Associations between lifetime classic psychedelic use and cardiometabolic diseases

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The objective of the current study was to investigate the associations between lifetime classic psychedelic use and cardiometabolic diseases. Using data from the National Survey on Drug Use and Health (2005–2014), the present study examined the associations between lifetime classic psychedelic use and two types of cardiometabolic disease: heart disease and diabetes. Respondents who reported having tried a classic psychedelic at least once in their lifetime had lower odds of heart disease in the past year (adjusted odds ratio (aOR) = 0.77 (0.65–0.92), p = .006) and lower odds of diabetes in the past year (adjusted odds ratio (aOR) = 0.88 (0.78–0.99), p = .036). Classic psychedelic use might be beneficial for cardiometabolic health, but more research is needed to investigate potential causal pathways of classic psychedelics on cardiometabolic diseases.

Cardiometabolic diseases such as heart disease and diabetes are leading contributors to the global burden of disease. While pharmacological treatment, intensive lifestyle modification, or both can delay or reverse the development of cardiometabolic diseases, no study has thus far investigated the long-term cardiometabolic effects of classic psychedelics, which could potentially be administered both as a pharmacological treatment and as part of a program to facilitate healthy lifestyle changes.

The term classic psychedelics broadly refers to psychoactive substances known to act as agonists primarily at serotonin 2A receptors, which are often categorized into three main classes: tryptamines, lysergamides, and phenethylamines. Most notably, tryptamines include N,N-dimethyltryptamine (DMT), the DMT-containing admixture ayahuasca, and psilocybin; lysergic acid diethylamide (LSD) comprises the lysergamide class; and phenethylamines include mescaline and the mescaline-containing cacti peyote and San Pedro. The evidence to date suggests that classic psychedelics have a good risk profile and can be effective in the treatment of several mental health conditions, but recent research indicates that classic psychedelics may also have beneficial effects for a range of physical illnesses, including cardiometabolic diseases such as heart disease and diabetes.

There are several mechanisms through which classic psychedelics might influence cardiometabolic health. First, research suggests that classic psychedelics may facilitate healthy lifestyle changes associated with a beneficial impact on cardiometabolic risk factors (e.g., diet, alcohol and tobacco consumption, and exercise). Second, classic psychedelics administered in a safe and supportive setting have been shown to improve mental health conditions associated with cardiometabolic diseases. Third, classic psychedelics have anti-inflammatory and immunomodulatory properties of importance for both mental and cardiometabolic health. Fourth, classic psychedelics have high affinity to serotonin receptor subtypes associated with cardiometabolic diseases (e.g., serotonin 2A and 2C receptors) and in sum, classic psychedelics could have both direct and indirect effects that lead to better cardiometabolic health.

Previous research has found associations between lifetime classic psychedelic use and lower odds of being overweight or obese as well as lower odds of having hypertension in the past year, which are risk factors of cardiometabolic disease. Using pooled data from the National Survey on Drug Use and Health (2005–2014), the present study therefore sought to investigate the associations between lifetime classic psychedelic use and two types of cardiometabolic disease: heart disease and diabetes. We hypothesized that lifetime classic psychedelic use would be associated with lower odds of heart disease in the past year as well as lower odds of diabetes in the past year.
Results
Table 1 displays the percentage of respondents reporting heart disease or diabetes in the past year. As seen in the table, the prevalence of heart disease or diabetes in the past year among respondents who had ever used a classic psychedelic was approximately 51% and 52%, respectively, of that among respondents who had never used a classic psychedelic. Notably, the prevalence of heart disease or diabetes in the past year among respondents who had ever used a tryptamine (DMT, ayahuasca, or psilocybin) was approximately 45% and 41%, respectively, of that among respondents who had never used a tryptamine. It is noted, however, that these relationships do not control for the range of potential confounding factors.

Table 2 presents results from the regressions on the associations between lifetime classic psychedelic use and heart disease in the past year as well as diabetes in the past year. As illustrated below, lifetime classic psychedelic use was uniquely associated with a 23% lower odds of heart disease in the past year and a 12% lower odds of diabetes in the past year. Among the three main classes of classic psychedelics, neither lifetime tryptamine use, lifetime LSD use, nor lifetime phenethylamine use were uniquely associated with heart disease or diabetes in the past year when simultaneously entered into the regression models, though the association between lifetime tryptamine use and diabetes in the past year approached conventional levels of significance.

Discussion
The results of this national survey-based study showed that lifetime classic psychedelic use was associated with both lower odds of heart disease in the past year and lower odds of diabetes in the past year, which indicates that classic psychedelic use might be beneficial for cardiometabolic health. The findings are novel and build on previous findings on the associations between lifetime classic psychedelic use and various markers of physical health22–24, but there are several limitations inherent in the study design that merit consideration. First, the cross-sectional design used in the present study limits causal inference. The regression models controlled for several potential confounding factors, but the associations could have been affected by latent variables that were not included in the dataset and could not be controlled for (e.g., a common factor that predisposes respondents to classic psychedelic use might also predispose them to salubrious lifestyle behaviors associated with cardiometabolic health). Second, there was no information in the dataset on the context of classic psychedelic use, dose used, or frequency of use. The analysis could therefore not evaluate context, dose, or frequency-specific associations. Third, the term “heart disease” covers a wide range of conditions and the term “diabetes” can refer to several

| Lifetime classic psychedelic use | Heart disease in the past year |
|---------------------------------|-------------------------------|
|                                 | Yes | No |
| Yes                              | 658 (2.29%) | 54,077 (97.71%) |
| No                               | 6,495 (4.49%) | 314,977 (95.51%) |
| Lifetime tryptamine use          | Yes | No |
| Yes                              | 383 (1.95%) | 39,683 (98.05%) |
| No                               | 6,770 (4.41%) | 329,371 (95.59%) |
| Lifetime LSD use                 | Yes | No |
| Yes                              | 529 (2.50%) | 36,836 (97.50%) |
| No                               | 6,624 (4.38%) | 332,218 (95.62%) |
| Lifetime phenethylamine use      | Yes | No |
| Yes                              | 303 (3.59%) | 13,007 (96.41%) |
| No                               | 6,850 (4.22%) | 356,047 (95.78%) |
| Lifetime classic psychedelic use | Diabetes in the past year   |
|                                 | Yes | No |
| Yes                              | 1,322 (3.95%) | 53,400 (96.05%) |
| No                               | 12,913 (7.69%) | 308,532 (92.31%) |
| Lifetime tryptamine use          | Yes | No |
| Yes                              | 722 (3.06%) | 39,336 (96.94%) |
| No                               | 13,513 (7.59%) | 322,596 (92.41%) |
| Lifetime LSD use                 | Yes | No |
| Yes                              | 1,013 (4.13%) | 36,341 (95.87%) |
| No                               | 13,222 (7.53%) | 325,591 (92.47%) |
| Lifetime phenethylamine use      | Yes | No |
| Yes                              | 546 (5.72%) | 12,758 (94.28%) |
| No                               | 13,689 (7.25%) | 349,174 (92.75%) |
metabolic disorders, including type 1 and type 2 diabetes. It is therefore possible that associations might vary across types of heart disease and diabetes.

There has been extensive research during the last decades on prevention and treatment of cardiometabolic diseases, including several comprehensive interventions designed to reduce lifestyle risk factors. Yet the potential long-term effects of classic psychedelic use on cardiometabolic health remains largely unknown. The findings in the present study reveal associations between lifetime classic psychedelic use and lower odds of heart disease in the past year as well as lower odds of diabetes in the past year. It demonstrates the need for further research to investigate potential causal pathways of classic psychedelics on cardiometabolic health (i.e., lifestyle changes, mental health benefits, anti-inflammatory and immunomodulatory characteristics, and affinity to specific serotonin receptor subtypes).

**Methods**

**Data and population.** The National Survey on Drug Use and Health (NSDUH) is an annual survey designed to measure the prevalence of substance use and mental health issues in the United States. The present study used pooled data from NSDUH survey years 2005 to 2014, which were the only survey years with items on heart disease and diabetes in the past year. While previous research has investigated the association between lifetime classic psychedelic use and having a heart condition and/or cancer in the past year (composite measure; \( p = 0.09 \))\(^{23} \), this study examined the unique associations with heart disease and diabetes in the past year. The NSDUH public-use data files are available on their homepage: [https://www.datafiles.samhsa.gov/study-series/national-survey-drug-use-and-health-nsduh-nid13517](https://www.datafiles.samhsa.gov/study-series/national-survey-drug-use-and-health-nsduh-nid13517).

**Variables.** The dependent variables were: (1) having been told to have heart disease in the past year and (2) having been told to have diabetes in the past year. Both dependent variables derived from the following question:

> Which, if any, of these conditions did a doctor or other medical professional tell you that you had in the past 12 months?

### Table 2. Lifetime classic psychedelic use and cardiometabolic diseases. The number of observations in the models with heart disease in the past year as dependent variable was 375,473; the number of observations in the models with diabetes in the past year as dependent variable was 375,434; aOR adjusted Odds Ratio, CI confidence interval. Odds ratios were adjusted for age, sex, ethnoracial identity, educational attainment, annual household income, marital status, self-reported engagement in risky behavior, lifetime use of cocaine, other stimulants, sedatives, tranquilizers, heroin, pain relievers, marijuana, phencyclidine (PCP), 3,4-methylenedioxymethamphetamine (MDMA/ecstasy), inhalants, smokeless tobacco, pipe tobacco, cigarette daily, and age of first alcohol use; see Supplementary Table S1 for additional analysis.

| Variable                        | aOR (95% CI) | p value |
|---------------------------------|--------------|---------|
| **Heart disease in the past year** |               |         |
| Model 1 Lifetime classic psychedelic use | 0.77 (0.65–0.92) | .006    |
| Model 2 Lifetime tryptamine use | 0.85 (0.69–1.06) | .152    |
| Lifetime LSD use                | 0.88 (0.73–1.07) | .199    |
| Lifetime phenethylamine use     | 0.92 (0.75–1.13) | .402    |
| **Diabetes in the past year**   |               |         |
| Model 1 Lifetime classic psychedelic use | 0.88 (0.78–0.99) | .036    |
| Model 2 Lifetime tryptamine use | 0.86 (0.74–1.00) | .055    |
| Lifetime LSD use                | 0.92 (0.80–1.06) | .236    |
| Lifetime phenethylamine use     | 1.01 (0.86–1.19) | .891    |
lifetime inhalants use; lifetime other stimulants use; lifetime sedatives use; lifetime smokeless tobacco use; lifetime pipe tobacco use; lifetime pain relievers use; lifetime cigarette use; and age of first alcohol use (less than 13 years of age [Preteen], 13–19 years of age [Teen], more than 19 years of age [Adult], or never used). The control variables were coded as separate covariates and were the same as those used in a recent study analyzing the same NSDUH survey years22.

**Statistical analyses.** The present study first used descriptive statistics to present an overview of the zero-order relationships of lifetime psychedelic use and subcategories of lifetime use of tryptamines (DMT, ayahuasca, or psilocybin), LSD, and phenethylamines (mescaline, peyote, or San Pedro) with both heart disease in the past year and diabetes in the past year (Table 1). These zero-order relationships were then interrogated further with logistic regression, which was used to calculate adjusted odds ratios with 95 percent confidence intervals and examine the unique associations between lifetime classic psychedelic use and cardiometabolic diseases while adjusting for the control variables listed above (Table 2). The analyses used weights provided by the NSDUH. “Bad Data,” "Don’t Know,” "Refused,” “Blank” were coded as missing values. The analyses were conducted using Stata version 1726.

**Ethical approval.** The current study was a secondary analysis of publicly available data files and was exempt from review by the Research Ethics Committee of the Department of Sociology (DREC) at the University of Oxford.

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**References**
1. Roth, G. A. et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the global burden of disease study 2017. *Lancet* **392**(10139), 1736–1788 (2018).
2. Arnett, D. K. et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J. Am. Coll. Cardiol.* **74**(10), e177–e232 (2019).
3. Artinian, N. T. et al. Interventions to promote physical activity and dietary lifestyle changes for cardiovascular risk factor reduction in adults: a scientific statement from the American Heart Association. *Circulation* **122**(4), 406–441 (2010).
4. Chatterjee, S., Khunti, K. & Davies, M. J. Type 2 diabetes. *Lancet* **389**(10085), 2239–2251 (2017).
5. Tuomilehto, J. et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N. Engl. J. Med.* **344**(18), 1343–1350 (2001).
6. Nutt, D. & Carhart-Harris, R. The current status of psychedelics in psychiatry. *JAMA Psychiat.* **78**(2), 121–122 (2021).
7. Szabo, A. Psychedelics and immunomodulation: Novel approaches and therapeutic opportunities. *Front. Immunol.* **6**, 358 (2015).
8. Sexton, J. D. et al. Prevalence and epidemiological associates of novel psychedelic use in the United States adult population. *J. Psychopharmacol.* **33**(9), 1058–1067 (2019).
9. Nutt, D. J., King, L. A. & Phillips, L. D. Drug harms in the UK: A multicriteria decision analysis. *Lancet* **376**(9752), 1558–1565 (2010).
10. Freeska, E., Bokor, P. & Winkelman, M. The therapeutic potentials of ayahuasca: Possible effects against various diseases of civilization. *Front. Pharmacol.* **7**, 35 (2016).
11. Frese, P. J. et al. Psychedelics and health behaviour change. *J. Psychopharmacol.* 02698811211008554 (2021).
12. Carhart-Harris, R. et al. Trial of psilocybin versus escitalopram for depression. *N. Engl. J. Med.* **384**(15), 1402–1411 (2021).
13. Chaddha, A., Robinson, E. A., Kline-Rogers, E., Alexandris-Soupis, T. & Rubenfire, M. Mental health and cardiovascular disease. *Am. J. Med.* **129**(11), 1145–1146 (2016).
14. Davis, A. K. et al. Effects of psilocybin-assisted therapy on major depressive disorder: A randomized clinical trial. *JAMA Psychiat.* **78**(5), 481–489 (2021).
15. Luoma, J. B., Chwyl, C., Bathje, G. I., Davis, A. K. & Lancelotta, R. A Meta-analysis of placebo-controlled trials of psychedelic-assisted therapy. *J. Psychoactive Drugs* **2**, 1–11 (2020).
16. Sartorius, N. Depression and diabetes. *Dialogues Clin. Neurosci.* **20**(1), 47 (2018).
17. Nicholls, C. D. Serotonin 5-HT2A receptor function as a contributing factor to both neuropsychiatric and cardiovascular diseases. *Cardiovasc. Psychiatry Neurol.* (2009).
18. Flanagan, T. W. & Nichols, C. D. Psychedelics as anti-inflammatory agents. *Int. Rev. Psychiatry* **30**(4), 363–375 (2018).
19. Furman, D. et al. Chronic inflammation in the etiology of disease across the life span. *Nat. Med.* **25**(12), 1822–1832 (2019).
20. Thompson, C. & Szabo, A. Psychedelics as a novel approach to treating autoimmune conditions. *Cardiovasc. Psychiatry Neurol.* (2009).
21. Zhou, L. et al. Serotonin 2C receptor agonists improve type 2 diabetes via melanocortin-4 receptor signaling pathways. *Cell Metab.* **8**(5), 398–405 (2007).
22. Simonsson, O., Hendricks, P. S., Carhart-Harris, R., Ketten, H. & Osika, W. Association between lifetime classic psychedelic use and hypertension in the Past Year. *Hypertension* **77**(5), 1510–1516 (2021).
23. Simonsson, O., Sexton, J. D. & Hendricks, P. S. Associations between lifetime classic psychedelic use and markers of physical health. *J. Psychopharmacol.* **35**(4), 447–452 (2021).
24. Ona, G. et al. Ayahuasca and public health: Health status, psychosocial well-being, lifestyle, and coping strategies in a large sample of ritual ayahuasca users. *J. Psychoactive Drugs* **51**(2), 135–145 (2019).
25. Hendricks, P. S. et al. The relationships of classic psychedelic use with criminal behavior in the United States adult population. *J. Psychopharmacol.* **32**(1), 37–48 (2018).
26. StataCorp. *Stata statistical software: Release 17* (StataCorp LLC, 2021).

**Author contributions**
O.S. conceived of the study and the hypothesis. O.S. was the primary author who cleaned data, conducted analyses, and drafted the manuscript summarizing the findings. W.O. contributed meaningful expertise on cardiometabolic health. R.C.-H. contributed meaningful expertise on classic psychedelics and commented on...
draft manuscripts. P.S.H. contributed meaningful expertise to inform methodology and statistical analyses, and
on classic psychedelics. P.S.H. and W.O. supervised and commented on draft manuscripts.

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**Additional information**

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