BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016025
Article Type:	Research
Date Submitted by the Author:	23-Jan-2017
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Primary Subject Heading:	Public health
Secondary Subject Heading:	Evidence based practice, Epidemiology, Mental health
Keywords:	sex workers, psychedelics, hallucinogens, MENTAL HEALTH, Suicide & self-harm < PSYCHIATRY

Psychedelic use predicts reduced suicidality: Findings from a longitudinal study of women sex workers

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Word Count: 2769

ABSTRACT

Objective: This study aimed to longitudinally investigate whether ever having used a psychedelic drug can have a protective effect on incidence of suicidality among sex workers.

Design: Longitudinal cohort study.

Setting: Data were drawn from a prospective, community-based cohort of women sex workers, known as AESHA (An Evaluation of Sex Workers Health Access), in Vancouver, Canada.

Participants: 766 sex workers completed the AESHA baseline questionnaire between January 2010 and August 2014. Participants who did not report suicidality at baseline and who completed at least one follow-up visit were included.

Main outcome measure: Extended Cox regression was used to model predictors of new suicidality (suicide ideation or attempts) over 54 months follow-up.

Results: Nearly half (46%; n=355) of participants reported suicidality and were thus excluded from the present analyses. Of 290 sex workers eligible at baseline, 11% (n=31) reported recent suicidality during follow-up, with an incidence density of 4.42 per 100 person-years (95% Confidence Interval [CI] 3.10 to 6.30). In multivariable analysis, reported lifetime psychedelic drug use was associated with a 60% reduced hazard for suicidality (Adjusted Hazard Ratio [AHR] 0.40; 95%CI 0.17 to 0.94). Crystal methamphetamine use (AHR 3.25; 95%CI 1.47 to 7.21) and childhood abuse (AHR 3.54; 95%CI 1.49 to 8.40) remained independent predictors of suicidality.

Conclusion: The high rate of suicidality among sex workers is of major concern. Alongside emerging evidence on the potential of psychedelic-assisted therapy to treat mental health and addiction issues, our findings demonstrate that non-medical psychedelic drug use is independently associated with reduced suicidality, while other illicit drug use and childhood trauma predispose sex workers to suicidality. While observational, this study supports calls for further research and innovative interventions to address suicide risk, including investigation of the therapeutic utility of psychedelics.

Word Count: 287
Keywords: *sex workers, psychedelics, hallucinogens, suicide prevention, mental health, substance use*

Strengths and limitations of this study

- This is the first study to longitudinally investigate the impact of psychedelic drug use on suicidality among sex workers.
- This community-based study among women sex workers demonstrates that historical psychedelic drug use independently predicts reduced suicidality and supports calls for further research and innovative interventions to address suicide risk, including investigation of the therapeutic utility of psychedelics.
- The study population included women from a wide-ranging representation of sex work environments, increasing generalizability.
- The mapping of working areas and time–location sampling helped to ensure a representative sample and to minimize selection bias.
- Data were self-reported and variables examined included highly stigmatized topics, introducing the potential for recall bias, social desirability and reporting bias.

INTRODUCTION

Despite efforts to improve mental health over the last 60 years, suicide remains a critical public health concern worldwide [1,2]. Suicide was the second leading cause of death globally in 2012 among 15-29 year olds [2], with an estimated 80-90% of suicide deaths attributable to mental health or substance use disorders [3,4]. Significant gaps remain in empirical research examining suicidality among marginalized populations. Women sex workers experience disproportionately high levels of social and health-related risks and harms, including stigma, discrimination, and violence [5–7], and previous studies highlight the unmet mental health needs of sex workers, underscoring the associations of social exclusion, depression, and post-traumatic stress disorder (PTSD) with suicidality [8–12]. Research demonstrates greater risk for suicidality among those with a history of trauma [1,13] and among women sex workers who report historical experiences of violence and childhood abuse [8–10,14,15]. Further, Indigenous women are vastly overrepresented among street-based sex workers in North America, and face devastating and multigenerational effects of trauma and social dislocation (e.g., high burden of mental illness and suicidality) as a result of colonialism, racialized policies, and displacement from land and home communities [16,17].

Various biological, interpersonal, and socio-structural factors (e.g., social exclusion/isolation, education level, employment) contribute to our understanding of suicidal behaviors [1,18]. Given the complex etiological pathways to suicide and ineffectiveness of interventions to reduce the burden of suicidality, the US National Institute of Mental Health has called for innovative research on suicide prevention and treatment for suicidality [19].

A number of psychedelic drug therapies are being revisited following a 40-year hiatus in research for the treatment of depression, anxiety, PTSD, eating disorders, and addiction [20]. Psychedelic drugs include lysergic acid diethylamide (LSD), psilocybin, dimethyltryptamine (DMT), mescaline, and methylenedioxymethamphetamine (MDMA), many of which are being investigated in clinical/pre-clinical studies for their neuropharmacological functions and potential as adjuncts to psychotherapy [21,22]. While renewed interest in psychedelic medicine is challenged by various funding, methodological, and legal impediments, the emerging evidence indicating improved outcomes for some individuals suffering from mental health and addiction issues has generated new scientific inquiry and an imposing obligation to advance this research [20,23,24]. Recent observational studies in the US demonstrate significant associations between lifetime psychedelic use and reduced recidivism and intimate partner violence among populations of prison inmates [25,26], and reduced psychological distress and suicidality among the general adult population [27–29].

Despite the multifaceted vulnerabilities experienced by sex workers, there remains a paucity of data on suicide rates and research that systematically examines factors that potentiate or mitigate suicidality among sex workers, particularly in the global north. Some evidence suggests that psychedelic drug use may be protective with regard to suicidality [27–29] and is associated with significant improvements in psychological wellbeing and reductions in depression and anxiety in clinical settings [30–35], yet existent research is characterized by large gaps. Given the urgency of addressing and preventing suicide and calls for prioritizing innovative treatments in the wake of largely ineffective interventions, this study aimed to longitudinally investigate whether lifetime psychedelic drug use is associated with a reduced incidence of suicidality (suicide

ideation or attempts) among women sex workers. We postulated that psychedelic drug use would have an independent protective effect on suicidality over the study period.

METHODS

Study Design and Participants

Data for this study were drawn from a large, community-based, prospective cohort of over 800 women sex workers initiated in 2010, known as AESHA (An Evaluation of Sex Workers Health Access). Eligibility criteria for study participants included cisgender or transgender women, 14 years of age or older, who exchanged sex for money within the last 30 days. AESHA participants completed interviewer-administered questionnaires and HIV/STI/HCV serology testing at enrollment and biannually. Interview, outreach and nursing staff included experiential individuals (current/former sex workers) with substantial community experience. Participants were recruited across Metro Vancouver using time-location sampling and community mapping strategies, with day and late-night outreach to outdoor sex work locations (i.e., streets, alleyways), indoor sex work venues (i.e., massage parlors, micro-brothels, and in-call locations), and online. Weekly outreach is conducted to over 100 sex work venues by outreach/nursing teams operating a mobile van, with regular contact as well as encouraging drop-in to women-only spaces at the research office, contributing to an annual retention rate of >90% for AESHA participants.

The main interview questionnaire elicits responses related to socio-demographics (e.g., sexual identity, ethnicity, housing), the work environment (e.g., access to services, violence/safety, policing, incarceration), client characteristics (e.g., types/fees of services, condom use), intimate

partners (e.g., sexual history, cohabitation, financial support), trauma and violence (e.g., lifetime and childhood trauma, exposure to intimate partner and workplace violence), and comprehensive injection and non-injection drug use patterns. The clinical questionnaire relates to overall physical, mental, and emotional health, and HIV testing and treatment experiences to support education, referral, and linkages with care. The research team works in close partnership with the affected community and a diversity of stakeholders (e.g., legal/human rights experts, community-based organizations, service providers, health authorities, government officials, and international policy bodies) and regularly engages in knowledge exchange efforts. AESHA is monitored by a Community Advisory Board of over 15 sex work, women's health and HIV service agencies, as well as representatives from the health authority and policy experts, and holds ethical approval through Providence Health Care/University of British Columbia Research Ethics Board. All participants receive an honorarium of $40 CAD at each bi-annual visit for their time, expertise and travel.

Statistical Analyses

Analyses were restricted to AESHA participants who had never thought about or attempted suicide at baseline and completed at least one follow-up visit between January 2010 and August 2014. The outcome of interest was a first episode of suicidality, defined as responding 'yes' to having thought about or attempted suicide in the last six months. Time-fixed variables examined included age (continuous), gender/sexual minority (lesbian, gay, bisexual, trans, or two-spirit), Indigenous ancestry (inclusive of First Nations, Metis, and Inuit), being an im/migrant worker (versus Canadian born), education (high school or greater), and physical and/or sexual childhood abuse (before age 18). Variables treated as time-updated covariates based on bi-annual follow-up

data included HIV/STI serostatus, recent homelessness, recent physical and/or sexual violence by clients, recent police harassment and/or arrest, and primary place to solicit clients. Time-updated injection and non-injection drug use variables included use of psychedelics (any hallucinogens, including LSD/acid, magic mushrooms/psilocybin, salvia, ecstasy/MDMA), marijuana, pharmaceutical opioids (any street methadone/suboxone, dilaudid, morphine, oxycontin, percocet/vicodin/demerol, or T3s/T4s), crack, cocaine, crystal methamphetamine, and heroin.

Using extended Cox regression, unadjusted and adjusted hazard ratios (HR and AHR) and 95% confidence intervals (CI) were calculated to identify predictors of suicidality. Variables hypothesized a priori to be predictors of suicidality and those that were significantly correlated with the outcome at the $p<0.05$ level in bivariate analyses were subsequently fitted into a multivariable Cox model. Backward model selection was used to determine the final multivariable model with the best overall fit, as indicated by the lowest Akaike information criterion (AIC) value. A complete case analysis was used, where observations with missing data were excluded from analyses, and participants who were lost to follow-up were right censored at their most recent study visit. All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA). Two-sided p-values are reported.

RESULTS

Of the total 766 sex workers who completed the AESHA baseline questionnaire, 46% (n=355) reported ever experiencing suicidality (45%; n=343 reported suicidal thoughts, 32%; n=245 attempted suicide) and were thus excluded from this analysis. Those with missing observations

for suicidality at baseline (n=50/766; 6.5%) were excluded from analysis, and one additional participant was excluded because reported suicidality was missing at follow-up. A total of 290 sex workers without suicidality who completed at least one follow-up visit were eligible for inclusion in the present analysis. Participants were followed for a total of 53.5 months (median = 29.9 months). Baseline characteristics of participants who reported suicidality during follow-up compared to those who did not are displayed in Table 1.

Overall, 11% (n=31) thought about or attempted suicide for the first time during follow-up, with an incidence density of 4.42 per 100 person-years (95%CI 3.10 to 6.30). The median age was 36 (interquartile range [IQR] 29 to 42) and 16% (n=45) of participants identified as gender or sexual minorities. One third (n=93) reported Indigenous ancestry and one quarter (n=73) had been homeless in the last six months. Half of participants (49%; n=142) solicited clients on the streets, and 37% (n=106) solicited clients in indoor establishments. In terms of occupational violence, 14% (n=41) and 37% (n=107) reported physical/sexual violence from clients and police harassment/arrest, respectively. Nearly half (47%; n=136) of participants reported ever being physically and/or sexually abused before age 18, and among those who reported suicidality, 77% (n=24/31) experienced childhood abuse compared to 43% (n=112/259) among those who did not report suicidality (p<0.001). Overall HIV prevalence was 11% (n=33).

The majority of participants (63%, n=184) reported ever using crack and 56% (n=162) reported ever using cocaine, with higher proportions of crack and cocaine use among those reporting suicidality than those who did not (p=0.003). Close to half (49%, n=141) reported lifetime heroin use, which was significantly higher among those who reported suicidality than those who did not

(68% vs. 46%, p=0.02). Approximately one third (31%, n=90) of participants had ever used crystal methamphetamine, and this was significantly higher among those who reported suicidality than those who did not (58% vs. 28%, p<0.001). Overall, 27% (n=79) of participants reported ever using a psychedelic substance.

Unadjusted and adjusted hazard ratios for factors associated with a first episode of suicidality during follow-up are displayed in Table 2. In the final multivariable model, crystal methamphetamine use (AHR 3.25; 95%CI 1.47 to 7.21) and physical and/or sexual childhood abuse (AHR 3.54; 95%CI 1.49 to 8.40) remained independently associated with time to suicidality. Psychedelic use was associated with a 60% reduced hazard of suicidality (AHR 0.40; 95%CI 0.17 to 0.94).

DISCUSSION

This study demonstrated that among women sex workers, a population at disproportionately elevated risk for psychological distress and suicide, lifetime psychedelic drug use predicted a reduced hazard for suicidality. Crystal methamphetamine use and childhood abuse predisposed sex workers to suicidality corresponding to more than a three-fold increased hazard. Suicidality was highly prevalent, with almost half of sex workers reporting lifetime suicidality at baseline, and 11% reporting a first episode of suicidality in the last six months during follow-up. Few studies have longitudinally examined predictors of suicidality among sex workers, and of the available data, most are cross-sectional and/or conducted in lower and middle income settings [8,15,36,37]. The present study, based on a community-based, prospective cohort of sex workers,

adds to a growing body of literature documenting the protective and therapeutic potentials of psychedelic substances [20,23,33,38,39].

Data were self-reported, and questions pertaining to events that occurred in the past may be subject to recall bias. Variables examined included sensitive and highly stigmatized topics such as childhood trauma, violence, and illicit drug use, which introduce the potential for social desirability and reporting bias. However, the likelihood of these biases is reduced by the community-based nature of the study. Suicidality among sex workers is influenced by complex individual, interpersonal and structural variables, some of which may have not been measured in this study. While lifetime psychedelic drug use was found to reduce the hazard of suicidality, the associations uncovered in this analysis cannot be determined as causal. The study population included women from a wide-ranging representation of sex work environments, yet findings may not be fully generalizable to sex workers in other settings. The mapping of working areas and time–location sampling helped to ensure a representative sample and to minimize selection bias.

Prior cross-sectional research conducted in Sydney, Australia demonstrated significant links between depression, trauma, and suicidality, where an estimated 42% of street-based female sex workers reported attempting suicide and 74% reported lifetime suicidal ideation [10,36]. While estimates of mental illness vary significantly across sex work settings, up to three-quarters of sex workers in a US study reported severe depression, anxiety, or PTSD [12]. In studies conducted in Asia, recent suicide attempts ranged from 19% among sex workers in Goa, India [15] to 38% among sex workers in China [8,11,40]. Transgender women involved in sex work, a population experiencing significant psychosocial vulnerability, report notably further elevated rates of

suicidality: three quarters of participants in San Francisco reported suicide ideation, of whom 64% attempted suicide [41]. Our findings extend upon research establishing associations between lifetime use of illicit drugs and increased risk for suicidality: in bivariate analysis, all classes of illicit drugs were demonstrated to increase the hazard of suicidality with the exception of psychedelics. In multivariable analysis, psychedelics were independently associated with a 60% reduced hazard for suicidality, contributing to emergent evidence on the potential of psychedelics to mitigate risks for suicide.

Among the various scientific studies examining the potential benefits of psychedelic drug use, a recent and large (n>190,000) longitudinal study conducted among the general US adult population demonstrated that psychedelics are associated with reduced psychological distress and suicidality [27]. A recent open-label trial conducted in the UK demonstrated the safety and efficacy of psilocybin for treating major depression [30], and another open-label trial in Brazil found rapid and sustained anti-depressant effects from the Amazonian psychedelic brew ayahuasca administered in a clinical setting [32]. The ways in which psychedelics may alleviate suffering associated with mental health is undoubtedly a complex phenomenon. It has been hypothesized that psychedelics modify neurobiological processes involved in suicidality by down-regulating 5-HT_{2A} serotonin receptors, as increased binding (and up-regulation) of this receptor has been implicated in major depression and suicide [33,39,42]. Further, psychedelics are evidenced to alter neural network connectivity and enhance recall of autobiographical memories, which may facilitate positive reprocessing of trauma [21,43,44]. Recent randomized, placebo-controlled, cross-over studies found that psilocybin (among n=25 adults) and LSD (among n=20 adults) were associated with increased positive mood and psychological wellbeing

[31,33], supporting other work demonstrating the anti-depressive/anxiolytic effects of psychedelics [22,34,45,46]. The potential of psychedelics to elicit "mystical-type" experiences, with profound and sustained positive changes in attitudes and mood, may play a key role in addiction treatment interventions [35,39,47,48]. For example, psilocybin-assisted psychotherapy demonstrated high success in smoking cessation outcomes at six months follow-up (abstinence rates of 80%), with significant correlations found between psilocybin sessions and elevated ratings of personal meaningfulness, wellbeing, and life satisfaction [49]. Randomized control trials in the US and Switzerland have demonstrated significant long-term improvements among patients with treatment-resistant PTSD following MDMA-assisted psychotherapy [50,51], and similar research has commenced in Vancouver, Canada.

Sex workers experience complex and synergistic effects between trauma, mental health comorbidities, and risk for suicidality. Sex workers report high rates of childhood abuse [52–54], which is associated with an increased likelihood of experiencing subsequent physical or sexual violence, as well as initiating injection drug use [55–57]. For those suffering from emotional trauma stemming from violence, including indirect violence (i.e., witnessing violence), there may be a proclivity to use drugs for self-medication [58,59]. Violence and sexual coercion have been found to be significantly associated with suicidality among sex worker populations in China and India [8,9,15,60]. As demonstrated in this study, having an early traumatic life event is a key risk factor for suicide among sex workers, a high proportion of whom are Indigenous, and experiencing historical trauma can have harmful intergenerational impacts [1,16]. Given that historical experiences of violence and trauma denote significant risk for suicide, there is an urgent need to provide integrated, trauma-informed intervention services for sex workers and

other marginalized populations. Currently available interventions and pharmacological treatments for suicidality show limited efficacy, and concerted efforts should be made not only to increase access to evidence-based treatments, but also to explore alternative approaches to improving mental health and wellbeing. Emerging research and evidence show positive outcomes with psychedelic-assisted treatments, which have demonstrated an excellent record of safety with few to no serious adverse effects reported [20,22,30,61]. This study suggests psychedelic substances may hold promise as useful tools in addressing mental health issues and remediating risks for psychological distress and suicide.

CONCLUSION

The high rate of suicidality among sex workers identified in this study is a critical public health concern. In the context of emerging research and evidence on the therapeutic potential of psychedelics to treat mental health issues, our findings demonstrated that historical psychedelic use was independently associated with reduced suicidality among sex workers, while other drug use and childhood trauma increased the hazard for suicidality. This study supports calls for further research and innovative treatments and interventions to address and prevent suicide, including further investigation of the therapeutic utility of psychedelic drugs in treating mental illness and promoting mental wellness.

Acknowledgments: We thank all those who contributed their time and expertise to this project, particularly participants, AESHA community advisory board members and partner agencies. We wish to acknowledge Chrissy Taylor, Jill Chettiar, Jennifer Morris, Tina Ok, Avery Alder, Emily Groundwater, Jane Li, Sylvia Machat, Lauren Martin McCraw, Minshu Mo, Chris Rzepa, Brittany Udall, Rachel Nicoletti, Emily Sarah Leake, Ray Croy, Natalie Blair, Anita Dhanoa, Emily Sollows, Nelly Gomez, Zoe Hassall, Bridget Simpson, Krista Butler, and Peter Vann for their research and administrative support.

Contributors: EA and KS conceptualized and designed the study. EA, SAS, MB, and KS contributed to the interpretation and analysis of data. EA wrote the first draft of the manuscript. SAS, KT, MB, EW and KS contributed to reviewing and editing the manuscript. EA, SAS, KT, MB, EW and KS critically revised the manuscript and approved the final draft. KS is the guarantor.

Funding: This study was supported by the US National Institutes of Health (R01DA028648), the Canadian Institutes of Health Research (HHP-98835), and MacAIDS. KS is partially supported by a Canada Research Chair in Global Sexual Health and HIV/AIDS and the Michael Smith Foundation for Health Research. EA is supported by a Canadian Institutes of Health Research Doctoral Award. SAS is partially supported by a NIDA merit award (R37DA019829). EW is supported in part by a Tier 1 Canada Research Chair in Inner-City Medicine award. The study funders had no role in the study design, data collection, analysis, interpretation, writing of the report, or decision to submit the paper for publication.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: This study holds ethical approval through Providence Health Care/University of British Columbia Research Ethics Board.

Transparency: The study guarantor (KS) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies with the study as planned have been explained.

Data sharing: no additional data available.

REFERENCES

1 Hawton K, van Heeringen K. Suicide. *Lancet* 2009;**373**:1372–81.
2 World Health Organization. Preventing Suicide: A Global Imperative. Geneva, Switzerland: 2014. http://www.who.int/mental_health/suicide-prevention/world_report_2014/en/ (accessed Dec 2016).
3 Whiteford HA, Degenhardt L, Rehm J, *et al.* Global burden of disease attributable to mental and substance use disorders: Findings from the Global Burden of Disease Study 2010. *Lancet* 2013;**382**:1575–86.
4 Statistics Canada. Suicide Rates: An Overview. Ottawa: 2015. http://www.statcan.gc.ca/pub/82-624-x/2012001/article/11696-eng.htm (accessed Dec 2016).
5 Shannon K, Strathdee SA, Goldenberg SM, *et al.* Global epidemiology of HIV among female sex workers: Influence of structural determinants. *Lancet* 2015;**385**:55–71.
6 Argento E, Muldoon K, Duff P, *et al.* High prevalence and partner correlates of physical and sexual violence by intimate partners among street and off-street sex workers. *PLoS One* 2014;**9**:e102129.
7 Deering K, Amin A, Shoveller J, *et al.* A systematic review of the global magnitude and drivers of violence against sex workers. *Am J Public Health* 2014;**104**:e42–54.
8 Gu J, Lau JTF, Li M, *et al.* Socio-ecological factors associated with depression, suicidal ideation and suicidal attempt among female injection drug users who are sex workers in China. *Drug Alcohol Depend* 2014;**144**:102–10.
9 Zhang L, Li X, Wang B, *et al.* Violence, stigma and mental health among female sex workers in China: a structural equation modeling. *Women Health* 2016;**242**.
10 Roxburgh A, Degenhardt L, Copeland J. Posttraumatic stress disorder among female street-based sex workers in the greater Sydney area, Australia. *BMC Psychiatry* 2006;**6**:1–12.
11 Lau JTF, Tsui HY, Ho SPY, *et al.* Prevalence of psychological problems and relationships with condom use and HIV prevention behaviors among Chinese female sex workers in Hong Kong. *AIDS Care* 2010;**22**:659–68.
12 Surratt HL, Kurtz SP, Chen M, *et al.* HIV risk among female sex workers in Miami: the impact of violent victimization and untreated mental illness. *AIDS Care* 2012;**24**:553–61.
13 Hadland SE, Wood E, Dong H, *et al.* Suicide attempts and childhood maltreatment among street youth: A prospective cohort study. *Pediatrics* 2015;**136**:440–9.
14 Gilchrist G, Gruer L, Atkinson J. Comparison of drug use and psychiatric morbidity between prostitute and non-prostitute female drug users in Glasgow, Scotland. *Addict Behav* 2005;**30**:1019–23.
15 Shahmanesh M, Wayal S, Cowan F, *et al.* Suicidal behavior among female sex workers in Goa, India: The silent epidemic. *Am J Public Health* 2009;**99**:1239–46.
16 Bingham B, Leo D, Zhang R, *et al.* Generational sex work and HIV risk among Indigenous women in a street-based urban Canadian setting. Cult. Health Sex. 2014;**16**:440–52.
17 Benoit C, Carroll D, Chaudhry M. In search of a Healing Place: Aboriginal women in Vancouver's Downtown Eastside. *Soc Sci Med* 2003;**56**:821–33.
18 Li Z, Page A, Martin G, *et al.* Attributable risk of psychiatric and socio-economic factors for suicide from individual-level, population-based studies: A systematic review. *Soc Sci*

Med 2011;**72**:608–16.
19 National Action Alliance for Suicide Prevention: Research Prioritization Task Force. A Prioritized Research Agenda for Suicide Prevention: An Action Plan to Save Lives. Rockville, MD: 2014. www.suicide-research-agenda.org (accessed Dec 2016).
20 Tupper KW, Wood E, Yensen R, *et al.* Psychedelic medicine: a re-emerging therapeutic paradigm. *Can Med Assoc J* 2015;**187**:1054–9.
21 Carhart-Harris RL, Leech R, Williams TM, *et al.* Implications for psychedelic-assisted psychotherapy: Functional magnetic resonance imaging study with psilocybin. *Br J Psychiatry* 2012;**200**:238–44.
22 dos Santos RG, Osorio FL, Crippa JAS, *et al.* Antidepressive, anxiolytic, and antiaddictive effects of ayahuasca, psilocybin and lysergic acid diethylamide (LSD): a systematic review of clinical trials published in the last 25 years: antidepressive effects of ayahuasca, psilocybin and LSD. *Ther Adv Psychopharmacol* Published Online First: 2016. doi:10.1177/2045125316638008
23 Sessa B. Shaping the renaissance of psychedelic research. *Lancet* 2012;**380**:200–1.
24 Sessa B, Johnson MW. Can psychedelic compounds play a part in drug dependence therapy? *Br J Psychiatry* 2015;**206**:1–3.
25 Hendricks PS, Clark CB, Johnson MW, *et al.* Hallucinogen use predicts reduced recidivism among substance-involved offenders under community corrections supervision. *J Psychopharmacol* 2014;**28**:62–6.
26 Walsh Z, Hendricks PS, Smith S, *et al.* Hallucinogen use and intimate partner violence: Prospective evidence consistent with protective effects among men with histories of problematic substance use. *J Psychopharmacol* Published Online First: 2016. doi:10.1177/0269881116642538
27 Hendricks PS, Thorne CB, Clark CB, *et al.* Classic psychedelic use is associated with reduced psychological distress and suicidality in the United States adult population. *J Psychopharmacol* 2015;**29**:280–8.
28 Krebs TS, Johansen P-Ø. Psychedelics and mental health: a population study. *PLoS One* 2013;**8**:e63972. doi:10.1371/journal.pone.0063972
29 Johansen P-Ø, Krebs TS. Psychedelics not linked to mental health problems or suicidal behavior: A population study. *J Psychopharmacol* 2015;**29**:270–9.
30 Carhart-Harris RL, Bolstridge M, Rucker J, *et al.* Psilocybin with psychological support for treatment-resistant depression: An open-label feasibility study. *The Lancet Psychiatry* 2016;**3**:619–27.
31 Carhart-Harris RL, Kaelen M, Bolstridge M, *et al.* The paradoxical psychological effects of lysergic acid diethylamide (LSD). *Psychol Med* 2016;:1–12. doi:10.1017/S0033291715002901
32 Sanches R, de Lima Osorio F, dos Santos R, *et al.* Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: A SPECT study. *J Clin Psychopharmacol* 2016;**36**:77–81.
33 Kraehenmann R, Preller KH, Scheidegger M, *et al.* Psilocybin-induced decrease in amygdala reactivity correlates with enhanced positive mood in healthy volunteers. *Biol Psychiatry* 2015;**78**:572–81.
34 Grob CS, Danforth AL, Chopra GS, *et al.* Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Arch Gen Psychiatry* 2011;**68**:71–8.
35 Griffiths RR, Johnson MW, Richards WA, *et al.* Psilocybin occasioned mystical-type

experiences: Immediate and persisting dose-related effects. *Psychopharmacology (Berl)* 2011;**218**:649–65.

36 Roxburgh A, Degenhardt L, Copeland J, *et al.* Drug dependence and associated risks among female street-based sex workers in the Greater Sydney Area. Australia. *Subst Use Misuse* 2008;**43**:1202–17.

37 Hong Y, Zhang C, Li X, *et al.* Partner violence and psychosocial distress among female sex workers in China. *PLoS One* 2013;**8**:e62290. doi:10.1371/journal.pone.0062290

38 Dyck E. LSD: A new treatment emerging from the past. *Can Med Assoc J* 2015;**187**:1079–80.

39 Bogenschutz MP, Johnson MW. Classic hallucinogens in the treatment of addictions. *Prog Neuro-Psychopharmacology Biol Psychiatry* 2015;**64**:250–8.

40 Jung M. Associations of physical and sexual health with suicide attempts among female sex workers in South Korea. *Sex Disabil* 2013;**31**:275–86.

41 Nemoto T, Boedeker B, Iwamoto M. Social support, exposure to violence and transphobia, and correlates of depression among male-to-female transgender women with a history of sex work. *Am J Public Health* 2011;**101**:1980–8.

42 Anisman H, Du L, Palkovits M, *et al.* Serotonin receptor subtype and p11 mRNA expression in stress-relevant brain regions of suicide and control subjects. *J Psychiatry Neurosci* 2008;**33**:131–41.

43 Carhart-Harris RL, Leech R, Hellyer PJ, *et al.* The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs. *Front Hum Neurosci* 2014;**8**. doi:10.3389/fnhum.2014.00020

44 Carhart-Harris RL, Erritzoe D, Williams T, *et al.* Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proc Natl Acad Sci U S A* 2012;**109**:2138–43.

45 Osório FL, Sanches RF, Macedo LR, *et al.* Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a preliminary report. *Rev Bras Psiquiatr* 2016;**37**:13–20.

46 Gasser P, Holstein D, Michel Y, *et al.* Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. *J Nerv Ment Dis* 2014;**202**:513–20.

47 Griffiths RR, Richards WA, McCann U, *et al.* Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology (Berl)* 2006;**187**:268–83.

48 Bouso JC, Palhano-Fontes F, Rodriguez-Fornells A, *et al.* Long-term use of psychedelic drugs is associated with differences in brain structure and personality in humans. *Eur Neuropsychopharmacol* 2015;**25**:483–92.

49 Johnson MW, Garcia-Romeu A, Cosimano MP, *et al.* Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction. *J Psychopharmacol* 2014;**28**:983–92.

50 Mithoefer MC, Wagner MT, Mithoefer AT, *et al.* Durability of improvement in post-traumatic stress disorder symptoms and absence of harmful effects or drug dependency after 3,4-methylenedioxymethamphetamine-assisted psychotherapy: a prospective long-term follow-up study. *J Psychopharmacol* 2013;**27**:28–39.

51 Oehen P, Schnyder U. A randomized, controlled pilot study of MDMA (± 3,4 methylenedioxymethamphetamine)-assisted psychotherapy for treatment of resistant, chronic Post-Traumatic Stress Disorder (PTSD). *J Psychopharmacol* 2013;**27**:40–52.

52 Rio Navarro J, Cohen J, Rocillo Arechaga E, *et al.* Physical and sexual violence, mental health indicators, and treatment seeking among street-based population groups in Tegucigalpa, Honduras. *Pan Am J Public Heal* 2012;**31**:388–95.

53 Stolz J-A, Shannon K, Kerr T, *et al.* Associations between childhood maltreatment and sex work in a cohort of drug-using youth. *Soc Sci Med* 2007;**65**:1214–21.

54 Argento E, Chettiar J, Nguyen P, *et al.* Prevalence and correlates of nonmedical prescription opioid use among a cohort of sex workers in Vancouver, Canada. *Int J Drug Policy* 2015;**26**:59–66.

55 Kerr T, Stoltz J, Marshall BDL, *et al.* Childhood Trauma and Injection Drug Use among High-Risk Youth. *J Adolesc Heal* 2009;**45**:300–2.

56 Ulibarri MD, Strathdee S a, Lozada R, *et al.* Intimate partner violence among female sex workers in two Mexico-U.S. border cities: partner characteristics and HIV risk-behaviors as correlates of abuse. *Psychol Trauma Theory, Res Pract Policy* 2010;**2**:318–25.

57 Argento E, Strathdee S, Goldenberg S, *et al.* Violence, trauma and living with HIV: Longitudinal predictors of initiating crystal methamphetamine injection among sex workers. *Drug Alcohol Depend* 2016 (submitted).

58 Tull MT, Gratz KL, Aklin WM, *et al.* A preliminary examination of the relationships between posttraumatic stress symptoms and crack/cocaine, heroin, and alcohol dependence. *J Anxiety Disord* 2010;**24**:55–62.

59 Romero-Daza N, Weeks M, Singer M. Conceptualizing the impact of indirect violence on HIV risk among women involved in street-level prostitution. *Aggress Violent Behav* 2005;**10**:153–70.

60 Wang B, Li X, Stanton B, *et al.* Sexual coercion, HIV-related risk, and mental health among female sex workers in China. *Health Care Women Int* 2007;**28**:745–62.

61 Morgan CJA, Muetzelfeldt L, Muetzelfeldt M, *et al.* Harms associated with psychoactive substances: findings of the UK National Drug Survey. *J Psychopharmacol* 2010;**24**:147–53.

Table 1: Baseline characteristics of sex workers in Vancouver who thought about or attempted suicide over follow-up, compared to those who did not (N=290)

Characteristics	Suicidality n=31 (11%)	No Suicidality n=259 (89%)	p-value
Age (median, IQR)	34 (27 to 47)	36 (29 to 42)	0.767
Gender/sexual minority	7 (22.6)	38 (14.7)	0.291
Born in Canada	29 (93.6)	156 (60.2)	<0.001
Indigenous ancestry	18 (58.1)	75 (29.0)	0.001
Education, high school or greater	10 (32.3)	142 (54.8)	0.017
HIV seropositivity†	7 (22.6)	26 (10.0)	0.065
STI seropositivity†	3 (9.7)	35 (13.5)	0.778
Homelessness†	10 (32.3)	63 (24.3)	0.336
Psychedelic use	8 (25.8)	71 (27.4)	0.849
Marijuana use	27 (87.1)	152 (58.7)	0.002
Prescription opioid use	12 (38.7)	77 (29.7)	0.306
Crack use	27 (87.1)	157 (60.6)	0.004
Cocaine use	25 (80.7)	137 (52.9)	0.003
Crystal meth use	18 (58.1)	72 (27.8)	<0.001
Heroin use	21 (67.7)	120 (46.3)	0.024
Non-injection drug use†	27 (87.1)	148 (57.1)	0.001
Injection drug use†	16 (51.6)	81 (31.3)	0.023
Physical/sexual client violence†	5 (16.1)	36 (13.9)	0.784
Physical/sexual childhood abuse	24 (77.4)	112 (43.2)	<0.001
Police harassment/arrest†	16 (51.6)	91 (35.1)	0.072
Primary place to solicit clients†			
Street/public space	24 (77.4)	118 (45.6)	0.002
Indoor/in-call venue	3 (9.7)	103 (39.8)	-
Independent/self-advertising (e.g., newspapers, online)	4 (12.9)	38 (14.7)	-

† In the last 6 months

Table 2: Unadjusted and adjusted hazard ratios for predictors of time to suicidality among sex workers in Vancouver, 2010-2014 (N=290)

Characteristics	Unadjusted Hazard Ratio (95%CI)	p-value	Adjusted Hazard Ratio (95%CI)	p-value
Psychedelic use	1.00 (0.45 to 2.23)	0.995	0.40 (0.17 to 0.94)	0.036
Marijuana use	3.44 (1.21 to 9.79)	0.021	-	-
Prescription opioid use	1.88 (0.91 to 3.90)	0.089	-	-
Crack use	3.06 (1.07 to 8.74)	0.037	-	-
Cocaine use	2.53 (1.03 to 6.22)	0.043	-	-
Crystal meth use	3.73 (1.75 to 7.97)	<0.001	3.25 (1.47 to 7.21)	0.004
Heroin use	2.26 (0.99 to 5.13)	0.053	-	-
HIV seropositivity†	2.15 (0.92 to 5.06)	0.078	-	-
Childhood abuse	3.92 (1.69 to 9.09)	0.002	3.54 (1.49 to 8.40)	0.004
Indigenous ancestry	2.76 (1.34 to 5.67)	0.006	-	-
Canadian born	6.72 (1.62 to 27.95)	0.009	-	-
Homelessness†	2.55 (1.19 to 5.44)	0.016	1.95 (0.91 to 4.17)	0.085
Primary place to solicit clients†				
Indoor venue (vs. street)	0.19 (0.06 to 0.66)	0.009	-	-
Independent (vs. street)	0.38 (0.14 to 1.05)	0.061	-	-

† In the last 6 months

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page, 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3, 4
Objectives	3	State specific objectives, including any prespecified hypotheses	4, 5
Methods			
Study design	4	Present key elements of study design early in the paper	5, 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5, 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	5, 10
Study size	10	Explain how the study size was arrived at	6, 7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6, 7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6, 7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how loss to follow-up was addressed	7
		(*e*) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7, 8
		(b) Give reasons for non-participation at each stage	6, 7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-9, 19, 20
		(b) Indicate number of participants with missing data for each variable of interest	7, 8
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 20, 7
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9, 10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Does psychedelic drug use reduce risk of suicidality? Evidence from a longitudinal community-based cohort of marginalized women in a Canadian setting

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016025.R1
Article Type:	Research
Date Submitted by the Author:	13-Jun-2017
Complete List of Authors:	Argento, Elena; BC Centre for Excellence in HIV/AIDS; University of British Columbia, Interdisciplinary Studies Strathdee, Steffanie; University of California San Diego, Medicine Tupper, Kenneth; University of British Columbia, School of Population and Public Health Braschel, Melissa; BC Centre for Excellence in HIV/AIDS, Gender and Sexual Health Initiative Wood, Evan; BC Centre for Excellence in HIVAIDS Shannon, Kate; British Columbia Centre for Excellence in HIVAIDS; University of British Columbia, Division of AIDS Department of Medicine
Primary Subject Heading:	Public health
Secondary Subject Heading:	Evidence based practice, Epidemiology, Mental health
Keywords:	sex workers, psychedelics, hallucinogens, MENTAL HEALTH, Suicide & self-harm < PSYCHIATRY

Does psychedelic drug use reduce risk of suicidality? Evidence from a longitudinal community-based cohort of marginalized women in a Canadian setting

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Word Count: 3197

ABSTRACT

Objective: This study aimed to longitudinally investigate whether ever having used a psychedelic drug can have a protective effect on incidence of suicidality among marginalized women.

Design: Longitudinal community-based cohort study.

Setting: Data were drawn from a prospective, community-based cohort of marginalized women in Metro Vancouver, Canada.

Participants: 766 women completed the baseline questionnaire between January 2010 and August 2014. Participants who did not report suicidality at baseline and who completed at least one follow-up visit were included.

Main outcome measure: Extended Cox regression was used to model predictors of new suicidality (suicide ideation or attempts) over 54 months follow-up.

Results: Nearly half (46%; n=355) of participants reported prior suicidality and were thus excluded from the present analyses. Of 290 women eligible at baseline, 11% (n=31) reported recent suicidality during follow-up, with an incidence density of 4.42 per 100 person-years (95% Confidence Interval [CI] 3.10 to 6.30). In multivariable analysis, reported lifetime psychedelic drug use was associated with a 60% reduced hazard for suicidality (Adjusted Hazard Ratio [AHR] 0.40; 95%CI 0.17 to 0.94). Crystal methamphetamine use (AHR 3.25; 95%CI 1.47 to 7.21) and childhood abuse (AHR 3.54; 95%CI 1.49 to 8.40) remained independent predictors of suicidality.

Conclusion: The high rate of suicidality identified in this study is of major concern. Alongside emerging evidence on the potential of psychedelic-assisted therapy to treat some mental illness and addiction issues, our findings demonstrate that naturalistic psychedelic drug use is independently associated with reduced suicidality, while other illicit drug use and childhood trauma predispose women to suicidality. While observational, this study supports calls for further investigation of the therapeutic utility of psychedelic drugs in treating mental illness and promoting mental wellness.

Word Count: 277
Keywords: *women, psychedelics, hallucinogens, suicide prevention, mental health, substance use*

Strengths and limitations of this study

- This is the first study to longitudinally investigate the potential protective effect of psychedelic drug use on suicidality, drawing from a large, community-based cohort of marginalized women.
- Multivariable Cox regression analyses were used to examine the impact of lifetime psychedelic drug use on incidence of suicidality among a marginalized population.
- The associations between specific psychedelics, contexts of their use, and suicidality were not explored in this study.
- Not all potential confounding variables could be controlled for in this study and the associations uncovered cannot be determined as causal.
- Data were self-reported and variables examined included highly stigmatized topics, introducing the potential for recall bias, social desirability and reporting bias.

INTRODUCTION

Despite efforts to improve mental health over the last 60 years, suicide remains a critical public health concern worldwide [1,2]. Suicide was the second leading cause of death globally in 2012 among 15-29 year olds [2], with an estimated 80-90% of suicide deaths attributable to mental health or substance use disorders [3,4]. Significant gaps remain in empirical research examining suicidality among marginalized populations. Marginalized women, such as sex workers who are street-involved or use drugs, experience disproportionately high levels of social and health-related risks and harms, including stigma, discrimination, and violence [5–7] as a result of dynamic structural drivers including poverty, criminalization, and racism. While sex workers are a diverse population working from indoor in-call and out-call venues to street-based settings, previous studies highlight substantial unmet mental health needs of more marginalized and street-involved sex workers. Studies among street-based sex workers and those who use drugs underscore the associations of social exclusion, depression, and post-traumatic stress disorder (PTSD) with suicidality [8–12]. Research demonstrates greater risk for suicidality among those with a history of trauma [1,13,14] and among women sex workers who report historical experiences of violence and childhood abuse [8–10,15,16]. Further, Indigenous women are vastly overrepresented among street-based sex workers in North America, and face devastating and multigenerational effects of trauma and socio-economic dislocation (e.g., high burden of mental illness and suicidality) as a result of colonialism, racialized policies, and displacement from land and home communities [17,18].

Various biological, interpersonal, and socio-structural factors (e.g., social exclusion/isolation, education level, employment) contribute to our understanding of suicidal behaviors [1,19]. While

evidence has demonstrated that some forms of cognitive behavioral therapy and pharmacological interventions may reduce suicidality, the literature is hampered by publication bias and significant heterogeneity of strategies and outcome measures [14,20]. There remains an urgency to better understand pathways to suicidality, with data highlighting the need for tailored intervention approaches for key marginalized populations [20,21]. Given the complex etiological pathways to suicide and limited effectiveness of well-established evidence-based interventions to reduce the burden of suicidality, the US National Institute of Mental Health has called for innovative research on suicide prevention and treatment for suicidality [22].

A number of psychedelic drug therapies are being revisited following a 40-year hiatus in research into their potential for the treatment of depression, anxiety, PTSD, eating disorders, and addiction [23]. Psychedelic drugs include the classic serotonergic psychedelics or "hallucinogens" lysergic acid diethylamide (LSD), psilocybin, dimethyltryptamine (DMT), and mescaline, as well as the "enactogen" or "empathogen" methylenedioxymethamphetamine (MDMA) [23–25], all of which are being investigated in clinical/pre-clinical studies for their neuropharmacological functions and potential as adjuncts to psychotherapy [26–28]. While renewed interest in psychedelic medicine is challenged by various funding, methodological, and legal impediments, the emerging evidence indicating improved outcomes for some individuals suffering from mental health and addiction issues has generated new scientific inquiry and an imposing obligation to advance this research [23,29,30]. Recent observational studies in the US demonstrate significant associations between lifetime psychedelic use and reduced recidivism and intimate partner violence among populations of prison inmates [31,32], and reduced psychological distress and suicidality among the general adult population [33–35].

Despite the multifaceted vulnerabilities experienced by marginalized sex workers, there remains a paucity of data on suicide rates and research that systematically examines factors that potentiate or mitigate suicidality among sex workers, particularly in the global north. Some evidence suggests that psychedelic drug use may be protective with regard to suicidality [33–35] and is associated with significant improvements in psychological wellbeing and reductions in depression and anxiety in clinical settings [36–41], yet existent research is characterized by large gaps. Given the urgency of addressing and preventing suicide and calls for prioritizing innovative interventions, this study aimed to longitudinally investigate whether lifetime psychedelic drug use is associated with a reduced incidence of suicidality (suicide ideation or attempts) among a cohort of marginalized women. We postulated that psychedelic drug use would have an independent protective effect on suicidality over the study period.

METHODS

Study Design and Participants

Data for this study were drawn from a large, community-based, prospective cohort of women sex workers initiated in 2010, known as AESHA (An Evaluation of Sex Workers Health Access). Eligibility criteria for study participants included cisgender or transgender women, 14 years of age or older, who exchanged sex for money within the last 30 days. AESHA participants completed interviewer-administered questionnaires and HIV/STI/HCV serology testing at enrollment and biannually. Interview, outreach and nursing staff included experiential individuals (current/former sex workers) with substantial community experience. Participants were recruited across Metro Vancouver using time-location sampling and community mapping

strategies, with day and late-night outreach to outdoor sex work locations (i.e., streets, alleyways), indoor sex work venues (i.e., massage parlors, micro-brothels, and in-call locations), and online. Weekly outreach is conducted to over 100 sex work venues by outreach/nursing teams operating a mobile van, with regular contact as well as encouraging drop-in to women-only spaces at the research office, contributing to an annual retention rate of >90% for AESHA participants.

The main interview questionnaire elicits responses related to socio-demographics (e.g., sexual identity, ethnicity, housing), the work environment (e.g., access to services, violence/safety, policing, incarceration), client characteristics (e.g., types/fees of services, condom use), intimate partners (e.g., sexual history, cohabitation, financial support), trauma and violence (e.g., lifetime and childhood trauma, exposure to intimate partner and workplace violence), and comprehensive injection and non-injection drug use patterns. The clinical questionnaire relates to overall physical, mental, and emotional health, and HIV testing and treatment experiences to support education, referral, and linkages with care. The research team works in close partnership with the affected community and a diversity of stakeholders (e.g., legal/human rights experts, community-based organizations, service providers, health authorities, government officials, and international policy bodies) and regularly engages in knowledge exchange efforts. AESHA is monitored by a Community Advisory Board of over 15 sex work, women's health and HIV service agencies, as well as representatives from the health authority and policy experts, and holds ethical approval through Providence Health Care/University of British Columbia Research Ethics Board. All participants receive an honorarium of $40 CAD at each bi-annual visit for their time, expertise and travel.

Analyses for this study were restricted to AESHA participants who had never thought about or attempted suicide at baseline and completed at least one follow-up visit between January 2010 and August 2014. Those with missing observations for suicidality at baseline (n=50/766; 6.5%) were excluded from analysis, and one additional participant was excluded because reported suicidality was missing at follow-up.

Statistical Analyses

The outcome of interest was a first episode of suicidality, defined as responding 'yes' to having thought about or attempted suicide in the last six months. Time-fixed variables examined included age (continuous), gender/sexual minority (lesbian, gay, bisexual, trans, or two-spirit), Indigenous ancestry (inclusive of First Nations, Métis, and Inuit), being an im/migrant worker (versus Canadian born), education (high school or greater), and physical and/or sexual childhood abuse (before age 18). Variables treated as time-updated covariates based on bi-annual follow-up data included HIV/STI serostatus, recent homelessness, recent physical and/or sexual violence by clients, recent police harassment and/or arrest, and primary place to solicit clients. Time-updated injection and non-injection drug use variables included lifetime use of psychedelics (including LSD/acid, magic mushrooms/psilocybin, ecstasy/MDMA), cannabis, pharmaceutical opioids (any street methadone/suboxone, dilaudid, morphine, oxycontin, percocet/vicodin/demerol, or T3s/T4s), crack, cocaine, crystal methamphetamine, and heroin.

Using extended Cox regression, unadjusted and adjusted hazard ratios (HR and AHR) and 95% confidence intervals (CI) were calculated to identify predictors of suicidality. Variables

hypothesized a priori to be predictors of suicidality (e.g., psychedelic drug use) and those that were significantly correlated with the outcome at the $p<0.05$ level in bivariate analyses were subsequently fitted into a multivariable Cox model. Backward model selection was used to determine the final multivariable model with the best overall fit, as indicated by the lowest Akaike information criterion (AIC) value. A complete case analysis was used, where observations with missing data were excluded from analyses, and participants who were lost to follow-up were right censored at their most recent study visit. All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA). Two-sided p-values are reported.

RESULTS

Socio-Demographic Characteristics

Of the total 766 women who completed the baseline questionnaire, 46% (n=355) reported ever experiencing suicidality (45%; n=343 reported suicidal thoughts, 32%; n=245 attempted suicide) and were thus excluded from this analysis. A total of 290 women without suicidality who completed at least one follow-up visit were eligible for inclusion in the present analysis. Participants were followed for a total of 53.5 months (median = 29.9 months). Baseline characteristics of participants who reported suicidality during follow-up compared to those who did not are displayed in Table 1.

Overall, 11% (n=31) thought about or attempted suicide for the first time during follow-up, with an incidence density of 4.42 per 100 person-years (95%CI 3.10 to 6.30). The median age was 36 (interquartile range [IQR] 29 to 42) and 16% (n=45) of participants identified as gender or sexual

minorities. One third (n=93) identified as Indigenous and one quarter (n=73) had been homeless in the last six months. Half of participants (49%; n=142) solicited clients on the streets, and 37% (n=106) solicited clients in indoor establishments. In terms of workplace violence, 14% (n=41) and 37% (n=107) reported physical/sexual violence from clients and police harassment/arrest, respectively. Nearly half (47%; n=136) of participants reported ever being physically and/or sexually abused before age 18, and among those who reported suicidality, 77% (n=24/31) experienced childhood abuse compared to 43% (n=112/259) among those who did not report suicidality (p<0.001).

Substance Use

Over half of participants reported ever using crack (63%, n=184) or cocaine (56%; n=162), with higher proportions of crack and cocaine use among those reporting suicidality than those who did not (p=0.003). Close to half (49%, n=141) reported lifetime heroin use, which was significantly higher among those who reported suicidality than those who did not (68% vs. 46%, p=0.02). Approximately one third (31%, n=90) of participants had ever used crystal methamphetamine, and this was significantly higher among those who reported suicidality than those who did not (58% vs. 28%, p<0.001). Overall, 27% (n=79) of participants reported ever using a psychedelic substance, and of those, 75% (n=59) had used MDMA/ecstasy, 35% (n=28) had used LSD/acid, and 30% (n=24) had used psilocybin/magic mushrooms.

Bivariate and Multivariable Cox Analyses

Unadjusted and adjusted hazard ratios for factors associated with a first episode of suicidality during follow-up are displayed in Table 2. In the final multivariable model, crystal

methamphetamine use (AHR 3.25; 95%CI 1.47 to 7.21) and physical and/or sexual childhood abuse (AHR 3.54; 95%CI 1.49 to 8.40) remained independently associated with time to suicidality. Psychedelic use was associated with a 60% reduced hazard of suicidality (AHR 0.40; 95%CI 0.17 to 0.94).

DISCUSSION

This study demonstrated that among marginalized women, many of whom are street-involved and experience a disproportionate burden of violence, trauma, psychological distress and suicide, naturalistic psychedelic drug use predicted a significantly reduced hazard for suicidality. Crystal methamphetamine use and childhood abuse predisposed women to suicidality corresponding to more than a three-fold increased hazard. Suicidality was highly prevalent, with almost half of women reporting lifetime suicidality at baseline, and 11% reporting a first episode of suicidality in the last six months during follow-up. Few studies have longitudinally examined predictors of suicidality among marginalized sex workers, and of the available data, most are cross-sectional and/or conducted in lower and middle income settings [8,16,42,43]. The present study, based on a community-based, prospective cohort of marginalized women, adds to a growing body of literature documenting the protective and therapeutic potentials of psychedelic substances [23,29,39,44,45].

Data were self-reported, and questions pertaining to events that occurred in the past may be subject to recall bias. Variables examined included sensitive and highly stigmatized topics such as childhood trauma, violence, and illicit drug use, which introduce the potential for social desirability and reporting bias. However, the likelihood of these biases is reduced by the

community-based nature of the study. While lifetime psychedelic drug use was found to reduce the hazard of suicidality, the associations uncovered in this analysis cannot be determined as causal. Suicidality is influenced by complex individual, interpersonal and structural variables, and not all potential confounding variables could be controlled for in this study. For example, women who use psychedelics may also possess some characteristic(s) associated with a reduced likelihood of being suicidal (e.g., openness to experience, curiosity, or spirituality), which were not examined in this study. Despite the relative safety of psychedelic drug use as evidenced from the clinical and non-clinical literature [36,46–49], it should be noted that the use of psychedelics, particularly with unknown doses sourced from unregulated street markets, is not without risk, highlighting the importance of set and setting [23]; the doses and contexts of psychedelic use among women in the present study could not be determined. The standard error for the association between psychedelic use and suicidality was somewhat high, resulting in a wider confidence interval. However, a large and significant protective effect was demonstrated in multivariable analysis, despite the relatively small number of events for suicidality over follow-up. With a larger sample size, we would expect a narrower confidence interval for this association. The study population included women from a wide-ranging representation of sex work environments, yet findings may not be fully generalizable to sex workers in other settings. The mapping of working areas and time–location sampling helped to ensure a representative sample and to minimize selection bias.

This study is the first to longitudinally investigate associations with suicidality among women sex workers in North America, and builds upon prior cross-sectional research highlighting significantly elevated rates of suicidality and unmet mental health needs in this population. For

example, a study conducted in Sydney, Australia demonstrated significant links between depression, trauma, and suicidality, where an estimated 42% of street-based female sex workers reported attempting suicide and 74% reported lifetime suicidal ideation [10,42]. While estimates of mental illness vary significantly across sex work settings, up to three-quarters of street- and drug-involved sex workers in a US study reported severe depression, anxiety, or PTSD [12]. Notably, our study demonstrated a lower risk of suicidality among women working indoors in bivariate analysis (HR 0.19, p=0.009), lending support to the critical role of safer workplace environments in mitigating risk. In studies conducted in Asia, recent suicide attempts ranged from 19% among sex workers in Goa, India [16] to 38% among sex workers in China [8,11,50], many of whom work in marginalized settings with few workplace protections. Transgender women involved in sex work, a sub-population experiencing significant psychosocial vulnerability and discrimination, report notably further elevated rates of suicidality: three quarters of participants in San Francisco reported suicide ideation, of whom 64% attempted suicide [51]. Our findings extend upon research establishing associations between lifetime use of illicit drugs and increased risk for suicidality: in bivariate analysis, all classes of illicit drugs were demonstrated to increase the hazard of suicidality with the exception of psychedelics. In multivariable analysis, psychedelics were independently associated with a 60% reduced hazard for suicidality, contributing to emergent evidence on the potential of psychedelics to mitigate risks for suicide.

Among the various scientific studies examining the potential benefits of psychedelic drug use, a recent and large (n>190,000) population study conducted among adult respondents in the US demonstrated that psychedelics are associated with reduced psychological distress and suicidality

[33]. A recent open-label trial conducted in the UK demonstrated the safety and efficacy of psilocybin for treating major depression [36], and another open-label trial in Brazil found rapid and sustained anti-depressant effects from the Amazonian psychedelic brew ayahuasca administered in a clinical setting [38]. The ways in which psychedelics may alleviate suffering associated with some mental illness is undoubtedly a complex phenomenon. It has been hypothesized that psychedelics modify neurobiological processes that may be involved in suicidality by down-regulating 5-HT_{2A} serotonin receptors, as increased binding (and up-regulation) of this receptor has been implicated in major depression and suicide [39,45,52]. Further, there is evidence that psychedelics alter neural network connectivity and enhance recall of autobiographical memories, which may facilitate positive reprocessing of trauma [26,53,54]. Recent randomized, placebo-controlled, cross-over studies found that psilocybin (among n=25 adults) and LSD (among n=20 adults) were associated with increased positive mood and psychological wellbeing [37,39], supporting other work demonstrating the anti-depressive/anxiolytic effects of psychedelics [27,40,55,46]. The potential of psychedelics to elicit "mystical-type" experiences, with profound and sustained positive changes in attitudes and mood, may play a key role in addiction treatment interventions [41,45,56,57]. For example, psilocybin-assisted psychotherapy demonstrated high success in smoking cessation outcomes at six months follow-up (abstinence rates of 80%), and mystical experiences generated from the psilocybin sessions were significantly correlated with elevated ratings of personal meaningfulness, wellbeing, and life satisfaction [58]. Randomized control trials in the US and Switzerland have demonstrated significant long-term improvements among patients with treatment-resistant PTSD following MDMA-assisted psychotherapy [59,28], and further research is continuing in an international multi-site phase 3 clinical trial.

Marginalized and street-based sex workers experience complex and synergistic effects between trauma, lack of workplace safety, and mental health/substance use comorbidities that elevate risk of suicidality. Marginalized women and sex workers who use drugs report high rates of childhood abuse [60–62], which is associated with an increased likelihood of experiencing subsequent physical or sexual violence, as well as initiating injection drug use [63–65]. For those suffering from emotional trauma stemming from violence, including indirect violence (i.e., witnessing violence), there may be a proclivity to use drugs for self-medication [66,67]. Violence and sexual coercion have been found to be significantly associated with suicidality among sex worker populations in China and India [8,9,16,68]. As demonstrated in this study, having an early traumatic life event is a key risk factor for suicide among sex workers, a high proportion of whom are Indigenous, and experiencing historical trauma can have harmful intergenerational impacts [1,17]. Given that historical experiences of violence and trauma denote significant risk for suicide, there is an urgent need to provide integrated, trauma-informed intervention services for sex workers and other marginalized populations. Currently available interventions and pharmacological treatments for suicidality show limited efficacy, and concerted efforts should be made not only to increase access to evidence-based treatments, but also to explore alternative approaches to improving mental health and wellbeing. Emerging research and evidence show positive outcomes with psychedelic-assisted treatments, which have demonstrated an excellent record of safety with few to no serious adverse effects reported [23,27,36,69]. This study suggests psychedelic substances may hold promise as useful tools in addressing mental health issues and remediating risks for psychological distress and suicide.

CONCLUSION

The high rate of suicidality among marginalized women identified in this study is a critical public health concern. In the context of emerging research and evidence on the therapeutic potential of psychedelics to treat mental health issues, our findings demonstrated that naturalistic psychedelic use was independently associated with reduced suicidality among sex workers, while other drug use and childhood trauma increased the hazard for suicidality. This is the first study to longitudinally investigate the relationship between psychedelic drug use and suicidality. While observational, this study supports calls for further investigation of the therapeutic utility of psychedelic drugs in treating mental illness and promoting mental wellness.

Acknowledgments: We thank all those who contributed their time and expertise to this project, particularly participants, AESHA community advisory board members and partner agencies. We wish to acknowledge Chrissy Taylor, Jill Chettiar, Jennifer Morris, Tina Ok, Avery Alder, Emily Groundwater, Jane Li, Sylvia Machat, Lauren Martin McCraw, Minshu Mo, Chris Rzepa, Brittany Udall, Rachel Nicoletti, Emily Sarah Leake, Ray Croy, Natalie Blair, Anita Dhanoa, Emily Sollows, Nelly Gomez, Zoe Hassall, Bridget Simpson, Krista Butler, and Peter Vann for their research and administrative support.

Contributors: EA and KS conceptualized and designed the study. EA, SAS, MB, and KS contributed to the interpretation and analysis of data. EA wrote the first draft of the manuscript. SAS, KT, MB, EW and KS contributed to reviewing and editing the manuscript. EA, SAS, KT, MB, EW and KS critically revised the manuscript and approved the final draft. KS is the guarantor.

Funding: This study was supported by the US National Institutes of Health (R01DA028648), the Canadian Institutes of Health Research (HHP-98835), and MacAIDS. KS is partially supported by a Canada Research Chair in Global Sexual Health and HIV/AIDS and the Michael Smith Foundation for Health Research. EA is supported by a Canadian Institutes of Health Research Doctoral Award. SAS is partially supported by a NIDA merit award (R37DA019829). EW is supported in part by a Tier 1 Canada Research Chair in Inner-City Medicine award. The study funders had no role in the study design, data collection, analysis, interpretation, writing of the report, or decision to submit the paper for publication.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: This study holds ethical approval through Providence Health Care/University of British Columbia Research Ethics Board.

Transparency: The study guarantor (KS) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies with the study as planned have been explained.

Data sharing: no additional data available.

REFERENCES

1 Hawton K, van Heeringen K. Suicide. *Lancet* 2009;**373**:1372–81.
2 World Health Organization. Preventing Suicide: A Global Imperative. Geneva, Switzerland: 2014. http://www.who.int/mental_health/suicide-prevention/world_report_2014/en/ (accessed Dec 2016).
3 Whiteford HA, Degenhardt L, Rehm J, *et al.* Global burden of disease attributable to mental and substance use disorders: Findings from the Global Burden of Disease Study 2010. *Lancet* 2013;**382**:1575–86.
4 Statistics Canada. Suicide Rates: An Overview. Ottawa: 2015. http://www.statcan.gc.ca/pub/82-624-x/2012001/article/11696-eng.htm (accessed Dec 2016).
5 Shannon K, Strathdee SA, Goldenberg SM, *et al.* Global epidemiology of HIV among female sex workers: Influence of structural determinants. *Lancet* 2015;**385**:55–71.
6 Argento E, Muldoon K, Duff P, *et al.* High prevalence and partner correlates of physical and sexual violence by intimate partners among street and off-street sex workers. *PLoS One* 2014;**9**:e102129.
7 Deering K, Amin A, Shoveller J, *et al.* A systematic review of the global magnitude and drivers of violence against sex workers. *Am J Public Health* 2014;**104**:e42–54.
8 Gu J, Lau JTF, Li M, *et al.* Socio-ecological factors associated with depression, suicidal ideation and suicidal attempt among female injection drug users who are sex workers in China. *Drug Alcohol Depend* 2014;**144**:102–10.
9 Zhang L, Li X, Wang B, *et al.* Violence, stigma and mental health among female sex workers in China: a structural equation modeling. *Women Health* 2016;**242**. \
10 Roxburgh A, Degenhardt L, Copeland J. Posttraumatic stress disorder among female street-based sex workers in the greater Sydney area, Australia. *BMC Psychiatry* 2006;**6**:1–12.
11 Lau JTF, Tsui HY, Ho SPY, *et al.* Prevalence of psychological problems and relationships with condom use and HIV prevention behaviors among Chinese female sex workers in Hong Kong. *AIDS Care* 2010;**22**:659–68.
12 Surratt HL, Kurtz SP, Chen M, *et al.* HIV risk among female sex workers in Miami: the impact of violent victimization and untreated mental illness. *AIDS Care* 2012;**24**:553–61.
13 Hadland SE, Marshall BDL, Kerr T, *et al.* Suicide and history of childhood trauma among street youth. *J Affect Disord* 2012;**136**:377–80.
14 O'Connor RC, Nock MK. The psychology of suicidal behaviour. *The Lancet Psychiatry* 2014;**1**:73–85.
15 Gilchrist G, Gruer L, Atkinson J. Comparison of drug use and psychiatric morbidity between prostitute and non-prostitute female drug users in Glasgow, Scotland. *Addict Behav* 2005;**30**:1019–23.
16 Shahmanesh M, Wayal S, Cowan F, *et al.* Suicidal behavior among female sex workers in Goa, India: The silent epidemic. *Am J Public Health* 2009;**99**:1239–46.
17 Bingham B, Leo D, Zhang R, *et al.* Generational sex work and HIV risk among Indigenous women in a street-based urban Canadian setting. Cult. Health Sex. 2014;**16**:440–52.
18 Benoit C, Carroll D, Chaudhry M. In search of a Healing Place: Aboriginal women in Vancouver's Downtown Eastside. *Soc Sci Med* 2003;**56**:821–33.

19 Li Z, Page A, Martin G, *et al.* Attributable risk of psychiatric and socio-economic factors for suicide from individual-level, population-based studies: A systematic review. *Soc Sci Med* 2011;**72**:608–16.

20 Zalsman G, Hawton K, Wasserman D, *et al.* Suicide prevention strategies revisited: 10-year systematic review. *The Lancet Psychiatry* 2016;**3**:646–59.

21 Klonsky ED, May AM, Saffer BY. Suicide, Suicide Attempts, and Suicidal Ideation. *Annu Rev Clin Psychol* 2016;**12**:307–30.

22 National Action Alliance for Suicide Prevention: Research Prioritization Task Force. A Prioritized Research Agenda for Suicide Prevention: An Action Plan to Save Lives. Rockville, MD: 2014. www.suicide-research-agenda.org (accessed Dec 2016).

23 Tupper K, Wood E, Yensen R, *et al.* Psychedelic medicine: a re-emerging therapeutic paradigm. *Can Med Assoc J* 2015;**187**:1054–9.

24 Nichols DE. Hallucinogens. *Pharmacol Ther* 2004;**101**:131–81.

25 Bedi G, Hyman D, De Wit H. Is ecstasy an 'empathogen'? Effects of 3,4-methylenedioxymethamphetamine on prosocial feelings and identification of emotional states in others. *Biol Psychiatry* 2010;**68**:1134–40.

26 Carhart-Harris RL, Leech R, Williams TM, *et al.* Implications for psychedelic-assisted psychotherapy: Functional magnetic resonance imaging study with psilocybin. *Br J Psychiatry* 2012;**200**:238–44.

27 dos Santos RG, Osorio FL, Crippa JAS, *et al.* Antidepressive, anxiolytic, and antiaddictive effects of ayahuasca, psilocybin and lysergic acid diethylamide (LSD): a systematic review of clinical trials published in the last 25 years: antidepressive effects of ayahuasca, psilocybin and LSD. *Ther Adv Psychopharmacol* 2016;**6**:193-213.

28 Oehen P, Schnyder U. A randomized, controlled pilot study of MDMA (± 3,4 methylenedioxymethamphetamine)-assisted psychotherapy for treatment of resistant, chronic Post-Traumatic Stress Disorder (PTSD). *J Psychopharmacol* 2013;**27**:40–52.

29 Sessa B. Shaping the renaissance of psychedelic research. *Lancet* 2012;**380**:200–1.

30 Sessa B, Johnson MW. Can psychedelic compounds play a part in drug dependence therapy? *Br J Psychiatry* 2015;**206**:1–3.

31 Hendricks PS, Clark CB, Johnson MW, *et al.* Hallucinogen use predicts reduced recidivism among substance-involved offenders under community corrections supervision. *J Psychopharmacol* 2014;**28**:62–6.

32 Walsh Z, Hendricks PS, Smith S, *et al.* Hallucinogen use and intimate partner violence: Prospective evidence consistent with protective effects among men with histories of problematic substance use. *J Psychopharmacol* 2016;**30**:601-607.

33 Hendricks PS, Thorne CB, Clark CB, *et al.* Classic psychedelic use is associated with reduced psychological distress and suicidality in the United States adult population. *J Psychopharmacol* 2015;**29**:280–8.

34 Krebs TS, Johansen P-Ø. Psychedelics and mental health: a population study. *PLoS One* 2013;**8**:e63972. doi:10.1371/journal.pone.0063972

35 Johansen P-Ø, Krebs TS. Psychedelics not linked to mental health problems or suicidal behavior: A population study. *J Psychopharmacol* 2015;**29**:270–9.

36 Carhart-Harris RL, Bolstridge M, Rucker J, *et al.* Psilocybin with psychological support for treatment-resistant depression: An open-label feasibility study. *The Lancet Psychiatry* 2016;**3**:619–27.

37 Carhart-Harris R, Kaelen M, Bolstridge M, *et al.* The paradoxical psychological effects of

lysergic acid diethylamide (LSD). *Psychol Med* 2016;1–12. doi:10.1017/S0033291715002901

38 Sanches R, de Lima Osorio F, dos Santos R, *et al.* Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: A SPECT study. *J Clin Psychopharmacol* 2016;**36**:77–81.

39 Kraehenmann R, Preller KH, Scheidegger M, *et al.* Psilocybin-induced decrease in amygdala reactivity correlates with enhanced positive mood in healthy volunteers. *Biol Psychiatry* 2015;**78**:572–81.

40 Grob CS, Danforth AL, Chopra GS, *et al.* Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Arch Gen Psychiatry* 2011;**68**:71–8.

41 Griffiths RR, Johnson MW, Richards WA, *et al.* Psilocybin occasioned mystical-type experiences: Immediate and persisting dose-related effects. *Psychopharmacology (Berl)* 2011;**218**:649–65.

42 Roxburgh A, Degenhardt L, Copeland J, *et al.* Drug dependence and associated risks among female street-based sex workers in the Greater Sydney Area. Australia. *Subst Use Misuse* 2008;**43**:1202–17.

43 Hong Y, Zhang C, Li X, *et al.* Partner violence and psychosocial distress among female sex workers in China. *PLoS One* 2013;**8**:e62290. doi:10.1371/journal.pone.0062290

44 Dyck E. LSD: A new treatment emerging from the past. *Can Med Assoc J* 2015;**187**:1079–80.

45 Bogenschutz MP, Johnson MW. Classic hallucinogens in the treatment of addictions. *Prog Neuro-Psychopharmacology Biol Psychiatry* 2015;**64**:250–8.

46 Gasser P, Holstein D, Michel Y, *et al.* Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. *J Nerv Ment Dis* 2014;**202**:513–20.

47 Mithoefer, Wagner M, Mithoefer A, *et al.* The safety and efficacy of ±3,4-methylenedioxymethamphetamine-assisted psychotherapy in subjects with chronic, treatment-resistant posttraumatic stress disorder: the first randomized controlled pilot study. *J Psychopharmacol* 2011;**25**:439–52.

48 Winstock A, Barratt M, Ferris J, *et al.* Global Drug Survey. London: 2017. https://www.globaldrugsurvey.com/wp-content/themes/globaldrugsurvey/results/GDS2017_key-findings-report_final.pdf (accessed June 2017).

49 Nutt DJ, King LA, Phillips LD. Drug harms in the UK: A multicriteria decision analysis. *Lancet* 2010;**376**:1558–65.

50 Jung M. Associations of physical and sexual health with suicide attempts among female sex workers in South Korea. *Sex Disabil* 2013;**31**:275–86.

51 Nemoto T, Boedeker B, Iwamoto M. Social support, exposure to violence and transphobia, and correlates of depression among male-to-female transgender women with a history of sex work. *Am J Public Health* 2011;**101**:1980–8.

52 Anisman H, Du L, Palkovits M, *et al.* Serotonin receptor subtype and p11 mRNA expression in stress-relevant brain regions of suicide and control subjects. *J Psychiatry Neurosci* 2008;**33**:131–41.

53 Carhart-Harris RL, Leech R, Hellyer PJ, *et al.* The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs. *Front Hum Neurosci* 2014;**8**. doi:10.3389/fnhum.2014.00020

54 Carhart-Harris RL, Erritzoe D, Williams T, *et al.* Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proc Natl Acad Sci U S A* 2012;**109**:2138–43.

55 Osório FL, Sanches RF, Macedo LR, *et al.* Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a preliminary report. *Rev Bras Psiquiatr* 2016;**37**:13–20.

56 Griffiths RR, Richards WA, McCann U, *et al.* Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology (Berl)* 2006;**187**:268–83.

57 Bouso JC, Palhano-Fontes F, Rodriguez-Fornells A, *et al.* Long-term use of psychedelic drugs is associated with differences in brain structure and personality in humans. *Eur Neuropsychopharmacol* 2015;**25**:483–92.

58 Johnson MW, Garcia-Romeu A, Cosimano MP, *et al.* Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction. *J Psychopharmacol* 2014;**28**:983–92.

59 Mithoefer MC, Wagner MT, Mithoefer AT, *et al.* Durability of improvement in post-traumatic stress disorder symptoms and absence of harmful effects or drug dependency after 3,4-methylenedioxymethamphetamine-assisted psychotherapy: a prospective long-term follow-up study. *J Psychopharmacol* 2013;**27**:28–39.

60 Rio Navarro J, Cohen J, Rocillo Arechaga E, *et al.* Physical and sexual violence, mental health indicators, and treatment seeking among street-based population groups in Tegucigalpa, Honduras. *Pan Am J Public Heal* 2012;**31**:388–95.

61 Stolz J-A, Shannon K, Kerr T, *et al.* Associations between childhood maltreatment and sex work in a cohort of drug-using youth. *Soc Sci Med* 2007;**65**:1214–21.

62 Argento E, Chettiar J, Nguyen P, *et al.* Prevalence and correlates of nonmedical prescription opioid use among a cohort of sex workers in Vancouver, Canada. *Int J Drug Policy* 2015;**26**:59–66.

63 Kerr T, Stoltz J, Marshall BDL, *et al.* Childhood Trauma and Injection Drug Use among High-Risk Youth. *J Adolesc Heal* 2009;**45**:300–2.

64 Ulibarri MD, Strathdee S a, Lozada R, *et al.* Intimate partner violence among female sex workers in two Mexico-U.S. border cities: partner characteristics and HIV risk-behaviors as correlates of abuse. *Psychol Trauma Theory, Res Pract Policy* 2010;**2**:318–25.

65 Argento E, Strathdee SA, Goldenberg S, *et al.* Violence, trauma and living with HIV: Longitudinal predictors of initiating crystal methamphetamine injection among sex workers. *Drug Alcohol Depend* 2017;**175**:198-204.

66 Tull MT, Gratz KL, Aklin WM, *et al.* A preliminary examination of the relationships between posttraumatic stress symptoms and crack/cocaine, heroin, and alcohol dependence. *J Anxiety Disord* 2010;**24**:55–62.

67 Romero-Daza N, Weeks M, Singer M. Conceptualizing the impact of indirect violence on HIV risk among women involved in street-level prostitution. *Aggress Violent Behav* 2005;**10**:153–70.

68 Wang B, Li X, Stanton B, *et al.* Sexual coercion, HIV-related risk, and mental health among female sex workers in China. *Health Care Women Int* 2007;**28**:745–62.

69 Morgan CJA, Muetzelfeldt L, Muetzelfeldt M, *et al.* Harms associated with psychoactive substances: findings of the UK National Drug Survey. *J Psychopharmacol* 2010;**24**:147–53.

Table 1: Baseline characteristics of sex workers in Vancouver who thought about or attempted suicide over follow-up, compared to those who did not (N=290)

Characteristics	Suicidality n=31 (11%)	No Suicidality n=259 (89%)	p-value
Age (median, IQR)	34 (27 to 47)	36 (29 to 42)	0.767
Gender/sexual minority	7 (22.6)	38 (14.7)	0.291
Born in Canada	29 (93.6)	156 (60.2)	<0.001
Indigenous ancestry	18 (58.1)	75 (29.0)	0.001
Education, high school or greater	10 (32.3)	142 (54.8)	0.017
HIV seropositivity†	7 (22.6)	26 (10.0)	0.065
STI seropositivity†	3 (9.7)	35 (13.5)	0.778
Homelessness†	10 (32.3)	63 (24.3)	0.336
Psychedelic use	8 (25.8)	71 (27.4)	0.849
Cannabis use	27 (87.1)	152 (58.7)	0.002
Prescription opioid use	12 (38.7)	77 (29.7)	0.306
Crack use	27 (87.1)	157 (60.6)	0.004
Cocaine use	25 (80.7)	137 (52.9)	0.003
Crystal meth use	18 (58.1)	72 (27.8)	<0.001
Heroin use	21 (67.7)	120 (46.3)	0.024
Non-injection drug use†	27 (87.1)	148 (57.1)	0.001
Injection drug use†	16 (51.6)	81 (31.3)	0.023
Physical/sexual client violence†	5 (16.1)	36 (13.9)	0.784
Physical/sexual childhood abuse	24 (77.4)	112 (43.2)	<0.001
Police harassment/arrest†	16 (51.6)	91 (35.1)	0.072
Primary place to solicit clients†			
Street/public space	24 (77.4)	118 (45.6)	
Indoor/in-call venue	3 (9.7)	103 (39.8)	
Independent/self-advertising (e.g., newspapers, online)	4 (12.9)	38 (14.7)	0.002

† In the last 6 months

Table 2: Unadjusted and adjusted hazard ratios for predictors of time to suicidality among sex workers in Vancouver, 2010-2014 (N=290)

Characteristics	Unadjusted Hazard Ratio (95%CI)	p-value	Adjusted Hazard Ratio (95%CI)	p-value
Psychedelic use	1.00 (0.45 to 2.23)	0.995	0.40 (0.17 to 0.94)*	0.036
Cannabis use	3.44 (1.21 to 9.79)	0.021		
Prescription opioid use	1.88 (0.91 to 3.90)	0.089		
Crack use	3.06 (1.07 to 8.74)	0.037		
Cocaine use	2.53 (1.03 to 6.22)	0.043		
Crystal meth use	3.73 (1.75 to 7.97)	<0.001	3.25 (1.47 to 7.21)*	0.004
Heroin use	2.26 (0.99 to 5.13)	0.053		
HIV seropositivity†	2.15 (0.92 to 5.06)	0.078		
Childhood abuse	3.92 (1.69 to 9.09)	0.002	3.54 (1.49 to 8.40)*	0.004
Indigenous ancestry	2.76 (1.34 to 5.67)	0.006		
Canadian born	6.72 (1.62 to 27.95)	0.009		
Homelessness†	2.55 (1.19 to 5.44)	0.016	1.95 (0.91 to 4.17)*	0.085
Primary place to solicit clients†				
Indoor venue (vs. street)	0.19 (0.06 to 0.66)	0.009		
Independent (vs. street)	0.38 (0.14 to 1.05)	0.061		

† In the last 6 months
*Final multivariable model determined using backward selection with best overall fit, as indicated by the lowest Akaike information criterion (AIC) value.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page, 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3, 4
Objectives	3	State specific objectives, including any prespecified hypotheses	4, 5
Methods			
Study design	4	Present key elements of study design early in the paper	5, 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5, 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	5, 10
Study size	10	Explain how the study size was arrived at	6, 7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6, 7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6, 7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how loss to follow-up was addressed	7
		(*e*) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7, 8
		(b) Give reasons for non-participation at each stage	6, 7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-9, 19, 20
		(b) Indicate number of participants with missing data for each variable of interest	7, 8
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 20, 7
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9, 10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Does psychedelic drug use reduce risk of suicidality? Evidence from a longitudinal community-based cohort of marginalized women in a Canadian setting

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016025.R2
Article Type:	Research
Date Submitted by the Author:	18-Jul-2017
Complete List of Authors:	Argento, Elena; BC Centre for Excellence in HIV/AIDS, Gender and Sexual Health Initiative ; University of British Columbia, Interdisciplinary Studies Strathdee, Steffanie; University of California San Diego, Medicine Tupper, Kenneth; University of British Columbia, School of Population and Public Health; BC Centre on Substance Use Braschel, Melissa; BC Centre for Excellence in HIV/AIDS, Gender and Sexual Health Initiative Wood, Evan; BC Centre on Substance Use; University of British Columbia, Faculty of Medicine Shannon, Kate; British Columbia Centre for Excellence in HIVAIDS; University of British Columbia, Division of AIDS Department of Medicine
Primary Subject Heading:	Public health
Secondary Subject Heading:	Evidence based practice, Epidemiology, Mental health
Keywords:	sex workers, psychedelics, hallucinogens, MENTAL HEALTH, Suicide & self-harm < PSYCHIATRY

Does psychedelic drug use reduce risk of suicidality? Evidence from a longitudinal community-based cohort of marginalized women in a Canadian setting

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Word Count: 3544

ABSTRACT

Objective: This study aimed to longitudinally investigate whether ever having used a psychedelic drug can have a protective effect on incidence of suicidality among marginalized women.

Design: Longitudinal community-based cohort study.

Setting: Data were drawn from a prospective, community-based cohort of marginalized women in Metro Vancouver, Canada.

Participants: 766 women completed the baseline questionnaire between January 2010 and August 2014. Participants who did not report suicidality at baseline and who completed at least one follow-up visit were included.

Main outcome measure: Extended Cox regression was used to model predictors of new suicidality (suicide ideation or attempts) over 54 months follow-up.

Results: Nearly half (46%; n=355) of participants reported prior suicidality and were thus excluded from the present analyses. Of 290 women eligible at baseline, 11% (n=31) reported recent suicidality during follow-up, with an incidence density of 4.42 per 100 person-years (95% Confidence Interval [CI] 3.10 to 6.30). In multivariable analysis, reported lifetime psychedelic drug use was associated with a 60% reduced hazard for suicidality (Adjusted Hazard Ratio [AHR] 0.40; 95%CI 0.17 to 0.94). Crystal methamphetamine use (AHR 3.25; 95%CI 1.47 to 7.21) and childhood abuse (AHR 3.54; 95%CI 1.49 to 8.40) remained independent predictors of suicidality.

Conclusion: The high rate of suicidality identified in this study is of major concern. Alongside emerging evidence on the potential of psychedelic-assisted therapy to treat some mental illness and addiction issues, our findings demonstrate that naturalistic psychedelic drug use is independently associated with reduced suicidality, while other illicit drug use and childhood trauma predispose women to suicidality. While observational, this study supports calls for further investigation of the therapeutic utility of psychedelic drugs in treating poor mental health and promoting mental wellness.

Word Count: 278
Keywords: *women, psychedelics, hallucinogens, suicide prevention, mental health, substance use*

Strengths and limitations of this study

- To the best of our knowledge, this is the first study to longitudinally investigate the potential protective effect of psychedelic drug use on suicidality, drawing from a large, community-based cohort of marginalized women.
- Multivariable Cox regression analyses were used to examine the impact of lifetime psychedelic drug use on incidence of suicidality among a marginalized population.
- The associations between specific psychedelics, contexts of their use, and suicidality were not explored in this study.
- Not all potential confounding variables could be controlled for in this study and the associations uncovered cannot be determined as causal.
- Data were self-reported and variables examined included highly stigmatized topics, introducing the potential for recall bias, social desirability and reporting bias.

INTRODUCTION

Despite efforts to improve mental health over the last 60 years, suicide remains a critical public health concern worldwide [1,2]. Suicide was the second leading cause of death globally in 2012 among 15-29 year olds [2], with an estimated 80-90% of suicide deaths attributable to mental health or substance use disorders [3,4]. Significant gaps remain in empirical research examining suicidality among marginalized populations. Marginalized women, such as sex workers who are street-involved or use drugs, experience disproportionately high levels of social and health-related risks and harms, including stigma, discrimination, and violence [5–7] as a result of dynamic structural drivers including poverty, criminalization, and racism. While sex workers are a diverse population working from indoor in-call and out-call venues to street-based settings, previous studies highlight substantial unmet mental health needs of more marginalized and street-involved sex workers. Studies among street-based sex workers and those who use drugs underscore the associations of social exclusion, depression, and post-traumatic stress disorder (PTSD) with suicidality [8–12]. Research demonstrates greater risk for suicidality among those with a history of trauma [1,13,14] and among street-involved sex workers who report historical experiences of violence and childhood abuse [8–10,15,16]. Further, Indigenous women are vastly overrepresented among street-based sex workers in North America, and face devastating and multigenerational effects of trauma and socio-economic dislocation (e.g., high burden of mental illness and suicidality) as a result of colonialism, racialized policies, and displacement from land and home communities [17,18].

Various biological, interpersonal, and socio-structural factors (e.g., social exclusion/isolation, education level, employment) contribute to our understanding of suicidal behaviors [1,19]. While

evidence has demonstrated that some forms of cognitive behavioral therapy and pharmacological interventions may reduce suicidality, the literature is hampered by publication bias and significant heterogeneity of strategies and outcome measures [14,20]. Due to ethical challenges and limitations to studying suicide and its proxies (i.e., ideation and attempts), there remains a paucity of evidence from randomized controlled trials to support the efficacy of prevention interventions [20]. Researchers have largely focused on examining suicidality outcomes (rather than suicide itself), which may not be fully generalizable to understanding suicide or accurately evaluating treatment approaches [21]. Further, stigma continues to hinder research and reporting of suicidality [21]. There remains an urgency to better understand pathways to suicidality, with literature highlighting the need for innovative psychological and psychosocial treatments [14] and tailored intervention approaches for key marginalized populations [20,21]. Given the complex etiological pathways to suicide and limited effectiveness of well-established evidence-based interventions to reduce the burden of suicidality, the US National Institute of Mental Health has called for innovative research on suicide prevention and treatment for suicidality [22].

A number of psychedelic drug therapies are being revisited following a 40-year hiatus in research into their potential for the treatment of depression, anxiety, PTSD, eating disorders, and addiction [23]. Psychedelic drugs include the classic serotonergic psychedelics or "hallucinogens" lysergic acid diethylamide (LSD), psilocybin, dimethyltryptamine (DMT), and mescaline, as well as the "enactogen" or "empathogen" methylenedioxymethamphetamine (MDMA) [23–25], all of which are being investigated in clinical/pre-clinical studies for their neuropharmacological functions and potential as adjuncts to psychotherapy [26–28]. While renewed interest in psychedelic medicine is challenged by various funding, methodological, and

legal impediments, the emerging evidence indicating improved outcomes for some individuals suffering from mental health and addiction issues has generated new scientific inquiry and an imposing obligation to advance this research [23,29,30]. Recent observational studies in the US demonstrate significant associations between lifetime psychedelic use and reduced recidivism and intimate partner violence among populations of prison inmates [31,32], and reduced psychological distress and suicidality among the general adult population [33–35].

Despite the multifaceted structural and social inequities that shape poor mental health burden among marginalized and street-involved sex workers, there remains a paucity of data on suicide rates and research that systematically examines factors that potentiate or mitigate suicidality among sex workers, particularly in the global north. Some evidence suggests that psychedelic drug use may be protective with regard to suicidality [33–35] and is associated with significant improvements in psychological wellbeing and reductions in depression and anxiety in clinical settings [36–41], yet existent research is characterized by large gaps. Given the urgency of addressing and preventing suicide and calls for prioritizing innovative interventions, this study aimed to longitudinally investigate whether lifetime psychedelic drug use is associated with a reduced incidence of suicidality (suicide ideation or attempts) among a community-based prospective cohort of marginalized women. We postulated that psychedelic drug use would have an independent protective effect on suicidality over the study period.

METHODS

Study Design and Participants

Data for this study were drawn from a large, community-based, prospective cohort of women sex workers initiated in 2010, known as AESHA (An Evaluation of Sex Workers Health Access). Eligibility criteria for study participants included cisgender or transgender women, 14 years of age or older, who exchanged sex for money within the last 30 days. AESHA participants completed interviewer-administered questionnaires and HIV/STI/HCV serology testing at enrollment and biannually. Experiential staff (current/former sex workers) are represented across interview, outreach and nursing teams, including coordinators with substantial community experience. Participants were recruited across Metro Vancouver using time-location sampling and community mapping strategies, with day and late-night outreach to outdoor sex work locations (i.e., streets, alleyways), indoor sex work venues (i.e., massage parlors, micro-brothels, and in-call locations), and online. Weekly outreach by experiential staff is conducted to over 100 sex work venues by outreach/nursing teams operating a mobile van, with regular contact as well as encouraging drop-in to women-only spaces at the research office, contributing to an annual retention rate of >90% for AESHA participants.

The main interview questionnaire elicits responses related to socio-demographics (e.g., sexual and gender identities, ethnicity, housing), the work environment (e.g., access to services, violence/safety, policing, incarceration), client characteristics (e.g., types/fees of services, male condom use), intimate partners (e.g., sexual history, cohabitation, financial support), trauma and violence (e.g., lifetime and childhood trauma, exposure to intimate partner and workplace violence), and comprehensive injection and non-injection drug use patterns. The clinical questionnaire relates to overall physical, mental, and emotional health, and HIV testing and treatment experiences to support education, referral, and linkages with care. The research team

works in close partnership with the affected community and a diversity of stakeholders (e.g., legal/human rights experts, community-based organizations, service providers, health authorities, government officials, and international policy bodies) and regularly engages in knowledge exchange efforts. AESHA is monitored by a Community Advisory Board of over 15 sex work, women's health and HIV service agencies, as well as representatives from the health authority and policy experts, and holds ethical approval through Providence Health Care/University of British Columbia Research Ethics Board. All participants receive an honorarium of $40 CAD at each bi-annual visit for their time, expertise and travel.

To capture initial episodes of suicidality, analyses for this study were restricted to AESHA participants who had never thought about or attempted suicide at baseline and completed at least one follow-up visit between January 2010 and August 2014. Those with missing observations for suicidality at baseline (n=50/766; 6.5%) were excluded from analysis, and one additional participant was excluded because reported suicidality was missing at follow-up.

Statistical Analyses

The outcome of interest was a first episode of suicidality, defined as responding 'yes' to having thought about or attempted suicide in the last six months. Time-fixed variables examined included age (continuous), gender/sexual minority (lesbian, gay, bisexual, trans, or two-spirit), Indigenous ancestry (inclusive of First Nations, Métis, and Inuit), being an im/migrant worker (versus Canadian born), education (high school or greater), and physical and/or sexual childhood abuse (before age 18). Variables treated as time-updated covariates based on bi-annual follow-up data included HIV/STI serostatus, recent homelessness, recent physical and/or sexual violence

by clients, recent police harassment and/or arrest, and primary place to solicit clients. Time-updated injection and non-injection drug use variables included lifetime use of psychedelics (including LSD/acid, magic mushrooms/psilocybin, ecstasy/MDMA), cannabis, pharmaceutical opioids (any street methadone/suboxone, dilaudid, morphine, oxycontin, percocet/vicodin/demerol, or T3s/T4s), crack, cocaine, crystal methamphetamine, and heroin.

Using extended Cox regression, unadjusted and adjusted hazard ratios (HR and AHR) and 95% confidence intervals (CI) were calculated to identify predictors of suicidality. Psychedelic drug use, hypothesized a priori to be a predictor of suicidality, and variables that were significantly correlated with the outcome at the $p<0.10$ level in bivariate analyses were subsequently fitted into a multivariable Cox model. Backward model selection was used to determine the final multivariable model with the best overall fit, as indicated by the lowest Akaike information criterion (AIC) value. A complete case analysis was used, where observations with missing data were excluded from analyses, and participants who were lost to follow-up were right censored at their most recent study visit. All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA). Two-sided p-values are reported.

RESULTS

Socio-Demographic Characteristics

Of the total 766 women who completed the baseline questionnaire, 46% (n=355) reported ever experiencing suicidality (45%; n=343 reported suicidal thoughts, 32%; n=245 attempted suicide) and were thus excluded from this analysis. A total of 290 women without suicidality who completed at least one follow-up visit were eligible for inclusion in the present analysis.

Participants were followed for a total of 53.5 months (median = 29.9 months). Baseline characteristics of participants who reported suicidality during follow-up compared to those who did not are displayed in Table 1.

Overall, 11% (n=31) thought about or attempted suicide for the first time during follow-up, with an incidence density of 4.42 per 100 person-years (95%CI 3.10 to 6.30). The median age was 36 (interquartile range [IQR] 29 to 42) and 16% (n=45) of participants identified as gender or sexual minorities. One third (n=93) identified as Indigenous and one quarter (n=73) had been homeless in the last six months. Half of participants (49%; n=142) solicited clients on the streets, and 37% (n=106) solicited clients in indoor establishments. In terms of workplace violence and harassment, 14% (n=41) and 37% (n=107) reported recent exposure to physical and/or sexual violence from clients/dates and recent police harassment without arrest, respectively. Nearly half (47%; n=136) of participants reported ever being physically and/or sexually abused before age 18, and among those who reported suicidality, 77% (n=24/31) experienced childhood abuse compared to 43% (n=112/259) among those who did not report suicidality (p<0.001).

Substance Use

Over half of participants reported ever using crack (63%, n=184) or cocaine (56%; n=162), with higher proportions of crack and cocaine use among those reporting suicidality than those who did not (p=0.003). Close to half (49%, n=141) reported lifetime heroin use, which was significantly higher among those who reported suicidality than those who did not (68% vs. 46%, p=0.02). Approximately one third (31%, n=90) of participants had ever used crystal methamphetamine, and this was significantly higher among those who reported suicidality than those who did not

(58% vs. 28%, p<0.001). Overall, 27% (n=79) of participants reported ever using a psychedelic substance, and of those, 75% (n=59) had used MDMA/ecstasy, 35% (n=28) had used LSD/acid, and 30% (n=24) had used psilocybin/magic mushrooms.

Bivariate and Multivariable Cox Analyses

Unadjusted and adjusted hazard ratios for factors associated with a first episode of suicidality during follow-up are displayed in Table 2. In the final multivariable model, crystal methamphetamine use (AHR 3.25; 95%CI 1.47 to 7.21) and physical and/or sexual childhood abuse (AHR 3.54; 95%CI 1.49 to 8.40) remained independently associated with time to suicidality. Psychedelic use was associated with a 60% reduced hazard of suicidality (AHR 0.40; 95%CI 0.17 to 0.94).

DISCUSSION

This study demonstrated that among marginalized women, many of whom are street-involved and experience a disproportionate burden of violence, trauma, psychological distress and suicide, naturalistic psychedelic drug use predicted a significantly reduced hazard for suicidality. Crystal methamphetamine use and childhood abuse predisposed women to suicidality corresponding to more than a three-fold increased hazard. Suicidality was highly prevalent, with almost half of women reporting lifetime suicidality at baseline, and 11% reporting a first episode of suicidality in the last six months during follow-up. Few studies have longitudinally examined predictors of suicidality among marginalized sex workers, and of the available data, most are cross-sectional and/or conducted in lower and middle income settings [8,16,42,43]. The present study, based on a community-based, prospective cohort of marginalized women, adds to a growing body of

literature documenting the protective and therapeutic potentials of psychedelic substances [23,29,39,44,45].

Data were self-reported, and questions pertaining to events that occurred in the past may be subject to recall bias. Variables examined included sensitive and highly stigmatized topics such as childhood trauma, violence, and illicit drug use, which introduce the potential for social desirability and reporting bias. However, the likelihood of these biases is reduced by the community-based nature of the study. While lifetime psychedelic drug use was found to reduce the hazard of suicidality, the associations uncovered in this analysis cannot be determined as causal. However, the use of Cox regression analysis in this study was able to determine a temporal relationship between psychedelic use and suicidality. The sample was restricted to participants who had not experienced suicidal ideation or attempt at baseline, ensuring that psychedelic use preceded suicidality and thus providing evidence that psychedelics have a protective effect. Due to a lack of statistical power, analyses evaluating the effects of more nuanced indicators of psychedelic use (e.g., frequency of use or recent use), as well as separate analyses for ideation and attempt outcomes, were not feasible. Further examination of these variables would certainly be interesting and important in future analyses with additional data from follow-up questionnaires. Suicidality is influenced by complex individual, interpersonal and structural variables, and not all potential confounding variables could be controlled for in this study. For example, women who use psychedelics may also possess some characteristic(s) associated with a reduced likelihood of being suicidal (e.g., openness to experience, curiosity, or spirituality), which were not examined in this study. Despite the relative safety of psychedelic drug use as evidenced from the clinical and non-clinical literature [36,46–49], it should be noted

that the use of psychedelics, particularly with unknown doses sourced from unregulated street markets, is not without risk, highlighting the importance of set and setting [23]; the doses and contexts of psychedelic use among women in the present study could not be determined. The standard error for the association between psychedelic use and suicidality was somewhat high, resulting in a wider confidence interval. However, a large and significant protective effect was demonstrated in multivariable analysis, despite the relatively small number of events for suicidality over follow-up. With a larger sample size, we would expect a narrower confidence interval for this association. The study population included women from a wide-ranging representation of sex work environments, yet findings may not be fully generalizable to sex workers in other settings. The mapping of working areas and time–location sampling helped to ensure a representative sample and to minimize selection bias.

To the best of our knowledge, this study is the first to longitudinally investigate associations with suicidality among marginalized and street-involved sex workers in North America, and builds upon prior cross-sectional research highlighting significantly elevated rates of suicidality and unmet mental health needs in this population. For example, a study conducted in Sydney, Australia demonstrated significant links between depression, trauma, and suicidality, where an estimated 42% of street-based female sex workers reported attempting suicide and 74% reported lifetime suicidal ideation [10,42]. While estimates of mental illness vary significantly across sex work settings, up to three-quarters of street- and drug-involved sex workers in a US study reported severe depression, anxiety, or PTSD [12]. Notably, our study demonstrated a lower risk of suicidality among women working indoors in bivariate analysis (HR 0.19, p=0.009), lending support to the critical role of safer workplace environments in mitigating risk. In studies

conducted in Asia, recent suicide attempts ranged from 19% among sex workers in Goa, India [16] to 38% among sex workers in China [8,11,50], many of whom work in marginalized settings with few workplace protections. Transgender women involved in sex work, a sub-population experiencing significant psychosocial vulnerability and discrimination, report notably further elevated rates of suicidality: three quarters of participants in San Francisco reported suicide ideation, of whom 64% attempted suicide [51]. The global evidence is unequivocal that in settings where sex work is criminalized, sex workers are unable to access essential social, health, and legal protections (e.g., against violence), highlighting the need for structural (e.g., decriminalization) and community-led interventions to improve health and human rights [5]. A structural approach to mitigating suicidality risk requires a reform of laws and policies that perpetuate stigma, discrimination, violence, and unequal access to health and social supports among sex workers. Increased support for community-driven interventions that are gender and culturally appropriate are urgently needed, and any clinical treatment utilizing psychedelics must be developed alongside sex worker-led interventions and community empowerment.

Our findings extend upon research on associations between lifetime use of illicit drugs and increased risk for suicidality: in bivariate analysis, all classes of illicit drugs were demonstrated to increase the hazard of suicidality with the exception of psychedelics. In multivariable analysis, psychedelics were independently associated with a 60% reduced hazard for suicidality, contributing to emergent evidence on the potential of psychedelics to mitigate risks for suicide. Among the various scientific studies examining the potential benefits of psychedelic drug use, a recent and large (n>190,000) population study conducted among adult respondents in the US demonstrated that psychedelics are associated with reduced psychological distress and suicidality

[33]. A recent open-label trial conducted in the UK demonstrated the safety and efficacy of psilocybin for treating major depression [36], and another open-label trial in Brazil found rapid and sustained anti-depressant effects from the Amazonian psychedelic brew ayahuasca administered in a clinical setting [38]. The ways in which psychedelics may alleviate suffering associated with some mental illness is undoubtedly a complex phenomenon. It has been hypothesized that psychedelics modify neurobiological processes that may be involved in suicidality by down-regulating 5-HT_{2A} serotonin receptors, as increased binding (and up-regulation) of this receptor has been implicated in major depression and suicide [39,45,52]. Further, there is evidence that psychedelics alter neural network connectivity and enhance recall of autobiographical memories, which may facilitate positive reprocessing of trauma [26,53,54]. Recent randomized, placebo-controlled, cross-over studies found that psilocybin (among n=25 adults) and LSD (among n=20 adults) were associated with increased positive mood and psychological wellbeing [37,39], supporting other work demonstrating the anti-depressive/anxiolytic effects of psychedelics [27,40,46,55]. The potential of psychedelics to elicit "mystical-type" experiences, with profound and sustained positive changes in attitudes and mood, may play a key role in addiction treatment interventions [41,45,56,57]. For example, psilocybin-assisted psychotherapy demonstrated high success in smoking cessation outcomes at six months follow-up (abstinence rates of 80%), and mystical experiences generated from the psilocybin sessions were significantly correlated with elevated ratings of personal meaningfulness, wellbeing, and life satisfaction [58]. Randomized control trials in the US and Switzerland have demonstrated significant long-term improvements among patients with treatment-resistant PTSD following MDMA-assisted psychotherapy [28,59], and further research is continuing in an international multi-site phase 3 clinical trial.

Marginalized and street-based sex workers experience complex and synergistic effects between trauma, lack of workplace safety, and mental health/substance use comorbidities that elevate risk of suicidality. Marginalized women and sex workers who use drugs report high rates of childhood abuse [60–62], which is associated with an increased likelihood of experiencing subsequent physical or sexual violence, as well as initiating injection drug use [63–65]. For those suffering from emotional trauma stemming from violence, including indirect violence (i.e., witnessing violence), there may be a proclivity to use drugs for self-medication [66,67]. Violence and sexual coercion have been found to be significantly associated with suicidality among sex worker populations in China and India [8,9,16,68]. As demonstrated in this study, having an early traumatic life event is a key risk factor for suicide among sex workers, a high proportion of whom are Indigenous, and experiencing historical trauma can have harmful intergenerational impacts [1,17]. Given that historical experiences of violence and trauma denote significant risk for suicide, there is an urgent need to provide integrated, trauma-informed intervention services for sex workers and other marginalized populations. Currently available interventions and pharmacological treatments for suicidality show limited efficacy, and concerted efforts should be made not only to increase access to evidence-based treatments, but also to explore alternative approaches to improving mental health and wellbeing. Emerging research and evidence show positive outcomes with psychedelic-assisted treatments, which have demonstrated an excellent record of safety with few to no serious adverse effects reported [23,27,36,69]. This study suggests psychedelic substances may hold promise as useful tools in addressing mental health issues and remediating risks for psychological distress and suicide.

CONCLUSION

The high rate of suicidality among marginalized women identified in this study is a critical public health concern. In the context of emerging research and evidence on the therapeutic potential of psychedelics to treat mental health issues, our findings demonstrated that naturalistic psychedelic use was independently associated with reduced suicidality among sex workers, while other drug use and childhood trauma increased the hazard for suicidality. To the best of our knowledge, this is the first study to longitudinally investigate the relationship between psychedelic drug use and suicidality. While observational, this study supports calls for further investigation of the therapeutic utility of psychedelic drugs in treating mental illness and promoting mental wellness.

Acknowledgments: We thank all those who contributed their time and expertise to this project, particularly participants, AESHA community advisory board members and partner agencies, and the AESHA team, including: Sarah Moreheart, Jennifer Morris, Sylvia Machat, Jane Li, Minshu Mo, Sherry Wu, Sylvia Machat, Emily Leake, Anita Dhanoa, Meaghan Thumath, Alka Murphy, Jenn McDermid, Tave Cole, Jaime Adams. We also thank Abby Rolston, Peter Vann, Erin Seatter and Patricia McDonald for their research and administrative support

Contributors: EA and KS conceptualized and designed the study. EA, SAS, MB, and KS contributed to the interpretation and analysis of data. EA wrote the first draft of the manuscript. SAS, KT, MB, EW and KS contributed to reviewing and editing the manuscript. EA, SAS, KT, MB, EW and KS critically revised the manuscript and approved the final draft. KS is the guarantor.

Funding: This study was supported by the US National Institutes of Health (R01DA028648) and MacAIDS. KS is partially supported by a Canada Research Chair in Global Sexual Health and HIV/AIDS and the Michael Smith Foundation for Health Research. EA is supported by a Canadian Institutes of Health Research Doctoral Award. SAS is partially supported by a NIDA merit award (R37DA019829). EW is supported in part by a Tier 1 Canada Research Chair in Inner-City Medicine award. The study funders had no role in the study design, data collection, analysis, interpretation, writing of the report, or decision to submit the paper for publication.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: This study holds ethical approval through Providence Health Care/University of British Columbia Research Ethics Board.

Transparency: The study guarantor (KS) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies with the study as planned have been explained.

Data sharing: no additional data available.

REFERENCES

1 Hawton K, van Heeringen K. Suicide. *Lancet* 2009;**373**:1372–81.
2 World Health Organization. Preventing Suicide: A Global Imperative. Geneva, Switzerland: 2014. http://www.who.int/mental_health/suicide-prevention/world_report_2014/en/ (accessed Dec 2016).
3 Whiteford HA, Degenhardt L, Rehm J, *et al.* Global burden of disease attributable to mental and substance use disorders: Findings from the Global Burden of Disease Study 2010. *Lancet* 2013;**382**:1575–86.
4 Statistics Canada. Suicide Rates: An Overview. Ottawa: 2015. http://www.statcan.gc.ca/pub/82-624-x/2012001/article/11696-eng.htm (accessed Dec 2016).
5 Shannon K, Strathdee SA, Goldenberg SM, *et al.* Global epidemiology of HIV among female sex workers: Influence of structural determinants. *Lancet* 2015;**385**:55–71.
6 Argento E, Muldoon K, Duff P, *et al.* High prevalence and partner correlates of physical and sexual violence by intimate partners among street and off-street sex workers. *PLoS One* 2014;**9**:e102129.
7 Deering K, Amin A, Shoveller J, *et al.* A systematic review of the global magnitude and drivers of violence against sex workers. *Am J Public Health* 2014;**104**:e42–54.
8 Gu J, Lau JTF, Li M, *et al.* Socio-ecological factors associated with depression, suicidal ideation and suicidal attempt among female injection drug users who are sex workers in China. *Drug Alcohol Depend* 2014;**144**:102–10.
9 Zhang L, Li X, Wang B, *et al.* Violence, stigma and mental health among female sex workers in China: a structural equation modeling. *Women Health* 2016;**242**. \
10 Roxburgh A, Degenhardt L, Copeland J. Posttraumatic stress disorder among female street-based sex workers in the greater Sydney area, Australia. *BMC Psychiatry* 2006;**6**:1–12.
11 Lau JTF, Tsui HY, Ho SPY, *et al.* Prevalence of psychological problems and relationships with condom use and HIV prevention behaviors among Chinese female sex workers in Hong Kong. *AIDS Care* 2010;**22**:659–68.
12 Surratt HL, Kurtz SP, Chen M, *et al.* HIV risk among female sex workers in Miami: the impact of violent victimization and untreated mental illness. *AIDS Care* 2012;**24**:553–61.
13 Hadland SE, Marshall BDL, Kerr T, *et al.* Suicide and history of childhood trauma among street youth. *J Affect Disord* 2012;**136**:377–80.
14 O'Connor RC, Nock MK. The psychology of suicidal behaviour. *The Lancet Psychiatry* 2014;**1**:73–85.
15 Gilchrist G, Gruer L, Atkinson J. Comparison of drug use and psychiatric morbidity between prostitute and non-prostitute female drug users in Glasgow, Scotland. *Addict Behav* 2005;**30**:1019–23.
16 Shahmanesh M, Wayal S, Cowan F, *et al.* Suicidal behavior among female sex workers in Goa, India: The silent epidemic. *Am J Public Health* 2009;**99**:1239–46.
17 Bingham B, Leo D, Zhang R, *et al.* Generational sex work and HIV risk among Indigenous women in a street-based urban Canadian setting. Cult. Health Sex. 2014;**16**:440–52.
18 Benoit C, Carroll D, Chaudhry M. In search of a Healing Place: Aboriginal women in Vancouver's Downtown Eastside. *Soc Sci Med* 2003;**56**:821–33.

19 Li Z, Page A, Martin G, *et al.* Attributable risk of psychiatric and socio-economic factors for suicide from individual-level, population-based studies: A systematic review. *Soc Sci Med* 2011;**72**:608–16.

20 Zalsman G, Hawton K, Wasserman D, *et al.* Suicide prevention strategies revisited: 10-year systematic review. *The Lancet Psychiatry* 2016;**3**:646–59.

21 Klonsky ED, May AM, Saffer BY. Suicide, Suicide Attempts, and Suicidal Ideation. *Annu Rev Clin Psychol* 2016;**12**:307–30.

22 National Action Alliance for Suicide Prevention: Research Prioritization Task Force. A Prioritized Research Agenda for Suicide Prevention: An Action Plan to Save Lives. Rockville, MD: 2014. www.suicide-research-agenda.org (accessed Dec 2016).

23 Tupper K, Wood E, Yensen R, *et al.* Psychedelic medicine: a re-emerging therapeutic paradigm. *Can Med Assoc J* 2015;**187**:1054–9.

24 Nichols DE. Hallucinogens. *Pharmacol Ther* 2004;**101**:131–81.

25 Bedi G, Hyman D, De Wit H. Is ecstasy an 'empathogen'? Effects of 3,4-methylenedioxymethamphetamine on prosocial feelings and identification of emotional states in others. *Biol Psychiatry* 2010;**68**:1134–40.

26 Carhart-Harris RL, Leech R, Williams TM, *et al.* Implications for psychedelic-assisted psychotherapy: Functional magnetic resonance imaging study with psilocybin. *Br J Psychiatry* 2012;**200**:238–44.

27 dos Santos RG, Osorio FL, Crippa JAS, *et al.* Antidepressive, anxiolytic, and antiaddictive effects of ayahuasca, psilocybin and lysergic acid diethylamide (LSD): a systematic review of clinical trials published in the last 25 years: antidepressive effects of ayahuasca, psilocybin and LSD. *Ther Adv Psychopharmacol* 2016;**6**:193-213.

28 Oehen P, Schnyder U. A randomized, controlled pilot study of MDMA (± 3,4 methylenedioxymethamphetamine)-assisted psychotherapy for treatment of resistant, chronic Post-Traumatic Stress Disorder (PTSD). *J Psychopharmacol* 2013;**27**:40–52.

29 Sessa B. Shaping the renaissance of psychedelic research. *Lancet* 2012;**380**:200–1.

30 Sessa B, Johnson MW. Can psychedelic compounds play a part in drug dependence therapy? *Br J Psychiatry* 2015;**206**:1–3.

31 Hendricks PS, Clark CB, Johnson MW, *et al.* Hallucinogen use predicts reduced recidivism among substance-involved offenders under community corrections supervision. *J Psychopharmacol* 2014;**28**:62–6.

32 Walsh Z, Hendricks PS, Smith S, *et al.* Hallucinogen use and intimate partner violence: Prospective evidence consistent with protective effects among men with histories of problematic substance use. *J Psychopharmacol* 2016;**30**:601-607.

33 Hendricks PS, Thorne CB, Clark CB, *et al.* Classic psychedelic use is associated with reduced psychological distress and suicidality in the United States adult population. *J Psychopharmacol* 2015;**29**:280–8.

34 Krebs TS, Johansen P-Ø. Psychedelics and mental health: a population study. *PLoS One* 2013;**8**:e63972. doi:10.1371/journal.pone.0063972

35 Johansen P-Ø, Krebs TS. Psychedelics not linked to mental health problems or suicidal behavior: A population study. *J Psychopharmacol* 2015;**29**:270–9.

36 Carhart-Harris RL, Bolstridge M, Rucker J, *et al.* Psilocybin with psychological support for treatment-resistant depression: An open-label feasibility study. *The Lancet Psychiatry* 2016;**3**:619–27.

37 Carhart-Harris R, Kaelen M, Bolstridge M, *et al.* The paradoxical psychological effects of

lysergic acid diethylamide (LSD). *Psychol Med* 2016;1–12. doi:10.1017/S0033291715002901

38 Sanches R, de Lima Osorio F, dos Santos R, *et al.* Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: A SPECT study. *J Clin Psychopharmacol* 2016;**36**:77–81.

39 Kraehenmann R, Preller KH, Scheidegger M, *et al.* Psilocybin-induced decrease in amygdala reactivity correlates with enhanced positive mood in healthy volunteers. *Biol Psychiatry* 2015;**78**:572–81.

40 Grob CS, Danforth AL, Chopra GS, *et al.* Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Arch Gen Psychiatry* 2011;**68**:71–8.

41 Griffiths RR, Johnson MW, Richards WA, *et al.* Psilocybin occasioned mystical-type experiences: Immediate and persisting dose-related effects. *Psychopharmacology (Berl)* 2011;**218**:649–65.

42 Roxburgh A, Degenhardt L, Copeland J, *et al.* Drug dependence and associated risks among female street-based sex workers in the Greater Sydney Area. Australia. *Subst Use Misuse* 2008;**43**:1202–17.

43 Hong Y, Zhang C, Li X, *et al.* Partner violence and psychosocial distress among female sex workers in China. *PLoS One* 2013;**8**:e62290. doi:10.1371/journal.pone.0062290

44 Dyck E. LSD: A new treatment emerging from the past. *Can Med Assoc J* 2015;**187**:1079–80.

45 Bogenschutz MP, Johnson MW. Classic hallucinogens in the treatment of addictions. *Prog Neuro-Psychopharmacology Biol Psychiatry* 2015;**64**:250–8.

46 Gasser P, Holstein D, Michel Y, *et al.* Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. *J Nerv Ment Dis* 2014;**202**:513–20.

47 Mithoefer, Wagner M, Mithoefer A, *et al.* The safety and efficacy of ±3,4-methylenedioxymethamphetamine-assisted psychotherapy in subjects with chronic, treatment-resistant posttraumatic stress disorder: the first randomized controlled pilot study. *J Psychopharmacol* 2011;**25**:439–52.

48 Winstock A, Barratt M, Ferris J, *et al.* Global Drug Survey. London: 2017. https://www.globaldrugsurvey.com/wp-content/themes/globaldrugsurvey/results/GDS2017_key-findings-report_final.pdf (accessed June 2017).

49 Nutt DJ, King LA, Phillips LD. Drug harms in the UK: A multicriteria decision analysis. *Lancet* 2010;**376**:1558–65.

50 Jung M. Associations of physical and sexual health with suicide attempts among female sex workers in South Korea. *Sex Disabil* 2013;**31**:275–86.

51 Nemoto T, Boedeker B, Iwamoto M. Social support, exposure to violence and transphobia, and correlates of depression among male-to-female transgender women with a history of sex work. *Am J Public Health* 2011;**101**:1980–8.

52 Anisman H, Du L, Palkovits M, *et al.* Serotonin receptor subtype and p11 mRNA expression in stress-relevant brain regions of suicide and control subjects. *J Psychiatry Neurosci* 2008;**33**:131–41.

53 Carhart-Harris RL, Leech R, Hellyer PJ, *et al.* The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs. *Front Hum Neurosci* 2014;**8**. doi:10.3389/fnhum.2014.00020

54 Carhart-Harris RL, Erritzoe D, Williams T, *et al.* Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proc Natl Acad Sci U S A* 2012;**109**:2138–43.

55 Osório FL, Sanches RF, Macedo LR, *et al.* Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a preliminary report. *Rev Bras Psiquiatr* 2016;**37**:13–20.

56 Griffiths RR, Richards WA, McCann U, *et al.* Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology (Berl)* 2006;**187**:268–83.

57 Bouso JC, Palhano-Fontes F, Rodriguez-Fornells A, *et al.* Long-term use of psychedelic drugs is associated with differences in brain structure and personality in humans. *Eur Neuropsychopharmacol* 2015;**25**:483–92.

58 Johnson MW, Garcia-Romeu A, Cosimano MP, *et al.* Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction. *J Psychopharmacol* 2014;**28**:983–92.

59 Mithoefer MC, Wagner MT, Mithoefer AT, *et al.* Durability of improvement in post-traumatic stress disorder symptoms and absence of harmful effects or drug dependency after 3,4-methylenedioxymethamphetamine-assisted psychotherapy: a prospective long-term follow-up study. *J Psychopharmacol* 2013;**27**:28–39.

60 Rio Navarro J, Cohen J, Rocillo Arechaga E, *et al.* Physical and sexual violence, mental health indicators, and treatment seeking among street-based population groups in Tegucigalpa, Honduras. *Pan Am J Public Heal* 2012;**31**:388–95.

61 Stolz J-A, Shannon K, Kerr T, *et al.* Associations between childhood maltreatment and sex work in a cohort of drug-using youth. *Soc Sci Med* 2007;**65**:1214–21.

62 Argento E, Chettiar J, Nguyen P, *et al.* Prevalence and correlates of nonmedical prescription opioid use among a cohort of sex workers in Vancouver, Canada. *Int J Drug Policy* 2015;**26**:59–66.

63 Kerr T, Stoltz J, Marshall BDL, *et al.* Childhood Trauma and Injection Drug Use among High-Risk Youth. *J Adolesc Heal* 2009;**45**:300–2.

64 Ulibarri MD, Strathdee S a, Lozada R, *et al.* Intimate partner violence among female sex workers in two Mexico-U.S. border cities: partner characteristics and HIV risk-behaviors as correlates of abuse. *Psychol Trauma Theory, Res Pract Policy* 2010;**2**:318–25.

65 Argento E, Strathdee SA, Goldenberg S, *et al.* Violence, trauma and living with HIV: Longitudinal predictors of initiating crystal methamphetamine injection among sex workers. *Drug Alcohol Depend* 2017;**175**:198-204.

66 Tull MT, Gratz KL, Aklin WM, *et al.* A preliminary examination of the relationships between posttraumatic stress symptoms and crack/cocaine, heroin, and alcohol dependence. *J Anxiety Disord* 2010;**24**:55–62.

67 Romero-Daza N, Weeks M, Singer M. Conceptualizing the impact of indirect violence on HIV risk among women involved in street-level prostitution. *Aggress Violent Behav* 2005;**10**:153–70.

68 Wang B, Li X, Stanton B, *et al.* Sexual coercion, HIV-related risk, and mental health among female sex workers in China. *Health Care Women Int* 2007;**28**:745–62.

69 Morgan CJA, Muetzelfeldt L, Muetzelfeldt M, *et al.* Harms associated with psychoactive substances: findings of the UK National Drug Survey. *J Psychopharmacol* 2010;**24**:147–53.

Table 1: Baseline characteristics of women in Vancouver who thought about or attempted suicide over follow-up, compared to those who did not (N=290)

Characteristics	Suicidality n=31 (11%)	No Suicidality n=259 (89%)	p-value
Age (median, IQR)	34 (27 to 47)	36 (29 to 42)	0.767
Gender/sexual minority	7 (22.6)	38 (14.7)	0.291
Born in Canada	29 (93.6)	156 (60.2)	<0.001
Indigenous ancestry	18 (58.1)	75 (29.0)	0.001
Education, high school or greater	10 (32.3)	142 (54.8)	0.017
HIV seropositivity†	7 (22.6)	26 (10.0)	0.065
STI seropositivity†	3 (9.7)	35 (13.5)	0.778
Homelessness†	10 (32.3)	63 (24.3)	0.336
Psychedelic use	8 (25.8)	71 (27.4)	0.849
Cannabis use	27 (87.1)	152 (58.7)	0.002
Prescription opioid use	12 (38.7)	77 (29.7)	0.306
Crack use	27 (87.1)	157 (60.6)	0.004
Cocaine use	25 (80.7)	137 (52.9)	0.003
Crystal meth use	18 (58.1)	72 (27.8)	<0.001
Heroin use	21 (67.7)	120 (46.3)	0.024
Non-injection drug use†	27 (87.1)	148 (57.1)	0.001
Injection drug use†	16 (51.6)	81 (31.3)	0.023
Physical/sexual client violence†	5 (16.1)	36 (13.9)	0.784
Physical/sexual childhood abuse	24 (77.4)	112 (43.2)	<0.001
Police harassment/arrest†	16 (51.6)	91 (35.1)	0.072
Primary place to solicit clients†			
Street/public space	24 (77.4)	118 (45.6)	
Indoor/in-call venue	3 (9.7)	103 (39.8)	
Independent/self-advertising (e.g., newspapers, online)	4 (12.9)	38 (14.7)	0.002

† Time-updated, last 6 months as reference

Table 2: Unadjusted and adjusted hazard ratios for predictors of time to suicidality among women in Vancouver, 2010-2014 (N=290)

Characteristics	Unadjusted Hazard Ratio (95%CI)	p-value	Adjusted Hazard Ratio (95%CI)	p-value
Psychedelic use	1.00 (0.45 to 2.23)	0.995	0.40 (0.17 to 0.94)*	0.036
Cannabis use	3.44 (1.21 to 9.79)	0.021		
Prescription opioid use	1.88 (0.91 to 3.90)	0.089		
Crack use	3.06 (1.07 to 8.74)	0.037		
Cocaine use	2.53 (1.03 to 6.22)	0.043		
Crystal meth use	3.73 (1.75 to 7.97)	<0.001	3.25 (1.47 to 7.21)*	0.004
Heroin use	2.26 (0.99 to 5.13)	0.053		
HIV seropositivity†	2.15 (0.92 to 5.06)	0.078		
Childhood abuse	3.92 (1.69 to 9.09)	0.002	3.54 (1.49 to 8.40)*	0.004
Indigenous ancestry	2.76 (1.34 to 5.67)	0.006		
Canadian born	6.72 (1.62 to 27.95)	0.009		
Homelessness†	2.55 (1.19 to 5.44)	0.016	1.95 (0.91 to 4.17)*	0.085
Primary place to solicit clients†				
Indoor venue (vs. street)	0.19 (0.06 to 0.66)	0.009		
Independent (vs. street)	0.38 (0.14 to 1.05)	0.061		

† Time-updated, last 6 months as reference
*Final multivariable model determined using backward selection with best overall fit, as indicated by the lowest Akaike information criterion (AIC) value.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page, 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3, 4
Objectives	3	State specific objectives, including any prespecified hypotheses	4, 5
Methods			
Study design	4	Present key elements of study design early in the paper	5, 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5, 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	5, 10
Study size	10	Explain how the study size was arrived at	6, 7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6, 7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6, 7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how loss to follow-up was addressed	7
		(*e*) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7, 8
		(b) Give reasons for non-participation at each stage	6, 7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-9, 19, 20
		(b) Indicate number of participants with missing data for each variable of interest	7, 8
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 20, 7
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9, 10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.