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# Use of Lysergic Acid Diethylamide by Major Depression Status

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**IMPORTANCE** Renewed interest in the clinical potential of hallucinogens may lead people with depression to a generally more positive view of the use of lysergic acid diethylamide (LSD). Therefore, past-year LSD use among people with depression may be increasing in prevalence.

**OBJECTIVE** To assess time trends in the prevalence of past-year nonmedical LSD use by past-year major depression status and the variation in this association by sociodemographic characteristics.

**DESIGN, SETTING, AND PARTICIPANTS** This survey study used pooled publicly available data from 478 492 adults aged 18 years or older who were administered the National Survey on Drug Use and Health from 2008 through 2019. Statistical analysis was conducted from December 2022 to June 2023.

**MAIN OUTCOME AND MEASURES** Past-year major depression diagnoses per criteria from the *DSM-IV* were analyzed. Logistic regression models examined whether time trends in past-year nonmedical LSD use differed between adults with vs without past-year depression, adjusting for sociodemographic characteristics. Secondary analyses examined whether the trends in LSD use by depression status differed between sociodemographic subgroups.

**RESULTS** The analytic sample included 478 492 adults, of whom 51.8% were female, 56.1% were younger than 50 years, 11.7% were Black, 15.1% were Hispanic, 65.8% were White, and 7.5% were another race. Weighted interview response rates ranged from 64.9% to 75.6% during the study time frame. From 2008 to 2019, past-year use of LSD increased significantly more among adults with major depression (2008 prevalence, 0.5%; 2019 prevalence, 1.8%; prevalence difference [PD], 1.3% [95% CI, 1.0%-1.6%]) compared with adults without major depression (2008 prevalence, 0.2%; 2019 prevalence, 0.8%; PD, 0.6% [95% CI, 0.5%-0.7%]) (difference in difference, 0.8% [95% CI, 0.5%-1.1%]). This difference was particularly pronounced among young adults aged 34 years or younger (PD among those aged 18-25 years with depression, 3.3% [95% CI, 2.5%-4.2%]; PD among those aged 26-34 years with depression, 2.7% [95% CI, 1.6%-3.8%]) and individuals with incomes less than $75 000 per year (PD among those with income <$20 000, 1.9% [95% CI, 1.3%-2.6%]; PD among those with income $20 000-$49 999, 1.5% [95% CI, 1.0%-2.1%]; PD among those with income $50 000-$74 999, 1.3% [95% CI, 0.7%-2.0%]).

**CONCLUSIONS AND RELEVANCE** This study suggests that, from 2008 to 2019, there was a disproportionate increase in the prevalence of past-year LSD use among US adults with past-year depression. Among those with depression, this increase was particularly strong among younger adults and those with lower household incomes. Among individuals with depression who also report LSD use, clinicians should discuss potential strategies for mitigating harm and maximizing benefits in medically unsupervised settings.

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Supplemental content

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Lysergic acid diethylamide (LSD) is a potent, semisynthetic hallucinogen that causes psychoactive effects, such as hallucinations (eg, color or movement of objects) and alterations in sense of identity.[1] After its discovery in the US in 1943,[2] LSD became a target for psychiatric research given its potent mind-altering effects[3] and mechanism of action on central serotonin 2A receptors.[4,5] Lysergic acid diethylamide was studied as a potential treatment for psychiatric and substance use disorders until the mid-1970s[6-8]; because LSD became illegal in the US in 1970 when the Controlled Substances Act was signed into law,[9] research was halted quickly after due to concerns about increases in recreational use.[10] Although LSD remains classified as a Schedule I substance under the US Controlled Substances Act,[11] the past decade has been marked by a resurgence of clinical research suggesting promise of hallucinogens, including LSD, for treating psychiatric or substance use disorders.[12] There has also been substantial renewed interest in LSD within popular culture and private industry, such as venture capital and biotech investors funding privately owned psychedelic companies.[13] As popular media outlets increasingly present hallucinogens as beneficial for mental health, and as practices such as microdosing of LSD (defined as taking a subhallucinogenic dose of the drug with the goal of improving mood[14]) gain popularity, LSD use may be viewed as appealing among individuals with depression more so than in previous years.

Although empirical evidence regarding the efficacy of hallucinogens in the treatment of mood disorders remains preliminary, 1 double-blind trial demonstrated improvement in internalizing symptoms after LSD administration among adults with depression or anxiety.[15] However, this pilot study was small and limited to adults with a life-threatening illness. Results of trials testing the efficacy of LSD among adults with depression without the presence of a co-occurring illness are yet to be published, although 1 phase 2 trial studying the role of LSD in the treatment of depression is currently under way.[16] Nevertheless, the global psychedelic therapeutic market is projected to be valued at $8.3 billion in the US by 2028,[17] underscoring the burgeoning role hallucinogens are expected to play as an alternative to more conventional treatments for mental disorders in psychiatry.

Although LSD use may prove beneficial for some individuals, there can also be adverse consequences, particularly in medically unsupervised settings. Administration of LSD can result in acute physical effects (eg, hypertension, tachycardia, increased body temperature, and body tremors)[2] and in unpleasant experiences, such as delusions, panic attacks, fear, or paranoia (colloquially referred to as a "bad trip"), particularly when taken in high doses.[18] Although these experiences are typically resolved as the psychotropic effects wear off, some individuals may continue to experience "flashbacks" to bad trips while not under the influence of LSD[19] or may develop hallucinogen-persisting perception disorder, a condition in which individuals continue experiencing changes in perception long after drug administration.[20] Because the risk of adverse experiences may be dose dependent,[21] those using LSD in unsupervised settings may be at a higher risk due to unclear dosing information, and effects may be disturbing to individuals with depression who may expect a positive experience after drug exposure. Finally, individuals seeking LSD from illegal sources cannot verify the contents of the substances they buy. An example of this risk is one compound of synthetic psychedelic substances, NBOMe, that has recently emerged on the illicit drug market and was marketed as LSD by illegal drug sources.[22-24] Case reports of NBOMe ingestion have documented toxic effects and fatalities as a result of drug administration and overdose.[25] Therefore, given the renewed interest in the therapeutic use of LSD in psychiatry, understanding trends in the association between LSD use and depression in unsupervised, nonmedical settings has become an important public health issue.

Some recent population studies show that adults with psychiatric disorders, suicidal ideation, or serious psychological distress are more likely than those without these conditions to use LSD.[26-28] However, other studies found a reduced likelihood of past-month psychological distress or major depression among those who used hallucinogens recreationally in their lifetime,[29,30] while still other studies found no association between mental health problems and hallucinogen use.[31,32] These inconsistencies may be in part due to the grouping of different hallucinogens into combined categories rather than assessing commonly used hallucinogens (such as LSD) in distinct categories and the use of different within-study time frames for assessing hallucinogen use and psychiatric problems.

Nonetheless, studies in the overall population demonstrate a consistent increase in LSD use over time. Specifically, 1 National Survey on Drug Use and Health (NSDUH) study showed that, whereas use of other hallucinogen classes either decreased or increased only among select age groups or time frames, the use of LSD consistently increased among every observed age group (12-17 years, 18-25 years, and ≥26 years) from 2002 to 2019.[33] Increases in LSD use were observed in tandem with a decreasing perception of LSD use as risky and were consistent with studies showing increases in LSD use among other populations, such as youths enrolled in the Monitoring the Future study[34] and other potentially high-risk populations, such as attendees of electronic dance music parties.[35]

### Key Points

**Question** Did trends in the prevalence of past-year lysergic acid diethylamide (LSD) use differ between adults with and adults without depression between 2008 and 2019?

**Findings** In this survey study of data from 478 492 adults aged 18 years or older who were administered the National Survey on Drug Use and Health, between 2008 and 2019, the proportion of adults who reported past-year LSD use increased more among those with depression than those without depression. Disproportionate increases in past-year LSD use were more pronounced among young adults with depression than their older counterparts.

**Meaning** Although past-year LSD use is increasing in the overall US population, these findings suggest that young adults with depression are increasingly likely to use LSD in medically unsupervised settings.

Changing trends in the prevalence of hallucinogen use has particular relevance to young adults. Specifically, longitudinal analysis of alcohol and drug use in a nationally representative sample of young adults showed that in 2021, young adults had historically low prevalences of cigarette, alcohol, and narcotic opioid use, while at the same time, hallucinogen use was at a historic high.[34] Therefore, given the recent overall increases in LSD use, further study of this increase among potentially high-risk populations (ie, those with a current mood disorder) is warranted. Although there is evidence of an association between recreational LSD use and depression among US adults in pooled data from recent years (2015-2020),[27] whether this association is changing over time is unknown (ie, whether the prevalence of LSD use is increasing at a disproportionately greater rate among individuals with depression compared with those without).

Therefore, we used nationally representative data from the NSDUH of the US adult population to investigate 2 research aims. First, we compared trends in past-year LSD use from 2008 to 2019 between adults with and adults without past-year depression. Second, we further investigated whether the differences in trends varied between sociodemographic subgroups (age, sex, race and ethnicity, income, educational level, and marital status) to assess whether use of LSD in nonmedical settings may be associated with specific subgroups. We hypothesized that we would observe a larger increase in past-year LSD use among adults with depression compared with those without depression.

## Methods

### Sample

Data were from the NSDUH, a nationally representative, annual, cross-sectional survey administered by the Substance Abuse and Mental Health Services Administration (SAMHSA).[36] The NSDUH uses multistage probability sampling to recruit noninstitutionalized civilians aged 12 years or older in the 50 US states and the District of Columbia. Interviews are conducted face to face at the home of the respondent. Data collection occurs electronically through computer-assisted interviewing devices (eg, tablets or laptops).[37] Sensitive modules of the interview are collected using audio computer-assisted self-interviewing, in which respondents listen to the question on the device and input their responses directly, to encourage high-quality data. After data collection, NSDUH sample weights are calculated to adjust for nonresponse rates and to represent the US target population, per the US Census Bureau's population estimates. For the current analysis, new sample weights were calculated when combining the data across years by dividing the original sample weight by the total number of data sets, as recommended by SAMHSA.[37] Study procedures were approved by the institutional review board of RTI International. The current study analyzed data from the publicly available, deidentified NSDUH data files from 2008 through 2019. Due to questionnaire changes in 2008, major depression variables in the 2008 NSDUH and later are not directly comparable to depression variables prior to 2008. In addition, because of limited data collection due to the COVID-19 pandemic, 2020 NSDUH estimates are not comparable to prior years' estimates.[38] As a result, adult trends in LSD use by depression status are assessed from 2008 to 2019. Because equivalent major depression modules are not displayed to adolescents, the current study included only adults aged 18 years or older. Written informed consent was obtained from adults, and respondents received $30 as compensation after completing the interview. Weighted interview response rates ranged from 64.9% to 75.6% during the study time frame.[37] Variables included in the analysis were imputation revised by NSDUH and therefore contain no missing data. This study followed the American Association for Public Opinion Research (AAPOR) reporting guideline.

### Measures

#### Past-Year LSD Use

The presence of past-year LSD use was assessed with 2 questions. First, respondents were asked, "Have you ever, even once, used LSD, also called 'acid'?" Those who reported lifetime use were subsequently asked, "How long has it been since you last used LSD?" A binary variable indicating past-year LSD use was positive for those who responded, "Within the past 30 days" or "More than 30 days ago, but within the past 12 months."

#### Past-Year Major Depression

The presence of past-year major depression was assessed based on procedures outlined by the NSDUH's methodological definitions.[39] Past-year depression was dichotomized and coded "yes" if respondents reported 5 or more of 9 of the *DSM-IV* major depressive episode criteria, with at least 1 of the criteria being a period of depressed mood or loss of interest or pleasure in daily activities for 2 or more weeks.

#### Sociodemographic Characteristics

Sociodemographic subgroups included age (18-25 years, 26-34 years, 35-49 years, and ≥50 years), sex (male or female), race and ethnicity (Black, Hispanic, White, or non-Hispanic other groups [American Indian or Alaska Native, Asian, and Native Hawaiian or Other Pacific Islander]), total family income (<$20 000, $20 000-$49 999, $50 000-$74 999, or >$75 000), educational level (<high school, high school graduate, some college, or college), and marital status (not married or married).

### Statistical Analysis

Statistical analysis was conducted from December 2022 to June 2023. Data were analyzed using adjusted multivariable logistic regression models with past-year depression as the primary variable and past-year LSD use as the primary outcome. First, a logistic regression model tested the change in the overall prevalence of LSD use in the pooled data from 2008 through 2019, adjusting for age, sex, race and ethnicity, total family income, educational level, marital status, and year. Second, to test trends in LSD use by depression status from 2008 through 2019, an interaction term, year × depression, was included in the model, with survey year treated as a continuous variable.

Log-odd estimates from the logistic models were back transformed to generate estimated marginal prevalences (ie, prevalences standardized to the distribution of sociodemographic characteristics of the sample) in each year by major depressive episode status (yes or no). Interaction was evaluated on the additive scale, wherein a modified marginal effect is calculated from models including all hypothesized confounders, thereby allowing for the calculation of adjusted prevalence estimates (refer to the eMethods and eTable 1 in Supplement 1 for further detail). Adjusted prevalence estimates were then compared using prevalence differences (PDs), which were themselves compared using difference in differences, or the comparison of the differences in PDs between 2008 and 2019 between adults with and adults without depression. The Wald *t* test was used to assess the statistical significance of the PDs and the difference in PDs.

To test whether the comparison of LSD use between those with depression and those without depression varied by demographic subgroup, models were rerun including 3-way interactions between time, depression, and demographic variables (eg, time × depression × sex). Separate models were used to test each demographic variable while controlling for all others. To assess for statistical significance, difference-in-difference estimates were calculated for each subgroup individually and compared using difference in PD differences and the Wald *t* test.

Finally, the analysis included 2 sensitivity tests. First, the main 2-way interaction model was updated to adjust for past-year use of alcohol, cannabis, cocaine, and heroin. Second, the model was run again to adjust for only past-year use of cannabis, cocaine, and heroin. All models were conducted using SUDAAN, version 11.0.4 software (RTI International). All analyses accounted for the complex survey design and weighting of the NSDUH. All *P* values were from 1-sided tests and results were deemed statistically significant at $P < .05$.

Table 1. Sociodemographic Characteristics of the Overall Sample, NSDUH 2008-2019 (N = 478 492)[a,b]

| Characteristic | % (SE) |
|---|---|
| Sex | |
| Male | 48.2 (0.1) |
| Female | 51.8 (0.1) |
| Age, y | |
| 18-25 | 14.3 (0.1) |
| 26-34 | 15.9 (0.1) |
| 35-49 | 25.9 (0.1) |
| ≥50 | 43.9 (0.1) |
| Educational level | |
| Less than high school | 13.6 (0.1) |
| High school graduate | 27.8 (0.1) |
| Some college | 28.3 (0.1) |
| College graduate | 30.4 (0.1) |
| Race and ethnicity | |
| Hispanic | 15.1 (0.1) |
| Non-Hispanic Black | 11.7 (0.1) |
| Non-Hispanic White | 65.8 (0.1) |
| Other[c] | 7.5 (0.1) |
| Income, $ | |
| <20 000 | 17.3 (0.1) |
| 20 000-49 999 | 31.1 (0.1) |
| 50 000-74 999 | 16.7 (0.1) |
| ≥75 000 | 35.0 (0.1) |
| Marital status | |
| Unmarried | 47.4 (0.1) |
| Married | 52.6 (0.1) |

Abbreviation: NSDUH, National Survey on Drug Use and Health.

[a] Sample listed is the unweighted analytic sample.

[b] All reported estimates account for the complex survey design and weighting of the NSDUH.

[c] American Indian or Alaska Native, Asian, and Native Hawaiian or Other Pacific Islander.

## Results

### Sociodemographic Characteristics

The final analytic sample included 478 492 US adults (**Table 1**). Pooled across all study years (2008-2019), 51.8% of respondents were female, 65.8% were non-Hispanic White, 15.1% were Hispanic, 11.7% were non-Hispanic Black, and 7.5% were of another race and ethnicity. By age group, 14.3% were young adults aged 18 to 25 years, 15.9% were aged 26 to 34 years, 25.9% were aged 35 to 49 years, and 43.9% were aged 50 years or older. A total of 13.6% had less than a high school education, and 48.4% had a total family income of $49 999 or less. Full details regarding sample characteristics can be found in Table 1.

### Overall Prevalence of and Trends in LSD Use From 2008 to 2019

From 2008 to 2019, the overall prevalence of past-year LSD use increased significantly from 0.2% to 0.9% (PD, 0.7% [95% CI, 0.6%-0.8%]) (**Table 2**; eFigure in Supplement 1). Among adults without depression, the prevalence of past-year LSD use increased from 0.2% in 2008 to 0.8% in 2019 (PD, 0.6% [95% CI, 0.5%-0.7%]). In contrast, among adults with past-year depression, the prevalence of past-year LSD use increased from 0.5% in 2008 to 1.8% in 2019 (PD, 1.3% [95% CI, 1.0%-1.6%]). The difference in difference was 0.8% (95% CI, 0.5%-1.1%), indicating a significantly greater increase in past-year LSD use among participants with depression. Trends in LSD use among adults with vs without depression from 2008 to 2019 can be found in the eFigure in Supplement 1.

### Trends in LSD Use and Depression by Demographic Subgroup

Overall, the prevalence of past-year LSD use increased significantly among those with or without depression across nearly all sociodemographic subgroups (**Table 3**). However, examining differential trends in LSD use by depression status between demographic subgroups indicated significant differences only for age and income level. Specifically, young adults with depression showed the greatest increase in LSD use of any demographic subgroup (PD among those aged 18-25 years with depression, 3.3% [95% CI, 2.5%-4.2%], PD among those aged

Table 2. Trends in LSD Use by Depression Status in the US Adult Population, NSDUH 2008-2019 (N = 478 492)[a,b]

| Depression status | Adjusted prevalence, % (SE)[c] | | Prevalence difference, % (95% CI)[c,d] | Difference in prevalence difference, % (95% CI)[c] |
|---|---|---|---|---|
| | 2008 | 2019 | | |
| All | 0.2 (0.01) | 0.9 (0.04) | 0.7 (0.6-0.8)[e] | NA |
| Without past-year depression | 0.2 (0.01) | 0.8 (0.03) | 0.6 (0.5-0.7)[e] | Reference |
| With past-year depression | 0.5 (0.1) | 1.8 (0.1) | 1.3 (1.0-1.6)[e] | 0.76 (0.45-1.07)[e] |

Abbreviations: LSD, lysergic acid diethylamide; NA, not applicable; NSDUH, National Survey on Drug Use and Health.

[a] Sample listed is the unweighted analytic sample.

[b] All reported estimates account for the complex survey design and weighting of the NSDUH.

[c] Adjusted for year, age, sex, race and ethnicity, income, educational level, and marital status.

[d] Prevalence for 2019 minus prevalence for 2008.

[e] Statistically significant at the $P < .05$ level.

26-34 years with depression, 2.7% [95% CI, 1.6%-3.8%]). Those aged 35 to 49 years and those 50 years or older had a lesser difference in PD from 2008 to 2019 by depression status than those aged 18 to 25 years (difference in PD difference, −1.7% [95% CI, −2.7% to −0.8%] and −1.8% [95% CI, −2.7% to −0.9%], respectively). The difference was particularly pronounced among individuals with incomes less than $75 000 per year (PD among those with income <$20 000, 1.9% [95% CI, 1.3%-2.6%]; PD among those with income $20 000-$49 999, 1.5% [95% CI, 1.0%-2.1%]; PD among those with income $50 000-$74 999, 1.3% [95% CI, 0.7%-2.0%]). Similarly, those with annual incomes of $75 000 or more had a lesser difference in PD from 2008 to 2019 by depression status than those with incomes of less than $20 000 (difference in PD difference, −1.2% [95% CI, −2.0% to −0.4%]). In 2019, the greatest prevalence of LSD use was observed among adults with depression who were aged 18 to 25 years (4.9% vs 1.6% in 2008) or 26 to 34 years (3.2% vs 0.5% in 2008), men (2.4% vs 0.7% in 2008), had some college education (2.1% vs 0.6% in 2008), were non-Hispanic White (2.2% vs 0.7% in 2008), and had income less than $20 000 (2.4% vs 0.5% in 2008).

### Sensitivity Analysis

eTable 2 and eTable 3 in Supplement 1 present results from sensitivity tests that reran the 2-way interaction additionally controlling for alcohol and other illicit substance use. In both sensitivity tests, difference in differences were attenuated compared with the original model, but they remained significant (alcohol and other illicit drug use difference in difference, 0.3% [95% CI, 0.04%-0.5%]; other illicit drug use only difference in difference, 0.2% [95% CI, 0.04%-0.5%]).

## Discussion

This study compared trends in past-year nonmedical LSD use by past-year depression status between 2008 and 2019 in a national sample of US adults. Past-year LSD use increased in the overall population and increased at a disproportionately higher rate among participants with depression. These trends were particularly strong among young adults aged 18 to 25 years and 26 to 34 years, suggesting that young adults with depression may be disproportionately at risk for nonmedical LSD use.

Disproportionate increases in LSD use among those with depression occurred in parallel with increases in the prevalence of major depression in the past decade, with diagnoses of past-year depression among US adults increasing from 13.7 million in 2005 to 17.5 million in 2018.[40,41] If the rates of depression continue to increase in tandem with popular media and research reports presenting psychedelics as beneficial,[42,43] the number of individuals who use LSD in the context of major depression will likely continue to increase. Although more longitudinal research is needed, it is possible that LSD may become increasingly popular as a means of self-medication for depressive symptoms, especially as LSD continues to be studied as a therapeutic agent in highly publicized research. Therefore, trends in LSD use should continue to be monitored in this population. Our results also coincide with findings showing a decrease in the perception of regular LSD use as risky,[44] suggesting that individuals with depression may be trying LSD without an expectation of adverse events. One systematic review demonstrated an association between LSD use and increased risk of paranoia or transient anxiety compared with other hallucinogens (eg, psilocybin or ayahuasca).[45] Given that the trend in LSD use is increasing in the overall population as well as among those with depression, public health messaging informing safe practices of LSD use to mitigate harm in medically unsupervised settings is warranted.

Our finding that younger adults with depression (ie, those aged 18-25 years and 26-34 years) are more likely to use LSD compared with their older counterparts is noteworthy because this age group is also increasingly likely over time to have depression[41] and because young adults increasingly perceive LSD as easy to obtain.[44] There is a decreasing public perception that LSD use is risky[44] and/or has great risk of harm when used regularly, particularly among young adults aged 18 to 25 years.[33] Young adults may also be more engaged online and, therefore, may learn of new practices, such as microdosing, which are increasing in popularity.[46] However, population surveys, such as the NSDUH, do not ascertain information regarding microdosing behaviors, so it is currently unknown whether young adults are more prone to microdosing than older adults. Future research among those who use LSD should also query respondents on microdosing to illuminate potential patterns of use in the population.

Although the greatest increases in LSD use were observed among young adults (with 4.9% of adults aged 18-25 years using LSD in 2019), adults with depression had significantly greater prevalences and increases in LSD use across nearly all sociodemographic subgroups compared with those

Table 3. Trends Over Time of Major Depressive Episode With LSD on an Additive Scale by Sociodemographic Characteristics, Past Year, NSDUH (N = 478 492)[a,b]

| Characteristic | Major depressive episode | | | No major depressive episode | | | % (95% CI) | |
|---|---|---|---|---|---|---|---|---|
| | % (SE)[c] | | PD, % (95% CI)[d] | % (SE)[c] | | PD, % (95% CI)[d] | Difference in PD[e] | Difference in PD difference[f] |
| | 2008 | 2019 | | 2008 | 2019 | | | |
| Sex | | | | | | | | |
| Male | 0.7 (0.1) | 2.4 (0.2) | 1.7 (1.1 to 2.2)[g] | 0.3 (0.02) | 1.1 (0.1) | 0.8 (0.7 to 0.9)[g] | 0.9 (0.3 to 1.4)[g] | 0.3 (−0.3 to 0.9) |
| Female | 0.3 (0.04) | 1.2 (0.1) | 0.9 (0.7 to 1.2)[g] | 0.1 (0.01) | 0.5 (0.03) | 0.3 (0.3 to 0.4)[g] | 0.6 (0.3 to 0.9)[g] | Reference |
| Marital status | | | | | | | | |
| Not married | 0.6 (0.1) | 2.3 (0.2) | 1.6 (1.2 to 2.0)[g] | 0.3 (0.01) | 1.0 (0.04) | 0.7 (0.6 to 0.8)[g] | 0.9 (0.5 to 1.3)[g] | 0.2 (−0.7 to 1.0) |
| Married | 0.1 (0.04) | 1.1 (0.4) | 1.0 (0.3 to 1.8)[g] | 0.04 (0.01) | 0.3 (0.1) | 0.3 (0.1 to 0.4)[g] | 0.8 (0.01 to 1.5)[g] | Reference |
| Age category, y | | | | | | | | |
| 18-25 | 1.6 (0.2) | 4.9 (0.4) | 3.3 (2.5 to 4.2)[g] | 0.8 (0.1) | 2.2 (0.1) | 1.4 (1.1 to 1.6)[g] | 1.9 (1.1 to 2.8)[g] | Reference |
| 26-34 | 0.5 (0.2) | 3.2 (0.5) | 2.7 (1.6 to 3.8)[g] | 0.2 (0.03) | 1.2 (0.1) | 1.1 (0.8 to 1.3)[g] | 1.6 (0.5 to 2.8)[g] | −0.3 (−1.6 to 1.0) |
| 35-49 | 0.2 (0.1) | 0.7 (0.2) | 0.5 (−0.1 to 1.0) | 0.1 (0.02) | 0.3 (0.1) | 0.3 (0.2 to 0.4)[g] | 0.2 (−0.4 to 0.8) | -1.7 (−2.7 to −0.8)[g] |
| ≥50 | 0.02 (0.02) | 0.2 (0.2) | 0.2 (−0.2 to 0.6) | 0.01 (0.01) | 0.1 (0.02) | 0.1 (0.01 to 0.1)[g] | 0.1 (−0.2 to 0.5) | -1.8 (−2.7 to −0.9)[g] |
| Educational level | | | | | | | | |
| <High school | 0.5 (0.1) | 1.3 (0.3) | 0.8 (0.2 to 1.4)[g] | 0.2 (0.02) | 0.5 (0.1) | 0.3 (0.1 to 0.4)[g] | 0.5 (−0.1 to 1.1) | Reference |
| High school | 0.4 (0.1) | 1.6 (0.2) | 1.3 (0.8 to 1.8)[g] | 0.2 (0.01) | 0.7 (0.1) | 0.5 (0.3 to 0.6)[g] | 0.8 (0.3 to 1.4)[g] | 0.3 (−0.6 to 1.1) |
| Some college | 0.6 (0.1) | 2.1 (0.2) | 1.5 (1.0 to 2.0)[g] | 0.3 (0.02) | 0.9 (0.1) | 0.6 (0.5 to 0.7)[g] | 0.9 (0.4 to 1.4)[g] | 0.4 (−0.4 to 1.1) |
| College degree | 0.5 (0.2) | 2.0 (0.4) | 1.5 (0.6 to 2.4)[g] | 0.2 (0.03) | 1.1 (0.1) | 0.9 (0.7 to 1.1)[g] | 0.7 (−0.3 to 1.6) | 0.1 (−1.0 to 1.3) |
| Race and ethnicity | | | | | | | | |
| Hispanic | 0.3 (0.1) | 1.6 (0.3) | 1.3 (0.7 to 1.9)[g] | 0.1 (0.02) | 0.6 (0.1) | 0.5 (0.3 to 0.6)[g] | 0.8 (0.2 to 1.4)[g] | −0.02 (−0.9 to 0.8) |
| Non-Hispanic Black | 0.2 (0.1) | 0.9 (0.3) | 0.7 (0.1 to 1.4)[g] | 0.03 (0.01) | 0.3 (0.04) | 0.2 (0.1 to 0.3)[g] | 0.5 (−0.2 to 1.2) | −0.3 (−1.1 to 0.4) |
| Non-Hispanic White | 0.7 (0.1) | 2.2 (0.2) | 1.5 (1.0 to 2.0)[g] | 0.3 (0.02) | 1.0 (0.1) | 0.7 (0.6 to 0.8)[g] | 0.8 (0.4 to 1.3)[g] | Reference |
| Other[h] | 0.1 (0.1) | 2.1 (0.6) | 2.0 (0.7 to 3.2)[g] | 0.1 (0.02) | 0.8 (0.1) | 0.7 (0.4 to 0.9)[g] | 1.3 (−0.04 to 2.6) | 0.5 (−1.0 to 2.0) |
| Income, $ | | | | | | | | |
| <20 000 | 0.5 (0.1) | 2.4 (0.3) | 1.9 (1.3 to 2.6)[g] | 0.3 (0.02) | 0.9 (0.1) | 0.6 (0.5 to 0.8)[g] | 1.3 (0.7 to 1.9)[g] | Reference |
| 20 000-49 999 | 0.4 (0.1) | 1.9 (0.2) | 1.5 (1.0 to 2.1)[g] | 0.2 (0.02) | 0.8 (0.1) | 0.6 (0.5 to 0.8)[g] | 0.9 (0.3 to 1.5)[g] | −0.4 (−1.2 to 0.4) |
| 50 000-74 999 | 0.4 (0.1) | 1.7 (0.2) | 1.3 (0.7 to 2.0)[g] | 0.2 (0.02) | 0.8 (0.1) | 0.6 (0.4 to 0.8)[g] | 0.8 (0.1 to 1.4)[g] | −0.5 (−1.4 to 0.4) |
| ≥75 000 or more | 0.7 (0.2) | 1.3 (0.2) | 0.6 (0.01 to 1.1)[g] | 0.2 (0.02) | 0.7 (0.1) | 0.5 (0.4 to 0.6)[g] | 0.1 (−0.5 to 0.7) | -1.2 (−2.0 to −0.4)[g] |

Abbreviations: LSD, lysergic acid diethylamide; NSDUH, National Survey on Drug Use and Health; PD, prevalence difference.

[a] Sample listed is the unweighted analytic sample.

[b] All reported estimates account for the complex survey design and weighting of the NSDUH.

[c] Models are adjusted for year, age, sex, race and ethnicity, income, educational level, and marital status and a year × major depression × sociodemographic 3-way interaction term. Interactions were included in separate models and adjusted for all other demographic characteristics. Models also included all 2-way interaction terms (ie, year × major depression, year × sociodemographic characteristic, and major depression × sociodemographic characteristic).

[d] Prevalence for 2019 minus prevalence for 2008.

[e] Difference in prevalence difference between 2008 and 2019 for those with major depression minus those without major depression.

[f] The difference in prevalence difference between 2008 and 2019 for those with major depression minus those without major depression, compared between each sociodemographic category.

[g] Statistically significant at the $P < .05$ level.

[h] American Indian or Alaska Native, Asian, and Native Hawaiian or Other Pacific Islander.

without depression. Thus, our findings demonstrating the increase in LSD use over time are consistent with prior studies using national data,[28,33,47] and they provide evidence suggesting that this trend is partially associated with young adults with depression. Although LSD carries relatively low risks for physical health or dependence compared with other substances,[18]

individuals with depression are more likely to experience problematic substance use compared with those without a mood disorder[48] or to experience adverse events, such as paranoia or a "bad trip," when using LSD nonmedically.[45] As research and media reports on psychedelics as therapeutics increase, recreational use patterns among those with depression should continue to be monitored.

### Limitations

This study has some limitations. First, due to the use of self-reporting in the NSDUH, the resulting data are subject to response bias or underreporting. Second, the NSDUH does not ask respondents about their motives for LSD use, and we therefore cannot attribute the trends to specific causes. Third, measures of frequency of LSD use or of microdosing vs use at higher doses were lacking. Fourth, NSDUH data are cross-sectional, precluding inference about the directionality of associations (ie, if LSD use occurs before or after symptoms of depression). Fifth, while our sensitivity analysis yielded a similar pattern in the trend of LSD use by depression status as the main model, results were attenuated after controlling for use of alcohol and other drugs. These findings indicate that LSD use may be occurring in the context of other substance use in the population. Sixth, trends assessed in the current study are from the period from 2008 through 2019, and further studies into how trends may have changed since the COVID-19 pandemic (2020) are warranted. Future studies should also provide more detail on (1) the dose amount, (2) the frequency of use, (3) motivations or reasons for use (eg, potential self-medicating behaviors), and (4) a comparison of the trend in LSD use by depression status with trends in other substance use (such as cannabis or opioids).

## Conclusions

This survey study on the trends in LSD use by major depression status offers evidence that, over time, increases in LSD use are occurring at disproportionately higher rates among adults with depression compared with those without depression. From 2008 to 2019, past-year LSD use increased by 1.3% among adults with depression, in contrast to a 0.6% increase in LSD use among those without depression. This trend was particularly pronounced among young adults with depression aged 18 to 34 years, among whom approximately 5% used LSD in 2019 as opposed to approximately 2% in 2008. Future research should aim to understand the motivations for LSD use as well as the directionality between nonmedical LSD use and depression. As the evaluation of LSD as a potential psychiatric treatment continues, public health efforts to promote safe and evidence-based use of psychedelics are critical.


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