

**Title: Anxiety, mood disorders and injection risk behaviors among cocaine users: results  
from the COSMO study**

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## **Abstract**

*Background and Objectives:* Despite being common among cocaine users, mental health problems and their relationship with HIV and hepatitis C high risk injection behaviors are poorly documented. This study was undertaken to examine the relationships between mood and anxiety disorders and the sharing of drug injection equipment among cocaine users who inject drugs.

*Methods:* The sample was drawn from a prospective cohort study and comprises 387 participants. The outcome of interest was "sharing injection material" in the past three months. The presence of mood and anxiety disorders during the past year was assessed using the CIDI questionnaire. Statistical analyses were conducted on baseline data using logistic regression.

*Results:* Most participants were male (84.5%) and were aged 25 or over (92.2%); 43.0% qualified for an anxiety disorder diagnosis and 29.3% for a mood disorder diagnosis. Participants with anxiety disorders were more likely to share needles (Adjusted Odds Ratio (AOR): 2.13, 95%CI: 1.15-3.96) and other injection material (AOR: 1.81, 95%CI: 1.12-2.92). No significant association was found between mood disorders and sharing behaviors.

*Discussion and Conclusions:* Primary anxiety disorders but not mood disorders increases injection risk behaviors among cocaine users. These results bring to light another negative outcome of mental health comorbidity in this vulnerable population.

*Scientific Significance:* This study underlines the need to fine-tune therapeutic approaches targeting specific mental health problems in individuals with cocaine use disorders. Longitudinal studies that assess impulsivity and other correlates of psychiatric disorders are needed to examine underlying mechanisms of high risk injection behaviors in comorbid populations.

## **Introduction**

Cocaine is one of the major illicit drugs used internationally. According to the World Drug Report (2013), cocaine use is on the rise in many regions of the world including Africa, Eastern Europe, Oceania and several parts of Asia.<sup>1</sup> In North America and Western and Central Europe, over one percent of the adult population used cocaine in 2011. In Canada, consumption of cocaine in the past year varies greatly according to age, with prevalence of 2.7% for Canadians 15 to 24 years old, and of 0.3% for 25 and older cohort in 2010.<sup>2</sup>

Cocaine misuse is an important public health threat, especially when it comes to its role in the transmission of HIV and hepatitis C viruses (HCV).<sup>3-6</sup> This phenomenon is of major concern in Canada where problematic cocaine use remains one of the main risk factors in stake in HIV and hepatitis C epidemics, primarily among people who inject drugs (PWID).<sup>7</sup> In this regard, drug injection among cocaine users poses a significant challenge for harm reduction programs. Studies have shown that patterns of consumption are complex and dynamic among problematic cocaine users, particularly with respect to polysubstance use and routes of drug administration.<sup>8</sup> This significantly impacts risk taking behaviors which causes negative health outcomes among users.

Overall, illicit drug use disorders are associated with a high prevalence of mental health disorders.<sup>9-12</sup> Cocaine use disorders are specifically linked to increased prevalence of mood and anxiety disorders<sup>10</sup> which in turn are associated with altered cognitive functions involved in decision-making and at-risk behaviors.<sup>13</sup> Therefore, studying the relationships between mental

health problems and high-risk behaviors among cocaine users who inject drugs is of great clinical interest. Relatively few studies, mainly based on symptom assessment, have examined the relationship between mood and anxiety disorders and injection risk behaviors. Although studies often included cocaine users, none focused on this particular group.

According to a meta-analysis on depression and substance-related behaviors among PWID,<sup>14</sup> most studies relied on clinical samples of opioid users, mainly conducted in methadone treatment settings. Only 13 out of the 55 identified studies examined sharing behaviors, mainly needle sharing. The results indicated a significant but weak association with depression. Only few observational studies have examined the relationship between depression and injection risk behaviors using measurement tools that allow diagnosis of psychiatric disorders. In Canada, a multisite study of street-based opiate users showed that those suffering from a diagnosis of depression were more likely to share injection equipment than those who did not.<sup>15</sup> In the United States, a study conducted in Providence, Rhode Island, revealed that depression severity was associated with receptive needle sharing among PWID diagnosed with a depression.<sup>16</sup> In contrast, a diagnosis of primary major depression was not found to be associated with injection risk behaviors among young PWID in Chicago, Illinois.<sup>17</sup>

Inconsistent evidence exists regarding the relationship between anxiety and injection risk behaviors. In the United States, needle sharing was found positively associated with symptoms of increased anxiety<sup>18</sup> and anxiety or tension.<sup>19</sup> A positive association was also found between severity of anxious symptoms and several sharing behaviors including sharing needles, backloading, sharing filter/cookers, and sharing rinse water.<sup>20</sup> Conversely, one recent study

showed a negative association between anxiety symptoms and needle sharing among PWID in India.<sup>21</sup> Furthermore, in the young PWID study, although anxiety disorders were more prevalent among injectors who shared syringes, the association was not statistically significant.<sup>17</sup>

The available data does not allow to estimate the magnitude of the relationship between mood and anxiety disorders and high risk injection practices among cocaine users. This gap in the literature hampers the ability of clinicians to accurately assess potential significant predisposing factors of at-risk injection behaviors. Such information could also pave way to more targeted preventive interventions. This study was thus carried out to estimate the prevalence of mood and anxiety disorders and their relationship with high risk injection behaviors among street-based cocaine users who were concomitantly injecting drugs. We hypothesized that both mood and anxiety disorders would be positively associated with injection risk behaviors in this population.

The sample included in this analysis was drawn from a prospective cohort study of out-of-treatment cocaine users initiated in Montréal, Canada, which the aim was to examine the relationship between HIV/HCV risk behaviors and mental health. Of the 605 cocaine users who were recruited in the cohort, 387 reported drug injection in the three months prior to baseline and formed the sample for this investigation. Age and gender distribution of both the full sample and the sample included in the analyses were similar with mean age being respectively 39.4 years (SD: 11.1) and 39.8 years (SD: 10.4) and gender distribution, 86.0% and 84.5% males. Compared to participants reporting injection, mean age and gender distribution of participants denying injection (n=218) were also similar (38.7 years; SD : 12.2 and 88.5% males), and there was no statistical difference.

## **Materials and Methods**

Baseline data was collected between October 2010 and April 2013. The methodology was described in detail elsewhere.<sup>22</sup> To be eligible, participants needed to have used cocaine in the last month, either by smoking crack or by injection. They also had to speak French or English, be able to consent and be at least 14 years old. This research was approved by the ethical boards of the Faculty of medicine and health sciences of l'Université de Sherbrooke and the Centre Hospitalier de l'Université de Montréal.

Study participants were, for the most part, recruited in community-based programs located in downtown Montréal, including homelessness day programs, shelters, and needle exchange programs. After providing informed consent, participants underwent an interviewer-administered questionnaire lasting between 60 and 90 minutes. Interviews were conducted in a research office located in this same neighbourhood as recruitment sites. Participants were offered a 30\$ financial compensation for their time. For this investigation, we included only participants who reported drug injection in the three months prior to baseline.

### *Measurements*

The outcome of interest for this study was “sharing injection material” in the past three months. Sharing injection material was defined as using injection paraphernalia that had already been used by someone else. These could be either needles or other injection materials. The sharing of other injection materials included i) the sharing of rinse or dilution water, cookers or filters, ii) backloading/frontloading (defined as sharing drug using a syringe that has already been used by

another person) and iii) “doing a wash” (defined as injecting drug residues extracted from a cotton, a filter or a container used by another person). The “life history calendar” technique was used to help situate participants in time in order to minimise recall bias.<sup>23</sup> Recent life events were put on a visual calendar that was used to better define the time period assessed during the interview.

The main independent variables for this study were the presence of mood and anxiety disorders during the past year. The World Mental Health Composite International Diagnostic Interview (CIDI) version 2.1 was used in assessing mood disorder diagnoses (major depression, bipolar disorders and dysthymia).<sup>24</sup> The CIDIS developed by Kovess and colleagues was used to assess anxiety disorder diagnoses.<sup>25</sup> Both instruments are well-validated tools that can be administered by lay interviewers and produce psychiatric diagnoses according to the fourth version of the Diagnostic and Statistical Manual of Mental Health Disorders published by the American Psychiatric Association.<sup>26</sup> An inter-rater study of the CIDI has shown an excellent reliability with Kappa statistics of 0.9 and more for most diagnoses.<sup>27</sup> Furthermore, using the CIDI and CIDIS allowed us to distinguish primary disorders from substance-induced disorders. The CIDI (for each symptom) and CIDIS are designed to assess whether disorders are primary or induced by substance use. Subjects are asked whether symptoms always occur as a result of medication, drugs or alcohol and if this is the case, then they do not qualify for the diagnosis. This approach reduces the chance of mental disorder overdiagnosis in drug using populations. At the same time, only drug users whose symptoms occur always when they consumed, disqualify themselves for the disorder diagnosis which allows the possibility of eliciting primary mental disorders among drug users. In the general population, while there was some initial concerns that the CIDI

strategy would lead to underestimate prevalence of psychiatric disorders, this has proved not to be the case.<sup>28</sup>

Co-variables considered as potential confounders included age (younger than 25 years old versus older), gender, ethnicity (born in Canada versus outside), level of education (less than high school versus higher level), living with a partner, homelessness (defined as having lived or slept at least once in a shelter or in any place not intended for housing in the past 3 months), having an unstable income (defined as having a marginal or criminal source of income in the past 3 months), reporting being HIV-antibody positive or HCV-antibody positive and level of dependence to cocaine using the severity of dependence scale (SDS).<sup>29</sup> The SDS is a five items tool measuring the intensity of dependence to a drug over the past 3 months. The score ranges between 0 and 15. Cocaine dependence was determined by a SDS score of 4 or higher.<sup>30</sup>

### *Analyses*

Proportions of participants who qualified for each category of psychiatric disorders, either mood or anxiety disorders, were calculated. Two series of univariate logistic regression analyses were conducted to assess the association between each disorder and other covariates and 1) “needle sharing” and 2) “sharing of injection material other than needle”. Two-tailed tests were used. Then, multivariate models considering all variables with a p-value  $\leq 0.20$  in univariate analyses, were carried out. Following the purposeful selection procedure, significant variables with a p-value  $< 0.05$  and those with a confounding effect were kept in the final models. A variable was considered confounding if its removal from the model changed a significant coefficient by more than 20%. Interactions between each psychiatric disorder and HIV or HCV self-report status



were also examined. Adjusted odds ratios (AOR) and 95% confidence intervals were derived from the final models. SPSS 18.0 and R 2.14.2 softwares were used to perform the analyses.

## **Results**

The 387 participants who reported drug injection in the three months prior to baseline were mostly male (85.5%), aged 25 or older (92.2%) and born in Canada (96.6%) (table 1). Less than a fifth was living with a partner and two thirds had been homeless at least once in the past 3 months. Almost half of the sample had less than a high school diploma and three quarters had relied at least once on marginal or criminal sources of income in the past three months. An HCV-positive status was reported by 46.1%, while 17.4% reported being HIV-positive. More than half of participants had a high cocaine SDS score.

In the three months prior to study entry, the vast majority of participants injected powder cocaine or crack cocaine (92.0%), followed by prescriptions opioids (55.6%), heroin (37.7%) and speedballs (a mixture of heroin and cocaine; 16.3%). Other injected substances included stimulants other than cocaine, such as amphetamines or methamphetamines (9.3%), psychotherapeutic medications (anxiolytics, hypnotics or antipsychotic; 5.4%), synthetic drugs (ecstasy, ketamine, GHB or hallucinogens; 5.2%) and two other prescription drugs (0.6%). Overall, 61% of participants injected at least two drugs. With respect to risk-taking behaviors, almost a third of participants had shared at least one injection material (including needles) in the past three months (29.5%). Sharing of cookers, needles and rinse or dilution water were the three

most common sharing practices. “Doing a wash”, sharing of filters and backloading/frontloading were reported by 10% or less of the sample.

Mental health problems were frequent, with 43.0% of participants qualifying for anxiety disorders (phobic: 34.11%; panic: 17.45%; generalised anxiety: 16.93%) and 29.3% for mood disorders (major depression: 20.37%; bipolar: 8.09%; dysthymic : 3.39%). Results of univariate and multivariate logistic regression analyses are showed in Tables 2 and 3, respectively. Recent mood disorders were not associated to neither needle sharing or sharing of injection material other than needles during the past 3 months. However, in multivariate analyses, participants with recent anxiety disorders were more likely to share needles (AOR : 2.13, 95% CI : 1.15-3.96) and to share injection material other than needles (AOR : 1.81, 95% CI : 1.12-2.92) after adjusting for sociodemographic and serostatus co-variates.

## **Discussion**

Participants to this study were all active cocaine users who were also injecting drugs. Using validated instruments, we were able to identify some of their primary mental disorders, which was one of our main objectives. We also examined the relationship between mood and anxiety disorders and high-risk injection behaviors.

A diagnosis of recent mood disorder was found among 29.3% of participants whereas 43.0% had a diagnosis of recent anxiety disorders. There is much variability in the rates of mental disorders

reported among cocaine users in the literature. In a study carried out in a sample of cocaine users entering inpatient cocaine dependence treatment in Connecticut, 10% rates of recent mood and anxiety disorder diagnoses were documented using the Structured Clinical Interview for DSM Disorders.<sup>31</sup> Among out of treatment cocaine users, using the DIS, a study conducted in St. Louis, Missouri, found that 10% of participants were suffering of major depression.<sup>32</sup> In Spain, 43% of young out-of-treatment cocaine users that were administered the CIDI had a lifetime mental disorder.<sup>33</sup> The most common diagnosis was depression (37.5%) and a fifth of the sample had a recent mental disorder. These variations are probably due to methodological differences, including different diagnosis tools, recruitment strategies and study populations.

Our study found that the presence of a mood disorder diagnosis was not significantly associated with injection risk behaviors among cocaine users who inject drugs. This finding is consistent with that of a recent study showing that there was no association between primary major depression and injection risk behaviors among young PWID in Chicago.<sup>17</sup> It contrasts with the Canadian study that looked at the association between a diagnosis of depression and injection risk behaviors among street-based opiate users.<sup>15</sup> In this latter study, participants suffering from major depression were more likely than users without depression to share injection equipment, either needles or other paraphernalia. Similarly, studies based on depressive symptoms assessment showed that severe depressive symptomatology was associated with a small increase in the probability of needle sharing.<sup>14,21,34,35</sup> It was also the case for the sharing of cotton or cookers, but only among injectors with a co-occurrence of high boredom.<sup>35</sup>

The absence of a correlation between sharing and a primary mood disorder diagnosis in our study raises the possibility that high risk behaviors could be better explained by mood symptomatology than by an actual mood disorder diagnosis among cocaine users who inject drugs. The neurobiological correlates of chronic cocaine exposure and those of depression are very similar, suggesting that there may be a number of common etiological factors for these two disorders.<sup>36</sup> Furthermore, according to DSM-5, cocaine withdrawal is characterized by fatigue, change in appetite, dysphoria, sleep alteration, and psychomotor agitation or retardation, a syndrome that is very similar to depression, while many intoxication criteria mimic hypomania or mania (euphoria, tension, changes in sociability, psychomotor agitation). It is thus plausible that individuals with or without a diagnosis of primary mood disorders all show significant mood symptoms (with related neurobiological alterations) which, as reported in the literature, increase the risk of sharing behaviors. Unfortunately, we could not test this hypothesis within the current study.

There is a dearth of research on the relationship between anxiety and injection risk behaviors among PWID not in treatment, and the few published studies available show contradictory results.<sup>19-21,37</sup> Our results showed increased risk behaviors among PWID with a primary anxiety disorder, suggesting a specific contributions of anxiety that is not induced by substances. Anxiety symptoms induced by stimulants are often panic-like or similar to generalized anxiety, which thus can be observed in both users with and without a primary disorder. However, as opposed to mood disorders, specific symptoms linked to primary specific anxiety disorders (eg phobia) rarely occurs in the context of cocaine use alone. They could potentially explain the differences observed in our study among users with a diagnosis of primary anxiety disorders and

those without. Investigators have proposed several underlying mechanisms for the association between anxiety disorders and injection risk behaviors. Impulsivity, high tension or low self-efficacy could be among the factors that jeopardize the capacity of drug injectors to have safe injection practices.<sup>16</sup> Studies looking at the contribution and impact of each specific anxiety disorders may thus prove to be critical in order to truly address this research question.

A major strength of this study is the accrual of a large sample of out-of-treatment chronic cocaine users who are often underrepresented in studies on mental health and injection risk behaviors. Another strength is that participants were administered a well-validated tool allowing for the assessment of mental disorder diagnoses in the context of an epidemiological study. Data collection by interview-administered questionnaires, using self-report information may have led to the minimization of certain stigmatized behaviors and a recall bias, which is a study limitation. Our study may not be generalized to other settings since female users accounted for only 15.5% of the sample. However these statistics are not surprising because they correspond to figures observed in other adult street-based populations in our region.<sup>38</sup> Multicenter studies are needed to recruit sufficient numbers of street-based female cocaine users and achieve better representation of this vulnerable population. Finally, the cross-sectional design could not ascertain causality. The longitudinal follow-up of this cohort will help better understand the direction of the association, adding a temporal consideration to the analyses.

## **Conclusion**

The results of this study underline the need to fine-tune our therapeutic approaches targeting individuals with mental health problems and cocaine use disorders. It certainly challenges the common practice of “wait and see”, an approach that suggests to wait before intervening on anxiety because it is thought to be substance-induced until proven otherwise. On the contrary, our results suggest that interventions that decrease anxiety in cocaine dependent individuals should be developed to evaluate their ability to alleviate risky behaviors. Studies examining the specific chronology of anxiodepressive symptoms and risky behaviors could help to elucidate the main focus and timing of such potential new approaches. Exploring which neurobiological correlates of anxiodepressive symptoms and chronic cocaine exposure are involved and mediate the behaviors leading to risk-taking could also help to develop targeted intervention. Overall, the ability to conduct longitudinal studies that assess simultaneously multiple domains, correlates and dimensions of psychiatric disorders (e.g. biological markers, cognitive testing, personality traits) could be tremendously helpful to successfully move forward in understanding and addressing the destructive combination of substance use, mental health problems and risky behaviors.

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## **Declaration of Interest**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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**Table 1.** Sociodemographic characteristics, serostatus, mental health disorders and drug injection material sharing of study participants at study entry (n=387).

	n	%
<b>Sociodemographic characteristics</b>		
Gender, female	60	15.5
Age $\geq$ 25 years old	357	92.2
Born outside Canada	13	3.4
Less than high school	186	48.1
Living with a partner <sup>†</sup>	60	15.5
Had $\geq$ 1x an unstable source of income <sup>†</sup>	284	73.4
Mainly homeless <sup>†</sup>	245	63.3
<b>Serostatus</b>		
Report an HIV-positive status <sup>a</sup>	67	17.4
Report an HCV-positive status <sup>b</sup>	177	46.1
<b>Mental health disorders</b>		
Anxiety disorders <sup>b‡</sup>	165	43.0
Mood disorders <sup>c‡</sup>	112	29.3
<b>Dependence to cocaine</b>		
High SDS score ( $\geq$ 4) <sup>b</sup>	224	58.3
<b>Drug injection material sharing</b>		
Needle sharing <sup>a†</sup>	58	15.0
Sharing of cookers <sup>a†</sup>	61	15.8

Sharing of filters <sup>a†</sup>	35	9.1
Sharing of rinse or dilution water <sup>a†</sup>	48	12.4
Backloading/ Frontloading <sup>a†</sup>	27	7.0
“Doing a wash” <sup>a†</sup>	39	10.1
Sharing of injection material other than needles <sup>a†</sup>	95	24.6
Sharing of injection material including needles <sup>a†</sup>	114	29.5

<sup>a</sup>1 missing value, <sup>b</sup>3 missing values; <sup>c</sup>5 missing values; <sup>†</sup>Past 3 months; <sup>‡</sup>Past 12 months.

“Doing a wash”, injection drug residues extracted from a cotton, a filter or a container used by another person; sharing of injection material, injection material sharing including dilution water, cookers, filters, sharing while backloading/frontloading and “doing a wash”.

**Table 2.** Univariate logistic regression analyses of correlates of drug injection material sharing behaviors (n=387 )

	No n (%)	Yes n (%)	OR (95%CI)	P*
<b>Needle sharing, past 3 months</b>				
Mood disorders <sup>‡</sup>	96 (85.7)	16 (14.3)	0.93 (0.50 to 1.73)	0.812
Anxiety disorders <sup>‡</sup>	129 (78.2)	36 (21.8)	2.49 (1.40 to 4.42)	0.002
Gender, female	45 (75.0)	15 (25.0)	2.19 (1.13 to 4.27)	0.019
Age ≥25 years old	309 (86.6)	48 (13.4)	0.30 (0.13 to 0.67)	0.005 <sup>†</sup>
Born outside Canada	10 (76.9)	3 (23.1)	1.74 (0.46 to 6.50)	0.424 <sup>†</sup>
Less than high school	159 (85.9)	26 (14.1)	0.86 (0.49 to 1.51)	0.608
Living with a partner	41 (68.3)	19 (31.7)	3.41 (1.80 to 6.46)	<0.001
Unstable source of income	237 (83.7)	46 (16.3)	1.47 (0.75 to 2.91)	0.263
Homelessness	200 (82.0)	44 (18.0)	2.01 (1.06 to 3.82)	0.030
Knowledge HIV-positive status	50 (74.6)	17 (25.4)	2.36 (1.24 to 4.49)	0.007
Knowledge HCV-positive status	142 (80.2)	35 (19.8)	1.96 (1.11 to 3.47)	0.019
High SDS score (≥4)	184 (82.1)	40 (17.9)	1.70 (0.94 to 3.10)	0.079
<b>Sharing of injection material other than needle, past 3 months</b>				
Mood disorders <sup>‡</sup>	83 (74.1)	29 (25.9)	1.08 (0.65 to 1.78)	0.780

Anxiety disorders <sup>‡</sup>	112 (67.9)	53 (32.1)	1.98 (1.24 to 3.17)	0.004
Gender, female	41 (68.3)	19 (31.7)	1.52 (0.84 to 2.78)	0.167
Age $\geq$ 25 years old	275 (77.0)	82 (23.0)	0.37 (0.17 to 0.79)	0.009
Born outside Canada	10 (76.9)	3 (23.1)	0.92 (0.25 to 3.40)	>0.999 <sup>†</sup>
Less than high school	145 (78.4)	40 (21.6)	0.73 (0.46 to 1.17)	0.191
Living with a partner	36 (60.0)	24 (40.0)	2.39 (1.34 to 4.28)	0.003
Unstable source of income	206 (72.8)	77 (27.2)	1.77 (1.00 to 3.13)	0.050
Homelessness	179 (73.4)	65 (26.6)	1.36 (0.83 to 2.22)	0.225
Knowledge HIV-positive status	47 (70.1)	20 (29.9)	1.40 (0.78 to 2.52)	0.254
Knowledge HCV-positive status	123 (69.5)	54 (30.5)	1.77 (1.11 to 2.82)	0.017
High SDS score ( $\geq$ 4)	153 (68.3)	71 (31.7)	1.25 (0.80 to 1.96)	0.326

\*P-Value by Pearson chi-square test unless indicated otherwise; <sup>†</sup>P-Value by Fisher's exact test. <sup>‡</sup>Past 12 months.

OR: Odd Ratio; CI: Confidence Interval.



**Table 3.** Multivariate logistic regression analyses of the association between material sharing outcomes and anxiety disorders, accounting for sociodemographic and serostatus co-variates.

	Sharing of injection material					
	Needle sharing, past 3 months			other than needle, past 3 months		
	AOR	95% CI	<i>P</i>	AOR	95% CI	<i>P</i>
Anxiety disorders <sup>†</sup>	2.13	1.15 to 3.96	0.017	1.81	1.12 to 2.92	0.016
Age ≥25 years old	0.29	0.11 to 0.73	0.008	0.38	0.17 to 0.84	0.017
Living with a partner	5.08	2.44 to 10.59	<0.001	2.31	1.27 to 4.18	0.006
Homelessness	3.25	1.52 to 6.95	0.002	-	-	-
Knowledge HIV- positive status	4.18	2.01 to 8.68	<0.001	-	-	-
Knowledge HCV- positive status	-	-	-	1.83	1.13 to 2.98	0.014
Constant	0.08	-	<0.001	0.39	-	0.024

AOR: Adjusted Odd Ratio; CI: Confidence Interval. †Past 12 months