Odds Ratio[c]	95% CI
Any cannabis use	1.38	0.47, 2.29	6.16	3.41, 11.01	1.21	0.56, 1.86	2.83	1.92, 4.17
Frequent cannabis use	0.73	−0.15, 1.61	3.70	1.57, 8.69	2.11	0.89, 3.33	4.25	2.63, 6.87
Daily/near-daily cannabis use	0.61	−0.23, 1.45	3.26	1.25, 8.49	1.84	0.55, 3.13	3.82	2.21, 6.59
Cannabis use disorder	2.28	0.18, 4.38	9.60	4.10, 22.58	2.70	1.03, 4.37	5.19	3.03, 8.89
Proxy DSM-5 cannabis use disorder[d]	2.53	0.35, 4.71	10.64	4.77, 23.71	2.65	1.00, 4.30	5.12	2.98, 8.79

[a] Data are from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) survey and the 2012–2013 NESARC-III survey. Nonmedical cannabis use is defined as use without a prescription or other than prescribed, for example, to get high.
[b] Effects estimated on the additive scale: prevalence difference indicates the prevalence difference of psychotic disorders between those with the cannabis-related predictor and those without cannabis use in 2001–2002 and 2012–2013. These effects are considered significant when the 95% confidence interval does not include 0.
[c] Effects estimated on the multiplicative scale: odds ratio indicates the ratio of the odds of psychotic disorders between those with and without the cannabis predictor in 2001–2002 and 2012–2013. These effects are considered significant when the 95% confidence interval does not include 1.
[d] Includes six DSM-IV cannabis use disorder criteria plus proxy for cannabis withdrawal syndrome (three or more of five symptoms: nervousness/anxiety; sleep disturbances; restlessness; depressed mood; and any physical symptoms: sweating/fast heartbeat; fever; shaking; nausea, vomiting, stomach pain; or headache) or using cannabis to avoid withdrawal symptoms.

TABLE 3. Across-survey associations of past-year cannabis indicators with self-reported psychotic disorders[a]

	2012–2013 Versus 2001–2002, Estimated on the Additive Scale[b]		2012–2013 Versus 2001–2002, Estimated on the Multiplicative Scale[c]	
Cannabis Indicator	Difference in Prevalence Differences	95% CI	Ratio of Odds Ratios	95% CI
Any cannabis use	−0.17	−1.24, 0.90	0.46	0.24, 0.90
Frequent cannabis use	1.38	−0.09, 2.85	1.15	0.44, 3.00
Daily/near-daily cannabis use	1.23	−0.28, 2.74	1.17	0.40, 3.47
Cannabis use disorder	0.42	−2.15, 2.99	0.54	0.21, 1.41
Proxy DSM-5 cannabis use disorder[d]	0.12	−2.47, 2.71	0.48	0.19, 1.21

[a] Data are from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) survey and the 2012–2013 NESARC-III survey. Nonmedical cannabis use is defined as use without a prescription or other than prescribed, for example, to get high.
[b] Effects estimated on the additive scale: prevalence difference indicates the prevalence difference of psychotic disorders between those with and without the cannabis-related predictor in 2001–2002 and 2012–2013, while difference in prevalence differences indicates the difference between those differences. These effects are significant when the 95% confidence interval does not include 0.
[c] Effects estimated on the multiplicative scale: odds ratio indicates the ratio of the odds (likelihood) of psychotic disorders between those with and without the cannabis predictor in 2001–2002 and 2012–2013, while ratio of odds ratios indicates the ratio between those ratios. These effects are significant when the 95% confidence interval does not include 1.
[d] Includes six DSM-IV cannabis use disorder criteria plus proxy for cannabis withdrawal syndrome (three or more of five symptoms: nervousness/anxiety; sleep disturbances; restlessness; depressed mood; and any physical symptoms: sweating/fast heartbeat; fever; shaking; nausea, vomiting, stomach pain; or headache) or using cannabis to avoid withdrawal symptoms.

with nonusers in 2012–2013 (2.52% compared with 0.68%; prevalence difference=1.84, 95% CI=0.55, 3.13), but not in 2001–2002 (Tables 1, 2).

DSM-IV cannabis use disorder. Self-reported psychotic disorders were more prevalent among participants with DSM-IV cannabis use disorder compared with nonusers in 2001–2002 (2.55% compared with 0.27%; prevalence difference=2.28, 95% CI=0.18, 4.38) and in 2012–2013 (3.38% compared with 0.68%; prevalence difference=2.70, 95% CI=1.03, 4.37) (Tables 1, 2).

Relative Scale

On the relative scale, any past-year nonmedical cannabis use, frequent use, daily/near-daily use, and DSM-IV cannabis use disorder were all significantly associated with self-reported psychosis in both 2001–2002 and 2012–2013 (Table 2). Except for any past-year nonmedical cannabis use, there were no changes in the magnitude of association over time (Table 3). When withdrawal was added, cannabis use disorder remained significantly associated with self-reported psychosis in both time periods (Table 2), with no significant differences in the strength of the association (Table 3).

Between-Survey Change in Strength of Associations

Although frequent and daily/near-daily use was not associated with self-reported psychosis in 2001–2002 but was associated with it in 2012–2013, none of the difference-in-difference tests indicating between-survey change in the strength of the associations were significant (Table 3).

Sensitivity Analyses

After adding cannabis withdrawal to the dependence criteria, cannabis use disorder remained associated with self-reported psychosis in both time periods (Table 2). When medical cannabis law status was added as a covariate, results were similar to those from the original models (see Tables S1–S3 in the online supplement).

DISCUSSION

In this study, we examined associations between several cannabis use indicators and self-reported psychotic disorders, along with changes over time in these associations, in the adult U.S. general population. In recent decades, the U.S. cannabis landscape has shifted substantially, including increased public perception of cannabis as a safe substance and increasing state cannabis legalization. Although the nature of the cannabis-psychosis relationship has been debated, cannabis use is widely considered to play a partial role in the risk of psychosis (27, 28). Thus, investigating changes in associations between psychotic disorders and cannabis use indicators over time is warranted. The present study shows that the prevalence of self-reported psychosis increased among U.S. adults between 2001 − 2002 and 2012–2013. The results demonstrate that all nonmedical cannabis use indicators were associated with self-reported psychosis in 2012–2013. Further, any nonmedical cannabis use and cannabis use disorder were associated with self-reported psychosis in both 2001–2002 and 2012–2013. Nevertheless, the magnitude of these associations did not change significantly across survey years.

Our finding that the prevalence of past-year self-reported psychosis increased significantly between 2001–2002 and 2012–2013 is the first reported change in prevalence of self-reported psychotic disorders based on large-scale, nationally representative samples of U.S. adults. This finding contrasts with earlier studies based on hospitalization records, whose methods of recording may be imprecise and variable over time. The present study adds to the literature by providing

evidence that psychotic disorders have been on the rise in the United States in recent decades, based on comparison of prevalence of self-reported psychosis between two national surveys that used identical measures of psychosis.

The finding that self-reported psychotic disorders were significantly more prevalent among survey respondents with any past-year cannabis use compared with nonusers in both surveys is consistent with results from past studies (55–58) and adds to the literature by reporting standardized prevalences of psychotic disorders among past-year adult cannabis users. Clinicians and policy makers should be aware of this increased likelihood of psychosis among individuals reporting any past-year cannabis use. In addition, self-reported psychosis was significantly associated with frequent and daily/near-daily cannabis use in the more recent survey, supporting previous findings on a dose-response relationship between cannabis use and psychotic disorders (59), which should be further investigated. While not possible with the available data, a study design that would allow assessment of a true dose-response relationship as a function of a more fine-grained measure of cannabis use frequency and quantity would shed further light on the matter. While none of these associations significantly changed across survey years on the absolute difference scale, on the relative scale, the odds of self-reported psychosis among any past-year nonmedical cannabis users was significantly weaker in 2012–2013 (odds ratio=2.83) than 2001–2002 (odds ratio=6.16). One possible explanation for the weaker odds ratio in the more recent survey could be the higher proportion of nonfrequent cannabis users among all users in 2012–2013 (5.84%) than in 2001–2002 (2.86%). Changing marijuana norms (e.g., decreased perception of marijuana use as risky) may have led to more experimental, one- or two-time users in 2012–2013, who are less likely to be diagnosed with psychotic disorders compared with regular and frequent cannabis users, as indicated in numerous studies (22, 60–62).

The study findings indicate that participants with cannabis use disorder are at increased risk of reporting being diagnosed with a psychotic disorder compared with non–cannabis users, a finding that has also been reported in previous non-U.S. studies (25, 26). Notably, the highest absolute prevalence of self-reported psychotic disorders in this study (3.38%) was seen in past-year cannabis users reporting DSM-IV cannabis use disorder in the 2012–2013 survey. Findings from sensitivity analyses show that cannabis use disorder with withdrawal (a combination that is closer to the DSM-5 diagnostic criteria for cannabis use disorder) was associated with self-reported psychotic disorders in both surveys. Although differences in associations across surveys were not significant, one plausible explanation for the high rates of self-reported psychotic disorders among those with cannabis use disorder in 2012–2013 is the increase in availability of high-potency cannabis products, which have been associated with higher prevalence of psychosis (59, 63).

In sensitivity analyses, the inclusion of state medical cannabis law status in the model did not affect the associations between cannabis use variables and psychosis over time. However, early evidence suggests a stronger effect of recreational cannabis laws than medical cannabis laws in increasing adult cannabis use and associated problems (64). Therefore, incorporating recreational cannabis law effects in studies of the relationship of cannabis use to psychosis is warranted, and may be highly valuable in informing policy makers, clinicians, and researchers about increased risk of psychosis associated with state recreational cannabis laws.

This study had several limitations. First, self-reported psychotic disorders were indicated by a single item rather than physician assessment, as in a previous NESARC study (31). While future national studies of substance use should measure psychotic disorders more extensively, a growing number of studies have explored the validity and reliability of various self-reported measures of psychotic disorders, including the present study's measure, and have reported prevalences that are similar to studies using clinical diagnoses (41, 65, 66). Furthermore, unlike other large-scale national surveys, such as the National Survey on Drug Use and Health, which includes a broad measure of "severe mental illness" that is not diagnosis specific, NESARC is the only national epidemiologic survey to utilize a variable specific to psychosis.

Second, cannabis use variables were based on self-report and could be subject to social desirability bias (34). Further, this study did not address self-reported psychotic disorders among individuals using cannabis exclusively for medical purposes. The NESARC did not include a question about medical use of cannabis, precluding examination of this question in NESARC data. While the NESARC-III did include such a question, very few NESARC-III participants (weighted percentage, 0.22%, SE=0.04) used cannabis for medical purposes only who did not also use cannabis nonmedically (67), and those who used it exclusively for medical reasons were not asked about frequency of use or cannabis use disorder criteria. Given the small numbers of medical-only users, their omission seems unlikely to have altered the relationships found. However, when relevant data become available, future studies should address changes in the association of psychotic disorders with cannabis variables over time among those using cannabis exclusively for medical purposes. Further, this study did not examine negative control psychiatric conditions (i.e., those unrelated to cannabis use, such as autism or obsessive-compulsive disorder) because the data were unavailable, but future studies should do so.

Third, directionality of the relationship cannot be determined in cross-sectional data. Additionally, since DSM-IV mental disorders were diagnosed in NESARC and DSM-5 diagnoses were made in NESARC-III, we could not adjust for the presence of other psychiatric disorders. If national data with consistent DSM or ICD mental disorder diagnoses over time can be found, studies should explore such

adjustments. This also meant that DSM-5 cannabis use disorder could not be assessed in both surveys. However, an extensive literature (42) shows that the criteria for DSM-IV cannabis abuse and dependence are unidimensional, justifying their combination (as has been done in many other studies), and that DSM-IV cannabis disorder diagnoses correspond closely with DSM-5 cannabis use disorder (68).

Fourth, the NESARC and NESARC-III survey items about psychosis did not differentiate between types of psychotic disorders. Therefore, we could not account for time trends in specific disorders or differentiate between primary and secondary psychotic disorders. Future studies should account for specific types of psychotic disorders. Additionally, considering increasing rates of cannabis use among women in recent years (69, 70) and, conversely, higher rates of psychosis among men compared with women (12), associations reported in the present study may have differed by gender. Examination of effect modification by gender was beyond the scope of this study but should be addressed in future research.

Finally, the NESARC and NESARC-III were surveys of household residents and did not include medically institutionalized participants (perhaps less likely than the general population to use cannabis), or incarcerated participants (more likely to use cannabis and often mentally ill). Thus, the study results are not generalizable to these populations.

CONCLUSIONS

The prevalence of self-reported psychotic disorders in the adult U.S. population significantly increased from 2001–2002 to 2012–2013. Nonmedical cannabis use and cannabis use disorder were consistently associated with self-reported psychotic disorders over time, while frequent and daily/near-daily use were also associated with self-reported psychotic disorders in the more recent survey. The increasing perception of cannabis as a harmless substance may deter the general public as well as health care providers from recognizing that nonmedical cannabis use may play a role in exacerbating the risk for psychotic disorders. Therefore, improving public knowledge and educating providers about this risk may serve a useful function. In particular, identifying cannabis use disorder may help indicate individuals at increased risk of psychotic disorders. This information can inform addiction specialists and other clinicians about the need for evaluation and appropriate interventions and therapeutic modalities for individuals at risk. Further, although not directly examined in this study, policy makers should be aware of the increase in cannabis use and cannabis use disorder among U.S. adults, and any possible subsequent increase in cannabis-related outcomes, including psychotic disorders.

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