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Past-Year Hallucinogen Use in Relation to Psychological Distress, Depression, and Suicidality among US Adults

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Abstract

Background: There is renewed interest in the clinical application of hallucinogenic substances to treat a range of psychiatric conditions. However, there is mixed evidence regarding how use of such substances outside of medical settings relates to psychological distress, depression, and suicidality.

Methods: We examined data from a US representative sample of noninstitutionalized adults from the 2015-2020 National Survey on Drug Use and Health (N=241,675). We evaluated whether past-year use of specific hallucinogens (i.e., LSD, DMT/AMT/Foxy, *salvia divinorum*, ecstasy (MDMA/Molly), ketamine) is associated with reporting past-year serious psychological distress (SPD), major depressive episode (MDE), and suicidality. Generalized linear models using Poisson and log link were used to estimate adjusted prevalence ratios (aPRs), controlling for sociodemographic characteristics and past-year use of various other illegal drugs.

Results: LSD use was associated with an increased likelihood of MDE (aPR=1.23, 95% CI: 1.10-1.37) and suicidal thinking (aPR=1.21, 95% CI: 1.09-1.34). Similar associations were observed between *salvia divinorum* use and suicidal thinking (aPR=1.41, 95% CI: 1.00-1.98) and between DMT/AMT/Foxy use and suicidal planning (aPR=1.81 95% CI: 1.17-2.81). On the other hand, ecstasy use was associated with a decreased likelihood of SPD (aPR=0.83, 95% CI: 0.77-0.89), MDE (aPR=0.91, 95% CI: 0.83-0.99), and suicidal thinking (aPR=0.86, 95% CI: 0.75-0.99).

Conclusion: Findings suggest there are differences among specific hallucinogens with respect to depression and suicidality. More research is warranted to understand consequences of and risk factors for hallucinogen use outside of medical settings among adults experiencing depression or suicidality.
Keywords: hallucinogens; depression; suicidality; psychedelics
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**Conclusion:** Findings suggest there are differences among specific hallucinogens with respect to depression and suicidality. More research is warranted to understand consequences of and risk factors for hallucinogen use outside of medical settings among adults experiencing depression or suicidality.

**Keywords:** hallucinogens; depression; suicidality; psychedelics
1. Introduction

Depressive disorders are common in the US, affecting more than 10% of adults in any given year (Hasin et al., 2018). They are a leading cause of disability worldwide and associated with significant psychological distress and economic burden (Greenberg et al., 2015). Studies have shown that depression is one of the strongest risk factors for suicidal behavior, which is the tenth leading cause of death in the US (Esang & Ahmed, 2018). Depression and suicidality are also highly associated with psychoactive substance use among adults—particularly use of alcohol, cannabis, and opioids (Esang & Ahmed, 2018). As such, it appears that adults experiencing depression or suicidality may be at risk for other psychoactive substance use as well.

Recent years have witnessed a re-emergence in use of hallucinogens for their clinical efficacy in treating a range of psychiatric disorders. Hallucinogens including lysergic acid diethylamide (LSD), 3,4-methylenedioxymethamphetamine (MDMA), ketamine, and N,N-dimethyltryptamine (DMT) (a natural psychoactive component in ayahuasca) have been demonstrated in clinical trials to be efficacious in managing psychological distress (Grof et al., 1973; Mitchell et al., 2021), depression (Murrough et al., 2013; Palhano-Fontes et al., 2019), and
suicidality (Murrough et al., 2015; Zeifman et al., 2019) among other conditions. However, outside of clinical settings, these hallucinogens have misuse potential (Heal et al., 2018), and little is known about how use of these substances relate to psychiatric symptoms on a population level.

Few nationally representative studies have evaluated the associations between hallucinogen use and serious psychological distress (SPD), major depressive episode (MDE), and suicidality among adults. These results have been mixed, with studies finding positive (Killion et al., 2021; Nesvåg et al., 2015; Salas-Wright et al., 2021; Yockey et al., 2019), negative (Hendricks, Johnson, et al., 2015; Hendricks, Thorne, et al., 2015; Jones & Nock, 2022a, 2022b; Sexton et al., 2020), and null associations (Johansen & Krebs, 2015; Krebs & Johansen, 2013) between hallucinogen use and these conditions. Most of these studies evaluated lifetime use of hallucinogens, but examining more recent use may allow for better examination of potential associations. Furthermore, many studies compiled hallucinogens into classes (i.e., classic psychedelics) rather than examining each substance separately. Given the unique structure and pharmacodynamics of each hallucinogen, each yields distinct effects and each may also have distinct populations more inclined to use select substances. Thus, we use national data to determine how past-year use of specific hallucinogens is associated with adults reporting past-year SPD, MDE, and suicidality.

2. Methods

2.1 Data Source and Study Population

We examined aggregated data (N=241,675) from adults aged 18 and older, from the 2015-2020 National Survey on Drug Use and Health (NSDUH). NSDUH is a nationally
representative annual cross-sectional survey of non-institutionalized individuals in the US. The
survey employed a multistage area probability sample for each of the 50 states and the District of
Columbia (Substance Abuse and Mental Health Services Administration, 2020). We focused on
adults as only adults were asked about depressive symptomology.

2.2 Measures

Participants were asked about use of LSD (e.g., “Have you ever, even once, used LSD, also called ‘acid’?”), salvia divinorum, ecstasy or “Molly” (MDMA), and ketamine, and they were also asked about use of DMT, alpha-methyltryptamine (AMT), and “Foxy” via a single item. Participants who reported use were then asked about recency of use for each substance (e.g., “How long has it been since you last used LSD?”). Participants who reported use “Within the past 30 days” or “More than 30 days ago but within the past 12 months” were coded as reporting past-year use. Participants were also asked about past-year use of cannabis, cocaine, methamphetamine, and heroin, as well as misuse of prescription tranquilizers, sedatives, stimulants, and opioids. Misuse was defined as using in any way not directed by a doctor, including use without a prescription, use in greater amounts, more often, or longer than instructed to take them, or use in any other way a doctor did not direct.

We defined hallucinogens in the present study to include LSD, DMT/AMT/Foxy, salvia divinorum, ecstasy/MDMA, and ketamine. These drugs were included as examples in the list for hallucinogens provided to participants in the NSDUH (Lipari et al., 2013), they have been used in prior studies evaluating hallucinogens (Salas-Wright et al., 2021), and were defined as hallucinogens in the Handbook of Medical Hallucinogens (Grob & Grigsby, 2021). Of note, we
were unable to evaluate past-year use of psilocybin, peyote, or mescaline because only lifetime use was queried for these substances.

NSDUH used the Kessler-6 (K6) distress scale to assess nonspecific psychological distress over the past 30 days. The K6 includes six items that respondents answer via a five-point Likert scale, with a summary score range of 0-24. A score of ≥13 was identified as SPD. The K6 is a validated measure of mental distress (Kessler et al., 2010). MDE in the past year was coded as affirmative when participants reported experiencing at least five of the nine MDE Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria (American Psychiatric Association, 1994). The MDE questionnaire in NSDUH has been used in prior studies to estimate prevalence of MDE and has been shown to have good predictive validity (Hedden et al., 2012; Lipari et al., 2013; Weinberger et al., 2018). NSDUH also assessed past-year suicidality by asking: “At any time during the past 12 months, did you seriously think about trying to kill yourself?” Further, those who answered affirmatively were asked whether they experienced suicidal planning and attempts.

2.3 Analyses

First, we estimated prevalence of past-year use of each drug and all dependent variables included in this analysis. Next, bivariable comparisons were conducted using Rao-Scott chi-square to determine potential differences in prevalence of use of each drug with regard to SPD, MDE, and suicidality. We then utilized generalized linear models using Poisson and log link to determine whether use of specific hallucinogens was associated with each separate outcome. These models produced adjusted prevalence ratios (aPRs) for each drug in relation to SPD, MDE, and suicidality, adjusting for survey year, sex, age, race/ethnicity, annual household
income, education, marital status, and use of cannabis, cocaine, methamphetamine, and heroin, and misuse of prescription tranquilizers/sedatives, stimulants, and opioids. Stata SE 17 (StataCorp, College Station, TX) was used for all analyses and weights were used to account for the complex survey design, non-response, selection probability, and population distribution. This secondary analysis was exempt from review at the New York University Langone Medical Center’s Institutional Review Board.

3. Results

An estimated 1.0% used ecstasy/MDMA in the past year, 0.8% used LSD, 0.2% used ketamine, 0.2% used DMT/AMT/Foxy, and 0.1% used salvia divinorum. Over a tenth (11.6%) of individuals experienced past-year SPD, 7.3% experienced MDE, 4.4% experienced suicidal ideation, 1.3% experienced suicidal planning, and 0.6% had suicidal attempts.

Table 1 presents results from bivariable tests examining hallucinogen use in relation to SPD, MDE, and suicidality. Those who used each hallucinogen were more likely to experience SPD, MDE, and suicidality (p<0.001). Supplemental Table 1 presents estimates for non-hallucinogenic drugs.

Table 2 presents results from the multivariable models. Results suggest that LSD use was associated with an increased likelihood of reporting MDE (aPR=1.23, 95% CI: 1.10-1.37) and suicidal thinking (aPR=1.21, 95% CI: 1.09-1.34). Similar associations were observed between salvia divinorum use and suicidal thinking (aPR=1.41, 95% CI: 1.00-1.98) and between DMT/AMT/Foxy use and suicidal planning (aPR=1.81, 95% CI: 1.17-2.81). On the other hand, ecstasy/MDMA use was associated with a decreased likelihood of SPD (aPR=0.83, 95% CI: 0.77-0.89), MDE (aPR=0.91, 95% CI: 0.83-0.99), and suicidal thinking (aPR=0.86, 95% CI:
For multivariable results including estimates for non-hallucinogenic drugs, see Supplemental Table 2 with results suggesting that (mis)use of cannabis, methamphetamine, tranquilizers/sedatives, and opioids in particular were consistent risk factors for all outcomes.

4. Discussion

Findings suggest there are differences among use of specific hallucinogens with respect to depression and suicidality. Although all hallucinogens were associated with increased risk in bivariable models, only some associations held in multivariable models. We found that adults reporting past-year use of LSD, *salvia divinorum*, and/or DMT/AMT/Foxy were more likely to report experiencing depression and/or suicidality in the same year while the opposite was observed for ecstasy/MDMA use. These results begin to address the gap that exists in the literature regarding associations between recreational use of specific hallucinogens and depression and suicidality.

Our findings are consistent with previous epidemiologic studies evaluating associations between hallucinogen use and depression and suicidality. For example, positive associations have been estimated between past-year LSD use and MDE using 2002-2018 NSDUH data (Killion et al., 2021). Our study confirms this positive association using more recent data while also suggesting additional associations with suicidal thinking. Positive associations have also been estimated between lifetime LSD use and MDE (Salas-Wright et al., 2021) and suicidal thinking (Jones & Nock, 2022b; Yockey et al., 2019). Our study suggests that these positive associations are applicable to past-year use and not just lifetime use, which may indicate a stronger association between these factors. Furthermore, (Jones & Nock, 2022a, 2022b) determined that lifetime ecstasy/MDMA use was associated with reduced MDE and suicidal
thinking. Our study suggests this finding holds when examining past-year use, and we also discovered that these associations further extend to SPD.

Our findings, however, are inconsistent with several epidemiologic studies. (Hendricks, Thorne, et al., 2015) estimated negative associations between lifetime classic psychedelic use and suicidality, although further analysis suggests these results were driven by psilocybin specifically (Hendricks, Johnson, et al., 2015). Additionally, (Sexton et al., 2020) estimated associations between lifetime classic tryptamine use (e.g. DMT) and decreased suicidal thinking, while our study determined that DMT/AMT/Foxy use is associated with increased risk for suicidal planning. Lastly, two studies found no associations between lifetime psychedelic use and the aforementioned outcomes (Johansen & Krebs, 2015; Krebs & Johansen, 2013), although (Nesvåg et al., 2015), using the same data with different analyses, estimated psychedelic use to be positively associated with all the outcomes evaluated. We believe these conflicting findings may be due to a combination of compiling hallucinogens into classes and examining lifetime use instead of more recent use. We sought to overcome these limitations in the extant literature by examining past-year use of specific hallucinogens in relation to SPD, MDE, and suicidality.

Several potential explanations may underlie the associations estimated in our study between LSD, salvia divinorum, and DMT/AMT/Foxy use and depression and/or suicidality. First, there may be direct causal links between individual hallucinogens and specific psychological and behavioral consequences. For example, case reports have documented depression and suicidality following LSD use (Bose et al., 2021; Larsen, 2016). Additionally, studies suggest that salvia divinorum and DMT/AMT/Foxy can precipitate psychosis in some users (Dos Santos et al., 2017; Mahendran et al., 2016), which could explain their associations with suicidality despite not having increased risk for depression. Similarly, although rare,
hallucinogen persisting perception disorder may result in increased suicidality (Brodrick & Mitchell, 2016). With regard to risk factors for suicide, hallucinogens may be associated with impaired cognitive functioning (Pokorny et al., 2020) and impulsivity (Grant et al., 2019), and can therefore be risky if used in non-clinical contexts for some users. However, more information on the prevalence of such adverse outcomes is needed, and such outcomes may be rare compared to more beneficial outcomes associated with use.

Second, our observed associations may be a result of adults using hallucinogens for self-medicaiton for depressive disorders (Lea et al., 2020; Matzopoulos et al., 2022). In fact, studies have shown that increased media coverage of the beneficial effects of hallucinogens might be influencing people to use nonmedically (Grabski et al., 2022; Palamar & Le, 2021). More research is therefore warranted to determine risk factors for hallucinogen use among adults experiencing psychiatric symptoms, and whether their use might be affected by potential shifts in acceptance of these drugs.

Similarly, our findings of negative associations between ecstasy/MDMA and SPD, MDE, and suicidal thinking may reflect its potential beneficial effects or relatively better initial mental health among these users. There could also be indirect pathways regarding such associations such as use in party settings or access to the drug. Although the present study estimated negative associations between ecstasy/MDMA use and the outcomes evaluated on a population level, research has shown that chronic use, at least on an individual level, is positively associated with depression (MacInnes et al., 2001; McCardle et al., 2004). Therefore, future longitudinal studies evaluating these associations will be beneficial.

Finally, we found no associations between ketamine and SPD, MDE, or suicidality in multivariable models. However, use of ketamine was indeed a risk factor in bivariable models,
and epidemiologic research has demonstrated that past-year recreational ketamine use is a risk factor for reporting current depressive symptoms among adolescents (Palamar et al., 2022). Therefore, further research on its misuse potential and relationship to psychiatric symptoms are needed.

4.1. Limitations

The findings should be interpreted in the context of several limitations. First, NSDUH is a survey and is thus subject to social desirability and recall bias. Second, the survey did not differentiate between those using hallucinogens for recreational versus medical purposes. Third, individuals living in institutionalized settings were not represented. Fourth, we could not examine past-year use of psilocybin, peyote, or mescaline because only lifetime use was queried. Fifth, we were unable to examine frequency or intensity of substance use as these were not queried. Sixth, as this is a cross-sectional study, we were unable to determine the directionality of the associations between hallucinogen use and SPD, MDE, and suicidality. Finally, although we assessed past-year substance use and mental health, temporality cannot be established, in part, because it is possible that the mental health problems may be chronic.

Notwithstanding these limitations, a strength of the present study is the large sample size to allow evaluation of potential associations given the low prevalence of many hallucinogens explored. Future cross-sectional and longitudinal studies that include detailed assessments of frequency and intensity of use and reasons for use are needed to better understand the potential associations observed.

5. Conclusions
Findings provide epidemiological evidence supporting differences among use of specific hallucinogens with respect to depression and suicidality. Understanding why past-year use of certain hallucinogens is associated with reporting better or worse mental health is necessary to minimize harms and may inform future clinical research and policy efforts.

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https://doi.org/10.1017/S0033291719002393


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https://doi.org/10.1017/S0033291717002781


Table 1 – Bivariate comparisons of past-year hallucinogen use according to past-year serious psychological distress, major depressive episode, and suicidality

<table>
<thead>
<tr>
<th></th>
<th>Serious Psychological Distress</th>
<th>Major Depressive Episode</th>
<th>Suicidal Thinking</th>
<th>Suicide Planning</th>
<th>Suicide Attempt</th>
</tr>
</thead>
<tbody>
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<td>Yes Weighted %</td>
<td>No Weighted %</td>
<td>Yes Weighted %</td>
<td>No Weighted %</td>
</tr>
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<td></td>
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</tr>
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<td>0.6</td>
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<td>97.2</td>
<td>2.8</td>
<td>96.1</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<tr>
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<td>0.5</td>
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<td></td>
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<td>Ecstasy/MDMA</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>99.2</td>
<td>0.8</td>
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<tr>
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<td>97.3</td>
<td>2.7</td>
<td>96.4</td>
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<td>Ketamine</td>
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<td></td>
<td></td>
</tr>
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<td>No</td>
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</table>

Note: all ps<0.001. Data from years 2015-2020 are pooled. All percentages are reported as row percentages and weighted estimates.
Table 2 – Multivariable associations between past-year hallucinogen use and past-year serious psychological distress, major depressive episode, and suicidality

<table>
<thead>
<tr>
<th></th>
<th>Serious Psychological Distress</th>
<th>Major Depressive Episode</th>
<th>Suicidal Thinking</th>
<th>Suicide Planning</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>aPR (95% CI)</td>
<td>aPR (95% CI)</td>
<td>aPR (95% CI)</td>
<td>aPR (95% CI)</td>
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<td>LSD</td>
<td>1.06 (0.99-1.14)</td>
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<td>1.21 (1.09-1.34)</td>
<td>1.14 (0.96-1.33)</td>
</tr>
<tr>
<td>DMT/AMT/Foxy</td>
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<td>1.00 (0.81-1.26)</td>
<td>1.14 (0.87-1.48)</td>
<td>1.81 (1.17-2.89)</td>
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<td>Salvia divinorum</td>
<td>1.09 (0.86-1.39)</td>
<td>0.97 (0.67-1.42)</td>
<td>1.41 (1.00-1.98)</td>
<td>1.74 (0.93-3.26)</td>
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<td>Ecstasy/MDMA</td>
<td>0.83 (0.77-0.89)</td>
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<td>Ketamine</td>
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<td>1.07 (0.81-1.40)</td>
<td>1.19 (0.67-2.18)</td>
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</tbody>
</table>

Note: **Bold** = statistically significant. *a*p<.05, **b**p<.001. aPR = adjusted prevalence ratio; CI = confidence interval. Data from years 2015-2020 are pooled. Adjusted analyses controlled for survey year, sex, age, race/ethnicity, annual household income, education, marital status, and use of cannabis, cocaine, methamphetamine, and heroin, and misuse of prescription tranquilizers/sedatives, stimulants, and opioids.

Supplemental Table 1 – Bivariable comparisons between past-year (mis)use of other illegal drugs and past-year serious psychological distress, major depressive episode, and suicidality

<table>
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<th>Suicidal Thinking</th>
<th>Suicide Planning</th>
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<td>5.6</td>
<td>94.6</td>
<td>5.4</td>
</tr>
<tr>
<td>Cocaine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>No</td>
<td>99.5</td>
<td>0.5</td>
<td>99.5</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>97.2</td>
<td>2.8</td>
<td>97.3</td>
</tr>
<tr>
<td>Heroin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prescription Tranquilizers or Sedatives (Misuse)</td>
<td>No</td>
<td>98.2</td>
<td>1.8</td>
<td>98.0</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>91.7</td>
<td>8.3</td>
<td>91.5</td>
</tr>
<tr>
<td>Prescription Stimulants (Misuse)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>98.5</td>
<td>1.5</td>
<td>98.3</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>94.2</td>
<td>5.8</td>
<td>94.3</td>
</tr>
<tr>
<td>Prescription Opioids (Misuse)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>96.9</td>
<td>3.1</td>
<td>96.6</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>89.1</td>
<td>10.9</td>
<td>89.3</td>
</tr>
</tbody>
</table>

Note: All ps <0.001. Data from years 2015-2020 are pooled. All percentages are reported as row percentages and weighted estimates.
Supplemental Table 2 – Multivariable associations between past-year (mis)use of other illegal drugs and past-year serious psychological distress, major depressive episode, and suicidality

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>Serious Psychological Distress</th>
<th>Major Depressive Episode</th>
<th>Suicidal Thinking</th>
<th>Suicide Planning</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>aPR (95% CI)</td>
<td>aPR (95% CI)</td>
<td>aPR (95% CI)</td>
<td>aPR (95% CI)</td>
</tr>
<tr>
<td>Marijuana</td>
<td>1.66 (1.59-1.73)(^b)</td>
<td>1.71 (1.65-1.78)(^b)</td>
<td>1.74 (1.63-1.85)(^b)</td>
<td>1.82 (1.65-2.01)(^b)</td>
</tr>
<tr>
<td>Cocaine</td>
<td>1.00 (0.93-1.08)</td>
<td>0.95 (0.87-1.04)</td>
<td>1.21 (0.99-1.27)</td>
<td>1.20 (0.96-1.48)</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>1.51 (1.37-1.65)(^b)</td>
<td>1.55 (1.34-1.79)(^b)</td>
<td>1.58 (1.37-1.82)(^b)</td>
<td>1.87 (1.46-2.42)(^b)</td>
</tr>
<tr>
<td>Heroin</td>
<td>1.11 (0.98-1.25)</td>
<td>0.96 (0.78-1.17)</td>
<td>1.03 (0.84-1.27)</td>
<td>1.07 (0.78-1.44)</td>
</tr>
<tr>
<td>Tranquilizers or Sedatives</td>
<td>1.58 (1.50-1.66)(^b)</td>
<td>1.67 (1.57-1.78)(^b)</td>
<td>1.62 (1.47-1.79)(^b)</td>
<td>1.77 (1.50-2.08)(^b)</td>
</tr>
<tr>
<td>Stimulants</td>
<td>1.03 (0.98-1.07)</td>
<td>1.04 (0.96-1.13)</td>
<td>1.06 (0.92-1.10)</td>
<td>0.90 (0.75-1.08)</td>
</tr>
<tr>
<td>Pain Reliever Misuse</td>
<td>1.61 (1.52-1.70)(^b)</td>
<td>1.60 (1.47-1.73)(^b)</td>
<td>1.94 (1.78-2.12)(^b)</td>
<td>2.33 (2.06-2.64)(^b)</td>
</tr>
</tbody>
</table>

Note: **Bold** = statistically significant. ^p<.05, ^b<.001. Tranquilizers, sedatives, stimulants, and opioids refer to misuse of prescriptions of these drug classes. aPR = adjusted prevalence ratio; CI = confidence interval. Data from years 2015-2020 are pooled. Adjusted analyses controlled for survey year, sex, age, race/ethnicity, annual household income, education, marital status, and use of cannabis, cocaine, methamphetamine, and heroin, and misuse of prescription tranquilizers/sedatives, stimulants, and opioids.

Highlights

- Hallucinogens differ with respect to their link with depression and suicidality.
- LSD use was associated with an increased likelihood of major depressive episode and suicidal thinking.
- *Salvia divinorum* use was associated with an increased likelihood of suicidal thinking.
- DMT/AMT/Foxy use was associated with an increased likelihood of suicidal planning.
- Ecstasy/MDMA use was associated with a decreased likelihood of psychological distress, major depressive episode, and suicidal thinking.