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Recent national trends in *Salvia divinorum* use and substance-use disorders among recent and former *Salvia divinorum* users compared with nonusers

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Abstract

Context—Media and scientific reports have indicated an increase in recreational use of *Salvia divinorum*. Epidemiological data are lacking on the trends, prevalence, and correlates of *S. divinorum* use in large representative samples, as well as the extent of substance use and mental health problems among *S. divinorum* users.

Objective—To examine the national trend in prevalence of *S. divinorum* use and to identify sociodemographic, behavioral, mental health, and substance-use profiles of recent (past-year) and former users of *S. divinorum*.

Design—Analyses of public-use data files from the 2006–2008 United States National Surveys on Drug Use and Health (N = 166,453).

Setting—Noninstitutionalized individuals aged 12 years or older were interviewed in their places of residence.

Main measures—Substance use, *S. divinorum*, self-reported substance use disorders, criminality, depression, and mental health treatment were assessed by standardized survey questions administered by the audio computer-assisted self-interviewing method.

Results—Among survey respondents, lifetime prevalence of *S. divinorum* use had increased from 0.7% in 2006 to 1.3% in 2008 (an 83% increase). *S. divinorum* use was associated with ages 18–25 years, male gender, white or multiple race, residence of large metropolitan areas, arrests for criminal activities, and depression. *S. divinorum* use was particularly common among recent drug

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Ethical approval

This work was approved by the Duke University Institutional Review Board.

Disclosure

GE Woody is a member of the RADARS post-marketing study external advisory group, whose job is to assess abuse of prescription medications. Denver Health administers RADARS, and nine pharmaceutical companies currently support its work.

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users, including users of lysergic acid diethylamide (53.7%), ecstasy (30.1%), heroin (24.2%), phencyclidine (22.4%), and cocaine (17.5%). Adjusted multinomial logistic analyses indicated polydrug use as the strongest determinant for recent and former *S. divinorum* use. An estimated 43.0% of past-year *S. divinorum* users and 28.9% of former *S. divinorum* users had an illicit or nonmedical drug-use disorder compared with 2.5% of nonusers. Adjusted logistic regression analyses showed that recent and former *S. divinorum* users had greater odds of having past-year depression and a substance-use disorder (alcohol or drugs) than past-year alcohol or drug users who did not use *S. divinorum*.

Conclusion—*S. divinorum* use is prevalent among recent or active drug users who have used other hallucinogens or stimulants. The high prevalence of substance use disorders among recent *S. divinorum* users emphasizes the need to study health risks of drug interactions.

Keywords

alcohol-use disorders; drug-use disorders; ecstasy; lysergic acid diethylamide; major depression; multiple race; nicotine dependence; phencyclidine; prescription drug abuse

Introduction

Recreational use of *Salvia divinorum* has become a matter of increasing concern in the United States and elsewhere, but epidemiological data from large representative samples are lacking to delineate the prevalence of its use across different population groups and the profiles of emerging users.[1–8] *S. divinorum*, also known as Maria Pastora, Pastora, Sage of the Seers, Diviner's Sage, Sally-D, or Magic Mint, is a perennial herb in the mint family.[9] Its main active ingredient, salvinorin A, is a kappa opioid receptor agonist and is considered one of the most potent naturally occurring hallucinogens.[2,9–11] In the United States, *S. divinorum* and salvinorin A have no approved medical use.[9] *S. divinorum* leaves and salvinorin A have been used to produce hallucinogenic effects. The half-life of salvinorin A in nonhuman primates is estimated to be 56.6 ± 24.8 minutes.[10] However, the potential toxicity and metabolism of salvinorin A have not been fully investigated in laboratory animals or humans.[10,12]

To date, studies of *S. divinorum* have focused mainly on its effects, which have been found to be intense, short-lived, and diverse. In a study of qualitative data from 10 *S. divinorum* users collected by email interviews, Dalgarno[13] found that subjective experiences due to *S. divinorum* use were quite similar to those of ketamine use. In another study of 32 recreational users of *S. divinorum* and other psychedelics, González et al[14] found that smoking *S. divinorum* produced intense and short-lived psychedelic-like changes in visual perception, mood, and somatic sensations, as well as a highly modified perception of external reality and the self. Additionally, Albertson and Grubbs[15] found a greater number of users who reported *S. divinorum* experiences as being more similar to those of marijuana use than to experiences produced by psychedelic mushrooms or lysergic acid diethylamide (LSD). More recently, Johnson et al[12] used a controlled design to study four healthy hallucinogen-using adults and found that salvinorin A appeared to produce dose-related changes in subjective effects similar to those from use of classic hallucinogens. Recent data from a United States statewide poison control system have shown that, among patients who intentionally used *S. divinorum*, whether alone or in combination with alcohol or other drugs, psychiatric, neurologic, cardiovascular, or gastrointestinal effects were evident and that polysubstance use could result in more serious adverse effects (eg, seizures, intubations) than use of *S. divinorum* alone.[4]

Because of its ready availability, its legality, its hallucinogenic effects, and the lack of empirical data on long-term safety of *S. divinorum* in humans, *S. divinorum* has become a drug of increasing concern.[1–10] In particular, it is easily obtained from sources that may increase exposure opportunity to psychoactive drug use. *S. divinorum* and salvinorin A are not currently controlled under the Controlled Substances Act in the United States, although, as of September 2010, 24 states have enacted legislation placing regulatory controls on *S. divinorum* and/or salvinorin A.[9] Because it is legal to use and sell *S. divinorum* products in many jurisdictions and *S. divinorum* can be cultivated, the Internet has become one of the venues for the distribution of information about and sources of *S. divinorum* and other psychoactive substances.[5,16] For example, Hoover et al[5] found that many websites that sell *S. divinorum* products either encourage its use (eg, providing potentially erroneous information about the substance) or promote it as a safe or legal alternative to scheduled hallucinogens or cannabis, and that very few websites provide anti-use information. A recent study of college students found that friends and head shops serve as the primary information providers or sources of *S. divinorum*, suggesting that *S. divinorum* use can occur in groups.[17]

Moreover, although little is presently known about salvinorin A's long-term health risks in repeated users,[10] case reports have demonstrated that repeated use of *S. divinorum* can be associated with serious psychiatric conditions in young or vulnerable individuals.[2] For instance, Przekop and Lee[8] reported on a 21-year-old man with no family or personal psychiatric history who developed persistent psychosis associated with *S. divinorum* use. Breton et al[18] described a case of a bipolar 17-year-old girl who developed prolonged hallucinations and dissociative self-destructive behaviors following *S. divinorum* use. Similarly, Singh[19] discussed a 15-year-old boy with a history of *S. divinorum* and marijuana use who presented to psychiatric emergency services with acute onset of mental status changes characterized by paranoia, déjà vu, blunted affect, thought blocking, and slow speech of 3 days' duration. Together, these findings point towards a need to investigate the extent of use of this novel substance and *S. divinorum* users' sociodemographic, behavioral, mental health, and substance use profiles to inform research, prevention, and policy-making efforts. As noted in several research reports, epidemiological data on the prevalence of *S. divinorum* use in representative samples are lacking.[5,7,20,21]

To date, there are only a few studies of prevalence and correlates of *S. divinorum* use, and they have focused primarily on college students.[17,21,22] In a convenience sample of undergraduate students at a large public university in the southeastern United States (N = 825), 10.9% of men and 3.8% of women reported lifetime use of any *S. divinorum*; *S. divinorum* use was associated with male sex, white race, a high level of family income, marijuana use, and a low level of self-control.[17,21] In another study of college students drawn from a large public university in the southwestern United States (N = 1516), Lange et al[22] found that 4.4% of the sample reported using *S. divinorum* at least once in the past 12 months, and that whites, males, fraternity members, illicit drug users, and heavy episodic drinkers reported a higher prevalence than other groups. However, after controlling for the other covariates in the logistic regression analysis, only past-year drug use was associated with *S. divinorum* use, suggesting drug use as a robust correlate for *S. divinorum* use.[22]

Of note, no studies have explored the trend in *S. divinorum* use despite the fact that several reports have mentioned its increasing popularity among young people. Here, we seek to address the gaps in knowledge regarding population-based prevalence estimates and correlates of *S. divinorum* use by examining prevalence rates of recent (past-year) and former (prior to the past year) *S. divinorum* use and their correlates in a large nationally representative sample of individuals aged 12 years or older. The data are drawn from multiple waves of the United States National Surveys on Drug Use and Health (NSDUH). Beginning in 2006, the NSDUH added assessments of *S. divinorum* use to the annual

survey.[23] In a recent NSDUH report, past-year *S. divinorum* use (1.7%) among young adults aged 18–25 years in 2006 was found to be less common than past-year ecstasy use (3.8%) but more common than past-year use of LSD (1.2%) and phencyclidine (PCP) (0.2%).[23] Since the inclusion of *S. divinorum* use questions, the NSDUH data have not been utilized fully to explore changes in the prevalence of *S. divinorum* use across diverse population subgroups and correlates of use.

This study examines a geographically diverse national sample to inform recent trends in *S. divinorum* use (with a higher level of generalizability to population subgroups than a convenience sample) and to elucidate *S. divinorum* users' sociodemographic (age, sex, race/ethnicity, total family income, and population density of the respondent's residence), behavioral (criminal behaviors), mental health (depression, use of mental health treatment), and substance use (tobacco, alcohol, illicit or nonmedical drug use) profiles. Recent (in the past year) and former (prior to the past year) *S. divinorum* use is distinguished in the analysis to inform research and prevention efforts. These research questions have not been systematically addressed in prior NSDUH reports.

Four main questions are addressed:

1. Are there increases in *S. divinorum* use across different sociodemographic groups?
2. To what extent are sociodemographic, behavioral, mental health, and substance-use characteristics associated with recent or former *S. divinorum* use?
3. Are recent *S. divinorum* users more likely than former *S. divinorum* users and nonusers to have depression and substance-use disorders (nicotine, alcohol, and drug-use disorders)?
4. Among recent *S. divinorum* users, to what extent are sociodemographic, behavioral, mental health, and substance-use characteristics associated with having a substance-use disorder?

Methods

Data source

Data were from the public-use data file of the 2006–2008 NSDUH, the only survey designed to provide ongoing national estimates of substance use and disorders in the United States.[24–26] The target population includes residents of households from the 50 states (including shelters, rooming houses, and group homes; civilians residing on military base) plus the District of Columbia. Participants are selected by multistage area probability methods to ensure that each independent and cross-sectional sample is representative of persons aged 12 years or older.

Respondents are interviewed privately at their places of residence. Prospective respondents are assured that their names will not be recorded and their responses will be kept strictly confidential, and all study procedures and protections are carefully explained. For adolescents aged 12–17 years, the field interviewer first seeks verbal consent from their parents/guardians. Once parental permission is granted, field interviewers then approach the adolescents and obtain their agreement to participate in the study. Parents are then asked to leave the interview setting to ensure the confidentiality of their children's responses.

The interview uses computer-assisted interviewing to increase valid reports of substance use behaviors. Sociodemographic questions are administered by interviewers using computer-assisted personal interviewing. Other questions of a sensitive nature (substance use and disorders, criminal behaviors, mental health) are administered with audio computer-assisted

self-interviewing (ACASI), which provides respondents with a highly confidential means of responding to questions to increase honest reporting of sensitive behaviors. In this mode, respondents read questions on the computer screen, or questions are read to them through headphones, and they enter responses directly into a computer provided by the interviewer.

The survey is conducted from January through December in every independent survey year. Participants are offered a US$30 incentive for participation in the interview. In 2006–2008, approximately 67,500 unique persons aged 12 years or older were interviewed annually; weighted response rates for household screening and interviewing were 89.0%–90.6% and 73.9%–74.5%, respectively.[24–26] The public-use de-identified data file contains about 55,000 respondents yearly due to exclusions to ensure anonymity. In response to reports suggesting the emergence of *S. divinorum* use, specific questions about this hallucinogen were added to the survey beginning in 2006.[23] This study examined data from 2006 to 2008 to determine recent national trends in *S. divinorum* use and to identify subgroups showing elevated odds of use (N = 55,279 in 2006; N = 55,435 in 2007; N = 55,739 in 2008). The same survey items were examined across the years. Per NSDUH designs, the use of the pooled data from 3 years to examine yearly changes in prevalence rates of use is appropriate.[24,25]

Study variables

Substance use—NSDUH assessments of substance use were conducted via ACASI. Tobacco, alcohol, and another nine drug classes (not including *S. divinorum*) were assessed separately in 11 different sections. Each section included a detailed description of the substance class and a list of substances belonging to the class; for nonmedical use of prescription drugs, respondents were provided with pill cards showing color pictures of tablets for opioid analgesics, tranquilizers, stimulants, and sedatives. The survey asked each respondent about his/her use of each substance group and recency of use. Past-year tobacco use included use of cigarettes, chewing tobacco, snuff, dip, or pipe tobacco in the 12 months prior to the interview. Binge alcohol use was defined as drinking five or more drinks on the same occasion (ie, at the same time or within a couple of hours of each other) on at least 1 day in the past 30 days.

Drug use—Drug use included illicit use of marijuana or hashish, cocaine or crack, heroin, or hallucinogens (eg, LSD, PCP, ecstasy/3,4-methylenedioxymethamphetamine [MDMA]); inhalant use (eg, nitrous oxide, amyl nitrite, cleaning fluids, gasoline, spray paint, glue); and nonmedical use of prescription analgesic opioids, stimulants (amphetamines), tranquilizers, or sedatives. Nonmedical use was defined as self-reported use of prescription drugs (pain relievers/opioids, stimulants, sedatives, and tranquilizers) that were not prescribed for the respondent or that the respondent took only for the experience or feeling they caused; use of over-the-counter drugs and legitimate use of prescription drugs were not included.

***S. divinorum* use—**Questions about *S. divinorum* use were included in a separate ‘Special drugs’ section. Lifetime *S. divinorum* use was based on the following question: “Have you ever, even once, used *Salvia divinorum*?” Among respondents who responded affirmatively to this question, the survey then asked about recency of use: “The computer recorded that you have used *Salvia divinorum*. How long has it been since you last used *Salvia divinorum* (eg, within the past 12 months or more than 12 months ago)?” Based on responses to these two questions, we categorized respondents into three mutually exclusive groups: nonuser, past-year *S. divinorum* users (use within the past 12 months), and former users (use prior to the past 12 months).

Diagnostic and Statistical Manual of Mental Disorders

(DSM)-IV alcohol- or drug-use disorders (abuse, dependence): Respondents who reported alcohol or drug use in the past year were asked a set of structured and substance-specific questions designed to operationalize DSM-IV criteria for abuse of or dependence on each substance class in question.[26,27]

Nicotine (cigarette) dependence: Nicotine dependence was defined as specified by the nicotine dependence syndrome scale (NDSS) and the Fagerstrom test of nicotine dependence (FTND).[28–30] NDSS questions assess dependence similar to the concepts specified by the DSM-IV, while FTND discriminates between dependent smokers and nondependent smokers by assessing how soon after waking that smokers have their first cigarette. To optimize the number of respondents classified as having current nicotine dependence, the NSDUH categorizes respondents as having nicotine dependence in the past month if they meet criteria for dependence as specified either by the NDSS or FTND.[26] Past-year measurement of nicotine dependence was not available.

Criminal activities and mental health: Guided by prior research showing an association of hallucinogen use with criminality and depression,[31–33] criminality, depression, and mental health treatment variables were examined as potential correlates of *S. divinorum* use. Lifetime criminal activity was assessed by the following question: “Not counting minor traffic violations, have you ever been arrested and booked for breaking the law?”. The survey explicitly defined “being booked” as having ever been taken into custody and processed by the police or by someone connected with the courts, even if the respondent was then released. Among respondents who gave a positive response to this question, the survey then asked the number of times during the past 12 months that they had been arrested and booked.

Questions assessing major depressive episodes (MDE) were based on DSM-IV criteria and were adapted from the National Comorbidity Survey-Replication.[26,27,34] A respondent was defined as having an MDE in the past year if he/she met criteria for a lifetime MDE (ie, having met at least five criteria in the same 2-week period, in which at least one of the symptoms was a depressed mood or loss of interest or pleasure in daily activities) and had a period of time in the past 12 months when he/she felt depressed or lost interest or pleasure in daily activities for 2 weeks or longer while also having other symptoms of a lifetime MDE.[26]

The survey defined mental health treatment for adolescents aged 12–17 years as receiving treatment or counseling for emotional or behavioral problems from specific mental health or other health professionals in school, home, outpatient, or inpatient settings within the 12 months prior to the interview; for adults aged 18 years or older, it was defined as treatment or counseling for any problem with emotions, nerves, or mental health in the 12 months prior to the interview in any inpatient or outpatient setting, or the use of prescription medication for treatment of a mental or emotional condition. Treatment for a substance-use problem only was excluded for adolescents and adults.

Sociodemographics: Respondents’ age, sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Native American [American Indian/Alaska Native], Asian/Pacific Islander/Native Hawaiian, multiple-race, Hispanic), total family income, and population density of residence were examined as potential correlates for *S. divinorum* use.[17,21,22,31–33] For adolescents who were unable to respond to the income questions, proxy responses were accepted from a household member. NSDUH-defined population density was based on 2000 census data and the June 2003 Core-Based Statistical Area (CBSA) classifications, and was

categorized into large metro (area with at least 1 million population), small metro (area with less than 1 million population), and nonmetropolitan (area not in a CBSA) areas.

Data analysis—The distribution of study variables by survey year were determined by χ^2 tests. Lifetime prevalence rates of *S. divinorum* use in each year by demographic, behavioral, mental health, and substance use variables were then determined. To ease interpretation, the percentages of increase between years are reported. Next, we examined the prevalence and correlates of past-year and former use using χ^2 and unadjusted multinomial logistic regression procedures to distinguish between characteristics of past-year users and former users as compared with nonusers. In the total sample, adjusted multinomial logistic regression analyses were then conducted to estimate the strength of associations between each covariate and *S. divinorum* use while adjusting for other variables to mitigate for their confounding effects on the estimated associations.

Finally, we determined whether past-year *S. divinorum* users had higher prevalence rates of depression and substance-use disorders than former users, and whether both groups had higher prevalence rates of these conditions than individuals who had never used *S. divinorum*. Adjusted logistic regression analyses also were conducted to evaluate further whether former and past-year *S. divinorum* users had greater odds of having depression and substance-use disorders than past-year alcohol or drug users who did not use *S. divinorum* and to identify subgroups of past-year *S. divinorum* users that had elevated odds of having a substance-use disorder. All analyses were conducted with SUDAAN®to take into account NSDUH's complex designs (eg, weighting, clustering).[35] All results reported here are weighted figures except for sample sizes, which are unweighted figures.

Results

Demographic characteristics of the study sample

There were no significant differences in the distribution of respondents' age, sex, and racial/ethnic groups across the 3 years. In the total sample (N = 166,453), males (49%) and females (51%) were equally distributed; 10% were adolescents aged 12–17 years; 27% were young adults aged 18–34 years; and 32% were of nonwhite race (blacks, 12%; American Indians/Alaska Natives, 0.5%; Asians/Pacific Islanders/Native Hawaiians, 4.5%; multiple-race individuals, 1%; Hispanics, 14%).

Prevalence and characteristics of lifetime *S. divinorum* use (Table 1 and Figure 1)

Among individuals aged 12 years or older, 0.7% (95% confidence interval [CI] 0.63–0.79) reported having ever used *S. divinorum* in 2006, and the prevalence increased to 1.0% (95% CI 0.94–1.12) in 2007 and to 1.3% (95% CI 1.19–1.42) in 2008.

Table 1 shows that lifetime *S. divinorum* use was associated with all study variables examined in each year ($P < 0.01$). In 2008, comparatively high rates of lifetime use were noted among adults aged 18–25 years (6.1%), multiple-race individuals (3.0%), individuals arrested for criminal activities (7.8%), or those who had depression (2.5%) in the past year.

Of note, *S. divinorum* use was common among individuals who used hallucinogens or stimulant drugs in the past year. Figure 1 indicates that, in 2008, lifetime *S. divinorum* use was prevalent among past-year users of LSD (53.7%), ecstasy (30.1%), heroin (24.2%), PCP (22.4%), cocaine (17.5%), tranquilizers (15.3%), inhalants (15.2%), sedatives (12.3%), opioid analgesics (10.5%), or marijuana (9.9%).

Past-year *S. divinorum* users versus former *S. divinorum* users (Tables 2 and 3)

Table 2 distinguishes between past-year *S. divinorum* use and former use. Among all lifetime *S. divinorum* users, 40% were recent *S. divinorum* users in the past 12 months.

Demographic, behavioral, and mental health characteristics

Young adults aged 18–25 years (2.0% and 2.9%, respectively) and individuals who were arrested for criminal activities (2.5% and 3.6%, respectively) showed comparatively high rates of past-year use and former use, respectively (Table 2). Additional groups showing higher rates of past-year use and former use than other groups included: males (0.6%, 1.0%), multiple-race individuals (0.8%, 1.5%), and individuals who reported depression (0.8%, 1.2%) or who received treatment for mental health problems (0.7%, 0.9%) in the past year.

Substance-use characteristics

As displayed in Table 3, past-year and former use of *S. divinorum* were more prevalent among illicit or nonmedical drug users (3.3%–21.3% and 3.9%–20.2%, respectively) than among alcohol or tobacco users (1.0%–1.2% and 1.6%–1.8%, respectively). Specifically, users of LSD (21.3%) had the highest prevalence of past-year *S. divinorum* use, followed by users of PCP (13.4%), ecstasy (11.1%), heroin (9.8%), inhalants (6.6%), stimulants (6.1%), cocaine (5.8%), tranquilizers (5.7%), and other drugs (3%–4%). A similar pattern was noted for former use.

Multinomial logistic regression of *S. divinorum* use (Table 4)

Adjusted multinomial logistic regression analyses of *S. divinorum* use were conducted to estimate the strength of associations with each covariate. To account for correlations among various drug use and produce stable estimates, the 11 drug classes (marijuana, inhalants, cocaine, heroin, ecstasy, LSD, PCP, opioids, stimulants, sedatives, tranquilizers) were summed and examined as a categorical polydrug use variable in the adjusted model. The adjusted model included survey year, age, sex, race/ethnicity, annual family income, population density of residence, arrest for criminal activity, depression, mental health treatment, tobacco use, binge drinking, and polydrug use.

Adjusted analysis conf irmed an increased rate of *S. divinorum* use in 2007 and 2008 and revealed illicit/nonmedical drug use as the strongest correlate for either past-year or former *S. divinorum* use (Table 4). There was a graded association of past-year *S. divinorum* use with polydrug use in the past year; that is, individuals who used one drug class were about nine times more likely than individuals who did not use any illicit/nonmedical drug in the past year to use *S. divinorum* in the past year (adjusted odds ratios [AOR] 8.95, 95% CI 6.18–12.96). The strength of associations increased to about 19 times (AOR 18.51, 95% CI 13.27–25.82) and 46 times (AOR 45.98, 95% CI 32.99–64.10) for individuals who used two drug classes and three or more drug classes, respectively. A similar pattern of association, but of lesser magnitude, was noted for polydrug use and former *S. divinorum* use (AOR ranging from 6.17 to 17.36).

Adjusted analysis also showed that young adults aged 18–25 years, males, individuals who used treatment for mental health problems, and tobacco users had elevated odds of using *S. divinorum* in the past year, while blacks as compared with whites and those in the lowest income group as compared with those in the highest income group had decreased odds of past-year *S. divinorum* use.

Regarding former use, young adults aged 18–25 years or 26–34 years, males, residents of large or small metropolitan areas, individuals who were arrested for criminal activity recently, and tobacco users exhibited elevated odds of former *S. divinorum* use, while

blacks, American Indians/Alaska Natives, and Hispanics had lower odds of former use than whites.

Depression and substance use disorders among *S. divinorum* users (Figure 2)

Prevalence rates of depression and all substance-use disorders (abuse or dependence) were markedly higher among past-year and former users of *S. divinorum* than among nonusers (χ^2, degrees of freedom [df] = 2, P, < 0.001 for each disorder by *S. divinorum* use status). Approximately 15% of past-year (95% CI 11.2–19.0) and 14% of former (95% CI 11.7–16.1) *S. divinorum* users had self-reported depression in the past year compared with 7.2% (95% CI 6.9–7.4) of nonusers of *S. divinorum*.

As summarized in Figure 2, 69.7% of past-year *S. divinorum* users and 66.9% of former users had a self-reported nicotine, alcohol, or drug use disorder in the past year compared with 19.7% of nonusers. Past-year *S. divinorum* users had higher rates of alcohol and most drug use disorders (ie, any drug, alcohol, marijuana, opioid, cocaine, hallucinogen, and stimulant use disorders) than former users, but they had a similar rate of nicotine dependence and of heroin, sedative, and tranquilizer use disorders. Specifically, an estimated 43.0% of past-year users and 28.9% of former users had a drug-use disorder compared with only 2.5% of nonusers of *S. divinorum*. Alcohol (42.8%, 35.8%, respectively), marijuana (33.0%, 21.5%, respectively), nicotine (31.0%, 36.1%, respectively), opioid (10.5%, 6.0%, respectively), and cocaine (10.5%, 5.0%, respectively) use disorders were comparatively common among past-year and former users of *S. divinorum*, respectively. Prevalence rates of these disorders, however, were comparatively low among nonusers of *S. divinorum*(0.6%–13.8%).

Logistic regression of depression and substance use disorders among *S. divinorum* users compared with other substance users (Table 5)

Adjusted logistic regression analyses were conducted to determine whether *S. divinorum*users were more likely than other substance users to have depression or a substance-use disorder. Table 5 shows that former and past-year *S. divinorum* users were about 1.4 times more likely than past-year alcohol or drug users who did not use *S. divinorum* to have depression in the past year. Both groups of *S. divinorum* users also were about 3–4 times more likely than past-year alcohol or drug users who did not use *S. divinorum* to have an alcohol or drug-use disorder in the past year.

Logistic regression of substance-use disorders among *S. divinorum* users (Table 6)

Finally, adjusted logistic regression analyses were conducted to identify subgroups of past-year *S. divinorum* users that had elevated odds of having a substance-use disorder (Table 6). Among past-year *S. divinorum* users (N = 1585): young adults aged 26–34 years, low- and middle-level income groups, individuals who were arrested for criminal activities or who had depression, and binge drinkers had elevated odds of nicotine dependence; depression, use of mental health treatment, and binge drinking increased odds of having an alcohol-use disorder; and American Indian/Alaska Native race, being arrested for criminal activity, depression, use of mental health treatment, tobacco use, and binge drinking increased odds of having a drug-use disorder.

Discussion

Main findings

This study of a large nationally representative sample documents a significant increase in *S. divinorum* use, identifies several groups showing elevated odds of *S. divinorum* use, and provides a comprehensive profile of substance-use disorders for *S. divinorum* users. These

findings are useful to concerned citizens and health professionals, and have implications for prevention and research efforts. First, over a 3-year period, the prevalence of *S. divinorum* use nationally had increased moderately, suggesting a need to monitor the trend in *S. divinorum* use. Females, individuals with middle-level family income (US$40,000–US $74,999), and residents of small metropolitan areas showed a substantial (<100%) increase in use. Second, while *S. divinorum* use in the general population is infrequent, young adults aged 18–25 years and individuals who were arrested for criminal activity had a disproportionally high rate of lifetime and recent use. Third, *S. divinorum* use was particularly common among past-year users of hallucinogens or stimulants, and the odds of past-year use increased with polydrug use, suggesting that polydrug users who used hallucinogens or stimulants have an increased probability of using *S. divinorum*. Fourth, the majority of former (70%) and past-year (67%) *S. divinorum* users were affected by symptoms of nicotine, alcohol, or drug-use disorders in the past year, and past-year *S. divinorum* users (especially binge drinkers and individuals with depression or other mental health problems) manifested the most problems related to alcohol and drug-use disorders. Adjusted analysis helps to reveal that either former or past-year *S. divinorum* users were more likely than past-year substance users who did not use *S. divinorum* to have depression or a substance-use disorder in the past year.

What this study adds

This study represents the first effort to examine recent trends in the prevalence of *S. divinorum* use. Previous studies of prevalence or correlates of *S. divinorum* use have relied on convenience samples, and some findings are constrained by a small sample.[17,21,22,36] State-level variations in legal status of *S. divinorum* use also might influence the access to or use of *S. divinorum*, resulting in regional variations in use. Of note, results from these NSDUH data, which include a large probability sample from all 50 states plus the District of Columbia, delineate recent changes in *S. divinorum* use across diverse age, sex, and racial/ethnic groups. Findings reveal a significant 83% increase within a 3-year period, and an increase was noted across different sex and income groups, suggesting that this increase is robust. These findings are in line with results from studies on *S. divinorum* use among YouTube users, *S. divinorum* and salvinorin A seized data, and Internet access to *S. divinorum*, which have indirectly suggested the rising popularity in use of *S. divinorum*.[5,37,38]

The findings also are consistent with recent results from studies of college students showing that whites, males, and individuals of a higher level of family income have an elevated rate of *S. divinorum* use.[17,21,22] Additionally, with these national data, we found that residents of metropolitan areas, individuals who were arrested for criminal activities, and individuals with depression or who use treatment for mental health problems have increased odds of recent *S. divinorum* use. These findings suggest some regional variations in *S. divinorum* use and show that *S. divinorum* users, like users of other hallucinogens and substance users in general, have a higher likelihood of exhibiting externalizing or internalizing problems than nonusers of *S. divinorum*.[31–33] Moreover, because *S. divinorum* use was robustly associated with other drugs connected with use in group settings,[31] such as ecstasy and LSD (http://www.clubdrugs.gov/), one possibility is raised that *S. divinorum* is being used in groups.[17] Given that *S. divinorum*'s subjective effects are reportedly similar to those of marijuana, LSD, and ketamine,[13–15] research is warranted to explore the context of *S. divinorum* use and to assess health risks associated with its use in conjunction with other substances (eg, risk for intoxication, accidents, injuries, psychiatric events, and overdose).[1,2,4,8,11,19]

Furthermore, multiple-race individuals were the only group in the adjusted model that showed greater odds of both recent and former *S. divinorum* use than whites. Prior research

on club drug use (ie, use of methamphetamine, ecstasy, LSD, ketamine, gamma hydroxybutyrate, or flunitrazepam; http://www.clubdrugs.gov/) among youth aged 16–23 years also found a high prevalence of lifetime club drug use (29%) among multiple-race youth compared with 24% of whites or American Indians/Alaska Natives and 5%–15% of other racial/ethnic groups.[31] Thus, in addition to whites and young adults, multiple-race groups need research to explore contextual and psychological factors that may promote their use of *S. divinorum* and other hallucinogenic or stimulant drugs.

Additional research also is recommended to monitor *S. divinorum* use among females (eg, young white females), as they demonstrate the highest level of increase (163%). Although the majority of *S. divinorum* users were males, recent results from an online survey of self-identified *S. divinorum* users (N = 219) showed that females were about twice as likely than males to be in the young age group (<22 years).[36] Possible research efforts might explore whether ease of access, legal status, use of club drugs, and the perception of *S. divinorum* as a legal or safer alternative to illicit drugs promote experimentation or continued use of *S. divinorum*.[5–7,39]

Lastly, these findings reveal that *S. divinorum* is most likely to be used by active illicit drug users, particularly substance users who have used hallucinogenic or stimulant drugs, and that the vast majority of *S. divinorum* users were affected by symptoms and consequences indicative of substance use problems (eg, role interference, use in hazardous conditions that increase risk for injuries, physical dependence on substances, compulsive drug use or seeking behaviors, repeated substance use despite having substance-related health problems). *S. divinorum* users also have a higher rate of depression than nonusers, and *S. divinorum* users who had depression or used treatment for mental health problems were particularly more likely than those without mental health conditions to have alcohol or drug-use disorders. Therefore, repeated *S. divinorum* use for the purpose of “getting high” or “obtaining hallucinogenic effects” could pose a health concern (eg, drug interaction, intoxication) or increase the likelihood of medical and other psychiatric conditions for subsets of users who have been affected by other substance use or psychiatric disorders.[2,4,8,18,19]

Limitations and strengths

These findings should be interpreted with caution. NSDUH uses a cross-sectional design and relies on self-reports, which can be influenced by memory error and underreporting. All results are considered estimates, and no causal inference can be drawn. For example, the causal relation between substance use and depression cannot be determined by the NSDUH data. Study findings also are limited by the lack of data on contextual factors associated with *S. divinorum* use, motives or detailed frequency of use, and *S. divinorum*-specific problems. Studies of con-submit venience samples of *S. divinorum* users have suggested that *S. divinorum* was used for a variety of reasons (eg, for fun, curiosity, social purposes, drug-induced states of consciousness, getting high, self-defined spiritual purposes, relieving boredom, reducing medical or psychological problems) and that a very small subset of users were frequent users.[36,40,41] However, these results from small or convenience samples need to be confirmed and extended using data from surveys of a probability sample or controlled studies.[36,40,41] In addition, NSDUH assessments of substance-use disorders and major depression are based on standardized questions designed to operationalize DSM-IV criteria for these disorders. These results are self-reported, survey-based estimates and not clinical diagnoses (ie, not being validated by clinicians). Moreover, because of a lack of research data, there are no established criteria for assessing abuse of or dependence on *S. divinorum*.[27] Results from this study also are not applicable to institutionalized and homeless individuals because these groups are not included in the NSDUH sampling.

Nonetheless, NSDUH has noteworthy strengths not available in small-scale studies. NSDUH is the first national United States survey to add *S. divinorum* use questions to the assessment beginning in 2006.[23] Because *S. divinorum* and salvinorin A are not controlled substances under the Controlled Substances Act in the United States and have no approved medical use, there is a scarcity of data about their use and adverse effects.[38] For example, the annual reports of the American Association of Poison Control Centers (AAPCC), IMS National Prescription Audit Plus™ (a database of prescription drugs), the Aggregate Production Quota (a database for the maximum amount of Schedule I and II substances manufactured in the United States), and the ongoing United States Drug Abuse Warning Network (DAWN) reports have not included data on use and problems associated with *S. divinorum* and salvinorin A.[38] Given the lack of data, this study makes a timely and unique contribution by presenting the most recent national trends in S. divinorum use and by documenting a comprehensive profile of substance-use problems among *S. divinorum* users.

These findings also have a higher level of generalizability to population subgroups than those of a convenience or regional sample due to the large representative sample consisting of geographically diverse racial/ethnic groups. Lastly, the survey has high levels of response rates for household screening and interviewing, uses the most sophisticated survey methods available to improve respondents' honest reporting of substance-use behaviors (ie, computer-assisted self-administered interviewing and anonymous data collection), includes detailed probes and color pictures of prescription drugs to facilitate assessments for substance use behaviors, and applies the 2000 census to improve sample weight calibration.[24–26]

Conclusion and implications

Nationally, the rate of *S. divinorum* use has increased moderately. While young adults aged 18–25 years show an elevated likelihood of recent *S. divinorum* use, *S. divinorum* is most likely to be used by recent or active drug users who have used hallucinogens or stimulants. Polydrug use is the most robust determinant of *S. divinorum* use. *S. divinorum* users who engaged in binge drinking, experienced depression, or used treatment for mental health problems had particularly high odds of having substance use disorders. The high prevalence of past-year substance use disorders among recent *S. divinorum* users emphasizes the need for research to address several open issues for *S. divinorum* use, including its addictive potential, its influence on continuance of drug-use behaviors or escalation to addiction (eg, as an alternative to other drugs, cross-tolerance), adverse effects from drug interactions (eg, intoxications, accidents, injuries, health risk), and long-term effects on human health.[1,2,4,8,10,39] Health care professionals and individuals involved in substance abuse care or services need to be aware of this new drug.[39] Assessments of recreational *S. divinorum* use need to be improved and considered for addition to the clinical assessment for addiction problems. Finally, continuous surveillance of *S. divinorum* use among high-risk groups is warranted.

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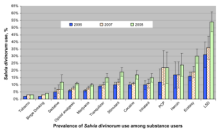

Figure 1.
Prevalence of lifetime *Salvia divinorum* use among past-year substance users aged 12 years or older by type of substance used: 2006–2008 National Surveys on Drug Use and Health (N = 166,453). Lines extending from bars indicate 95% confidence intervals of the estimates; due to a very narrow range of 95% confidence intervals for the prevalence of lifetime *Salvia divinorum* use among tobacco users and binge drinkers, they are not shown in the figure.
Abbreviations: LSD, lysergic acid diethylamide; PCP, phencyclidine.

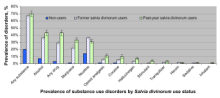

Figure 2.

Prevalence of substance use disorders (abuse or dependence) among past-year and former (prior to the past 12 months) users of *Salvia divinorum* compared with nonusers aged 12 years or older: 2006–2008 National Surveys on Drug Use and Health (N = 166,453). χ^2 (degrees of freedom = 2) $P < 0.001$ for each disorder by *Salvia divinorum* use status. Any drug abuse or dependence included abuse of or dependence on marijuana, inhalants, cocaine, heroin, hallucinogens, opioid analgesics, stimulants, sedatives, and tranquilizers in the past year. Except for nicotine dependence, which refers to dependence in the past month, all other substance use disorders include abuse of or dependence on that substance class in the past year. Lines extending from bars indicate 95% confidence intervals of the estimates; due to a very narrow range of 95% confidence intervals for nonusers, they are not shown in the figure.

Table 1

Lifetime prevalence of *Salvia divinorum* use among individuals aged 12 years or older: 2006–2008 National Surveys on Drug Use and Health (N = 166,453)

Prevalence of *Salvia divinorum* use by study variables	2006	2007	2008	2006 versus 2007: increase in %	2006 versus 2008: increase in %
Sample size	N = 55,279	N = 55,435	N = 55,739		
Overall prevalence, % (SE)	0.71 (0.04)	1.02 (0.05)	1.30(0.06)[a]	44[b]	83[b]
Age group in years					
12–17	0.88 (0.09)[c]	1.18 (0.11)[c]	1.57 (0.13)[c]	34	78[b]
18–25	3.39 (0.20)	5.00 (0.22)	6.10 (0.26)	32[b]	80[b]
26–34	0.78 (0.12)	1.15 (0.19)	1.73 (0.23)	47	122b
≥35	0.09 (0.02)	0.13 (0.03)	0.15 (0.04)	44	67
Sex					
Male	1.17 (0.07)[c]	1.59 (0.07)[c]	1.93 (0.09)[c]	36[b]	65[b]
Female	0.27 (0.03)	0.49 (0.04)	0.71 (0.06)	81[b]	163[b]
Race/ethnicity					
White	0.86 (0.05)[c]	1.22 (0.05)[c]	1.58 (0.08)[c]	42[b]	84[b]
Black	0.11 (0.04)	0.23 (0.08)	0.21 (0.05)	109	91
American indian/Alaska native	0.68 (0.48)	2.04 (1.26)	1.18 (0.35)	200	74
Asian/Native Hawaiian/Pacific Islander	0.32 (0.1 1)	0.45 (0.28)	0.40 (0.1 1)	41	25
Multiple race	1.18 (0.39)	2.35 (0.61)	2.95 (0.81)	99	150
Hispanic	0.56 (0.10)	0.80 (0.13)	1.01 (0.14)	43	80
Total family income (USD)					
$0–$39,999	0.85 (0.06)[c]	1.20 (0.08)[d]	1.61 (0.10)[c]	41[b]	89[b]
$40,000–$74,999	0.56 (0.06)	0.82 (0.08)	1.15 (0.10)	46[b]	105[b]
≥ $75,000	0.65 (0.08)	0.99 (0.09)	1.07 (0.07)	52[b]	65[b]
Population density of residence					
Large metro areas	0.75 (0.06)[c]	1.03 (0.07)[c]	1.22 (0.08)[c]	37[b]	63[b]
Small metro areas	0.70 (0.07)	1.12 (0.07)	1.50 (0.09)	60[b]	114[b]

Prevalence of *Salvia divinorum* use by study variables	2006	2007	2008	2006 versus 2007: increase in %	2006 versus 2008: increase in %
Nonmetro areas	0.37 (0.08)	0.41 (0.09)	0.60 (0.1 1)	11	62
Past-year arrest for criminal activity					
Yes	4.75 (0.59)[c]	5.75 (0.66)[c]	7.80 (0.75)[c]	21	64[b]
No	0.59 (0.03)	0.89 (0.04)	1.10 (0.05)	51[b]	86[b]
Past-year depression					
Yes	1.44 (0.20)[c]	2.12 (0.26)[c]	2.46 (0.28)[c]	47	71[b]
No	0.64 (0.04)	0.93 (0.04)	1.21 (0.05)	45[b]	89[b]
Past-year mental health treatment					
Yes	1.05 (0.11)[c]	1.56 (0.14)[c]	2.01 (0.19)[c]	49[b]	91[b]
No	0.66 (0.04)	0.94 (0.05)	1.19 (0.06)	42[b]	80[b]

Notes:

[a] χ^2 test = 62.15, degrees of freedom = 2, $P < 0.001$;

[b] $P \leq 0.05$;

[c] χ^2 test for survey year and the covariate in the first column: $P < 0.001$;

[d] χ^2 test for survey year and the covariate in the first column: $P < 0.01$.

Abbreviation: SE, standard error.

Table 2

Demographic, behavioral, and mental health characteristics of recent (past-year) and former (prior to past year) use of *Salvia divinorum* among individuals aged 12 years or older: 2006–2008 National Surveys on Drug Use and Health (N = 166,453)

Prevalence of *Salvia divinorum* use	Past-year use, % (SE)	Crude odds ratio of past-year use versus never use	Former use, % (SE)	Crude odds ratio of former use versus never use
Overall prevalence, % (SE)	0.40 (0.02)		0.61 (0.02)	
Year				
2006	0.28 (0.02)	1.00	0.42 (0.03)	1.00
2007	0.41 (0.03)	1.46 (1.21–1.77)[a]	0.61 (0.03)	1.45 (1.19–1.76)[a]
2008	0.49 (0.03)	1.76 (1.44–2.14)[a]	0.81 (0.05)	1.91 (1.54–2.36)[a]
Age group in years				
12–17	0.76 (0.05)	1.00	0.45 (0.04)	1.00
18–25	1.98 (0.08)	2.70 (2.34–3.11)[a]	2.85 (0.10)	6.62 (5.48–7.99)[a]
26–34	0.26 (0.06)	0.34 (0.22–0.54)[a]	0.96 (0.09)	2.15(1.70–2.70)[a]
≥35	0.03 (0.01)	0.04 (0.02–0.08)[a]	0.09 (0.02)	0.19 (0.13–0.29)[a]
Sex				
Male	0.62 (0.03)	3.29 (2.76–3.91)[a]	0.95 (0.04)	3.19 (2.73–3.73)[a]
Female	0.19 (0.02)	1.00	0.30 (0.02)	1.00
Race/ethnicity				
White	0.47 (0.02)	1.00	0.75 (0.03)	1.00
Black	0.08 (0.02)	0.17 (0.10–0.28)[a]	0.10 (0.03)	0.13 (0.08-0.23)[a]
American Indian/Alaska Native	0.88 (0.47)	1.89 (0.64–5.57)	0.43 (0.12)	0.57 (0.32–1.00)[b]
Asian/Native Hawaiian/Pacific Islander	0.18 (0.04)	0.38 (0.24–0.61)[a]	0.21 (0.09)	0.28 (0.12–0.67)[c]
Multiple race	0.75 (0.17)	1.62 (1.02–2.57)[b]	1.46 (0.34)	1.96 (1.21–3.16)[c]
Hispanic	0.35 (0.06)	0.75 (0.54–1.05)	0.44 (0.06)	0.58 (0.43–0.78)[a]
Total family income (USD)				
$0–$39,999	0.43 (0.02)	1.09 (0.90–1.31)	0.78 (0.05)	1.51 (1.25–1.83)a
$40,000–$74,999	0.36 (0.03)	0.91 (0.72–1.14)	0.49 (0.04)	0.94 (0.76–1.17)
≥ $75,000	0.39 (0.03)	1.00	0.52 (0.04)	1.00
Population density of residence				
Large metro areas	0.39 (0.03)	1.00	0.61 (0.03)	1.00
Small metro areas	0.43 (0.02)	1.12 (0.96–1.30)	0.68 (0.04)	1.11 (0.94–1.31)
Nonmetro areas	0.25 (0.04)	0.65 (0.46–0.92)[b]	0.21 (0.03)	0.33 (0.24–0.46)[c]
Past-year arrest for criminal activity				
Yes	2.51 (0.22)	7.93 (6.47–9.71)[a]	3.62 (0.34)	7.25 (5.92–8.87)[a]
No	0.33 (0.02)	1.00	0.53 (0.02)	1.00
Past-year depression				
Yes	0.82 (0.08)	2.30 (1.88–2.82)[a]	1.18 (0.11)	2.10 (1.72–2.56)[a]
No	0.36 (0.02)	1.00	0.57 (0.02)	1.00

Prevalence of *Salvia divinorum* use	Past-year use, % (SE)	Crude odds ratio of past-year use versus never use	Former use, % (SE)	Crude odds ratio of former use versus never use
Past-year mental health treatment				
Yes	0.65 (0.06)	1.83 (1.51-2.22)[a]	0.89 (0.07)	1.56 (1.33–1.83)[a]
No	0.36 (0.02)	1.00	0.57 (0.02)	1.00

Abbreviation: SE, standard error.

Notes:

[c] $P < 0.001$,

[b] $P < 0.01$,

[a] $P < 0.05$.

Table 3

Substance use characteristics of recent (past-year) and former (prior to past year) use of *Salvia divinorum* among individuals aged 12 years or older: 2006–2008 National Surveys on Drug Use and Health (N = 166,453)

Prevalence of *Salvia divinorum* use	Past-year use, % (SE)	Crude odds ratio of past-year use versus never use	Former use, % (SE)	Crude odds ratio of former use versus never use
Past-year tobacco use				
Yes	1.04 (0.05)	17.32 (13.05–22.99)[a]	1.56 (0.06)	13.27 (10.79–16.32)[a]
No	0.06 (0.01)	1.00	0.12 (0.01)	1.00
Past-month binge drinking				
Yes	1.19 (0.05)	7.88 (6.69–9.28)[a]	1.80 (0.08)	7.19 (6.06–8.53)[a]
No	0.16 (0.01)	1.00	0.26 (0.02)	1.00
Past-year marijuana use				
Yes	3.34 (0.15)	21.40 (16.89–27.11)[a]	4.53 (0.18)	10.47 (8.38–13.09)[a]
No	0.06 (0.01)	1.00	0.17 (0.01)	1.00
Past-year inhalant use				
Yes	6.55 (0.69)	21.40 (16.89–27.11)[a]	5.35 (0.54)	10.47 (8.38–13.09)[a]
No	0.34 (0.01)	1.00	0.57 (0.02)	1.00
Past-year cocaine use				
Yes	5.77 (0.38)	24.43 (20.76–28.75)[a]	7.19 (0.51)	17.85 (15.15–21.03)[a]
No	0.27 (0.01)	1.00	0.46 (0.02)	1.00
Past-year heroin use				
Yes	9.84 (2.03)	31.98 (20.11–50.85)[a]	9.70 (1.81)	19.97 (13.12–30.38)[a]
No	0.38 (0.02)	1.00	0.60 (0.02)	1.00
Past-year ecstasy use				
Yes	11.06 (0.83)	46.22 (37.37–57.16)[a]	10.67 (0.92)	25.66 (20.61–31.96)[a]
No	0.30 (0.01)	1.00	0.53 (0.02)	1.00
Past-year LSD use				
Yes	21.27 (1.79)	107.78 (84.40–137.65)[a]	20.19 (1.93)	61.44 (47.17–80.03)[a]
No	0.33 (0.01)	1.00	0.56 (0.02)	1.00
Past-year PCP use				
Yes	13.36 (3.07)	41.25 (23.47–72.51)[a]	4.29 (1.63)	8.42 (3.67–19.32)[a]
No	0.39 (0.02)	1.00	0.61 (0.02)	1.00
Past-year opioid analgesic use				
Yes	3.96 (0.23)	20.31 (17.15–24.07)[a]	4.36 (0.25)	11.26 (9.37–13.06)[a]
No	0.21 (0.01)	1.00	0.42 (0.02)	1.00
Past-year stimulant use				
Yes	6.14 (0.52)	21.36 (17.39–26.24)[a]	7.04 (0.62)	14.94 (12.16–18.35)[a]
No	0.33 (0.01)	1.00	0.54 (0.02)	1.00
Past-year sedative use				
Yes	3.63 (0.61)	10.06 (7.02–14.42)[a]	3.90 (0.74)	6.90 (4.62–10.29)[a]

Prevalence of *Salvia divinorum* use	**Past-year use, % (SE)**	**Crude odds ratio of past-year use versus never use**	**Former use, % (SE)**	**Crude odds ratio of former use versus never use**
No	0.39 (0.02)	1.00	0.60 (0.02)	1.00
Past-year tranquilizer use				
Yes	5.68 (0.42)	22.24 (18.20–27.19)[a]	5.95 (0.42)	13.27 (11.19–15.74)[a]
No	0.29 (0.01)	1.00	0.50 (0.02)	1.00

Note:

[a] $P < 0.001$.

Abbreviations: LSD, lysergic acid diethylamide; PCP, phencyclidine.

Table 4

AORs[a] of past-year and former (prior to past year) use of *Salvia divinorum* among individuals aged 12 years or older: 2006–2008 National Surveys on Drug Use and Health (N = 166,453)

Selected characteristics of *Salvia divinorum* use	Past-year *Salvia divinorum* use versus never use AOR (95% CI)	Former *Salvia divinorum* use versus never use AOR (95% CI)
Year (versus 2006)		
2007	1.66 (1.36–2.03)[b]	1.56 (1.28–1.91)[b]
2008	2.19 (1.78–2.70)[b]	2.24 (1.81–2.78)[b]
Age group in years (versus 12–17 years)		
18–25	1.33 (1.12–1.58)[c]	3.27 (2.66–4.03)[b]
26–34	0.25 (0.15–0.41)[b]	1.57 (1.23–2.02)[b]
≥35	0.08 (0.04–0.15)[b]	0.29 (0.20–0.42)[b]
Sex (versus female)		
Male	2.78 (2.27–3.39)[b]	2.58 (2.16–3.07)[b]
Race/ethnicity (versus white)		
Black	0.20 (0.13–0.33)[b]	0.13 (0.07–0.22)[b]
American Indian/Alaska Native	1.52 (0.58–3.98)	0.48 (0.27–0.87)[d]
Asian/Native Hawaiian/Pacific Islander	0.71 (0.44–1.13)	0.43 (0.17–1.09)
Multiple race	1.32 (0.82–2.11)	1.56 (0.89–2.75)
Hispanic	0.78 (0.54–1.11)	0.54 (0.40–0.74)[b]
Total family income (USD) (versus $75,000+)		
$0–$39,999	0.74 (0.61–0.91)[c]	1.05 (0.85–1.30)
$40,000–$74,999	0.85 (0.67–1.08)	0.84 (0.67–1.05)
Population density (versus nonmetro areas)		
Large metro areas	1.32 (0.92–1.88)	2.71 (1.90–3.86)[b]
Small metro areas	1.35 (0.96–1.90)	2.60 (1.83–3.71)[b]
Past-year arrest for criminal activity (versus no)		
Yes	1.14 (0.91–1.42)	1.28 (1.03–1.60)[d]
Past-year depression (versus no)		
Yes	1.24 (0.98–1.58)[e]	1.24 (0.98–1.56)[e]
Past-year mental health treatment (versus no)		
Yes	1.33 (1.06–1.67)[d]	1.21 (0.99–1.49)[f]
Past-year tobacco use (versus no)		
Yes	2.76 (2.03–3.76)[b]	2.62 (2.03–3.40)[b]
Past-month binge drinking (versus no)		
Yes	1.16 (0.93–1.44)	1.19 (0.97–1.46)
Past-year polydrug use, number of the 11 drug classes used in the past yearg (versus none)		
1	8.95 (6.18–12.96)[b]	6.17 (4.81–7.90)[b]

Selected characteristics of *Salvia divinorum* use	Past-year *Salvia divinorum* use versus never use AOR (95% CI)	Former *Salvia divinorum* use versus never use AOR (95% CI)
2	18.51 (13.27–25.82)[b]	9.08 (6.86–12.02)[b]
≥3	45.98 (3 2.99–64. 10)[b]	17.36 (13.51–22.31)[b]

Notes:

[a] Adjusted multinomial logistic model included all variables listed in the first column;

[b] $P < 0.001$;

[c] $P < 0.01$;

[d] $P < 0.05$;

[e] $P = 0.07$;

[f] $P = 0.06$;

[g] Including marijuana, inhalants, cocaine, heroin, ecstasy/MDMA, LSD, PcP, analgesic opioids, stimulants, sedatives, and tranquilizers.

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; LSD, lysergic acid diethylamide; MDMA, 3,4-methylenedioxymethamphetamine (ecstasy); PCP, phencyclidine.

Table 5

AORs of depression and substance-use disorders among *Salvia divinorum* users compared with alcohol or drug users who did not use *Salvia divinorum* in the past year: 2006–2008 National Surveys on Drug Use and Health (N = 106,042)

Substance use status	AOR of depression[1] (95% CI)	AOR of alcohol or drug use disorders[1] (95% CI)
Former *Salvia divinorum* users	1.44 (1.13–1.82) $P < 0.01$	2.97 (2.54–3.48) $P < 0.01$
Past-year *Salvia divinorum* users	1.45 (1.12–1.88) $P < 0.01$	4.33 (3.55–5.29) $P < 0.01$
Past-year alcohol or drug users who did not use *Salvia divinorum*[2]	1.00	1.00

Notes:

[1]The adjusted logistic regression model controlled for survey year, age, sex, race/ethnicity, population density, arrests for criminal activity, and mental heath treatment;

[2]Including past-year users of alcohol, marijuana, inhalants, cocaine, heroin, ecstasy, LSD, PcP, analgesic opioids, stimulants, sedatives, and tranquilizers.

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; LSD, lysergic acid diethylamide; PCP, phencyclidine.

Table 6

AORs[a] of substance use disorders among past-year *Salvia divinorum* users aged 12 years or older: 2006–2008 National Surveys on Drug Use and Health (N = 1585)

Selected characteristics of *Salvia divinorum* users	AOR of nicotine dependence (95% CI)	AOR of alcohol use disorders (95% CI)	AOR of drug use disorders (95% CI)
Year (versus 2006)			
2007	1.13 (0.76–1.67)	0.95 (0.64–1.41)	0.85 (0.53–1.37)
2008	1.01 (0.69–1.50)	1.22 (0.84–1.75)	1.03 (0.68–1.56)
Age group (versus 12–17 years)			
18–25	1.06 (0.74–1.52)	1.07 (0.74–1.57)	0.73 (0.51–1.05)
26–34	2.80 (1.20–6.55)[b]	1.48 (0.57–3.80)	0.73 (0.30–1.80)
≥35 years	1.15 (0.79–1.68)	1.27 (0.30–5.26)	0.59 (0.21–1.66)
Sex (versus female)			
Male	1.15 (0.79–1.68)	0.88 (0.58–1.34)	1.05 (0.73–1.52)
Race/ethnicity (versus white)			
Black	0.65 (0.18–2.32)	1.10 (0.37–3.28)	2.06 (0.71–5.97)
American Indian/Alaska Native	0.18 (0.03–1.05)	0.70 (0.19–2.66)	14.63 (2.20–97.15)[c]
Asian/Native Hawaiian/Pacific Islander	1.15 (0.45–2.91)	1.18 (0.38–3.68)	0.66 (0.24–1.84)
Multiple race	1.21 (0.55–2.66)	1.94 (0.79–4.76)	1.26 (0.62–2.58)
Hispanic	0.85 (0.44–1.63)	0.71 (0.37–1.36)	0.77 (0.39–1.50)
Total family income (USD) (versus $75,000+)			
$0–$39,999	1.55 (1.03–2.34)[b]	0.86 (0.55–1.36)	1.05 (0.65–1.70)
$40,000–$74,999	1.56 (1.10–2.20)[b]	1.01 (0.63–1.62)	0.96 (0.60–1.53)
Population density (versus nonmetro)			
Large metro areas	0.91 (0.47–1.79)	1.12 (0.45–2.81)	1.10 (0.45–2.66)
Small metro areas	1.10 (0.55–2.21)	1.31 (0.54–3.16)	1.08 (0.49–2.37)
Arrested for criminal activity (versus no)			
Yes	2.06 (1.27–3.34)[c]	1.51 (0.95–2.40)	1.85 (1.25–2.73)[c]
Past-year depression (versus no)			
Yes	1.85 (1.1 5–2.99)[b]	1.76 (1.05–2.93)[b]	2.24 (1.32–3.83)[c]
Mental health treatment (versus no)			
Yes	1.22 (0.77–1.92)	1.17 (0.72–1.9 1)[b]	2.97 (1.91–4.62)[d]
Current tobacco use (versus no)			
Yes	-[e]	1.35 (0.70–2.58)	2.01 (1.07–3.77)[b]
Binge drinking (versus no)			
Yes	1.65 (1.11–2.45)[b]	7.87 (5.16–12.02)[d]	1.72 (1.13–2.62)[b]

Notes:

[a] Adjusted logistic model included all variables listed in the first column;

[b] $P < 0.05$;

[c] $P < 0.01$;

[d] $P < 0.001$;

[e] Tobacco use was not included in the model due to a high level of correlation.

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval.