Associations of substance use patterns with attempted suicide among persons who inject drugs: Can distinct use patterns play a role?

Andreea Adelina Artenie[a,b], Julie Bruneau[a,b,c], Geng Zang[a], François Lespérance[a,d], Johanne Renaud[e], Joël Tremblay[f], Didier Jutras-Aswad[a,d]

[a] Research Center, Centre Hospitalier de l'Université de Montréal (CHUM), 900 Saint-Denis, Montréal, QC, Canada H2X 0A9

[b] Department of Family Medicine, Faculty of Medicine, McGill University, 5858 Chemin de la Côte-des-Neiges, Montréal, QC, Canada H3S 1Z1

[c] Department of Family and Emergency Medicine, Faculty of Medicine, Université de Montréal, C.P. 6128, succursale Centre-ville, Montréal, QC, Canada H3C 3J7

[d] Department of Psychiatry, Faculty of Medicine, Université de Montréal, C.P. 6128, succursale Centre-ville, Montréal, QC, Canada H3C 3J7

[e] Department of Psychiatry, Faculty of Medicine, McGill University, 1033 Pine Avenue West, Montréal, QC, Canada H3A 1A1

[f] Department of psychoeducation, Université du Québec à Trois-Rivières, C.P. 500, Trois-Rivières, QC, Canada G9A 5H7

Contact information (Corresponding author):

Didier Jutras-Aswad, MD, MSc

Research Center, Centre Hospitalier de l'Université de Montréal (CHUM)

Tour Viger

900, Saint-Denis, office R06-444

Montréal, QC, Canada

Phone: +1 (514) 890-8000 Ext.35703 Fax:+1 (514) 412-7320

E-mail: didier.jutras-aswad@umontreal.ca

Structured abstract

Background: While the elevated risk of suicide attempt among persons who inject drugs (PWID) is well documented, whether use of different substances is associated with varying degrees of risk remains unclear. We sought to examine the associations between substance use patterns and attempted suicide in a prospective cohort of PWID in Montreal, Canada.

Methods: Between 2004 and 2011, participants completed an interviewer-administered questionnaire eliciting information on socio-demographic, substance use patterns, related behaviors, and mental health markers. Generalized estimating equations were used to model the relationship between self-reported use of six common substances (cocaine, amphetamine, opioids, sedative-hypnotics, cannabis and alcohol), associated patterns of use (chronic, occasional and none), and a recent (past six-month) suicide attempt.

Results: At baseline, of 1,240 participants (median age: 39.1, 83.7% male), 71 (5.7%) reported a recent suicide attempt. Among 5,621 observations collected during follow-up, 221 attempts were reported by 143 (11.5%) participants. In multivariate analyses adjusting for socio-demographic and psychosocial stressors, among primary drugs of abuse, chronic [Adjusted Odds Ratio (AOR): 1.97] and occasional (AOR: 1.92) cocaine use, and chronic amphetamine use (AOR: 1.96) were independently associated with attempted suicide. Among co-used substances, chronic sedative-hypnotic use was independently associated with an attempt (AOR: 2.29). No statistically significant association was found for the remaining substances.

Conclusion: Among PWID at high risk of attempted suicide, stimulant users appear to constitute a particularly vulnerable sub-group. While the mechanisms underlying these associations remain to be elucidated, findings suggest that stimulant-using PWID should constitute a prime focus of suicide prevention efforts.

Keywords

suicide, injection, drug use, risk factor, epidemiology, stimulant

Abbreviations

PWID: persons who inject drugs

1.0 Introduction

Substance misuse constitutes a significant risk factor for suicide, second only to depression and other affective disorders (Cavanagh et al., 2003). Among illicit drug-users, suicide is a substantial contributor to excess mortality, estimated to account for more than 10% of deaths (Darke et al., 2007). Further, lifetime histories of suicide attempt in this population range between 17% and 43% (Darke et al., 2007). These proportions are far in excess to prevalences reported in the general population, estimated to vary between 3% and 5% (Health Canada, 2009; Kessler et al., 1999).

Persons who inject drugs (PWID) seem to exhibit the greatest risk. Compared to the general population, intravenous drug use carries a nearly 14-fold elevated risk of completed suicide (Wilcox et al., 2004), and PWID are estimated to be four times more likely to experience an attempt compared to non-injection drug users (Darke and Kaye, 2004). Studies conducted in the United States (Havens et al., 2004) and Canada (Marshall et al., 2011) among street-based PWID reported six-month prevalences of suicide attempt of 7.0% and 8.0%, respectively.

While the relationship between substance misuse and risk of suicidal behavior is well established, it is unclear how this association varies across different types of substances among drug-using populations (Center for Substance Abuse Treatment, 2008). An extensive literature has focused on cocaine- (Darke and Kaye, 2004; Roy, 2001) and heroin-users (Darke et al., 2005; Roy, 2002, 2010) and reported comparable prevalences of attempted suicide, suggesting that both drugs may carry a similar risk of suicidal behaviors. Investigations conducted among broader drug-using populations noted a positive association between suicide attempt, and use of cocaine (Britton and Conner, 2010) and amphetamine (Marshall et al., 2011). Use of licit non-injectable substances, including sedative-hypnotics and alcohol, which are often co-used by illicit drug users (Darke and Hall, 1995; Public Health Agency of Canada, 2006), has also been

reported to be associated with increased odds of attempted suicide (Backmund et al., 2011; Rossow and Lauritzen, 1999). In contrast, a number of studies failed to report an association between use of specific substances and suicide attempt (Havens et al., 2004; Roy, 2003; Wines et al., 2004). Although polysubstance use is highly prevalent among street-based PWID (Leri et al., 2004), few investigations have examined a broad range of commonly used substances within the same study sample (Wines et al., 2004), making it difficult to compare associations with attempted suicide across substances. Moreover, other findings are limited by a lack of control for important confounding factors implicated in suicidal behaviors, such as mental health status (Marshall et al., 2011).

Given that one of the most powerful predictors of death by suicide is a previous suicide attempt (Christiansen and Jensen, 2007), it is important to identify drug users who are most likely to engage in suicidal behaviors. Having a better understanding of the possible risks carried by use of specific substances in this population provides a way to guide and prioritize suicide prevention efforts (Center for Substance Abuse Treatment, 2008). In this study, we sought to examine the relationship between patterns of substance use and attempted suicide using data collected as part of a prospective cohort study of polysubstance-using PWID recruited in Montreal, Canada.

2.0 Methods

2.1 Participants

The study sample was selected from the HEPatitis COhort (HEPCO), an ongoing prospective investigation of PWID established in Montreal, in 2004, to study determinants of Hepatitis C Virus (HCV) transmission. Cohort recruitment and follow-up procedures have been described in detail previously (Bruneau et al., 2012). Briefly, eligibility criteria included having injected drugs within the previous six months, being 18 years of age or older, residing in the

Greater Montreal area and providing informed consent in compliance with institutional review board regulations of the Centre Hospitalier de l'Université de Montréal (CHUM). Participant recruitment occurred through street-level strategies such as word-of-mouth and community program referrals.

At baseline and each six-month follow-up visit, participants provided blood samples for HCV testing and completed an interviewer-administered questionnaire eliciting information on socio-demographic characteristics, detailed information on substance use patterns and related behaviors in the past month and past six months, and mental health status indicators. The interviewers and nurses present on-site offered information about, and referrals to addiction, mental health and HCV treatment or support services on a case-by-case basis. A CAD 15.00$ stipend was offered to all study participants upon completion of the questionnaire, as compensation for their time. Ethical approval for this study was provided through the Ethics Review Board of the CHUM.

Between November, 2004 and March, 2011, a total of 1,243 PWID were recruited in the HEPCO cohort, and were eligible for this study. Three participants were excluded from the present analyses, as they had missing data for the outcome of interest.

2.2 Measures

Consistent with previous reports (Marshall et al., 2011), the outcome of interest was a dichotomous measure of suicide attempt assessed by the following question: "In the past six months, have you attempted suicide?".

The primary exposure variables were substance use patterns. Participants were questioned on the types of substances used in the previous six months, and on the corresponding number of days of use. A conceptual domain assessing substance use patterns was created, and

included the types of substances used and associated patterns of use. Six types of commonly used substances were assessed: cocaine, amphetamine, opioids, including heroin and prescription opioids, cannabis, alcohol and sedative-hypnotics, including barbiturates and benzodiazepines. Given that eligible participants must have injected drugs in the previous six months, cocaine, amphetamine and opioids constitute the primary drugs of abuse in our sample, whereas the remaining substances are typically co-used. Patterns of substance use were operationalized in three groups: chronic, occasional or none, based on the number of days of use in the previous six months. In the absence of formal guidelines distinguishing between chronic and occasional substance use, we relied on the definition used by the United States Office of National Drug Control Policy to describe patterns of illegal drug use (Office of National Drug Control Policy, 2012). Accordingly, chronic drug use is defined as consumption that occurs once a week or more, and occasional use as consumption that takes place less frequently. A similar definition has been successfully employed in a previous study assessing patterns of drug use in relation to suicidal behaviors among drug users (Wines et al., 2004). In line with this definition, in our study, chronic substance use, with the exception of alcohol, was defined as having consumed on 26 days or more in the previous six months, and occasional use as having consumed up to 25 days over the same time period. As alcohol is more widely consumed compared to all of the other drugs, we opted for a less conservative definition to describe chronic use. As such, chronic use of alcohol was defined as having consumed, on average, every other day or more in the past six months (i.e., ≥90 days), and occasional use as having consumed less frequently. A third category (none), indicating no consumption in the previous six months, was also included for all substance use variables.

Potential confounders included measured variables previously identified as significant

correlates of suicide attempt among drug-using populations (Havens et al., 2004; Marshall et al., 2011), and were grouped into two conceptual domains: socio-demographic characteristics and psychosocial stressors. Age, gender and education were assessed as part of the socio-demographic domain. Variables examined in the psychosocial stressors domain included living in unstable housing conditions, prostitution, incarceration, characteristics of injection drug use relevant to the study population, including the frequency of injection (>30 versus ≤30 injections, past month), age at first injection and duration of injection drug use, and markers of psychological distress. Two variables were assessed as markers of psychological distress, and included history of a diagnosed psychological disorder and treatment for anxiety or depression. Detailed information regarding the type of psychological disorder was not collected. Consistent with previous studies (Bruneau et al., 2012), unstable housing was defined as living on the street, in shelters or in apartment-hotels rented on a monthly basis, indicating rapid turnover compared to typical 12-month rent–lease accommodation standards in Montreal. All factors in the psychosocial stressors domain were assessed in reference to the past six months, with the exception of diagnosed psychological disorder, which was in reference to lifetime.

2.3 Statistical analyses

Descriptive statistics were used to characterize the study sample at baseline, and included medians and corresponding interquartile ranges (IQR), and frequency distributions for continuous and categorical variables, respectively. To compare the characteristics of participants who did and did not experience a suicide attempt at baseline, chi-square tests were conducted for categorical variables and nonparametric Mann-Whitney U-tests for continuous variables, given their non-normal distribution.

To examine factors associated with reports of suicide attempt throughout the entire 77–month period, while accounting for within-subject correlation as a result of repeated measurements, we used generalized estimating equations (GEE) analyses for binary outcomes with autoregressive order 1 covariance structure (Zeger et al., 1988). In a first step, bivariate GEE analyses were conducted for substance use patterns and potential confounders, and suicide attempt to calculate crude odds ratios (OR) and corresponding 95% Confidence Intervals (CI). Subsequently, a multivariate GEE model was constructed to identify substance use patterns that were independently associated with attempted suicide. Model building was carried out by introducing, in a sequential manner, blocks of variables pertaining to each of the three pre-defined domains. Specifically, substance use patterns were entered first, followed by the socio-demographic and the psychosocial stressor domains. This sequential introduction of variables permitted the assessment of socio-demographic characteristics and psychosocial stressors as potential confounders of the associations between substance use patterns and suicide attempt. To ensure that only the most informative variables were retained, those that were statistically significant at the p-value<0.10 level within each domain were selected through a process of backward elimination, and subsequently introduced in the final, multivariate model. For all analyses, p-values were two-sided. Statistical analyses were performed using SAS 9.3 software (SAS Institute).

3.0 Results

3.1 Sample characteristics

Table 1 presents baseline characteristics among the 1,240 participants eligible for the analyses. Median age was 39.1(IQR: 30.2 – 45.6), the majority (83.7%) was male and less than two-thirds (60.2%) completed high-school education. Regarding substance use patterns, among

primary drugs of abuse, cocaine was the most commonly used drug (56.7% chronic and 30.1% occasional), followed by opioids (36.2% chronic and 21.1% occasional) and amphetamine (2.5% chronic and 13.3% occasional). Among co-used substances, more than two-thirds of participants indicated using alcohol (8.1% chronic and 71.0% occasional) and cannabis (49.6% chronic and 22.8% occasional), and nearly half reported using sedative-hypnotics (23.3% chronic and 18.4% occasional). Overall, participants presented characteristics often associated with drug addiction severity and chronicity. Approximately one in two PWID reported living in unstable housing conditions (42.4%) and a high-injection frequency (50.5%). The median time of injection duration was 12.6 years (IQR: 6.7 – 21.3). Further, a significant proportion of participants had a history of a diagnosed psychological disorder (28.2%) and received recent treatment for anxiety or depression (26.4%).

At baseline, seventy-one PWID (5.7%) reported a suicide attempt in the preceding six months. Table 1 compares baseline characteristics between attempters and non-attempters. Attempters were more likely to be female (26.8% versus 15.7%). Regarding substance use patterns, they were also more likely to report chronic (7.2% versus 2.3%) and occasional (17.4% versus 13.1%) use of amphetamine, and chronic use of sedative-hypnotics (44.3% versus 22.0%). No statistically significant differences were found for the remaining substances. Participants who attempted suicide were also more likely to report characteristics of greater psychological distress. For instance, compared to non-attempters, a significantly higher proportion of attempters reported a history of a diagnosed psychological disorder (52.9% versus 26.7%).

3.2 Associations of substance use patterns with suicide attempt

Overall, participants contributed to 5,621 observations during the 77-month follow-up. Eight hundred and seventy-nine (70.9%) had at least one follow-up visit, and the median number of visits was 4 (IQR: 2–8). A total of 221 suicide attempts were reported during follow-up by 143 (11.5%) participants. Among participants who experienced a suicide attempt, the median number of attempts during follow-up was 1 (IQR: 1 – 2).

Table 2 presents crude associations between socio-demographic characteristics, substance use patterns and psychosocial stressors, and suicide attempt from bivariate GEE analyses. Among socio-demographic characteristics, older age and male were statistically significantly associated with lower odds of attempting suicide. Overall, substance use patterns pertaining to all three primary drugs of abuse were significantly associated with increased odds of reporting an attempt, whereas among co-used substances, only chronic and occasional use of sedative-hypnotics was significantly associated with the outcome. In addition, several markers of psychosocial stress were associated with increased odds of reporting an attempt, including recent treatment for anxiety or depression, and having a history of a diagnosed psychological disorder.

Results from the multivariate GEE analyses illustrating the associations between substance use patterns and suicide attempt, adjusting, sequentially, for socio-demographic characteristics and markers of psychosocial stress, are presented in Table 3. Model A presents the odds ratios for having experienced a suicide attempt according to all substance use patterns that met the inclusion criterion for retention in the multivariate model, and included chronic [Adjusted Odds Ratios (AOR): 2.09, 95% CI: 1.22 – 3.58)] and occasional (AOR: 1.79, 95% CI: 1.06 – 3.04) use of cocaine, chronic (AOR: 2.35, 95% CI: 1.18 – 4.70) and occasional (AOR: 1.61, 95% CI: 1.10 – 2.35) use of amphetamine, and chronic (AOR: 2.75, 95% CI: 1.96 – 3.86) and occasional (AOR: 1.65, 95% CI: 1.08 – 2.50) use of sedative-hypnotics. The addition of

socio-demographic factors in Model B resulted in small changes (10-13%) in the estimates of cocaine and amphetamine use patterns, whereas negligible changes were noted in the estimates of sedative-hypnotics. Further adjustment for psychosocial stressors in Model C led to a reduction in the AOR of all substance use patterns of up to 15%. For the most part, substance use patterns remained independently associated with suicide attempt in the final model. Specifically, the odds of reporting a suicide attempt were greater for chronic (AOR: 1.97, 95% CI: 1.14 – 3.41) and occasional (AOR: 1.92, 95% CI: 1.12 – 3.30) use of cocaine, chronic (AOR: 1.96, 95% CI: 1.01 – 3.80) and occasional (AOR: 1.41, 95% CI: 0.95 – 2.09) use of amphetamine, and chronic (AOR: 2.29, 95% CI: 1.61 – 3.26) and occasional (AOR: 1.48, 95% CI: 0.95 – 2.29) use of sedative-hypnotics.

4.0 Discussion

Consistent with previous reports (Havens et al., 2004; Marshall et al., 2011), our findings indicate that suicide attempt is a frequent event among PWID in Montreal. At baseline, nearly 6% of participants reported an attempt within the previous six months. The present study sought to examine the associations between patterns of substance use and attempted suicide in this high-risk population.

4.1 Main findings

Findings indicate that among primary drugs of abuse, use of stimulants is, by and large, associated with elevated odds of reporting a suicide attempt, whereas use of opioids is not, after controlling for use of other drugs and important confounders, including history of a psychological disorder. We noted that chronic and occasional use of cocaine and chronic use of amphetamine was associated with nearly two-fold greater odds of reporting an attempt. Similarly, among substances that are typically co-used by illicit drug-using populations, chronic

use of sedative-hypnotics was associated with two-fold elevated odds of attempted suicide. This study uniquely adds to the literature by examining a broad range of commonly used substance types and associated patterns of use within a large sample of polydrug-using PWID, while controlling for several factors previously linked to suicidal behaviors.

4.2 Associations of stimulant use patterns with suicide attempt

Our findings illustrating a positive association between suicide attempt and use of cocaine and amphetamine are in agreement with a number of previous studies. In a multi-city study conducted in the United States among a clinical sample of drug users, participants reporting cocaine use as their primary drug of choice had three-fold greater odds of attempting suicide at one-year follow-up (Britton and Conner, 2010). Among street-based PWID in Vancouver, methamphetamine injection was found to increase the risk of attempted suicide by 80% (Marshall et al., 2011). Though previous research has reported elevated prevalences of suicidal behaviors among opioid-dependent individuals compared to the general population (Darke and Ross, 2002), to our knowledge, no study has reported an independent association between opioid use and suicidality among drug-using populations. Altogether, these findings suggest that, while substance use, in and out itself, carries a significant risk for suicidal behaviors, stimulant users may be a particularly vulnerable population, and should constitute a focal target group of suicide prevention efforts among the broader PWID community.

A range of neurobiological, behavioral and social differences between stimulant and opioid users could account for these findings. First, the anhedonic state often associated with use of stimulants may play a role in heightening vulnerability to suicidal behaviors. Supporting this presumption, several imaging studies reported dopamine hypoactivity among long-term cocaine and amphetamine users (Volkow et al., 2001; Volkow et al., 1997), which has been implicated in

inducing a chronic state of anhedonia and heightened vulnerability to suicide (Dackis and O'Brien, 2001). A second possible explanation for our finding relates to the varying degrees of impulsivity seen across users of stimulants and opioids. There is evidence to suggest that, compared to opiate users, cocaine and amphetamine users have poorer levels of impulse control (Badiani et al., 2011), and impulsive behaviors have been implicated in a substantial proportion of attempted suicides (Simon et al., 2001). It is unclear, however, whether differences in impulsivity are due to the drug itself or pre-existing differences, though preliminary evidence points toward the former possibility (Badiani et al., 2011).

Finally, the more limited opportunities for engagement in care made available to stimulant users, compared to opiate users, are also likely to account for our findings. Traditionally, addiction treatment services have been structured around opiate users, and have been slower to adapt to patterns of stimulant misuse (Foers et al., 2004). Among heroin users, opiate substitution therapy has been linked to greater linkage with health care services (Spire et al., 2007), and a plethora of positive health and social outcomes, including reductions in drug use (Sees et al., 2000), susceptibility to infection with Human Immunodeficiency Virus (MacArthur et al., 2012), non-fatal overdose (Kerr et al., 2007) and involvement in crime (Keen et al., 2000). By establishing timely contacts with health care services and helping improve the overall health of drug users, opiate substitution therapy may have a positive impact on their vulnerability to suicidal behaviors. In support of this hypothesis, a study conducted in New South Wales, Australia noted significant reductions in depression and suicidal thoughts, plans and attempts in a sample of 387 heroin-users, three years following entry in drug addiction treatment (Darke et al., 2009). For stimulant users, pharmacological therapies are still under development (Ciccarone, 2011), and the effectiveness of psychosocial interventions is compromised by poor treatment

initiation and retention rates (Shearer, 2007). Compared to heroin users, stimulant users are substantially less likely to initiate drug treatment (John et al., 2001) and are more prone to relapse following cessation of drug use (Nosyk et al., 2014), suggesting that health care services may fail to reach and engage stimulant users into care as effectively as opiate users. Innovative care models involving assertive outreach, adapted to the unique profile of stimulant users, may prove useful in reaching this difficult-to-engage sub-group of PWID. Research conducted in Rotterdam, Netherlands illustrated that such models can have positive impacts on treatment engagement, and physical and mental health among chronic high-risk crack cocaine users who were previously inadequately engaged in care (Henskens et al., 2008).

4.3 Associations of sedative-hypnotic use patterns with suicide attempt

In our study, chronic use of sedative-hypnotics was associated with approximately two-fold greater odds of reporting a suicide attempt, finding that is consistent with a previous study conducted among PWID (Backmund et al., 2011). Given that nearly half of participating PWID reported using sedative-hypnotics, regular screening regarding the use of such drugs in this population is deemed necessary.

A number of explanations could account for this finding. First, the elevated odds of suicide attempt among PWID using sedative-hypnotics could reflect an attempt to self-medication as a result of an underlying psychiatric comorbidity (Rigg and Ibanez, 2010). In our study, chronic use of sedative-hypnotics remained associated with suicide attempt even after controlling for the presence of a diagnosed psychological condition. Though, it is possible that our definition missed conditions that have never been clinically diagnosed. Second, finding could also be attributed to the disinhibiting properties of certain sedatives. Increased impulsivity and aggressive behavior following use of these drugs has been reported in some individuals (5-10%),

which may lead to a reduced threshold for taking action on suicidal thoughts. Finally, the observed positive association with attempted suicide may also reflect easy access to a common means for attempting suicide (Darke and Ross, 2002).

4.4 Associations of psychosocial stressors with suicide attempt

Among psychosocial stressors, high-injection frequency and history of a diagnosed psychological disorder were found to be positively associated with suicide attempt. The association with high injection frequency may be reflective of a sub-group of PWID who has a more drug-affected lifestyle and therefore, is more vulnerable to experiencing multiple risk factors for suicidal behaviors (Harris et al., 2013). The role of psychological distress in elevating the risk of suicidal behaviors is well-established (Cavanagh et al., 2003). Given the preponderance of psychological disorders among drug-using populations, mental health assessment should constitute an integral part of addiction treatment and community-based support services.

4.5 Limitations

Our findings must be considered in light of several limitations. Given the observational nature of our study and the absence of information regarding the sequence of events, causal inferences regarding the associations between substance use patterns and suicide attempt cannot be made. While the socio-demographic and drug use characteristics of participants are, by and large, reflective of the PWID population in Quebec (Public Health Agency of Canada, 2006), the HEPCO cohort is not a random sample, thereby limiting the generalisability of our findings. Moreover, as data for this study were collected through self-report, social desirability bias might arise as a result of eliciting information on socially sensitive behavior, though self-reported data collected from drug-using populations appear to be generally reliable and valid (Darke, 1998).

Furthermore, though we controlled for markers of psychological distress, results should be interpreted with caution given the absence of validated instruments assessing mental health. The lack of detailed characteristics of suicide attempts (e.g. severity of attempt) also limited our ability to identify specific factors relevant to different types of suicidal behaviors. Finally, other factors previously linked to suicidal behaviors, including childhood abuse and a family history of suicide (Hawton and van Heeringen, 2009), were not measured in our study, and therefore, residual confounding may explain the observed associations with attempted suicide.

4.6 Conclusion

Altogether, our study points toward a unique link between stimulant use and suicide attempt that does not seem to pertain to use of opioids, thereby providing preliminary evidence that distinct substance use patterns may play a role in shaping PWID's vulnerability to suicidal behaviors. Although further research is needed to delineate the possible direction of causality between substance use and suicide attempt, findings suggest that stimulant-using PWID should constitute a prime focus of suicide prevention efforts among the broader injecting community. Future studies coupling behavioral and basic sciences may be fruitful in better understanding the neurobiological, behavioral and social factors that possibly work to increase the risk of suicide attempt in this group. Finally, as simultaneous use of multiple substances is a common behavior among drug-using populations, future research should focus on examining the role of substances overlap in relation to suicidal behaviors.

References

Backmund, M., Meyer, K., Schutz, C., Reimer, J., 2011. Factors associated with suicide attempts among injection drug users. Subst. Use Misuse 46, 1553-1559.

Badiani, A., Belin, D., Epstein, D., Calu, D., Shaham, Y., 2011. Opiate versus psychostimulant addiction: the differences do matter. Nat. Rev. Neurosci. 12, 685-700.

Britton, P.C., Conner, K.R., 2010. Suicide attempts within 12 months of treatment for substance use disorders. Suicide Life Threat. Behav. 40, 14-21.

Bruneau, J., Roy, E., Arruda, N., Zang, G., Jutras-Aswad, D., 2012. The rising prevalence of prescription opioid injection and its association with hepatitis C incidence among street-drug users. Addiction 107, 1318-1327.

Cavanagh, J.T., Carson, A.J., Sharpe, M., Lawrie, S.M., 2003. Psychological autopsy studies of suicide: a systematic review. Psychol. Med. 33, 395-405.

Center for Substance Abuse Treatment, 2008. Substance abuse and suicide prevention: evidence and implications- A white paper. Substance Abuse and Mental Health Services Administration, Rockville, Maryland.

Christiansen, E., Jensen, B.F., 2007. Risk of repetition of suicide attempt, suicide or all deaths after an episode of attempted suicide: a register-based survival analysis. Aust. N. Z. J. Psychiatry 41, 257-265.

Ciccarone, D., 2011. Stimulant abuse: pharmacology, cocaine, methamphetamine, treatment, attempts at pharmacotherapy. Prim. Care. 38, 41-58, v-vi.

Dackis, C.A., O'Brien, C.P., 2001. Cocaine dependence: a disease of the brain's reward centers. J. Subst. Abuse Treat. 21, 111-117.

Darke, S., 1998. Self-report among injecting drug users: a review. Drug Alcohol Depend. 51, 253-263; discussion 267-258.

Darke, S., Degenhardt, L., Mattick, R., 2007. Mortality amongst Illicit Drug Users. Epidemiology, Causes and Intervention. Cambridge University Press, Cambridge, New York.

Darke, S., Hall, W., 1995. Levels and correlates of polydrug use among heroin users and regular amphetamine users. Drug Alcohol Depend. 39, 231-235.

Darke, S., Kaye, S., 2004. Attempted suicide among injecting and noninjecting cocaine users in Sydney, Australia. J. Urban Health 81, 505-515.

Darke, S., Mills, K., Teesson, M., Ross, J., Williamson, A., Havard, A., 2009. Patterns of major depression and drug-related problems amongst heroin users across 36 months. Psychiatry Res. 166, 7-14.

Darke, S., Ross, J., 2002. Suicide among heroin users: rates, risk factors and methods. Addiction 97, 1383-1394.

Darke, S., Williamson, A., Ross, J., Teesson, M., 2005. Attempted suicide among heroin users: 12-month outcomes from the Australian Treatment Outcome Study (ATOS). Drug Alcohol Depend. 78, 177-186.

Foers, J., Mathers, N., Glendenning, R., Keen, J., 2004. Stimulant use: an investigation into population characteristics and service provision. Fam. Pract. 21, 370-371.

Harris, J.L., Lorvick, J., Wenger, L., Wilkins, T., Iguchi, M.Y., Bourgois, P., Kral, A.H., 2013. Low-frequency heroin injection among out-of-treatment, street-recruited injection drug users. Journal of urban health : bulletin of the New York Academy of Medicine 90, 299-306.

Havens, J.R., Strathdee, S.A., Fuller, C.M., Ikeda, R., Friedman, S.R., Des Jarlais, D.C., Morse, P.S., Bailey, S., Kerndt, P., Garfein, R.S., 2004. Correlates of attempted suicide among young injection drug users in a multi-site cohort. Drug Alcohol Depend. 75, 261-269.

Hawton, K., van Heeringen, K., 2009. Suicide. Lancet 373, 1372-1381.

Health Canada, 2009. Suicide prevention. Available at: http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/diseases-maladies/suicide-eng.php. Accessed on 10 July, 2014.

Henskens, R., Garretsen, H., Bongers, I., Van Dijk, A., Sturmans, F., 2008. Effectiveness of an outreach treatment program for inner city crack abusers: compliance, outcome, and client satisfaction. Subst. Use Misuse 43, 1464-1475.

John, D., Kwiatkowski, C.F., Booth, R.E., 2001. Differences among out-of-treatment drug injectors who use stimulants only, opiates only or both: implications for treatment entry. Drug Alcohol Depend. 64, 165-172.

Keen, J., Rowse, G., Mathers, N., Campbell, M., Seivewright, N., 2000. Can methadone maintenance for heroin-dependent patients retained in general practice reduce criminal conviction rates and time spent in prison? Br. J. Gen. Pract. 50, 48-49.

Kerr, T., Fairbairn, N., Tyndall, M., Marsh, D., Li, K., Montaner, J., Wood, E., 2007. Predictors of non-fatal overdose among a cohort of polysubstance-using injection drug users. Drug Alcohol Depend. 87, 39-45.

Kessler, R.C., Borges, G., Walters, E.E., 1999. Prevalence of and risk factors for lifetime suicide attempts in the National Comorbidity Survey. Arch. Gen. Psychiatry 56, 617-626.

Leri, F., Stewart, J., Tremblay, A., Bruneau, J., 2004. Heroin and cocaine co-use in a group of injection drug users in Montreal. J. Psychiatry Neurosci. 29, 40-47.

MacArthur, G.J., Minozzi, S., Martin, N., Vickerman, P., Deren, S., Bruneau, J., Degenhardt, L., Hickman, M., 2012. Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. BMJ 345, e5945.

Marshall, B.D., Galea, S., Wood, E., Kerr, T., 2011. Injection methamphetamine use is associated with an increased risk of attempted suicide: a prospective cohort study. Drug and alcohol dependence 119, 134-137.

Nosyk, B., Li, L., Evans, E., Huang, D., Min, J., Kerr, T., Brecht, M.L., Hser, Y.I., 2014. Characterizing longitudinal health state transitions among heroin, cocaine, and methamphetamine users. Drug Alcohol Depend. 140, 69-77.

Office of National Drug Control Policy, 2012. What America's users spend on illegal drugs, 2002-2006. Executive Office of the President, Washington, DC.

Public Health Agency of Canada, 2006. I-Track: Enhanced Surveillance of Risk Behaviors among People who Inject Drugs. Public Health Agency of Canada.

Rigg, K.K., Ibanez, G.E., 2010. Motivations for non-medical prescription drug use: a mixed methods analysis. J. Subst. Abuse Treat. 39, 236-247.

Rossow, I., Lauritzen, G., 1999. Balancing on the edge of death: suicide attempts and life-threatening overdoses among drug addicts. Addiction 94, 209-219.

Roy, A., 2001. Characteristics of cocaine-dependent patients who attempt suicide. Am. J. Psychiatry 158, 1215-1219.

Roy, A., 2002. Characteristics of opiate dependent patients who attempt suicide. J. Clin. Psychiatry 63, 403-407.

Roy, A., 2003. Characteristics of drug addicts who attempt suicide. Psychiatry Res. 121, 99-103.

Roy, A., 2010. Risk factors for attempting suicide in heroin addicts. Suicide Life Threat. Behav. 40, 416-420.

Sees, K.L., Delucchi, K.L., Masson, C., Rosen, A., Clark, H.W., Robillard, H., Banys, P., Hall, S.M., 2000. Methadone maintenance vs 180-day psychosocially enriched detoxification for treatment of opioid dependence: a randomized controlled trial. JAMA 283, 1303-1310.

Shearer, J., 2007. Psychosocial approaches to psychostimulant dependence: a systematic review. J. Subst. Abuse Treat. 32, 41-52.

Simon, O.R., Swann, A.C., Powell, K.E., Potter, L.B., Kresnow, M.J., O'Carroll, P.W., 2001. Characteristics of impulsive suicide attempts and attempters. Suicide Life Threat. Behav. 32, 49-59.

Spire, B., Lucas, G.M., Carrieri, M.P., 2007. Adherence to HIV treatment among IDUs and the role of opioid substitution treatment (OST). The International journal on drug policy 18, 262-270.

Volkow, N.D., Chang, L., Wang, G.J., Fowler, J.S., Leonido-Yee, M., Franceschi, D., Sedler, M.J., Gatley, S.J., Hitzemann, R., Ding, Y.S., Logan, J., Wong, C., Miller, E.N., 2001. Association of dopamine transporter reduction with psychomotor impairment in methamphetamine abusers. Am. J. Psychiatry 158, 377-382.

Volkow, N.D., Wang, G.J., Fowler, J.S., Logan, J., Gatley, S.J., Hitzemann, R., Chen, A.D., Dewey, S.L., Pappas, N., 1997. Decreased striatal dopaminergic responsiveness in detoxified cocaine-dependent subjects. Nature 386, 830-833.

Wilcox, H.C., Conner, K.R., Caine, E.D., 2004. Association of alcohol and drug use disorders and completed suicide: an empirical review of cohort studies. Drug Alcohol Depend. 76 Suppl, S11-19.

Wines, J.D., Jr., Saitz, R., Horton, N.J., Lloyd-Travaglini, C., Samet, J.H., 2004. Suicidal behavior, drug use and depressive symptoms after detoxification: a 2-year prospective study. Drug Alcohol Depend. 76 Suppl, S21-29.

Zeger, S.L., Liang, K.Y., Albert, P.S., 1988. Models for longitudinal data: a generalized estimating equation approach. Biometrics 44, 1049-1060.

Table 1: Descriptive characteristics of the study sample at baseline, stratified by whether or not participants experienced a suicide attempt in the previous six months (N=1,240 participants)

Category	Total participants N=1240 n (%)	Attempted suicide N=71 n (%)	Did not attempt suicide N=1169 n (%)	*p*-value [a]
Socio-demographic factors				
Age				
Median (IQR)	39.1 (30.2 - 45.6)	38.7 (29.2-49.4)	39.1 (30.3 – 45.6)	0.110
Gender				
Male	1038 (83.7)	52 (73.2)	983 (84.3)	0.014
Female	202 (16.3)	19 (26.8)	183 (15.7)	
Completed high-school education				
Yes	746 (60.2)	42 (59.2)	704 (60.2)	0.858
No	494 (39.8)	29 (40.8)	465 (39.8)	
Substance use patterns past six months [b]				
Cocaine				
Chronic	693 (56.7)	44 (62.9)	649 (56.2)	0.408
Occasional	369 (30.1)	20 (28.6)	349 (30.2)	
None	162 (13.2)	6 (8.6)	156 (13.5)	
Amphetamine				
Chronic	31 (2.5)	5 (7.2)	26 (2.3)	0.019
Occasional	163 (13.3)	12 (17.4)	151 (13.1)	
None	1029 (84.1)	52 (75.4)	977 (84.7)	
Opioids				
Chronic	436 (36.2)	31 (44.9)	405 (35.7)	0.059
Occasional	254 (21.1)	18 (26.1)	236 (20.8)	
None	515 (42.7)	20 (29.0)	495 (43.6)	
Sedative-hypnotics				
Chronic	284 (23.3)	31 (44.3)	253 (22.0)	<0.001
Occasional	225 (18.4)	10 (14.3)	215 (18.7)	
None	711 (58.3)	29 (41.4)	682 (59.3)	
Cannabis				
Chronic	605 (49.6)	34 (49.3)	571 (49.6)	0.914
Occasional	278 (22.8)	17 (24.6)	261 (22.7)	
None	338 (27.7)	18 (26.1)	320 (27.8)	
Alcohol				

Chronic	99 (8.1)	6 (8.5)	93 (8.1)	0.966
Occasional	870 (71.0)	51 (71.8)	819 (71.0)	
None	256 (20.9)	14 (19.7)	242 (21.0)	
Psychosocial stressors				
Living in unstable housing conditions past six months				
Yes	525 (42.4)	25 (35.2)	500 (42.8)	0.209
No	714 (57.6)	46 (64.8)	668 (57.2)	
Prostitution past six months				
Yes	142 (11.5)	17 (23.9)	125 (10.7)	<0.001
No	1098 (88.5)	54 (76.1)	1044 (89.3)	
Incarceration past six months				
Yes	272 (22.0)	11 (15.5)	261 (22.4)	0.174
No	965 (78.0)	60 (84.5)	905 (77.6)	
Treatment for anxiety or depression past 6 months				
Yes	327 (26.4)	32 (45.1)	295 (25.2)	<0.001
No	913 (73.6)	39 (54.9)	874 (74.8)	
History of a psychological disorder				
Yes	348 (28.2)	37 (52.9)	311 (26.7)	<0.001
No	888 (71.8)	33 (47.1)	855 (73.3)	
Number of injections past month				
>30	626 (50.5)	41 (57.8)	585 (50.0)	0.208
≤30	614 (49.5)	30 (42.3)	584 (50.0)	
Age at first injection				
Median (IQR)	21.0 (17.0 – 28.0)	20 (17.0 - 28.0)	20 (17.0 – 29.0)	0.427
Duration of injection (years)				
Median (IQR)	12.6 (6.7 – 21.3)	11.1 (7.9 - 20.1)	12.7 (6.7 – 21.3)	0.669

Abbreviation: IQR, interquartile range

[a] *p*-value derived from the χ^2 test for categorical variables and the Mann-Whitney U-test for continuous variables

[b] Chronic and occasional use of cocaine, amphetamine, opioids, sedative-hypnotic drugs and cannabis: ≥26 and <26 days in the previous six months, respectively; Chronic and occasional use of alcohol: ≥90 and <90 days in the previous six months, respectively

Table 2: Associations between socio-demographic factors, substance use patterns and psychosocial stressors, and suicide attempt, by univariate generalized estimating equation analyses (N=5,621 observations)

Variable	Unadjusted Odds Ratio (95% Confidence Intervals)
Socio-demographic factors	
Age (per 5 year older)	0.90 (0.82 - 0.99)*
Male gender	0.47 (0.30 - 0.74)*
Completed high-school education	0.78 (0.55 - 1.10)
Substance use patterns past six months [a]	
Cocaine	
Chronic	2.13 (1.28 – 3.55)**
Occasional	1.85 (1.11 – 3.09)*
Amphetamine	
Chronic	2.73 (1.47 – 5.05)**
Occasional	1.88 (1.31 - 2.71)**
Opioids	
Chronic	1.74 (1.23 – 2.47)**
Occasional	1.64 (1.12 – 2.39)*
Sedative-hypnotics	
Chronic	2.89 (2.08 – 4.01)**
Occasional	1.87 (1.24 – 2.82)**
Cannabis	
Chronic	1.17 (0.80 – 1.70)
Occasional	1.25 (0.85 – 1.84)
Alcohol	
Chronic	1.35 (0.78 – 2.34)
Occasional	1.21 (0.87 – 1.67)
Psychosocial stressors	
Living in unstable housing conditions past six months	1.31 (0.97 - 1.78)
Prostitution past six months	2.06 (1.26 - 3.38)**
Incarceration past six months	1.32 (0.98 - 1.76)
Treatment for anxiety or depression past six months	2.56 (1.84 - 3.56)**
History of a psychological disorder	3.25 (2.39 - 4.41)**
>30 injections past month	1.48 (1.14 - 1.93)**
Age at first injection (per year older)	0.98 (0.96 - 1.01)
Duration of injection (per year older)	0.99 (0.97 - 1.01)

[a] The reference category is "none"

*p-value< 0.05; **p-value< 0.01

Table 3: Associations between substance use patterns and suicide attempt, with incremental introduction of variables pertaining to the socio-demographic and psychosocial stressors domains, by multivariate generalized estimating equation analyses (N=5,621 observations)

Variable	*Model A* *Substance use patterns* AOR (95% CI)	*Model B* *+Socio-demographic characteristics* AOR (95% CI)	*Model C* *+Psychosocial stressors* AOR (95% CI)
Substance use patterns past six months [a]			
Cocaine			
Chronic	2.09** (1.22 – 3.58)	2.31** (1.19 – 3.40)	1.97* (1.14 – 3.41)
Occasional	1.79* (1.06 – 3.04)	2.01** (1.37 – 3.91)	1.92* (1.12 – 3.30)
Amphetamine			
Chronic	2.35* (1.18 – 4.70)	2.04* (1.02 – 4.07)	1.96* (1.01 – 3.80)
Occasional	1.61* (1.10 – 2.35)	1.42 (0.97 – 2. 08)	1.41 (0.95 – 2.09)
Sedative-hypnotics			
Chronic	2.75** (1.96 – 3.86)	2.76** (1.94 – 3.92)	2.29**(1.61 – 3.26)
Occasional	1.65* (1.08 – 2.50)	1.61* (1.06 – 2.45)	1.48 (0.95 – 2.29)
Socio-demographic characteristics			
Age		0.91 (0.82 - 1.01)	0.91 (0.82 - 1.01)
Male gender		0.56* (0.34 - 0.93)	0.65 (0.40 - 1.07)
Psychosocial stressors			
Unstable housing conditions past six months			1.26 (0.90 - 1.76)
Prostitution past six months			1.20 (0.71 - 2.03)
History of a psychological disorder			2.84** (2.05 - 3.95)
>30 injections past month			1.35* (1.01 - 1.81)

[a] The reference category is "none"

Abbreviations: AOR, adjusted odds ratios; CI, confidence interval

*p-value< 0.05; **p-value< 0.01