Psychedelic Medicine
Volume XX, Number X, 2024

DOI: 10.1089/psymed.2023.0027

psychedelic medicine

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Perceived Risk of Trying Lysergic Acid Diethylamide in the United States from 2015 to 2019: Are Americans Assessing Lysergic Acid Diethylamide's Risk Profile More Favorably?

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Abstract

Background: Though lysergic acid diethylamide (LSD) use is rising in the United States amid expanding research into the therapeutic potential of psychedelics, little scholarly work exists on whether perceived risk of trying LSD (prLSD) is changing or factors influencing prLSD among the general public. Therefore, we sought to investigate changes in prLSD from 2015 to 2019 and identify characteristics associated with prLSD among respondents to the National Survey on Drug Use and Health (NSDUH).

Methods: Using NDSUH data from 2015 to 2019, we investigated correlates of and temporal trends in prLSD, reporting results for the entire sample, as well under age 18 (<18) and age 18 and older (18+) subgroups. Orthogonal polynomial contrasts were used to evaluate trends across survey years. Multivariable models were constructed to identify factors associated with prLSD.

Results: On multivariable modeling for respondents age 18+, lower prLSD had statistically significant associations with later survey year, personal LSD use, younger age, higher education level, male gender, identifying as a sexual minority, past year psychological distress, and other factors. Higher prLSD was associated with identifying as Black or Hispanic, past year suicide attempt, and having children in the home. Notable differences in the age <18 subgroup were no association between prLSD and identifying as Hispanic and male gender being associated with higher prLSD. From 2015 to 2019, there was a statistically significant linear decreasing trend in proportion of respondents who perceived "great" risk in trying LSD [from 70.5% to 64.8%; ($p < 0.0001$)]. Similar trends were observed in most subgroups that were analyzed.

Conclusions: We observed differences in prLSD among subgroups, suggesting that factors such as age, gender, race, ethnicity, and personal history of LSD may be related to prLSD. Overall, Americans appear to be assessing LSD's risk profile more favorably in recent years, though most Americans still perceive great risk in trying LSD.

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This manuscript was previously submitted to Research Square (www.researchsquare.com) as a preprint, which can be found at: https://doi.org/10.21203/rs.3.rs-2667155/v2

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Keywords: lysergic acid, LSD, psychedelics, risk perception, survey, National Survey on Drug Use and Health (NSDUH)

Introduction

Risk perception is one of several factors influencing decision-making around drug use.[1–5] Greater risk perception is associated with lower lifetime use of many drugs, and decreasing risk perception has previously coincided with increased use of various drugs at the population level.[6] Recent reports indicate a decrease in the perceived risk of smoking cigarettes[7,8] and using marijuana[9] in the United States, while perceived risk of alcohol use has remained stable.[10] Although past year lysergic acid diethylamide (LSD) use in the United States rose 56% from 2015 to 2018 (0.55–0.86%),[11] minimal research has been conducted exploring the perceived risk of trying LSD (prLSD) in the United States and whether it is changing.

According to data from the National Survey on Drug Use and Health (NSDUH), most Americans perceive LSD use as posing a ''great'' risk of harm.[12] NSDUH data reveal that the percentage of Americans 12 and older perceiving ''great'' risk from trying LSD fell from 73.7% in 2002 to 68.0% in 2014.[13] Recent analysis also indicates that perceived risk of using LSD once or twice per week has fallen from 2002 to 2019.[14] Relative to other drugs with routinely gathered national data on risk perceptions, LSD sits approximately in the middle of the risk perception hierarchy. According to the 2019 NSDUH,[15] 64.8% of respondents considered trying LSD a ''great'' risk, compared to 85.1% for trying heroin. In addition, 79.5% believed using LSD weekly poses a ''great'' risk, compared to 93.7% for heroin, 85.7% for cocaine, 44.8% for binge drinking, and 29.0% for marijuana.

To better understand prLSD, it is helpful to briefly review important facets of LSD's risk profile. In the United Kingdom, experts ranked LSD as one of the least harmful drugs to both users and others in a 2010 analysis.[16] They based this on an evaluation of nine harm potential categories, including four categories of physical harm, three categories of psychological harm, and two categories of social harm. Regarding medical risks, most LSD-related adverse events are mild or moderate,[17] with the majority resolving within 24 h.[18] There is little evidence of lethal LSD overdose potential in physically healthy individuals, even at extremely high doses.[19,20] LSD also has low addictive potential.[21] It does not produce repetitive self-administration in animal models,[22] and physical dependence is extremely rare.[23] No evidence of carcinogenic potential for LSD has been identified in humans.[24,25] In a recent survey of more than 10,000 past year LSD users, 0.2% of LSD use events resulted in need for emergency medical attention, most commonly for anxiety, panic, and confusion.[18]

Although LSD use is usually associated with few severe adverse events, such events can be life-changing or life-threatening. Accidental deaths have been reported,[26,27] as well as a small number of toxicity-related deaths, which are usually due to overdoses or the use of police restraints.[21,28,29] Suicide,[30–32] nonsuicidal self-harm,[33] solar maculopathy,[34] acute and prolonged psychosis,[30] catatonia,[35] and hallucinogen persisting perception disorder[36] have also been reported. Seizures[37] and rhabdomyolysis[38] can also occur. Potentially serious cardiovascular adverse effects of LSD include arrhythmia,[39] myocardial infarction,[40] carotid artery obstruction,[41,42] and vasospasm,[43] with at least one cardiovascular-related death reported in a patient with Brugada syndrome.[39]

Legal penalties related to LSD possession and trafficking are also important risks associated with LSD use. These penalties vary by jurisdiction, with possession being a felony in nearly all U.S. states. As an example, a person convicted of possessing small amounts of LSD in Vermont can be imprisoned for up to 1 year or fined up to $2,000, or both.[44] A person convicted of selling small amounts of LSD in Vermont can be imprisoned for up to 5 years, fined up to $25,000, or both. Based on the limited publicly available data, arrest or imprisonment for LSD possession or trafficking appears uncommon.[45,46]

Social disapproval is another important risk associated with LSD use. We are unaware of longitudinal data on social disapproval of LSD use among American adults. However, among American 12th graders, social disapproval of people 18 years of age and older trying LSD is high, though it has been in steady decline since 2009, when it was 88.2%, falling to 68.7% in 2021, down significantly from the last measurement of 76.1% in 2019.[47]

Possible factors that could be affecting contemporary prLSD include recent clinical trials suggesting therapeutic potential for LSD in psychiatric conditions[48,49] and growing interest in psychedelic microdosing.[50] Considering recent increases in LSD consumption and the limited scholarship on prLSD in the United States, we sought to determine demographic correlates of prLSD and how prLSD has changed among the general population and subpopulations in recent years using NSDUH data from 2015 to 2019. Given the particularly limited scholarship on prLSD in adolescents, we opted to investigate this issue in both adolescents (under age 18) and adults (age 18 and older), reporting findings for the entire sample

as well as each age-based subgroup separately where applicable. We hypothesized that age, race/ethnicity, gender, education level, and personal history of LSD use would be influential determinants of prLSD and that prLSD would fall during the study period.

Methods

Data source description

The NSDUH is conducted annually nationwide by the U.S. Substance Abuse and Mental Health Services Administration (SAMHSA).[51] It is administered in person to randomly selected, noninstitutionalized civilians and inquires about substance use, mental health, and other health-related issues, as well as treatments received for mental health conditions and substance-use disorders. To improve generalizability, the NSDUH employs a sample-weighted design with weight adjustments for demographics, nonresponse, and other factors.[52]

We used pooled data from NSDUH survey years 2015 to 2019 on all respondents (age 12 and older), which included 282,768 people. Although 2020 survey data were available, data collection that year was disrupted due to COVID-19, and comparing that year's data to previous years' has been advised against.[53] The primary outcome for this study was prLSD, as ascertained by respondent answers to the question: ''How much do people risk harming themselves physically and in other ways when they try LSD once or twice?.'' The four responses ranged from ''no risk'' to ''great risk'' and were coded on a four-point ordinal scale. Eight thousand nine hundred fifty-one respondents did not answer this question and were excluded.

Statistical analysis

Survey analysis procedures were used due to the complex survey design, utilizing the NSDUH respondent weight, replicate, and variance strata. Since this study utilizes 5 years of survey data, the respondent weight was divided by five for analyses that included all study years, as recommended by the NSDUH.[54] Significance was assessed at $p < 0.05$. Analysis was conducted in SAS 9.4 (SAS Institute, Cary, NC, USA).

Continuous variables were summarized with weighted medians and interquartile ranges, and comparisons between levels of risk perception were evaluated with log-transformed linear regression. Categorical factors were summarized with weighted percentages and 95% confidence intervals, and comparisons between levels of risk perception were evaluated using Rao–Scott chi-square tests. Collinearity and confounding were assessed with the goal of limiting the number of factors in final models. First, the associations between respondent factors were evaluated using correlations, effect sizes, and tests for association. Second, the variance inflation factor was calculated for all variables included in the final models; none were larger than 1.4 indicating no evidence of collinearity.[55] Multiple comparisons adjustments were not needed due to the consistency of the significant results across all variables (most $p < 0.001$) and similar results across similar covariates.[56]

Several cumulative logistic regressions were performed with prLSD as the outcome variable to calculate adjusted odds ratios for the increase in prLSD across the four risk responses. Analysis was first done with all respondents together and then stratified by age group (under age 18, and age 18+). Variable reduction methods were used to find the most parsimonious models.[57] Orthogonal polynomial contrasts were used to evaluate trends in categorical variables,[54,58–61] and graphs were created to visually evaluate the trend. All models were adjusted for demographic factors. For more details about methods, including a full list of model variables and rationale for variable inclusion (see Supplementary Appendix SA1).

Ethics

This study was approved by the Cleveland Clinic Institutional Review Board.

Results

Univariable associations between participant factors and prLSD among the entire sample

The final unweighted sample size was $N = 273{,}817$ with 165,942 respondents (60.6%) who perceived ''great risk'' in trying LSD; 58,989 (21.5%) who perceived ''moderate risk''; 37,038 (13.5%) who perceived ''slight risk''; and 11,848 (4.3%) who perceived ''no risk.'' On univariable tests, ''great'' prLSD was associated with, among other characteristics, disproportionately higher numbers of respondents who were: female (in the age 18 and older subgroup), age 35 or older, Black race or Hispanic ethnicity, heterosexual (data only available for respondents 18 and older), living in a nonmetropolitan area, married, divorced/separated, or pregnant, as well as those with: a high school diploma/GED or less education, children in the household, lower income, or no suicide attempts or serious psychological distress in the past year; $p < 0.001$ for all. Full results are reported in Table 1.

Lifetime use or misuse of nearly all psychoactive substances assessed, including LSD, was associated with disproportionately lower numbers of respondents with greater prLSD (Supplementary Table S1 in Supplemental Appendix SA2). Reporting that LSD was ''probably impossible'' to obtain was associated with disproportionately higher numbers of respondents reporting greater prLSD. While lifetime LSD users made up 10.0% of the sample, their distribution among levels of prLSD was 37.5% ''no risk,'' 27.3% ''slight risk,'' 12.8%

Table 1. Demographic Characteristics for National Survey on Drug Use and Health Survey Respondents by Perceived Risk of Lysergic Acid Diethylamide Use from 2015 to 2019

Factor	*Overall (N = 273,817)*	*Perceived risk of LSD use/once or twice ever*			
		No risk (N = 11,848)	*Slight risk (N = 37,038)*	*Moderate risk (N = 58,989)*	*Great risk (N = 165,942)*
Male gender by age	48.6 (48.3, 48.9)	64.9 (63.4, 66.5)	58.2 (57.4, 58.9)	53.3 (52.7, 54.0)	44.9 (44.6, 45.3)
Male gender, under age 18	51.1 (50.5, 51.7)	58.7 (56.1, 61.4)	48.6 (47.3, 49.9)	50.2 (49.4, 51.1)	51.7 (50.9, 52.5)
Male gender, age 18+	48.3 (48.0, 48.7)	65.7 (64.0, 67.5)	59.5 (58.6, 60.5)	53.9 (53.2, 54.6)	44.5 (44.1, 44.9)
Age groups					
Age: 12–17	8.8 (8.7, 9.0)	11.6 (11.1, 12.2)	12.8 (12.3, 13.2)	15.5 (15.1, 15.8)	6.4 (6.2, 6.5)
Age: 18–25	12.7 (12.5, 12.9)	20.9 (19.9, 22.0)	19.5 (19.1, 19.9)	18.1 (17.6, 18.5)	9.8 (9.6, 9.9)
Age: 26–34	14.5 (14.3, 14.8)	21.8 (20.8, 22.9)	19.2 (18.5, 19.9)	16.9 (16.4, 17.3)	12.8 (12.5, 13.1)
Age: 35–49	22.5 (22.3, 22.8)	20.0 (18.8, 21.1)	22.1 (21.4, 22.7)	20.3 (19.8, 20.9)	23.3 (22.9, 23.6)
Age: 50+	41.4 (41.0, 41.9)	25.7 (24.1, 27.2)	26.5 (25.5, 27.5)	29.3 (28.5, 30.0)	47.8 (47.3, 48.3)
Age groups (over/under age 18)					
Under18	8.8 (8.7, 9.0)	11.6 (11.1, 12.2)	12.8 (12.3, 13.2)	15.5 (15.1, 15.8)	6.4 (6.2, 6.5)
18+ Years	91.2 (91.0, 91.3)	88.4 (87.8, 88.9)	87.2 (86.8, 87.7)	84.5 (84.2, 84.9)	93.6 (93.5, 93.8)
Race/hispanicity					
NH White	63.3 (62.8, 63.8)	63.8 (62.4, 65.3)	73.1 (72.4, 73.7)	67.3 (66.5, 68.1)	60.7 (60.1, 61.2)
NH Black/African American	12.0 (11.6, 12.3)	9.5 (8.7, 10.3)	6.5 (6.1, 7.0)	9.2 (8.8, 9.7)	13.7 (13.3, 14.1)
NH Native American/Alaskan Native	0.55 (0.50, 0.59)	0.84 (0.66, 1.02)	0.44 (0.37, 0.51)	0.50 (0.42, 0.58)	0.56 (0.50, 0.63)
NH Native Hawaiian/Pacific Islander	0.37 (0.33, 0.42)	0.46 (0.30, 0.62)	0.25 (0.19, 0.32)	0.35 (0.29, 0.41)	0.40 (0.35, 0.44)
NH Asian	5.4 (5.2, 5.6)	5.9 (5.2, 6.6)	5.4 (4.9, 5.9)	6.0 (5.6, 6.5)	5.2 (4.9, 5.4)
NH more than one race	1.8 (1.8, 1.9)	2.2 (1.9, 2.5)	2.3 (2.1, 2.5)	2.0 (1.9, 2.1)	1.7 (1.6, 1.8)
Hispanic	16.6 (16.2, 17.0)	17.2 (16.2, 18.3)	12.0 (11.5, 12.5)	14.6 (14.1, 15.1)	17.9 (17.4, 18.3)
Sexual identity, age 18+					
Heterosexual, that is, straight	94.4 (94.3, 94.6)	87.5 (86.5, 88.5)	90.0 (89.5, 90.4)	92.5 (92.1, 92.8)	95.9 (95.8, 96.1)
Lesbian or gay	1.9 (1.8, 2.0)	3.7 (3.1, 4.3)	3.5 (3.2, 3.9)	2.6 (2.3, 2.8)	1.4 (1.3, 1.5)
Bisexual	3.1 (3.0, 3.2)	7.4 (6.6, 8.1)	6.1 (5.8, 6.4)	4.5 (4.3, 4.8)	2.1 (2.0, 2.2)
Don't know	0.52 (0.47, 0.57)	1.5 (1.10, 1.8)	0.42 (0.27, 0.58)	0.43 (0.31, 0.55)	0.50 (0.46, 0.55)
County metropolitan status					
Large metro	55.8 (55.3, 56.3)	60.9 (59.4, 62.5)	60.1 (59.0, 61.1)	56.7 (55.9, 57.5)	54.7 (54.1, 55.2)
Small metro	30.0 (29.5, 30.5)	28.5 (27.1, 29.9)	29.2 (28.3, 30.1)	30.4 (29.7, 31.1)	30.1 (29.5, 30.7)
Nonmetro	14.2 (13.8, 14.5)	10.6 (9.6, 11.5)	10.7 (10.1, 11.3)	12.9 (12.5, 13.4)	15.2 (14.8, 15.7)
Education level, under age 18					
Some HS, no diploma	98.9 (98.8, 99.0)	98.6 (97.8, 99.3)	98.9 (98.7, 99.2)	98.9 (98.7, 99.1)	98.9 (98.7, 99.0)
HS diploma/GED	0.91 (0.82, 1.00)	1.3 (0.63, 2.1)	0.88 (0.64, 1.1)	0.80 (0.66, 0.95)	0.95 (0.82, 1.07)
Some college, no degree	0.16 (0.11, 0.21)	0.08 (0.00, 0.17)	0.11 (0.02, 0.21)	0.23 (0.12, 0.34)	0.14 (0.09, 0.18)
2-Year college degree	0.00 (0.00, 0.01)	0	0	0.00 (0.00, 0.01)	0.00 (0.00, 0.01)
4-Year college degree	0.04 (0.01, 0.06)	0	0.06 (0.00, 0.13)	0.03 (0.00, 0.08)	0.03 (0.00, 0.06)
Education level, age 18+					
Some HS, no diploma	12.4 (12.2, 12.7)	13.4 (12.3, 14.5)	7.9 (7.4, 8.5)	8.6 (8.2, 9.1)	13.9 (13.6, 14.3)
HS diploma/GED	24.8 (24.5, 25.1)	23.0 (22.0, 24.1)	18.6 (18.0, 19.3)	22.0 (21.4, 22.5)	26.5 (26.1, 26.8)
Some college, no degree	21.6 (21.4, 21.9)	22.7 (21.3, 24.2)	22.2 (21.5, 22.8)	23.1 (22.4, 23.7)	21.2 (20.9, 21.5)
2-Year college degree	9.3 (9.1, 9.6)	7.4 (6.7, 8.2)	8.3 (7.8, 8.8)	9.2 (8.7, 9.7)	9.6 (9.3, 9.9)
4-Year college degree	31.8 (31.4, 32.3)	33.4 (31.8, 34.9)	42.9 (41.8, 44.1)	37.2 (36.4, 37.9)	28.8 (28.3, 29.3)
Marriage status, age 18+					
Married	51.8 (51.3, 52.2)	38.1 (36.3, 40.0)	42.2 (41.2, 43.2)	46.7 (45.7, 47.6)	55.1 (54.6, 55.6)
Widowed	5.8 (5.6, 6.0)	3.6 (2.8, 4.3)	2.8 (2.5, 3.2)	3.7 (3.4, 4.0)	6.9 (6.7, 7.1)
Divorced or separated	13.9 (13.6, 14.1)	10.6 (9.8, 11.4)	11.5 (10.7, 12.2)	12.1 (11.5, 12.6)	14.8 (14.5, 15.1)
Never been married	28.5 (28.2, 28.9)	47.6 (45.9, 49.3)	43.5 (42.5, 44.5)	37.5 (36.8, 38.3)	23.2 (22.9, 23.6)
Number of children under age 18 in household					
None	73.8 (73.5, 74.0)	79.2 (77.9, 80.5)	77.9 (77.1, 78.6)	75.3 (74.6, 75.9)	72.4 (72.1, 72.7)
One	10.9 (10.8, 11.1)	9.9 (8.9, 10.9)	9.2 (8.8, 9.6)	10.5 (10.0, 10.9)	11.4 (11.2, 11.6)

(*continued*)

Table 1. (Continued)

Factor	*Overall (N = 273,817)*	*Perceived risk of LSD use/once or twice ever*			
		No risk (N = 11,848)	*Slight risk (N = 37,038)*	*Moderate risk (N = 58,989)*	*Great risk (N = 165,942)*
Two	9.8 (9.6, 9.9)	7.1 (6.4, 7.9)	9.0 (8.5, 9.5)	9.3 (8.9, 9.6)	10.1 (9.9, 10.3)
Three or more	5.6 (5.4, 5.7)	3.8 (3.3, 4.2)	3.9 (3.6, 4.2)	5.0 (4.8, 5.2)	6.1 (5.9, 6.2)
Employment status, under age 18					
Employed full time	2.4 (2.3, 2.6)	2.4 (1.8, 3.0)	2.0 (1.6, 2.3)	2.0 (1.8, 2.3)	2.8 (2.6, 3.1)
Employed part time	12.8 (12.5, 13.2)	11.5 (10.0, 13.0)	12.4 (11.5, 13.3)	12.4 (11.7, 13.1)	13.3 (12.8, 13.9)
Unemployed	5.7 (5.4, 5.9)	7.2 (6.1, 8.4)	5.1 (4.5, 5.8)	5.2 (4.8, 5.5)	6.1 (5.7, 6.4)
Other	79.0 (78.6, 79.5)	78.9 (77.0, 80.8)	80.5 (79.4, 81.6)	80.4 (79.5, 81.2)	77.8 (77.2, 78.3)
Employment status, age 18+					
Employed full-time	49.7 (49.3, 50.1)	51.0 (49.4, 52.6)	55.5 (54.4, 56.5)	54.1 (53.3, 54.9)	47.8 (47.4, 48.1)
Employed part-time	13.1 (12.9, 13.4)	14.1 (12.8, 15.4)	16.2 (15.5, 16.9)	14.9 (14.4, 15.4)	12.2 (12.0, 12.5)
Unemployed	4.3 (4.2, 4.5)	7.3 (6.5, 8.1)	4.9 (4.5, 5.3)	4.9 (4.5, 5.2)	4.0 (3.8, 4.1)
Other	32.8 (32.5, 33.2)	27.7 (26.0, 29.4)	23.4 (22.5, 24.3)	26.2 (25.5, 26.9)	36.0 (35.6, 36.4)
US federal poverty level					
Living in poverty	14.6 (14.3, 14.9)	19.1 (17.9, 20.2)	12.6 (12.2, 13.1)	13.8 (13.3, 14.2)	14.9 (14.5, 15.2)
Income up to 2×threshold	19.8 (19.6, 20.1)	20.1 (19.1, 21.1)	16.1 (15.6, 16.7)	18.2 (17.6, 18.7)	20.9 (20.5, 21.2)
Income more than 2×threshold	65.6 (65.1, 66.1)	60.8 (59.6, 62.0)	71.2 (70.5, 72.0)	68.1 (67.4, 68.7)	64.3 (63.8, 64.8)
Arrested/ever	15.8 (15.5, 16.0)	23.3 (21.9, 24.7)	21.0 (20.5, 21.6)	16.8 (16.2, 17.4)	14.3 (14.0, 14.6)
Overnight stay in hospital, age 18+/12 months	9.6 (9.4, 9.8)	7.8 (7.0, 8.6)	7.3 (6.8, 7.8)	8.6 (8.3, 8.9)	10.3 (10.0, 10.5)
Serious psychological distress, age 18+/year	11.4 (11.2, 11.5)	18.6 (17.4, 19.7)	18.3 (17.7, 18.8)	14.4 (13.9, 14.9)	9.3 (9.1, 9.4)
Attempted to kill self, age 18+/year	0.56 (0.52, 0.60)	1.2 (0.95, 1.5)	0.79 (0.68, 0.90)	0.69 (0.60, 0.78)	0.46 (0.42, 0.51)

Frequencies presented are unweighted counts. All factors were significantly associated with prLSD, $p < 0.001$. SAS Survey Procedures used for all analyses.

GED, General Educational Development test; HS, high school; LSD, lysergic acid diethylamide; NH, non-Hispanic; prLSD, perceived risk of trying LSD.

''moderate risk,'' and 5.0% ''great risk.'' Additionally, perceiving binge drinking, cocaine use, heroin use, and marijuana use as higher risk was associated with disproportionately higher numbers of respondents perceiving ''great'' risk of LSD use, as well, $p < 0.0001$ for all (Supplementary Table S2).

Multivariable analysis of participant factors and prLSD for age 18 and older subgroup

All results in this section are reported from the multivariable cumulative logistic regression models for respondents age 18+, and all results were significant at $p < 0.0001$. Figure 1 is a forest plot of the relationship between most of the categorical factors assessed and prLSD in the age 18 and older subgroup.

Respondents were 14% more likely to perceive greater risk in trying LSD if they were older, 60% more likely if they were Black, 39% more likely if they were Hispanic, 4% more likely if they children living at home, 10% more likely if divorced or separated, 19% more likely if they had an arrest history, 11% more likely if they had a history of alcohol abuse, 35% more likely if they attempted suicide in the past year, and 8% more likely if they had been hospitalized in the past year ($p < 0.0001$ for all).

Respondents were 23% less likely to perceive greater risk in trying LSD if they had never been married, 12% less likely for each increase in level of education, 6% less likely if they were not employed full-time, 32% less likely if they were male, 9% less likely if they were Asian, 21% less likely if they lived in large metropolitan area, 11% less likely if they had a history of serious psychological distress over the past year, and 17% less likely if they were lesbian, gay, or bisexual. Past-year drug use was also negatively associated with prLSD, and the following groups were less likely to perceive great risk using LSD: 39% less likely with history of hallucinogen use, 33% less likely with a history of marijuana use, 27% less likely with a history of stimulant misuse, and 28% less likely with a history of sedative misuse.

Multivariable analysis of participant factors and prLSD for under age 18 subgroup

All results in this section are reported from the multivariable cumulative logistic regression models for respondents under the age of 18, and all results were significant at $p < 0.0001$. These respondents were 13% more likely to perceive greater risk in using LSD if they were older, 5% more likely if they were male, and 16% more likely if they were Black. Respondents were

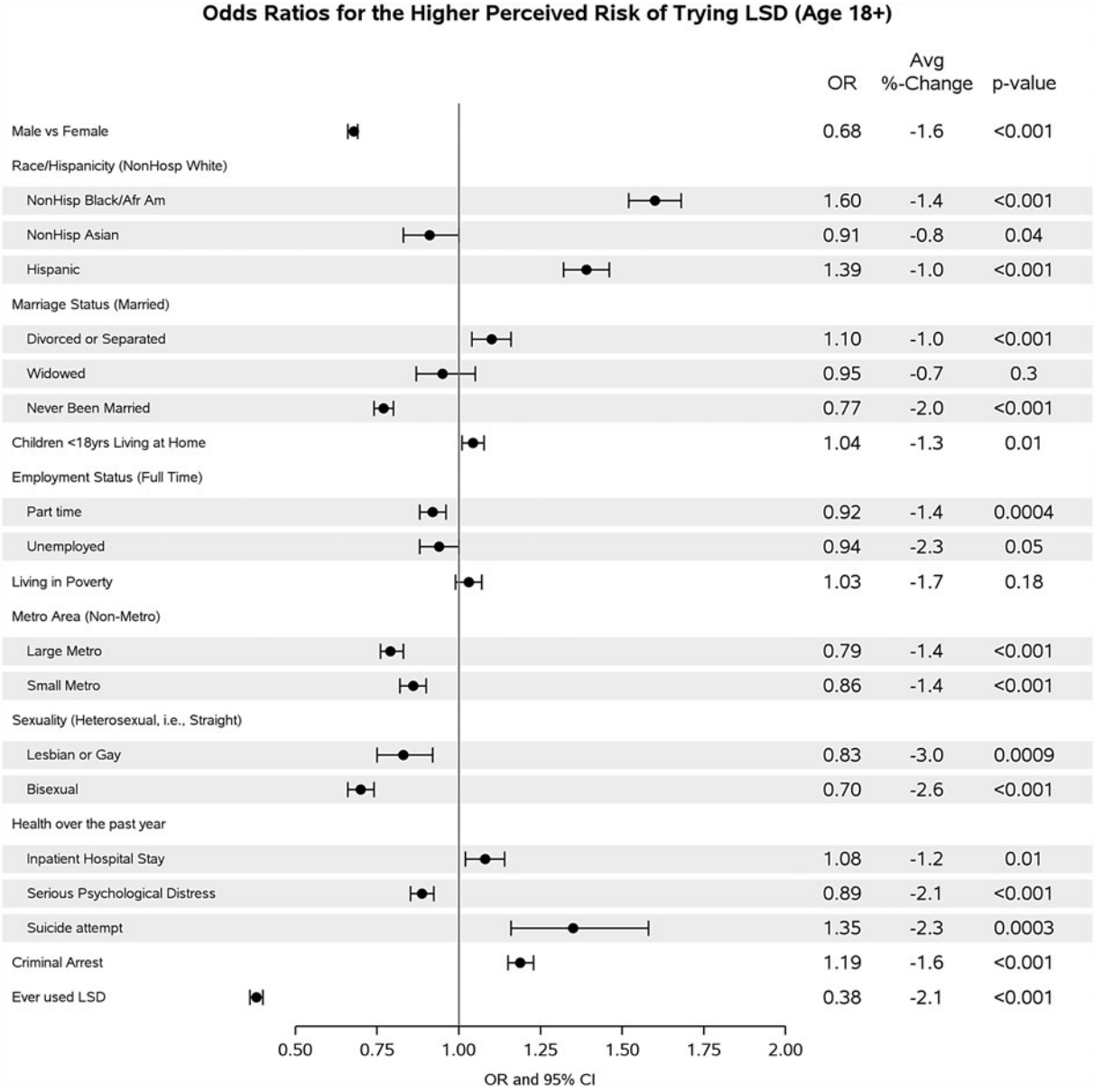

Fig. 1. Forest plot for odds of higher prLSD for select factors from the adult only (age 18+) multivariable cumulative logistic regression model (for all results see Supplementary Table S3). *p*-Values are reported for these ORs. Avg %, change is the average percentage change from 2015 to 2019 in respondents who perceived "great" risk of trying LSD (for full details see Supplementary Table S4). LSD, lysergic acid diethylamide; OR, odds ratio; prLSD, perceived risk of trying LSD.

16% less likely to perceive greater risk in LSD use if they were Asian, 11% less likely if living in a large metropolitan area, 62% less likely if they had a history of LSD use, 39% less likely if they had a history of other hallucinogen use, 20% less likely if they had a history of marijuana use, 40% less likely if they had a history of stimulant misuse, and 12% less likely if they had a history of sedative misuse.

For full results stratified by age group, see Supplementary Table S3.

prLSD trend analysis

The weighted proportion of respondents who reported ''great'' prLSD dropped 5.7% (from 70.5% to 64.8%) among the entire sample (trend $p < 0.0001$). It dropped 5.6% (from 72.3% to 66.7%) among the 18 and older subgroup (trend $p < 0.0001$) and 6.3% (from 51.7% to 45.4%) in the under-age 18 subgroup (trend $p < 0.0001$). For further details see Figure 2 shows descriptive statistics for each year in the study to visualize the trend for the entire sample, and Table 2 reports the results from a

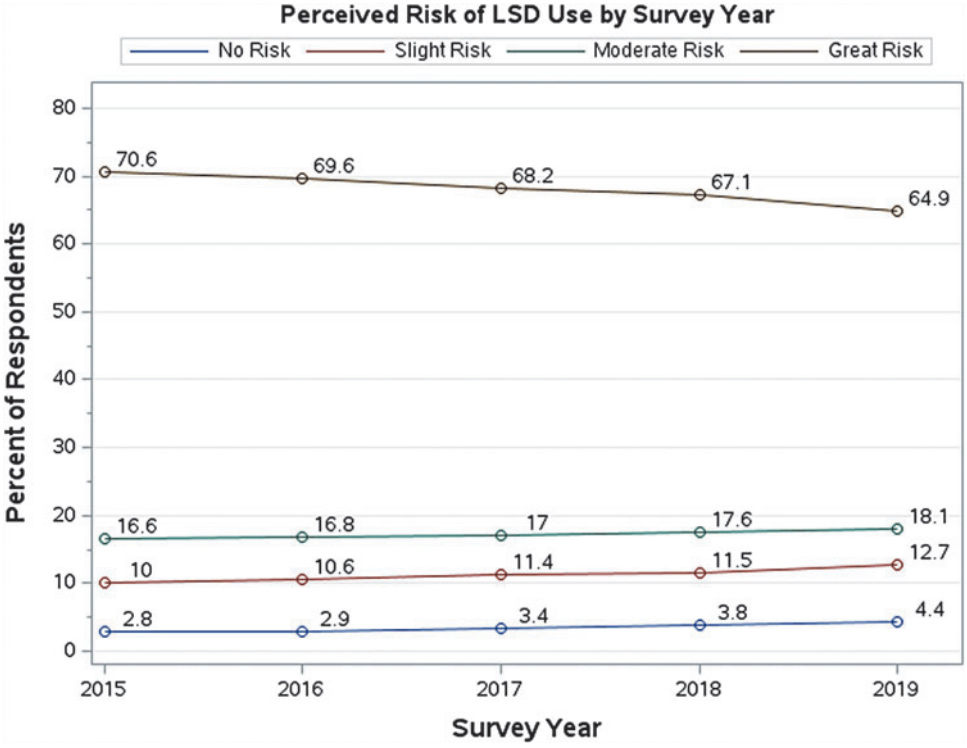

Fig. 2. Perceived risk of LSD use by survey year for all respondents. Percent signs omitted.

trend analysis for prLSD across the study period for the entire sample and the sample dichotomized at age 18.

There were significant decreasing linear trends in greater prLSD within most respondent factors. Those groups which showed no significant trend were Native American/Alaskan Native ($p=0.12$), Native Hawaiian/Other Pacific Islander ($p=0.88$), and, for factors only evaluated in those 18 and older, not knowing one's sexual identity ($p=0.11$), being widowed ($p=0.05$), and attempting suicide in the last year ($p=0.06$). Changes

Table 2. Trend Analysis for Lower Perceived Risk of Trying Lysergic Acid Diethylamide Once or Twice

	Percent of responses within each year							
Perceived risk	*2015 (%)*	*2016 (%)*	*2017 (%)*	*2018 (%)*	*2019 (%)*	*Percent Change (%)*	*Trend*	p
All respondents								
No risk	2.9	3.0	3.5	3.9	4.4	+1.5	Linear	<0.0001
Slight risk	10.0	10.6	11.3	11.4	12.6	+2.6		
Moderate risk	16.6	16.8	17.0	17.6	18.1	+1.5		
Great risk	70.5	69.6	68.2	67.0	64.8	−5.6		
Under age 18 only								
No risk	4.3	4.2	4.7	4.8	5.3	+1.1	Linear	<0.0001
Slight risk	14.4	15.7	16.1	16.3	18.4	+4.1		
Moderate risk	29.7	29.8	29.1	31.5	30.9	+1.1		
Great risk	51.7	50.2	50.2	47.4	45.4	−6.3		
Age 18 and older only								
No risk	2.8	2.9	3.3	3.8	4.3	+1.6	Linear	<0.0001
Slight risk	9.6	10.1	10.9	10.9	12.1	+2.5		
Moderate risk	15.3	15.6	15.8	16.3	16.9	+1.6		
Great risk	72.3	71.5	70.0	68.9	66.7	−5.6		

Trend analysis was conducted using orthogonal polynomial contrasts for survey year in multivariable logistic regression to test for linear trends in the perceived risk of LSD use across the study period and adjusted for all demographic factors described in the methods section of this article. All analysis was adjusted for the complex survey design of the NSDUH using respondent weight, replicate, and variance strata.

NSDUH, National Survey on Drug Use and Health.

over the study period in most subgroups among the 18 and older sample are included on the right side of Figure 1. We have highlighted data from this trend analysis for racial and ethnic groups among the entire sample in Table 3. Detailed information for all subgroups is in Supplementary Table S4. The largest annual decreases among subgroups were in respondents: identifying as lesbian or gay (3.03%), identifying as more than one race (2.85%), identifying as bisexual (2.63%), age 18–25 (2.48%), age 26–34 (2.40%), unemployed (2.30%), having serious psychological distress within the last year (2.06%), and never married (2.00%).

We also found statistically significant decreases from 2015 to 2019 in the proportion of respondents in the entire sample perceiving use of other drugs as ''great risk'': weekly cocaine use (−1.5%), weekly LSD use (−5.0%), weekly marijuana use (−7.1%), monthly cocaine use (−2.1%), and monthly marijuana use (−5.3%), all significant $p < 0.0001$. No trends were identified for perceived risk of trying heroin ($p = 0.76$), weekly heroin use ($p = 0.40$), or binge drinking twice weekly ($p = 0.52$). For further details see Supplementary Table S5.

Discussion

Three notable findings regarding prLSD emerged from this investigation. The first is that there is variation in prLSD in association with gender, race and ethnicity, education level, marital status, sexual orientation, urbanicity, personal history of LSD use, and other factors. The second is that there are some differences in factors associated with prLSD between people under age 18 and those 18 and older. The third is that prLSD declined throughout the study period in the entire sample, as well as most subgroups analyzed.

Our observation of elevated prLSD in adults identifying as Black and Hispanic is consistent with recent analysis from the 2019 NDSUH.[62] These groups also have lower rates of LSD use compared to Whites.[63] Differential risk perceptions for other drugs among people of different races and ethnicities have previously been observed, with past research identifying lower-risk perception of trying heroin among Blacks and Hispanics compared to Whites,[64] but higher-risk perception of regular cannabis use.[65] A prior study found US-born Latinos and Latino immigrants had higher prLSD than US-born Whites and non-Latino White immigrants.[66] One explanatory factor for higher prLSD being associated with identifying as Black may be the significant research abuses carried out against Black participants in early LSD studies.[67]

While LSD probably carries more stigma than most psychedelics, given the legacy of the 1960s, it is still the most commonly used classic psychedelic in the United States,[14] so it may serve as a suitable proxy for the perceived risk of psychedelics as a group. With approval by the US Food and Drug Administration of 3,4-methylenedioxymethamphetamine (MDMA) for posttraumatic stress disorder and psilocybin for treatment-resistant depression expected by 2024[68] and 2026,[69] respectively, our findings on prLSD suggest that Black and Hispanic patients may not be as amenable to these treatments as White patients due to concerns about risks. Of course, patients will likely view psychedelics as less risky when administered in a medical setting than a naturalistic one.

Table 3. Percent of Respondents According to Race/Ethnicity Who Perceived the Risk of Trying Lysergic Acid Diethylamide to Be "Great" by Survey Year with Test for Linearly Decreasing Trend Over Time (All Respondents Age 12+)

	2015	*2016*	*2017*	*2018*	*2019*	*Avg Ann*		
Race/Hispanicity	*(N = 35,317)*	*(N = 34,308)*	*(N = 33,134)*	*(N = 32,350)*	*(N = 30,833)*	*%Δ*	*Trend*	p
NH White	67.9 (67.0, 68.8)	66.9 (66.0, 67.9)	65.4 (64.5, 66.3)	64.0 (63.2, 64.7)	61.6 (60.7, 62.5)	−1.57	Linear ↓	<0.0001
NH Black/African American	80.1 (78.9, 81.2)	78.5 (77.0, 79.9)	78.4 (77.0, 79.9)	76.9 (75.5, 78.2)	74.9 (73.2, 76.6)	−1.30	Linear ↓	<0.0001
NH Native American/Alaskan	76.1 (71.8, 80.4)	65.8 (60.0, 71.7)	68.1 (62.6, 73.5)	69.1 (63.9, 74.4)	70.3 (63.5, 77.2)	−1.44	No trend	0.12
NH Native Hawaiian/ Pacific Island	71.5 (63.7, 79.3)	70.4 (61.8, 79.0)	74.2 (66.2, 82.3)	68.6 (62.2, 75.0)	75.1 (69.8, 80.4)	0.88	No trend	0.88
NH Asian	67.8 (64.6, 70.9)	66.9 (64.0, 69.8)	66.4 (63.7, 69.1)	61.9 (58.6, 65.2)	64.8 (61.0, 68.6)	−0.74	Linear ↓	0.03
NH more than one race	66.4 (62.6, 70.2)	66.0 (62.8, 69.3)	64.0 (59.4, 68.6)	65.7 (61.1, 70.2)	55.0 (51.6, 58.4)	−2.85	Linear ↓	<0.0001
Hispanic	74.7 (73.5, 76.0)	74.9 (73.5, 76.2)	72.6 (71.0, 74.2)	73.3 (72.2, 74.3)	70.2 (68.9, 71.5)	−1.12	Linear ↓	<0.0001

Frequencies presented are unweighted counts. All trend tests are adjusted for respondent age. Orthogonal polynomial contrasts were used to test for decreasing linear trends and were adjusted for age only. All analysis was adjusted for the complex survey design of the NSDUH using respondent weight, replicate, and variance strata.

Avg Ann %Δ, average annual percent-change; NH, Non-Hispanic.

Our finding of an association between greater prLSD and older age is consistent with previous findings.[6,62,70,71] The association we observed between lower prLSD and identifying as a sexual minority is in line with previous findings among people who have never used LSD.[72] The association observed between higher education level and lower prLSD contrasts with previous studies showing positive associations between education level and perceived risk of marijuana and heroin.[64]

The association observed between past-year serious psychological distress and lower prLSD is intriguing since level of current psychological distress was not associated with perceived risk of marijuana, tobacco, or alcohol use in a previous study.[73] However, medical marijuana users have higher rates of past-month psychological distress than recreational users,[74] and daily marijuana use is more common in people with past-month psychological distress.[75] LSD use is more common among people with past-year psychological distress.[76,77] Unfortunately, the NSDUH does not collect data on frequency of LSD use or reasons for use, which would allow investigation of the relationships between medical use of LSD, frequency of LSD use, past-year psychological distress, and prLSD. Notably, we found people with past-year suicide attempts were more likely to have higher prLSD, raising the question of whether there is awareness among this group that LSD use could be potentially dangerous for them given rare reports of suicide following use.[31,32,78,79]

There were a few noteworthy differences regarding prLSD in the under-age 18 subgroup compared to the adult subgroup. History of arrest, being approached by a drug seller, and history of alcohol or tobacco use were associated with higher prLSD among adults, but this was not the case in respondents under 18. While identifying as Hispanic or ''other'' race was associated with higher prLSD compared to non-Hispanic Whites among adults, there was no association between prLSD and these factors in respondents under 18. Additionally, the magnitude of the adjusted odds ratio for higher prLSD was substantially lower among respondents identifying as Black in the under-age 18 subgroup compared to those in the adult subgroup. Finally, male gender was associated with higher prLSD in respondents under 18, though it was associated with lower prLSD in adults.

Over the study period, there was a statistically significant linear decreasing trend (−5.7% from 2015 to 2019) in respondents reporting ''great'' prLSD. This trend was also observed in nearly all subgroups assessed. Large decreasing trends were found in people 18–34. Interestingly, data indicate that from 2015 to 2018 the relative change in LSD use prevalence among people age 18–25 was −24%, compared to +28.7% in people age 26–34.[11] We observed other large decreasing trends for prLSD in sexual minorities, with data indicating a relative change in LSD use prevalence of −3% in gay/lesbian people and +16% in bisexual people from 2015 to 2018.[11] These data demonstrate that changes in prLSD do not perfectly correlate with changes in LSD use.

Notably, people with serious psychological distress within the last year had one of the largest decreasing trends in prLSD. It is unclear whether this is related to self-treatment of mental health issues with LSD, though future research should investigate the relationship between anticipated health benefits from self-treating mental health issues with LSD and prLSD. There was also a decreasing trend for respondents among the entire sample who believed using LSD weekly represents ''great risk'' (−5.0% from 2015 to 2019). This was consistent with previous research using data from the NSDUH and the Monitoring the Future study, which showed a decreasing trend in this metric from 2002 to 2019.[14] Of the other substances for which perceived risk of weekly use was measured (binge alcohol use, cocaine, heroin, and marijuana), only marijuana experienced a larger drop in respondents reporting ''great risk'' over the study period (−7.1%). The results presented here suggest LSD and marijuana are experiencing uniquely large reductions in societal risk perception.

Risk perception can be significantly impacted by both social context and objective drug knowledge,[80] and there appear to be significant social changes occurring around LSD use, while information about LSD is easier than ever to access. It is unclear to what degree decreasing prLSD may reflect wider knowledge around the importance of set and setting[81] in reducing psychedelic-related harms. However, a relationship between risk perception and such knowledge has been observed in MDMA users.[80]

With LSD use in the United States growing recently,[11] it is intriguing to consider the potential contribution of decreased prLSD to this phenomenon. Though past studies indicate inverse associations between prLSD and rates of LSD use,[71] this relationship is not as clear-cut as it may initially appear. Risk perception is only one of multiple factors contributing to decision-making about drug use. Availability, as well as descriptive norms (perception of frequency of use among peers), injunctive norms (peer approval), and sensation-seeking are other important factors affecting drug use with varying levels of influence for different substances.

Supporting the importance of other factors besides prLSD in decision-making around LSD use is a previous study that found 63% of young women who used LSD in the past year reported half or more of their peers used LSD, versus 3% for those who used marijuana but not LSD in the past year, and 1% for those who used neither.[71] That study also found that young women who used LSD were less disapproving of people trying LSD than those who had used only marijuana or neither drug.

Changes in risk perception predict changes in use of tobacco, alcohol, and cannabis.[82] Previous population level studies of American adolescents suggest that changes in prLSD are a leading indicator of inverse changes in use.[83,84] However, one survey of college students, which did not inquire about LSD, found that for designer drugs such as MDMA, injunctive norms, sensation-seeking, and perceived availability were associated with past-year use, while risk perception was not.[85] Increased rates of use following decrease in risk perception (a phenomenon termed the ''motivational hypothesis'') has been observed for multiple drugs.[82] However, for marijuana, there is also evidence for the ''risk reappraisal hypothesis,'' in which users may readjust risk perceptions about a drug following its use. People have also been observed to change expectancies around alcohol use following initial consumption.[86] This may be the case with LSD.

Strikingly, we found that lifetime LSD use conferred a 62% decrease in likelihood of respondent report of higher prLSD, the largest reduction of any factor analyzed. However, we do not know the prLSD of LSD users in this sample before first use, and we are unaware of research analyzing the directionality of the relationship between prLSD and LSD use at the individual level. Intriguingly, previous research on marijuana indicates that though there are differences in risk perception between users and nonusers, risk perception among users is associated with neither frequency of use or experiencing drug-related consequences.[87] Unfortunately, the NSDUH does not collect data on frequency of use or history of LSD-associated adverse events to allow for a similar investigation here.

In addition to prospectively gathering data on how prLSD changes following first LSD use, future studies on prLSD and its relationship with LSD use should gather data from participants on descriptive norms, injunctive norms, what they consider the most important risks of LSD to be, and whether they know someone who has experienced an LSD-related adverse effect. Additionally, data on LSD use frequency, history of adverse effects, and reasons for use should be collected from LSD users. Finally, studies should prospectively investigate the relationship between prLSD in a cohort of people before and after initiation of naturalistic LSD use.

One final implication from this study is that since most respondents viewed LSD as a drug of great risk, education about the risks of LSD and efforts to mitigate these during administration in medical settings will be important for patients who might benefit from treatment, but be hesitant to pursue it if LSD is approved as medical treatment. In a study of 31 healthy participants receiving LSD, 26% reported pretreatment concerns about having a challenging experience with LSD, though these anxieties dissipated by the end of the study, with participants attributing this to the presence of dosing session attendants and a clear treatment structure.[88] While LSD appears safe in research settings with rigorous medical supervision, important risks remain, as demonstrated by a recent trial where one participant required medication to manage delusions during a dosing session.[89]

Strengths and limitations

The primary strength of this study is its use of data from multiple administrations of a large, rigorously conducted survey employing a nationally representative sample. The primary limitation is its cross-sectional nature, which prevents determination of a cause-and-effect relationship. Another important limitation is the use of retrospective self-reported data. However, the NSDUH's substance use self-report measures have high concordance with drug testing results.[90]

The NSDUH's restriction of respondents to the civilian noninstitutionalized population of the United States is another important limitation. While this represents 97% of the US population,[53] the NSDUH excludes people in institutional settings such as hospitals, prisons, nursing homes, and addiction treatment centers, who are likely to have important demographic and prLSD differences. One further limitation is that this study only investigated the prLSD once or twice. Results regarding correlates of perceived risk of LSD use are likely to differ if perceived risk is gauged differently in terms of frequency of use (e.g., using LSD once or twice a week).

Conclusions

This study identified important differences in prLSD based on survey year, age, gender, education level, sexual orientation, race and ethnicity, and other factors. Lifetime LSD use was the examined factor associated with lowest odds of reporting higher prLSD. Importantly, from 2015 to 2019, there was a statistically significant linear decreasing trend in prLSD, which was also observed in nearly all subgroups assessed, including most racial and ethnic groups. While Americans appear to be assessing LSD's risk profile more favorably in recent years, a majority still perceive great risk in trying LSD.

Authors' Contributions

B.S.B. conceived and designed the study and wrote the first draft of the article. A.A. designed the study, interpreted data, and substantively revised the article draft. E.N.D. designed the study, analyzed the data, and substantively revised the article draft. D.S., S.M.N., and D.B. interpreted the data and substantively revised the article draft. J.W. designed the study, interpreted data, and substantively revised the article draft. All authors approved the submitted version and have agreed both to be personally accountable for their own contributions and to ensure that questions related to the accuracy

or integrity of any part of the work are appropriately investigated, resolved, and the resolution documented in the literature.

Author Disclosure Statement

B.S.B. holds stock options in CB Therapeutics. He is an advisory board member of CB Therapeutics and Compass Pathways. He also receives monetary compensation for editorial work from DynaMed Plus (EBSCO Industries, Inc.) and from Cerebral and Janssen Pharmaceuticals for consulting services. He is primary investigator on a clinical trial funded by MindMed. Support for S.M.N. through the Johns Hopkins Center for Psychedelic and Consciousness Research was provided by Tim Ferriss, Matt Mullenweg, Blake Mycoskie, Craig Nerenberg, and the Steven and Alexandra Cohen Foundation. S.M.N. was also co-investigator on a psilocybin clinical trial funded by Usona Institute. The other authors report no potential conflicts of interest.

Funding Information

This work was supported by a nonmonetary scientific collaboration award from the Cleveland Clinic Center for Populations Health Research awarded to B.S.B.

Supplementary Material

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