



OPEN ACCESS

EDITED BY

Kunhua Lee,
National Tsing Hua University, Taiwan

REVIEWED BY

Maurizio Coppola,
Department of Addiction ASLGN1, Italy
Laura Roe,
University of St. Andrews, United Kingdom

*CORRESPONDENCE

Lionel Moulis
✉ l-moulis@chu-montpellier.fr

RECEIVED 02 June 2023

ACCEPTED 09 October 2023

PUBLISHED 01 November 2023

CITATION

Moulis L, Le SM, Hai VV, Huong DT, Minh KP, Oanh KTH, Rapoud D, Quillet C, Thi TTN, Vallo R, Hoang GT, Moles J-P, Laureillard D, Feelemyer J, Des Jarlais DC, Michel L, Nagot N and the DRIVE Study Team (2023) Gender, homelessness, hospitalization and methamphetamine use fuel depression among people who inject drugs: implications for innovative prevention and care strategies. *Front. Psychiatry* 14:1233844. doi: 10.3389/fpsy.2023.1233844

COPYRIGHT

© 2023 Moulis, Le, Hai, Huong, Minh, Oanh, Rapoud, Quillet, Thi, Vallo, Hoang, Moles, Laureillard, Feelemyer, Des Jarlais, Michel, Nagot and the DRIVE Study Team. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Gender, homelessness, hospitalization and methamphetamine use fuel depression among people who inject drugs: implications for innovative prevention and care strategies

Lionel Moulis^{1*}, Sao Mai Le², Vinh Vu Hai³, Duong Thi Huong², Khuê Pham Minh², Khuat Thi Hai Oanh⁴, Delphine Rapoud¹, Catherine Quillet¹, Tuyêt Thanh Nham Thi⁴, Roselyne Vallo¹, Giang Thi Hoang², Jean-Pierre Moles¹, Didier Laureillard^{1,5}, Jonathan Feelemyer⁶, Don C. Des Jarlais⁶, Laurent Michel⁷, Nicolas Nagot¹ and the DRIVE Study Team

¹PCCEI, University of Montpellier, INSERM, EFS, University of Antilles, Montpellier, France, ²Haiphong University of Medicine and Pharmacy, Haiphong, Vietnam, ³Department of Infectious and Tropical Diseases, Viet Tiep Hospital, Haiphong, Vietnam, ⁴Supporting Community Development Initiatives, Hanoi, Vietnam, ⁵Infectious Diseases Department, Caremeau University Hospital, Nimes, France, ⁶School of Global Public Health, New York, NY, United States, ⁷CESP Inserm UMRS, Pierre Nicole Center, Paris Saclay University, Fench Red Cross, Paris, France

Background: The co-occurrence of substance use disorder and mental disorder, known as dual diagnosis, has a distressingly high prevalence among individuals grappling with either of these conditions. Mood disorders, especially depression, constitute a substantial burden for People Who Inject Drugs (PWID) and a significant public health concern in Vietnam. Identifying risk factors for depression in PWID is imperative for the development of targeted interventions.

Methods: We enrolled PWID into a cohort using the respondent-driven sampling method. Over a 36-month period, we systematically tracked the emergence of depression and employed multiple imputation in conjunction with a mixed nonlinear model to pinpoint risk factors for depression in this demographic. At inclusion, depression was screened using the PHQ-2 questionnaire, and subsequent episodes of depression were assessed semi-annually using the CES-D8.

Results: Three hundred and ninety-one PWID (26.6%) were depressed. Major risk factors for depression included being female, not having a permanent residency, having been hospitalized and using methamphetamine more than weekly. Other risk factors included age, being single, not having a health insurance card and not being on methadone.

Limitations: The exclusion of missing visits and social desirability could have led to selection and information biases. In this observational study, confusion biases are possible despite our best efforts.

Conclusion: Depression is alarmingly frequent in PWID. In this study taking in account the chronological relationship between sociodemographic and clinical factors and depression, risk factors were identified in this specific setting of low-to-middle income country. The findings highlight the need to develop innovative targeted psychiatric interventions with the help of supporting peers.

KEYWORDS

mental health, mood disorder, substance abuse, Vietnam, PWID, depression, prevention, dual diagnosis

1. Introduction

Dual diagnosis, or the co-occurrence of substance use disorders (SUD) with psychiatric comorbidities (such as depression, anxiety disorders, suicidal tendencies, etc.), is relatively uncommon in the general population (approximately 2 to 3%) (1). However, it is found in an alarming prevalence ranging from 40 to 50% in patients presenting with either condition (2–5). While further elucidation is required to fully comprehend the reasons behind the frequent association of these two conditions (6, 7), it is observed that they tend to progress concurrently within the same individual, exerting mutual influence on each other's prognosis (8). Consequently, they lead to severe consequences in socio-professional aspects (9), clinical domains (physical comorbidities, risk behaviors) (10–13), delayed detection of viral illnesses (14), and hindered access to healthcare in general (15).

The most common psychiatric condition in patients with SUD are mood disorders, with prevalence rates varying from 17% in Canada to a broader range of 27 to 85% in Australia, as reported in a meta-analysis (1, 4). More specifically, the prevalence of major depressive disorders in community and clinical settings among individuals with SUD was found to be 25% in a comprehensive meta-analysis comprising 48 studies from around the world (16). However, these rates varied depending on the studied population, type of substance and country considered.

In Vietnam, as in numerous low- to middle-income countries (LMICs), psychiatric resources are sparse, resulting in a saturated mental health system (17) managing mainly the most severely ill patients because of a lack of human and material resources.

In this context, targeting specifically people who inject drugs (PWID) who are in need of mental health support is therefore crucial for they present, among other mental health issues, significantly higher rates of depression (18). Previous studies analyzing risk factors for depression were sparse among PWID living in LMIC (19), where the expression of depression is not as prevalent as in high income countries and where associated factors might differ. Moreover, these studies with cross-sectional designs (20) identified only factors associated with depression and not risk factors for depression whose estimating requires following up the population (21, 22). Indeed, the chronological knowledge of the situation must be taken in account in order to better understanding the mechanisms and offer tailored prevention strategies.

The aim of our project is to develop a community-based innovative intervention plan to prevent and limit the burden of depression in this specific population. In order to do so, we aimed in this study to explore longitudinal associations between depressive

symptoms and patient characteristics in people who inject drugs in Hai Phong, Vietnam.

2. Materials and methods

2.1. DRIVE study population and recruitment

The Drug use and Infections in Vietnam (DRIVE) program is an international project launched in 2016 whose goal was to end the HIV epidemic among PWID in Hai Phong, Vietnam (23). The DRIVE study relied on extensive HIV screening *via* community-based respondent-driven sampling (RDS) surveys combined with linkage to HIV care. The RDS method allows access to hard-to-reach populations, hidden from care and inaccessible through classic recruitment methods (24).

Three rounds of annual RDS surveys from November 2016 to November 2018 targeted 3,150 PWID. The inclusion criteria were being at least 18 years old, having a positive urine test for heroin or methamphetamine and having skin marks from a recent injection (23). Those unable to understand the study information or unwilling to consent were not enrolled.

Starting from the first RDS survey, two open cohorts were created: one with HIV-negative participants to estimate HIV incidence and another with HIV-positive participants to estimate the cascade of HIV care dynamics. All RDS HIV-positive participants were invited to be included in the cohort and were then provided counseling and peer support to help them connect with care and initiate or remain on antiretroviral treatment (ART) as well as encourage them to pursue methadone maintenance therapies (MMTs). HIV-negative participants were recruited until the target cohort size was reached, which was set to 400 for RDS1 and 400 for the next two RDS rounds, excluding those who reported already being treated with methadone (25). Participants were enrolled in the cohort for 12 to 36 months depending on their date of recruitment, with follow-up visits every 6 months.

2.2. Selection

In this study, sociodemographic, drug habit, psychological, behavioral and health event-related data from all PWID recruited in the previously described HIV+ and HIV- cohorts and who participated in at least one follow up visit were included.

2.3. Measures

2.3.1. Primary outcome

At baseline (RDS survey), depression was screened with a short form of the Patient Health Questionnaire (PHQ-2) (26), in face-to-face interview with trained community-based organization (CBO) member. Participants with a score strictly superior to 2 were considered depressive (27, 28).

During semiannual follow-up visits, depression was measured by trained doctors from the Hai Phong University of Medicine and Pharmacy using a short form of the Center for Epidemiologic Studies- Depression (CES-D8) questionnaire (29), shown to facilitate the efficiency of assessment during epidemiological studies (30). Because the original cutoff of ≥ 7 was determined in women, who represent 5% of PWID in Hai Phong, we used a lower cutoff of ≥ 6 (31).

2.3.2. Other psychiatric disorders

Participants were screened for anxiety at the time of the RDS survey with the short Generalized Anxiety Disorder questionnaire (GAD-2) developed to screen for anxiety in primary care patients and the general population, with a published cutoff of ≥ 3 (32).

Participants who screened positive for any mental health issue during the RDS survey or during follow-up were invited to meet with a psychiatrist for a full clinical assessment followed by other consultations when necessary at the study site.

2.3.3. Substance use

Data were collected by trained interviewers (CBO members) using a face-to-face questionnaire on drug and alcohol use. The questionnaire created for the study included questions on duration, age of initiation, frequency and substances injected, as well as on the use of other non-injected substances including alcohol. Its content has been described in greater detail elsewhere (25, 33). PWID were also screened for opiates, methadone, methamphetamine and cannabis by urine tests.

A *high heroin injection frequency* referred to PWID reporting more than 30 injections in the past month. *Methamphetamine use* had two categories, “no use or less than once per week” and “more than once per week” (34). We combined urine tests and questions about drug use in the past 6 months to define *polydrug use* as using any drug other than heroin or methamphetamine (ketamine, ecstasy, cocaine or cannabis) in addition to heroin, which was used by all participants.

Alcohol misuse was assessed through Audit-C, a 3-item questionnaire including the first questions of the AUDIT questionnaire, with a cutoff of ≥ 3 for women and ≥ 4 for men (35).

2.3.4. Other medical data

At the RDS visit, CBO members collected individual sociodemographic measures: *gender*, *age* and *education level*. During the cohort follow-up, they collected data on major health and life events (*overdoses* and *arrests*), as well as social and structural sociodemographic measures (*relationship status*, *stable housing* and *health insurance card*). PWID were also asked if they had *been hospitalized* during the past 6 months, whatever the reason, and were tested for HCV and HIV at every visit.

2.4. Statistical analysis

We analyzed risk factors for depressive syndrome among PWID over up to 3 years. These potential risk factors were sociodemographic (*gender*, *age*, *relationship status*, *stable housing* and *health insurance card*), drug habits (*methamphetamine use*, *high heroin injection frequency*, *polydrug use*, *alcohol misuse*, *being on MMT* and *more than 10 years since the first heroin injection*), and health events (*having been hospitalized in the past 6 months*, *HCV status* and *HIV status*). Anxiety was not entered in the model as cofounder because of anxiety-related questions within the CES-D scale (36). People with depressive syndrome at baseline according to the PHQ-2 were not included in our model. We censored participants from the time they began antidepressant treatment.

A mixed nonlinear model was used for the main analyzes in order to explore longitudinal associations between depression and patient characteristics. We developed multiple models that differed in the number of variables and the inclusion of random intercepts and then compared their quality to select the final model.

To deal with missing completely at random (MCAR) data for participants who had completed their follow-up visits, we selected complete outcome cases and used a multiple imputation technique: the model was apply to 20 datasets of possible values created *via* linear regression or discriminant function method depending on the variable and parameter estimates were combined to obtain final adjusted odds ratio and their 95% confidence intervals (CIs) (36–38).

The data analysis for this paper was performed using SAS software version 9.4. Copyright © 2013 SAS Institute Inc.

2.5. Ethics consideration

The DRIVE study was approved by the Institutional Review Boards of the Hai Phong University of Medicine and Pharmacy, the Icahn School of Medicine at Mount Sinai, and the New York University School of Medicine. All participants provided signed informed consent.

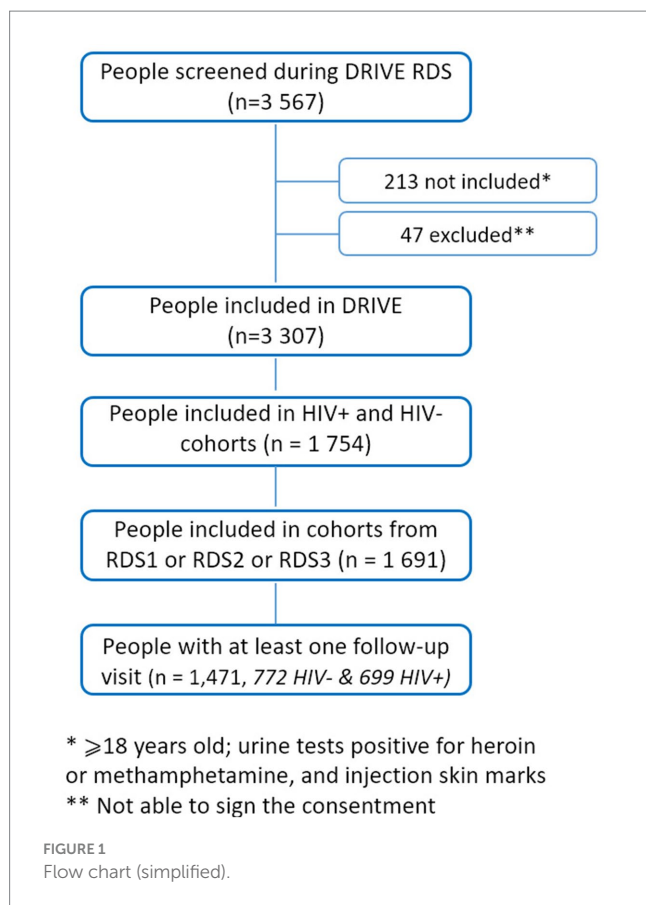
3. Results

3.1. Population selection

Of the 1,691 people included in the DRIVE cohort, 215 never returned for any follow-up visits, 2 died, and 3 began antidepressant treatment before the first follow-up. In total, 1,471 people were included in our study, 772 from the HIV-negative cohort and 699 from the HIV-positive cohort (Figure 1). They were followed up from 2 to 35 months (16 months on average) with a mean number of 3.3 visits. 771 PWID followed up during 6 visits, 371 during 4 visits and 329 during 2 visits were included at the first, second and last RDS survey, respectively (Supplementary Figure S1).

3.2. Population characteristics

All participants were heroin users, 93% were male, and their mean age was 41 years (Table 1). Overall, HIV-infected participants were less



educated (53% vs. 70%), injected heroin for longer (63% used it for more than 10 years vs. 37%), and were more often on MMT (35% vs. 12%).

Of our 6,768 planned follow-up visits, 5,201 (76.8%) were completed. During follow-up, 56 people had died, including 1 from suicide, 2 from overdoses and 2 for unknown reasons. Other causes of death had no direct link with depression. 394 (5.8%) visits were attended but had incomplete data on the CES-D8 questionnaire.

The 329 participants who dropped out (22%) were younger, were less likely to be in a relationship or in a stable housing, were more depressed at inclusion, and were more likely to use methamphetamine more than once per week. They were less likely to be enrolled in methadone maintenance therapy and less likely to be infected by HIV (Supplementary Table S1).

3.3. Prevalence of depression

The proportion of depressed participants was 11.9% at baseline. The number of PWID depressed at one or more visits was 391 (26.6%). Among people free from depression in the 2 weeks prior to inclusion based on the PHQ-2, 320 (23.8%) developed depression over the mean 16 months of follow-up.

3.4. Risk factors for depression

No permanent residency [OR = 5.6, 95% CI (2.2–14.6)], gender [female: OR = 4.0, 95% CI (2.0–7.9)], having been hospitalized and

using methamphetamine at least once a week [OR = 3.1, 95% CI (1.8–5.2)], not being in relationship nor on methadone [OR = 2.0, 95% CI (1.1–3.5)], not having an insurance card [OR = 1.7, 95% CI (1.2–2.4)], age [OR = 1.3, 95% CI (1.0–1.7) for every 10 years] were all significant risk factors for depression. Time since inclusion in the cohort was a protective factor against depression [OR = 0.6, 95% CI (0.5–0.8) for each year in the cohort]. Being infected with HCV tended to be associated with depression without statistically significant (Figure 2).

4. Discussion

4.1. Identifying PWID with a high depression risk

In this cohort of PWID recruited through RDS surveys, almost a quarter had depressive symptoms develop or reoccur during a follow-up of 16 months on average. This is more than previously found in a Canadian open cohort of PWID (39) but lower than in other PWID populations, whether in LMICs (40) or in high-income countries (41). This could be explained by the different methodologies (population selection, screening tools) used to measure the prevalence of depression. Furthermore, in Asian settings, the expressiveness of depressive symptoms has been shown to vary: depressive people from LMICs show fewer mood-related symptoms, which are what the CES-D8 mainly measures, and more somatic symptoms (42, 43).

The gender gap in depression has been extensively studied in the general population and could be attributed to various factors. Hormonal fluctuations (44, 45), differences in expressed genes and neural and cerebral circuitry architecture (44), personality traits (46, 47), societal factors such as the lower levels of education (48, 49), life stressors (50), and gender norms influencing answers of certain CES-D8 questions (51) could all be part of the explanation. Nevertheless, in this particular population of female PWID, the stigma associated with drug use could have a significant impact on depressive symptoms (52). This effect has been observed not only globally (53) but also in Vietnam, where female PWID experience higher levels of stigmatization, both from men and women (54), which may have concerning implications for their mental health (55).

Another potential explanation could be gender disparities in involvement in sex work. While we could not establish gender differences in sex work due to underreported or unanswered questions in this study, another article from the DRIVE project, focusing on a similar population, found that being a woman was linked to engagement in sex work (56), a known risk factor for depression (57). Although reaching sex workers is difficult (fear of stigma, desirability biases, conditions of life, night work, pimp control, etc.), psychological interventions, screening for mental health in health care services targeting female sex workers, and training “gatekeepers” to support women at risk, should be implemented (58). More generally, targeted prevention efforts should consider that women may be at a higher risk of depression and offer them dedicated interventions.

Other factors reflecting social precariousness emerged. “Living on the edge” without stable housing or a health insurance card has already been identified as a risk factor for mental illness (59). The concerns

TABLE 1 Characteristics of the population at inclusion.

Characteristics	HIV- (n = 772)	HIV+ (n = 699)	Total (n = 1,471)
Sociodemographic			
Male	710 (92.0)	659 (94.3)	1,369 (93.1)
Female	61 (7.9)	39 (5.6)	100 (6.8)
Transgender	1 (0.1)	1 (0.1)	2 (0.1)
Age	40.9 (± 9.4)	40.4 (± 6.5)	40.6 (± 8.1)
At least high school level	541 (70.1)	371 (53.1)	912 (62.0)
In a relationship	325 (42.1)	250 (35.8)	575 (39.1)
Income ≥ 6 VND ¹	353 (45.7)	258 (36.9)	611 (41.5)
Stable housing	744 (96.4)	680 (97.3)	1,425 (96.8)
Health insurance card	285 (36.9)	463 (66.2)	748 (50.9)
Sex work	23 (3.0)	9 (1.3)	32 (2.2)
Psychiatric data			
Anxiety	72 (9.3)	50 (7.1)	122 (8.3)
Depression (PHQ-2)	74 (9.6)	58 (8.3)	132 (9.0)
Suicidal ideation (past 2 weeks)	102 (13.2)	76 (10.8)	178 (12.1)
Drug habits			
Alcohol misuse (AUDIT-C)	315 (40.8)	260 (37.2)	576 (39.1)
Methamphetamine > once a week	166 (21.5)	101 (14.4)	267 (18.1)
Recent methamphetamine use ²	528 (68.4)	439 (62.8)	967 (65.7)
Polydrug use ³	121 (15.7)	97 (13.9)	218 (14.8)
Years of heroin injection			
< 5 years	212 (27.4)	43 (6.1)	255 (17.3)
5–10 years	210 (27.2)	158 (22.5)	368 (24.9)
10–15 years	174 (22.5)	180 (25.6)	354 (24.0)
> 15 years	177 (22.9)	321 (45.7)	498 (33.7)
Age at first heroin injection	31.4 (± 8.9)	27.3 (± 7.3)	29.4 (± 8.4)
High-frequency heroin use	603 (78.1)	501 (71.7)	1,109 (75.1)
Methadone Maintenance therapy	93 (12.0)	242 (34.6)	335 (22.8)
Cannabis (past 6 months)	103 (13.3)	123 (17.6)	226 (15.4)
Cocaine (past 6 months)	5 (0.6)	9 (1.3)	14 (0.9)
Ketamine (past 6 months)	43 (5.6)	28 (4.0)	71 (4.8)
Ecstasy (past 6 months)	40 (5.2)	30 (4.3)	70 (4.8)
Amphetamine (past 6 months)	124 (16.1)	95 (13.6)	219 (14.9)
Urine tests			
Heroin	768 (99.5)	697 (99.7)	1,465 (99.6)
Methamphetamine	271 (35.1)	213 (30.5)	484 (32.9)
Cannabis	47 (6.1)	205 (29.3)	252 (17.1)
Cocaine	0 (0)	0 (0)	0 (0)
Ketamine	0 (0)	0 (0)	0 (0)
Methadone	207 (26.8)	448 (64.1)	655 (44.5)
Infection status			
Undetectable HIV RNA ⁴	NA	490 (70.1)	NA
HCV-positive serology	445 (57.6)	611 (87.0)	1,053 (71.6)

¹Equivalent to ~260 USD per month; ²In the month; ³Cannabis, cocaine, ketamine or ecstasy; ⁴Undetectable or viral load lower than 20 copies/mL. The results are given as number (percentage) or mean (± standard deviation).

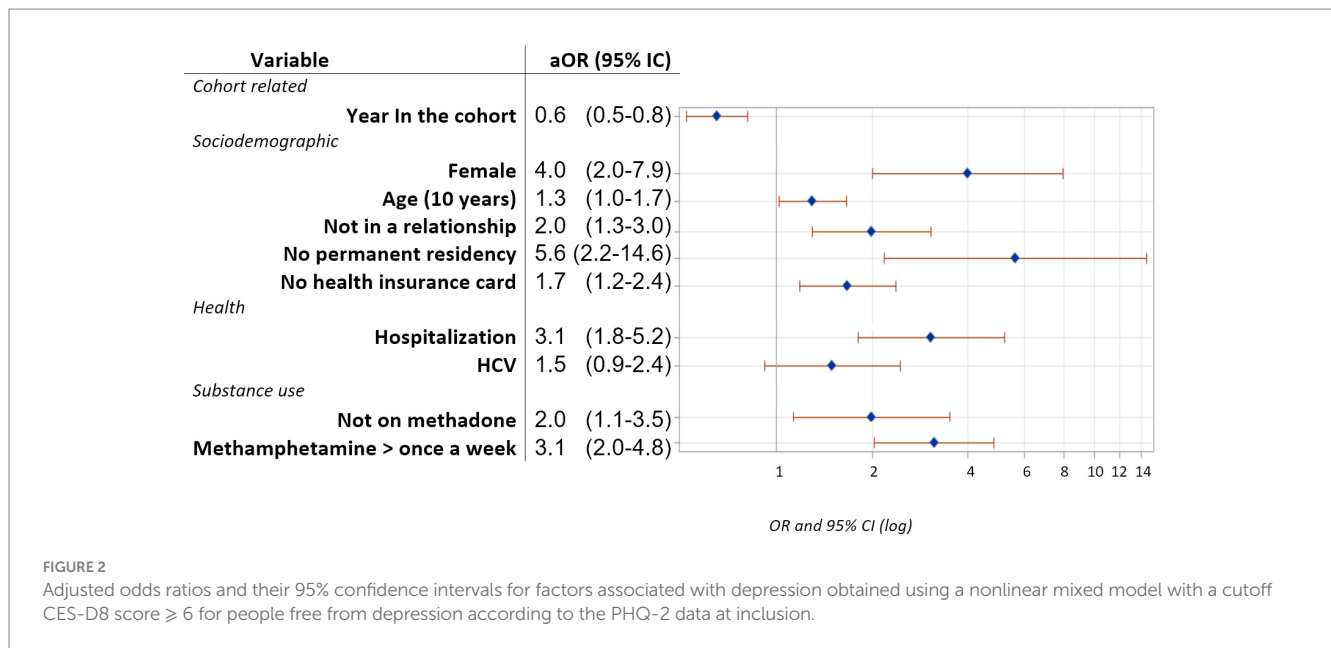


FIGURE 2

Adjusted odds ratios and their 95% confidence intervals for factors associated with depression obtained using a nonlinear mixed model with a cutoff CES-D8 score ≥ 6 for people free from depression according to the PHQ-2 data at inclusion.

and anxiety this causes could exacerbate or trigger the onset of mental illness, acting as additional stress on a potentially compromised state of mental resilience already affected by substance use. Similarly, social support, as defined in our study as being in a relationship, was a protective factor for depression, probably because of both its social and its emotional support impacts (60, 61).

The prevalence of depression increases with age in both the general population and PWID (62, 63). This may be explained by age-related biological changes and comorbidities or chronic conditions, all of which are strongly associated with depression (64). As we did not have data about comorbidities, it is possible that age acted as a proxy of chronic health problems (65). The association found between depression and hospitalization during follow-up, probably reflecting the decompensation of somatic comorbidities, is consistent with this hypothesis.

Indeed, having been hospitalized during the follow-up increased the risk of depression. Despite the fact that we had no information on the causes of these hospital admissions, they might be related to complications or treatments of infections, which are frequent in our cohort population, as well as a degraded state of health, commonly associated with depression (12).

We found that HCV had a tendency to increase the risk of depression, although not significantly. In literature, this observed association (66) has been described as linked to poor health-related quality of life and physical, mental and social illnesses due to the disease (67), the treatments (68), and even direct HCV neuro-invasion, and metabolic derangements (69). Nevertheless, as new cost-effective direct-acting antivirals for HCV have recently been developed with lower psychiatric side effects (70–72), we can see how they will become widespread, including among LMICs, thus reducing the mental health burden of HCV.

Generally, we observed that time since inclusion was a protective factor. Our patients participated in a research program offering them the opportunities to be tested, examined and treated. Furthermore, the positive social impact of being enrolled in a cohort and going to regular meetings with CBO-trained members for social support, harm

reduction and social and administrative counseling might have helped reduce the risk of depression. Being part of a community also offers, in the context of layered drug- and HIV-related stigma, the possibility to disclose their situation to someone (73).

4.2. Taking care of PWID with a high depression risk

In many countries, where access to psychiatric care is notably limited, alternative and original strategies that rely on nonprofessional or peer workers could be crucial. Using simple screening tools in the community to introduce drug users to their mental health may be the first step.

A simplified psychiatric screening tool adapted to nonprofessional/CBO members was developed as part of the DRIVE project. This 9-item questionnaire validated among PWID with acceptable psychometric characteristics and good acceptability (74, 75) allows a discussion of mental health, depression, psychiatric consequences of regular drug use and their treatment with trained CBO members, particularly for PWID with multiple risk factors. Depending on the score, a consultation with a psychiatrist *in situ* is proposed. Screening followed by delocalized psychiatric consultation is one of the innovative approaches that allows the care and monitoring of hard-to-reach vulnerable populations.

Psychiatric complications, particularly depression but also psychotic manifestations, are very common among frequent methamphetamine users and need special attention and tailored harm reduction interventions (76). Adapted information on drug use and the benefits of reducing should be provided by peers or social workers. For users who want to adapt their use, they should be given the means to change his or her behavior, thus limiting the risk of depression (77, 78).

Enrollment in MMT should be encouraged, since having the easiest possible access to MMT was found to be a protective factor (41, 79–81). Methadone-induced biological stabilization protected the patients from

craving phases and allowed them personal and social stabilization (82, 83). Regular opioid use could even have a protective effect against psychiatric comorbidities (84). Indeed, this enables a decline in risk practices and the patient to be in touch with care professionals (85). Of course, the decision to initiate a patient in an MMT program should be made by a physician, following a thorough assessment of contraindications and in agreement with the patient. This decision should be preceded by informed consent, which includes a discussion of the risks and benefits of such a program, as well as alternative treatments, to enable the patient to make an informed decision.

It has become necessary to promote the development of psychiatric interventions in environments dedicated to drug users (methadone or HIV clinics) (78). In this aim, basic training on the association between mental health and addiction is required for all stakeholders, which implies acceptance of delocalized psychiatric interventions in specialized settings or CBO offices (86). Reducing the stigma associated with drug use and mental health disorders is urgent, and recognizing mutual competencies and roles of peers and healthcare workers is crucial (87).

4.3. Study limitations

First, owing to limitations in resources, staffing, and organizational capacity, we were unable to conduct psychiatric evaluations based on international criteria. The PHQ-2 used at baseline has a sensitivity of 72% (28), meaning that we did not exclude some people with clinical depression. Moreover, the questionnaire relates only to symptoms in the past 2 weeks, which could have biased our selection of people without depression. Although the presence and severity of depressive symptoms are known to vary over time, we did not evaluate history of depression. Furthermore, the semiannual assessment of depression involved a different screening tool with different psychometric properties, the CES-D. This questionnaire focus on symptoms in the last week, and we use a short 8-item version. However, this version has a correlation of 0.93 with the complete scale (30). Additionally, in another part of the DRIVE project (not shown here), psychiatric evaluation and the CES-D8 were found to have good agreement, indicating that as imperfect as this outcome was, it still served as a suitable proxy for depression assessment. The limitations of using different questionnaires in the study are well acknowledged by the investigators but provide insight into the evolution of depressive symptoms in a context of participant attrition. If these limitations were to introduce biases, they would likely be of minor magnitude and should not undermine the findings.

Second, we had to restrict our data to people with at least one follow-up visit; some were lost to follow-up, and we considered only visits with completed outcomes. This could induce some selection biases because it is plausible that people with high depression risk are the least able to visit, meaning that the more severe cases of depression were not as represented as others. We observed this phenomenon when we compared people with missed or excluded visits with the rest; the former presented more risk factors for depression.

Third, sampling biases could occur because our recruitment method included a large majority of male PWID. Our findings are representative of Vietnam and South Asia (88) but might not

be extrapolated to populations of PWID with a lower proportion of males (approximately 75% around the world) (89). Similarly, our cohort overrepresented HIV-positive participants (approximately half), whereas the estimated prevalence of HIV among PWID is 30% in Hai Phong (24). In our analyzes, HIV status had no association with depression, which may seem surprising, as the link between depression and HIV status has been shown (90). In our cohort, however, we speculate that HIV-positive participants are less depressed because of greater support and free access to care offered by the DRIVE project.

Finally, avoided sensitive questions and missing data could be explained by desirability biases. For instance, questions about heroin experience and sex work were often not answered. Recall bias could also have occurred since questions were related to past behaviors.

5. Conclusion

The co-occurrence of addiction and depression is a scourge with catastrophic consequences for individuals affected by it. In this large longitudinal study focusing on people who inject drugs in a low-to-middle income country setting, we found a concerning high prevalence of depression.

This work was able for the first time in this setting to consider the temporal relationships of the factors studied and their impact on depressive symptomatology. We found that being a woman was strongly associated with depression. Certain factors of social precariousness were also identified as risk factors, as well as the consumption of methamphetamine in addition to substance injection. The beneficial effect of being on a MMT program was also emphasized.

All these results drive, in the context of limited psychiatric resources, the development of innovative interventions focusing on these vulnerable sub-populations, such as simple screening tools, delocalized psychiatric consultations, peer support, free treatment, etc.... Other interventions remain to be designed and tested in these specific settings.

Data availability statement

The original contributions presented in the study are included in the article/[Supplementary material](#), further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Institutional Review Board of the Hai Phong University of Medicine and Pharmacy, the Institutional Review Board of the Icahn School of Medicine at Mount Sinai, and the Institutional Review Board of the New York University School of Medicine. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

LiM: conceptualization, methodology, software, formal analysis, writing—original draft, and visualization. SL: investigation, validation, and writing—review and editing. VH: investigation and writing—review and editing. DH and DD: funding acquisition, supervision, and writing—review and editing. KM and J-PM: resources, supervision, and writing—review and editing. KO: funding acquisition and writing—review and editing. DR and CQ: resources, supervision, data curation, and writing—review and editing. TT: supervision and writing—review and editing. RV: data curation and writing—review and editing. GH: supervision, data curation, and writing—review and editing. DL and JF: writing—review and editing. LaM: supervision, conceptualization, methodology, and writing—review and editing. NN: funding acquisition, supervision, conceptualization, methodology, and writing—review and editing. All authors contributed to the article and approved the submitted version.

Funding

This work was cosupported by the French *Agence Nationale de Recherches sur le SIDA et les hépatites virales* (ANRS) [12299] and the *US National Institute of Drug Abuse* (NIDA) [P30DA011041].

References

- Rush B, Urbanoski K, Bassani D, Castel S, Wild TC, Strike C, et al. Prevalence of co-occurring substance use and other mental disorders in the Canadian population. *Can J Psychiatr.* (2008) 53:800–9. doi: 10.1177/070674370805301206
- Compton WM, Thomas YF, Stinson FS, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV drug abuse and dependence in the United States: results from the National Epidemiologic Survey on alcohol and related conditions. *Arch Gen Psychiatry.* (2007) 64:566–76. doi: 10.1001/archpsyc.64.5.566
- Conner KR, Pinquart M, Duberstein PR. Meta-analysis of depression and substance use and impairment among intravenous drug users (IDUs). *Addiction.* (2008) 103:524–34. doi: 10.1111/j.1360-0443.2007.02118.x
- Kingston REF, Marel C, Mills KL. A systematic review of the prevalence of comorbid mental health disorders in people presenting for substance use treatment in Australia: comorbidity in substance use treatment. *Drug Alcohol Rev.* (2017) 36:527–39. doi: 10.1111/dar.12448
- Schuckit MA. Comorbidity between substance use disorders and psychiatric conditions. *Addiction.* (2006) 101:76–88. doi: 10.1111/j.1360-0443.2006.01592.x
- Boumendjel M, Benyamina A. Les «pathologies duelles» en addictologie: état des lieux et prise en charge In: M Reynaud, editor. *Traité d'Addictologie*. Cachan: Lavoisier (2016). 139–49.
- Couteron JP, Blaise M, Julien JP, Berne E, Hans C, Péquart C, et al. *Addictions et troubles psychiatriques*. Fédération Addiction, p. 106. (2019). Available at: <https://fr.calameo.com/read/0055448589de9b5897807>.
- Benyamina A. Pathologie duelle, actualités et perspectives. *Ann Méd Psychol Rev Psychiatr.* (2018) 176:742–5. doi: 10.1016/j.amp.2018.08.016
- Steger ME, Kashdan TB. Depression and everyday social activity, belonging, and well-being. *J Couns Psychol.* (2009) 56:289–300. doi: 10.1037/a0015416
- Harris EC, Barraclough B. Suicide as an outcome for mental disorders. A meta-analysis. *Br J Psychiatry.* (1997) 170:205–28. doi: 10.1192/bjp.170.3.205
- Hutton HE, Lyketsos CG, Zenilman JM, Thompson RE, Erbeling EJ. Depression and HIV risk behaviors among patients in a sexually transmitted disease clinic. *AJP.* (2004) 161:912–4. doi: 10.1176/appi.ajp.161.5.912
- Kang HJ, Kim SY, Bae KY, Kim SW, Shin IS, Yoon JS, et al. Comorbidity of depression with physical disorders: research and clinical implications. *Chonnam Med J.* (2015) 51:8–18. doi: 10.4068/cmj.2015.51.1.8
- Levintow SN, Pence BW, Powers KA, Sripaipan T, Ha TV, Chu VA, et al. Estimating the effect of depression on HIV transmission risk behaviors among people who inject drugs in Vietnam: a causal approach. *AIDS Behav.* (2020) 25:438–46. doi: 10.1007/s10461-020-03007-9
- Swartz MS, Swanson JW, Hannon MJ, Bosworth HS, Osher FC, Essock SM, et al. Regular sources of medical care among persons with severe mental illness at risk of hepatitis C infection. *Psychiatr Serv.* (2003) 54:854–9. doi: 10.1176/appi.ps.54.6.854

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpsy.2023.1233844/full#supplementary-material>

- Ann Priester M, Browne T, Iachini A, Clone S, DeHart D, Seay KD. Treatment access barriers and disparities among individuals with co-occurring mental health and substance use disorders: an integrative literature review. *J Subst Abus Treat.* (2016) 61:47–59. doi: 10.1016/j.jsat.2015.09.006
- Hunt GE, Malhi GS, Lai HMX, Cleary M. Prevalence of comorbid substance use in major depressive disorder in community and clinical settings, 1990–2019: systematic review and meta-analysis. *J Affect Disord.* (2020) 266:288–304. doi: 10.1016/j.jad.2020.01.141
- Vuong DA, Van Ginneken E, Morris J, Ha ST, Busse R. Mental health in Vietnam: burden of disease and availability of services. *Asian J Psychiatr.* (2011) 4:65–70. doi: 10.1016/j.ajp.2011.01.005
- Pham Minh K, Vallo R, Duong Thi H, Khuat Thi Hai O, Jarlais DCD, Peries M, et al. Psychiatric comorbidities among people who inject drugs in Hai Phong, Vietnam: the need for screening and innovative interventions. *Biomed Res Int.* (2018) 20:1–13. doi: 10.1155/2018/8346195
- Shaw SA, El-Bassel N, Gilbert L, Terlikbayeva A, Hunt T, Primbetova S, et al. Depression among people who inject drugs and their intimate partners in Kazakhstan. *Community Ment Health J.* (2016) 52:1047–56. doi: 10.1007/s10597-015-9883-3
- Iskandar S, Kamal R, De Jong CA. Psychiatric comorbidity in injecting drug users in Asia and Africa. *Curr Opin Psychiatry.* (2012) 25:213–8. doi: 10.1097/YCO.0b013e3283523d66
- Barroga EF, Kojima T. Research study designs: an appraisal for peer reviewers and science editors. *Eur Sci Edit.* (2013) 39:2.
- Gordis L. *Epidemiology*. Fifth ed. Philadelphia, PA: Elsevier/Saunders (2014). 392 p.
- Jarlais DD, Huong DT, Pham MK, Oanh KTH, Thanh NTT, Arasteh K, et al. Integrated respondent driven sampling and peer support for persons who inject drugs in Haiphong, Vietnam: a case study with implications for interventions. *AIDS Care.* (2016) 28:1312–5. doi: 10.1080/09540121.2016.1178698
- Jarlais DD, Khue PM, Feelemyer J, Arasteh K, Huong DT, Oanh KTH, et al. Using dual capture/recapture studies to estimate the population size of persons who inject drugs (PWID) in the city of Hai Phong, Vietnam. *Drug Alcohol Depend.* (2018) 185:106–11. doi: 10.1016/j.drugalcdep.2017.11.033
- Michel L, Des Jarlais DC, Thi HD, Hai OKT, Minh KP, Peries M, et al. Intravenous heroin use in Haiphong, Vietnam: need for comprehensive care including methamphetamine use-related interventions. *Drug Alcohol Depend.* (2017) 179:198–204. doi: 10.1016/j.drugalcdep.2017.07.004
- Kroenke K, Spitzer RL, Williams JBW, Löwe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. *Psychosomatics.* (2009) 50:613–21. doi: 10.1176/appi.psy.50.6.613
- Kroenke K, Spitzer RL, Williams JBW. The patient health Questionnaire-2: validity of a two-item depression screener. *Med Care.* (2003) 41:1284–92. doi: 10.1097/01.MLR.0000093487.78664.3C

28. Levis B, Sun Y, He C, Wu Y, Krishnan A, Bhandari PM, et al. Accuracy of the PHQ-2 alone and in combination with the PHQ-9 for screening to detect major depression: systematic review and Meta-analysis. *JAMA*. (2020) 323:2290–300. doi: 10.1001/jama.2020.6504
29. Melchior LA, Huba GJ, Brown VB, Reback CJ. A short depression index for women. *Educ Psychol Meas*. (1993) 53:1117–25. doi: 10.1177/0013164493053004024
30. Santor DA, Coyne JC. Shortening the CES-D to improve its ability to detect cases of depression. *Psychol Assess*. (1997) 9:233–43. doi: 10.1037/1040-3590.9.3.233
31. Zauszniewski JA, Graham GC. Comparison of short scales to measure depressive symptoms in elders with diabetes. *West J Nurs Res*. (2009) 31:219–34. doi: 10.1177/0193945908326065
32. Kroenke K, Spitzer RL, Williams JBW, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med*. (2007) 146:317–25. doi: 10.7326/0003-4819-146-5-200703060-00004
33. Duong HT, Jarlais DD, Khuat OHT, Arasteh K, Feelemyer J, Khue PM, et al. Risk behaviors for HIV and HCV infection among people who inject drugs in Hai Phong, Viet Nam, 2014. *AIDS Behav*. (2018) 22:2161–71. doi: 10.1007/s10461-017-1814-6
34. McKetin R, McLaren J, Lubman DI, Hides L. The prevalence of psychotic symptoms among methamphetamine users. *Addiction*. (2006) 101:1473–8. doi: 10.1111/j.1360-0443.2006.01496.x
35. Dawson DA, Smith SM, Saha TD, Rubinsky AD, Grant BF. Comparative performance of the AUDIT-C in screening for DSM-IV and DSM-5 alcohol use disorders. *Drug Alcohol Depend*. (2012) 126:384–8. doi: 10.1016/j.drugalcdep.2012.05.029
36. Sterne JAC, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ*. (2009) 338:b2393. doi: 10.1136/bmj.b2393
37. Littell RC, Pendergast J, Natarajan R. Modelling covariance structure in the analysis of repeated measures data. *Stat Med*. (2000) 19:1793–819. doi: 10.1002/1097-0258(20000715)19:13<1793::AID-SIM482>3.0.CO;2-Q
38. Liu Y, De A. Multiple imputation by fully conditional specification for dealing with missing data in a large epidemiologic study. *Int J Stat Med Res*. (2015) 4:287–95. doi: 10.6000/1929-6029.2015.04.037
39. Reddon H, Pettes T, Wood E, Nosova E, Milloy MJ, Kerr T, et al. Incidence and predictors of mental health disorder diagnoses among people who inject drugs in a Canadian setting. *Drug Alcohol Rev*. (2018) 37 Suppl 1:S285–93. doi: 10.1111/dar.12631
40. Gu J, Lau JTF, Chen H, Chen X, Liu C, Liu J. Mental health and interpersonal factors associated with HIV-related risk behaviors among non-institutionalized female injection drug users who are also sex workers in China. *Women Health*. (2010) 50:20–36. doi: 10.1080/03630241003601137
41. Marammani AGI, Rovai L, Pani PP, Pacini M, Lamanna F, Rugani F, et al. Do methadone and buprenorphine have the same impact on psychopathological symptoms of heroin addicts? *Ann General Psychiatry*. (2011) 10:17. doi: 10.1186/1744-859X-10-17
42. Chee KY, Tripathi A, Avasthi A, Chong MY, Xiang YT, Sim K, et al. Country variations in depressive symptoms profile in Asian countries: findings of the research on Asia psychotropic prescription (REAP) studies: country variations in depressive profile. *Asia Pac Psychiatry*. (2015) 7:276–85. doi: 10.1111/appy.12170
43. Niemi M, Mälqvist M, Giang KB, Allebeck P, Falkenberg T. A narrative review of factors influencing detection and treatment of depression in Vietnam. *Int J Ment Health Syst*. (2013) 7:15. doi: 10.1186/1752-4458-7-15
44. Albert PR. Why is depression more prevalent in women? *J Psychiatry Neurosci*. (2015) 40:219–21. doi: 10.1503/jpn.150205
45. Cheslack-Postava K, Keyes KM, Lowe SR, Koenen KC. Oral contraceptive use and psychiatric disorders in a nationally representative sample of women. *Arch Womens Ment Health*. (2015) 18:103–11. doi: 10.1007/s00737-014-0453-4
46. Goodwin RD, Gotlib IH. Gender differences in depression: the role of personality factors. *Psychiatry Res*. (2004) 126:135–42. doi: 10.1016/j.psychres.2003.12.024
47. Jeronimus BF, Riese H, Sanderman R, Ormel J. Mutual reinforcement between neuroticism and life experiences: a five-wave, 16-year study to test reciprocal causation. *J Pers Soc Psychol*. (2014) 107:751–64. doi: 10.1037/a0037009
48. Eugenia Alvarado B, Victoria Zunzunegui M, Béland F, Sicotte M, Tellechea L. Social and gender inequalities in depressive symptoms among urban older adults of Latin America and the Caribbean. *J Gerontol B Psychol Sci Soc Sci*. (2007) 62:S226–36. doi: 10.1093/geronb/62.4.S226
49. Miech RA, Eaton WW, Brennan K. Mental health disparities across education and sex: a prospective analysis examining how they persist over the life course. *J Gerontol*. (2005) 60:S93–8. doi: 10.1093/geronb/60.Special_Issue_2.S93
50. Keita GP. Psychosocial and cultural contributions to depression in women: considerations for women midlife and beyond. *JMCP*. (2007) 13:12–5. doi: 10.18553/jmcp.2007.13.9.a.12
51. Carleton RN, Thibodeau MA, Teale MJN, Welch PG, Abrams MP, Robinson T, et al. The Center for Epidemiologic Studies Depression Scale: a review with a theoretical and empirical examination of item content and factor structure. *PLoS One*. (2013);e58067. doi: 10.1371/journal.pone.0058067
52. Khuat OT, Morrow M, Nguyen TN, Armstrong G. Social context, diversity and risk among women who inject drugs in Vietnam: descriptive findings from a cross-sectional survey. *Harm Reduct J*. (2015) 12:35. doi: 10.1186/s12954-015-0067-9
53. Meyers SA, Earnshaw VA, D'Ambrosio B, Courchesne N, Werb D, Smith LR. The intersection of gender and drug use-related stigma: a mixed methods systematic review and synthesis of the literature. *Drug Alcohol Depend*. (2021) 223:108706. doi: 10.1016/j.drugalcdep.2021.108706
54. Trang NT, Jauffret-Roustide M, Giang LM, Visier L. “I’m not like others”: stigma navigation by people who inject drugs in Vietnam. *Drugs*. (2022) 29:85–94. doi: 10.1080/09687637.2021.1874875
55. Wang DF, Zhou YN, Liu YH, Hao YZ, Zhang JH, Liu TQ, et al. Social support and depressive symptoms: exploring stigma and self-efficacy in a moderated mediation model. *BMC Psychiatry*. (2022) 22:117. doi: 10.1186/s12888-022-03740-6
56. Giang HT, Duc NQ, Khue PM, Quillet C, Oanh KTH, Thanh NTT, et al. Gender differences in HIV, HCV risk and prevention needs among people who inject drug in Vietnam. *AIDS Behav*. (2023) 27:1989–97. doi: 10.1007/s10461-022-03932-x
57. Rael CT, Davis A. Depression and key associated factors in female sex workers and women living with HIV/AIDS in the Dominican Republic. *Int J STD AIDS*. (2017) 28:433–40. doi: 10.1177/0956462416651374
58. Beattie TS, Smilenova B, Krishnaratne S, Mazzuca A. Mental health problems among female sex workers in low- and middle-income countries: a systematic review and meta-analysis. *PLoS Med*. (2020) 17:e1003297. doi: 10.1371/journal.pmed.1003297
59. McKee M, Reeves A, Clair A, Stuckler D. Living on the edge: precariousness and why it matters for health. *Arch Public Health*. (2017) 75:13. doi: 10.1186/s13690-017-0183-y
60. Gordillo V, Fekete EM, Platteau T, Antoni MH, Schneiderman N, Nöstlinger C, et al. Emotional support and gender in people living with HIV: effects on psychological well-being. *J Behav Med*. (2009) 32:523–31. doi: 10.1007/s10865-009-9222-7
61. Wang X, Cai L, Qian J, Peng J. Social support moderates stress effects on depression. *Int J Ment Health Syst*. (2014) 8:41. doi: 10.1186/1752-4458-8-41
62. Kessler RC, Birnbaum H, Bromet E, Hwang I, Sampson N, Shahly V. Age differences in major depression: results from the National Comorbidity Surveys Replication (NCS-R). *Psychol Med*. (2010) 40:225–37. doi: 10.1017/S0033291709990213
63. Li Y, Hershov R, Irwanto I, Praptoraharjo I, Setiawan M, Levy J. Factors associated with symptoms of depression among injection drug users receiving antiretroviral treatment in Indonesia. *J AIDS Clin Res*. (2014) 5:303. doi: 10.4172/2155-6113.1000303
64. Fiske A, Wetherell JL, Gatz M. Depression in older adults. *Annu Rev Clin Psychol*. (2009) 5:363–89. doi: 10.1146/annurev.clinpsy.032408.153621
65. Roberts RE, Kaplan GA, Shema SJ, Strawbridge WJ. Prevalence and correlates of depression in an aging cohort: the Alameda County Study. *J Gerontol B Psychol Sci Soc Sci*. (1997) 52B:S252–8. doi: 10.1093/geronb/52B.5.S252
66. Younossi Z, Park H, Henry L, Adeyemi A, Stepanova M. Extrahepatic manifestations of hepatitis C: a Meta-analysis of prevalence, quality of life, and economic burden. *Gastroenterology*. (2016) 150:1599–608. doi: 10.1053/j.gastro.2016.02.039
67. Modabbernia A, Poustchi H, Malekzadeh R. Neuropsychiatric and psychosocial issues of patients with Hepatitis C infection: a selective literature review. *Hepat Mon*. (2013) 13:e8340. doi: 10.5812/hepatmon.8340
68. Davoodi L, Masoum B, Moosazadeh M, Jafarpour H, Haghshenas MR, Mousavi T. Psychiatric side effects of pegylated interferon- α and ribavirin therapy in Iranian patients with chronic hepatitis C: a meta-analysis. *Exp Ther Med*. (2018) 16:971–8. doi: 10.3892/etm.2018.6255
69. Yarlott L, Heald E, Forton D. Hepatitis C virus infection, and neurological and psychiatric disorders – a review. *J Adv Res*. (2017) 8:139–48. doi: 10.1016/j.jare.2016.09.005
70. Due OT, Thakkinian A, Thavorncharoensap M, Sobhonslidsuk A, Wu O, Phuong NK, et al. Cost-utility analysis of direct-acting antivirals for treatment of chronic hepatitis C genotype 1 and 6 in Vietnam. *Value Health*. (2020) 23:1180–90. doi: 10.1016/j.jval.2020.03.018
71. Pockros PJ. New direct-acting antivirals in the development for hepatitis C virus infection. *Ther Adv Gastroenterol*. (2010) 3:191–202. doi: 10.1177/1756283X10363055
72. Sundberg I, Lannergård A, Ramklint M, Cunningham JL. Direct-acting antiviral treatment in real world patients with hepatitis C not associated with psychiatric side effects: a prospective observational study. *BMC Psychiatry*. (2018) 18:157. doi: 10.1186/s12888-018-1735-6
73. Rudolph AE, Davis WW, Quan VM, Ha TV, Minh NL, Gregowski A, et al. Perceptions of community- and family-level injection drug user (IDU)- and HIV-related stigma, disclosure decisions and experiences with layered stigma among HIV-positive IDUs in Vietnam. *AIDS Care*. (2012) 24:239–44. doi: 10.1080/09540121.2011.596517
74. Le SM, Trouiller P, Duong TH, Khuat THO, Pham MK, Vallo R, et al. Development and assessment of a community-based screening tool for mental health disorders among people who inject drugs. *Drug Alcohol Rev*. (2022) 41:697–705. doi: 10.1111/dar.13402
75. Michel L. *Screening for mental health disorders in the community (DRIVE project): Validation of a quick screening tool (QST) among people who inject drugs with community-based organizations (CBO)*. (2019). Available at: hri.global/abstracts/abstracthr19/719/print.

76. Glasner-Edwards S, Marinelli-Casey P, Hillhouse M, Ang A, Mooney LJ, Rawson R. Depression among methamphetamine users. *J Nerv Ment Dis.* (2009) 197:225–31. doi: 10.1097/NMD.0b013e31819db6fe
77. Parkes T, Matheson C, Carver H, Budd J, Liddell D, Wallace J, et al. Supporting harm reduction through peer support (SHARPS): testing the feasibility and acceptability of a peer-delivered, relational intervention for people with problem substance use who are homeless, to improve health outcomes, quality of life and social functioning and reduce harms: study protocol. *Pilot Feasibility Stud.* (2019) 5:64. doi: 10.1186/s40814-019-0447-0
78. Pinkham S, Stone K. *A global review of the harm reduction response to amphetamines: A 2015 update.* London: Harm Reduction International (2015).
79. Teesson M, Ross J, Darke S, Lynskey M, Ali R, Ritter A, et al. One year outcomes for heroin dependence: findings from the Australian treatment outcome Study (ATOS). *Drug Alcohol Depend.* (2006) 83:174–80. doi: 10.1016/j.drugalcdep.2005.11.009
80. Xiao L, Wu Z, Luo W, Wei X. Quality of life of outpatients in methadone maintenance treatment clinics. *J Acquir Immune Defic Syndr.* (2010) 53:S116–20. doi: 10.1097/QAI.0b013e3181c7dffb5
81. Yin W, Pang L, Cao X, McGoogan JM, Liu M, Zhang C, et al. Factors associated with depression and anxiety among patients attending community-based methadone maintenance treatment in China. *Addiction.* (2015) 110:51–60. doi: 10.1111/add.12780
82. Sun HM, Li XY, Chow EPF, Li T, Xian Y, Lu YH, et al. Methadone maintenance treatment programme reduces criminal activity and improves social well-being of drug users in China: a systematic review and meta-analysis. *BMJ Open.* (2015) 5:e005997. doi: 10.1136/bmjopen-2014-005997
83. Wang Y, Wang H, Li W, Zhu J, Gold MS, Zhang D, et al. Reduced responses to heroin-cue-induced craving in the dorsal striatum: effects of long-term methadone maintenance treatment. *Neurosci Lett.* (2014) 581:120–4. doi: 10.1016/j.neulet.2014.08.026
84. Le SM, Trouiller P, Duong Thi H, Khuat Thi Hai O, Pham Minh K, Vallo R, et al. Daily heroin injection and psychiatric disorders: a cross-sectional survey among people who inject drugs (PWID) in Haiphong, Vietnam. *Drug Alcohol Depend.* (2020) 216:108334. doi: 10.1016/j.drugalcdep.2020.108334
85. Woody G, Bruce D, Korthuis PT, Chhatre S, Hillhouse M, Jacobs P, et al. HIV risk reduction with buprenorphine-naloxone or methadone: findings from a randomized trial. *J Acquir Immune Defic Syndr.* (2014) 66:288–93. doi: 10.1097/QAI.0000000000000165
86. Castillo EG, Ijadi-Maghsoodi R, Shadravan S, Moore E, Mensah MO, Docherty M, et al. Community interventions to promote mental health and social equity. *Curr Psychiatry Rep.* (2019) 21:35. doi: 10.1007/s11920-019-1017-0
87. Livingston JD, Milne T, Fang ML, Amari E. The effectiveness of interventions for reducing stigma related to substance use disorders: a systematic review. *Addiction.* (2012) 107:39–50. doi: 10.1111/j.1360-0443.2011.03601.x
88. Nguyen VT, Scannapieco M. Drug abuse in Vietnam: a critical review of the literature and implications for future research. *Addiction.* (2008) 103:535–43. doi: 10.1111/j.1360-0443.2007.02122.x
89. Degenhardt L, Peacock A, Colledge S, Leung J, Grebely J, Vickerman P, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. *Lancet Glob Health.* (2017) 5:e1192–207. doi: 10.1016/S2214-109X(17)30375-3
90. Nyirenda M, Chatterji S, Rochat T, Mutevedzi P, Newell ML. Prevalence and correlates of depression among HIV-infected and -affected older people in rural South Africa. *J Affect Disord.* (2013) 151:31–8. doi: 10.1016/j.jad.2013.05.005