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Daily heroin injection and psychiatric disorders: a cross-sectional survey among People Who Inject Drugs (PWID) in Haiphong, Vietnam

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Abstract

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Contributors:

NN, DCDJ, DL, LM, SML and OKTH conceptualized the study. NN, DCDJ, LM, SML, OKTH, HDT, KPM, DL, JPM designed the questionnaires. SML, HDT, KPM, TNTTB, GHT, VVH, TLN, DR, CQ, HQD participated in the implementation of intervention, supervised the work with the Community Based Organizations and the data collection. PT and RV performed the data analysis with input from SML, LM and NN. SML drafted the manuscript, LM, NN, DCDJ, PT, JPM edited the manuscript, NN, DCDJ, LM, HDT, KPM, JF, PT, JPM provided critical revisions. All authors have approved the final version of the paper for submission.

Conflict of interest:

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Background: Psychiatric comorbidities are frequent among people who inject drugs, they are associated with a poorer prognosis and need to be addressed. Their interaction with daily heroin injection requires clarification.

Methods: A cross-sectional survey was conducted among PWID recruited in the city of Haiphong, Vietnam, by respondent-driven sampling. The inclusion criteria were age 18 or older and current injection drug use, verified by skin marks and positive urine tests for heroin or methamphetamine. Data on socio-demographic characteristics, drug use, sexual behaviour and access to treatment were collected using face-to-face questionnaires by trained interviewers. PWID were screened by trained psychiatrists for depression, psychotic disorder and suicidality, using the MINI questionnaire.

Results: 418 participants were included in the analyses. All were injected heroin users, 21% were diagnosed with a current major depressive disorder, 15% with a current psychotic disorder and 12% presented a suicide risk. In the bivariate analyses, regular meth use, cannabis use and ketamine use were positively associated with presenting at least one psychiatric condition while daily heroin injection and being currently treated with methadone were negatively associated. In the multivariate model, poly-substance use was positively associated with depression (methamphetamine and drinking in addition to heroin) and psychotic disorder (methamphetamine and/or hazardous drinking in addition to heroin) while daily heroin injection and current methadone treatment were negatively and independently associated with depression and psychotic syndrome.

Conclusions: Our survey confirms the burden of methamphetamine use and the protective effect of methadone but also a possible protective effect of daily heroin injection.

Keywords

Methamphetamine; Heroin; Psychosis; Depression; Dual Disorder

1. Introduction

Psychiatric comorbidities are very common among drug users and are associated with a poor prognosis of both psychiatric and substance-use disorders, with little chance of recovery (Buckley and Brown, 2006; Cuffel, 1996; EMCDDA, 2015; Kessler, 2004; Kessler et al., 1996). This is a key issue for national and international drug policies (EMCDDA, 2015). The most common disorders are mood, anxiety and personality disorders (Compton et al., 2007; Kingston et al., 2017; Regier et al., 1990) but there are considerable variations across study populations, the instruments used and the drugs considered (Kingston et al., 2017; Schuckit, 2006) raising the question of the nature of the links between substance use and psychiatric disorders.

Primary/independent psychiatric disorders can be defined as psychiatric conditions observed in the absence of any other major diagnosis for a given time interval, often preceding the substance use disorder. The mental disorder leads to the onset of substance use disorder possibly through increased exposure to drug use and self-medication. The second possibility is that substance use disorders induce psychiatric disorders through a combination of biological and environmental mechanisms. Common causes (genetic, environmental etc.)

can also underpin the two disorders, as is the case for nicotine dependence and depression. The two disorders can be independent (de Graaf et al., 2002; Kessler, 2004; Schuckit, 2006). The prevalence of psychiatric disorders is systematically higher among people who use drugs than in the general population, and a wide range of drugs are involved in the onset of mood disorders. Cannabis and stimulants are specifically associated with drug-induced psychotic disorders (Lev-Ran et al., 2012; Schuckit, 2006). In the last few years, methamphetamine use has dramatically increased in Asia, with major public health consequences, including exposure to HIV risk, social harm and frequent psychiatric complications (Darke et al., 2008; Degenhardt et al., 2010; Marshall and Werb, 2010; McKetin et al., 2019; Salo et al., 2011). The prevalence of current psychosis among methamphetamine users is 11 times higher than in the general population and around 1/4 of regular methamphetamine users experience clinically significant psychotic symptoms (McKetin et al., 2006). A recent meta-analysis confirmed the strong link between methamphetamine use and psychosis, in addition to associations with violence, depression and suicidality (McKetin et al., 2019).

The role of opioid use is more controversial. Opioid use is rarely described as a risk factor for drug-induced psychotic disorder (Arunogiri et al., 2018; Dalmau et al., 1999; Fiorentini et al., 2011). Overall, substance-induced conditions are observed less frequently among opioid-dependent individuals (Schuckit, 2006). They could be related to social impairment, stigma, or comorbidities associated to drug injection (HIV, HCV) more than the biological effects of opioids (Levintow et al., 2019; Li et al., 2013; Nguyen et al., 2019; Tomori et al., 2014). Among opioid-dependent patients, methadone and buprenorphine, which are opioid agonists, are associated with improved quality of life and mental health (Teesson et al., 2006; Tenore, 2008; Ward et al., 1999; Xiao et al., 2010) through biological stabilization, and also a rapid improvement of living conditions.

Suicide and suicide attempts are also strongly associated with substance misuse with a clear overlap between suicide and overdose, reaching up to 50% overdoses among subjects in addiction treatment involving suicidal intent (Bohnert et al., 2010; Gicquelais et al., 2020).

The objective of the present study was to describe the prevalence of depression, psychotic syndrome and suicide risk among people who inject heroin, and the associated factors, in order to design an improved community-based mental health intervention to prevent and treat the psychiatric complications of drug use. The role of daily heroin injection was particularly investigated, as it remains unclear in the literature.

2. Material and methods

2.1 Design and participants

The DRIVE RDS bio-behavioral survey was conducted from October 2019 to January 2020 among PWIDs in Hai Phong. Participants were recruited using a standard RDS strategy (Heckathorn, 1997, 2002) with twenty initial “seeds” who were each given three coupons to distribute to potentially eligible participants (details of the sampling strategy have been previously described (Des Jarlais, D. et al., 2016)). The RDS eligibility criteria were (1) age 18 or older, (2) ability to provide informed consent, and (3) current injection drug use,

verified by skin marks and positive urine test for opiates or methamphetamines. Participants previously recruited in any step of the DRIVE project were allowed to participate in the RDS. The target sample size was 1500, but the recruitment of new participants slowed considerably five weeks into the survey. As a result, “snowball” recruiting was initiated (Biernacki P, 1981) where each participant was asked to recruit as many new participants as they could (up to 20). We continued to use the RDS coupon system to track recruitment. The RDS procedure took place in 2 offices of the Community-Based Organisations (CBO) participating in the project in Hai Phong. CBO members contributed to all study procedures, and after specific training, they recruited the seeds, registered participants, presented the study, determined eligibility, collected data (particularly on drug use and sexual behavior), paid honoraria and distributed coupons for further recruitment (Des Jarlais, D. et al., 2016). Participants received 150,000 VND (\$7.50 USD) compensation for their participation and (\$2.50 USD for each PWID recruited, with a maximum of 3) for recruiting new participants.

2.2 Psychiatric disorder variables

In this paper, psychiatric disorders include current major depressive disorder, current psychotic disorder and suicide risk screened for by trained psychiatrists from Hai Phong University of Medicine and Pharmacy using the Mini International Neuropsychiatric Interview (MINI 5.0.0) (Sheehan et al., 1998) which was translated into Vietnamese following a translation–back translation–pre-test strategy (Brislin, 1986; Flaherty et al., 1988; Ghimire, 2011; Pham Minh et al., 2018). The psychiatrists were present full time in each CBO site for 4 weeks and then half-time in each CBO site. They met all the participants who were also on site during their time of presence. They were trained by the research coordinators (international and national experts from the field of mental health). Participants diagnosed with a mental health disorder were offered a psychiatric follow-up on site.

2.3 Study questionnaire

Data was collected by trained interviewers using a face-to-face questionnaire on socio-demographic characteristics, injecting and sexual behaviors and drug use, and blood samples for HIV and HCV screening were taken. The variable “daily heroin use” referred to the last 30 days. “Regular methamphetamine use” referred to use at least 4 times in the past month. Hazardous and binge drinking in the last six months were assessed using the Audit-C questionnaire (Bush et al., 1998; Dawson et al., 2012). The variable “regular poly-substance use” was defined as the number of substances regularly consumed among the following: alcohol (Audit-C score of 3 or more for women and 4 for men, over the last six months), heroin (injected at least once a day in the past month) and methamphetamines (at least 4 times in the past month).

2.4 Laboratory testing

The blood samples were tested for HIV and HCV. HIV serology followed national guidelines including an initial rapid test using SD BIOLINE HIV 1/2 3.0 (Standard Diagnostic Inc., South Korea), coupled with confirmation using two other rapid tests (Alere Determine HIV 1/2 (Abbott Alere Medical Co., Japan, and VIKIA[®]HIV1/2, Biomerieux,

France). HCV serology was based on a rapid test SD BIOLINE HCV (SD standard Diagnostic Inc, South Korea)).

2.5 Ethical considerations

The study was approved by the Institutional Review Board of the Haiphong University of Medicine and Pharmacy (Vietnam) and the Icahn School of Medicine at Mount Sinai (USA). All PWIDs included in the study signed informed consent.

2.6 Statistical analysis

Participants in RDS who met the eligibility criteria but had already been enrolled in previous steps of the DRIVE project were excluded from our analyses, leaving only the DRIVE-naive subjects who had not experienced any kind of intervention, including the study-related mental health intervention.

After estimating the prevalence of current depression, psychotic disorder and suicidality, a bivariate analysis was conducted to compare the two PWID groups for each variable: those who presented a psychiatric disorder and those who did not (table 2). Then two multivariate models were run to further examine the association between the daily injection of heroin and diagnoses of a current psychotic disorder and major depressive disorder (table 3). In these multivariate models, the independent variables were “daily heroin injection”, “current methadone treatment”, “heroin use duration”, and “regular poly-substance use”. In order to estimate prevalence ratios, a log-binomial regression was used (Petersen and Daddens, 2008). The selection of independent variables included in the model was based on epidemiological relevance and not on a statistical criterion: since we chose to focus on the link between daily heroin use and psychotic disorder or major depressive disorder, factors with a potentially confounding effect on these associations were included (i.e. factors associated with both heroin use and psychiatric disorders). Sensitivity analyses were performed to estimate the robustness of the results; a multivariate model was run including regular methamphetamine use, cannabis use and hazardous drinking (based on the AUDIT-C score) as independent covariates, instead of a synthetic “regular poly-substance use” variable. Because snowball sampling added at the end of the survey violates RDS assumptions, sampling weights were not used in our analyses; nevertheless weighted prevalences for psychiatric disorders are presented in the text for information (using RDS-II weights (Volz E, 2008)). These analyses were performed with R software version 3.5.1 (R Core Team, 2016).

The threshold for statistical significance was set at $p < 0.05$.

3. Results

3.1 Overall population

Overall, 1339 subjects agreed to participate in the DRIVE RDS study and 1268 met the eligibility criteria. Among them, 978 were randomly screened for psychiatric disorders using the MINI questionnaire but 560 had already been enrolled in previous steps of the DRIVE

project. Hence, data for 418 PWID was analyzed, representing around 8% of the estimated total population of PWID in the city of Haiphong (Des Jarlais et al., 2018).

3.2 Participant characteristics and prevalence of current psychiatric disorder

The study population characteristics are summarized in Table 1. The mean age in our sample was 40.3 years and 95% of participants were male. All participants were using injected heroin and screened positive for heroin in their urine, 28% reported receiving methadone treatment at the time of the survey, 27% reported the use of street methadone (median [IQR], the number of days of street methadone use during the last 30 days was 2 [2,4]) and 50% screened positive for methadone in their urine. Methamphetamine use in the past month was reported by 44% of the participants and 22.7% reported regular methamphetamine use. Around 25% of the participants reported regular use of two substances and 4% reported 3 substances among the following: daily heroin injection, hazardous drinking and methamphetamine use 4 times during the last 30 days. 24% of the women and 12% of the men reported a past history of suicide attempt. Regarding the psychiatric assessment, 21.3% (95% CI = [17.6 – 25.5]) of all participants presented a current major depressive episode (weighted estimation using RDS-II weights = 22.4%). A psychotic disorder was identified for 15.1% [11.9 – 18.8] of the participants (weighted % = 15.3), and suicide risk was identified for 12.2% [9.4 – 15.7] (weighted % = 13.5). Finally, 32.8 % [28.4 – 37.4] of all participants presented at least one of the above-mentioned three psychiatric disorders (weighted % = 35.2).

Figure 1 shows the distribution of the different psychiatric disorders among those with at least one disorder (N=137).

Among PWID reporting regular methamphetamine use (4 times in last 30 days), 28% were diagnosed with a current psychotic disorder (vs. 10% for those using methamphetamine <4 times in the last 30 days), 29% with a major depressive episode (vs. 20%) and 20% with suicide risk (vs. 10%).

Among the PWID reporting daily heroin injection, 12% were diagnosed with a current psychotic disorder (vs. 21% for those injecting heroin less than daily), 18% with a major depressive episode (vs. 27%) and 13% with suicide risk (vs. 10%).

3.3 Bivariate analysis: factors associated with current psychiatric disorder

Participant characteristics in relation to their psychiatric disorder status are described in table 2. Regular methamphetamine use was positively associated with each of the psychiatric disorders we focused on in this study, and especially with a current psychotic disorder (among those who presented this disorder 42.9% reported regular methamphetamine use vs. 19.2% among those who did not, $p < 0.001$). Cannabis use was associated with both current major depressive episode and psychotic disorder. Alcohol misuse assessed by AUDIT-C was only associated with psychotic disorder (39.7% vs 24.2%, $p = 0.016$).

Interestingly, the daily use of heroin seemed negatively associated with both current major depressive episode and current psychotic disorder. Indeed, in the group showing depressive symptoms, 58.4 % reported daily use of heroin vs. 69.9% in the other group ($p = 0.054$).

Likewise, among subjects presenting a psychotic disorder 54% reported daily use of heroin vs. 69.9% among those who did not ($p = 0.02$).

3.4 Multivariate analysis: relationship between regular heroin use and psychotic disorder

Results from the two multivariate models are presented in Table 3. Participants who reported daily use of heroin were less likely to present a major depressive episode (prevalence ratio (PR) : 0.52, $p < 0.001$) or a current psychotic disorder (prevalence ratio : 0.3, $p < 0.001$) after controlling for current methadone treatment, heroin use duration, and regular poly-substance use. Finally, the use of two or three substances, including alcohol, heroin or methamphetamine was strongly associated with a current psychotic disorder (prevalence ratio of 2.77 [1.21 – 6.50] and 9.35 [3.50 – 24.94], respectively).

3.5 Sensitivity analyses

Our sensitivity analysis presented in Table 4 showed that the daily use of heroin was still negatively associated with current psychotic disorder (PR : 0.64, $p = 0.049$) and major depressive disorder (PR: 0.68, $p = 0.039$) after including regular methamphetamine use, cannabis use and alcohol misuse (based on AUDIT-C score) as control variables, instead of a synthetic “regular poly-substance use” variable.

4. Discussion

More than one third of the PWID participating in this survey were diagnosed with at least one disorder, around a quarter with a current major depressive episode and more than one sixth with a current psychotic disorder.

The prevalence of major depressive disorder was lower in our population sample than in many other studies conducted among PWID (Colledge et al., 2020; Iskandar et al., 2012) in which the prevalence of anxiety disorders and depression ranged from 4% to 53% and 18% to 72% respectively. However, one third of our subjects had already been treated with methadone, which is associated with lower depression rates (Pani et al., 2010), and two-thirds were injecting heroin every day, which is associated with lower prevalence of depression. Suicide risk was difficult to compare with other studies, as both the populations and the assessment of suicide risk differs considerably from one study to another (Colledge et al., 2020; Iskandar et al., 2012). Indeed, previous studies showed prevalence rates of suicidal ideation and suicide attempts ranging from 50 to 93% and 43 to 87% respectively (Iskandar et al., 2012). The prevalence of psychotic disorder was higher than in other studies, (for example a study by Iskandar et al. showed a prevalence of psychotic disorders of around 12% (Iskandar et al., 2012)), but in line with what is observed among subjects using methamphetamines (Arunogiri et al., 2020), and 69% of the participants reported methamphetamine use in the last 30 days.

In our study, regular heroin injection was negatively and independently associated with being diagnosed with a current psychotic disorder and a major depressive disorder, even after adjustment on the many possible confounding factors. Diacetylmorphine (heroin) is a strong, full opioid agonist that is used in a therapeutic context as maintenance treatment (heroin-assisted treatment) for severely dependent opioid users. Controlled studies

have shown that diacetylmorphine or diacetylmorphine plus methadone were superior to methadone alone on different outcomes, including quality of life, psychological health, and psychosocial functioning (Ferri et al., 2011; Haasen et al., 2007; Karow et al., 2010; Oviedo-Joekes et al., 2010; Reimer et al., 2011; Schafer et al., 2010; van den Brink et al., 2003). Shafer *et al.* concluded that psychiatric comorbidity should be an inclusion criterion for heroin-assisted treatment (Schafer et al., 2010).

Although the context of our study is far removed from a therapeutic context, it can nevertheless be assumed that PWID injecting heroin daily could draw benefit from heroin on their psychiatric symptoms.

The many benefits of methadone initiation among heroin-dependent injection drug users are well documented (Connock et al., 2007; Gowing et al., 2011; MacArthur et al., 2014; Marks et al., 2019; Mattick et al., 2009, 2014; Molero et al., 2018) and one benefit is the improvement in mental health status, particularly for depression, but also for psychosis (Deglon, 2008; Gossop et al., 2006; Maremmani et al., 2011; Ward et al., 1999). Increasing methadone doses for heroin-dependent subjects hospitalized for psychiatric emergencies was found to reduce their needs for anti-manic and antipsychotic drugs (Pacini, 2005). Cases of psychosis related to methadone withdrawal have been described (Cobo et al., 2006). Overall, while psychotic disorders are more frequent among drug users than in the general population (Lev-Ran et al., 2012; Regier et al., 1990), opioids are rarely identified as being responsible for psychotic disorders, unlike stimulants, alcohol or cannabis (Arunogiri et al., 2018; Dalmau et al., 1999; Fiorentini et al., 2011; Schuckit, 2006), thus raising the question of the chronology of the occurrence of psychotic symptoms compared to opioid use initiation. The hypothesis of an antipsychotic or modulatory effect of opioids on dopamine or on the neurotransmitter system that controls mood has been suggested (Deglon, 2008; Maremmani et al., 2014; Schmauss and Emrich, 1985; Tenore, 2008).

In Vietnam, heroin has been the predominant substance of abuse since the early 90s and is mainly injected, but stimulant use and particularly methamphetamine use have increased rapidly since the beginning of the 2000s to become a major public health concern today (Giang et al., 2013). In 2016, up to 50% of the people who inject drugs (PWIDs) in the city of Haiphong were also inhaling methamphetamines (Feelemyer et al., 2018) and methamphetamine use was reported by 77% of the young people (16–24) using drugs in the cities of Haiphong, Ho Chi Minh City and Hanoi (Michel et al., 2020). Methamphetamine use, and particularly regular methamphetamine use, was positively and strongly associated with psychiatric disorders in our study, as in previous studies (McKetin et al., 2019). The proportion of PWID with regular methamphetamine use and with psychotic symptoms observed in our study is alarming, but very similar to proportions found in other studies (approximately 25%) (McKetin et al., 2006). This emphasizes the dramatic public health consequences of methamphetamine use and the need to inform, prevent its trivialization and work on the representations associated with it. Many people who use drugs in Vietnam and elsewhere see methamphetamine as a trendy, fashionable “social” drug, inhaled and not injected, associated with sex and fun, and also as helping to cope with stress; this contrasts with heroin, which is primarily injected, thus exposing PWID to HIV and overdose, and

is associated with loneliness and being identified as a “junkie”(Degenhardt et al., 2010; Hobkirk et al., 2016; Liu et al., 2018; Michel et al., 2020; Noroozi et al., 2018).

Regular poly-substance use (i.e. the association of regular methamphetamine use, daily heroin injection and hazardous drinking) is associated with the highest prevalence ratios for all disorders. The association between alcohol use disorder and psychiatric comorbidities has been well established, for major depressive disorder as well as psychotic disorder (Castillo-Carniglia et al., 2019; Dalmau et al., 1999; Hasin et al., 2007; Hjemsæter et al., 2019). The deleterious cumulative effect of regular methamphetamine use and hazardous drinking is not surprising, as outlined in previously documented studies (Chen et al., 2003; Connor et al., 2014; Dalmau et al., 1999; Woules et al., 2013).

These findings have clinical implications. In order to prevent psychiatric complications among PWID, regular methamphetamine use should be targeted first, particularly when it is associated with hazardous drinking. Screening for both substances using self-report questionnaires and rapid psychiatric screening should be routinely implemented, and brief interventions proposed, mainly based on information and harm reduction messages. Access to methadone treatment needs to be facilitated and persistence of heroin injection during methadone treatment should not be sanctioned, but a more comprehensive support and harm reduction approach should be offered. Access to psychiatric interventions also needs to be organized for those exhibiting significant symptoms and could involve peer support in low-middle income countries (Patel et al., 2007; Pham Minh et al., 2018; Sunkel, 2012; WHO, 2013).

Some limitations of this study should be noted. We used a cross-sectional design, which did not allow us to establish temporal relationships across variables. Psychiatric problems can occur before or after the onset of a drug addiction or share the same risk factors; it is likely that the chronology could have consequences for the approach to treatment and for understanding of the relationship between drug use and the incidence of psychiatric disorders. Although RDS sampling remains a method of choice to investigate hidden populations such as PWID, caution is needed when interpreting results based on this method. The weighted proportion we calculated, while it was not perfect for dealing with representativeness bias (McCreesh et al., 2012), suggests that a slight underestimation of the disorders is possible. In addition, our conclusions are limited to the profile of our population sample which included only people who inject heroin. Extending these conclusions to other populations of people who use drugs would need further studies. Finally, we cannot rule out a social desirability bias in self-report of behaviors (the variables explored here were self-reported and could present under-reporting bias, etc.).

5. Conclusions

Our survey confirms the dramatic mental health consequences of methamphetamine use and concern about its association with hazardous drinking, but it also suggests a protective effect of regular heroin injection, particularly when methadone treatment has already been initiated. Taken together, these results pinpoint the importance of routine screening for methamphetamine use and mental health disorders among people who use drugs, with

community-based links to care in countries where psychiatric facilities are limited. It also suggests that in places where psychosocial interventions associated with methadone treatment are sparse, daily heroin use could potentiate methadone treatment and should not be sanctioned but rather associated with comprehensive support and harm reduction interventions.

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Abbreviations

CBO	Community-based organization
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
MINI	Mini international neuropsychiatric interview
PR	Prevalence ratio
PWID	People who inject drugs
USD	US dollars
VND	Vietnamese dong

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Highlights

- Regular heroin injection could be protective for depression and psychotic symptoms.
- Psychiatric burden of methamphetamine use is high.
- PWID treated with methadone are less often depressed.
- Regular polysubstance use is associated with higher rate of psychiatric disorders.

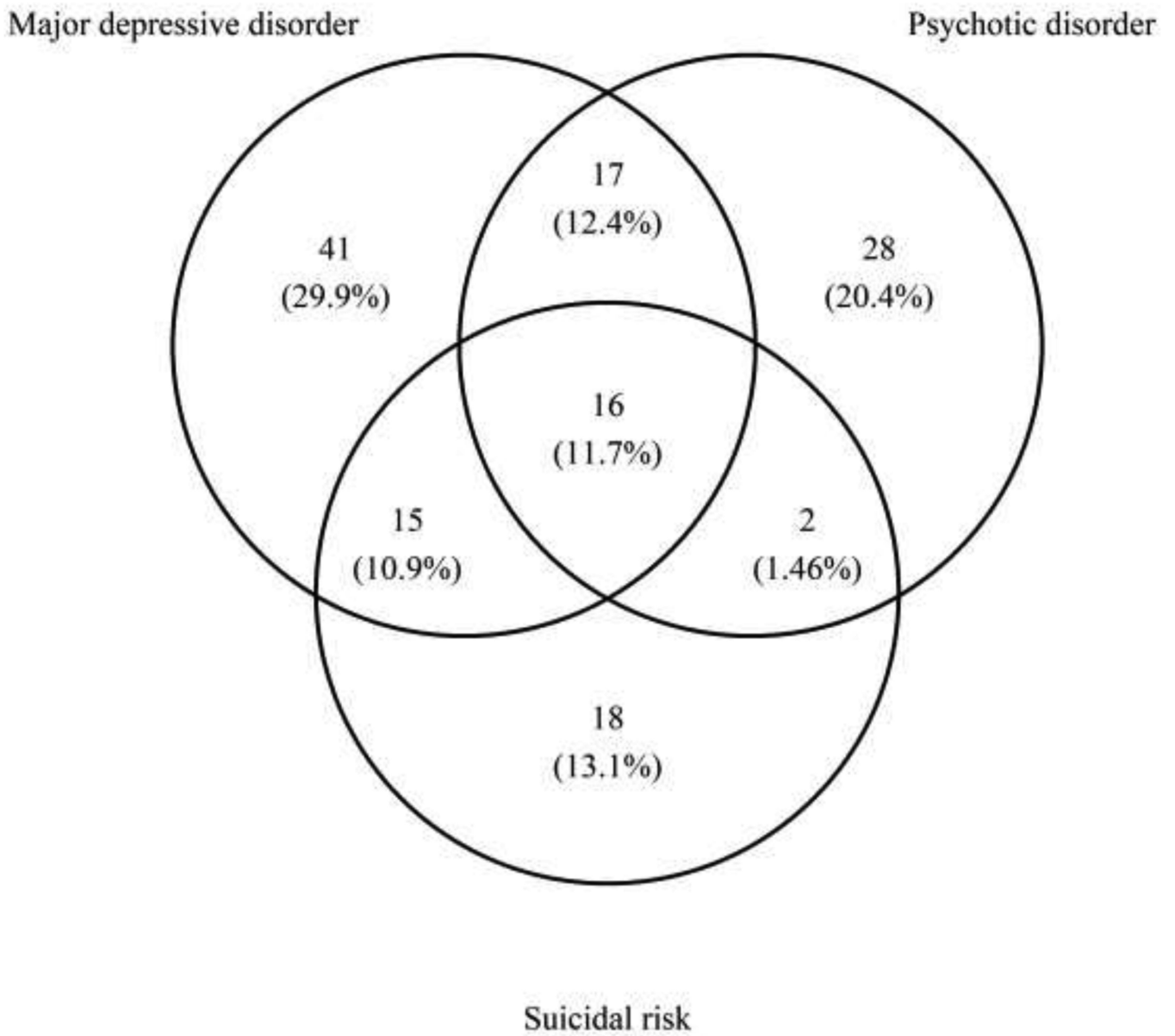


Fig. 1.
Venn Diagram for Psychiatric Disorders.

Table 1.

Participant characteristics (n = 418)

Socio-demographics	Age (mean (sd))	40.26 (8.69)
	Male (%)	397 (95.0)
	Female (%)	21 (5.0)
	Living with a partner (%)	168 (40.2)
	ID card (%)	313 (74.9)
	Health insurance (%)	169 (40.4)
	Sexual partner in the last 6 months (%)	253 (60.5)
Psychiatric disorder	Current major depressive episode (%)	89 (21.3)
	Current suicidality (%)	
	None	367 (87.8)
	Low	31 (7.4)
	Moderate	11 (2.6)
	High	9 (2.2)
	Suicidality (any level) (%)	51 (12.2)
	Lifetime suicide attempt (%)	26 (6.2)
	Current psychotic disorder (%)	63 (15.1)
	One disorder or more^a(%)	137 (32.8)
Drug/alcohol use	Methamphetamine use in the last 6 months (%)	268 (64.1)
	Methamphetamine use in the last 30 days (%)	184 (44.0)
	Regular methamphetamine use (4 times in the last 30 days) (%)	95 (22.7)
	Positive urine test for methamphetamine (%)	163 (39.0)
	Daily heroin use (in the past month) (%)	282 (67.5)
	Duration heroin use (%)	
	Less than 5 years	67 (16.0)
	5 to 10 years	119 (28.5)
	10 to 15 years	99 (23.7)
	15 years or more	133 (31.8)
	Cannabis use (%)	49 (11.7)
	Ketamine use (%)	26 (6.2)
	Street methadone use (%)	112 (26.8)
	Hazardous drinking (Audit-c score 3 in women and 4 in men) (%)	111 (26.6)
	Regular poly-substance use^b(%)	
	0	66 (15.8)
	1	233 (55.7)
2	102 (24.4)	
3	17 (4.1)	
Health	Positive serology for HCV (%)	287 (68.7)
	Positive serology for HIV (%)	71 (17.0)
	Past experience of overdose (%)	12 (2.9)
	Currently under methadone treatment (%)	132 (31.6)

Positive urine test for methadone (%)	223 (53.3)
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* Percentage (unless otherwise stated) taking into account the RDS sampling with RDS-II weights

^a one disorder or more among the following: major depressive episode, psychotic disorder, suicidality risk score > 0)

^b including daily heroin injection, regular methamphetamine use (≥ 4 times during the last 30 days), and alcohol misuse

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Table 2.

Participant characteristics according to psychiatric disorder (N=418)

	Current major depressive episode			Current psychotic disorder			Suicidality (any level)			One or more disorder		
	No	Yes	<i>p</i>	No	Yes	<i>p</i>	No	Yes	<i>p</i>	No	Yes	<i>p</i>
N =	329	89		355	63		367	51		281	137	
Age (mean (sd))	39.91 (8.55)	41.57 (9.14)	0.109	40.26 (8.59)	40.29 (9.31)	0.982	40.02 (8.55)	41.98 (9.57)	0.132	39.83 (8.53)	41.16 (8.98)	0.141
Male (%)	315 (95.7)	82 (92.1)	0.267	339 (95.5)	58 (92.1)	0.403	352 (95.9)	45 (88.2)	0.044	270 (96.1)	127 (92.7)	0.212
Living with a partner (%)	134 (40.7)	34 (38.2)	0.757	150 (42.3)	18 (28.6)	0.057	152 (41.4)	16 (31.4)	0.223	120 (42.7)	48 (35.0)	0.163
ID card (%)	245 (74.5)	68 (76.4)	0.813	269 (75.8)	44 (69.8)	0.399	275 (74.9)	38 (74.5)	1	212 (75.4)	101 (73.7)	0.794
Health insurance (%)	140 (42.6)	29 (32.6)	0.114	150 (42.3)	19 (30.2)	0.096	151 (41.1)	18 (35.3)	0.519	125 (44.5)	44 (32.1)	0.021
Sexual partner in the last 6 months (%)	210 (63.8)	43 (48.3)	0.011	216 (60.8)	37 (58.7)	0.86	225 (61.3)	28 (54.9)	0.469	178 (63.3)	75 (54.7)	0.114
Methamphetamine use in the last 6 months (%)	205 (62.3)	63 (70.8)	0.176	224 (63.1)	44 (69.8)	0.376	223 (60.8)	45 (88.2)	<0.001	168 (59.8)	100 (73.0)	0.011
Methamphetamine use in the last 30 days (%)	143 (43.5)	41 (46.1)	0.75	149 (42.0)	35 (55.6)	0.062	154 (42.0)	30 (58.8)	0.034	114 (40.6)	70 (51.1)	0.054
Regular methamphetamine use (< 4 times in the last 30 days) (%)	67 (20.4)	28 (31.5)	0.038	68 (19.2)	27 (42.9)	<0.001	76 (20.7)	19 (37.3)	0.014	52 (18.5)	43 (31.4)	0.005
Positive urine test for methamphetamine (%)	128 (38.9)	35 (39.3)	1	132 (37.2)	31 (49.2)	0.096	135 (36.8)	28 (54.9)	0.02	101 (35.9)	62 (45.3)	0.084
Daily heroin use (in the past month) (%)	230 (69.9)	52 (58.4)	0.054	248 (69.9)	34 (54.0)	0.02	245 (66.8)	37 (72.5)	0.504	199 (70.8)	83 (60.6)	0.047
Duration heroin use (%)			0.106 ^a			0.07 ^a			0.18 ^a			0.01^a
Less than 5 years	56 (17.0)	11 (12.4)		61 (17.2)	6 (9.5)		60 (16.3)	7 (13.7)		51 (18.1)	16 (11.7)	
5 to 10 years	95 (28.9)	24 (27.0)		102 (28.7)	17 (27.0)		106 (28.9)	13 (25.5)		82 (29.2)	37 (27.0)	
10 to 15 years	80 (24.3)	19 (21.3)		84 (23.7)	15 (23.8)		90 (24.5)	9 (17.6)		70 (24.9)	29 (21.2)	
15 years or more	98 (29.8)	35 (39.3)		108 (30.4)	25 (39.7)		111 (30.2)	22 (43.1)		78 (27.8)	55 (40.1)	
Cannabis use (%)	31 (9.4)	18 (20.2)	0.009	35 (9.9)	14 (22.2)	0.009	42 (11.4)	7 (13.7)	0.809	23 (8.2)	26 (19.0)	0.002
Ketamine use (%)	15 (4.6)	11 (12.4)	0.014	20 (5.6)	6 (9.5)	0.371	21 (5.7)	5 (9.8)	0.411	10 (3.6)	16 (11.7)	0.003
Street methadone use (%)	85 (25.8)	27 (30.3)	0.474	94 (26.5)	18 (28.6)	0.848	98 (26.7)	14 (27.5)	1	68 (24.2)	44 (32.1)	0.11
Hazardous drinking (Audit-c score < 3 in women and < 4 in men) (%)	84 (25.5)	27 (30.3)	0.438	86 (24.2)	25 (39.7)	0.016	96 (26.2)	15 (29.4)	0.746	68 (24.2)	43 (31.4)	0.149

	Current major depressive episode			Current psychotic disorder			Suicidality (any level)			One or more disorder		
	No	Yes	<i>p</i>	No	Yes	<i>p</i>	No	Yes	<i>p</i>	No	Yes	<i>p</i>
Lifetime suicide attempt (%)	15 (4.3)	11 (17.5)	<0.001	15 (4.3)	11 (17.5)	<0.001	0 (0.0)	26 (51.0)	<0.001	0 (0.0)	26 (19.0)	<0.001
Positive serology for HCV (%)	229 (69.6)	58 (65.2)	0.502	247 (69.6)	40 (63.5)	0.417	257 (70.0)	30 (58.8)	0.146	196 (69.8)	91 (66.4)	0.565
Positive serology for HIV (%)	58 (17.6)	13 (14.6)	0.607	60 (16.9)	11 (17.5)	1	60 (16.3)	11 (21.6)	0.465	48 (17.1)	23 (16.8)	1
Past experience of overdose (%)	7 (2.1)	5 (5.6)	0.164	7 (2.0)	5 (7.9)	0.028	7 (1.9)	5 (9.8)	0.007	5 (1.8)	7 (5.1)	0.109
Currently under methadone treatment (%)	110 (33.4)	22 (24.7)	0.15	116 (32.7)	16 (25.4)	0.318	119 (32.4)	13 (25.5)	0.402	98 (34.9)	34 (24.8)	0.049
Positive urine test for methadone (%)	181 (55.0)	42 (47.2)	0.233	195 (54.9)	28 (44.4)	0.161	199 (54.2)	24 (47.1)	0.417	157 (55.9)	66 (48.2)	0.169

^a
p for trend

Table 3.

Multivariate analysis across all subjects (N = 418): factors associated with major depressive episode and psychotic disorder

	Unadjusted prevalence Ratio	Prevalence Ratio	95% CI
Major depressive episode			
Daily heroin use (in the past month)	0.68	0.52	0.34 – 0.83
Duration heroin use ^{**}	1.16	1.15	0.97 – 1.38
Current methadone treatment	0.71	0.64	0.40 – 0.98
Regular poly-substance use (ref = 0) [*]			
One substance	0.91	1.27	0.73 – 2.30
Two substances	0.82	1.23	0.61 – 2.47
Three substances	1.81	2.72	1.09 – 6.23
Current psychotic disorder			
Daily heroin use (in the past month)	0.57	0.3	0.18 – 0.52
Duration heroin use ^{**}	1.22	1.17	0.95 – 1.47
Current methadone treatment	0.74	0.68	0.39 – 1.11
Regular poly-substance use (ref = 0) [*]			
One substance	0.94	1.82	0.92 – 3.97
Two substances	1.15	2.77	1.21 – 6.50
Three substances	3.45	9.35	3.50 – 24.94

^{*}Regular poly-substance use, including daily heroin injection, regular methamphetamine use (4 times in the last 30 days), and alcohol misuse

^{**}Levels were set as follows: less than 5 years (ref); 5–10 years; 10–15 years; 15+ years. Coefficient for each level increase

Table 4.

Sensitivity analysis. Factors associated with major depressive episode and psychotic disorder (multivariate model, N = 418)

	Prevalence Ratio	95% CI
Major depressive disorder		
Daily heroin use (in the past month)	0.68	0.46 – 0.98
Heroin use duration	1.18	0.99 – 1.40
Current methadone treatment	0.64	0.41 – 1.00
Hazardous drinking (Audit-c score 3 in women and 4 in men) (%)	1.02	0.69 – 1.51
Regular methamphetamine use (4 times in the last 30 days) (%)	1.31	0.88 – 1.93
Cannabis use	1.7	1.11 – 2.62
Psychotic Disorder		
Daily heroin use (in the past month)	0.64	0.41 – 0.99
Heroin use duration	1.17	0.95 – 1.45
Current methadone treatment	0.72	0.42 – 1.22
Hazardous drinking (Audit-c score 3 in women and 4 in men) (%)	1.52	0.97 – 2.39
Regular methamphetamine use (4 times in the last 30 days) (%)	2.16	1.37 – 3.41
Cannabis use	1.43	0.85 – 2.39