A case-control study on psychotropic substance use and risk of Axis I psychiatric disorders in HIV-infected gay or bisexual men in Hong Kong

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Abstract

Background: Psychotropic substance use is common in HIV-infected gay or bisexual men (GBM). This study examined the association between Axis I psychiatric disorders and active psychotropic substance use, and identified factors affecting the prevalence of psychiatric disorders in HIV-infected GBM.

Methods: This is a cross-sectional case-control study taken place in an HIV clinic and community organisations serving people living with HIV or GBM in Hong Kong. Participants were 62 HIV-infected self-identified GBM who reported psychotropic substance use in the past 1 year (cases), and 55 HIV-infected self-identified GBM without psychotropic substance use in the past 1 year and had negative toxicology tests at recruitment (controls).

The Chinese-bilingual Structured Clinical Interview for DSM-IV (Axis I, Patient version) was followed to establish the psychiatric diagnoses. Socio-demographic data, level of social support, HIV-related data, and pattern of psychotropic substance use were collected.

Results: Cases had lower level of social support (p=0.02), more depressive disorders (AOR 3.4, 95% CI 1.3-8.7, p=0.01) and psychotic disorders (AOR 7.2, 95% CI 1.2-41, p=0.03) but not anxiety disorders. Significant difference in the prevalence of psychiatric disorders was only evident for disorders with onset after HIV diagnosis. Methamphetamine dependence (AOR 6.63, 95% CI 1.53-228.72, p<0.01), weekly methamphetamine use for 2 years or more (AOR 18.6, 95% CI 1.26-274.69, p=0.03), using methamphetamine beyond chemsex (AOR 4.76, 95% CI 1.17-19.41, p=0.03*)* were significant predictors for psychiatric disorders in the cases in separate logistic regression models. Duration of HIV diagnosis was a significant independent predictor in all three models.

Conclusions: Active psychotropic substance use in HIV-infected gay or bisexual men was associated with a 3-fold increase in Axis I psychiatric disorders. This increase in psychiatric disorders was predicted by the severity, duration and context of methamphetamine use and the duration of HIV diagnosis.

Background

Psychotropic substance (PS) use is highly common in HIV-infected gay or bisexual men (GBM) with reported prevalence ranging from 30-60% over a 3- to 12-month period (1-4). Recently the pattern of PS use has shifted from with the predominate use of ‘club drugs’ such as 3,4-methylenedioxymethamphetmine (MDMA) and ketamine for socializing or dancing (5, 6) to methamphetamine and *g*-hydroxybutyrate (GHB) for enhancing their sexual experiences (7, 8). The latter phenomenon is now commonly known as ‘chemsex’ (9).

The use of PS has been shown to associate with higher risks of psychiatric disorders. Methamphetamine users were 11 times more likely to have psychosis than the general population (10) and that the intensity, defined as the product the of frequency and duration of methamphetamine use, was associated with more depressive symptoms (11). Frequent cannabis use was associated with elevated risks of schizophrenia (12, 13) and depression (14). The positive relationship between substance use disorder (SUD) and Axis I psychiatric disorders has been confirmed by decades of epidemiological studies and a meta-analysis (15). The risks for various psychiatric disorders were different for different PS (16).

As the sexual minority and living with HIV infection both increased the risks of having psychiatric disorders (17-20). Factors related to higher psychiatric morbidities in people living with HIV (PLHIV) included low nadir CD4 (21), symptomatic infections (22), co-occurring HCV infection (21, 23) and absence or non-adherence of antiretroviral treatment (ART) (22, 24-26). It is uncertain how the pattern of PS use among HIV-infected GBM associates with the profile of psychiatric disorders in this highly-stigmatised population.

In Hong Kong, a special administrative region in the southern part of China, a HIV epidemic in GBM was observed in the past decade (27). At the largest local HIV clinic, the proportion of new attendees with homosexually acquired HIV reported ever methamphetamine use increased from 24% in 2014 to 36% in 2016 (Chan K. Personal Communication. 7 June 2017). The earlier local studies of psychiatric aspect of PLHIV fell short of focusing in this sexual minority group (28) without examining the relationships between substance use and psychiatric disorders (29). There has been no published study using standard diagnostic tools on psychiatric and substance use disorders of HIV-infected GBM in Asian settings.

Methods

Aim

This study aimed to determine the association between Axis I psychiatric disorders and active PS use, and to identify the socio-demographic, HIV-related and substance-related factors affecting the prevalence of Axis I psychiatric disorders in HIV-infected GBM.

Study design

This was a cross-sectional case-control study.

Study settings

Subjects were recruited from Integrated Treatment Centre (ITC) and eight community non-governmental organisations (NGO) that provide HIV services to GBM or support services to PLHIV. ITC is the largest clinic serving 70% of local HIV infection caseloads (30).

Participants

Inclusion criteria were self-identified GBM diagnosed with HIV infection for 1 month or more. Cases were those reported any PS use in the previous 1 year. Controls were those reported no PS use in the previous 1 year with a negative urine toxicology screening result at the time of recruitment. Never PS use was uncommon in this population thus a one-year cut-off was chosen to differentiate the cases from the controls according to the symptoms duration required for diagnosing substance related disorders in DSM-IV. A one-month period from initial HIV diagnosis to recruitment allowed observation of any psychiatric symptoms emerged and persisted to fulfil any diagnostic criteria. HIV status was confirmed for those receiving HIV treatment from ITC or having two different HIV antibody tests tested positive. Those could not communicate in Chinese or English, could not provide an informed consent, aged below 16 or did not usually reside locally (<50% time in previous or coming 6 months) were excluded.

Study variables

Axis I psychiatric diagnosis

The modules on mood disorders, anxiety disorders, psychotic disorders and substance related disorders of the Chinese-Bilingual Structured Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (Axis I, Patient version) (CB-SCID-I/P) were followed to establish the current and lifetime psychiatric diagnosis. CB-SCID-I/P has been validated locally (31, 32) and is currently the most updated translated Chinese version available.

Pattern and severity of psychotropic substance use

The types and methods of PS use, its use in chemsex or other settings, frequency of use in past 1 year and days of use in the past 1 month were obtained.

Socio-demographic data and social support

Age, ethnicity, education attainment, relationship status, employment status, income level and living arrangement were collected by self-administered survey. Level of social support was measured by the Medical Outcomes Study Social Support Survey (MOS-SSS). It is a 19-item self-administered questionnaire that examined 4 domains of social support, including tangible support (TAN), affectionate support (AFF), positive social interaction (POS) and emotional or informational support (EMI) (33). This has been validated in Hong Kong Chinese (34) and has been used in a local study of PLHIV (35).

HIV - related data

Duration of HIV diagnosis, use of ART and adherence were collected by interviewer-administered questionnaire. The most recent CD4, HIV viral load (VL), hepatitis C (HCV) co-infection, and stage of HIV infection were obtained from the clinical system of ITC or from the blood samples collected at study recruitment. The definitions are shown in Table 1.

Study administration

Convenience sampling was used. Staff at the study sites invited potentially eligible subjects to contact the research coordinator who screened for their eligibility and arranged the interviews. The authors conducted the interviews in private rooms in ITC or the NGO. Subjects completed a questionnaire on demography, HIV-related data and MOS-SSS, followed by the assessment of PS use pattern and ascertainment of psychiatric diagnosis. Urine toxicology screening was performed by commercially available kits (Wondfo®) for the presence of amphetamines, barbituates, benzodiazepines, cocaine, marijuana, methamphetamine, MDMA, morphine, opiate, ketamine and synthetic cannabis. Subjects provided their unique clinic number and date of birth for data retrieval from ITC or provided blood samples for laboratory investigations. Subjects were referred to various treatment agencies when appropriate with their consent.

Sample size calculations and statistical analysis

Referenced from Bing et al. (2001), the cases were assumed to be 3 times more likely to have any mood, anxiety or psychotic disorders. With a 20% lifetime prevalence of psychiatric disorders (excluding substance related disorders) in the controls, 80% power and 5% Type I error, subjects required in each arm was estimated to be 60.

Odds ratios were calculated to compare the differences in psychiatric diagnoses between the cases and controls. Adjustments for potential confounding factors identified in univariate analysis were performed using multiple logistic regression. Univariate and multivariate analyses using logistic regressions were performed to identify factors affecting the prevalence of psychiatric diagnosis (excluding substance related disorders) in the cases and controls. Following earlier recommendations (36, 37), no adjustments were made for multiple comparison as selection of the factors under studied were informed by previous research. In this relatively small study, this would also avoid reduction in power thus missing possible significant findings for further investigations. All comparisons of CD4 counts were age and ethnicity-adjusted. All statistical analyses were performed using SPSS version 24.0 using two-sided tests and a p-value <0.05 was considered statistically significant.

Results

Subjects' description

During September 2017 to May 2018, 117 subjects were recruited. Their background characteristics are shown in Table 2. The cases scored significantly lower in the total and subscales of MOS-SSS except tangible support subscale. The cases had higher rate of HIV non-suppression after ART than the controls although the difference was statistically insignificant (Fisher exact test, p=0.06). The cases were comparable to the controls in terms of other demographic variables and stage of HIV infection. The subjects recruited from ITC and NGO were comparable except all non-Chinese subjects came from ITC (Fisher exact test, p=0.006).

Psychotropic substance use pattern **Table** 3 lists the specific types and number of PS used by the cases and controls. Methamphetamine was the most commonly used PS: 97% of the cases and 13% of the controls reported ever used. One-third of the controls reported previous PS use.

Table 4 details the methamphetamine use pattern in the cases. A quarter started methamphetamine use after HIV diagnosis and 55% of those started methamphetamine use before HIV diagnosis did not reduce the frequency of use afterwards. Only 3% reported regular injections. Methamphetamine use for sex i.e. chemsex, was highly common: 87% initiated and 95% ever used methamphetamine at chemsex. Methamphetamine was also the most frequently used PS with 22% using it for more than 14 days in the previous month, a frequency only reported by 2 cases for GHB and none for other substances (Supplementary data Table S1).

Pattern of DSM-IV Axis I psychiatric diagnosis

Table 5 and Table 6 list the lifetime and current SUD and other psychiatric diagnoses according to the DSM-IV criteria. Methamphetamine-related SUD was the most common SUD in the cases: 50% (n=31) fulfilled criteria for DSM-IV lifetime methamphetamine dependence and 8% (n=5) methamphetamine abuse. Depressive disorders were the most common diagnoses across all subjects, followed by psychotic disorders. Figure 1 illustrates the pattern of co-occurring psychiatric diagnoses in the cases and controls.

After adjustments with age, duration of HIV diagnosis and level of social support, cases were 6.1 times (95% CI 2.5-14.8, p<0.001) more likely to have lifetime psychiatric diagnosis and 3.1 times (95% CI 1.3-7.6, p<0.001) more likely to have lifetime psychiatric diagnosis excluding SUD (Table 7). Specifically, they were 7.2 times (95% CI 1.3-41, p=0.03) more likely to have lifetime psychotic disorders and 3.4 times (95% CI 1.3-8.7, p=0.01) more likely to have lifetime depressive disorders. After excluding substance-induced depressive episodes, cases were still 2.7 times (95% CI 1.0-6.9, p=0.04) more likely to have lifetime depressive disorders. The prevalence of lifetime anxiety disorders in the case and controls did not differ significantly (adjusted OR 1.1, 95% CI 0.3-4.7, p=0.86).

There was no statistical difference was observed in the prevalence of psychiatric disorders with onset prior to HIV diagnosis between the cases and controls, but the cases were 6 times (AOR 6.36, 95% CI 1.96-20.65, p=0.002) more likely to have any psychiatric disorders with onset after HIV diagnosis (Table 8).

Factors affecting the prevalence of DSM-IV Axis I psychiatric diagnosis

Table 9 shows the univariate analysis of factors affecting the prevalence of lifetime psychiatric disorders in the cases. Methamphetamine dependence was highly correlated with SUD, $r(62)$=0.822. p<0.01 and duration of weekly use of

methamphetamine, *r(62)*=0.769, *p*<0.01 (Supplementary data Table S2). Multivariate analyses excluding these highly-correlated variables were performed separately (Table 10). In the first two models, either methamphetamine dependence (AOR 6.63, 95% CI 1.53-28.72, *p*=0.01) or SUD (AOR 6.80, 95% CI 1.38-33.62, *p*=0.02) and duration of HIV diagnosis remained as significant predictors. In the third model which excluded methamphetamine dependence and SUD from the analysis, methamphetamine use beyond chemsex (AOR 4.76, 95% CI 1.17-19.41, *p*=0.03) and duration of HIV diagnosis remained as independent predictors. As methamphetamine use beyond chemsex was moderately correlated with methamphetamine dependence, *r*(60)=0.533, *p*<0.01 and weakly correlated with duration of weekly methamphetamine use, *r*(60)=0.464, *p*<0.01, a fourth model was built excluding methamphetamine dependence, methamphetamine use beyond chemsex and SUD. In this model, having weekly use of methamphetamine for 2 years or more (AOR 18.60, 95% CI 1.26-274.69, *p*=0.03) and duration of HIV diagnosis remained as independent predictors. All models showed satisfactory goodness-of-fit.

Multivariate analysis in the controls showed that SUD (AOR 17.51, 95% CI 1.42-300, *p*=0.03) and family history of mental illness (AOR 6.25, 95% CI 1.51-25.82, *p*=0.01) were independent significant predictors in the final model (Supplementary data Table S3-4).

Discussion

Our sample was characterised by relatively young age, more recent HIV diagnosis, low level of virological or immunological failure and a distinct PS use pattern. These were consistent with other local reports (29, 38, 39) and contrasted with overseas cohorts that often consisted of men of older age with less favourable HIV outcomes (2, 40). Methamphetamine was the most commonly and frequently used substance, unlike the more prevalent use of cannabis or cocaine elsewhere. IDU rate was of the lower range compared to studies from the UK and Australia (2, 4). Methamphetamine users in our study had less frequent, less injection and shorter duration of methamphetamine use compared to overseas cohorts whose sexual orientation or HIV status were unspecified (10, 41, 42).

Consistent with literature, depressive disorders were the most common psychiatric diagnosis in our sample. The risk of lifetime depressive disorders in our cases (AOR 3.40, 95% CI 1.33–8.69, *p* = 0.01) was different from the lack of significant association of depression with methamphetamine use, slightly stronger than that with cocaine use and was comparable to that with drug abuse reported by Skeer, Mimiaga (40). Although comparison of their cross-sectional measures with our lifetime diagnosis is difficult, the difference observed could be related to their use of PHQ-9 which is less specific than the standard diagnosing tool and the inclusion of active users of other PS in the comparison group hence weakening their associations. It may also be explained by the more severe substance use in our sample: 52% of our cases fulfilled DSM-IV dependence criteria, whereas Skeer, Mimiaga (40) reported in their study that 55% of their substance users fulfilled the less restrictive abuse criteria using PHQ. The lack of description of methamphetamine use pattern by Forrest, Metsch (43) rendered comparisons to their results difficult.

The rate of lifetime psychotic disorders in our cases was comparable to other studies (10, 44) despite different assessment methods were used in samples with heavier and longer methamphetamine use. The proportion of lifetime methamphetamine-induced psychotic disorder among subjects with methamphetamine dependence (32%) resembled previous findings (10, 45, 46). The lack of schizophrenia was likely related to our small sample size with less frequent and shorter duration of methamphetamine use, based on the conversion rate reported by Niemi-Pynttari, Sund (47).

The lack of significant association of anxiety disorders with PS use observed in our study was similarly reported by Skeer et al. (2012). As homelessness, HIV symptoms and IDU predicted the anxiety level in PLHIV (48, 49), the absence of homelessness, few IDU and immunological failure in our cases may explain the low prevalence of anxiety disorder observed.

Corroborated with previous research (10, 11, 41), methamphetamine dependence and duration of methamphetamine use significantly predicted lifetime psychiatric disorders in our cases. The difference in rates of psychotic disorders as reported by McKetin, McLaren (10) could be related to different outcome measures. The infrequent and short duration of methamphetamine use in our non-dependent cases could also have inflated our odds ratio (Supplementary data Table S5). We showed that weekly use of methamphetamine for 2 years or more significantly predicted psychiatric disorders, concurred with previous findings on the positive relationship between frequency and duration of methamphetamine use and psychotic symptoms (10, 44).

A prominent finding from this study was the positive association between active PS use and psychiatric disorders appeared only for those with onset after HIV diagnosis. Our findings showed that weekly methamphetamine use of more than 2 years, methamphetamine use beyond chemsex and methamphetamine dependence predicted psychiatric disorders, and that all these factors correlated with a report of initiating or increasing methamphetamine use after HIV diagnosis. These observations suggested the diagnosis of HIV may have a critical impact in influencing the pattern of PS use and psychiatric diagnosis, although the characteristics of such relationships such as causality and temporality needs further evaluation.

This postulation concurred with earlier studies showing methamphetamine use was associated with the purpose to avoid unpleasant emotions in mixed-HIV status GBM (50) and to deal with negative emotions associated with HIV (51–53). Low mood was a major reason for PS use in local HIV-infected drug users, majority of whom were MSM (29). Our findings extended this knowledgebase and illustrated that using methamphetamine at non-sexual settings correlated with methamphetamine dependence and duration of HIV diagnosis and predicted psychiatric disorders. To avoid ongoing HIV transmissions, instead of using methamphetamine in chemsex which commonly took place over weekends, some cases reported using methamphetamine at other situations such as masturbation that could happen more frequently. This shift in the setting of methamphetamine use was probably unique in GBM, as chemsex with methamphetamine was much less common in the general population (54, 55).

The finding that the duration of HIV diagnosis predicated psychiatric diagnosis echoed previous results (56, 57) although direct comparison between the lifetime diagnosis and the point prevalence used in the other studies was difficult. The lack of significant association of psychiatric disorders with the stage of HIV infection echoed previous findings (21, 58, 59).

To our knowledge, this is the first study that examined PS use and its relationship with psychiatric disorders in HIV-infected GBM using a standard diagnostic tool. The incorporation of socio-demographic, HIV-related and substance-related factors in examining psychiatric epidemiology generated new insights into the possible inter-relationships among them. A case-control study design was more efficient than a prevalence survey and it minimised the sampling and surveillance bias when the cases and controls were compared. Multiple recruitment sources allowed sampling of subjects not engaged in HIV treatment during the study period, a situation more common among those with active PS use. The close collaborations with NGOs provided flexibility in scheduling the interviews at locations familiar and convenient to the subjects, facilitating recruitment of this hard-to-reach group. The inclusion of psychotic disorders filled a research gap that is relevant to the common use of methamphetamine in this population. The use of laboratory and clinical markers minimised recall bias.

This study had several limitations. Firstly, there was selection bias in non-randomised samples that limited the generalisability of our results. Our cases were largely comparable to the sample reported by Lee, Chan (29) regarding the proportion of viral suppression and living alone, although they were older with lower CD4 level. This could be explained by the discrepancy in case-mix where the hospital-based clinics were more likely providing care for patients with more severe disease, the minority of heterosexual subjects sampled and the lower CD4 observed with ageing. The lack of local data on PS use pattern in this population made assessment of the representativeness regarding these aspects difficult. Individuals with more severe PS use might not have joined the study, like when the substance use took priority. Sampling at the NGOs

where free HIV testing services were provided might have resulted in sampling of subjects with relatively short duration of methamphetamine use. It is uncertain if our subjects joined the study for treatment leading to over-estimation of the prevalence of psychiatric disorders. Yet even if these exist, the comparisons between the cases and the controls should still be valid. Secondly, the results of this study could not indicate any causal relationships between the factors studied as our study was not powered to detect the differences in specific psychiatric diagnosis. Thirdly, there could be recall bias in substance use patterns, past psychiatric symptoms and ART adherence.

Conclusion

Active PS use in HIV-infected GBM was associated with a three-fold increase in psychiatric disorders. The increase was evident only for those with onset after HIV diagnosis and was predicted by the severity, duration and context of methamphetamine use and duration of HIV diagnosis. These findings supported regular screening of depression and PS use in HIV clinical care. The predictors for psychiatric disorders should be further explored as potentially effective harm reduction measures. With the continued HIV epidemic in GBM and the popularity of methamphetamine in Asia, a proportion of these highly-stigmatised individuals suffered multiple biopsychosocial disadvantages despite the availability of highly effective HIV treatment. Chemsex, a less described phenomenon in this region, has been the most important context where they explored and continued their methamphetamine use. Coordinated efforts from HIV, psychiatric and substance use services are needed to prevent harms arising from PS use and chemsex and to identify those in need and facilitate treatment access.

Declarations

Ethics approval and consent to participate

Approval by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster, Queen Mary Hospital (IRB reference number UW 16-406 and UW 18-387) and the Ethics Committees of the Department of Health, Hong Kong SAR Government (LM 366/2016) were obtained. Written informed consent was obtained from each participant before the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available due to sensitivity of the research questions but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LCK and CKK conceptualised the study and collected the data. LCK analyzed and interpreted the patient data and draft the manuscript. All authors read and approved the final manuscript.

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Abbreviations

AFF: affectionate support

CB-SCID-I/P: Chinese-Bilingual Structured Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (Axis I, Patient version)

EMI: and emotional or informational support

GBM: gay or bisexual men

GHB: *g*-hydroxybutyrate

HCV: hepatitis C

ITC: Integrated Treatment Centre

MDMA: 3,4-methylenedioxymethamphetmine

MOS-SSS: Medical Outcomes Study Social Support Survey

NGO: non-governmental organisations

PLHIV: people living with HIV

POS: positive social interaction

PS: Psychotropic substance

SUD: substance use disorder

TAN: tangible support

VL: viral load

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Tables

Table 1 Definitions of stage of HIV infection and HIV outcome measures

Measures	Definitions
Stage of HIV infection [1]	A – asymptomatic infection B – symptomatic infection without AIDS-defining illness C – symptomatic infection with AIDS-defining illness
Level of immunodeficiency [1]	1- CD4 >499/µL 2- CD4 200-499/µL 3- CD4 <200 /µL
HIV non-suppression & virologic failure [2]	Any detectable HIV viral load defines HIV non-suppression; failure to achieve undetectable HIV viral load 6 months after ART initiation defines virologic failure
ART adherence[3]	Number of doses taken over doses prescribed in the past 3 months; at least 95% was considered satisfactory
References: [1] Scientific Committee on AIDS (60) [2] European AIDS Clinical Society (61) [3] Ho, Fong (62), Paterson, Swindells (63)	

Table 2 Background characteristics of the subjects

		Case (n=62)		Control (n=55)		*p*-value[1]
Socio-demographic characteristics						
Non-Chinese		5	8%	3	6%	0.72
Age[2]		32	[28,40]	37	[27,46]	0.13
Bisexual		5	8%	2	4%	0.45
In a relationship/married		24	39%	21	38%	0.95
Lived alone		14	23%	14	25%	0.72
No tertiary education		16	26%	20	36%	0.21
Occupation	Part-time/unemployed	19	31%	11	20%	0.42
	Retired/student	3	5%	6	11%	
	Full-time	40	65%	38	69%	
Monthly income	$15000 or below	32	52%	27	49%	0.67
	$15001-40000	24	39%	18	33%	
	$40001 or above	6	10%	10	18%	
Social support[3,4]	MOS-SSS total	59.8	(14.9)	66.2	(15.1)	0.02
	EMI subscale	24.8	(7.3)	27.6	(6.8)	0.03
	AFF subscale	9.5	(2.6)	10.7	(2.5)	0.02
	TAN subscale	12.5	(4.2)	13.0	(4.1)	0.47
	POS subscale	10.1	(3.0)	11.5	(2.7)	0.01
HIV-related characteristics						
Duration of HIV diagnosis (year)[2]		2	[0,6]	2	[1,7]	0.13
Stage of HIV infection	A	36	58%	37	67%	0.36
	B or C	8	10%	13	24%	
	Not available	18	29%	5	9%	
Receiving ART		60	97%	50	91%	0.25
ART adherence <95%		7/59	12%	1	2%	0.07
HIV non-suppression[5]		7/56	13%	1/49	2%	0.06
CD4<200 µL		1/62	2%	2/53	4%	0.26
HCV co-infection		2/61	3%	0/53	0%	0.50

[1] t-test or Mann Whitney U test for continuous variable, chi-square or fisher exact test for categorical variables, logistic regression was used to adjust for age and ethnicity in comparing CD4

[2] median and inter-quartile ranges were presented

[3] MOS-SSS medical outcome survey, social support scale, EMI emotional or informational support, AFF affectionate support, TAN tangible support, POS positive experiences

[4] mean and standard deviations were presented

[5] Excluding those received ART <6 months

Table 3 Types and numbers of psychotropic substance use in the cases and controls

	Case (n=62)				Control (n=55)	
	Ever used		Active use (past 1 year)		Ever used	
Specific substance used						
Methamphetamine	60	97%	56	90%	7	13%
GHB	56	90%	46	74%	4	7%
Cannabis	46	74%	25	40%	10	18%
MDMA	44	71%	12	19%	8	15%
Ketamine	33	53%	3	5%	6	11%
Sedatives excluding GHB [1]	18	29%	9	15%	4	7%
5-methoxy-diisopropyltryptamine (Foxy)	16	26%	12	19%	0	
Cocaine	10	16%	3	5%	0	
Cough mixture	0		0		1	2%
Number of substance used						
0	0		0		35	64%
1	0		11	18%	8	15%
2-3	18	29%	30	48%	7	13%
4-5	22	35%	21	34%	4	7%
6 or more	22	35%	0		1	2%

[1] 6 of the 18 cases referred to nimetazepam (commonly known as ‘five’)

Table 4 Patterns of methamphetamine use in the cases

		Case (n=60)	
Age of first use [1]		29	(22,35)
Initiated use after HIV diagnosis		15	25%
Frequency after HIV diagnosis	Stopped	2	3%
	Reduced	13	22%
	Similar	10	17%
	Increased	15	25%
	Not applicable (ever used once only)	5	8%
Intravenous use	Ever	8	13%
	Past 1 year	7	12%
	Regular intravenous use	2	3%
Use in chemsex	Initiated at chemsex	52	87%
	Ever used for chemsex	57	95%
	Exclusive use in chemsex only	27	45%
Duration of regular use (at least monthly)	Irregular use (less frequent than monthly)	16	28%
	1 year or less	17	30%
	>1 year -2 years	12	20%
	>2 years -5 years	9	15%
	>5 years or more	6	8%
Duration of regular use (at least weekly)	Irregular use (less frequent than weekly)	24	40%
	1 year or less	17	30%
	>1 year -2 years	8	13%
	>2 years -5 years	8	13%
	>5 years or more	3	5%
Days of use in the past 1 month	0	24	40%
	1-2	12	20%
	3-6	7	12%
	7-14	4	7%
	15 or more	13	22%
Estimated monthly cost	Free	12	20%
	HKD$1000 or less	11	18%
	HKD$1000-2000	7	12%
	HKD$2000 or more	7	12%
	Missing	11	18%

Table 5 Lifetime and current DSM-IV substance use disorders in the cases and controls

	Lifetime diagnosis				Current diagnosis			
	Case (n=62)		Control (n=55)		Case (n=62)		Control (n=55)	
Amphetamine-like substances related								
Methamphetamine-related								
Abuse	5	8%	1	2%	1	2%	0	
Dependence	31	50%	1	2%	23	37%	0	
MDMA-related								
Abuse	0		1	2%	0		0	
Dependence	1	2%	1	2%	0		0	
Cannabis-related								
Abuse	1	2%	0		1	2%	0	
Dependence	1	2%	0		1	2%	0	
Hallucinogen-related (Ketamine)								
Abuse	0		0		0		0	
Dependence	1	2%	0		0		0	
Sedatives-related								
Abuse[1]	2	3%	0		0		0	
Dependence[2]	1	2%	0		1	2%	0	
Alcohol related								
Abuse	2	3%			0			

[1]Both were GHB-related; [2] Zopiclone-related

Table 6 Lifetime and current DSM-IV Axis I psychiatric diagnoses (excluding substance use disorders) in the cases and controls

	Lifetime diagnosis				Current diagnosis			
	Case (n=62)		Control (n=55)		Case (n=62)		Control (n=55)	
Any mood disorders	**25**	**40%**	**10**	**18%**	**9**	**15%**	**2**	**4%**
Any depressive disorders	25	40%	9	16%	9	15%	2	4%
Major depressive episode	15	24%	6	11%	4	6%	2	4%
Single episode	12	19%	5	9%	4	6%	1	2%
Recurrent	3	5%	1	2%	0		1	2%
Depressive episode NOS	5	8%	3	5%	1	2%	0	
Substance-induced mood disorder (with depressive features)	4	6%	0		3	5%	0	
Dysthymia	1	2%	0		1	2%	0	
Bipolar disorders	0		1	2%	0		0	
Any anxiety disorders	**6**	**10%**	**4**	**7%**	**3**	**5%**	**1**	**2%**
Agoraphobia	0		1	2%	0		0	
Panic disorder	1	2%	2	4%	0		0	
Social phobia	3	5%	0		1	2%	0	
PTSD[1]	2	3%	0		0		0	
Anxiety NOS[2]	3	5%	1	2%	2	3%	1	2%
Any psychotic disorders	**10**	**16%**	**2**	**4%**	**5**	**8%**	**0**	
Substance-induced	10	16%	1	2%	5	8%	0	
Brief psychotic disorder	0		1	2%	0		0	

[1] Post-traumatic stress disorders (PTSD)

[2] not otherwise specified (NOS)

Case (n=62)	Control (n=55)	Crude OR	(95% CI)	*p*-value	AOR[1]	(95% CI)	*p*-value	AOR[2]	(95% CI)	*p*-value			
Mood disorders			25 (40%)	10 (18%)	3.04	(1.30-7.13)	0.01	**2.96**	(1.19-7.36)	0.02	**3.48**	1.43-8.47	0.006
Depressive disorders			25 (40%)	9 (16%)	3.45	(1.44-8.30)	0.006	**3.40**	(1.33-8.69)	0.01	**4.03**	1.62-10.07	0.003
Excluding substance-induced mood disorder		21 (34%)	9 (16%)	2.62	(1.08-6.36)	0.03	**2.67**	(1.03-6.94)	0.04	**3.18**	1.26-8.04	0.01	
Anxiety disorders			6 (10%)	4 (7%)	1.37	(0.37-5.12)	0.57	**1.14**	(0.28-4.67)	0.86	**1.38**	0.34-5.53	0.65
Psychotic disorders			10 (16%)	2 (4%)	5.10	(1.07-24.39)	0.04	**7.18**	(1.27-41.65)	0.03	**8.64**	1.52-49.25	0.02
Excluding substance-induced			0	1 (2%)	-			**-**			-	-	-
Any psychiatric (mood, anxiety or psychotic) disorder			31 (50%)	14 (25%)	2.93	(1.34-6.42)	0.007	**3.10**	(1.28-7.56)	0.01	**3.69**	1.56-8.74	0.003
Substance use disorders (SUD)			37 (60%)	4 (7%)	18.87	(6.05-58.84)	<0.001	**19.41**	(5.75-65.58)	<0.001	**21.77**	6.55-72.34	<0.001
Any psychiatric disorder or SUD			44 (71%)	15 (27%)	6.52	(2.91-14.62)	<0.001	**6.11**	(2.52-14.80)	<0.001	**6.99**	3.00-16.29	<0.001
Co-occurring SUD and psychiatric disorders			24 (39%)	3 (5%)	10.95	(3.07-39.02)	<0.001	**16.27**	(3.85-68.87)	<0.001	**19.32**	4.57-81.66	<0.001

[1]Adjusted for MOS-SSS total score, age and duration of HIV diagnosis

[2] Adjusted for age and duration of HIV diagnosis

Abbreviations: AOR - adjusted odds ratio, CI - confidence interval, MOS-SSS - Medical Outcome Survey Social Support Scale, OR - odds ratio, SUD - substance use disorders

Table 7. Comparison of the prevalence of lifetime psychiatric disorders and substance use disorders between the cases and controls

Table 8. Comparisons of the prevalence of lifetime psychiatric disorders and substance use disorders with onset proior to and after HIV diagnosis between the cases and controls

	Psychiatric disorders prior to HIV diagnosis				Psychiatric disorders after HIV diagnosis			
	Case (n=62)	Control (n=55)	AOR (95% CI)[1]	*p*-value	Case (n=62)	Control (n=55)	AOR (95% CI)[1]	*p*-value
Mood disorders	6 (10%)	5 (9%)	1.05 (0.28-3.93)	0.95	19 (31%)	5 (9%)	4.73 (1.47-15.20)	0.009
Depressive disorders	6 (10%)	5 (9%)	1.02 (0.27-3.5)	0.97	19 (31%)	4 (7%)	6.22 (1.76-21.97)	0.005
Anxiety disorders	5 (8%)	2 (4%)	1.36 (0.24-7.81)	0.73	1 (2%)	2 (4%)	0.77 (0.06-10.69)	0.85
Psychotic disorders	1 (2%)	2 (4%)	0.37 (0.03-4.98)	0.45	9 (14%)	0	-	
Any psychiatric (mood, anxiety or psychotic) disorder	10 (16%)	9 (16%)	0.94 (0.33-2.62)	0.90	24 (39%)	7 (13%)	6.36 (1.96-20.65)	0.002
Substance use disorders (SUD)	24 (39%)	4 (7%)	10.8 (3.2-36.2)	<0.001	15 (24%)	0	-	
Any psychiatric disorder or SUD	27 (44%)	11 (20%)	2.71 (1.15-6.43)	0.02	27 (44%)	7 (13%)	6.66 (1.08-41.01)	0.04

[1]Adjusted for MOS-SSS total score, age and duration of HIV diagnosis
Abbreviations: AOR - adjusted odds ratio, CI - confidence interval, MOS-SSS - Medical Outcome Survey Social Support Scale, SUD - substance use disorders

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Table 9. Univariate analysis of the factors affecting the prevalence of lifetime psychiatric disorders in the cases

	Lifetime psychiatric diagnosis		*p*-value[2]
	Yes (n=31)[1]	No (n=31)[1]	
Sociodemographic factors			
Non-Chinese	3	2	0.64
Age[3]	34.68 (7.90)	33.19 (8.75)	0.45
Bisexual	4	1	0.16
Secondary education only	6	10	0.25
Unemployed	6	3	0.28
Monthly income $10000 or below	9	4	0.12
Single/divorced	21	17	0.30
Lived alone	8	6	0.54
Family history of psychiatric illness	9	7	0.56
MOS-SSS total[3]	55.74 (13.76)	63.84 (15.18)	0.03
HIV-related factors			
Duration of HIV diagnosis[4]	5 [1,7]	1 [0,2]	0.003
Stage B or C	3/21	5/23	0.70
ART initiated	31	30	1.00
ART adherence <95%	5	2/30	0.42
Virologic failure	4/28	3/29	0.71
CD4<200/μL	1	0	1.00
HCV co-infection	2	2/30	1.00
Substance-related factors			
Any SUD	24	13	0.004
Methamphetamine use factors			
Dependence	22	9	<0.001
Duration of regular use			0.004
Irregular or no use	8	18	
Weekly use for 2 years or less	13	12	
Weekly use for more than 2 years	10	1	
Days of use in last month[4]	2 [0,16]	1 [0,3]	0.17
Age of first use (n=60)[3]	30.03 (9.19)	29.61 (8.94)	0.86
Not exclusive in chemsex	22	11	0.006
Increased or started after HIV diagnosis	18	12	0.13
Other psychotropic substance use factors			
Ever monthly use of MDMA	11	5	0.08
Ever monthly use of GHB	15	11	0.30
Number of substances ever used[4]	5 [4,6]	4 [3,6]	0.11

[1] unless otherwise stated for specific variables

[2] *t* test or Mann Whitney U test for continuous variable, chi-square or Fisher exact test for categorical variables

[3] means and standard deviations are presented

[4] medians and interquartile ranges are presented

Abbreviations: ART - antiretroviral treatment, HCV - hepatitis C virus, GHB - *g*-hydroxybutyrate, MDMA - 3,4-methylenedioxymethamphetamine, MOS-SSS - Medical Outcome Survey Social Support Scale, SDS - Severity of Dependence Scale, SUD - substance use disorders

Table 10. Multivariate loistic regression analysis of the factors affecting the prevalence of lifetime psychiatric disorders in the cases

	Model 1		Model 2		Model 3		Model 4	
	AOR[1] (95% CI)	*p*-value	AOR[1] (95% CI)	*p*-value	AOR[1] (95% CI)	*p*-value	AOR[1] (95% CI)	*p*-value
Substance use disorders (Model 1)	6.80 (1.38-33.62)	0.02						
Methamphetamine dependence (Model 2)			6.63 (1.53-28.72)	0.01				
Methamphetamine use beyond chemsex (Model 3)					4.76 (1.17-19.41)	0.03		
weekly use of methamphetamine for 2 years or less (Model 4)							1.76 (0.38-8.09)	0.47
weekly use of methamphetamine for more than 2 years (Model 4)							18.60 (1.26-274.69)	0.03
Ever MDMA monthly use (Model 4)							4.41 (0.79-25.67)	0.10
Duration of HIV diagnosis (Models 1-4)	1.87 (1.28-2.72)	0.001	1.78 (1.23-2.52)	0.002	1.73 (1.23-2.43)	0.002	1.77 (1.22-2.58)	0.003
Model summary	Cox & Snell R^2 :0.41 Hosmer-Lemeshow test: Chi-square 3.7 df 7 p=0.82		Cox & Snell R^2 :0.42 Hosmer-Lemeshow test: Chi-square 6.8 df 7 p= 0.45		Cox & Snell R^2 :0.39 Hosmer-Lemeshow test: Chi-square 10.3 df 7 p= 0.18		Cox & Snell R^2 :0.42 Hosmer-Lemeshow test: Chi-square 12.0 df 7 p= 0.10	

[1] Factors were adjusted for the other variables as shown in individual models
Abbreviations: AOR – adjusted odds ratio, CI – confidence interval, MDMA - 3,4-methylenedioxymethamphetamine

Figures

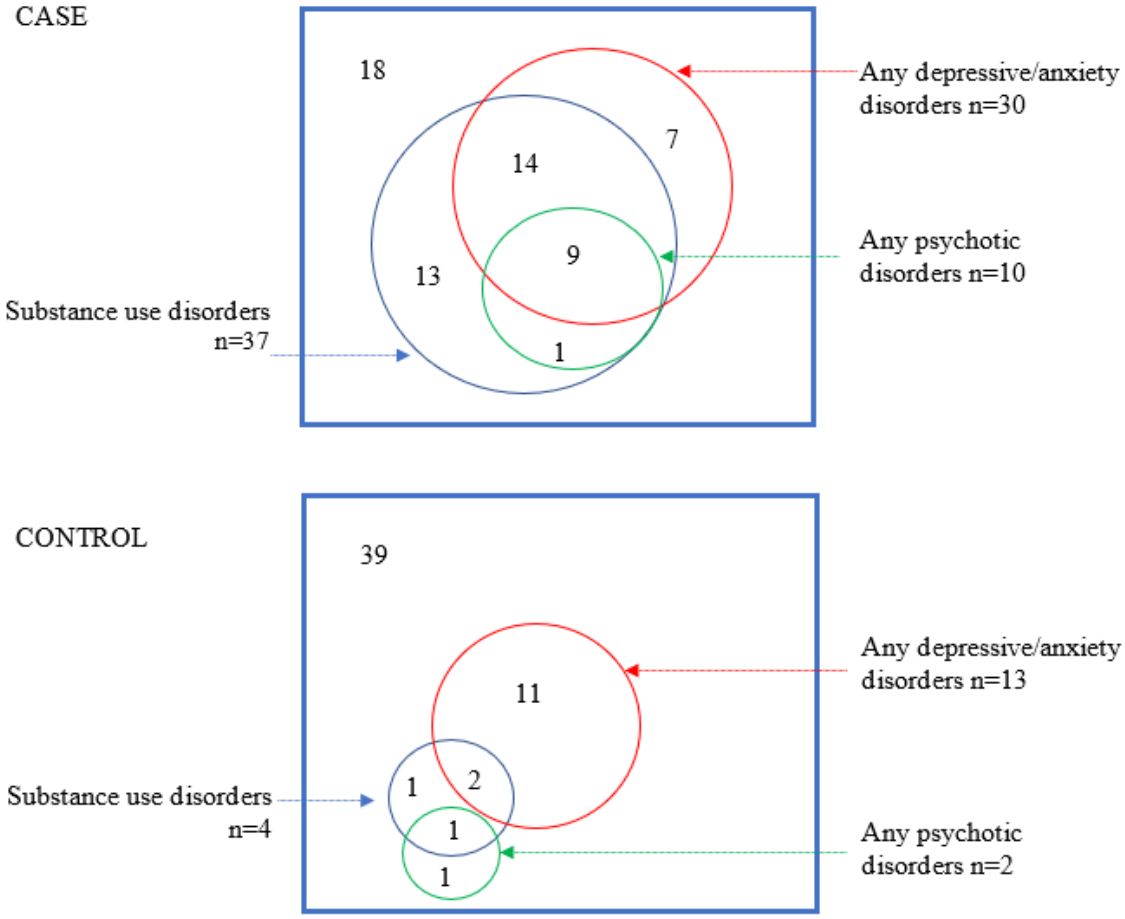
CASE
18
14
7
9
13
1
Any depressive/anxiety disorders n=30
Any psychotic disorders n=10
Substance use disorders n=37
CONTROL
39
11
1
2
1
1
Any depressive/anxiety disorders n=13
Any psychotic disorders n=2
Substance use disorders n=4

Figure 1