

**EXPLORING TRAJECTORIES OF DRUG USE, VIOLENCE, AND SUICIDALITY  
AMONG MARGINALIZED WOMEN: AVENUES OF INTERVENTION AND THE  
THERAPEUTIC POTENTIAL OF PSYCHEDELICS**

by

ELENA MARIA ARGENTO

MPH, Simon Fraser University, 2009

BA, The University of British Columbia, 2004

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF  
THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

in

THE FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES  
(Interdisciplinary Studies)

THE UNIVERSITY OF BRITISH COLUMBIA  
(Vancouver)

June 2019

© Elena Maria Argento, 2019

The following individuals certify that they have read, and recommend to the Faculty of Graduate and Postdoctoral Studies for acceptance, the dissertation entitled:

**Exploring trajectories of drug use, violence, and suicidality among marginalized women:  
Avenues of intervention and the therapeutic potential of psychedelics**

submitted by Elena Maria Argento in partial fulfillment of the requirements for

the degree of Doctor of Philosophy

in Interdisciplinary Studies

**Examining Committee:**

Dr. Kate Shannon, Medicine

Co-supervisor

Dr. Steffanie Strathdee, Medicine

Co-supervisor

Dr. Kenneth Tupper and Dr. Jean Shoveller, School of Population and Public Health

Supervisory Committee Members

Dr. Eugenia Oviedo-Joekes, School of Population and Public Health

University Examiner

Dr. Christian Schütz, Psychiatry

University Examiner

## **Abstract**

**Background:** Women who are marginalized due to social and/or economic disadvantage, including street-involved women, sex workers, and women who use drugs, experience numerous health and social inequities that disproportionately elevate risk of violence and suicidality. However, research and intervention programs to prevent violence and address systemic drivers of suicidality have been largely absent for this population and the socio-structural determinants remain poorly understood and under investigated. This dissertation therefore sought to explore trajectories of drug use, violence and suicidality among marginalized sex workers and aimed to identify avenues of intervention with a special focus on the therapeutic utility of psychedelics.

**Methods:** This dissertation drew on data collected from AESHA (An Evaluation of Sex Workers' Health Access), a community-based open prospective cohort of women sex workers across Metro Vancouver, Canada. Bivariate and multivariable logistic regression analyses using generalized estimating equations were employed to examine associations between various intersecting socio-structural factors and suicidality. Cox regression analyses were used to examine the impact of individual and socio-structural factors on incidence of crystal methamphetamine injection and suicidality, and assessed the independent effect of naturalistic psychedelic use on suicidality.

**Results:** This dissertation identified that sex workers experience elevated risk and rates of suicidality influenced by dynamic, interrelated socio-structural factors. Experiences of interpersonal violence, homelessness, trauma/mental illness and physical/sexual childhood abuse were among the strongest determinants shaping drug use trajectories and risk of suicidality.

Importantly, the study findings demonstrated that increased social cohesion had an independent protective effect on suicidality, as did psychedelic use, which was associated with a 60% reduced hazard of suicidality.

**Conclusion:** Socio-structural factors play a critical role in potentiating and mitigating risk of suicide. Strengthening social cohesion among sex workers may be an important protective strategy, and this dissertation provides some of the first empirical evidence of the potential benefits of psychedelic use for preventing suicidality. The collective findings of this dissertation offer critical insights into how integrated, trauma-informed, community-led structural interventions may mitigate risk of suicide, and underscore the need to advance research on the therapeutic utility of psychedelics alongside broader interventions that facilitate social cohesion and connectedness.

## **Lay Summary**

Women who are marginalized due to social and/or economic inequities, including those who are street-involved and/or use drugs, experience a disproportionate burden of violence and suicide; however, research and intervention programs to prevent violence and suicide have been largely absent for this population. This thesis examined the interplay between drug use, violence and suicidality among a community-based cohort of street and indoor sex workers in Metro Vancouver, Canada, and aimed to identify avenues of intervention including whether psychedelic use could have a protective effect on suicidality. This thesis demonstrated that key socio-structural factors shape risk of suicide, such as experiences of interpersonal violence, trauma, homelessness, and childhood abuse. Findings demonstrated that increased social cohesion and psychedelic use were protective against suicidality, underscoring the need to advance research on the therapeutic utility of psychedelics alongside broader trauma-informed structural interventions that facilitate social cohesion and connectedness.

## **Preface**

This statement certifies that the work presented in this dissertation was conceived, conducted, written, and disseminated by Elena Argento (EA). All research within this dissertation received ethical approval from the University of British Columbia/Providence Health Care Research Ethics Board (H09-02803). Co-authors of the manuscripts – Dr. Kate Shannon (KS), Dr. Steffanie Strathdee (SS), Dr. Jean Shoveller (JS), Dr. Kenneth Tupper (KT), Melissa Braschel (MB), Dr. Shira Goldenberg (SG), Dr. Julio Montaner (JM), and Dr. Evan Wood (EW) – made contributions only as is commensurate with supervisory committee, collegial, or co-author duties. KS is the principal investigator of the program of research from which the studies were derived (AESHA), and takes full responsibility for the integrity of the results and accuracy of the data.

With guidance from supervisors (KS and SS) and committee members (KT and JS), EA designed the studies and wrote the research protocols. SS, JS, MB, and KS provided contextual and scientific input and approved the final version of the manuscript presented in Chapter 2. SS, SG, MB, JM, and KS provided contextual and scientific input and approved the final version of the manuscript presented in Chapter 3. SS, KT, MB, EW, and KS provided contextual and scientific input and approved the final version of the manuscript presented in Chapter 4. The statistical analyses in Chapters 2, 3, and 4 were conducted by MB in collaboration with EA.

All chapters in this dissertation were prepared, written, and edited by EA. Final drafts of the manuscripts were prepared following inclusion of material based on comments from all co-authors, journal editors, and external peer reviewers. Chapters 1 and 5 are original, unpublished

products written by EA, with input from supervisors (KS and SS) and members of the supervisory committee (JS and KT). The analysis presented in Chapter 2 is currently under review. The analyses presented in Chapters 3 and 4 have been published.

#### Chapter 2:

**Argento E**, Strathdee SA, Shoveller JA, Braschel M, & Shannon K. (submitted for publication).

Correlates of suicidality among a community-based cohort of women sex workers: The protective effect of social cohesion.

#### Chapter 3:

**Argento E**, Strathdee SA, Goldenberg S, Braschel M, Montaner J, & Shannon K. (2017).

Violence, trauma and living with HIV: Longitudinal predictors of initiating crystal methamphetamine injection among sex workers. *Drug and Alcohol Dependence*, 175, 198-204.

#### Chapter 4:

**Argento E**, Strathdee SA, Tupper K, Braschel M, Wood E, & Shannon K. (2017). Does

psychedelic drug use reduce risk of suicidality? Evidence from a longitudinal community-based cohort of marginalized women in a Canadian setting. *BMJ Open*, 7, e016025.

# Table of Contents

<b>Abstract.....</b>	<b>iii</b>
<b>Lay Summary .....</b>	<b>v</b>
<b>Preface.....</b>	<b>vi</b>
<b>Table of Contents .....</b>	<b>viii</b>
<b>List of Tables .....</b>	<b>xi</b>
<b>List of Figures.....</b>	<b>xii</b>
<b>List of Abbreviations .....</b>	<b>xiii</b>
<b>Acknowledgements .....</b>	<b>xiv</b>
<b>Dedication .....</b>	<b>xvi</b>
<b>Chapter 1: Introduction .....</b>	<b>1</b>
1.1 Suicide risk among marginalized women .....	1
1.2 Theoretical orientation and conceptual framework .....	4
1.3 Literature review of socio-structural determinants of suicide risk among marginalized women.....	8
1.4 The therapeutic potential of psychedelics.....	19
1.5 Research objectives and aims .....	39
1.6 Study design and methods .....	40
1.7 Overview of the dissertation .....	42
<b>Chapter 2: Correlates of suicidality among a community-based cohort of women sex workers and the protective effect of social cohesion.....</b>	<b>44</b>
2.1 Introduction.....	44

2.2	Methods.....	45
2.3	Results.....	48
2.4	Discussion.....	49
2.5	Limitations.....	52
2.6	Conclusion.....	53
<b>Chapter 3: Violence, trauma and living with HIV: Longitudinal predictors of initiating crystal methamphetamine injection among sex workers .....</b>		<b>56</b>
3.1	Introduction.....	56
3.2	Methods.....	59
3.3	Results.....	61
3.4	Discussion.....	63
3.5	Limitations.....	68
3.6	Conclusion.....	68
<b>Chapter 4: Does psychedelic use reduce risk of suicidality? Evidence from a longitudinal community-based cohort of marginalized women in Canada .....</b>		<b>73</b>
4.1	Introduction.....	73
4.2	Methods.....	75
4.3	Results.....	77
4.4	Discussion.....	79
4.5	Limitations.....	82
4.6	Conclusion.....	84
<b>Chapter 5: Discussion, implications, and conclusions .....</b>		<b>87</b>
5.1	Summary of findings.....	87

5.2	Informing avenues of intervention and directions for future research.....	89
5.3	Study strengths and limitations.....	103
5.4	Conclusion .....	105
	<b>Bibliography .....</b>	<b>107</b>

## List of Tables

<b>Table 2.1:</b> Baseline socio-structural characteristics of women sex workers who reported suicidality in the last six months, compared to those who did not (N=867).....	54
<b>Table 2.2:</b> Unadjusted and adjusted odds ratios for correlates of recent suicidality among women sex workers in Vancouver, 2010-2017 (N=867) .....	55
<b>Table 3.1:</b> Baseline characteristics of sex workers in Vancouver who reported first time injection crystal methamphetamine use over follow-up compared to those who did not (N=455).....	70
<b>Table 3.2:</b> Unadjusted and adjusted hazard ratios (AHR) for predictors of time to initiating crystal methamphetamine injection among sex workers in Vancouver, 2010-2014 (N=455) .....	71
<b>Table 4.1:</b> Baseline characteristics of women in Vancouver who thought about or attempted suicide over follow-up, compared to those who did not (N=290) .....	85
<b>Table 4.2:</b> Unadjusted and adjusted hazard ratios for predictors of time to suicidality among women in Vancouver, 2010-2014 (N=290) .....	86

## List of Figures

<b>Figure 1.1</b> Conceptual model for iterative pathways to suicidality among marginalized women and potential avenues of intervention .....	7
<b>Figure 3.1</b> Time to initiation of crystal methamphetamine (CM) injection by physical/sexual workplace violence experiences .....	72
<b>Figure 3.2</b> Time to initiation of crystal methamphetamine (CM) injection by physical/sexual childhood abuse .....	72

## List of Abbreviations

AESHA	An Evaluation of Sex Workers' Health Access
ATS	Amphetamine-type stimulants
CGSHE	Centre for Gender & Sexual Health Equity
CBT	Cognitive Behavioral Therapy
CI	Confidence interval
CM	Crystal methamphetamine
DALY	Disability-adjusted life years
DMT	Dimethyltryptamine
DMN	Default Mode Network
DSM	Diagnostic and Statistical Manual of Mental Disorders
EMDR	Eye Movement Desensitization and Reprocessing
fMRI	Functional magnetic resonance imaging
GEE	Generalized estimating equations
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
LMIC	Low- and middle-income countries
LSD	Lysergic acid diethylamide
MAPS	Multidisciplinary Association for Psychedelic Studies
MDMA	Methylenedioxymethamphetamine
NIMH	National Institute of Mental Health
NSWP	Global Network of Sex Work Projects
PCEPA	Protection of Communities and Exploited Persons Act
PTSD	Post-traumatic stress disorder
SAMHSA	Substance Abuse and Mental Health Services Administration
SSRI	Selective serotonin reuptake inhibitor
STI	Sexually transmitted infection
UNAIDS	Joint United Nations Program on HIV/AIDS
UNODC	United Nations Office on Drugs and Crimes
YLL	Years of life lost

## **Acknowledgements**

I want to express my deep gratitude to my co-supervisors, Drs. Kate Shannon and Steffanie Stratheedee, and to my supervisory committee members, Drs. Kenneth Tupper and Jean Shoveller, for their ongoing mentorship and support. I am very appreciative to have had the opportunity to be guided by such an experienced, thoughtful, and supportive team. It was a privilege to learn from all four of these extraordinary scholars and their collective supervision has been fundamental to my growth as a researcher. In particular, I am grateful for the expert guidance and encouragement to pursue this work from Kate Shannon. Her unwavering commitment to the rights of marginalized women has been a source of great inspiration from the beginning. I also want to extend special thanks to Ken Tupper who has been a great mentor and friend over the years. He was one of the first people to discuss psychedelic research with me and our many conversations helped me to think through the complexities surrounding this work. I have also benefited greatly from the support and guidance offered by Shira Goldenberg, Andrea Krusi, Tara Lyons, Kathleen Deering, Zach Walsh, Peter Hendricks, Eugenia Socias and Evan Wood.

I offer my enduring appreciation to the AESHA participants who so generously shared their time, stories and expertise. Without them this dissertation would not have been possible. I also extend my sincerest thanks to the AESHA interview, outreach and nursing team and to past and present staff at the Centre for Gender & Sexual Health Equity for their immeasurable support, in particular Colette Ryan, Megan Bobetsis, Sylvia Machat, Sarah Moreheart and Jill Chettiar.

Thank you to Melissa Braschel for her patience and statistical expertise, and to Peter Vann for always making the administrative side of things easy, and to many others for their honest encouragement, feedback and camaraderie over the years. Special thanks to Putu Duff, Bronwyn

McBride, Margaret Erickson, Stephanie Lake, Tessa Cheng and Pauline Voon for the invaluable advice, encouragement and laughter. Brittany Barker and Mary Clare Kennedy, you made doctoral studies more fun than I could have ever imagined. I could not have done this without you.

My doctoral research was generously supported by a Canadian Institutes of Health Research Doctoral Award, a UBC Four Year Fellowship and a Killam Scholarship. I also thank the Centre for Gender & Sexual Health Equity for providing salary support during my doctoral training.

Finally, my deepest gratitude goes to my closest friends and family for their unconditional love and support. To my parents, Floriana and Elmiro, my brothers, Andrew and Michael, and my sister, Gianna, for always believing in me and supporting me in whatever I choose to do, even when it means gallivanting across the globe. I am truly grateful for all of the opportunities I have been afforded as a direct result of your love and support. I am also deeply grateful for my family in South Africa, Rentia & Stoffel, Martie & Chris, Van Wyk & Janette, and Zarine & Emile, whose love and kindness never cease to amaze me. I feel very fortunate to have you all in my life.

Last, but furthest from least, my husband Christiaan, without whom this dissertation would not exist. I am eternally grateful for your patience, support, thoughtful feedback, encouragement, and the balance you instilled in me throughout this journey. Thank you for helping me to remember what really matters and keeping me grounded and whole.

*To my parents,  
Floriana and Elmiro*

## **Chapter 1: Introduction**

### **1.1 Suicide risk among marginalized women**

Women who live at the margins of society experience a disproportionate burden of social and health inequities worldwide. Marginalized women, such as street-involved sex workers, Indigenous women, and women who use illegal drugs, continue to face multiple forms of violence and trauma driven by a matrix of interrelated socio-structural factors (Benoit, Carroll, & Chaudhry, 2003; Shannon et al., 2015; Ulibarri et al., 2013) that significantly elevate risk of psychological distress and suicide (Clifford, Doran, & Tsey, 2013; Gu et al., 2014; Hawton & van Heeringen, 2009; Roxburgh, Degenhardt, & Copeland, 2006; Zhang et al., 2016). Research and intervention programs to prevent suicide have paid inadequate attention to key sub-populations and marginalized individuals who experience elevated risks and harms, such as violence, stigma, criminalization, lack of social support, and concurrent mental and substance use disorders.

Globally, suicide is a critical public health concern and leading cause of morbidity and mortality (Hawton & van Heeringen, 2009; World Health Organization, 2014). Approximately 1 million people die each year from suicide, which translates to one death every 40 seconds (World Health Organization, 2014). It has been estimated that 80-90% of suicide deaths are attributable to mental or substance use disorders; in 2010 alone, such disorders accounted for 183.9 million disability-adjusted life years (DALYs) and 8.6 million years of life lost (YLLs) to premature mortality worldwide, equivalent to 232,000 deaths (Statistics Canada, 2015; Whiteford et al., 2013). The etiological pathways to suicide are multifaceted, involving a convergence of individual, social, cultural and environmental factors combined with experiences of trauma and

loss (Hawton & van Heeringen, 2009; O'Connor & Nock, 2014; Zalsman et al., 2016). As originally put forth by Emile Durkheim in 1897, suicide is not merely an individual-level issue, but rather can be understood from a sociological perspective whereby socio-structural forces (e.g., social disintegration or a lack of social solidarity) are key drivers of risk (Durkheim, 1951). Suicidal ideation and attempts (suicidality) and depression are some of the strongest predictors of suicide (Center for Addiction and Mental Health, 2011; Klonsky, May, & Saffer, 2016); however, efforts to improve mental health over the last few decades have been largely unsuccessful in reducing rates of suicide leading to a call by the US National of Mental Health for innovative research and treatment to prevent suicide (NIMH, 2014). The relatively recent medicalization of suicide as a primarily pathological problem internal to the individual elides a richer understanding of suicide as influenced by larger social and cultural constructs, and in turn overlooks alternative avenues of intervention (Marsh, 2010). Evidence has demonstrated that some forms of cognitive behavioral therapy and pharmacological interventions may reduce suicidality; however, the literature is hampered by publication bias and significant inconsistencies in strategies and outcome measures (O'Connor & Nock, 2014; Zalsman et al., 2016). There remains a paucity of evidence to support the efficacy of prevention interventions (Zalsman et al., 2016), and stigma continues to hinder research and reporting of suicidality (Klonsky et al., 2016).

There is significant heterogeneity in suicide rates across settings and populations, with rates generally higher among men than women, yet rates of suicidal ideation and attempts are higher among women (Center for Addiction and Mental Health, 2011; Klonsky et al., 2016), and suicide is the leading cause of death among female youth aged 15-19 (Klonsky et al., 2016; World

Health Organization, 2014). Suicidality is an undeniably complex phenomenon that cannot be explained by any single or set of risk factors, making broad generalizations about risk counterproductive. However, those who experience multiple simultaneous disadvantages (e.g., violence, trauma, stigma, discrimination, lack of social support, concurrent mental and substance use disorders) are at the highest risk of suicide (Center for Addiction and Mental Health, 2011; Hawton & van Heeringen, 2009), such as marginalized and street-entrenched sex workers who continue to endure elevated levels of social and health-related risks and harms as a result of dynamic structural drivers (e.g., poverty, criminalization, and racism). The literature highlights greater risk for suicide among people with a history of trauma (Hadland et al., 2012; Hawton & van Heeringen, 2009; O'Connor & Nock, 2014) and some research suggests increased risk among street-involved sex workers who report historical experiences of violence and childhood abuse (Gilchrist, Gruer, & Atkinson, 2005; Gu et al., 2014; Roxburgh et al., 2006; Shahmanesh et al., 2009; Zhang et al., 2016). Research has also reported significant associations between social exclusion, depression, post-traumatic stress disorder (PTSD), and suicidality among street-based sex workers and those who use drugs (Gu et al., 2014; Lau, Tsui, Ho, Wong, & Yang, 2010; Roxburgh et al., 2006; Surratt, Kurtz, Chen, & Mooss, 2012; Zhang et al., 2016). While data on suicidality among marginalized women is limited, global research has estimated that 19-75% of marginalized women involved in sex work report recent suicide ideation or attempts (Gu et al., 2014; Jung, 2013; Lau et al., 2010; Nemoto, Boedeker, & Iwamoto, 2011; Roxburgh et al., 2006; Shahmanesh et al., 2009).

Given the complex etiology of suicidality and limited effectiveness of well-established evidence-based interventions, there remains a critical need to explore and prioritize innovative approaches

to prevent and treat suicidality. One potential and novel avenue of intervention is psychedelic medicine – an area of renewed interest for treating depression, anxiety, PTSD, and addiction issues (Sessa, 2012; Tupper, Wood, Yensen, & Johnson, 2015). Various psychedelic compounds are currently being investigated in clinical trials for their neuropharmacological functions and uses as adjuncts to psychotherapy (Carhart-Harris, Leech, et al., 2012; dos Santos et al., 2016; Mithoefer et al., 2018). Large population studies have demonstrated strong correlations between naturalistic (non-medical) use of psychedelics and reduced recidivism, intimate partner violence, psychological distress, and suicidality (Hendricks, Clark, Johnson, Fontaine, & Cropsey, 2014; Johansen & Krebs, 2015; Thiessen, Walsh, Bird, & Lafrance, 2018; Walsh et al., 2016). Further, qualitative work has illuminated the potential role of psychedelics in increasing wellbeing among women who have experienced sexual trauma (Espinoza, 2014), eating disorders (Lafrance et al., 2017; Renelli et al., 2018), and among gender and sexual minorities (Cavnar, 2014). Despite the revitalization of psychedelic medicine in recent years, marginalized women have been largely excluded and underrepresented in these studies, and large gaps remain in the literature on how clinical psychedelic therapies or naturalistic psychedelic use might influence suicide risk, encouraging the advancement of psychedelic research with the inclusion of marginalized women.

## **1.2 Theoretical orientation and conceptual framework**

### **1.2.1 Structural determinants framework**

This research is guided by a structural determinants framework: one that emphasizes the role of social, structural, and environmental factors in shaping individual-level health outcomes (Rhodes, 2009; Shannon, Goldenberg, Deering, & Strathdee, 2014; Shannon et al., 2015). A structural determinants approach aims to elucidate how intersecting socio-structural factors (e.g.,

criminalization, laws/policies, stigma, wealth distribution, racism, cultural norms) influence and interact with community-level factors (e.g., interpersonal violence, partner-level dynamics, access to services, housing, social support, social isolation) and intrinsic factors such as biological predisposition (e.g., depression, anxiety, drug dependence) in determining health and wellbeing (Figure 1). Central to this framework is the notion that those who are marginalized or stigmatized in society are subjected to structural violence, whereby the social conditions embedded within the larger political, economic, and cultural organization of society inhibit individuals or populations from reaching their full potential, reproducing inequalities and powerlessness (Farmer, Nizeye, Stulac, & Keshavjee, 2006; Rhodes et al., 2012).

### **1.2.2 Drawing on intersectionality**

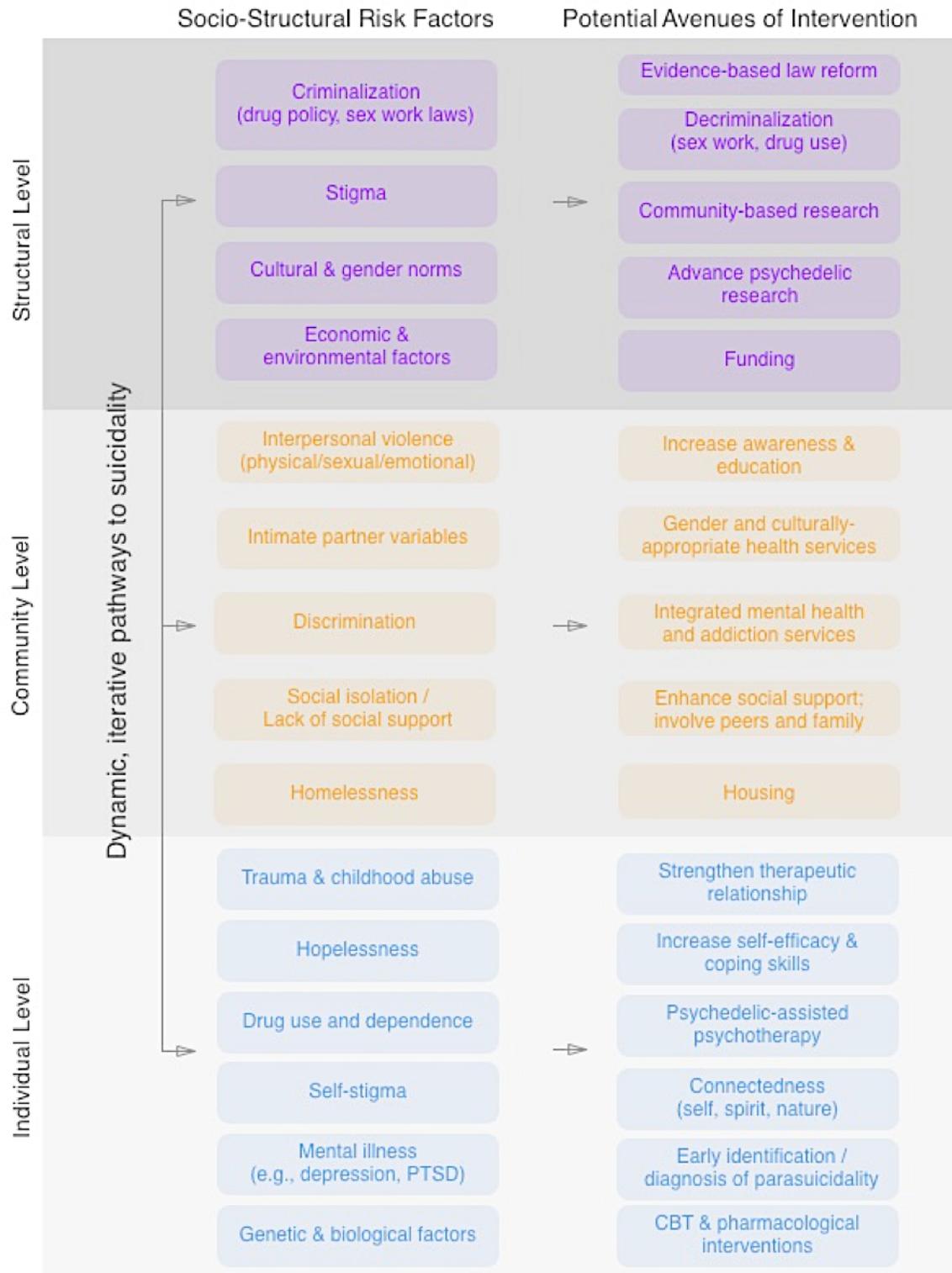
Alongside a structural determinants approach, this thesis draws from the theory of intersectionality, which offers a framework within which to examine how various social identities and positions shape disparities in health by focusing on the experiences of marginalized or oppressed populations as its vantage point (Bowleg, 2012). Approaches to modeling and operationalizing intersectionality remain challenged by the complexity of delineating the intersections between various marginalizing characteristics and the social inequalities related to them (Bowleg, 2008; Seng, Lopez, Sperlich, Hamama, & Reed Meldrum, 2012). The analyses for this thesis do not employ quantitative intersectional methodology, but rather draw from the theory of intersectionality to inform conceptual approaches to undertaking this research. An important yet necessary challenge to reducing and preventing suicide is to identify and examine synergistic effects among modifiable and protective factors that can be intervened upon to inform effective and evidence-based approaches (Nock et al., 2008). Thus,

intersectionality is critical to addressing complex, multidimensional health issues, such as suicidality, in that it embraces the complexities that are essential to understanding social and health inequalities and discovering novel approaches in which to intervene (Bowleg, 2012).

### **1.2.3 A rights-based approach and cognitive liberty**

A rights-based approach with an emphasis on cognitive liberty informs how criminalization and drug policies impact health, and is especially pertinent to the study of psychedelics. The legal and ethical notion of cognitive liberty is an extension of the fundamental right to freedom of thought (Government of Canada, 1982; United Nations, 1948), and acknowledges that individuals should “*have the right to autonomous self-determination over their own brain chemistry, a right that is currently infringed by the prohibition of psychedelics*” (Walsh, 2016). Within a rights-based approach, at a minimum cognitive liberty must mean that each person is “*free to direct one’s own consciousness; one’s own underlying mental processes, and one’s beliefs, opinions, and worldview*” (Boire, 1999). Such an approach builds upon the tenets of the harm reduction paradigm to advance the focus beyond negative consequences associated with drug use to one that works to ensure rights and maximize benefits (Walsh, 2016). Cognitive liberty has important implications for drug policy reform, as it posits that criminal drug prohibition (e.g., of psychedelics) essentially violates freedom of thought by infringing upon the fundamental right to self-determine one’s own mental states (Walsh, 2010, 2016).

**Figure 1.1 Conceptual model for iterative pathways to suicidality among marginalized women and potential avenues of intervention**



### **1.3 Literature review of socio-structural determinants of suicide risk among marginalized women**

#### **1.3.1 Structural violence and the impact of criminalization**

A well-established body of literature describes violence along a continuum of structural, everyday, symbolic, and physical dimensions (Bourdieu, 2001; Bourgois, Prince, & Moss, 2004; Bourgois & Schonberg, 2009; Farmer, 1996; Rhodes et al., 2012). Structural violence refers to the ways in which social suffering and harms at the individual level are shaped by social arrangements embedded in the political, economic, and cultural organization of societies (Farmer, 1996). Conceptualizing violence beyond merely physical phenomena helps us to understand how social inequities are reproduced and normalized by what Scheper-Hughes (2004) coined ‘everyday violence,’ rendering structural violence among those at the bottom of social hierarchies invisible (Bourgois et al., 2004; Scheper-Hughes, 1996).

Research and evidence demonstrate that criminalization of “vices” such as sex and drugs, along with punitive policing practices and the ensuing fear of law enforcement and incarceration, contribute to a lack of social and health protections (e.g., police protections from violence, community empowerment, access to services) and ultimately undermine the health needs of marginalized women (Argento et al., 2016; Csete & Cohen, 2010; Rhodes, 2009; Shannon et al., 2015). Violence among sex workers varies substantially by structural inequities (e.g., work environments) and community level protective factors (e.g., empowerment) ranging from as low as 7% to as high as 75% (Deering et al., 2014). Research has shown that violence among sex workers is largely shaped by the criminalized nature of sex work and contemporaneous stigma, discrimination, and social marginalization (Decker et al., 2015; Krüsi et al., 2012; Shannon et al.,

2015). Violence at the structural level (i.e., criminalization/laws, stigma, economic and cultural factors) strongly and negatively impacts health at the individual level, leading to increased physical risks and harms (e.g., injury, death, HIV/STI) (Deering et al., 2014; Shannon & Csete, 2010; World Health Organization, 2013) as well as poor mental health and emotional wellbeing (e.g., addiction, depression, anxiety, PTSD) (Roxburgh et al., 2006; World Health Organization, 2014; Zhang et al., 2016).

In Canada, so-called ‘end-demand’ legislation was implemented in 2014, known as the “Protection of Communities and Exploited Persons Act” (PCEPA), that criminalizes new aspects of sex work (communicating for the purpose of selling sex, purchasing and advertising of sexual services), targeting clients and third parties while leaving the sale of sex legal (Government of Canada Department of Justice, 2015). The impacts of the new laws on health and wellbeing of sex workers are beginning to emerge, and global research and evidence emphasize that criminal policies and punitive enforcement-based approaches to sex work continue to undermine the health and human rights of sex workers, leading numerous human rights and public health experts and international bodies, such as the World Health Organization, UNAIDS, and Amnesty International, along with sex work communities worldwide to strongly endorse full decriminalization of sex work (Amnesty International, 2015; Global Commission on HIV and the Law, 2012; World Health Organization, 2012). Research evaluating the impact of the PCEPA on sex workers’ access to health and community-led services and supports in Vancouver, Canada, found reduced access to these critical services and supports following implementation of end-demand laws (Argento et al., under review).

Additionally, a recent study from France found that end-demand laws had detrimental effects on sex workers' safety, health and overall living conditions – exacerbating, rather than reducing, the harms associated with previous laws against soliciting (Le Bail & Giametta, 2018).

Similar outcomes have been observed in the USA and Mexico, suggesting that high rates of depression and PTSD are both a product of and exacerbated by social isolation, stigma, and repeated violence and lack of recourse as a result of criminalized approaches to sex work (Nemoto et al., 2011; Surratt et al., 2012; Ulibarri et al., 2013). In contrast, in New Zealand where sex work has been decriminalized, sex workers experience improved safety and working conditions, including police protections against violence (Abel, 2014). Workplace violence (e.g., from clients, police, managers, pimps) among criminalized sex workers is a highly prevalent human rights violation due to a lack of safety and reduced ability among sex workers (across genders) to negotiate the terms of their work to ensure safe working conditions (Decker et al., 2015; Krüsi et al., 2012; Shannon et al., 2015). Recent research in Vancouver demonstrated that women sex workers working in more marginalized settings (i.e., the street or informal indoor settings) experienced a disproportionate burden of mental health problems (depression, anxiety, PTSD) (Puri, Shannon, Nguyen, & Goldenberg, 2017). The evidence is unequivocal that in criminalized settings sex workers are forced into adversarial relationships with police officers and are unable to access essential social, health, and legal protections (Csete & Cohen, 2010; Shannon et al., 2015), thereby contributing to a higher burden of mental illness.

Largely stemming from criminalization policies on sex work and drug use, stigma and discrimination and overall distrust of health care providers prevents many from seeking or accessing safe and non-judgmental health and support services (Corrigan, 2004; Lazarus et al.,

2012; Roxburgh, Degenhardt, Copeland, & Larance, 2008). Among gender and sexual minorities, severe forms of stigma/transphobia, prejudice and discrimination (e.g., hate crimes) have been linked to increased violence, trauma, and suicidality (Duncan & Hatzenbuehler, 2014; Haas et al., 2011; Lyons et al., 2015; Nemoto et al., 2011; Operario, Soma, & Underhill, 2008). Research in California among 573 trans women with a history of sex work uncovered significantly high rates of psychological vulnerability and suicidality: 74% reported lifetime suicidal ideation, of whom 64% had attempted suicide (Nemoto et al., 2011). Notably, the participants had experienced high rates of physical and sexual violence, transphobia and lack of social support and these intersecting social risk factors were strongly linked with depression and suicidality (Nemoto et al., 2011). Stigma in the form of internalized or self-stigma has a detrimental impact on psychological wellbeing (Corrigan, 2004), and has been associated with depression, emotional trauma, social isolation, and suicidality amongst sex worker and trans populations (Gu et al., 2014; Hong et al., 2010; Mizock & Lewis, 2008; Nemoto et al., 2011; Zhang et al., 2016).

Indigenous women in North America - a group vastly overrepresented among street-involved sex workers and women who use drugs in Canada (Duff et al., 2013; Shannon et al., 2007) - experience an unacceptably high burden of psychosocial vulnerability as a result of the devastating multigenerational trauma stemming from colonialism, racialized policies, and disconnection from traditions, language, culture and spirituality (Chansonneuve, 2007; Gracey & King, 2009). Suicide rates among Indigenous peoples in Canada are two to three times higher than the general population (Clifford et al., 2013). Further, the disproportionate criminalization of Indigenous women underscores the multidimensional social vulnerabilities of stigma, racism,

and historical trauma that continue to reproduce harms and inequalities (Benoit et al., 2003; Bingham, Leo, Zhang, Montaner, & Shannon, 2014; Culhane, 2003).

### **1.3.2 Interpersonal violence and community-level determinants**

At the community level, experiences of interpersonal violence substantially elevate risk of suicidality among women (Devries et al., 2011; World Health Organization, 2014). A comprehensive global review found physical and sexual interpersonal violence against women to be a major cause of morbidity and mortality, citing global and regional prevalence estimates for the first time in 2013; health outcomes included incident HIV/STI, induced abortion, depression, and suicide, and traumatic stress was highlighted as the primary mechanism linking interpersonal violence to suicide (World Health Organization, 2013). Stressful life events have been consistently linked to suicide risk (NIMH, 2014), and marginalized women (i.e., those subjected to poverty, ongoing stigma, and violent victimization) are often forced to cope with more challenging and harmful life events with less means and resources to do so (Benoit et al., 2003; Guillen, Panadero, Rivas, & Vazquez, 2015).

Qualitative and ethnographic research among marginalized groups of women (e.g., street-involved sex workers and women who use drugs) has documented the pervasiveness of controlling and abusive male intimate partners, underscoring the impact of gendered power imbalances and repeated exposures to violence that directly influences women's agency and ability to safeguard against risky sexual and drug-using behaviors, alongside the normalization of violence within the context of multiple and overwhelming forms of oppression such as poverty,

racism, and economic dependence on partners (Bourgois et al., 2004; Maher, 1997; Shannon et al., 2008).

Evidence from other settings (e.g., China and India) demonstrates significant links between interpersonal violence and suicidality among women sex workers. For example, cross-sectional research among female sex workers in China revealed strong correlations between intimate partner violence and suicidality, depression, loneliness, and drug use (Hong, Zhang, Li, Liu, & Zhou, 2013; Zhang et al., 2016). A study conducted among 200 female sex workers who inject drugs (of whom 45% reported suicidal ideation and 27% had attempted suicide in the last six months) found that self-stigma, depression, and having been physically or verbally abused by clients or managers were independently associated with recent suicidality (Gu et al., 2014). Likewise, among 454 sex workers working in entertainment establishments in China significant correlations were demonstrated between sexual coercion and recent suicidality (Wang et al., 2007). Among a cohort of 326 female sex workers in Goa, India, suicidality was independently associated with structural-level factors (e.g., gender disadvantage, context of sex work) and intimate partner violence was associated with a nearly 3-fold increased odds of suicidality (Shahmanesh et al., 2009).

While these findings across different cultures may not be generalizable to marginalized women in Canada, the authors signaled the importance of social support and community empowerment/mobilization in improving access to mental health services and preventing and reducing risk of suicide (Shahmanesh et al., 2009; Zhang et al., 2016). Social support is an important determinant of suicidality (Klonsky et al., 2016; NIMH, 2014; O'Connor & Nock,

2014), yet marginalized women who have experienced interpersonal violence may be less likely to seek or receive social support as a result of stigma surrounding interpersonal violence, in turn exacerbating internalized stigma (Overstreet & Quinn, 2013; Zhang et al., 2016). Given the demonstrated positive health impacts (e.g., reduced social discrimination, increased client condom use) of empowerment and social cohesion among sex workers (Argento et al., 2016; Fonner et al., 2014; Lippman et al., 2010), strengthening social networks and collectivization among marginalized women has great potential to protect against suicide risk, yet the research is scant.

### **1.3.3 Past trauma, re-victimization, and PTSD**

Both recent and historical experiences of violence have severe negative impacts upon psychological health and increase suicide risk by triggering depression and other emotional distress (World Health Organization, 2014). Trauma refers to shocking and overwhelming events or experiences that involve a major threat to the physical, emotional, or psychological safety and wellbeing of either the individual or a loved one (Courtois et al., 2017). A potential reaction to traumatic events is posttraumatic stress disorder (PTSD) – a “Trauma-and Stressor-Related Disorder” in the DSM-5 characterized by re-experiencing the traumatic event, involuntary and intrusive recollections, avoiding or numbing of triggers, negative alterations in mood, and hyperarousal/reactivity associated with the trauma (Courtois et al., 2017). The trauma incurred by childhood abuse and gender-based violence extends well beyond the violent act itself, into subsequent re-victimization and harmful impacts upon psychosocial domains (Kimerling, Alvarez, Pavao, Kaminski, & Baumrind, 2007; Noll, Horowitz, Bonanno, Trickett, & Putnam, 2003; Romero-Daza, Weeks, & Singer, 2005). Both direct experiences of violence, as well as

indirect violence (i.e., witnessing violence) contribute to suicide risk by precipitating emotional stressors such as depression, anxiety, and PTSD and increasing feelings of vulnerability, fear, and insecurities about one's own safety (Romero-Daza et al., 2005). The association between PTSD and suicidality (including suicide completion) is highly significant, and comorbid depression is known to substantially compound risk (Panagioti, Gooding, & Tarrier, 2012).

Among marginalized and street-entrenched populations globally, reported rates of childhood abuse are high (Argento, Chettiar, Nguyen, Montaner, & Shannon, 2015; Rio Navarro et al., 2012; Roxburgh et al., 2006). Recent research among women sex workers in Vancouver, Canada indicated that a large proportion (71%) of women had experienced physical and/or sexual abuse before age 18 (Argento, Chettiar, et al., 2015; Puri et al., 2017). Similarly, approximately 75% of street-based sex workers surveyed in Sydney, Australia reported childhood sexual abuse, and nearly half met the DSM-IV criteria for PTSD (Roxburgh et al., 2006). While estimates of psychological distress among sex workers vary across workplace and geographical settings, up to three-quarters of street-based female sex workers in the USA (n=562) reported high rates of severe depression, anxiety, and PTSD, and 88% reported lifetime histories of physical, sexual or emotional abuse (Surratt et al., 2012).

A growing body of literature elucidates the links between childhood abuse, re-victimization, and increased risk of trauma and suicidality later in life (Gilchrist et al., 2005; Noll et al., 2003; Roxburgh et al., 2006; Stoltz et al., 2007; World Health Organization, 2014). Physical and/or sexual childhood abuse among women sex workers in Vancouver was demonstrated to be positively associated with experiencing recent intimate partner violence (Argento et al., 2014).

Such re-victimization among women leads to markedly elevated risk of subsequent physical and sexual violence and mental health issues in adulthood (Kimerling et al., 2007; Noll et al., 2003; Roxburgh et al., 2006). Notably, a study of more than 11,000 women respondents in California demonstrated that re-victimization was associated with a 3-fold increased odds of depression and anxiety, and an extremely potent risk for PTSD (AOR=12.4,  $p<0.001$ ) (Kimerling et al., 2007). For street-involved sex workers who have been subjected to multiple forms of violence, childhood abuse and ensuing PTSD, re-exposure to ongoing trauma and violence as a result of dynamic structural/organizational-level factors (e.g., criminalization, stigma, lack of workplace protections) poses a substantial challenge to preventing and treating PTSD (Roxburgh et al., 2006).

#### **1.3.4 Drug use trajectories**

The ways in which drug use and experiences of violence and trauma intersect and influence risk of suicide is a multifaceted phenomenon. While substance use disorders are associated with substantially elevated risk of suicidality (Britton & Conner, 2010; Hawton & van Heeringen, 2009; World Health Organization, 2014), the mapping of drug use trajectories should be navigated within the paradigms of intersectionality using a socio-structural determinants framework. To understand addiction, it is imperative to recognize the relationships with various forms of violence (structural, interpersonal/everyday, symbolic, physical), trauma, and potential psychological motivations for using drugs: *“It is impossible to understand addiction without asking what relief the addict finds, or hopes to find, in the drug or the addictive behavior”* (Maté, 2009, p.33).

At the individual level, a growing body of literature documents drug use as a coping mechanism for psychological distress and emotional trauma such as PTSD (Romero-Daza et al., 2005; Roxburgh et al., 2008; Tull, Gratz, Aklin, & Lejuez, 2010), and addiction as an adaptation to sustained psychosocial dislocation (Alexander, 2012). It has been postulated that a lack of integration within the psychosocial fabrics of society leads to depression, anxiety, shame, anguish and suicide (Durkheim, 1951), and that addiction serves a compensatory function for people suffering from psychosocial dislocation, providing a theoretical basis for structural intervention and efforts to enhance supportive social relationships (Alexander, 2012). Many people with substance use disorders, especially with opioids, have complex relationships with both physical and emotional pain, with childhood trauma being strongly linked to subsequent substance use (Dasgupta, Beletsky, & Ciccarone, 2018). In turn, people with substance use disorders who have traumatic histories of physical or sexual abuse report elevated rates of suicidality (Fernández-Montalvo, López-Goñi, Arteaga, & Haro, 2018). Women who seek treatment for drug dependence suffer high rates of PTSD stemming from past experiences of violence; notably, the use of crystal methamphetamine is particularly high among those suffering from PTSD (Cohen, Greenberg, Uri, Halpin, & Zweben, 2007; Smith, Blumenthal, Badour, & Feldner, 2010). The literature cites sexual motivations for using drugs, particularly crystal methamphetamine, heroin, and ecstasy, among women involved in sex work (Ho, Le, & Dinh, 2013; Maher et al., 2011), suggesting that drug use among some sex workers may serve to diminish psychological distress potentially through emotional avoidance, especially among those already grappling with PTSD (Roxburgh et al., 2006). Ethnographic work among street-involved youth in Canada describes the use of crystal methamphetamine for treating both professionally and self-diagnosed depression and anxiety (Fast, Kerr, Wood, & Small, 2014). Among women

sex workers in Vancouver, Canada, exchanging sex while high, as well as intimate partner violence and police harassment were independently associated with non-medical use of pharmaceutical opioids (Argento, Chettiar, et al., 2015). Opioid-related overdoses have evolved into North America's most severe drug-overdose crisis in history – one that disproportionately impacts street-entrenched and Indigenous populations (Fischer & Argento, 2012; Fischer & Rehm, 2017) – driven by upstream socio-structural factors including homelessness, social exclusion, racism, and physical and psychological trauma (Dasgupta et al., 2018).

Among women who use drugs, research has demonstrated substantially elevated rates of childhood abuse and PTSD, and the emotional trauma from ongoing exposure to violence and re-victimization can shape patterns and frequency of drug use (El-Bassel, Gilbert, Wu, Go, & Hill, 2005; Meade et al., 2012; Romero-Daza et al., 2005; Tull et al., 2010). Street-based sex workers in Australia report highly prevalent risk factors associated with problematic substance use, including childhood abuse and exposure to multiple traumas, as well as depression, PTSD and suicidality (Roxburgh et al., 2008). Furthermore, the pervasiveness of gender inequality and male psychological dominance among couples who use drugs plays a key role in shaping interpersonal violence and impacts sexual- and drug use-related risks (Argento, Shannon, et al., 2015; El-Bassel et al., 2005; Shannon et al., 2008; Syvertsen et al., 2015; Ulibarri et al., 2015). For example, more than half of women interviewed in northern Mexico reported injecting drugs exclusively with their intimate sexual partners, and when sharing syringes with their male partners women often assume the more subordinate role, injecting after their partner (Firestone Cruz et al., 2007).

Elevated rates of suicidality have been demonstrated among people who inject drugs (Armstrong & Samson, 2016). According to a recent systematic review, 35-65% of female sex workers working predominantly in street-based settings in the US are estimated to inject drugs, with high poly-substance use (Abad et al., 2015). The pathways to initiating injection drug use among sex workers remain poorly understood and there is a critical need for further research on drug use trajectories and evidence-based addiction interventions tailored to the unique needs of marginalized women. Given the strong links between PTSD and crystal methamphetamine use among women, as well as elevated rates of suicidality among those with both substance use disorders and histories of violence and trauma, further research that focuses specifically on crystal methamphetamine injection initiation among women sex workers is needed to help elucidate socio-structural risk factors and develop interventions tailored to this population. Furthermore, criminal drug prohibition reinforces stigma and discrimination and infringes upon the health and safety of people who use illicit drugs, and various systemic, social, and cultural factors continue to shape gender disparities in access to health services, including addiction treatment and care for marginalized women globally (Csete & Cohen, 2010; UNODC, 2015).

#### **1.4 The therapeutic potential of psychedelics**

Psychedelics, also known as “hallucinogens” or “entheogens,” have a vibrant social, cultural, and medical history. Psychedelic plants have been used for centuries across diverse settings for a wide range of spiritual and therapeutic purposes and recent years have witnessed their expansion throughout mainstream global culture (McKenna & Riba, 2015; Tupper, 2008). The word ‘psychedelic’ was coined in Saskatchewan, Canada in 1956 by psychiatrist Humphrey Osmond in a letter he wrote to Aldous Huxley, which means ‘mind manifesting’ or ‘soul revealing’

(Osmond, 1957; Rucker, Iliff, & Nutt, 2018). During the 1950s and 60s, psychedelic drugs such as lysergic acid diethylamide (LSD), psilocybin, mescaline, dimethyltryptamine (DMT), and methylenedioxymethamphetamine (MDMA) were considered promising psychiatric medications for treating some mental and substance use disorders (Dyck, 2015; Nichols, 2004; Rucker, Jelen, Flynn, Frowde, & Young, 2016). Indeed, a robust body of research was conducted during this time, including some 40,000 individuals who were administered LSD within the context of these studies, yielding findings that deemed psychedelics to be generally safe and to hold considerable therapeutic potential (Garcia-Romeu & Richards, 2018). These earlier clinical trials, however, were suboptimal methodologically, often lacking proper controls, validated assessments, statistical analysis, and follow-up. Psychedelic research then endured a nearly half century long hiatus in large part due to the War on Drugs, but also new US regulations (the Drug Amendments of 1962) that introduced a formal requirement for randomized controlled trials and challenged some of the research. LSD-assisted psychotherapy had focused on therapeutic methodologies over trial design and was particularly challenged by these new regulations (Oram, 2014, 2016).

In what has been named a “renaissance”, psychedelics have re-emerged on the medical scene and their possible therapeutic utility and benefits to health and wellbeing are being re-examined with greater scientific rigor and more methodologically sound studies (Mithoefer, Grob, & Brewerton, 2016; Pollan, 2018; Sessa, 2012). This work not only explores psychedelics for alleviating clinical conditions such as addiction and mental health problems, but also for optimizing creativity and other cognitive and emotive functioning in “healthy” individuals (Garcia-Romeu & Richards, 2018).

### **1.4.1 Evidence of reduced suicide risk and mental health benefits**

Evidence from population studies and clinical research suggest psychedelics may be protective against suicide risk, highlighting the ways in which drugs like LSD, psilocybin, mescaline, and DMT interact with key risk factors. A recent and large ( $n > 190,000$ ) population study conducted among adult respondents in the US demonstrated that lifetime psychedelic drug use was associated with significantly reduced odds of past month psychological distress ( $p < 0.001$ ) and past year suicidality ( $p < 0.01$ ) (Hendricks, Thorne, Clark, Coombs, & Johnson, 2015). Another population study conducted among 130,000 adult respondents demonstrated several associations between lifetime psychedelic use and lower rates of mental health problems: psilocybin use (AOR 0.8,  $p = 0.009$ ), mescaline use (AOR 0.9,  $p = 0.04$ ), and past year LSD use (AOR 0.7,  $p = 0.01$ ) were all associated with lower rates of serious psychological distress; psilocybin use was also significantly associated with a lower rate of panic attacks (AOR 0.9,  $p = 0.006$ ) (Krebs & Johansen, 2013). Despite these findings, it is important to consider that the large sample sizes in these studies may be inflating the significance (i.e., p-values) of the observed associations, and that use of publicly available datasets preclude testing more nuanced associations between psychedelic use and psychological distress and suicidality.

In clinical settings, open-label trials in the UK limited to small samples of patients with treatment-resistant depression found psilocybin to be well-tolerated and associated with marked reductions in depressive symptoms and anxiety (Carhart-Harris, Bolstridge, et al., 2016; Carhart-Harris, Roseman, et al., 2017). Both psilocybin ( $n = 25$ ) and LSD ( $n = 20$ ) administered in small, randomized clinical trials were associated with increased positive mood and psychological wellbeing (Carhart-Harris et al., 2016; Kraehenmann et al., 2015). However, with such small

samples, one should be cautious of the potential for inflated effect sizes. Most recently, the first randomized clinical trial to test a psychedelic substance for treatment-resistant depression was conducted in Brazil. Findings (n=29) demonstrated significant and rapid antidepressant effects following a single dose of ayahuasca – an Amazonian plant brew (containing DMT) with a rich history of medicinal and ritualistic practices among Indigenous groups (Grob et al., 1996; McKenna & Riba, 2015) – compared to placebo (Palhano-Fontes et al., 2018). This study was conducted only among ayahuasca- and psychedelic-naïve individuals, and adopted a series of measures to ensure double blinding, including the use of a placebo that induced nausea and anxiety; 5/29 participants misclassified the placebo as ayahuasca (Palhano-Fontes et al., 2018). This evidence supports prior work demonstrating anti-depressive/anxiolytic effects of LSD, psilocybin, and ayahuasca (Gasser et al., 2014; Grob et al., 2011; Osório et al., 2015), summarized in a recent systematic review of clinical trials (dos Santos et al., 2016). Of note, ketamine, a dissociative anesthetic with a different mechanism of action (although it is sometimes classified as a psychedelic), is emerging as a promising treatment intervention for depression and addiction warranting further research with clinical trials (Morgan, McAndrew, Stevens, Nutt, & Lawn, 2017; Singh et al., 2017).

Two recent randomized double blind, placebo-controlled crossover trials in the USA explored the impact of psilocybin-assisted therapy on ameliorating end-of-life anxiety among 80 patients diagnosed with terminal cancer (Griffiths et al., 2016; Ross et al., 2016). A single dose of psilocybin produced substantial decreases in clinician- and self-rated measures of depression and anxiety, alongside increases in quality of life, optimism, life meaning, and spiritual wellbeing. At six-months follow-up, the anxiolytic and anti-depressant effects were sustained with 60-80% of

participants continuing to show clinically significant reductions in depression and anxiety (Griffiths et al., 2016; Ross et al., 2016).

Taken together, findings from epidemiological studies and clinical trials provide a strong rationale for conducting further controlled trials with larger samples and more diverse populations to determine how psychedelics might reduce psychological distress and suicidality, including anxiety and depression associated with life-threatening illnesses. Indeed, palliative care has been an area identified for the application of psychedelic-assisted therapy. In 1963, Aldous Huxley received LSD on his deathbed, which reportedly led him to experience death without fear and a sense of warmth and spiritual belonging (Dyck, 2015). By improving psychological wellbeing, and reducing fear among people suffering from end-of-life anxiety, it is plausible that in bestowing more meaning to death and life psychedelics may have a role to play in recalibrating how we die (Pollan, 2018), and in turn, how we live.

#### **1.4.2 Psychedelic research among marginalized populations and women**

While there remains a paucity of psychedelic research and evidence among marginalized women, a few notable studies have focused on marginalized populations, namely among people who have been incarcerated, Indigenous people, and sexual minorities. Recent evidence from observational studies in the US demonstrated that naturalistic psychedelic use was predictive of reduced arrest for intimate partner violence ( $p < 0.05$ ) among 302 incarcerated men with substance use disorders (Walsh et al., 2016), and associated with reduced recidivism among 25,000 substance-involved offenders ( $p = 0.002$ ) (Hendricks, Clark, Johnson, Fontaine, & Cropsey, 2014). Building on this work, a recent study among men and women demonstrated a

negative relationship between psychedelic use (LSD and/or psilocybin mushrooms) and intimate partner violence: men who used psychedelics were half as likely to report intimate partner violence perpetration and reported better emotional regulation than men with no history of psychedelic use; the association was not observed among women (Thiessen et al., 2018). Another observational study conducted with 12 members of a rural First Nations community in British Columbia, Canada, observed statistically significant improvements in measures of mental wellbeing and quality of life, as well as reductions in self-reported use of cocaine, alcohol, and tobacco following an ayahuasca-assisted intervention delivered in a retreat setting (Thomas, Lucas, Capler, Tupper, & Martin, 2013). Given the observational nature of these studies, causality could not be determined and biases in responding may have obscured the true associations in addition to potential sources of confounding. Furthermore, these findings have limited generalizability to other marginalized populations.

Qualitative phenomenological research among women has explored the impact of ayahuasca on sexuality and spirituality, and suggests that psychedelic-facilitated psychotherapy may have important therapeutic potential for women who have experienced sexual trauma. Findings from this qualitative study among seven North American women (aged 35-55) with histories of sexual trauma highlighted narratives of healing experiences on physical, emotional, mental, and spiritual levels following ceremonial ayahuasca use (Espinoza, 2014). Another qualitative study among 17 gay and lesbian individuals reported positive affirmation of social and sexual identities attributed to partaking in ritualistic ayahuasca use, with some describing profound experiences related to sexuality and sexual awakening/opening, including one woman who reported that her experience with ayahuasca facilitated healing from childhood sexual abuse (Cavnar, 2014).

Further qualitative work among 13 and 16 self-selected individuals, mostly women, diagnosed with eating disorders in North America who had experiences with ayahuasca suggested that ceremonial ayahuasca drinking may have potential to facilitate reductions in eating disorders and related mental illness symptoms (Lafrance et al., 2017; Renelli et al., 2018). Despite the inherent limitations to these exploratory studies, including self-selection that may have biased findings toward more positive effects of ayahuasca drinking, findings encourage further research with controlled trials that might inform integrative approaches marrying psychedelics or traditional healing modalities, such as ayahuasca, with conventional therapies. It is notable that one participant recalled a negative experience during an ayahuasca ceremony where she was touched inappropriately/sexually by a ceremony facilitator (Lafrance et al., 2017), underscoring the risk of sexual assault in such vulnerable states and the need for caution when selecting ceremonial settings in addition to ensuring safety and adequate support throughout the process.

Other psychedelic research involving women has focused on MDMA-assisted psychotherapy for treating PTSD from sexual abuse. A small pilot study among six women with chronic PTSD secondary to sexual assault was the first controlled study to investigate the safety of MDMA among a patient population, and demonstrated that low doses of MDMA administered as an adjunct to psychotherapy were safe and showed promise in efficacy to reduce PTSD (Bouso, Dublin, Farré, Alcazar, & Gomez-Jarabo, 2008). Since then, randomized controlled studies of MDMA-assisted psychotherapy have further demonstrated the safety and long-term efficacy among patients with treatment-resistant PTSD (Mithoefer et al., 2013; Oehen & Schnyder, 2013), including findings from a randomized clinical trial (n=26) where after two sessions with MDMA 68% of veterans and first responders no longer met clinical criteria for PTSD at 12

months follow-up (Mithoefer et al., 2018). However, this study was limited to a sample of mostly white men. In another study of predominantly women participants (85%), the vast majority (83%; 10/12) of participants in the MDMA treatment group experienced significant reductions in PTSD symptom severity, compared to 25% in the placebo group, with no serious adverse effects reported (Mithoefer, Wagner, Mithoefer, Jerome, & Doblin, 2010). This study reported that 40% of participants experienced childhood sexual abuse and the average duration of PTSD was estimated to be 19+ years. Interestingly, prior to 1985 when MDMA, also known as an ‘enactogen’ or ‘empathogen’ for its ability to enhance emotional empathy (Carlyle et al., 2019), was reclassified as a Schedule 1 drug in the US, an estimated 4000 psychiatrists and psychologists administered MDMA in the context of psychotherapy (Mithoefer et al., 2016; Oehen & Schnyder, 2013).

### **1.4.3 Evidence of reduced problematic substance use**

Emergent research and evidence lend support to the utility of psychedelics in treating substance use issues (Bogenschutz & Johnson, 2016; Sessa & Johnson, 2015). A systematic review of clinical trials published over the last 25 years summarizes some of the anti-depressive, anxiolytic, and anti-addictive effects of classic psychedelics (dos Santos et al., 2016), including promising findings from a meta-analysis of earlier controlled trials of LSD therapy (Krebs & Johansen, 2012) and a recent albeit small (n=10) open-label pilot study of psilocybin-assisted therapy for treating alcohol use disorder (Bogenschutz et al., 2015). Participants with DSM-IV alcohol dependence received one or two supervised psilocybin sessions in addition to Motivational Enhancement Therapy; in the first four weeks (without the psilocybin intervention) abstinence rates did not increase, but increased significantly following psilocybin-assisted

therapy and the improvements were mostly retained at 36-week follow-up (Bogenschutz et al., 2015). However, the open-label design and lack of control group, as well as the absence of biological verification of alcohol use, indicate caution is needed in extrapolating the findings.

High success was demonstrated in tobacco cessation following psilocybin-assisted therapy among 15 individuals in an open-label pilot study conducted at Johns Hopkins University. Eligible participants in the study smoked a minimum of 10 cigarettes per day and had multiple unsuccessful quit attempts. Following two or three moderate to high doses of psilocybin, in combination with cognitive behavioral therapy for smoking cessation, participants were assessed using biomarkers and self-reported measures of smoking status, which determined abstinence rates of 80% at 6-month follow-up and 67% at 12-month follow-up – rates that are substantially higher than any documented in the smoking cessation literature (Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014; Johnson, Garcia-Romeu, & Griffiths, 2017). Despite the small sample size and lack of control group, these findings suggest psilocybin-assisted therapy holds considerable promise for tobacco cessation and potentially other challenging addictions.

As mentioned above, ceremonial use of ayahuasca has been associated with significant reductions in treatment-resistant depression following a single dose of ayahuasca as demonstrated in a randomized clinical trial among 29 participants in Brazil (Palhano-Fontes et al., 2018), as well as reductions in self-reported problematic substance use as demonstrated in a preliminary observational study among 12 members of a First Nations community in British Columbia, Canada (Thomas et al., 2013). A qualitative follow-up analysis to the Thomas et al. (2013) study was recently conducted to further explore the impact of ayahuasca-assisted therapy

on addiction and elucidate the lived experiences of Indigenous participants; findings provided key contextual insights into the important role of connectedness (i.e., with self, others, nature/spirit) in reducing problematic substance use and cravings (Argento, Capler, Thomas, Lucas, & Tupper, under review). Other research from Brazil found significantly lower addiction issues (as assessed using the Addiction Severity Index) among regular, ritualistic ayahuasca drinkers (n=127) as compared to matched controls (n=115) at one year follow-up (Fábregas et al., 2010). A recent ethnographic, qualitative analysis of addiction recovery and ayahuasca use that drew on long-term fieldwork and in-depth interviews with participants who give or receive support within the context of ritualistic ayahuasca use in Italy and Brazil, concluded that practices of care within these ritual spaces play a key therapeutic role, highlighting the importance of community and caregiving in the success of addiction recovery (Talin & Sanabria, 2017).

Accumulating evidence on psychedelic-assisted therapy for opioid use disorder supports the need to advance this research (Argento, Tupper, & Socias, 2019). Increasing evidence links opioid use not only with overdoses, but also suicide (Bohnert & Ilgen, 2019), and many people who use opioids have complex relationships with both physical and emotional pain, including PTSD (Dasgupta et al., 2018; Hassan, Foll, Imtiaz, & Rehm, 2017). In the context of North America's most severe drug overdose crisis, largely driven by increasing contamination of the drug supply with illicitly manufactured synthetic opioids such as fentanyl (Wood, 2018), innovative responses and out-of-the-box thinking are urgently required to curb the epidemic. Available evidence from earlier randomized clinical trials suggests psychedelics may play a promising role: higher rates of abstinence were observed among participants receiving high dose LSD- and

ketamine-assisted therapies for heroin addiction compared to controls at long-term follow-ups (Krupitsky et al., 2002; Savage & McCabe, 1973). Recently, a large population study in the US among 44,000 people who use illicit drugs observed that lifetime use of psychedelics was significantly associated with a 40% reduced risk of past year opioid abuse (weighted risk ratio=0.60; p=0.006) and a 27% reduced risk of past year opioid dependence (weighted risk ratio=0.73; p=0.002), as defined by DSM-IV criteria (Pisano et al., 2017). The powerfully psychoactive plant from West Africa known as iboga (ibogaine) has garnered considerable attention for its tendency to generate transformative spiritual experiences associated with attenuation of opioid withdrawal symptoms/cravings and long-term abstinence (Alper, Lotsof, Frenken, Luciano, & Bastiaans, 1999; Brown, 2013; Brown & Alper, 2017; Cloutier-Gill, Wood, Millar, Ferris, & Socias, 2016; Malcolm, Polanco, & Barsuglia, 2018; Mash et al., 2001; Mash, Duque, Page, & Allen-Ferdinand, 2018; Noller, Frampton, & Yazar-Klosinski, 2018). An observational study among 30 individuals with heavy (daily) opioid use found that ibogaine treatment was associated with significantly reduced opioid withdrawal symptoms. Half of participants reported no drug use at 1-month follow-up – a sizable clinical effect (Brown & Alper, 2017). While preclinical research has lent support to the mainly anecdotal evidence suggesting ibogaine attenuates withdrawal symptoms and cravings, concerns over ibogaine's safety and potential toxicity, as well as a lack of solid data warrant further research with clinical trials (Brown, 2013; Noller et al., 2018).

#### **1.4.4 Possible mechanisms of action**

The precise mechanisms of action driving the relationships between psychedelics and suicide risk factors remain unknown, yet there is some evidence that psychedelics promote

neuroplasticity in the brain (Ly et al., 2018; Vollenweider & Kometer, 2010). The biological factor most consistently correlated with suicidality is a disturbance of the serotonergic system; disrupted functioning of serotonin is significantly associated with suicide (Hawton & van Heeringen, 2009; Nock et al., 2008; World Health Organization, 2014). Classic psychedelics primarily act as agonists of 5-HT<sub>2A</sub> serotonin receptors and are involved in down-regulation of these receptors whereas up-regulation of 5-HT<sub>2A</sub> receptors has been linked with depression and suicidality (Bogenschutz & Johnson, 2015; Carhart-Harris et al., 2012; Carhart-Harris et al., 2012; Kraehenmann et al., 2015; Vollenweider & Kometer, 2010). In fact, the discovery of LSD's psychoactive effects by Albert Hofmann in 1943 stimulated a new era of research in the field of neurochemistry in the 1950s that advanced understanding of serotonin as a key neurotransmitter influencing mood and behavior and ultimately led to the development of selective serotonin reuptake inhibitors (SSRIs) (Nichols, 2004). It has been hypothesized that psychedelics increase the permeability between the conscious and unconscious mind, and enhance recall of autobiographical memories that can facilitate more positive reprocessing of traumatic experiences (Carhart-Harris et al., 2012, 2014), which has important implications for marginalized women who have experienced childhood abuse and trauma.

Furthermore, nascent neuroimaging research with functional magnetic resonance imaging (fMRI) helps to explain how psychedelics may work to modulate mood and states of consciousness (Carhart-Harris et al., 2012, 2014). This emerging research with fMRI posits that psychedelics alter consciousness by producing disintegration of an area of the brain known as the Default Mode Network (DMN) and whole brain integration, thus increasing connectivity and communication between brain networks. The DMN, which develops from birth to adulthood

(and is undeveloped in young children), is responsible for “metacognitive” processes such as self-reflection and mental time travel (Carhart-Harris et al., 2014). The regions of the DMN are centers of dense connectivity thought to serve as important hubs for integrating information; for reasons still unclear, this area of the brain receives more blood flow and consumes significantly more energy than any other region of the brain (Carhart-Harris et al., 2014). In theory, the effect of psychedelics in creating more “entropy” or flexibility in the brain reverts the brain to a less constrained mode of cognition that helps normalize unhealthy or pathological patterns of thought as seen in people suffering from depression and other disorders (e.g., addictions, obsessive compulsive disorder) that are characterized by mental rigidity and “inflexible” self-criticism (Carhart-Harris et al., 2014). Thus, the therapeutic effect of psychedelics as explained by neuroscience, may be rooted in their ability to return the brain to a more balanced mode of cognition by increasing entropy and disrupting the overly aggressive self-critical focus that accompanies depression and suicidality.

#### **1.4.4.1 Mystical experiences and ego dissolution**

In addition to neurobiological explanations for how psychedelics might influence the brain, the effects may be dually attributable to the way psychedelics influence the mind and aspects of emotionality and spirituality. The existing literature on psychedelics describes deeply entwined physiological and psychological mechanisms of action (Nichols, 2016; Talin & Sanabria, 2017). In an environment of trust, safety, and compassion, psychedelics have the tendency to facilitate “mystical-type” experiences that can lead to profound changes in attitudes and behaviors, and the spiritual component of this process may play a key role in interventions. For example, in the study of psilocybin-assisted therapy for tobacco cessation, mystical-type experiences generated

from psilocybin sessions were significantly correlated with positive treatment outcomes (Garcia-Romeu, Griffiths, & Johnson, 2014); 13 out of 15 (87%) participants rated their psilocybin experience as among the five most personally meaningful and spiritually significant experiences of their lives (Johnson et al., 2017). Similarly, the mystical experiences occasioned by psilocybin sessions among patients with life-threatening cancer mediated the therapeutic effect of psilocybin on depression and anxiety (Griffiths et al., 2016; Ross et al., 2016). A recent randomized, double-blind, crossover study administered a single high dose of LSD to 16 “healthy” volunteers and found that 71% of participants rated their LSD experience as among the top 10 most meaningful experiences in their lives one year later (Schmid & Liechti, 2018).

Building on the mystical experience literature, a recent hypothesis proposes that the emotion awe is the primary psychological mechanism underlying psychedelic-occasioned mystical experiences. As the theory goes, awe (described as an emotion in the upper reaches of pleasure and bordering fear precipitated by encounters with something both vast and novel) has the effect of directing attention away from the self and towards the present moment and feelings of connectedness or oneness with others, thereby acting as both the ultimate collective emotion and principal catalyst for change within the psychedelic therapy paradigm (Hendricks, 2018). The burgeoning literature on the emotive and meaning-enhancing properties of psychedelics offer valuable clues in explicating their potential to instigate mystical experiences and therapeutic processes, and can inform prospective applications and directions for future research (Hartogsohn, 2018).

A key aspect of the mystical-type experience has been described as “ego dissolution” (Nichols, 2016; Nour, Evans, & Carhart-Harris, 2017). Indeed, it has been postulated that the DMN is the physical counterpart to the ego, and that in disorganizing DMN activity psychedelics relinquish the ego’s usual hold on reality (Carhart-Harris et al., 2014). A recent Internet-based survey involving 893 participants demonstrated that ego-dissolution elicited by participants’ most intense psychedelic experience was positively predictive of openness, connectedness to nature, and liberal political views (Nour et al., 2017). With respect to connectedness, recent qualitative work has highlighted the importance of participants’ experiences of enhanced connectedness in the context of psilocybin-assisted therapy for treatment-resistant depression (Watts, Day, Krzanowski, Nutt, & Carhart-Harris, 2017) and ayahuasca-assisted therapy for addiction and stress (Argento, Capler, et al., under review). Future work aims to determine whether increased connectedness is a primary component of successful psychedelic therapies by operationalizing connectedness as a phenomenon that straddles subjective, biological, and behavioral manifestations (Carhart-Harris, Erritzoe, Haijen, Kaelen, & Watts, 2017).

The field of transpersonal psychology is relevant to elucidating psychedelics’ therapeutic mechanisms inasmuch as this approach integrates spiritual and transcendent experiences (including culturally sensitive rituals and traditions) within the framework of modern psychology. Stanislov Grof, one of the founders of transpersonal psychology with over 60 years of research and experience in LSD/psychedelic psychotherapy, characterized psychedelics as unspecific amplifiers or catalysts for unconscious mental processes that are otherwise difficult to access, likening psychedelics and “*their potential significance for psychiatry and psychology to that of the microscope for medicine or the telescope for astronomy*” (Grof, 1973, p.18). It is

hypothesized that the unique ability of psychedelics to facilitate spiritual or transpersonal (literally meaning “beyond the personal”) experiences can be a source of therapeutic discovery. Such “non-ordinary” or “holotropic” states of consciousness elicited through psychedelics (but also attainable through other non-drug means such as meditation, breathing exercises and dancing) may induce experiences of reliving traumatic or positive life memories that can bring about dramatic healing and positive psychological transformation (Grof, 2007). Further, it has been observed that psychedelic experiences confront the individual with critical aspects of human existence related to dying and death and the consequence of such emotional or physical encounters with death is often a spiritual opening or insight: *“I have never seen a person who progressed in self-exploration beyond the point of ego death and still contemplated suicide”* (Grof, 1973, p.44).

A well-established body of literature cites several protective factors associated with lower risk of suicide, including religious beliefs and practices, spirituality, social support, and connectedness (Hawton & van Heeringen, 2009; Klonsky et al., 2016; NIMH, 2014; Nock et al., 2008; O’Connor & Nock, 2014). Thus, the ways in which psychedelics influence key characteristics such as spirituality, personal meaningfulness, life satisfaction, and connectedness may have important utility for reducing suicide risk and warrants further research.

#### **1.4.5 Potential risks and harms**

Physiologically, psychedelics are generally considered relatively safe compounds, with their primary effects being on consciousness. Adverse reactions and fatalities associated with psychedelics are rare as classic psychedelics possess low physiological toxicity and have not

been shown to cause organ damage or neuropsychological deficits; however, there are some concerns, mostly related to psychological risk (e.g., anxiety or ‘bad trips’) rather than physiological (Nichols, 2016). While adverse events have been more closely linked with newer synthetic compounds, as compared to classic psychedelics such as LSD, psilocybin, mescaline, and DMT, the potential risks and harms of psychedelics depend heavily on the context in which the substance is consumed.

Thorough investigation of the first wave of formal psychedelic studies in the 1950s and 1960s identified a small number of adverse outcomes (Mithoefer et al., 2016). However, given the methodological flaws in many of these earlier studies, adverse events may not have been accurately documented. Since the revival of psychedelic research in the 1990s, very few, if any serious adverse events have been reported (Rucker et al., 2018; Tupper et al., 2015). In the last 25 years, clinical trials that have administered LSD, psilocybin, and ayahuasca demonstrated that these compounds are comparatively safe pharmacological tools for treating drug dependence, anxiety, and depression, and no serious adverse reactions have been reported (dos Santos et al., 2016). However, sample sizes have been small and some studies lacked placebo and control groups. The most common adverse events cited in the literature associated with classic psychedelics administered in clinical settings are: transient anxiety, nausea, vomiting, mild increases in blood pressure and heart rate, and headache; no cases of psychosis or hallucinogen persisting perception disorder have been reported in modern trials using LSD, psilocybin or ayahuasca (Rucker et al., 2018). Psychedelics are not known to lead to addiction or dependence, given that they do not have direct effects on the brain’s dopaminergic system, and no overdose deaths have ever occurred with ingestion of LSD, psilocybin or mescaline (Nichols, 2016).

While not a classic psychedelic, MDMA has featured in recent clinical trials as a promising adjunct to psychotherapy, particularly for treatment refractory PTSD. In high-risk contexts, MDMA can be dangerous and deaths have been reported among recreational users (usually from heat stroke or dehydration when taken at raves). Research and evidence demonstrate that pure MDMA administered in moderate doses can be given safely to participants in controlled medical settings; however, the potential neurotoxic effects of MDMA among recreational users remain unclear (Mithoefer et al., 2016). In a phase 2 clinical trial of MDMA-assisted psychotherapy for treating chronic PTSD among 26 military personnel and first responders (between 2010 and 2015) the majority of adverse events reported were psychological symptoms (e.g., anxiety) that resolved shortly after the experimental session (Mithoefer et al., 2018).

Another psychoactive substance often included in the category of psychedelics due to its potent hallucinogenic and anti-addictive effects is ibogaine. No randomized clinical trials have been conducted with ibogaine; however, the main risk associated with ibogaine is cardiotoxicity and safety concerns appear to be heightened among those with poor cardiovascular health or those who have used opioids or cocaine in close proximity to ingesting ibogaine (Brown, 2013; Noller et al., 2018). A review of fatalities temporally associated with ibogaine from 1990 to 2008 reported that 19 individuals (15 men, 4 women) died within 1.5-76 hours of ingesting ibogaine, with pre-existing medical conditions (primarily cardiovascular) contributing to most of the deaths (12 of the 14 cases) where post-mortem data were available (Alper, Stajić, & Gill, 2012). The data on ibogaine has been limited to case reports and observational studies and further research with clinical trials is required to determine its safety and efficacy in treating addictions.

Despite some of the highly publicized deaths associated with ayahuasca tourism, the direct links between ayahuasca and fatalities remain unclear. A systematic review (supplemented by interviews with ceremony participants), concluded that the lethal dose of ayahuasca or DMT is likely 20 times greater than the typical ceremonial dose, and the risk of sustained psychological disturbance is minimal, with adverse psychological reactions typically resolving within a few hours (Gable, 2007). Another more recent systematic review of published case reports describing psychotic episodes following ingestion of ayahuasca or DMT concluded that incidence of such episodes appears to be rare in both ceremonial/ritual and recreational/non-controlled settings (dos Santos, Bouso, & Hallak, 2017). A review of calls to the US Poison Control Centers associated with ayahuasca consumption from 2005 to 2015 found that of the 538 reported exposures, there were some serious clinical manifestations, including 34% of reports for tachycardia, 16% for hypertension, 12 cases had seizures, seven cases were reported for respiratory arrest, four cases were reported for cardiac arrest, and three fatalities were reported (although two of these were marked as indirect) (Heise & Brooks, 2017). Ritualistic use of ayahuasca has spanned centuries, yet no scientific reports exist documenting toxic effects among pregnant women or their children (dos Santos, 2013). Acute and long-term consumption of ayahuasca does not seem to be toxic to humans or associated with loss of cognitive functioning (Bouso et al., 2015); however, more research is needed to better establish risks and possible toxicity of ayahuasca.

While the psychedelic research literature highlights the relative safety of psychedelic substances across various contexts (Carhart-Harris et al., 2016; Gasser et al., 2014; Krebs, 2015; Mithoefer

et al., 2011; Tupper et al., 2015), the importance of “set” (i.e., psychological intention and expectation) and “setting” (i.e., physical environment) cannot be emphasized enough (Carhart-Harris et al., 2018; Haden, Emerson, & Tupper, 2016; Tupper et al., 2015). The therapeutic action of psychedelics depends heavily on the psychological and environmental context (Carhart-Harris et al., 2018). The potential risks and harms are undoubtedly higher in non-medical/unsupervised settings (Tupper et al., 2015), especially in unregulated street markets where doses and purity are often unknown. Safety guidelines developed for psychedelic research, a key contribution by the Johns Hopkins research group, emphasize careful screening and exclusion of participants with personal or familial history of severe psychiatric disorders, alongside establishing safe and supportive environments and building strong rapport and trust between participants and therapists/guides in order to minimize adverse reactions (Johnson, Richards, & Griffiths, 2008). Finally, the current model of drug prohibition and classification of drugs within the international drug control regime correlates poorly with drug harms (Nutt, King, Saulsbury, & Blakemore, 2007). The latest Global Drug Survey (n>115,000) ranked psilocybin/mushrooms and LSD (along with cannabis) as the safest substances in a comparison of emergency medical treatment seeking for all substances (Winstock, Barratt, Ferris, & Maier, 2017). A 2010 Lancet report also ranked psilocybin/mushrooms, LSD, and MDMA/ecstasy among the least harmful drugs in terms of both organic toxicity and overall social harms – significantly less harmful than many other substances such as alcohol, heroin, crack, cocaine, amphetamines, benzodiazepines, and tobacco (Nutt, King, & Phillips, 2010). Rescheduling psychedelics out of Schedule 1 would certainly enable research that could elucidate not only the potential benefits, but also the potential harms and how to best mitigate risk.

## 1.5 Research objectives and aims

Drawing on a structural determinants framework (Shannon et al., 2014, 2015), this thesis aims to explore the trajectories of drug use, violence, and suicide risk among marginalized women, and potential avenues of intervention with a special focus on the therapeutic utility of psychedelics. This thesis will review the evidence on socio-structural risks for suicide beyond biological or individual-level processes and will examine the interplay between multilevel sources of violence and trauma (structural, interpersonal, physical, emotional) and drug use trajectories among marginalized women. Specifically, given the associations between trauma and crystal methamphetamine use among women and elevated risk of suicidality, this thesis will explore socio-structural risk factors for initiating crystal methamphetamine injection among women sex workers. Furthermore, this thesis will identify gaps in evidence around structural barriers (e.g., criminalization/laws, stigma, discrimination).

The overall aims of this research include: a) to explore the trajectories of drug use, violence, and suicidality among marginalized women using a structural determinants framework; and b) to identify potential avenues of intervention including an exploration of the therapeutic utility of psychedelics. The specific objectives of this research are as follows:

1. To better understand the burden of suicidality among marginalized women. Chapter 2 examines social and structural correlates of suicidality among women sex workers in Vancouver. Using Generalized Estimating Equations (GEE) logistic regression models, this longitudinal analysis estimates the prevalence of suicidality and explores socio-structural factors (e.g., experiences of violence, trauma, and homelessness) associated with recent suicidality. As one of the first prospective analyses on the prevalence and correlates of

suicide risk among sex workers in higher income settings worldwide, these findings provide important initial empirical evidence on how key socio-structural determinants shape suicide risk, including the role of social cohesion, which will be critical to informing intervention strategies tailored to the needs of women sex workers and recommendations for policy and programming that enable collectivization and connectedness.

2. To investigate socio-structural trajectories of crystal methamphetamine injection initiation among marginalized women. Chapter 3 longitudinally examines socio-structural predictors of crystal methamphetamine injection initiation among women sex workers using Kaplan Meier and Extended Cox regression models. This analysis provides key insights into how the gendered and social risk environment shape first-time crystal methamphetamine injection experiences among women sex workers. These findings will be used to inform recommendations for substance use interventions that are gender-sensitive and integrate trauma-informed mental health supports and couple-focused strategies for sex workers.
3. To explore the potentially protective effect of psychedelic use on suicidality among marginalized women. Chapter 4 provides a longitudinal analysis using Extended Cox regression to determine whether ever having used a psychedelic drug can have a protective effect on incidence of suicidality. This analysis is the first to prospectively investigate the protective effect of naturalistic psychedelic use on suicide risk among marginalized women. Findings from this analysis will guide the direction of future research and development of programs to advance the study of psychedelic-assisted therapies for improving mental health and wellbeing for marginalized women. The results point to upstream drivers of risk and will inform recommendations for multi-pronged structural interventions and policy reform.

## **1.6 Study design and methods**

The analyses for the empirical chapters of this thesis drew on data from a large, community-based, open prospective cohort of women sex workers initiated in 2010, known as AESHA: An Evaluation of Sex Workers Health Access. The NIH/CIHR-funded AESHA study is housed at

the Centre for Gender & Sexual Health Equity (CGSHE) and the University of British Columbia (UBC) and has a Community Advisory Board of more than 15 sex worker, women's health and HIV service agencies, as well as representatives from the health authority and policy experts. As previously described (Shannon et al., 2007), the AESHA study is based on longstanding partnerships with sex work agencies and community service providers since 2004 and has expanded to include women sex workers across Metro Vancouver working in both street and off-street settings. AESHA includes a diverse, experiential team of both current and former sex workers represented across interviewer, outreach, nursing, and coordinator staff.

Eligibility criteria for participants at baseline included cis or trans women, 14 years of age or older, who exchanged sex for money within the last 30 days. In the context of hard-to-reach populations, participants were recruited using systematic time-location sampling (Stueve, Duran, Doval, & Blome, 2001), 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. A combination of outreach methods and contact by mobile phone and Internet were used for follow-up. Participatory community mapping strategies were conducted to identify work venues. Regular contact and encouragement of drop-in to women-only spaces at the research office contributes to an annual retention rate of >90% for AESHA participants.

Participants completed interviewer-administered questionnaires and voluntary HIV/STI/HCV serology testing by a project nurse at enrollment and biannually. Urine samples were collected for gonorrhea and chlamydia, and blood was drawn for syphilis, HSV-2 antibody, and HCV. The questionnaires and clinical components were completed at one of two study offices or at a safe

location identified by participants. The main interview questionnaire elicits responses related to socio-demographics (e.g., sexual and gender identities, ethnicity, education, housing), the work environment (e.g., access to services, violence/safety, policing, incarceration), client characteristics (e.g., fees/types of services, condom use), intimate partner relationships (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 and behaviors. 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. All participants receive an honorarium of \$40 CAD at each bi-annual visit for their time, expertise and travel. The AESHA study holds ethical approval through the Providence Health Care /University of British Columbia Research Ethics Board.

## **1.7 Overview of the dissertation**

This dissertation consists of five chapters. The present chapter provides a review and synthesis of the literature pertaining to socio-structural determinants of suicide risk among marginalized women, an overview of the research and evidence on the therapeutic potential of psychedelics, and highlights gaps in knowledge. Chapter 1 also describes the theoretical orientation of this research and methodology. Chapters 2 through 4 present the empirical research, which describe detailed approaches and analyses used to conduct this study and address the aforementioned research objectives. Specifically, Chapter 2 explores the burden and correlates of suicidality and provides a broader picture of socio-structural risks used to inform subsequent chapters. Chapter 3 investigates socio-structural trajectories of crystal methamphetamine injection among sex workers, further documenting the dynamic interplay between violence, trauma, and drug use.

Chapter 4 examines the longitudinal impact of psychedelic use on incidence of suicidality, highlighting a 60% reduced hazard of suicidality among women who used psychedelics. Chapter 5 discusses overall findings from the empirical chapters, limitations and strengths of the research, and implications for policy and intervention programs, as well as directions for future research.

## **Chapter 2: Correlates of suicidality among a community-based cohort of women sex workers and the protective effect of social cohesion**

### **2.1 Introduction**

After decades of research and efforts to ameliorate mental health problems, suicide remains an intractable public health challenge worldwide (Hawton & van Heeringen, 2009; World Health Organization, 2014). Many marginalized populations, such as street-involved sex workers, experience a high burden of psychological distress and disproportionately elevated risk of suicidality as a result of dynamic and interrelated socio-structural determinants, such as historical and repeated violence, poverty, stigma, criminalization, and lack of social support (Argento et al., 2014; Deering et al., 2014; Shannon et al., 2015; Ulibarri et al., 2013). However, suicide prevention and intervention programs have been largely absent for women sex workers, and risk factors remain poorly understood and under investigated.

Depression has been identified as one of the strongest correlates of suicidality; however, risk is shaped by several, often overlapping individual and socio-structural factors such as other mental health and substance use disorders, trauma, and social disconnection (Center for Addiction and Mental Health, 2011; Hawton & van Heeringen, 2009; O'Connor & Nock, 2014; Zalsman et al., 2016). Suicidality is strongly predictive of suicide deaths, in addition to exerting a significant financial and psychosocial burden (Klonsky et al., 2016).

Of the limited available data among sex workers, research indicates that a history of violence, childhood abuse, and unaddressed mental health issues (e.g., depression, PTSD) may elevate risk of suicidality, particularly among women who work in street-based settings with fewer health and social supports (Gu et al., 2014; Lau et al., 2010; Roxburgh et al., 2006; Shahmanesh et al., 2009; Surratt et al., 2012; Zhang et al., 2016). Trans individuals and trans women sex workers in particular, experience considerable psychosocial challenges due to entrenched stigma and discrimination, and report elevated risk and rates of suicidality (Bourgois & Schonberg, 2009; Nemoto et al., 2011). Further, Indigenous women are vastly overrepresented among street-based sex workers in North America, and due to generations of racialized policies and social and cultural disconnection, experience comparatively higher risks and rates of poverty, HIV infection, substance use, trauma and suicidality (Benoit et al., 2003; Bingham et al., 2014; Clifford et al., 2013).

The literature is scarce regarding socio-structural correlates of suicidality and stigma continues to hamper research and prevention efforts among marginalized women. Thus, the objective of this study was to estimate the burden and identify socio-structural correlates of recent suicidality among a longitudinal cohort of women sex workers in Metro Vancouver, Canada.

## **2.2 Methods**

### **2.2.1 Study design and sample**

The present analysis drew on data from the AESHA study between January 2010 and August 2017. As previously mentioned, AESHA is an ongoing, open prospective cohort of 900+ street and off-street women sex workers across Metro Vancouver. The research team works in close partnership

with the affected community and a diversity of stakeholders, including legal/human rights experts, community-based organizations, service providers, health authorities, government officials, international policy bodies and regularly engages in knowledge exchange efforts. Experiential staff (current and former sex workers) and individuals with substantial community experience in sex work support services are represented across the interview, outreach, and nursing teams. Eligibility criteria for participants at baseline included cis or trans women, 14 years of age or older, who exchanged sex for money within the last month. Participants completed interviewer-administered questionnaires and voluntary HIV/STI/HCV serology testing at enrolment and biannually. All participants received an honorarium of \$40 CAD at each bi-annual visit for their time, expertise and travel. Methods are described fully in Chapter 1.

### **2.2.2 Study variables**

The dependent outcome of interest was recent suicidality, defined as responding ‘yes’ to having thought about or attempted suicide in the last six months based on the available data in the AESHA questionnaire. All data were self-reported and time-updated at each follow-up with the last six months as the reference, with the exception of time-fixed demographic variables considered at baseline: trans/gender minority, sexual minority (lesbian, gay, bisexual, queer, two-spirit, asexual), self-identification of Indigenous ancestry (inclusive of First Nations, Metis, and Inuit), being a migrant or new immigrant worker (versus Canadian born), and physical and/or sexual childhood abuse (before age 18). Time-updated variables included individual-level factors and those that reflect the social environment: age, HIV seropositivity, recent homelessness, recent injection and non-injection drug use, mental health issues (having ever been diagnosed with, treated for, or received counseling for depression, anxiety or PTSD), work-related variables (e.g., primary place

to solicit and service clients, police harassment, being arrested or put in jail), experiences of violence (e.g. physical/sexual violence by clients or police, any physical/sexual/emotional intimate partner violence), and social cohesion, captured using a continuous social cohesion scale (standardized with a mean of zero and standard deviation of one, with a higher score indicating greater social cohesion). Social cohesion was scored using an adapted scale first developed by Lippman, Kerrigan and colleagues that measures levels of perceived mutual aid, trust, solidarity and support within the community (Lippman et al., 2010). The scale has been previously adapted and validated with sex workers in low- and middle-income countries (LMICs) and among sex workers by our group in Canada (Argento et al., 2016; Duff et al., 2015; Fonner et al., 2014; Kerrigan, Telles, Torres, Overs, & Castle, 2008).

### **2.2.3 Statistical analyses**

Descriptive statistics at baseline were calculated for independent variables of interest, stratified by recent suicidality. Differences were assessed using the Wilcoxon rank-sum test for continuous variables and Pearson's chi-square test (or Fisher's exact test for small cell counts) for categorical variables. Correlates of recent suicidality were examined using bivariate and multivariable generalized estimating equations (GEE) with a logit link for the dichotomous outcome. To adjust the standard error and account for correlations between repeated measurements on the same participant over the follow-up, an exchangeable correlation matrix was used. Variables that were significantly correlated with suicidality at the  $p < 0.05$  level in bivariate analyses were subsequently fitted into a multivariable GEE model. Manual backward stepwise selection was used to identify the most parsimonious and best fitting model, as indicated by the lowest quasi-likelihood under the independence model criterion. Analyses were restricted to observations where participants

reported actively engaging in sex work in the last six months, and a complete case analysis was used such that observations with any missing data were removed. Two-sided p-values and unadjusted and adjusted odds ratios (OR and AOR) with 95% confidence intervals (95%CI) were generated. All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

## **2.3 Results**

### **2.3.1 Descriptive results**

A total of 867 women completed the baseline questionnaire between January 2010 and August 2017. Baseline socio-structural characteristics among women who reported recent suicidality compared to those who did not are displayed in Table 2.1. Within the study sample, 38% (n=333) identified as Indigenous, 34% (n=297) identified as a sexual minority, and 6% (n=54) identified as trans. The median age of the sample at baseline was 35 years (interquartile range [IQR]: 28 to 42). Nearly one third (30%; n=263) of women reported being homeless in the last six months, which was significantly more prevalent among those who reported suicidality than those who did not (46% vs. 27%;  $p<0.001$ ). In terms of experiences of violence and trauma, physical and/or sexual abuse (before age 18) was reported by 67% (n=584) of women in the study, and this was significantly higher among those who reported suicidality than those who did not (91% vs. 63%;  $p<0.001$ ). Recent bad dates (physical/sexual violence by clients) were reported by nearly one-fifth (18%; n=156) of women at baseline, as was recent intimate partner violence (any physical, sexual or emotional violence) (19%; n=163), both of which were significantly higher among women with suicidality ( $p<0.001$ ). Mental health issues (ever been diagnosed with, treated for, or received counseling for depression, anxiety or PTSD) were reported by 42% (n=365) of women.

Overall, 48% (n=413) reported any lifetime suicidality at baseline (46% [n=400] reported lifetime suicidal ideation; 33% [n=289] reported lifetime suicide attempts). At baseline, 16% (n=141) of women reported suicidality in the last six months, with 29% reporting suicidality at some point during the study. Of a total 4008 observations, there were 486 (12%) reports of suicidality over follow-up.

### **2.3.2 Bivariate and multivariable GEE analyses**

Longitudinal bivariate associations and adjusted odds ratios for independent correlates of recent suicidality are displayed in Table 2.2. In the final multivariable GEE model, factors independently associated with recent suicidality included physical and/or sexual childhood abuse (adjusted odds ratio [AOR] 2.99; 95% CI 1.75-5.10), mental health issues (depression, anxiety, or PTSD) (AOR 2.19; 95% CI 1.63-2.95), recent intimate partner violence (AOR 2.11; 95% CI 1.60-2.80), recent physical and/or sexual violence by clients (AOR 1.82; 95% CI 1.33-2.50), and recent homelessness (AOR 1.44; 95% CI 1.10-1.89). Older age (AOR 0.97; 95% CI 0.95-0.99) and higher social cohesion (AOR 0.88; 95% CI 0.78-0.99) were significantly associated with reduced odds of suicidality. Specifically, for every one standard deviation increase from the mean social cohesion score, the odds of suicidality decreased by 12% (p=0.036).

## **2.4 Discussion**

Findings from this analysis demonstrate that suicidality is highly prevalent among women sex workers in this setting – nearly half reported lifetime suicidality at baseline, highlighting a critical public health concern that warrants further attention. Factors independently associated with recent

suicidality in this study included physical/sexual childhood abuse as well as recent experiences of interpersonal violence. Notably, results indicate that social cohesion among workers had an independent protective effect on suicidality. The present prospective analysis is among the first to examine the prevalence and correlates of suicide risk among women sex workers in high-income settings worldwide. Given the dearth of epidemiological research examining suicide risk among marginalized populations, this analysis underscores the urgent need to scale-up innovative and evidence-based prevention and intervention strategies tailored to women sex workers.

Rates of suicidality vary substantially between settings and populations, with large gaps in research and reporting of suicidality among sex workers globally. Of the available data on suicidality among sex workers, most are cross-sectional and have been conducted in Australia and lower/middle-income settings such as in China and India, with prevalence rates ranging from 19-74% (Gu et al., 2014; Lau et al., 2010; Roxburgh et al., 2006; Shahmanesh et al., 2009). Research on suicidality among sex workers in North America remains largely absent. Of the limited available evidence, previous research conducted in the United States examined causes of mortality in a 30-year open cohort of nearly 2000 women sex workers and found that suicide accounted for 4.5% of deaths (Brody, Potterat, Muth, & Woodhouse, 2005; Potterat et al., 2004), as compared to 1.4% among the general population (Nock et al., 2008; World Health Organization, 2014). Research conducted in California demonstrated that trans women with histories of sex work and physical and sexual violence faced elevated risk of suicide; 74% reported lifetime suicidal ideation and 64% reported lifetime suicide attempts (Nemoto et al., 2011).

Ongoing stigma and systematic discrimination against sex workers continue to hamper efforts to advance research and interventions to reduce risk of suicidality, particularly among women who operate in environments that criminalize aspects of the sex work industry. Global evidence clearly demonstrates that sex workers' ability to access essential social, health, and legal protections (e.g., against violence) is severely compromised in settings where sex work is criminalized (Csete & Cohen, 2010; Shannon et al., 2015). New legislation in Canada, known as the "Protection of Communities and Exploited Persons Act" (PCEPA), criminalizes the buying and advertising of sex, and has serious implications for the health, safety and wellbeing of sex workers (Krüsi et al., 2014). Criminalization reduces the ability of sex workers to collectivize, which can be a powerful determinant of health: as evidenced in the present analysis, social cohesion among workers significantly reduced the odds of suicidality. Evidence from the USA echoes these findings where criminalized approaches to sex work coincide with social isolation, stigma, and repeated exposure to violence (Nemoto et al., 2011; Surratt et al., 2012). In settings where sex work has been decriminalized, such as in New Zealand, sex workers have experienced better access to health services and workplace safety (Abel, Fitzgerald, & Brunton, 2009). As such, numerous public health experts, international bodies, and sex work communities worldwide have endorsed full decriminalization of sex work (Amnesty International, 2015; Global Commission on HIV and the Law, 2012; World Health Organization, 2012).

Overall, multifaceted social (e.g., partner violence, social marginalization) and structural (e.g., laws, policies) inequities contribute to elevated risk of suicidality among sex workers. Some forms of cognitive behavioral therapy and pharmacological interventions have been evidenced to reduce depression and risk of suicide, yet the literature is hampered by stigma, publication bias

and inconsistencies in strategies and outcome measures (O'Connor & Nock, 2014; Zalsman et al., 2016), and psychotherapy treatments targeting depression have not been shown to significantly reduce suicidality (Cuijpers et al., 2013). Research and empirical evidence among sex worker populations remains largely absent and necessitates further investigation. There is an urgent need for trauma-informed care tailored to women sex workers, as well as integrated violence and couples-based interventions to address high rates of violent victimization and abuse. Mitigating risk of suicidality also necessitates a reform of laws and policies that perpetuate stigma/discrimination, violence, and unequal access to health and social support services for sex workers. Legislative reform is urgently needed alongside community-led interventions that facilitate collectivization and empowerment among sex workers to improve human rights, health, and overall wellbeing.

## **2.5 Limitations**

There are several limitations that should be considered. The definition of suicidality refers to suicidal ideation or attempts and does not include completed suicides, which introduces the potential for survivorship bias. Based on this study's linkages to vital statistics no completed suicides were observed during the study period. Suicide ideation and attempts were collapsed into one variable (due to a lack of statistical power), which may have led to some misclassification since thinking about suicide is less serious than attempting suicide. This study could not elucidate the impact of specific mental health problems (i.e., PTSD, depression, anxiety), as these were also collapsed into a single variable. Several study variables examined involved highly stigmatized and sensitive topics (e.g., childhood abuse, trauma, partner violence, drug use), which may have resulted in under-reporting or respondent-driven reporting biases by participants. However, the

community-based nature of the study reduced the likelihood of such biases, as interviews were conducted in safe and comfortable spaces by experienced interviewers (including by current and former sex workers) with strong community rapport. All data were self-reported and questions pertaining to events that occurred in the past may be subject to recall bias. A major strength of this analysis is the prospective design and use of GEE analyses, which increased statistical power and allowed for average estimates of the correlates of recent suicidality over the study period to be determined. Social cohesion was measured on a 5-point Likert scale from 2010-2013 and was revised to a 4-point Likert scale from 2014 onward in order to reflect the scale developed by Lippman, et al (Lippman et al., 2010). The scale was standardized as a z-score to account for this change. Findings may not be fully generalizable to other sex worker populations and women working more independently (e.g., escorts, online) may have been underrepresented. However, the mapping of working areas and time–location sampling likely helped to ensure a representative sample and to minimize selection bias.

## **2.6 Conclusion**

Findings reveal key socio-structural correlates of suicidality among sex workers, including experiences of violence, trauma, and homelessness. Strengthening social cohesion among workers may have a protective effect on suicidality. This analysis highlights the urgent need for trauma-informed community-led structural interventions tailored to sex workers and a legal framework that enables collectivization and connectedness.

**Table 2.1 Baseline socio-structural characteristics of women sex workers who reported suicidality in the last six months, compared to those who did not (N=867)**

Characteristic	Reported recent suicidality		p-value
	Yes n=141 (16.3%)	No n=726 (83.7%)	
Age (median, IQR)	33 (26 to 41)	35 (29 to 43)	0.005
Gender minority/trans	20 (14.2)	34 (4.7)	0.001
Sexual minority	63 (44.7)	234 (32.2)	0.005
Indigenous ancestry	64 (45.4)	269 (37.1)	0.064
Born in Canada	125 (88.7)	492 (67.8)	<0.001
HIV seropositivity	19 (13.5)	102 (14.1)	0.903
Homelessness <sup>†</sup>	65 (46.1)	198 (27.3)	<0.001
Standardized social cohesion score <sup>†</sup> (median, IQR)	-0.06 (-0.66 to 0.61)	0.18 (-0.54 to 0.91)	0.026
Depression, anxiety, or PTSD <sup>†*</sup>	95 (67.4)	270 (37.2)	<0.001
Non-injection drug use <sup>†</sup>	122 (86.5)	447 (61.6)	<0.001
Injection drug use <sup>†</sup>	82 (58.2)	265 (36.5)	<0.001
Physical/sexual childhood abuse	128 (90.8)	456 (62.8)	<0.001
Physical/sexual client violence <sup>†</sup>	48 (34.0)	108 (14.9)	<0.001
Any intimate partner violence <sup>†</sup>	57 (40.4)	106 (14.6)	<0.001
Police harassment <sup>†</sup>	55 (39.0)	227 (31.3)	0.076
Arrested/put in jail <sup>†</sup>	10 (7.1)	40 (5.5)	0.466
<i>Primary place to solicit clients<sup>†</sup></i>			
Street/public space	91 (64.5)	344 (47.4)	
Indoor/in-call venue	21 (14.9)	236 (32.5)	
Independent/self-advertising (e.g., newspapers, online)	28 (19.9)	138 (19.0)	<0.001
<i>Primary place to service clients<sup>†</sup></i>			
Outdoor/public space	71 (50.4)	269 (37.1)	
Informal indoor (e.g., bars, hotels, saunas, client's place)	50 (35.5)	193 (26.6)	
Formal in-call (e.g., brothel, massage parlour)	17 (12.1)	249 (34.3)	<0.001

<sup>†</sup> Last 6 months

<sup>\*</sup> Ever diagnosed with, treated for, or received support for depression, anxiety or PTSD

**Table 2.2 Unadjusted and adjusted odds ratios for correlates of recent suicidality among women sex workers in Vancouver, 2010-2017 (N=867)**

<b>Characteristic</b>	<b>Unadjusted Odds Ratio (95%CI)</b>	<b>p-value</b>	<b>Adjusted Odds Ratio (95%CI)</b>	<b>p-value</b>
Age (per year older)	0.96 (0.95 to 0.98)	<0.001	0.97 (0.95 to 0.99)	0.002
Gender minority/trans	2.41 (1.50 to 3.88)	0.003		
Sexual minority	1.92 (1.44 to 2.56)	<0.001		
Indigenous ancestry	1.51 (1.13 to 2.01)	0.005		
Born in Canada	4.38 (2.74 to 7.00)	<0.001		
HIV seropositivity	1.11 (0.75 to 1.65)	0.590		
Homelessness <sup>†</sup>	1.57 (1.26 to 1.96)	<0.001	1.44 (1.10 to 1.89)	0.008
Higher social cohesion (per standard deviation from the mean) <sup>†</sup>	0.83 (0.75 to 0.92)	<0.001	0.88 (0.78 to 0.99)	0.036
Depression, anxiety, or PTSD <sup>†*</sup>	2.47 (1.90 to 3.21)	<0.001	2.19 (1.63 to 2.95)	<0.001
Non-injection drug use <sup>†</sup>	1.77 (1.33 to 2.35)	<0.001		
Injection drug use <sup>†</sup>	1.75 (1.39 to 2.21)	<0.001		
Physical/sexual childhood abuse	5.85 (3.61 to 9.49)	<0.001	2.99 (1.75 to 5.10)	<0.001
Physical/sexual client violence <sup>†</sup>	2.25 (1.75 to 2.90)	<0.001	1.82 (1.33 to 2.50)	<0.001
Any intimate partner violence <sup>†</sup>	2.38 (1.88 to 3.02)	<0.001	2.11 (1.60 to 2.80)	<0.001
Police harassment <sup>†</sup>	1.29 (1.05 to 1.59)	0.017		
Arrested/put in jail <sup>†</sup>	1.88 (1.12 to 3.14)	0.017		
<i>Primary place to solicit clients<sup>†</sup></i>				
Indoor venue (vs. street)	0.59 (0.43 to 0.81)	0.001		
Independent (vs. street)	0.83 (0.67 to 1.02)	0.077		
<i>Primary place to service clients<sup>†</sup></i>				
Informal indoor (vs. outdoor)	0.73 (0.60 to 0.89)	0.002		
Formal in-call (vs. outdoor)	0.32 (0.21 to 0.49)	<0.001		

<sup>†</sup> Time-updated, last 6 months as reference

\*Ever diagnosed with, treated for, or received support for depression, anxiety or PTSD

## **Chapter 3: Violence, trauma and living with HIV: Longitudinal predictors of initiating crystal methamphetamine injection among sex workers**

### **3.1 Introduction**

In recent years, crystal methamphetamine (CM) has become one of the world's most commonly used illicit drugs; global use of amphetamine-type stimulants (ATS), which includes CM, is now second only to cannabis, with growing concern over the impacts of the increasing accessibility and availability of CM in North America and Europe (UNODC, 2015). CM is a potent and more commonly injected form of methamphetamine, and for many, a cheaper alternative to heroin that has significant potential for addiction and transmission of HIV and other blood-borne infections (Boddiger, 2005; Mathers et al., 2008). Injection use of CM appears to be more common in countries with the crystalline form of the drug (Strathdee & Stockman, 2010), such as Canada, the United States, Australia, New Zealand, Mexico, and a number of countries in Europe and East and Southeast Asia (e.g., Germany, Greece, Cambodia, Japan, and Thailand, among others) (Degenhardt et al., 2010; UNODC, 2015).

The evidence remains equivocal regarding elevated risk for HIV among those who inject CM compared to other drugs, with limited evidence documenting rates of HIV among CM injectors from only a few countries (Degenhardt et al., 2010; Marshall & Werb, 2010). CM use has been associated with risky sexual (Rusch et al., 2009; Schwarcz et al., 2007) and drug-related behaviors, such as transition from non-injection (e.g., inhalation) to injection drug use (Ahamad et al., 2014; Werb et al., 2013), and increased odds of HIV among key populations, primarily street-involved

youth and men who have sex with men (MSM) (Boddiger, 2005; Fairbairn et al., 2007; Strathdee and Stockman, 2010; Uhlmann et al., 2014). A wide range of other health and social harms have been linked to using CM, including homelessness or eviction from housing (Damon et al., 2018; Feng et al., 2013; Rusch et al., 2009; Shannon et al., 2011; Sasha Uhlmann et al., 2014), early age of incarceration (Milloy, Kerr, Buxton, Montaner, & Wood, 2009), and mental health problems (e.g., psychosis, suicidality, depression) (Cohen et al., 2007; Marshall & Werb, 2010; Semple, Grant, & Patterson, 2004).

Unlike other drugs, women may use CM at rates equal to those of men (Cohen et al., 2007), and women who use CM report high levels of social disadvantage, comorbid psychiatric problems (e.g., depression/anxiety), and sexual risk behaviors (Cohen et al., 2007; Lorvick, Martinez, Gee, & Kral, 2006; Semple et al., 2004). Women entering treatment for CM dependence are more likely than men to report suicide attempts and suffer from higher rates of depression/anxiety, PTSD and other psychological effects related to trauma from physical, sexual or emotional abuse (Cohen et al., 2007).

Among the limited available data, there is some evidence to suggest that harms associated with CM use are increasing in marginalized street-involved populations (e.g., youth) in Western Canada (Degenhardt et al., 2010; Fast et al., 2014; Wood, Stoltz, Montaner, & Kerr, 2006). In Vancouver, the use of CM has risen among various injection and non-injection drug using populations (Wood et al., 2006) and recently, the prevalence of CM injection among adults in Vancouver doubled from 4.9% to 10.5% between 2010 and 2011 (UHRI, 2013). Among street-involved youth, a significant association between smoking crack and subsequent initiation of CM was demonstrated

(Uhlmann et al., 2014). Research from Vancouver has estimated that one-quarter (24%) of street-based sex workers used CM in the last six months over a two-year follow-up period (Shannon et al., 2011).

Despite high and increasing levels of CM use in many settings worldwide, there remains a dearth of research on the initiation patterns of CM injection among sex workers. Compared to other drugs, CM is most often linked to sexual motivations for use and may be more prevalent among individuals in the sex industry (Chettiar, Shannon, Wood, Zhang, & Kerr, 2010; Meade et al., 2012; Rusch et al., 2009; Weiser et al., 2006). Qualitative research has elucidated the ways in which CM is used to stay awake and enhance sexual performance and pleasure (Maher et al., 2011) and is perceived by some sex workers as a superior and more modern alternative to heroin (Ho et al., 2013). While CM has been found to have direct effects on sexual desire, it may also lead to impaired judgment and increased likelihood of unprotected sex and syringe-sharing (Fairbairn et al., 2007; Lorvick et al., 2006; Strathdee & Stockman, 2010; Volkow et al., 2007).

Given the wide range of social and health-related harms associated with CM use, alongside stimulant effects including sexual dis-inhibition and prolonged awake-ness, this analysis aimed to investigate socio-structural predictors of initiating CM injection among women sex workers in Vancouver, Canada. Given prior evidence linking CM use and histories of violence/trauma among women, it was postulated that experiences of violence would be associated with a higher incidence of CM injection.

## **3.2 Methods**

### **3.2.1 Design and sample**

Data were drawn from the AESHA study between January 2010 and February 2014. Further details on the sampling procedures, eligibility criteria, and questionnaire content are described fully in Chapters one and two. Briefly, participants were recruited across Metro Vancouver using time-location sampling (Stueve et al., 2001), 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, in-call locations), and online. Eligibility criteria for participants included cis or trans women, 14 years of age or older, who exchanged sex for money within the last 30 days. For the present longitudinal analysis, the sample was restricted to CM injection-naïve participants who completed at least one follow-up visit.

### **3.2.2 Measures**

The outcome of interest was time to initiation of CM injection (i.e., participants who responded ‘yes’ to a first event of injection CM use 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 a migrant/new immigrant worker (versus Canadian born), education (high school or greater), and physical and/or sexual childhood abuse (before age 18). HIV/STI serostatus, homelessness, physical and/or sexual workplace violence (i.e., responded ‘yes’ to any of ‘abducted/kidnapped,’ ‘forced to have sex without a condom,’ ‘attempted sexual assault,’ ‘raped,’ ‘strangled,’ ‘physically assaulted/beaten,’ ‘locked/trapped in a car,’ ‘thrown out of moving car,’ ‘assaulted with weapon’ by clients; responded ‘yes’ to ‘physically assaulted’ or ‘coerced into providing sexual favors’ by

police), primary place to solicit and service clients (e.g., outdoor/public spaces, informal indoor venues, brothels/quasi-brothels), having a male intimate (non-paying) partner who injects drugs, and any injection and non-injection drug use (heroin, crack, cocaine, marijuana, alcohol) were considered time-varying and were updated to reflect their occurrence within the last six months.

### **3.2.3 Kaplan-Meier analyses**

The cumulative incidence of CM injection was calculated using Kaplan-Meier methods stratified by workplace violence and by participants with or without a history of childhood abuse at baseline. Survival curves were compared using the log-rank test. The date of CM injection initiation was estimated to be the midpoint between the last interview and interview date when CM injection initiation was reported. Participants who did not initiate CM injection were right-censored at the time of their most recent follow-up visit. Time zero was considered the date of recruitment into the cohort.

### **3.2.4 Extended Cox regression analyses**

Unadjusted and adjusted hazard ratios (HR and AHR) and 95% confidence intervals (95%CI) for factors associated with CM injection initiation were calculated using Extended Cox regression. All time-updated covariates were based on bi-annual follow-up data. For the final multivariable Cox analysis, a fixed model was built to adjust for all variables significantly correlated with CM injection initiation at  $p < 0.05$  in bivariate analyses. 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. All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA), and all p-values are two-sided.

### 3.3 Results

CM use was highly prevalent, with 42% (n=309/744) of the total AESHA cohort reporting ever using non-injection CM and 18% (n=132/744) reporting ever injecting CM who were thus excluded from this analysis. A total of 455 CM injection-naïve sex workers who completed at least one follow-up visit were eligible for inclusion in the present analysis. Baseline characteristics of participants who initiated CM injection compared to those who did not are displayed in Table 3.1. Overall, 14% (n=65) injected CM for the first time over the follow-up period, corresponding to an incidence density of 6.79 (95%CI: 5.30-8.69) per 100 person-years. The median age was 36 years old (interquartile range [IQR]=29-43) and those who initiated CM injection were a median age 5 years younger (32, IQR=28-39) than those who did not inject CM (37, IQR=29-43) (p=0.013). One quarter (24%; n=107) of participants identified as a gender or sexual minority and 39% (n=177) as Indigenous. Overall HIV prevalence was 12% (n=54), and those who initiated CM injection had a higher prevalence of HIV than those who did not initiate CM injection (25% vs. 10%, p<0.001).

At baseline, 32% (n=147) of participants had ever used non-injection CM, the majority (64%; n=291) reported non-injection crack use, and 28% (n=126) reported injecting heroin in the last six months. More than half (61%; n=276) of participants reported experiencing physical and/or sexual abuse before the age of 18, and among those who initiated CM injection, 75% experienced childhood abuse compared to 58% among those who did not inject CM (p=0.006). Overall, 21% (n=94) experienced recent physical and/or sexual violence from clients and 37% (n=168) experienced recent police harassment or arrest. Nearly one third (29%; n=131) were homeless in

the last six months and more than half (55%; n=252) solicited for clients on the streets, with 43% (n=196) providing services to clients in outdoor/public spaces.

Among those who initiated CM injection during the observational period (n=65), 20% (n=13) reported first-time use to be via injection, of which 85% (n=11/13) injected themselves. One third (31%; n=20) reported using CM for the first time with a friend/acquaintance, and 14% (n=9) with a boyfriend. The most frequently reported location for using CM in the last six months was the participant's own place (65%; n=42), followed by outdoors (35%; n=23), a friend's place (32%; n=21), a boyfriend's place (20%; n=13), a client's place (18%; n=12), and Vancouver's supervised injection site, Insite (18%; n=12). Approximately 40% (n=26) reported using CM while working, either indoors (n=18/26; 69%) or outdoors (n=15/26; 58%).

After 48 months, the cumulative incidence of CM injection was higher among participants who reported physical and/or sexual workplace violence than those who did not (25.6% vs. 14.1%;  $p<0.01$ ) (Figure 3.1). Similarly, the cumulative incidence of CM injection after follow-up was 21.9% among those who experienced childhood abuse compared with 16.3% among those who did not ( $p=0.014$ ) (Figure 3.2).

Unadjusted and adjusted hazard ratios for factors associated with initiating CM injection over follow-up are reported in Table 3.2. In the final multivariable model, injection heroin use (AHR 6.11; 95%CI 3.24-11.52), having an intimate partner who injects drugs (AHR 2.93; 95%CI 1.57-5.46), workplace violence (AHR 2.85; 95%CI 1.74-4.67), HIV seropositivity (AHR 2.69; 95%CI 1.45-5.00), and a history of physical and/or sexual childhood abuse (AHR 1.86; 95%CI 0.99-3.49)

remained independently associated with time to CM injection initiation. For each year increase in age, the hazard of initiating CM injection decreased by 5% (AHR 0.95; 95%CI 0.92-0.98). In a sub-analysis where non-injection CM use was included, the hazard associated with childhood abuse was smaller and less significant (AHR 1.68; 95%CI 0.89-3.17).

### **3.4 Discussion**

This prospective analysis reports on the incidence of and characteristics associated with first-time CM injection among a community-based cohort of women sex workers. Findings demonstrate that injection heroin use, having an intimate partner who injects drugs, HIV seropositivity, workplace and historical physical/sexual violence, and younger age are independently associated with initiating CM injection in this setting.

Current evidence demonstrates that sex workers who inject drugs are at elevated risk for HIV and other blood-borne infections, shaped by dual drug and sexual-risk pathways (Argento, Shannon, et al., 2015; Kerr et al., 2016; Shannon et al., 2011; Strathdee & Stockman, 2010). It has been hypothesized that CM use increases risk for HIV due to a reduced likelihood of using condoms and increased likelihood of engaging in riskier sexual behaviors (Meade et al., 2012; Patterson et al., 2008; Volkow et al., 2007; Zule et al., 2007). Among sex workers in northern Mexico, snorting or smoking CM was associated with three-fold increased odds of HIV infection (Patterson et al., 2008). Multivariable analyses among women who use CM in California found that injecting CM was independently associated with anal sex, >5 sexual partners, and syringe-sharing (Lorvick et al., 2006). Similar findings were observed among sex workers in Cambodia, with the use of CM/ATS being significantly associated with having more partners and STI infection (Couture et

al., 2012). Conversely, previous research did not find significant associations between CM use and enhanced sexual risks (i.e., number of clients, unprotected sex) among sex workers in Vancouver (Shannon et al., 2011).

Global and systematic reviews report insufficient evidence of elevated risk for HIV among those who inject CM compared to those who inject other drugs (Degenhardt et al., 2010; Marshall & Werb, 2010). Importantly, the present analysis suggests that the associations between CM injection and HIV infection may be bi-directional. While injecting CM has been linked to heightened risk for HIV and other blood-borne infections via risky sex (Patterson et al., 2008) and syringe-sharing (Fairbairn et al., 2007; Lorvick et al., 2006; Rusch et al., 2009), this study found an almost three-fold increased hazard of initiating CM injection among sex workers living with HIV, after adjusting for potential confounders. CM use may be a coping mechanism for psychosocial stressors, as using CM (via injection or non-injection routes) can help to alleviate the emotional and psychological stress associated with living with HIV (Boddiger, 2005). This study underscores the complex and potentially bi-directional associations between HIV and CM injection among sex workers, compounded by psychosocial distress, and the critical need to integrate trauma-informed addiction treatment within HIV care.

Sex workers in North America report high levels of violence and childhood abuse, and while data on mental illness were not directly captured in the present analysis, mental illness may be mediating the association between experiences of traumatic events and drug use-related risk behaviours (Argento et al., 2014; Surratt et al., 2012). Historical experiences of violence, as well as indirect violence (i.e., witnessing violence), can contribute to risk by shaping the propensity to

use drugs to escape emotional trauma (Romero-Daza et al., 2005). Among female CM users (of whom 22% were sex workers) surveyed in San Diego, 38% reported having a psychiatric disorder, with only 15% reporting current use of psychiatric medication (Semple et al., 2004). A US-based review of women with CM dependence underscores the high prevalence of comorbid mental disorders and history of violence and abuse (Cohen et al., 2007). This study provides temporal evidence for the relationship between sex workers' experiences of violence/abuse and initiation of CM injection. In multivariable analyses, physical/sexual violence independently predicted time to initiation of CM injection, which may imply that sex workers are self-medicating with CM for trauma or mental illness. Ethnographic research among street-involved youth in Vancouver supports this hypothesis, where narratives describe using CM as treatment for both professionally and self-diagnosed mental illness (Fast et al., 2014). A systematic review demonstrated consistent associations between CM use and psychosis and depression among youth (Marshall & Werb, 2010). The association of CM injection initiation with younger age in the present study highlights the vulnerability faced by younger sex workers to HIV and drug-related harms, amplified by the criminalized and stigmatized nature of sex work (Shannon et al., 2015; Uhlmann et al., 2014).

Findings extend upon prior research demonstrating a significant association between CM use and heroin injection (Shannon et al., 2011), and reveal that recent heroin injection is a strong predictor of subsequent CM injection. Given that heroin is known to be self-medicating for those suffering from PTSD (Tull et al., 2010), sex workers who have experienced violence and other traumatic life events may be self-medicating with injection CM. Higher rates of CM use have been observed among individuals with PTSD than without (Smith et al., 2010), and PTSD has been associated

with poorer CM treatment outcomes (Glasner-Edwards, Mooney, Ang, Hillhouse, & Rawson, 2013).

For sex workers in this setting, injection heroin use preceding CM injection could be attributable to the availability or relative purity of heroin in Vancouver, or the perception that CM is a better substance. In the context of a highly contaminated drug supply (i.e., with synthetic opioids such as fentanyl), it is plausible that some people may be switching from heroin to CM to reduce risk of overdose. The global literature highlights sexual motivations for CM use among women, including elevated energy and mood, weight loss, and enhanced sexual desire (Semple et al., 2004; Volkow et al., 2007). Qualitative work in Southeast Asia explicates the varied motivations for using CM among women sex worker populations who described increased feelings of confidence, happiness, and euphoria, highlighting the effect of enhanced sexual pleasure and performance (Ho et al., 2013; Maher et al., 2011). CM has been described as a highly functional “power drug” that facilitates a sense of agency and increases strength and endurance, allowing sex workers to see more clients and for longer hours (Maher et al., 2011). Sex workers in this region also report replacing heroin with CM, which they perceive a more fashionable and less addictive alternative that enables them to perform better at work (Ho et al., 2013).

The present analysis highlights the critical role of having an intimate partner who injects drugs and identifies important, gendered risk factors for injecting CM among sex workers, as well as a key area for intervention. Previous studies indicate that CM use may be closely connected to use with regular clients and non-commercial partners. Research has identified the pervasiveness of male psychological dominance and gender inequality among drug-using couples in the US and

its association with increased violence (El-Bassel et al., 2005). Sex workers who used CM in Vancouver have been shown to be more likely to have an intimate partner procure drugs for them (Shannon et al., 2011), and earlier ethnographic work has highlighted the physical and emotional vulnerability of women in unequal power relations, often relying on pimps to obtain drugs (Maher, 1997; Shannon et al., 2008). In Cape Town, South Africa, CM users were more likely than non-users to have experienced various forms of interpersonal violence: close to 50% experienced violence from intimate partners and nearly a quarter experienced childhood abuse (Meade et al., 2012). These findings evidence more nuanced gendered risk for injecting CM, tied closely to psychosocial relationships with sexual partners and experiences of violence and abuse. Given that injection drug use by intimate partners alongside recent heroin injection exemplify key risk pathways to CM injection, future research should seek to include male intimate partners and inform evidence-based interventions that actively involve couples within the context of understanding drug-related risks and harms.

The research and policy implications of these findings point to the critical need for evidence-based interventions that incorporate gender- and couple-focused strategies, integrating harm reduction, violence prevention, and mental health supports within HIV prevention and care for sex workers. Given the role of socio-structural factors in shaping CM injection initiation patterns, future research should address the broader risk environment for sex workers, including the physical and emotional aspects of the work environment, violence and abuse, as well as drug use patterns within sex workers' intimate sexual partnerships. Prior qualitative work has elucidated the importance of increasing access to safer indoor sex work environments, which offer critical protections against victimization and violence by increasing sex workers' capacity to control and negotiate safer

transactions (Krüsi et al., 2012). In light of disproportionate trauma and mental health burden (primarily depression, anxiety, and PTSD) experienced by sex workers, alongside the potential for self-medicating with CM or other drugs, insufficient access to mental health and addiction services remains a critical concern.

### **3.5 Limitations**

Data used for this analysis were largely self-reported, and the variables examined included sensitive topics such as childhood abuse and highly stigmatized illicit drug use, which introduces the potential for social desirability and reporting bias. However, interviews were conducted in safe and comfortable spaces by experienced interviewers (including current/former sex workers) with strong rapport, and the community-based nature of the study reduces the likelihood of these biases. Questions pertaining to events that occurred within the past six months of the interview may be subject to recall bias. Initiation of CM injection among sex workers may be influenced by complex individual, interpersonal and structural variables not measured in our study (e.g., psychiatric disorders). The study population included women from wide-ranging sex work environments, yet findings may not be fully generalizable to sex workers in other settings. Although eligibility criteria for participants included sex workers 14 years of age or older, our sample had few participants <18; therefore, younger sex workers may be underrepresented.

### **3.6 Conclusion**

This analysis underscores the gendered and social risk environment of first-time CM injection experiences among women sex workers. Drug use patterns within intimate sexual partners were evidenced to shape initiation of CM injection. The critical roles of workplace and historical

violence, coupled with heroin injection (known to be self-medicating for PTSD) as the strongest predictor of initiating CM injection, emphasize the importance of increasing access to evidence-based addiction treatment for key populations both living with and affected by HIV. Findings elucidate the urgent need for gender-sensitive and integrated, trauma-informed HIV and addiction services for marginalized women.

**Table 3.1 Baseline characteristics of sex workers in Vancouver who reported first time injection crystal methamphetamine use over follow-up compared to those who did not (N=455)**

Characteristic	Initiated crystal methamphetamine injection		p-value
	Yes n=65 (14.3%)	No n=390 (85.7%)	
Age (median, IQR)	32 (28-39)	37 (29-43)	0.013
HIV seropositivity <sup>†</sup>	16 (24.6)	38 (9.7)	<0.001
STI seropositivity <sup>†</sup>	13 (20.0)	43 (11.0)	0.063
Canadian-born	62 (95.4)	270 (69.2)	<0.001
Indigenous ancestry	32 (49.2)	145 (37.2)	0.065
Sexual minority	21 (32.3)	86 (22.1)	0.071
Education, high school or greater	26 (40.0)	205 (52.6)	0.061
Homelessness <sup>†</sup>	30 (46.2)	101 (25.9)	<0.001
Coerced into sex work	7 (10.8)	35 (9.0)	0.644
Childhood abuse	49 (75.4)	227 (58.2)	0.006
Physical/sexual violence by clients <sup>†</sup>	23 (35.4)	71 (18.2)	0.002
Physical/sexual violence by police <sup>†</sup>	7 (10.8)	15 (3.9)	0.026
Police harassment/arrest <sup>†</sup>	36 (55.4)	132 (33.9)	<0.001
<i>Primary place to solicit clients<sup>†</sup></i>			
Indoor establishment <sup>†</sup>	2 (3.1)	129 (33.1)	
Street/public <sup>†</sup>	53 (81.5)	199 (51.0)	
Independent <sup>†</sup>	10 (15.4)	62 (15.9)	<0.001
<i>Primary place to service clients<sup>†</sup></i>			
Outdoor/public space <sup>†</sup>	41 (63.1)	155 (39.7)	
Informal indoor <sup>†</sup>	19 (29.2)	105 (26.9)	
Formal/managed indoor space <sup>†</sup>	5 (7.7)	130 (33.3)	<0.001
<i>Drug use variables</i>			
Intimate partner injects drugs <sup>†</sup>	10 (15.4)	26 (6.7)	0.013
Non-injection heroin use <sup>†</sup>	23 (35.4)	55 (14.1)	<0.001
Injection heroin use <sup>†</sup>	36 (55.4)	90 (23.1)	<0.001
Cocaine use (non-injection) <sup>†</sup>	17 (26.2)	64 (16.4)	0.057
Cocaine use (injection) <sup>†</sup>	24 (36.9)	32 (8.2)	<0.001
Crack use (non-injection) <sup>†</sup>	60 (92.3)	231 (59.2)	<0.001
Crack use (injection) <sup>†</sup>	3 (4.6)	6 (1.5)	0.124
Marijuana use <sup>†</sup>	31 (47.7)	132 (33.9)	0.031

<sup>†</sup> Last six months

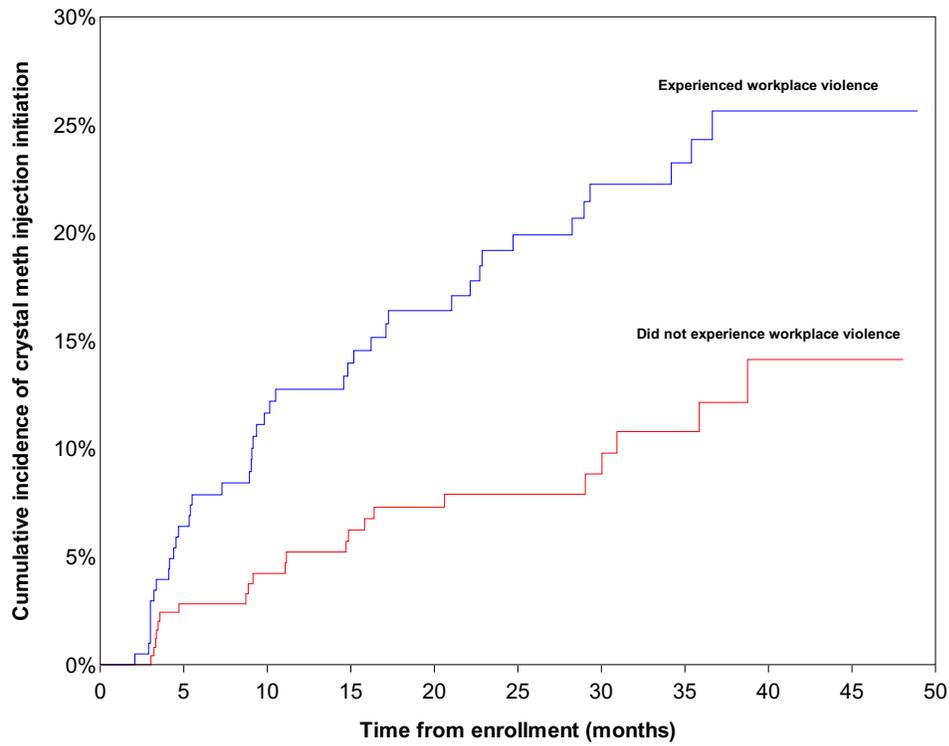
**Table 3.2 Unadjusted and adjusted hazard ratios (AHR) for predictors of time to initiating crystal methamphetamine injection among sex workers in Metro Vancouver, 2010-2014 (N=455)**

Characteristic	Unadjusted hazard ratio (95% CI)	Adjusted hazard ratio (95% CI)	AHR p-value
Age (per year older)	0.96 (0.93 - 0.98)*	0.95 (0.92 - 0.98)	0.001
HIV seropositivity†	2.49 (1.42 - 4.37)*	2.69 (1.45 - 5.00)	0.002
STI seropositivity†	2.38 (1.32 - 4.31)*		
Canadian-born	6.83 (2.13 - 21.89)*		
Indigenous ancestry	1.41 (0.86 - 2.31)		
Sexual minority	1.62 (0.96 - 2.73)		
Education, high school or greater	0.69 (0.42 - 1.14)		
Homelessness†	1.86 (1.08 - 3.22)**	-	
Coerced into sex work	1.08 (0.49 - 2.36)		
Childhood abuse	2.05 (1.15 - 3.65)**	1.86 (0.99 - 3.49)	0.054
Physical/sexual violence by clients†	4.25 (2.56 - 7.06)*		
Physical/sexual violence by police†	1.50 (0.20 - 11.44)		
Police harassment/arrest†	2.76 (1.65 - 4.62)*		
Workplace violence (police, clients)†		2.85 (1.74 - 4.67)	<0.001
<i>Primary place to solicit clients†</i>			
Indoor establishment (vs. street)†	0.22 (0.09 - 0.57)*		
Independent (vs. street)†	0.68 (0.39 - 1.18)		
<i>Primary place to service clients†</i>			
Informal indoor (vs. outdoor)†	0.82 (0.49 - 1.36)		
Brothel (vs. outdoor)†	0.14 (0.04 - 0.48)*		
<i>Drug use variables</i>			
Intimate partner injects drugs†	5.17 (2.92 - 9.14)*	2.93 (1.57 - 5.46)	0.001
Non-injection heroin use†	1.72 (0.90 - 3.26)		
Injection heroin use†	10.13 (5.59 - 18.34)*	6.11 (3.24 - 11.52)	<0.001
Cocaine use (non-injection)†	2.45 (1.37 - 4.39)*	-	
Cocaine use (injection)†	10.68 (6.55 - 17.42)*	-	
Crack use (non-injection)†	5.64 (2.56 - 12.42)*	-	
Crack use (injection)†	9.15 (4.17 - 20.07)*	-	
Marijuana use†	2.47 (1.51 - 4.05)*		

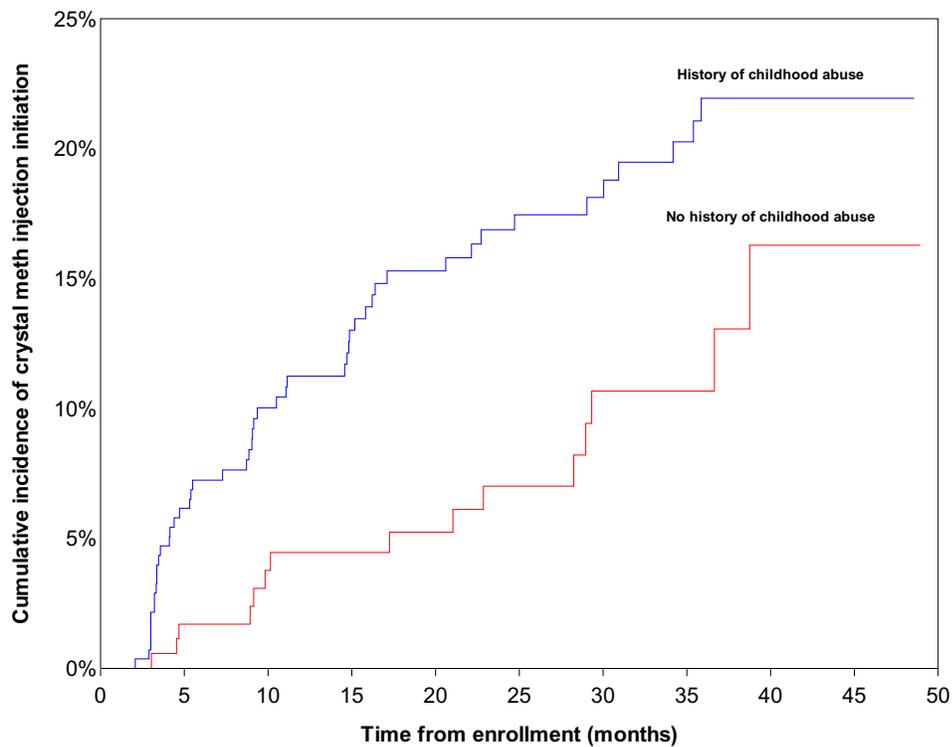
† Time-updated, last 6 months as reference

\* $p < 0.01$  \*\* $p \leq 0.05$

**Figure 3.1 Time to initiation of crystal methamphetamine (CM) injection by workplace violence experiences**



**Figure 3.2 Time to initiation of crystal methamphetamine (CM) injection by childhood abuse**



## **Chapter 4: Does psychedelic use reduce risk of suicidality? Evidence from a longitudinal community-based cohort of marginalized women in Canada**

### **4.1 Introduction**

Despite efforts to improve mental health over the last 60 years, rates of suicide have not significantly declined in much of the world (NIMH, 2014; Värnik, 2012). Suicidality remains a critical public health concern with no highly effective treatments (Klonsky et al., 2016; Nock et al., 2008). Significant gaps remain in empirical research examining suicidality among marginalized women, such as street-involved sex workers or women who use drugs, who experience disproportionately high levels of stigma, discrimination, criminalization, violence (Argento et al., 2014; Deering et al., 2014; Shannon et al., 2015) and other structural drivers that elevate risk of suicidality.

Rates of suicide vary significantly across settings and populations; however, global research and evidence demonstrate that nearly half (45%) of marginalized women (sex workers who use injection drugs) surveyed in China reported suicide ideation in the last six months (Gu et al., 2014); nearly one-fifth (19%) of female sex workers in India reported suicide attempts in the last 3 months (Shahmanesh et al., 2009); and nearly three-quarters (74%) of street-based sex workers in Sydney, Australia reported lifetime suicidal ideation or attempts (Roxburgh et al., 2006). Sex workers are a diverse population working from indoor in-call and out-call venues to street-based settings; however, previous studies highlight substantial unmet mental health needs of more marginalized and street-involved sex workers (Puri et al., 2017). Street-based sex workers who report histories

of trauma or childhood abuse are at greater risk of experiencing depression, PTSD, and suicidality (Gu et al., 2014; Hawton & van Heeringen, 2009; Roxburgh et al., 2006; Surratt et al., 2012; Zhang et al., 2016). Substantial structural barriers to accessing safe and non-judgmental health and support services exist for marginalized and street-involved women sex workers, and few evidence-based mental health or addiction interventions are tailored to the needs of such key populations both in Canada and internationally (Benoit et al., 2003; Jeal, Macleod, Turner, & Salisbury, 2015; Puri et al., 2017).

A number of psychedelic drugs, including the classic serotonergic psychedelics or “hallucinogens” LSD, psilocybin, DMT, and mescaline, as well as the “enactogen” or “empathogen” MDMA, are being revisited following a 40-year hiatus in research for their potential in improving mental wellbeing and addiction issues (Sessa, 2012; Tupper et al., 2015). While not considered a classic psychedelic, MDMA has featured over the years in research and clinical trials as a promising adjunct to psychotherapy, particularly for treating PTSD. Re-emerging clinical research and evidence lend mounting support to psychedelic-assisted therapy as an alternative treatment for refractory substance use disorders and treatment-resistant depression, end-of-life anxiety, and PTSD (Carhart-Harris & Goodwin, 2017; dos Santos et al., 2016; Johnson et al., 2017; Mithoefer et al., 2018). Congruent with the evidence from clinical trials, large epidemiological studies among the US adult population recently found significantly reduced psychological distress and suicidality associated with non-medical psychedelic use (Hendricks et al., 2015; Krebs & Johansen, 2013). Two other recent observational studies in the US demonstrated significant associations between lifetime psychedelic use and reduced recidivism and intimate partner violence among populations of prison inmates (Hendricks et al., 2014; Walsh et al., 2016). The literature remains characterized

by large gaps, however, and a paucity of evidence on how clinical psychedelic therapies or naturalistic (i.e., non-medical) psychedelic drug use might influence suicidality among marginalized women.

Despite the multifaceted structural and social inequities that shape poor mental health among marginalized women, little data and research exist on suicide rates or factors that may potentiate or mitigate suicidality, particularly in the global north. 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 among a community-based prospective cohort of marginalized women. Based on the currently available evidence on the therapeutic effects of psychedelics, it was postulated that psychedelic use would have an independent protective effect on suicidality over the study period.

## **4.2 Methods**

### **4.2.1 Study design and participants**

This longitudinal analysis drew on data from the AESHA described in detail in Chapters one and two. To capture initial episodes of suicidality, the present longitudinal analysis was 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.

#### 4.2.2 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 at baseline were excluded from analysis ( $n=50/766$ ; 6.5%), 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.

### **4.3 Results**

#### **4.3.1 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 4.1.

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 having 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 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 ( $p<0.001$ ).

#### **4.3.2 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 who reported 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.

#### **4.3.3 Bivariate and multivariable Cox analysis**

Unadjusted and adjusted hazard ratios for factors associated with a first episode of suicidality during follow-up are displayed in Table 4.2. 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).

#### 4.4 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 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 (Gu et al., 2014; Hong et al., 2013; Roxburgh et al., 2008; Shahmanesh et al., 2009). The present study, based on a community-based, prospective cohort of marginalized women, adds to a growing body of literature documenting the therapeutic effects of psychedelic substances (Bogenschutz & Johnson, 2016; Dyck, 2015; Kraehenmann et al., 2015; Sessa, 2012; Tupper et al., 2015). To the best of my knowledge, this is the first study to longitudinally investigate the relationship between psychedelic use and suicidality. This study also offers some of the first empirical evidence of the potential benefits of psychedelics for ameliorating mental health issues among marginalized women.

Findings extend upon research describing associations between illicit drug use 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 re-emerging evidence on the potential of psychedelics to mitigate risks for suicide and research citing

benefits to health and wellbeing in both clinical and non-clinical settings (Carhart-Harris, Kaelen, et al., 2016; dos Santos et al., 2016; Garcia-Romeu & Richards, 2018; Hendricks et al., 2015; Krebs & Johansen, 2013; Palhano-Fontes et al., 2018). A detailed overview of the available evidence and limitations to these studies is described in Chapter 1. Notably, in the context of the deadliest drug-overdose epidemic in North American history (largely driven by illicitly manufactured synthetic opioids such as fentanyl), and lack of addiction services tailored to marginalized women, further longitudinal observational research conducted by our team in Vancouver examined the moderating effect of psychedelic use on the relationship between other illicit drug use (specifically pharmaceutical opioids) and suicide risk. Findings from this secondary analysis found a significantly protective moderating effect of psychedelic use on the relationship between pharmaceutical opioid use and suicide risk among marginalized women (Argento, Braschel, Walsh, Socias, & Shannon, 2018). While observational and limited to self-reported data, these findings underscore the critical need for evidence-based and innovative approaches to addressing complex mental health and substance use comorbidities and risk of suicide among marginalized women.

The way in which psychedelics may alleviate suffering associated with mental health problems is undoubtedly a complicated phenomenon and warrants further investigation. The complex mechanisms by which psychedelics may influence suicidality likely involves activity at the 5-HT<sub>2A</sub> serotonin receptors (Anisman et al., 2008; Bogenschutz & Johnson, 2016; Vollenweider & Kometer, 2010). As described more fully in Chapter 1, neuroimaging research suggests that psychedelics alter neural network connectivity and may enhance recall of autobiographical memories to facilitate more positive reprocessing and reconciliation of traumatic memories

(Bogenschutz & Pommy, 2012; Carhart-Harris et al., 2014; Carhart-Harris, Leech, et al., 2012), in addition to eliciting powerful mystical-type experiences that can lead to sustained positive changes in attitudes and mood (Griffiths et al., 2011; Griffiths, Richards, McCann, & Jesse, 2006). The emotion awe has been postulated to be the underlying characteristic of psychedelic-occasioned mystical experiences, and in its extreme form may be analogous to experiencing ego-dissolution (Hendricks, 2018). Further, ego-dissolution elicited by psychedelic experiences may facilitate personal insights and self-reflection (Nour et al., 2017) and has been demonstrated to influence key characteristics such as personal meaningfulness, life satisfaction, spirituality, and connectedness that play a crucial role in problematic substance use and risk of suicidality (Carhart-Harris, Erritzoe, et al., 2017; Garcia-Romeu et al., 2014; Watts et al., 2017). However, this research is in the early stages and there remains a need for larger randomized controlled studies in more diverse populations, as well as continued research on potential risks and mechanisms of action.

Marginalized and street-based sex workers experience dynamic, synergistic effects between historical trauma, lack of workplace safety, and mental health/substance use comorbidities that elevate risk of suicidality. Notably, the present analysis 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. Marginalized women and sex workers who use drugs report high rates of childhood abuse (Argento, Chettiar, et al., 2015; Rio Navarro et al., 2012; Roxburgh et al., 2006), which is associated with an increased likelihood of experiencing subsequent physical or sexual violence, as well as initiating injection drug use (Argento et al., 2017; Kerr et al., 2009; Ulibarri et al., 2010). For those suffering from emotional trauma stemming from violence, including indirect violence or witnessing violence, there may be

a proclivity to use drugs for self-medication (Romero-Daza et al., 2005; Tull et al., 2010). As demonstrated, having an early traumatic life event is a key risk factor for suicide among sex workers in this study, a high proportion of whom are Indigenous and have experienced historical trauma that can have harmful intergenerational impacts (Bingham et al., 2014; Hawton & van Heeringen, 2009).

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. In the context of accumulating evidence demonstrating positive outcomes with psychedelic-assisted treatments, with few serious adverse events reported (Carhart-Harris, Bolstridge, et al., 2016; dos Santos et al., 2016; Morgan, Muetzelfeldt, Muetzelfeldt, Nutt, & Curran, 2010; Tupper et al., 2015), this study supports advancing research on psychedelics to explore their potential to be useful tools in addressing mental health issues and remediating risks for psychological distress and suicide.

#### **4.5 Limitations**

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 or recency of use), as well as separate analyses for ideation and attempt outcomes, were not feasible. This study could not elucidate the effect of specific psychedelics as they were collapsed into a single variable. Further examination of these variables would certainly be interesting and important in future analyses with additional data from follow-up questionnaires. Given that the majority of participants in the study had used MDMA, it would be interesting to examine the specific effects of MDMA use alone in future analyses. 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 personality characteristics 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 (Carhart-Harris, Bolstridge, et al., 2016; Gasser et al., 2014; Mithoefer et al., 2010; Nutt et al., 2010; Winstock et al., 2017), 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 (Tupper et al., 2015); 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 might 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.

#### **4.6 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 health problems and promoting mental wellness. Increased support for community-driven interventions that are gender and culturally appropriate are urgently needed to prevent suicidality, and any clinical treatment utilizing psychedelics must be developed alongside sex worker-led interventions and community empowerment.

**Table 4.1 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 <sup>†</sup>	7 (22.6)	26 (10.0)	0.065
STI seropositivity <sup>†</sup>	3 (9.7)	35 (13.5)	0.778
Homelessness <sup>†</sup>	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
Pharmceutical 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 <sup>†</sup>	27 (87.1)	148 (57.1)	0.001
Injection drug use <sup>†</sup>	16 (51.6)	81 (31.3)	0.023
Physical/sexual client violence <sup>†</sup>	5 (16.1)	36 (13.9)	0.784
Physical/sexual childhood abuse	24 (77.4)	112 (43.2)	<0.001
Police harassment/arrest <sup>†</sup>	16 (51.6)	91 (35.1)	0.072
<i>Primary place to solicit clients<sup>†</sup></i>			
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

<sup>†</sup> Last 6 months

**Table 4.2 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		
Pharmaceutical 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 <sup>†</sup>	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 <sup>†</sup>	2.55 (1.19 to 5.44)	0.016	1.95 (0.91 to 4.17)*	0.085
<i>Primary place to solicit clients<sup>†</sup></i>				
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		

<sup>†</sup> 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.

## **Chapter 5: Discussion, implications, and conclusions**

### **5.1 Summary of findings**

To date, there has been little research to understand and prevent suicide and improve mental health and wellbeing among marginalized women. While interest and scientific inquiry into the therapeutic potential of psychedelics has been revitalized in recent years, marginalized women have been excluded from most of this research. Coincident with substantial gaps in knowledge and evidence surrounding the socio-structural trajectories of drug use, violence, and suicidality, the field remains hampered by inadequate intervention strategies that meet the unique needs of this population.

Guided by a structural determinants framework, this dissertation aimed to explore trajectories of drug use, violence, and suicide risk among marginalized women, and to identify avenues of intervention including the therapeutic potential of psychedelics. Chapter 2 empirically examined the burden and correlates of suicidality among sex workers. These results revealed key socio-structural factors associated with suicidality, including experiences of historical and interpersonal violence, trauma/mental health issues, and homelessness. At the same time, increased social cohesion among women was demonstrated to have a protective effect on suicidality, underscoring the critical need for facilitating collectivization and connectedness among sex workers. Chapter 3 longitudinally investigated predictors of crystal methamphetamine injection initiation, further elucidating complex relationships between experiences of violence, trauma, and drug use. These findings identified how the gendered and social risk environment (e.g., drug use patterns with intimate partners, workplace violence),

coupled with heroin injection (known to be self-medicating for PTSD), influence first-time experiences of injection drug use.

Building on these findings, the longitudinal analysis described in Chapter 4 determined that psychedelic drug use had an independent protective effect on suicidality. This analysis was the first to prospectively examine the effect of psychedelic use on suicide risk among marginalized women, and demonstrated that those who used psychedelics had a 60% reduced hazard of suicidality. Crystal methamphetamine use and childhood trauma independently predicted increased risk of suicidality. These findings point to the therapeutic potential of psychedelics even when used in non-medical settings presumably without explicit therapeutic intent, and support calls to further investigate the utility of psychedelics and advance research on psychedelic-assisted therapy for improving mental health and preventing suicidality. Taken together, findings from these analyses suggest that key socio-structural factors can potentiate or mitigate risk of suicide among marginalized women, informing the development of potentially efficacious community-led and structural interventions implemented alongside innovative individual-level clinical interventions.

In applying a structural determinants framework and drawing on the theory of intersectionality, this thesis empirically explored how various intersecting socio-structural factors (e.g., interpersonal and workplace violence, homelessness, social cohesion, criminalization, stigma) are synergistically linked to individual-level markers of health and wellbeing (e.g., drug use, mental health and trauma), which dynamically work to shape risk of suicidality. This thesis highlights how social and health inequalities faced by marginalized women are embedded within

the larger structural organization of society that continues to reproduce inequalities through criminalization and the harmful effects of current laws and policies on drug use and sex work. Further informed by a rights-based approach emphasizing cognitive liberty, this thesis has important implications for policy reform to ensure fundamental rights (i.e., to health and freedom of thought) by enabling the advancement of psychedelic research alongside other key individual- and community-level (e.g., strengthening social cohesion, connectedness, and social support) strategies to prevent suicide. Findings extend the limited body of evidence on suicidality and unmet health needs among marginalized women, as well as the growing research and literature on psychedelics for treating mental health and substance use disorders.

## **5.2 Informing avenues of intervention and directions for future research**

### **5.2.1 Structural-level intervention**

There is a need to investigate and better understand synergistic risk pathways to suicidality using a structural determinants approach. Future research and efforts to mitigate suicidality should aim to identify and target socio-structural level factors that are amenable to intervention. This includes advocating for evidence-based law reform, as discussed above, and conveying the urgency of such pressing health issues faced by marginalized women to the general public and policymakers.

For example, the findings presented in this thesis underscore and provide critical insights into how criminalization (i.e., of non-medical drug use and of sex work) is a form of social marginalization that violates human rights and most negatively impacts the health of those who are already marginalized and stigmatized in society (Csete & Cohen, 2010; Shannon et al., 2015;

Walsh, 2016). A structural approach to mitigating suicidality necessitates at its heart a reform of laws and policies that perpetuate stigma, discrimination, violence, and unequal access to health and social support services (Corrigan, 2004; Csete & Cohen, 2010). The criminalization of sex work and drug use entrenches individuals in cycles of social exclusion, violence, incarceration, problematic substance use, and psychological distress, infringing upon the health and human rights of many marginalized women worldwide (Amnesty International, 2015; Bruckert & Hannem, 2013; Csete & Cohen, 2010).

It is imperative that sex work legislation and drug policy reflect a structural determinants approach and understanding of risk and harms based on evidence. Decriminalization of sex work (e.g., in New Zealand, parts of Australia) is evidenced to lead to better coverage and access to health services and workplace safety for sex workers (Abel et al., 2009; Shannon et al., 2015). By contrast, sex work legislation in Canada (*Protection of Communities and Exploited Persons Act*) continues to criminalize most aspects of the sex industry. The emerging evidence suggests this approach continues to reproduce stigma and restrict sex workers' ability to access health, social, and legal protections (Krüsi et al., 2014). Recent studies from Vancouver and France have reported reduced access to critical health and community-led services, reinforced marginalization, and increased violence and impoverishment following implementation of end-demand laws (Argento, Goldenberg, et al., under review; Le Bail & Giametta, 2018). Decriminalization of the use and possession of illicit drugs, as modeled in Portugal since 2001, can lead to reductions in problematic use and drug-related harms, as well as increased uptake of drug treatment and reduced burden on the criminal justice system (Hughes & Stevens, 2010). Criminal drug prohibition – with drug harms demonstrated to be poorly correlated with their

legal classifications, as is the case with psychedelics (Nutt et al., 2010; Winstock et al., 2017) - violates freedom of thought and cognitive liberty, and restricts access by researchers, clinicians, and individuals who wish to explore the ways in which psychoactive substances might facilitate healing and wellbeing (Krebs, 2015; Walsh, 2016).

Community-based research that is responsive to the needs and priorities of marginalized populations is fundamental to successfully identifying and targeting upstream drivers of risk, as is conducting more rigorous evaluation of suicidality interventions tailored to specific subpopulations of marginalized women (e.g., sex workers, women who use drugs, Indigenous women, and trans women) (Bauer, Scheim, Pyne, Travers, & Hammond, 2015; Clifford et al., 2013; Jeal et al., 2015; Roxburgh et al., 2006). A recent systematic review and meta-analysis of estimates of suicide attempts among adult sexual minorities offers some important insights into the need for more population health and community-based data to generate greater accuracy in estimates of health disparities among marginalized groups, and in turn, inform the prioritization of prevention policies and programs (Salway Hottes, Bogaert, Rhodes, Brennan, & Gesink, 2016). Further qualitative research would certainly facilitate a better understanding of the lived experiences of marginalized women and help to inform compassion-based policies and practices.

To address suicidality among Indigenous populations, there is a critical need for future research and intervention strategies led by Indigenous academics and communities that take a decolonizing perspective, with an emphasis on health promotion and cultural revitalization (Chandler & Lalonde, 2008; Dell et al., 2011). A significant structural problem remains in that the contrast between standard Western and Indigenous perspectives continues to hamper efforts

to advance research on suicide risk among Indigenous people. For example, a focus on individual-level determinants is somewhat at odds with a broader perspective that views life and experience within historical, social, environmental, and spiritual contexts (Chansonneuve, 2007; Dell et al., 2011; Wexler et al., 2015). Research indicates that positive cultural markers within Indigenous communities, such as self-governance, settled land claims, control over education and health care, and use of Indigenous language, correspond with significantly lower rates of suicide (Chandler & Lalonde, 2008; Hallett, Chandler, & Lalonde, 2007). To address mental health and substance use problems, a trauma-informed (SAMHSA, 2018) approach across the lifespan has been identified as necessary to sustain strong kinship with families and community and foster healing (First Nations Health Authority, British Columbia Ministry of Health, & Health Canada, 2013). Many Indigenous peoples in Canada, and elsewhere, recognize an interconnectedness of all things (e.g., people, animals, earth, nature), whereby the process of healing and recovery emphasizes a renewal of spirituality, connectedness, self-actualization, and the therapeutic power of the natural world (Chansonneuve, 2007; Dell et al., 2011).

Conventional, reductionist approaches to medicine may therefore represent a dismissal of key social, historical, and cultural contexts of healing – and perhaps also ontological and epistemological concepts – that are fundamental to understanding suicidality and other aspects of mental health and trajectories of drug use among Indigenous people (First Nations Health Authority et al., 2013; Wexler et al., 2015). The academic literature underscores the importance of culturally appropriate mental health and addiction services that are developed and implemented using participatory and community-based approaches to reflect the needs of Indigenous people within an integrative model of care (Benoit et al., 2003; Bingham et al., 2014;

Dell et al., 2011; Shannon et al., 2007). Indeed, recent community-led research utilizing Indigenous methodologies (i.e., talking circles) in Vancouver's Downtown Eastside described the ways in which healthcare inequalities among Indigenous people who use illicit drugs are perpetuated by systemic racism and discrimination, calling for traditional medicines and cultural practices to be integrated into mainstream healthcare services as paramount to addressing the evident gaps in health and access to care (Goodman et al., 2017).

### **5.2.2 Community-level intervention**

Given the fundamental role of social factors in driving risk of suicide, efforts to understand and prevent suicide must consider social disintegration and social solidarity as targets for community-level intervention (Durkheim, 1951). As evidenced in Chapter 2, building social cohesion among sex workers can be a powerfully protective strategy against suicidality after adjusting for potential confounding variables such as physical/sexual childhood abuse, partner violence, mental health disorders, and homelessness. The analysis described in Chapter 2 found that there were approximately 500 missed opportunities on which to intervene (486 reports of suicidality over follow-up). Given that social support and connectedness are crucial protective factors against suicidality, and are most impactful when implemented within and across multiple levels in society (NIMH, 2014), developing multi-pronged approaches that aim to increase social cohesion among marginalized women is essential to preventing further suicides. Prior research among sex workers globally has demonstrated that social cohesion is also associated with a number of health-related benefits, such as reduced social discrimination, increased condom use and ability to negotiate use with male sexual partners, and increased police protection (Argento et al., 2016; Duff et al., 2015; Fonner et al., 2014; Lippman et al., 2010).

Enhanced connectedness within communities has been identified as an effective protective strategy against suicide risk among other marginalized groups. For example, Bella Bella, an Indigenous community in British Columbia that once had the highest youth suicide rate in Canada, reversed the crisis through reconnecting youth to land, language, and traditional cultural practices; there has not been a suicide death in over 15 years and the graduation rate has reached 85%, up from 2% in the 1970s (Macdonald, 2016). Furthermore, mounting evidence points to social inequality in driving mental illness and problematic substance use, and reducing income gaps could result in significant improvements in health and wellbeing for the population as a whole. In societies where income is more equally distributed the prevalence of mental illness and problematic substance use is lower, and this relationship is likely mediated by the impact of better social connections (Ribeiro et al., 2017). The social environment has a powerful influence on mental health: inequality affects the nature of our social relationships and in turn, how we feel (Pickett & Wilkinson, 2019).

Global evidence highlights the success of community empowerment-based approaches in reducing sexual and drug-use related risks for HIV/STIs among sex workers (Argento et al., 2016; Deering et al., 2011; Kerrigan et al., 2015; Kim et al., 2015; Shannon et al., 2015), which can be extrapolated to interventions for suicidality. Community empowerment, a process by which sex workers take collective ownership of programs to achieve the most effective outcomes and address social and structural barriers to health and human rights, is a powerful factor in potentiating better health outcomes. The defining features of community empowerment among sex workers are that they are community-led, committed to ensuring health and human rights,

recognize sex work as work, and driven by the needs and priorities of sex workers themselves (Kerrigan et al., 2015). However, despite decades of grassroots organizing among sex workers in Canada, there is a dearth of data on community empowerment in high-income countries, with available global data largely restricted to lower- and middle-income settings, namely India and Brazil.

One example is the St. James Infirmery in San Francisco, a peer-based occupation health and safety clinic for sex workers of all genders that provides integrated mental and physical health care, as well as linkages to a number of support services and advocacy efforts (NSWP, 2012). In Canada, grassroots sex worker organizing led to one of the largest charter challenge cases at the Supreme Court (*Bedford*) that ultimately struck down criminalized sex work laws (Supreme Court of Canada, 2013). Sex worker-led mobile outreach has been independently linked with increased access to HIV testing and addiction treatment among women sex workers who use drugs in Vancouver (Deering et al., 2011). Community empowerment and access to safer/indoor work environments enables sex workers to connect with social and legal supports, health and harm reduction services, and increases capacity to mitigate violence (Anderson et al., 2015; Deering et al., 2014; Krüsi et al., 2012). The evidence base for community empowerment is building, yet needs to be strengthened both globally and locally. Increased support for community/peer-led interventions is urgently needed as they facilitate a deeper understanding of the challenges faced by marginalized women and target socio-structural barriers to health and human rights.

Broadly, community-level suicidality prevention and intervention strategies highlighted in the literature include means restriction (e.g., access to firearms), health professional education (e.g., management of depression), and school-based programs; however, the quality of evidence supporting these approaches is poor (Klonsky et al., 2016; World Health Organization, 2014; Zalsman et al., 2016), and there is an overall absence of research and evidence among marginalized populations. Public health programs must work to de-stigmatize mental health and substance use disorders, and increase awareness and education within professional training programs (e.g., physician residency programs, social work, nursing) around suicidality among marginalized women.

As demonstrated in this thesis, high prevalence and incidence of suicidality associated with mental health and substance use issues necessitates timely and effective access to health services (Center for Addiction and Mental Health, 2011; World Health Organization, 2014), and these services must be tailored to the unique and diverse needs of marginalized women. Unfortunately, most individuals (~60%) struggling with suicidality do not receive treatment (O'Connor & Nock, 2014), and the mental health system reaches only a small fraction of marginalized women given the substantial socio-structural barriers to accessing care, in addition to few evidence-based mental health or addiction interventions tailored to the needs of key sub-populations (Jeal et al., 2015; Shannon et al., 2015).

Strengthening positive connections with others can work to mitigate the negative effects of childhood trauma (NIMH, 2014). This study has shown that childhood trauma plays a primary role in influencing trajectories of injection drug use and risk of suicidality, and thus community-

driven services that are gender and culturally appropriate should integrate trauma-informed mental health support within substance use treatment and care (Armstrong & Samson, 2016; Haas et al., 2011; SAMHSA, 2018; Shannon et al., 2007). This includes targeting key psychosocial determinants of suicidality that extend beyond basic needs (e.g., affordable housing, education, protections against violence) to strengthening and re-building supportive social networks and connectedness to self, family/friends/community, and spirituality. The role of enhanced connectedness in reducing risk of suicidality within specific cultural and social contexts should be explored in further research (Benoit et al., 2003; Hendricks et al., 2015; Nock et al., 2008; Ross et al., 2016).

### **5.2.3 Individual-level and clinical interventions**

The literature and evidence on the effectiveness of cognitive behavioral therapies and pharmacological interventions have been hampered by publication bias, a lack of randomized clinical trials, and significant heterogeneity of outcome measures (NIMH, 2014; O'Connor & Nock, 2014; Zalsman et al., 2016). Due to ethical challenges and limitations to studying suicide and its proxies (i.e., ideation and attempts), there remains a paucity of evidence from controlled trials to support the efficacy of prevention interventions (Zalsman et al., 2016), and given that researchers have largely focused on examining suicidality outcomes (rather than suicide itself), findings may not be generalizable to understanding suicide or accurately evaluating treatment approaches (Klonsky et al., 2016). There remains an urgency to better understand pathways to suicide, with literature highlighting the need for innovative psychological and psychosocial treatments (O'Connor & Nock, 2014) and tailored intervention approaches for key marginalized populations (Klonsky et al., 2016; Zalsman et al., 2016).

Research findings on the use of selective serotonin reuptake inhibitors (SSRIs) are equivocal, and highlight the potential of SSRIs to potentiate a paradoxical increase in suicidality, particularly among youth (Hawton & van Heeringen, 2009; Nock et al., 2008). This has been recently corroborated by findings from a systematic review and meta-analysis where risk of suicidality doubled among children and adolescents receiving antidepressant medications (Sharma, Schow Guski, Freund, & Gotzsche, 2016). Evaluations of clinical interventions to prevent and treat suicidality underscore the complexity and challenges around identifying modifiable risk factors, and highlight the paucity of highly effective treatments (Klonsky et al., 2016; Nock et al., 2008). While treatment guidelines recommend treating suicidal patients for depression, the available data provide insufficient evidence to support that psychotherapy for depression can be considered an effective treatment in reducing suicidality (Cuijpers et al., 2013). Some evidence-based psychotherapeutic interventions warranting further research include: dialectical behavioral therapy (DBT), cognitive behavioral therapy (CBT), and interpersonal therapy (IP) (Center for Addiction and Mental Health, 2011; Klonsky et al., 2016). Clinical practice guidelines for adults with PTSD suggest the use of eye movement desensitization and reprocessing (EMDR) (Courtois et al., 2017), which may also benefit those with depression and/or suicidality, but further research is needed. Despite the availability of some potentially beneficial clinical interventions, marginalized women face considerable barriers to accessing even basic health and support services and the efficacy of such clinical approaches remains unclear, especially in the context of ongoing, structural and stigma-related drivers of poor health and access to care.

A vital aspect of managing and preventing suicidality is cultivating a positive and supportive therapeutic relationship (Center for Addiction and Mental Health, 2011; Klonsky et al., 2016; Tatarsky & Kellogg, 2010). An integrative, flexible, client-centered therapeutic approach that views mental health and substance use problems through the lens of a biopsychosocial framework has significantly greater potential to effectively support individuals through the healing process by enhancing self-reflection and self-management skills (Tatarsky & Kellogg, 2010).

In the context of psychedelic-assisted therapy, the therapeutic alliance is regarded as one of the most important factors influencing treatment outcomes (Garcia-Romeu & Richards, 2018; Tupper et al., 2015). The development of psychedelic therapist training programs, such as the first credentialed program housed at the California Institute of Integral Studies, is largely founded upon the framework of transpersonal psychology – a holistic approach that pays particular attention to the ways in which mystical, spiritual and other human experiences are associated with positive psychological outcomes, healing, and transformation (Phelps, 2017). This approach is especially pertinent given that the therapeutic alliance, as well as the mindset of the patient and the broader physical environment (‘set’ and ‘setting’) are powerful factors that codetermine how the experience and outcomes of psychedelic-assisted therapy unfold (Grof, 1973).

#### **5.2.4 Advancement of psychedelic research**

Emergent research and evidence lend considerable support to the therapeutic utility of psychedelics and encourage the advancement of more rigorous scientific research (Mithoefer et

al., 2016; Sessa, 2012; Walsh, 2016). Findings from recent clinical trials indicate that psychedelic-assisted psychotherapy has the potential to expand treatment options for those who experience refractory mental health and substance use problems when administered to carefully-screened individuals in structured clinical settings (Carhart-Harris et al., 2012; Haden et al., 2016; Mithoefer et al., 2016; Tupper et al., 2015). Further, the ceremonial use of psychedelics, especially for Indigenous peoples where this approach could be integrated within existing traditional/spiritual healing practices, may lead to greater therapeutic outcomes (Argento, Capler, et al., under review; Thomas et al., 2013). Much of the new wave of psychedelic research has relied on studies conducted among people of higher socio-economic status, and there remains a critical need to extend this work and potential therapeutic benefits to marginalized and underserved populations, with careful recognition of the unique needs of women who experience violence and trauma. As demonstrated in Chapter 4, non-medical use of psychedelics among marginalized women was associated with significantly reduced risk of suicidality, and the benefits have the potential to be maximized in safe and supportive therapeutic settings that carefully consider one's intention, preparation, set, setting, dose, and integration of the experience.

The current research has generated the strongest evidence to lend support to psychedelic-assisted therapy in ameliorating treatment-resistant depression (Carhart-Harris, Bolstridge, et al., 2016; Carhart-Harris, Roseman, et al., 2017; Palhano-Fontes et al., 2018), substance use disorders (Bogenschutz et al., 2015; Bogenschutz & Pommy, 2012; Fábregas et al., 2010; Johnson et al., 2014, 2017; Krebs & Johansen, 2012; Thomas et al., 2013), and end-of-life anxiety associated cancer and other life-threatening diseases (Gasser et al., 2014; Griffiths et al., 2016; Grob et al.,

2011; Ross et al., 2016). MDMA-assisted psychotherapy for PTSD has also demonstrated safety, efficacy, and long-term success in clinical trials, including among women with histories of sexual abuse, veterans, and first responders (Bouso et al., 2008; Mithoefer et al., 2018, 2013; Oehen & Schnyder, 2013). Future research should continue to examine the therapeutic applications of psychedelics for these and other novel targets such as suicidality, eating disorders, criminal recidivism, obsessive-compulsive disorders, gambling, cluster headaches, and inflammatory diseases (Garcia-Romeu & Richards, 2018). “Microdosing” – consuming regular, tiny fractions of psychedelic substances – is also gaining momentum as another promising area of novel research (Anderson et al., 2018; Fadiman, 2011; Johnstad, 2018; Polito & Stevenson, 2019; Prochazkova et al., 2018; Yanakieva et al., 2018), and warrants further investigation under controlled conditions. Microdosing studies are underway at Imperial College London and the University of Toronto (Imperial College London/Beckley Foundation, 2018; University of Toronto, 2018). The evidence regarding the therapeutic applications of psychedelics thus far indicates that the physiological and psychological mechanisms at play are deeply enmeshed. Alongside the clinical work, ethnographic analysis of people’s psychedelic experiences would serve to extend understanding of the efficacy of psychedelic-assisted interventions to the underlying psychosocial mechanisms.

There are significant clinical, legal and socio-political challenges to conducting psychedelic research. Given that most psychedelic drugs that have been studied for therapeutic efficacy are generic and cannot be patented, and that therapeutic doses in supportive clinical settings show benefit after only one to three administrations, the pharmaceutical industry has shown little interest in supporting this work. Funding to date has largely been obtained through private

donors and small, narrowly focused institutions, such as the Multidisciplinary Association for Psychedelic Studies (MAPS), the Beckley Foundation, and the Heffter Research Institute. Despite these barriers, researchers in scientific settings worldwide are pioneering investigations on the role of psychedelics in ameliorating intractable health issues primarily focused on treatment-resistant depression, anxiety, PTSD, and addictions, and many are urging the public and policy-makers to concentrate on evidence-based approaches rather than negative biases and pitfalls from the past around drug use (Sessa, 2015). Academic freedom and funding are necessary to further investigate the potential of psychedelic-assisted therapies in treating mental health and addiction issues.

The suppression of psychedelic research for decades in the latter part of the 20<sup>th</sup> century emboldened the ongoing systemic stigma that surrounds psychedelics and remains a significant barrier to advancing academic and scientific inquiry. Stemming in part from the ‘War on Drugs’, alongside the introduction of randomized double-blind controlled trials as the gold standard following the US Drug Amendments of 1962, which challenged the therapeutic methodologies used for psychedelics (Oram, 2014, 2016), the long pause in psychedelic research coincided with strict prohibitive regulations that leave psychedelics under the most stringent controls in most countries. The categorization and legal control of psychedelics can be traced back to the United Nations 1971 Convention on Psychotropic Substances (United Nations, 1971), whereby compounds such as MDMA, psilocybin and LSD were deemed to have no medical benefit (despite promising findings from studies in the 1950s and 60s) and thus research became extremely difficult, requiring approval from a government agency and hampered by misperceptions that psychedelics pose a significant danger to humans (Nutt, King, & Nichols,

2013). In practice, research with psychedelics almost completely ceased due to their Schedule I status, which was not based on the relative harms of these drugs, and may rather reflect socio-political objectives instead of health-related ones (Nutt et al., 2013), and perhaps a rejection of the questions psychedelics raised around the epistemology of scientific research and challenges to popular discourse (Tupper & Labate, 2014). Restricted access to these compounds among researchers is a significant and unfortunate outcome of such heavy controls placed on psychedelics, severely limiting what we might learn about their therapeutic applications (such as in addictions, depression, PTSD, and suicidality) as well as their potential harms and ways to mitigate adverse effects. Moving psychedelics from Schedule I to Schedule II would make them more accessible to researchers; however, there remains no agreed upon policy for re-scheduling drugs out of Schedule I, even if medical utility is discovered (Nutt et al., 2013). Given the importance of context – across psychological, environmental, and cultural domains (Carhart-Harris et al., 2018) – the success of advancing psychedelic research depends much on acceptance among scientists, clinicians, and policy-makers of a somewhat profound paradigm shift in treatment models and understandings of health and wellbeing.

### **5.3 Study strengths and limitations**

The AESHA study is built upon long-standing partnerships within the community since 2004 and is comprised of a diverse experiential team of both current and former sex workers represented across interviewer, outreach, nursing, and coordinator staff. AESHA has a Community Advisory Board of over 15 women’s health, sex work and HIV agencies, as well as representatives from health authorities and policy experts. As such, and given the excellent rapport established with marginalized women in Vancouver, the community-based nature of the

study is believed to have reduced the likelihood of social desirability and reporting biases common to this type of research. The close ties between the AESHA team and sex worker/community-led groups allowed for expert consultations to inform my research questions and provided valuable context for interpretation of the findings. The use of longitudinal analytic methods described in Chapters 2-4 is a major strength of the study, increasing statistical power and the validity of the results. Specifically, the use of Cox regression analyses in Chapters 3 and 4 were able to determine temporal relationships between correlates of CM injection initiation and psychedelic use and suicidality, respectively.

The limitations of each analysis are discussed in Chapters 2-4. Broadly, the study findings may not be fully generalizable to other populations of marginalized women or sex workers, and those working independently (e.g., escorts, online industry) may have been underrepresented.

However, community mapping of working areas and time–location sampling likely helped to mitigate this limitation, ensure a more representative sample, and minimize selection bias. Data for the analyses were largely based on self-report and involved highly stigmatized and sensitive topics (e.g., physical/sexual violence, childhood trauma, mental health, illicit drug use), which introduced the potential for social desirability and recall biases. However, interviews were conducted in safe and comfortable spaces by experienced interviewers with strong community rapport, which reduced the likelihood of this form of response bias. As previously mentioned, in Chapters 2 and 4, the measure for suicidality included both suicidal ideation and attempts, which could not be parsed out due to a lack of statistical power. This may have led to some misclassification given the difference in severity between suicidal thoughts and attempts.

Further, as completed suicides were not included as an outcome measure, there is potential for

survivorship bias. Previous research indicates that the surveillance of suicide is vulnerable to undercounting or underestimating, particularly among marginalized populations (Salway Hottes et al., 2016), and that even a small percentage of suicide deaths misclassified as other deaths (e.g., overdoses, undetermined deaths) can result in substantial underreporting of suicides (Bohnert et al., 2013). No completed suicides were observed during this study, according to linkages to vital statistics. Finally, outcome measures of interest in this study (i.e., suicidality, injection drug use) are influenced by complex individual, interpersonal and structural variables not all of which could be measured, thus associations uncovered cannot be determined as causal.

#### **5.4 Conclusion**

This thesis examined trajectories of drug use, violence, and suicidality among marginalized women, and highlighted the key role of upstream socio-structural factors in driving risk. This thesis further identified critical gaps in evidence and structural barriers to reducing suicidality, and explored novel avenues of intervention by reviewing the research and extending evidence on the therapeutic potential of psychedelics. Structural violence and the ongoing criminalization of sex work and drug use continue to reinforce stigma and discrimination, underscoring the urgent need for evidence-based law reform and integrated, trauma-informed mental health and addiction services tailored to marginalized women. Historical and interpersonal experiences of physical and sexual violence, trauma/PTSD, and depression substantially elevate risk of suicidality, and are interrelated with patterns of drug use.

Findings from this study suggest that increasing social cohesion can be an important and effective strategy to prevent suicidality. Further, psychedelic use was observed to significantly

reduce risk of suicidality in this study, and the ways in which psychedelics may modulate and influence primary risk factors (e.g., psychological distress, addiction, mood, spirituality, connectedness) is highly relevant to addressing an intractable public health problem for which conventional treatment approaches have shown limited success. Given the multilevel determinants of suicidality among marginalized women, the advancement of clinical interventions with psychedelics must be developed alongside community-led approaches that prioritize the unique needs of the population.

Suicidality among marginalized women is not only a critical public health concern, but also a matter of human rights. Research and intervention programs to prevent suicide have paid inadequate attention to this population, and there remains an urgency to improve understanding and prevent risk of suicide using a structural determinants framework. Ultimately, the success of interventions to improve mental health and wellbeing for marginalized women depends on the willingness of healthcare providers, researchers, governments, and policy-makers to acknowledge and target multilevel determinants of risk guided by a trauma-informed framework and careful evaluation and interpretation of the evidence. Substantial reform across legal, medical, and psychosocial domains is necessary to cultivate new understandings of health and innovative models of care that might unify science, spirituality, and psychopharmacology to foster the importance of connectedness within and amongst us.

## Bibliography

- Abad, N., Baack, B. N., O’Leary, A., Mizuno, Y., Herbst, J. H., & Lyles, C. M. (2015). A systematic review of HIV and STI behavior change interventions for female sex workers in the United States. *AIDS and Behavior, 19*, 1701–1719.
- Abel, G. M. (2014). A decade of decriminalization: Sex work ‘down under’ but not underground. *Criminology and Criminal Justice, 14*(5), 580–592.
- Abel, G. M., Fitzgerald, L. J., & Brunton, C. (2009). The impact of decriminalisation on the number of sex workers in New Zealand. *Journal of Social Policy, 38*(03), 515–531.
- Ahamad, K., DeBeck, K., Feng, C., Sakakibara, T., Kerr, T., & Wood, E. (2014). Gender influences on initiation of injecting drug use. *The American Journal of Drug and Alcohol Abuse, 40*(2), 151–156.
- Alexander, B. K. (2012). Addiction: The urgent need for a paradigm shift. *Substance Use and Misuse, 47*, 1475–1482.
- Alper, K., Lotsof, H. S., Frenken, G. M., Luciano, D. J., & Bastiaans, J. (1999). Treatment of acute opioid withdrawal with ibogaine. *The American Journal on Addictions, 8*(3), 234–242.
- Alper, K., Stajić, M., & Gill, J. R. (2012). Fatalities temporally associated with the ingestion of ibogaine. *Journal of Forensic Sciences, 57*(2), 398–412.
- Amnesty International. (2015). Sex Worker’s Rights are Human Rights. Retrieved from <https://www.amnesty.org/en/latest/news/2015/08/sex-workers-rights-are-human-rights/>
- Anderson, S., Jia, J. X., Liu, V., Chattier, J., Krüsi, A., Allan, S., ... Shannon, K. (2015). Violence prevention and municipal licensing of indoor sex work venues in the Greater Vancouver Area: Narratives of migrant sex workers, managers and business owners. *Culture, Health & Sexuality, 17*(7), 825–41.
- Anderson, T., Petranker, R., Dinh-Williams, L., Rosenbaum, D., Weissman, C., Hapke, E., ... Farb, N. (2018). Microdosing psychedelics: Personality, mental health, and creativity differences in microdosers. *Psychopharmacology, 69*(2), 283–291.
- Anisman, H., Du, L., Palkovits, M., Faludi, G., Kovacs, G. G., Szontagh-Kishazi, P., ... Poulter, M. O. (2008). Serotonin receptor subtype and p11 mRNA expression in stress-relevant brain regions of suicide and control subjects. *Journal of Psychiatry and Neuroscience, 33*(2), 131–141.

- Argento, E., Braschel, M., Walsh, Z., Socias, M., & Shannon, K. (2018). The moderating effect of psychedelics on the prospective relationship between prescription opioid use and suicide risk among marginalized women. *Journal of Psychopharmacology*, *32*(12), 1385–1391.
- Argento, E., Capler, R., Thomas, G., Lucas, P., & Tupper, K. W. (under review). Exploring ayahuasca-assisted therapy for addiction: A qualitative analysis of preliminary findings among an Indigenous community in Canada. *Drug and Alcohol Review*.
- Argento, E., Chettiar, J., Nguyen, P., Montaner, J., & Shannon, K. (2015). Prevalence and correlates of nonmedical prescription opioid use among a cohort of sex workers in Vancouver, Canada. *International Journal of Drug Policy*, *26*(1), 59–66.
- Argento, E., Duff, P., Bingham, B., Chapman, J., Nguyen, P., Strathdee, S. A., & Shannon, K. (2016). Social cohesion among sex workers and client condom refusal in a Canadian setting: Implications for structural and community-led interventions. *AIDS and Behavior*, *20*(6), 1275–1283.
- Argento, E., Goldenberg, S. M., Braschel, M., Machat, S., Strathdee, S. A., & Shannon, K. (under review.). The impact of end-demand legislation on sex workers' access to health and sex worker support services: A community-based prospective cohort study in Canada. *Journal of Urban Health*.
- Argento, E., Muldoon, K., Duff, P., Simo, A., Deering, K., & Shannon, K. (2014). High prevalence and partner correlates of physical and sexual violence by intimate partners among street and off-street sex workers. *PLOS ONE*, *9*(7), e102129.
- Argento, E., Shannon, K., Nguyen, P., Dobrer, S., Chettiar, J., & Deering, K. N. (2015). The role of dyad-level factors in shaping sexual and drug-related HIV/STI risks among sex workers with intimate partners. *Drug & Alcohol Dependence*, *157*, 166–173.
- Argento, E., Strathdee, S., Goldenberg, S., Braschel, M., Montaner, J., & Shannon, K. (2017). Violence, trauma and living with HIV: Longitudinal predictors of initiating crystal methamphetamine injection among sex workers. *Drug & Alcohol Dependence*, *175*, 198–204.
- Argento, E., Tupper, K. W., & Socias, M. (2019). The tripping point: The potential role of psychedelic-assisted therapy in the response to the opioid crisis. *International Journal of Drug Policy*, *66*, 80–81.
- Armstrong, G., & Samson, L. (2016). The imperative to integrate suicide prevention within community-based harm reduction programs for people who inject drugs: Informed by the situation in Delhi, India. *International Journal of Drug Policy*, *28*, 133–135.

- Bauer, G. R., Scheim, A. I., Pyne, J., Travers, R., & Hammond, R. (2015). Intervenable factors associated with suicide risk in transgender persons: a respondent driven sampling study in Ontario, Canada. *BMC Public Health, 15*(525).
- Benoit, C., Carroll, D., & Chaudhry, M. (2003). In search of a Healing Place: Aboriginal women in Vancouver's Downtown Eastside. *Social Science and Medicine, 56*(4), 821–833.
- Bingham, B., Leo, D., Zhang, R., Montaner, J., & Shannon, K. (2014). Generational sex work and HIV risk among Indigenous women in a street-based urban Canadian setting. *Culture, Health & Sexuality, 16*(4), 440-452.
- Boddiger, D. (2005). Metamphetamine use linked to rising HIV transmission. *Lancet, 365*(9466), 1217–1218.
- Bogenschutz, M. P., Forcehimes, A. A., Pommy, J. A., Wilcox, C. E., Barbosa, P. C. R., & Strassman, R. J. (2015). Psilocybin-assisted treatment for alcohol dependence: A proof-of-concept study. *Journal of Psychopharmacology, 29*(3), 289–299.
- Bogenschutz, M. P., & Johnson, M. W. (2016). Classic hallucinogens in the treatment of addictions. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 64*, 250–258.
- Bogenschutz, M. P., & Pommy, J. M. (2012). Therapeutic mechanisms of classic hallucinogens in the treatment of addictions: From indirect evidence to testable hypotheses. *Drug Testing and Analysis, 4*(1), 543–555.
- Bohnert, A. S. B., & Ilgen, M. A. (2019). Understanding links among opioid use, overdose, and suicide. *New England Journal of Medicine, 380*(1), 71–79.
- Bohnert, A. S. B., McCarthy, J. F., Ignacio, R. V., Ilgen, M. A., Eisenberg, A., & Blow, F. C. (2013). Misclassification of suicide deaths: Examining the psychiatric history of overdose decedents. *Injury Prevention, 19*(5), 326–330.
- Boire, R. G. (1999). On cognitive liberty (part 1). *Journal of Cognitive Liberties, 1*(1), 7–13.
- Bourdieu, P. (2001). *Masculine Domination*. Stanford, California: Stanford University Press.
- Bourgois, P., Prince, B., & Moss, A. (2004). The everyday violence of hepatitis C among young women who inject drugs in San Francisco. *Human Organization, 63*(3), 253–264.
- Bourgois, P., & Schonberg, J. (2009). *Righteous Dopefiend*. Berkeley: University of California Press.
- Bouso, J. C., Doblin, R., Farré, M., Alcazar, M., & Gomez-Jarabo, G. (2008). MDMA-assisted psychotherapy using low doses in a small sample of women with chronic posttraumatic stress disorder. *Journal of Psychoactive Drugs, 40*(3), 225–236.

- Bouso, J. C., Palhano-Fontes, F., Rodriguez-Fornells, A., Ribeiro, S., Sanches, R., Crippa, J. A. S., ... Riba, J. (2015). Long-term use of psychedelic drugs is associated with differences in brain structure and personality in humans. *European Neuropsychopharmacology*, *25*(4), 483–492.
- Bowleg, L. (2008). When Black + lesbian + woman  $\neq$  Black lesbian woman: The methodological challenges of qualitative and quantitative intersectionality research. *Sex Roles*, *59*(5–6), 312–325.
- Bowleg, L. (2012). The problem with the phrase women and minorities: Intersectionality-an important theoretical framework for public health. *American Journal of Public Health*, *102*(7), 1267–1273.
- Britton, P. C., & Conner, K. R. (2010). Suicide attempts within 12 months of treatment for substance use disorders. *Suicide and Life-Threatening Behavior*, *40*(1), 14–21.
- Brody, S., Potterat, J. J., Muth, S. Q., & Woodhouse, D. E. (2005). Psychiatric and characterological factors relevant to excess mortality in a long-term cohort of prostitute women. *Journal of Sex and Marital Therapy*, *31*(2), 97–112.
- Brown, T. K. (2013). Ibogaine in the treatment of substance dependence. *Current Drug Abuse Reviews*, *6*(1), 3–16.
- Brown, T. K., & Alper, K. (2017). Treatment of opioid use disorder with ibogaine: detoxification and drug use outcomes. *The American Journal of Drug and Alcohol Abuse*, 1–13.
- Bruckert, C., & Hannem, S. (2013). Rethinking the prostitution debates: Transcending structural stigma in systemic responses to sex work. *Canadian Journal of Law and Society*, *28*(1), 43–63.
- Carhart-Harris, R. L., Bolstridge, M., Rucker, J., Day, C. M. J., Erritzoe, D., Kaelen, M., ... Nutt, D. J. (2016). Psilocybin with psychological support for treatment-resistant depression: An open-label feasibility study. *The Lancet Psychiatry*, *3*(7), 619–627.
- Carhart-Harris, R. L., Erritzoe, D., Haijen, E., Kaelen, M., & Watts, R. (2017). Psychedelics and connectedness. *Psychopharmacology*, 1–4.
- Carhart-Harris, R. L., Erritzoe, D., Williams, T., Stone, J. M., Reed, L. J., Colasanti, A., ... Nutt, D. J. (2012). Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(6), 2138–43.
- Carhart-Harris, R. L., & Goodwin, G. M. (2017). The therapeutic potential of psychedelic drugs: Past, present and future. *Neuropsychopharmacology*, 1–9.

- Carhart-Harris, R. L., Kaelen, M., Bolstridge, M., Williams, T. M., Williams, L., Underwood, R., ... Nutt, D. J. (2016). The paradoxical psychological effects of lysergic acid diethylamide (LSD). *Psychological Medicine*, (1), 1–12.
- Carhart-Harris, R. L., Leech, R., Hellyer, P. J., Shanahan, M., Feilding, A., Tagliazucchi, E., ... Nutt, D. J. (2014). The entropic brain: A theory of conscious states informed by neuroimaging research with psychedelic drugs. *Frontiers in Human Neuroscience*, 8(20).
- Carhart-Harris, R. L., Leech, R., Williams, T. M., Erritzoe, D., Abbasi, N., Bargiotas, T., ... Nutt, D. J. (2012). Implications for psychedelic-assisted psychotherapy: Functional magnetic resonance imaging study with psilocybin. *British Journal of Psychiatry*, 200(3), 238–244.
- Carhart-Harris, R. L., Roseman, L., Bolstridge, M., Demetriou, L., Pannekoek, J. N., Wall, M. B., ... Nutt, D. J. (2017). Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms. *Scientific Reports*, 7(13187), 1–11.
- Carhart-Harris, R. L., Roseman, L., Haijen, E., Erritzoe, D., Watts, R., Branchi, I., & Kaelen, M. (2018). Psychedelics and the essential importance of context. *Journal of Psychopharmacology*, 32(7), 725–731.
- Carlyle, M., Stevens, T., Fawaz, L., Marsh, B., Kosmider, S., & Morgan, C. J. (2019). Greater empathy in MDMA users. *Journal of Psychopharmacology*, 1–10.
- Cavnar, C. (2014). The effects of ayahuasca ritual participation on gay and lesbian identity. *Journal of Psychoactive Drugs*, 46(3), 252–260.
- Center for Addiction and Mental Health. (2011). *Suicide Prevention and Assessment Handbook*. Toronto, ON. Retrieved from papers3://publication/uuid/E20B95DF-C102-4001-B984-FBB3031ACCB1
- Chandler, M. J., & Lalonde, C. E. (2008). Cultural continuity as a moderator of suicide risk among Canada's First Nations. In L. Kirmayer & G. Valaskakis (Eds.), *Healing Traditions: The Mental Health of Aboriginal Peoples in Canada* (pp. 221–248). Vancouver, BC: UBC Press.
- Chansonneuve, D. (2007). *Addictive Behaviours Among Aboriginal People in Canada. The Aboriginal Healing Foundation Research Series*. Ottawa, ON. Retrieved from <http://www.ahf.ca/downloads/addictive-behaviours.pdf>
- Chettiar, J., Shannon, K., Wood, E., Zhang, R., & Kerr, T. (2010). Survival sex work involvement among street-involved youth who use drugs in a Canadian setting. *Journal of Public Health*, 32(3), 322–327.

- Clifford, A. C., Doran, C. M., & Tsey, K. (2013). A systematic review of suicide prevention interventions targeting indigenous peoples in Australia, United States, Canada and New Zealand. *BMC Public Health, 13*(463).
- Cloutier-Gill, L., Wood, E., Millar, T., Ferris, C., & Socias, M. (2016). Remission of severe opioid use disorder with ibogaine: A case report. *Journal of Psychoactive Drugs, 48*(3), 214–217.
- Cohen, J. B., Greenberg, R., Uri, J., Halpin, M., & Zweben, J. E. (2007). Women with methamphetamine dependence: Research on etiology and treatment. *Journal of Psychoactive Drugs, 39*(sup4), 347–351.
- Corrigan, P. (2004). How stigma interferes with mental health care. *American Psychologist, 59*(7), 614–625.
- Courtois, C. A., Sonis, J., Fairbank, J. A., Friedman, M., Jones, R., Roberts, J., & Schulz, P. (2017). *Clinical Practice Guideline for the Treatment of Posttraumatic Stress Disorder (PTSD) in adults*. American Psychological Association. Washington, DC. Retrieved from <https://www.apa.org/about/offices/directorates/guidelines/ptsd.pdf>
- Couture, M.-C., Evans, J. L., Sothy, N. S., Stein, E. S., Sichan, K., Maher, L., & Page, K. (2012). Correlates of amphetamine-type stimulant use and associations with HIV-related risks among young women engaged in sex work in Phnom Penh, Cambodia. *Drug and Alcohol Dependence, 120*(1–3), 119–126.
- Csete, J., & Cohen, J. (2010). Health benefits of legal services for criminalized populations: The case of people who use drugs, sex workers and sexual and gender minorities. *Journal of Law, Medicine and Ethics, 38*(4), 816–831.
- Cuijpers, P., De Beurs, D. P., Van Spijker, B. A. J., Berking, M., Andersson, G., & Kerkhof, A. J. F. M. (2013). The effects of psychotherapy for adult depression on suicidality and hopelessness: A systematic review and meta-analysis. *Journal of Affective Disorders, 144*(3), 183–190.
- Culhane, D. (2003). Their spirits live within us: Aboriginal women in Downtown Eastside Vancouver emerging into visibility. *American Indian Quarterly, 27*(3/4), 593–606.
- Damon, W., McNeil, R., Milloy, M.-J., Nosova, E., Kerr, T., & Hayashi, K. (2018). Residential eviction predicts initiation of or relapse into crystal methamphetamine use among people who inject drugs: a prospective cohort study. *Journal of Public Health, 1–10*.
- Dasgupta, N., Beletsky, L., & Ciccarone, D. (2018). Opioid crisis: No easy fix to its social and economic determinants. *American Journal of Public Health, 108*(2), 182–186.

- Decker, M. R., Crago, A. L., Chu, S. K. H., Sherman, S. G., Seshu, M. S., Buthelezi, K., ... Beyrer, C. (2015). Human rights violations against sex workers: burden and effect on HIV. *The Lancet*, 385(9963), 186–199.
- Deering, K. N., Amin, A., Shoveller, J. A., Nesbitt, A., Garcia-Moreno, C., Duff, P., ... Shannon, K. (2014). A systematic review of the global magnitude and drivers of violence against sex workers. *American Journal of Public Health*, 104(5), e42–e54.
- Deering, K. N., Kerr, T., Tyndall, M. W., Montaner, J. S. G., Gibson, K., Irons, L., & Shannon, K. (2011). A peer-led mobile outreach program and increased utilization of detoxification and residential drug treatment among female sex workers who use drugs in a Canadian setting. *Drug and Alcohol Dependence*, 113(1), 46–54.
- Degenhardt, L., Mathers, B., Guarinieri, M., Panda, S., Phillips, B., Strathdee, S. a., ... Howard, J. (2010). Meth/amphetamine use and associated HIV: Implications for global policy and public health. *International Journal of Drug Policy*, 21(5), 347–358.
- Dell, C. A., Seguin, M., Hopkins, C., Tempier, R., Mehl-Madrona, L., Dell, D., ... Mosier, K. (2011). From benzos to berries: Treatment offered at an aboriginal youth solvent abuse treatment centre relays the importance of culture. *Canadian Journal of Psychiatry*, 56(2), 75–83.
- Devries, K., Watts, C., Yoshihama, M., Kiss, L., Schraiber, L. B., Deyessa, N., ... Garcia-Moreno, C. (2011). Violence against women is strongly associated with suicide attempts: Evidence from the WHO multi-country study on women's health and domestic violence against women. *Social Science and Medicine*, 73(1), 79–86.
- dos Santos, R. G. (2013). Safety and side effects of ayahuasca in humans - An overview focusing on developmental toxicology. *Journal of Psychoactive Drugs*, 45(1), 68–78.
- dos Santos, R. G., Bouso, J. C., & Hallak, J. E. C. (2017). Ayahuasca, dimethyltryptamine, and psychosis: A systematic review of human studies. *Therapeutic Advances in Psychopharmacology*, 7(4), 141–157.
- dos Santos, R. G., Osorio, F. L., Crippa, J. A. S., Riba, J., Zuardi, A. W., & Hallak, J. E. C. (2016). 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. *Therapeutic Advances in Psychopharmacology*, 6(3), 193–213.
- Duff, P., Shoveller, J. A., Dobrer, S., Ogilvie, G., Montaner, J., Chettiar, J., & Shannon, K. (2015). The relationship between social, policy and physical venue features and social cohesion on condom use for pregnancy prevention among sex workers: A safer indoor work environment scale. *Journal of Epidemiology & Community Health*, 1–7.

- Duff, P., Tyndall, M. W., Buxton, J., Zhang, R., Kerr, T., & Shannon, K. (2013). Sex-for-crack exchanges: associations with risky sexual and drug use niches in an urban Canadian city. *Harm Reduction Journal, 10*(29).
- Duncan, D. T., & Hatzenbuehler, M. L. (2014). Lesbian, gay, bisexual, and transgender hate crimes and suicidality among a population-based sample of sexual-minority adolescents in Boston. *American Journal of Public Health, 104*(2), 272–278.
- Durkheim, E. (1951). *Suicide: A study in sociology*. New York: Free Press.
- Dyck, E. (2015). LSD: A new treatment emerging from the past. *Canadian Medical Association Journal, 187*(14), 1079–1080.
- El-Bassel, N., Gilbert, L., Wu, E., Go, H., & Hill, J. (2005). HIV and intimate partner violence among methadone-maintained women in New York City. *Social Science & Medicine, 61*(1), 171–183.
- Espinoza, Y. (2014). Sexual healing with Amazonian plant teachers: A heuristic inquiry of women's spiritual–erotic awakenings. *Sexual and Relationship Therapy, 29*(1), 109–120.
- Fábregas, J. M., González, D., Fondevila, S., Cutchet, M., Fernández, X., Barbosa, P. C. R., ... Bouso, J. C. (2010). Assessment of addiction severity among ritual users of ayahuasca. *Drug and Alcohol Dependence, 111*(3), 257–261.
- Fadiman, J. (2011). *The Psychedelic Explorer's Guide: Safe, Therapeutic, and Sacred Journeys*. Rochester, VA: Park Street Press.
- Fairbairn, N., Kerr, T., Buxton, J. A., Li, K., Montaner, J. S., & Wood, E. (2007). Increasing use and associated harms of crystal methamphetamine injection in a Canadian setting. *Drug and Alcohol Dependence, 88*(2–3), 313–316.
- Farmer, P. E. (1996). On suffering and structural violence: A view from below. *Daedalus, 125*(1), 261–283.
- Farmer, P. E., Nizeye, B., Stulac, S., & Keshavjee, S. (2006). Structural violence and clinical medicine. *PLoS Medicine, 3*(10), 1686–1691.
- Fast, D., Kerr, T., Wood, E., & Small, W. (2014). The multiple truths about crystal meth among young people entrenched in an urban drug scene: A longitudinal ethnographic investigation. *Social Science and Medicine, 110*, 41–48.
- Feng, C., Debeck, K., Kerr, T., Mathias, S., Montaner, J., & Wood, E. (2013). Homelessness independently predicts injection drug use initiation among street-involved youth in a Canadian setting. *Journal of Adolescent Health, 52*(4), 499–501.

- Fernández-Montalvo, J., López-Goñi, J. J., Arteaga, A., & Haro, B. (2018). Suicidal ideation and attempts among patients with lifetime physical and/or sexual abuse in treatment for substance use disorders. *Addiction Research and Theory*, 1–6.
- Firestone Cruz, M., Mantsios, A., Ramos, R., Case, P., Brouwer, K. C., Ramos, M. E., ... Strathdee, S. A. (2007). A qualitative exploration of gender in the context of injection drug use in two US-Mexico border cities. *AIDS and Behavior*, 11(2), 253–262.
- First Nations Health Authority, British Columbia Ministry of Health, & Health Canada. (2013). *A Path Forward: BC First Nations and Aboriginal People's Mental Wellness and Substance Use - 10 Year Plan*. Retrieved from [http://www.fnhc.ca/pdf/FNHA\\_MWSU.pdf](http://www.fnhc.ca/pdf/FNHA_MWSU.pdf)
- Fischer, B., & Argento, E. (2012). Prescription opioid related misuse, harms, diversion and interventions in Canada: a review. *Pain Physician*, 15, ES191-203.
- Fischer, B., & Rehm, J. (2017). Revisiting the 'paradigm shift' in opioid use: Developments and implications 10 years later. *Drug and Alcohol Review*, 37(1), S199-202.
- Fonner, V. A., Kerrigan, D., Mnisi, Z., Ketende, S., Kennedy, C. E., & Baral, S. (2014). Social cohesion, social participation, and HIV related risk among female sex workers in Swaziland. *PLOS ONE*, 9(1), e87527.
- Gable, R. S. (2007). Risk assessment of ritual use of oral dimethyltryptamine (DMT) and harmala alkaloids. *Addiction*, 102(1), 24–34.
- Garcia-Romeu, A., Griffiths, R. R., & Johnson, M. W. (2014). Psilocybin-occasioned mystical experiences in the treatment of tobacco addiction. *Current Drug Abuse Reviews*, 7(3), 157–164.
- Garcia-Romeu, A., & Richards, W. A. (2018). Current perspectives on psychedelic therapy: use of serotonergic hallucinogens in clinical interventions. *International Review of Psychiatry*, 1–26.
- Gasser, P., Holstein, D., Michel, Y., Doblin, R., Yazar-Klosinski, B., Passie, T., & Brenneisen, R. (2014). Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. *The Journal of Nervous and Mental Disease*, 202(7), 513–20.
- Gilchrist, G., Gruer, L., & Atkinson, J. (2005). Comparison of drug use and psychiatric morbidity between prostitute and non-prostitute female drug users in Glasgow, Scotland. *Addictive Behaviors*, 30(5), 1019–1023.
- Glasner-Edwards, S., Mooney, L. J., Ang, A., Hillhouse, M., & Rawson, R. (2013). Does Posttraumatic Stress Disorder affect post-treatment methamphetamine use? *Journal of Dual Diagnosis*, 9(2), 123–128.

- Global Commission on HIV and the Law. (2012). *Risks, Rights & Health*. New York. Retrieved from <http://www.hivlawcommission.org/>
- Goodman, A., Fleming, K., Markwick, N., Morrison, T., Lagimodiere, L., & Kerr, T. (2017). “They treated me like crap and I know it was because I was Native”: The healthcare experiences of Aboriginal peoples living in Vancouver’s inner city. *Social Science and Medicine*, 178, 87–94.
- Government of Canada. (1982). Canadian Charter of Rights and Freedoms.
- Government of Canada Department of Justice. (2015). *Technical Paper: Bill C-36, Protection of Communities and Exploited Persons Act*. Ottawa, ON. Retrieved from <http://www.justice.gc.ca/eng/rp-pr/other-autre/protect/p1.html>
- Gracey, M., & King, M. (2009). Indigenous health part 1: determinants and disease patterns. *The Lancet*, 374(9683), 65–75.
- Griffiths, R. R., Johnson, M. W., Carducci, M. A., Umbricht, A., Richards, W. A., Richards, B. D., ... Klinedinst, M. A. (2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *Journal of Psychopharmacology*, 30(12), 1181–1197.
- Griffiths, R. R., Johnson, M. W., Richards, W. A., Richards, B. D., McCann, U., & Jesse, R. (2011). Psilocybin occasioned mystical-type experiences: Immediate and persisting dose-related effects. *Psychopharmacology*, 218(4), 649–665.
- Griffiths, R. R., Richards, W. A., McCann, U., & Jesse, R. (2006). Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology*, 187(3), 268–283.
- Grob, C. S., Danforth, A. L., Chopra, G. S., Hagerty, M., McKay, C. R., Halberstadt, A. L., & Greer, G. R. (2011). Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Archives of General Psychiatry*, 68(1), 71–78.
- Grob, C. S., McKenna, D. J., Callaway, J. C., Brito, G. S., Neves, E. S., Oberlaender, G., ... Boone, K. B. (1996). Human psychopharmacology of hoasca, a plant hallucinogen used in ritual context in Brazil. *The Journal of Nervous and Mental Disease*, 184(2), 86–94.
- Grof, S. (1973). Theoretical and empirical basis of transpersonal psychology and psychotherapy: Observations from LSD research. *Journal of Transpersonal Psychology*, 5(1), 15–53.
- Grof, S. (2007). New perspectives in understanding and treatment of emotional disorders. In M. Winkelman & T. Roberts (Eds.), *Psychedelic Medicine: New Evidence for Hallucinogenic Substances as Treatments* (Volume 2, pp. 255–283). London: Praeger.

- Gu, J., Lau, J. T. F., Li, M., Li, H., Gao, Q., Feng, X., ... Hao, Y. (2014). Socio-ecological factors associated with depression, suicidal ideation and suicidal attempt among female injection drug users who are sex workers in China. *Drug and Alcohol Dependence, 144*, 102–110.
- Guillen, A. I., Panadero, S., Rivas, E., & Vazquez, J. J. (2015). Suicide attempts and stressful life events among female victims of intimate partner violence living in poverty in Nicaragua. *Scandinavian Journal of Psychology, 56*(3), 349–356.
- Haas, A. P., Eliason, M., Mays, V. M., Mathy, R. M., Cochran, S. D., D'Augelli, A. R., ... Clayton, P. J. (2011). Suicide and suicide risk in lesbian, gay, bisexual, and transgender populations: Review and recommendations. *J Homosex, 58*(1), 10–51.
- Haden, M., Emerson, B., & Tupper, K. W. (2016). A public-health-based vision for the management and regulation of psychedelics. *Journal of Psychoactive Drugs, 48*(4), 243–252.
- Hadland, S. E., Marshall, B. D. L., Kerr, T., Qi, J., Montaner, J. S., & Wood, E. (2012). Suicide and history of childhood trauma among street youth. *Journal of Affective Disorders, 136*(3), 377–380.
- Hallett, D., Chandler, M. J., & Lalonde, C. E. (2007). Aboriginal language knowledge and youth suicide. *Cognitive Development, 22*(3), 392–399.
- Hartogsohn, I. (2018). The meaning-enhancing properties of psychedelics and their mediator role in psychedelic therapy, spirituality, and creativity. *Frontiers in Neuroscience, 12*(129), 1–5.
- Hassan, A. N., Foll, B. Le, Imtiaz, S., & Rehm, J. (2017). The effect of post-traumatic stress disorder on the risk of developing prescription opioid use disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions III. *Drug and Alcohol Dependence, 179*, 260–266.
- Hawton, K., & van Heeringen, K. (2009). Suicide. *The Lancet, 373*(9672), 1372–1381.
- Heise, C. W., & Brooks, D. E. (2017). Ayahuasca exposure: Descriptive analysis of calls to US Poison Control Centers from 2005 to 2015. *Journal of Medical Toxicology, 13*(3), 245–248.
- Hendricks, P. (2018). Awe: a putative mechanism underlying the effects of classic psychedelic-assisted psychotherapy. *International Review of Psychiatry, 30*(4), 1–12.
- Hendricks, P., Clark, C., Johnson, M. W., Fontaine, K., & Cropsey, K. (2014). Hallucinogen use predicts reduced recidivism among substance-involved offenders under community corrections supervision. *Journal of Psychopharmacology, 28*(1), 62–66.

- Hendricks, P., Thorne, C. B., Clark, C. B., Coombs, D. W., & Johnson, M. W. (2015). Classic psychedelic use is associated with reduced psychological distress and suicidality in the United States adult population. *Journal of Psychopharmacology*, *29*(3), 280–288.
- Ho, H. T., Le, G. M., & Dinh, T. T. (2013). Female sex workers who use amphetamine-type stimulants (ATS) in three cities of Vietnam: use and sexual risks related to HIV/AIDS. *Global Public Health*, *8*(5), 552–569.
- Hong, Y., Fang, X., Li, X., Liu, Y., Li, M., & Tai-Seale, T. (2010). Self-perceived stigma, depressive symptoms, and suicidal behaviors among female sex workers in China. *Journal of Transcultural Nursing*, *21*(1), 29–34.
- Hong, Y., Zhang, C., Li, X., Liu, W., & Zhou, Y. (2013). Partner violence and psychosocial distress among female sex workers in China. *PLOS ONE*, *8*(4), e62290.
- Hughes, C., & Stevens, A. (2010). What can we learn from the Portuguese decriminalization of illicit drugs? *The British Journal of Criminology*, *50*(6), 999–1022.
- Imperial College London/Beckley Foundation. (2018). LSD Microdosing Research. Retrieved from <http://beckleyfoundation.org/microdosing-bsd/>
- Jeal, N., Macleod, J., Turner, K., & Salisbury, C. (2015). Systematic review of interventions to reduce illicit drug use in female drug-dependent street sex workers. *BMJ Open*, *5*(11), e009238–e009238.
- Johansen, P.-Ø., & Krebs, T. S. (2015). Psychedelics not linked to mental health problems or suicidal behavior: A population study. *Journal of Psychopharmacology*, *29*(3), 270–279.
- Johnson, M. W., Garcia-Romeu, A., Cosimano, M. P., & Griffiths, R. R. (2014). Pilot study of the 5-HT<sub>2A</sub>R agonist psilocybin in the treatment of tobacco addiction. *Journal of Psychopharmacology*, *28*(11), 983–92.
- Johnson, M. W., Garcia-Romeu, A., & Griffiths, R. R. (2017). Long-term follow-up of psilocybin-facilitated smoking cessation. *American Journal of Drug and Alcohol Abuse*, *43*(1), 55–60.
- Johnson, M. W., Richards, W. A., & Griffiths, R. R. (2008). Human hallucinogen research: Guidelines for safety. *Journal of Psychopharmacology*, *22*(6), 603–620.
- Johnstad, P. G. (2018). Powerful substances in tiny amounts: An interview study of psychedelic microdosing. *Nordic Studies on Alcohol and Drugs*, *35*(1), 39–51.
- Jung, M. (2013). Associations of physical and sexual health with suicide attempts among female sex workers in South Korea. *Sexuality and Disability*, *31*(3), 275–286.

- Kerr, T., Shannon, K., Ti, L., Strathdee, S., Hayashi, K., Nguyen, P., ... Wood, E. (2016). Sex work and HIV incidence among people who inject drugs. *AIDS*, *30*, 627–634.
- Kerr, T., Stoltz, J., Marshall, B. D. L., Lai, C., Strathdee, S. A., & Wood, E. (2009). Childhood trauma and injection drug use among high-risk youth. *Journal of Adolescent Health*, *45*(3), 300–302.
- Kerrigan, D., Kennedy, C. E., Morgan-Thomas, R., Reza-Paul, S., Mwangi, P., Win, K. T., ... Butler, J. (2015). A community empowerment approach to the HIV response among sex workers: Effectiveness, challenges, and considerations for implementation and scale-up. *The Lancet*, *385*(9963), 172–185.
- Kerrigan, D., Telles, P., Torres, H., Overs, C., & Castle, C. (2008). Community development and HIV/STI-related vulnerability among female sex workers in Rio de Janeiro, Brazil. *Health Education Research*, *23*(1), 137–145.
- Kim, S. R., Goldenberg, S. M., Duff, P., Nguyen, P., Gibson, K., & Shannon, K. (2015). Uptake of a women-only, sex-work-specific drop-in center and links with sexual and reproductive health care for sex workers. *International Journal of Gynecology and Obstetrics*, *128*(3), 201–205.
- Kimerling, R., Alvarez, J., Pavao, J., Kaminski, A., & Baumrind, N. (2007). Epidemiology and consequences of women's revictimization. *Women's Health Issues*, *17*(2), 101–106.
- Klonsky, E. D., May, A. M., & Saffer, B. Y. (2016). Suicide, suicide attempts, and suicidal ideation. *Annual Review of Clinical Psychology*, *12*(1), 307–330.
- Kraehenmann, R., Preller, K. H., Scheidegger, M., Pokorny, T., Bosch, O. G., Seifritz, E., & Vollenweider, F. X. (2015). Psilocybin-induced decrease in amygdala reactivity correlates with enhanced positive mood in healthy volunteers. *Biological Psychiatry*, *78*(8), 572–581.
- Krebs, T. S. (2015). Protecting the human rights of people who use psychedelics. *The Lancet Psychiatry*, *2*(4), 294–295.
- Krebs, T. S., & Johansen, P.-Ø. (2012). Lysergic acid diethylamide (LSD) for alcoholism: meta-analysis of randomized controlled trials. *Journal of Psychopharmacology*, *26*(7), 994–1002.
- Krebs, T. S., & Johansen, P.-Ø. (2013). Psychedelics and mental health: a population study. *PLOS ONE*, *8*(8), e63972.
- Krupitsky, E., Burakov, A., Romanova, T., Dunaevsky, I., Strassman, R., & Grinenko, A. (2002). Ketamine psychotherapy for heroin addiction: Immediate effects and two-year follow-up. *J Subst Abuse Treat*, *23*(4), 273–283.

- Krüsi, A., Chettiar, J., Ridgway, A., Abbott, J., Strathdee, S. A., & Shannon, K. (2012). Negotiating safety and sexual risk reduction with clients in unsanctioned safer indoor sex work environments: a qualitative study. *American Journal of Public Health, 102*(6), 1154–1159.
- Krüsi, A., Pacey, K., Bird, L., Taylor, C., Chettiar, J., Allan, S., ... Shannon, K. (2014). Criminalisation of clients: reproducing vulnerabilities for violence and poor health among street-based sex workers in Canada - A qualitative study. *BMJ Open, 4*(e005191).
- Lafrance, A., Loizaga-Velder, A., Fletcher, J., Renelli, M., Files, N., & Tupper, K. W. (2017). Nourishing the spirit: Exploratory research on ayahuasca experiences along the continuum of recovery from eating disorders. *Journal of Psychoactive Drugs, 45*(5), 427–435.
- Lau, J. T. F., Tsui, H. Y., Ho, S. P. Y., Wong, E., & Yang, X. (2010). Prevalence of psychological problems and relationships with condom use and HIV prevention behaviors among Chinese female sex workers in Hong Kong. *AIDS Care, 22*(6), 659–668.
- Lazarus, L., Deering, K. N., Nabess, R., Gibson, K., Tyndall, M. W., & Shannon, K. (2012). Occupational stigma as a primary barrier to health care for street-based sex workers in Canada. *Culture, Health & Sexuality, 14*(2), 139–150.
- Le Bail, H., & Giametta, C. (2018). *What do Sex Workers Think About the French Prostitution Act? A Study on the Impact of the Law from 13 April 2016 Against the “Prostitution System” in France*. Paris. Retrieved from <https://www.medecinsdumonde.org/sites/default/files/ENGLISH-Synthèse-Rapport-prostitution-BD.PDF>
- Lippman, S., Donini, A., Díaz, J., Chinaglia, M., Reingold, A., & Kerrigan, D. (2010). Social-environmental factors and protective sexual behavior among sex workers: the Encontros intervention in Brazil. *American Journal of Public Health, 100*(S1), S216–S223.
- Lorvick, J., Martinez, A., Gee, L., & Kral, A. H. (2006). Sexual and injection risk among women who inject methamphetamine in San Francisco. *Journal of Urban Health, 83*(3), 497–505.
- Ly, C., Greb, A. C., Cameron, L. P., Wong, J. M., Barragan, E. V., Wilson, P. C., ... Olson, D. E. (2018). Psychedelics promote structural and functional neural plasticity. *Cell Reports, 23*(11), 3170–3182.
- Lyons, T., Krüsi, A., Pierre, L., Kerr, T., Small, W., & Shannon, K. (2015). Negotiating violence in the context of transphobia and criminalization: The experiences of trans sex workers in Vancouver, Canada. *Qualitative Health Research, 1*–9.
- Macdonald, N. (2016). Bella Bella, BC: The town that solved suicide. *Maclean's*. Retrieved from <https://www.macleans.ca/news/bella-bella-the-town-that-solved-suicide/>

- Maher, L. (1997). *Sexed work: Gender, race and resistance in a Brooklyn drug market (Clarendon Studies in Criminology)*. Oxford: Clarendon Press.
- Maher, L., Phlong, P., Mooney-Somers, J., Keo, S., Stein, E., Couture, M. C., & Page, K. (2011). Amphetamine-type stimulant use and HIV/STI risk behaviour among young female sex workers in Phnom Penh, Cambodia. *International Journal of Drug Policy*, 22(3), 203–209.
- Malcolm, B. J., Polanco, M., & Barsuglia, J. P. (2018). Changes in withdrawal and craving scores in participants undergoing opioid detoxification utilizing ibogaine. *Journal of Psychoactive Drugs*, 1–10.
- Marsh, I. (2010). *Suicide: Foucault, history and truth*. New York: Cambridge University Press.
- Marshall, B. D. L., & Werb, D. (2010). Health outcomes associated with methamphetamine use among young people: A systematic review. *Addiction*, 105(6), 991–1002.
- Mash, D. C., Duque, L., Page, B., & Allen-Ferdinand, K. (2018). Ibogaine detoxification transitions opioid and cocaine abusers between dependence and abstinence: Clinical observations and treatment outcomes. *Frontiers in Pharmacology*, 9(529).
- Mash, D. C., Kovera, C. a, Pablo, J., Tyndale, R., Ervin, F. R., Kamlet, J. D., & Hearn, W. L. (2001). Ibogaine in the treatment of heroin withdrawal. In K. Apler & G. Cordell (Eds.), *The Alkaloids* (Vol. 56, pp. 155–171). New York: Academic Press.
- Maté, G. (2009). *In the Realm of Hungry Ghosts: Close Encounters with Addiction*. Toronto: Vintage Canada.
- Mathers, B. M., Degenhardt, L., Phillips, B., Wiessing, L., Hickman, M., Strathdee, S. A., ... Mattick, R. P. (2008). Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. *The Lancet*, 372(9651), 1733–1745.
- McKenna, D., & Riba, J. (2015). New world tryptamine hallucinogens and the neuroscience of ayahuasca. *Current Topics in Behavioral Neurosciences*.
- Meade, C. S., Watt, M. H., Sikkema, K. J., Deng, L. X., Ranby, K. W., Skinner, D., ... Kalichmann, S. C. (2012). Methamphetamine use is associated with childhood sexual abuse and HIV sexual risk behaviors among patrons of alcohol-serving venues in Cape Town, South Africa. *Drug and Alcohol Dependence*, 126(1–2), 232–239.
- Milloy, M.-J., Kerr, T., Buxton, J., Montaner, J., & Wood, E. (2009). Methamphetamine use and rates of incarceration among street-involved youth in a Canadian setting: a cross-sectional analysis. *Substance Abuse Treatment, Prevention, and Policy*, 4(17), 1–6.

- Mithoefer, M. C., Grob, C. S., & Brewerton, T. D. (2016). Novel psychopharmacological therapies for psychiatric disorders: Psilocybin and MDMA. *The Lancet Psychiatry*, 3(5), 481–488.
- Mithoefer, M. C., Mithoefer, A. T., Feduccia, A. A., Jerome, L., Wagner, M., Wymer, J., ... Doblin, R. (2018). 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for post-traumatic stress disorder in military veterans, firefighters, and police officers: A randomised, double-blind, dose-response, phase 2 clinical trial. *The Lancet Psychiatry*, 5(6), 486–497.
- Mithoefer, M. C., Wagner, M., Mithoefer, A. T., Jerome, L., & Doblin, R. (2010). The safety and efficacy of  $\pm$ 3,4-methylenedioxymethamphetamine-assisted psychotherapy in subjects with chronic, treatment-resistant posttraumatic stress disorder: The first randomized controlled pilot study. *Journal of Psychopharmacology*, 25(4), 439–452.
- Mithoefer, M. C., Wagner, M. T., Mithoefer, A. T., Jerome, L., Martin, S. F., Yazar-Klosinski, B., ... Doblin, R. (2013). 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. *Journal of Psychopharmacology*, 27(1), 28–39.
- Mizock, L., & Lewis, T. (2008). Trauma in transgender populations: Risk, resilience, and clinical care. *Journal of Emotional Abuse*, 8(3), 335–354.
- Morgan, C. J., McAndrew, A., Stevens, T., Nutt, D., & Lawn, W. (2017). Tripping up addiction: the use of psychedelic drugs in the treatment of problematic drug and alcohol use. *Current Opinion in Behavioral Sciences*, 13, 71–76.
- Morgan, C. J. A., Muetzelfeldt, L., Muetzelfeldt, M., Nutt, D. J., & Curran, H. V. (2010). Harms associated with psychoactive substances: Findings of the UK National Drug Survey. *Journal of Psychopharmacology*, 24(2), 147–153.
- Nemoto, T., Boedeker, B., & Iwamoto, M. (2011). Social support, exposure to violence and transphobia, and correlates of depression among male-to-female transgender women with a history of sex work. *American Journal of Public Health*, 101(10), 1980–1988.
- Nichols, D. E. (2004). Hallucinogens. *Pharmacology and Therapeutics*, 101(2), 131–181.
- Nichols, D. E. (2016). Psychedelics. *Pharmacological Reviews*, 68, 264–355.
- NIMH. (2014). *A Prioritized Research Agenda for Suicide Prevention: An Action Plan to Save Lives*. Rockville, MD. Retrieved from [www.suicide-research-agenda.org](http://www.suicide-research-agenda.org)
- Nock, M. K., Borges, G., Bromet, E. J., Cha, C. B., Kessler, R. C., & Lee, S. (2008). Suicide and suicidal behavior. *Epidemiologic Reviews*, 30(1), 133–154.

- Noll, J., Horowitz, L., Bonanno, G., Trickett, P., & Putnam, F. (2003). Revictimization and self-harm in females who experienced childhood sexual abuse: results from a prospective study. *Journal of Interpersonal Violence, 18*(12), 1452–1471.
- Noller, G. E., Frampton, C. M., & Yazar-Klosinski, B. (2018). Ibogaine treatment outcomes for opioid dependence from a twelve-month follow-up observational study. *American Journal of Drug and Alcohol Abuse, 44*(1), 37–46.
- Nour, M. M., Evans, L., & Carhart-Harris, R. L. (2017). Psychedelics, personality and political perspectives. *Journal of Psychoactive Drugs, 1*–10.
- NSWP. (2012). *St James Infirmary posters presented at international conference. Global Network of Sex Work Projects*. Retrieved from <http://dev.nswp.org/news-story/st-james-infirmary-posters-presented-international-conference>
- Nutt, D. J., King, L. A., & Phillips, L. D. (2010). Drug harms in the UK: A multicriteria decision analysis. *The Lancet, 376*(9752), 1558–1565.
- Nutt, D. J., King, L. A., Saulsbury, W., & Blakemore, C. (2007). Development of a rational scale to assess the harm of drugs of potential misuse. *Lancet, 369*(9566), 1047–1053.
- Nutt, D. J., King, L. a, & Nichols, D. E. (2013). Effects of Schedule I drug laws on neuroscience research and treatment innovation. *Nature Reviews, 14*, 577–585.
- O'Connor, R. C., & Nock, M. K. (2014). The psychology of suicidal behaviour. *The Lancet Psychiatry, 1*(1), 73–85.
- Oehen, P., & Schnyder, U. (2013). A randomized, controlled pilot study of MDMA ( $\pm$  3,4 methylenedioxymethamphetamine)-assisted psychotherapy for treatment of resistant, chronic Post-Traumatic Stress Disorder (PTSD). *Journal of Psychopharmacology, 27*(1), 40–52.
- Operario, D., Soma, T., & Underhill, K. (2008). Sex work and HIV status among transgender women - Systematic review and meta-analysis. *Journal of Acquired Immune Deficiency Syndromes, 48*(1), 97–103.
- Oram, M. (2014). Efficacy and enlightenment: LSD psychotherapy and the drug amendments of 1962. *Journal of the History of Medicine and Allied Sciences, 69*(2), 221–250.
- Oram, M. (2016). Prohibited or regulated? LSD psychotherapy and the United States Food and Drug Administration. *History of Psychiatry, 27*(3), 290–306.
- Osmond, H. (1957). A review of the clinical effects of psychotomimetic agents. *Annals of the New York Academy of Sciences, 66*(3), 418–434.

- Osório, F. L., Sanches, R. F., Macedo, L. R., dos Santos, R. G., Maia-de-Oliveira, J. P., Wichert-Ana, L., ... Hallak, J. E. (2015). Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a preliminary report. *Revista Brasileira de Psiquiatria*, 37(1), 13–20.
- Overstreet, N. M., & Quinn, D. M. (2013). The intimate partner violence stigmatization model and barriers to help seeking. *Basic and Applied Social Psychology*, 35(1), 109–122.
- Palhano-Fontes, F., Barreto, D., Onias, H., Andrade, K. C., Novaes, M., Pessoa, J., ... Araujo, D. B. de. (2018). Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: A randomised placebo-controlled trial. *Psychological Medicine*, 1–9.
- Panagioti, M., Gooding, P. A., & Tarriner, N. (2012). A meta-analysis of the association between posttraumatic stress disorder and suicidality: The role of comorbid depression. *Comprehensive Psychiatry*, 53(7), 915–930.
- Patterson, T. L., Semple, S. J., Staines, H., Lozada, R., Orozovich, P., Bucardo, J., ... Strathdee, S. A. (2008). Prevalence and correlates of HIV infection among female sex workers in 2 Mexico–US border cities. *The Journal of Infectious Diseases*, 197(5), 728–732.
- Phelps, J. (2017). Developing guidelines and competencies for the training of psychedelic therapists. *Journal of Humanistic Psychology*, 57(5), 450–487.
- Pickett, K., & Wilkinson, R. (2019). *The Inner Level*. New York: Penguin Press.
- Pisano, V. D., Putnam, N. P., Kramer, H. M., Franciotti, K. J., Halpern, J. H., & Holden, S. C. (2017). The association of psychedelic use and opioid use disorders among illicit users in the United States. *Journal of Psychopharmacology*, 31(5), 1–8.
- Polito, V., & Stevenson, R. J. (2019). A systematic study of microdosing psychedelics. *PLoS ONE*, 14(2), e0211023.
- Pollan, M. (2018). *How to Change Your Mind: What the New Science of Psychedelics Teaches Us About Consciousness, Dying, Addiction, Depression, and Transcendence*. New York: Penguin Press.
- Potterat, J. J., Brewer, D. D., Muth, S. O., Rothenberg, R. B., Woodhouse, D. E., Muth, J. B., ... Brody, S. (2004). Mortality in a long-term open cohort of prostitute women. *American Journal of Epidemiology*, 159(8), 778–785.
- Prochazkova, L., Lippelt, D. P., Colzato, L. S., Kuchar, M., Sjoerds, Z., & Hommel, B. (2018). Exploring the effect of microdosing psychedelics on creativity in an open-label natural setting. *Psychopharmacology*, 235, 3401–3413.

- Puri, N., Shannon, K., Nguyen, P., & Goldenberg, S. M. (2017). Burden and correlates of mental health diagnoses among sex workers in an urban setting. *BMC Women's Health*, *17*(1), 1–9.
- Renelli, M., Fletcher, J., Tupper, K. W., Files, N., Loizaga-Velder, A., & Lafrance, A. (2018). An exploratory study of experiences with conventional eating disorder treatment and ceremonial ayahuasca for the healing of eating disorders. *Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity*, (Epub ahead of print).
- Rhodes, T. (2009). Risk environments and drug harms: a social science for harm reduction approach. *International Journal of Drug Policy*, *20*(3), 193–201.
- Rhodes, T., Wagner, K., Strathdee, S. A., Shannon, K., Davidson, P., & Bourgois, P. (2012). Structural Violence and Structural Vulnerability within the Risk Environment: Theoretical and Methodological Perspectives for a Social Epidemiology of HIV Risk among Injection Drug Users and Sex Workers. In P. O'Campo & J. Dunn (Eds.), *Rethinking social epidemiology: Towards a science of change*. Toronto: University of Toronto Press.
- Ribeiro, W. S., Bauer, A., Andrade, M. C. R., York-Smith, M., Pan, P. M., Pingani, L., ... Evans-Lacko, S. (2017). Income inequality and mental illness-related morbidity and resilience: A systematic review and meta-analysis. *The Lancet Psychiatry*, *4*(7), 554–562.
- Rio Navarro, J., Cohen, J., Rocillo Arechaga, E., Zuñiga, E., Médecins Sans Frontières Evaluation, & Action Team-Honduras. (2012). Physical and sexual violence, mental health indicators, and treatment seeking among street-based population groups in Tegucigalpa, Honduras. *Pan American Journal of Public Health*, *31*(3), 388–395.
- Romero-Daza, N., Weeks, M., & Singer, M. (2005). Conceptualizing the impact of indirect violence on HIV risk among women involved in street-level prostitution. *Aggression and Violent Behavior*, *10*(2), 153–170.
- Ross, S., Bossis, A., Guss, J., Agin-Liebes, G., Malone, T., Cohen, B., ... Schmidt, B. L. (2016). Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: A randomized controlled trial. *Journal of Psychopharmacology*, *30*(12), 1165–1180.
- Roxburgh, A., Degenhardt, L., & Copeland, J. (2006). Posttraumatic stress disorder among female street-based sex workers in the greater Sydney area, Australia. *BMC Psychiatry*, *6*(24), 1–12.
- Roxburgh, A., Degenhardt, L., Copeland, J., & Larance, B. (2008). Drug dependence and associated risks among female street-based sex workers in the Greater Sydney Area, Australia. *Substance Use & Misuse*, *43*, 1202–1217.
- Rucker, J. J. H., Iliff, J., & Nutt, D. J. (2018). Psychiatry & the psychedelic drugs. Past, present & future. *Neuropharmacology*, *142*, 200–218.

- Rucker, J. J. H., Jelen, L. A., Flynn, S., Frowde, K. D., & Young, A. H. (2016). Psychedelics in the treatment of unipolar mood disorders: A systematic review. *Journal of Psychopharmacology*, *30*(12), 1220–1229.
- Rusch, M. L., Lozada, R., Pollini, R. A., Vera, A., Patterson, T. L., Case, P., & Strathdee, S. A. (2009). Polydrug use among IDUs in Tijuana, Mexico: Correlates of methamphetamine use and route of administration by gender. *Journal of Urban Health*, *86*(5), 760–775.
- Salway Hottes, T., Bogaert, L., Rhodes, A. E., Brennan, D. J., & Gesink, D. (2016). Lifetime prevalence of suicide attempts among sexual minority adults by study sampling strategies: A systematic review and meta-analysis. *American Journal of Public Health*, *106*(5), e1–e12.
- SAMHSA. (2018). *Trauma-Informed Approach and Trauma-Specific Interventions*. Rockville, MD. Retrieved from <https://www.samhsa.gov/nctic/trauma-interventions>
- Savage, C., & McCabe, O. (1973). Residential psychedelic ( LSD ) for the narcotic addict: A controlled study. *Archives of General Psychiatry*, *28*, 808–814.
- Scheper-Hughes, N. (1996). Small wars and invisible genocides. *Social Science and Medicine*, *43*(5), 889–900.
- Schmid, Y., & Liechti, M. E. (2018). Long-lasting subjective effects of LSD in normal subjects. *Psychopharmacology*, *235*(2), 535–545.
- Schwarcz, S., Scheer, S., McFarland, W., Katz, M., Valleroy, L., Chen, S., & Catania, J. (2007). Prevalence of HIV infection and predictors of high-transmission sexual risk behaviors among men who have sex with men. *American Journal of Public Health*, *97*(6), 1067–1075.
- Semple, S., Grant, I., & Patterson, T. (2004). Female methamphetamine users: Social characteristics and sexual risk behavior. *Women & Health*, *40*(3), 77–94.
- Seng, J. S., Lopez, W. D., Sperlich, M., Hamama, L., & Reed Meldrum, C. D. (2012). Marginalized identities, discrimination burden, and mental health: Empirical exploration of an interpersonal-level approach to modeling intersectionality. *Social Science and Medicine*, *75*(12), 2437–2445.
- Sessa, B. (2012). Shaping the renaissance of psychedelic research. *The Lancet*, *380*(9838), 200–201.
- Sessa, B. (2015). Turn on and tune in to evidence-based psychedelic research. *The Lancet Psychiatry*, *2*(1), 10–12.

- Sessa, B., & Johnson, M. W. (2015). Can psychedelic compounds play a part in drug dependence therapy? *British Journal of Psychiatry*, *206*(1), 1–3.
- Shahmanesh, M., Wayal, S., Cowan, F., Mabey, D., Copas, A., & Patel, V. (2009). Suicidal behavior among female sex workers in Goa, India: The silent epidemic. *American Journal of Public Health*, *99*(7), 1239–1246.
- Shannon, K., Bright, V., Allinott, S., Alexson, D., Gibson, K., & Tyndall, M. W. (2007). Community-based HIV prevention research among substance-using women in survival sex work: The Maka Project Partnership. *Harm Reduction Journal*, *4*(20).
- Shannon, K., & Csete, J. (2010). Violence, condom negotiation, and HIV/STI risk among sex workers. *JAMA*, *304*(5), 573–574.
- Shannon, K., Goldenberg, S. M., Deering, K. N., & Strathdee, S. A. (2014). HIV infection among female sex workers in concentrated and high prevalence epidemics: Why a structural determinants framework is needed. *Current Opinion in HIV and AIDS*, *9*(2), 174–182.
- Shannon, K., Kerr, T., Allinott, S., Chettiar, J., Shoveller, J. A., & Tyndall, M. W. (2008). Social and structural violence and power relations in mitigating HIV risk of drug-using women in survival sex work. *Social Science and Medicine*, *66*, 911–921.
- Shannon, K., Strathdee, S. A., Goldenberg, S. M., Duff, P., Mwangi, P., Rusakova, M., ... Boily, M. C. (2015). Global epidemiology of HIV among female sex workers: Influence of structural determinants. *Lancet*, *385*, 55–71.
- Shannon, K., Strathdee, S., Shoveller, J., Zhang, R., Montaner, J., & Tyndall, M. (2011). Crystal methamphetamine use among female street-based sex workers: Moving beyond individual-focused interventions. *Drug and Alcohol Dependence*, *113*(1), 76–81.
- Sharma, T., Schow Guski, L., Freund, N., & Gotzsche, P. (2016). Suicidality and aggression during antidepressant treatment: Systematic review and meta-analyses based on clinical study reports. *BMJ*, *352*(i65).
- Singh, I., Morgan, C. J., Curran, V., Nutt, D., Schlag, A., & McShane, R. (2017). Ketamine treatment for depression: Opportunities for clinical innovation and ethical foresight. *The Lancet Psychiatry*, *4*(5), 419–426.
- Smith, R. C., Blumenthal, H., Badour, C., & Feldner, M. T. (2010). An investigation of relations between crystal methamphetamine use and posttraumatic stress disorder. *Addictive Behaviors*, *35*(6), 625–627.
- Statistics Canada. (2015). *Suicide Rates: An Overview. Health at a Glance*. Ottawa. Retrieved from <http://www.statcan.gc.ca/pub/82-624-x/2012001/article/11696-eng.htm>

- Stoltz, J. A. M., Shannon, K., Kerr, T., Zhang, R., Montaner, J. S., & Wood, E. (2007). Associations between childhood maltreatment and sex work in a cohort of drug-using youth. *Social Science and Medicine*, *65*(6), 1214–1221.
- Strathdee, S. A., & Stockman, J. K. (2010). Epidemiology of HIV among injecting and non-injecting drug users: Current trends and implications for interventions. *Current HIV/AIDS Reports*, *7*(2), 99–106.
- Stueve, A., Duran, R., Doval, A. S., & Blome, J. (2001). Time-space sampling in minority communities: Results with young Latino men who have sex with men. *American Journal of Public Health*, *91*(6), 922–926.
- Supreme Court of Canada. (2013). *Canada (Attorney General) vs. Bedford*. Ottawa SCC 72. Ottawa, ON. Retrieved from <https://scc-csc.lexum.com/scc-csc/scc-csc/en/item/13389/index.do>
- Surratt, H. L., Kurtz, S. P., Chen, M., & Mooss, A. (2012). HIV risk among female sex workers in Miami: The impact of violent victimization and untreated mental illness. *AIDS Care*, *24*(5), 553–561.
- Syvetsen, J. L., Bazzi, A. R., Martinez, G., Rangel, M. G., Ulibarri, M. D., Fergus, K. B., ... Strathdee, S. A. (2015). Love, trust, and HIV risk among female sex workers and their intimate male partners. *American Journal of Public Health*, e1–e9.
- Talin, P., & Sanabria, E. (2017). Ayahuasca's entwined efficacy: An ethnographic study of ritual healing from 'addiction.' *International Journal of Drug Policy*, *44*, 23–30.
- Tatarsky, A., & Kellogg, S. (2010). Integrative harm reduction psychotherapy: A case of substance use, multiple trauma, and suicidality. *Journal of Clinical Psychology*, *66*(2), 123–135.
- Thiessen, M. S., Walsh, Z., Bird, B. M., & Lafrance, A. (2018). Psychedelic use and intimate partner violence: The role of emotion regulation. *Journal of Psychopharmacology*, 1–7.
- Thomas, G., Lucas, P., Capler, N. R., Tupper, K. W., & Martin, G. (2013). Ayahuasca-assisted therapy for addiction: Results from a preliminary observational study in Canada. *Current Drug Abuse Reviews*, *6*(1), 30–42.
- Tull, M. T., Gratz, K. L., Aclin, W. M., & Lejuez, C. W. (2010). A preliminary examination of the relationships between posttraumatic stress symptoms and crack/cocaine, heroin, and alcohol dependence. *Journal of Anxiety Disorders*, *24*(1), 55–62.
- Tupper, K. W. (2008). The globalization of ayahuasca: Harm reduction or benefit maximization? *International Journal of Drug Policy*, *19*(4), 297–303.

- Tupper, K. W., & Labate, B. (2014). Ayahuasca, psychedelic studies and health sciences: The politics of knowledge and inquiry into an Amazonian plant brew. *Current Drug Abuse Reviews*, 7(2), 71–80.
- Tupper, K. W., Wood, E., Yensen, R., & Johnson, M. W. (2015). Psychedelic medicine: a re-emerging therapeutic paradigm. *Canadian Medical Association Journal*, 187(14), 1054–1059.
- Uhlmann, S., DeBeck, K., Simo, A., Kerr, T., Montaner, J. S. G., & Wood, E. (2014). Crystal methamphetamine initiation among street-involved youth. *American Journal of Drug and Alcohol Abuse*, 40(1), 31–36.
- Uhlmann, S., DeBeck, K., Simo, A., Kerr, T., Montaner, J. S. G., & Wood, E. (2014). Health and social harms associated with crystal methamphetamine use among street-involved youth in a Canadian setting. *The American Journal on Addictions*, 23(4), 393–8.
- Ulibarri, M. D., Hiller, S. P., Lozada, R., Rangel, M. G., Stockman, J. K., Silverman, J. G., & Ojeda, V. D. (2013). Prevalence and characteristics of abuse experiences and depression symptoms among injection drug-using female sex workers in Mexico. *Journal of Environmental and Public Health*, 1–11.
- Ulibarri, M. D., Roesch, S., Rangel, M. G., Staines, H., Amaro, H., & Strathdee, S. A. (2015). “Amar te Duele” (“Love Hurts”): Sexual relationship power, intimate partner violence, depression symptoms and HIV risk among female sex workers who use drugs and their non-commercial, steady partners in Mexico. *AIDS and Behavior*, 19, 9–18.
- Ulibarri, M. D., Strathdee, S. a, Lozada, R., Magis-Rodriguez, C., Amaro, H., O’Campo, P., & Patterson, T. L. (2010). Intimate partner violence among female sex workers in two Mexico-U.S. border cities: Partner characteristics and HIV risk-behaviors as correlates of abuse. *Psychological Trauma: Theory, Research, Practice and Policy*, 2(4), 318–325.
- United Nations. Universal Declaration of Human Rights (1948). Geneva.
- United Nations. (1971). *Convention on Psychotropic Substances*. Vienna. Retrieved from [http://www.unodc.org/pdf/convention\\_1971\\_en.pdf](http://www.unodc.org/pdf/convention_1971_en.pdf)
- University of Toronto. (2018). Rethinking psychedelics: Microdosing to ease anxiety and sharpen focus. U of T News. Retrieved from <https://www.utoronto.ca/news/rethinking-psychedelics-u-t-study-looks-practice-microdosing-ease-anxiety-and-sharpen-focus>
- UNODC. (2015). *World Drug Report 2015*. Vienna. Retrieved from [http://www.unodc.org/documents/wdr2015/World\\_Drug\\_Report\\_2015.pdf](http://www.unodc.org/documents/wdr2015/World_Drug_Report_2015.pdf)
- Urban Health Research Initiative. (2013). *Drug Situation in Vancouver* (Second Edition). Vancouver. Retrieved from <http://uhri.cfenet.ubc.ca>

- Värnik, P. (2012). Suicide in the world. *International Journal of Environmental Research and Public Health*, 9(3), 760–771.
- Volkow, N. D., Wang, G. J., Fowler, J. S., Telang, F., Jayne, M., & Wong, C. (2007). Stimulant-induced enhanced sexual desire as a potential contributing factor in HIV transmission. *American Journal of Psychiatry*, 164(1), 157–160.
- Vollenweider, F. X., & Kometer, M. (2010). The neurobiology of psychedelic drugs: implications for the treatment of mood disorders. *Nature Reviews Neuroscience*, 11, 642–651.
- Walsh, C. (2010). Drugs and human rights: Private palliatives, sacramental freedoms and cognitive liberty. *International Journal of Human Rights*, 14(3), 425–441.
- Walsh, C. (2016). Psychedelics and cognitive liberty: Reimagining drug policy through the prism of human rights. *International Journal of Drug Policy*, 29, 80–87.
- Walsh, Z., Hendricks, P., Smith, S., Kosson, D. S., Thiessen, M. S., Lucas, P., & Swogger, M. T. (2016). Hallucinogen use and intimate partner violence: Prospective evidence consistent with protective effects among men with histories of problematic substance use. *Journal of Psychopharmacology*, 30(7), 601–607.
- Wang, B., Li, X., Stanton, B., Fang, X., Yang, H., Zhao, R., & Hong, Y. (2007). Sexual coercion, HIV-related risk, and mental health among female sex workers in China. *Health Care for Women International*, 28(8), 745–762.
- Watts, R., Day, C., Krzanowski, J., Nutt, D. J., & Carhart-Harris, R. L. (2017). Patients' accounts of increased “connectedness” and “acceptance” after psilocybin for depression. *Journal of Humanistic Psychology*, 57(5), 520–564.
- Weiser, S., Dilworth, S., Neilands, T., Cohen, J., Bangsberg, D., & Riley, E. (2006). Gender-specific correlates of sex trade among homeless and marginally housed individuals in San Francisco. *Journal of Urban Health*, 83(4), 736–740.
- Werb, D., Kerr, T., Buxton, J., Mhsc, M., Shoveller, J., & Richardson, C. (2013). Crystal methamphetamine and initiation of injection drug use among street-involved youth in a Canadian setting. *Canadian Medical Association Journal*, 1–7.
- Wexler, L., Chandler, M., Gone, J. P., Cwik, M., Kirmayer, L. J., La Fromboise, T., ... Allen, J. (2015). Advancing suicide prevention research with rural American Indian and Alaska Native populations. *American Journal of Public Health*, 105(5), 891–899.

- Whiteford, H. A., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E., ... Vos, T. (2013). Global burden of disease attributable to mental and substance use disorders: Findings from the Global Burden of Disease Study 2010. *The Lancet*, 382(9904), 1575–1586.
- Winstock, A., Barratt, M., Ferris, J., & Maier, L. (2017). *Global Drug Survey*. London. Retrieved from [https://www.globaldrugsurvey.com/wp-content/themes/globaldrugsurvey/results/GDS2017\\_key-findings-report\\_final.pdf](https://www.globaldrugsurvey.com/wp-content/themes/globaldrugsurvey/results/GDS2017_key-findings-report_final.pdf)
- Wood, E. (2018). Strategies for reducing opioid-overdose deaths: Lessons from Canada. *New England Journal of Medicine*, 378(17), 1565–1567.
- Wood, E., Stoltz, J.-A., Montaner, J. S., & Kerr, T. (2006). Evaluating methamphetamine use and risks of injection initiation among street youth: The ARYS study. *Harm Reduction Journal*, 3(18).
- World Health Organization. (2012). *Prevention and Treatment of HIV and Other Sexually Transmitted Infections for Sex Workers in Low- and Middle-Income Countries*. Geneva. Retrieved from [http://www.who.int/hiv/pub/guidelines/sex\\_worker/en/index.html](http://www.who.int/hiv/pub/guidelines/sex_worker/en/index.html)
- World Health Organization. (2013). *Global and regional estimates of violence against women: Prevalence and health effects of intimate partner violence and non-partner sexual violence*. Geneva. Retrieved from <http://www.who.int/reproductivehealth/publications/violence/9789241564625/en/>
- World Health Organization. (2014). *Preventing Suicide: A Global Imperative*. Geneva, Switzerland. Retrieved from [https://www.who.int/mental\\_health/suicide-prevention/world\\_report\\_2014/en/](https://www.who.int/mental_health/suicide-prevention/world_report_2014/en/)
- Yanakieva, S., Polychroni, N., Family, N., Williams, L. T. J., Luke, D. P., & Terhune, D. B. (2018). The effects of microdose LSD on time perception: A randomised, double-blind, placebo-controlled trial. *Psychopharmacology*.
- Zalsman, G., Hawton, K., Wasserman, D., van Heeringen, K., Arensman, E., Sarchiapone, M., ... Zohar, J. (2016). Suicide prevention strategies revisited: 10-year systematic review. *The Lancet Psychiatry*, 3(7), 646–659.
- Zhang, L., Li, X., Wang, B., Shen, Z., Zhou, Y., Xu, J., ... Bonita, S. (2016). Violence, stigma and mental health among female sex workers in China: A structural equation modeling. *Women & Health*, 57(6), 685–704.
- Zule, W., Costenbader, E., Coomes, C. M., Meyer, W. J., Riehman, K., Poehlman, J., & Wechsberg, W. M. (2007). Stimulant use and sexual risk behaviors for HIV in rural North Carolina. *The Journal of Rural Health*, 23, 73–78.