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ORIGINAL PAPER

Prevalence and Risks of Depression and Substance Use Among Adults Living with HIV in the Asia–Pacific Region

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Abstract

Despite the mental health and substance use burden among people living with HIV (PLHIV) in the Asia–Pacific, data on their associations with HIV clinical outcomes are limited. This cross-sectional study of PLHIV at five sites assessed depression and substance use using PHQ-9 and ASSIST. Among 864 participants, 88% were male, median age was 39 years, 97% were on ART, 67% had an HIV viral load available and < 1000 copies/mL, 19% had moderate-to-severe depressive symptoms, and 80% had ever used at least one substance. Younger age, lower income, and suboptimal ART adherence were associated with moderate-to-severe depressive symptoms. Moderate-to-high risk substance use, found in 62% of users, was associated with younger age, being male, previous stressors, and suboptimal adherence. Our findings highlight the need for improved access to mental health and substance use services in HIV clinical settings.

Keywords HIV · Asia · Depression · Substance use · ART adherence

Introduction

In 2020, the Asia–Pacific region was home to 5.8 million people living with HIV (PLHIV) [1]. In the era of effective combination antiretroviral therapy (cART), with increasing rates of ART coverage and virologic suppression, attention has shifted towards the management of HIV as a chronic disease and the need to better address comorbid conditions among PLHIV [2]. Continued HIV treatment cascade gains and reaching the UNAIDS '95–95–95' targets (95% of PLHIV diagnosed, 95% initiating ART, and 95% achieving virologic suppression by 2030) will not be achieved without addressing mental health and substance use disorders among PLHIV [3].

The burden of mental health disorders and substance use among adult PLHIV is high and rates are often higher than those among HIV-negative counterparts [4–6]. Mental health disorders and use of certain substances are also associated with a higher risk of mortality among adult PLHIV [7–9]. Research among adult PLHIV cohorts, predominantly in developed countries, indicate that mental health and substance use disorders are associated with negative HIV clinical and treatment outcomes, such as poorer ART adherence and retention in care, and virologic failure [10–15]. However, similar evidence from the Asia–Pacific region is sparse.

Studies of depression among different adult PLHIV populations in the Asia–Pacific region indicate a prevalence of between 3 and 60% depending on the study population, study

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methodology, and screening tool used [16–21]. Data on the prevalence of substance use disorders among adult PLHIV in the region have often focused on opiate use in countries where it has historically driven local HIV epidemics, with more limited data on other substance use, such as amphetamines, sedatives and cannabis. Addressing the substantial mental health and substance use burden among PLHIV in the region would also have to be achieved in the context of persistent underfunding and scarcity of human resources for mental health services in the Asia–Pacific region [22]. We therefore conducted a cross-sectional study of depression and substance use among adult PLHIV under care at five HIV clinical centers in the Asia–Pacific region, and assessed risk factors for recent depression and substance use.

Methods

Study Design and Study Population

Adults living with HIV aged 18 years or older and under care at five sites were eligible to participate in this cross-sectional study. Participating sites are all tertiary care centers located in the following urban areas: Hong Kong SAR, China; Kuala Lumpur, Malaysia; Muntinlupa City, Metro Manila, Philippines; Seoul, South Korea; and Bangkok, Thailand. All study participants were consented and enrolled as they attended routine HIV clinical visits between July 2019 and June 2020.

Data Collection

Patient Health Questionnaire-9 (PHQ-9) was used to assess for depression over the past two weeks [23], and the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST v3.1) was used to assess ever using a substance, substance use in the past three months, and substance use risk [24]. If available, locally validated versions of PHQ-9 and ASSIST v3.1were used. If validated versions were not available, these screening tools were translated and reviewed by local investigators with related clinical or research experience. In one participating site a cultural adaptation process was developed that included a combination of translation, expert review, and local testing. Data on employment, household income, education level, HIV disclosure status, recent traumatic events or stressors, and family history of mental health diagnoses were collected as part of a study-specific questionnaire. PHQ-9 and ASSIST screenings were conducted by trained study staff or self-administered using electronic tablets. Positive screening results triggered clinical follow-up according to local standards of care, including urgent referrals of participants with suicidal thoughts for further psychiatric assessment and management.

Demographic data (i.e., age, sex, ethnicity, marital status), medical history (i.e., comorbid chronic conditions, sexually transmitted infections), laboratory data (i.e., weight, systolic and diastolic blood pressure, hemoglobin, complete blood count, lipid profile, liver function tests, glucose, creatinine, hepatitis serology), and HIV clinical data (i.e., HIV exposure category, date of HIV diagnosis, history of CDC stage C illness, CD4 cell count, HIV viral load, ART regimen, adverse events, adherence) were collected from existing medical records, as available. We collected all available CD4 cell count and HIV viral load test results for study participants up to the date of their last clinic visit, and Visual Analog Scale adherence assessments from the 12 months preceding the start of this study.

Statistical Analyses

We conducted risk factor analyses to assess associations with the following outcomes: (i) moderate-to-severe depressive symptoms; and (ii) moderate-to-high risk substance use of any drug. Patients were classified as having moderate-to-severe depressive symptoms if they had a PHQ-9 total score of 10 to 27. Moderate-to-high risk substance use was classified as having an ASSIST score ≥ 11 for alcohol or an ASSIST score ≥ 4 for other substances.

Patients with missing questionnaire responses to PHQ-9 and ASSIST were included in the analysis with missing responses imputed using the "hot deck" imputation method [25]. This imputation method replaces the missing value with a single data point imputed from randomly selected patients with complete dataset, who have similar characteristics to those with missing responses. The method was applied consistently across all other questionnaires within the study that required calculations of survey scores.

To account for heterogeneity across sites, we adjusted for World Bank country income grouping in all analyses. Logistic regression was used to analyse factors associated with moderate-to-severe depressive symptoms, and moderate-to-high risk substance use. Covariates included were demographics and HIV clinical characteristics, as well as socioeconomic risk factors on education, employment, household income, and previous life stressors obtained from the study-specific questionnaire. Not reported or unknown values were included in the regression as a separate category. Regression analyses were fitted using backward stepwise selection process. Covariates with $p < 0.10$ in the univariate analysis were included in the multivariate model. Covariates with $p < 0.05$ in the multivariate regression model were considered statistically significant.

Data management and statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary,

NC, USA) and Stata software version 16.1 (Stata Corp., College Station, TX, USA).

Ethical Considerations

All participating study sites, the study coordinating center (TREAT Asia, amfAR/The Foundation for AIDS Research, Thailand), and the data management center (The Kirby Institute, University of New South Wales, Australia) obtained institutional review board (IRB) approvals for study participation. Study participants were consented using standard informed consent and study information forms.

Results

A total of 864 patients participated in the study (Table 1). Of the 864 study participants, 793 (92%) had at least a high school education, 622 (72%) were in full- or part-time employment, and 334 (39%) were from high income countries. Their median age at enrolment was 39 years (IQR 31–47), 758 (88%) were male, 460 (53%) acquired HIV through male-to-male sex, and 841 (97%) were on ART. Among those on ART, median duration of ART was 6 years (IQR 2–11).

Of the 609 participants with a CD4 measurement available, median CD4 cell count was 519 cells/μL (IQR 333–725). Of the 625 participants with an available VL within six months of the study assessment, 576 (92%) had VL < 1000 copies/mL. Current ART regimens were nucleoside reverse transcriptase inhibitors (NRTI) plus non-nucleoside reverse transcriptase inhibitors (NNRTI) in 455 (53%), integrase inhibitors (INSTI) in 320 (37%), and NRTI plus protease inhibitors (PI) in 55 (6%). Overall, 639 (74%) had no previous mental health diagnosis, and 389 (45%) had experienced no traumatic event or stressors in the past five years.

Prevalence of Depressive Symptoms

On depression screening, 693 (80%) had a total PHQ-9 score above 0 (95% CI 77–83). There were 282 (33%) participants with minimal depressive symptoms (PHQ-9 score 1–4), 250 (29%) with mild depressive symptoms (PHQ-9 score 5–9), 103 (12%) with moderate depressive symptoms (PHQ-9 score 10–14), 39 (5%) with moderately severe depressive symptoms (PHQ-9 score 15–19), and 19 (2%) with severe depressive symptoms (PHQ-9 score 20–27) (Fig. 1). Suicidal thoughts on at least several days over the past two weeks were reported in 164 (19%) participants as indicated by a PHQ-9 question 9 score of 1 or above.

Factors Associated with Depressive Symptoms

Overall, 161 (19%) reported moderate-to-severe depressive symptoms, and associated risk factors are shown in Table 2. In the multivariate analysis, moderate-to-severe depressive symptoms were less likely in patients with older age at time of study assessment (41–50 years: aOR = 0.39, 95% CI 0.23–0.66, p < 0.001; > 50 years: aOR = 0.21, 95% CI 0.21–0.75, p = 0.004) compared to age ≤ 30 years, and those with higher monthly household income (> $501-$2000 USD: aOR = 0.52, 95% CI 0.31–0.87, p = 0.013; and > $2000 USD: aOR = 0.31, 95% CI 0.16–0.58, p < 0.001) compared to ≤ $500 USD. Participants reporting previous stressors (aOR = 3.05, 95% CI 1.95–4.75, p < 0.001) compared to no previous stressors, a previous mental health disorder (aOR = 2.97, 95% CI 1.65–5.32, p < 0.001) compared to none, and suboptimal ART adherence (< 95%) in the previous year (aOR = 2.41, 95% CI 1.23–4.75, p = 0.011) compared to adherence ≥ 95% were more likely to experience moderate-to-severe depressive symptoms. Moderate-to-high risk substance use was not found to be associated with moderate-to-severe depressive symptoms.

Prevalence of Substance Use and Substance Use Risk

On screening with ASSIST, 681 (80%) participants reported ever using at least one substance, and 553 (64%) reported using at least one substance in the past three months. Of those who ever used at least one substance, 407 (60%) used tobacco, 597 (88%) alcohol, 130 (19%) cannabis, 36 (5%) cocaine, 151 (22%) amphetamines, 33 (5%) inhalants, 101 (15%) sedatives, 43 (6%) hallucinogens, and 21 (3%) opioids (Table 3). Of those who used at least one substance in the past three months, 282 (51%) used tobacco, 443 (80%) alcohol, 40 (7%) cannabis, 7 (1%) cocaine, 69 (12%) amphetamines, 14 (3%) inhalants, 62 (11%) sedatives, 7 (1%) hallucinogens, and 2 (0%) opioids.

Of the 681 study participants who ever used at least one substance, 425 (62%) were classified as having moderate-to-high risk ASSIST scores to any drug. This included 284/407 (70%) of those that ever used tobacco, 221/597 (37%) alcohol, 29/130 (22%) cannabis, 5/36 (14%) cocaine, 76/151 (51%) amphetamine, 14/33 (42%) inhalants, 54/101 (54%) sedatives, 4/43 (9%) hallucinogens, and 4/21 (19%) of those that ever used opioids.

Factors Associated with Substance Use Risk

Overall, 425 (49%) were classified as having moderate-to-high risk substance use to any drug. Multivariate analyses indicated that those age > 50 years (aOR = 0.60, 95% CI 0.37–0.96, p = 0.033) compared to age ≤ 30 years, and females (aOR = 0.38, 95% CI 0.23–0.61, p < 0.001) compared to males,

Table 1 Participant characteristics

	Total patients (%)
Total	864 (100)
Sociodemographic characteristics	
Age at study assessment (years)	Median = 39, IQR (31–47)
≤ 30	203 (24)
31–40	270 (31)
41–50	255 (30)
> 50	136 (16)
Sex	
Male	758 (88)
Female	106 (12)
Employment status	
No	180 (21)
Yes, full-time	499 (58)
Yes, part-time, or occasionally	123 (14)
No response/not reported	62 (7)
Total household income	
≤ 500 USD/local currency equivalent per month	212 (24)
501–2000 USD/local currency equivalent per month	258 (30)
> 2000 USD/local currency equivalent per month	257 (30)
No response/unknown/not reported	137 (16)
Highest education level	
No formal education	4 (0)
Primary school	46 (5)
High school	231 (27)
College/vocational training	125 (14)
University	437 (51)
No response/not reported	21 (2)
HIV-related characteristics	
HIV mode of exposure	
Heterosexual contact	276 (32)
MSM	460 (53)
Injecting drug use	15 (2)
Other/Unknown	113 (13)
Year of ART initiation	
< 2010	236 (27)
2010–2012	115 (13)
2013–2015	189 (22)
2016–2020	313 (36)
No ART/unknown	11 (1)
Viral Load at study assessment (copies/mL)	Median = 33, IQR (19–39)
< 50	535 (62)
50–399	37 (4)
400–999	4 (0.5)
≥ 1000	49 (6)
Not tested	239 (28)
Median (IQR) viral load among those with VL ≥ 1000 (copies/mL)	107,644 (IQR 45,556–406,000)
CD4 at study assessment (cells/μL)	Median = 519, IQR (333–725)
≤ 200	73 (8)
201–350	94 (11)
351–500	123 (14)

Table 1 (continued)

	Total patients (%)
> 500	319 (37)
Not tested	255 (30)
Current ART	
NRTI + NNRTI	455 (53)
NRTI + PI	55 (6)
INSTI	320 (37)
Other	11 (1)
None/unknown	23 (3)
ART adverse events in the previous year	
No	603 (70)
Yes	93 (11)
Not reported/unknown	168 (19)
ART adherence in the previous year	
≥ 95	566 (66)
< 95	58 (7)
Not reported/unknown	240 (28)
Prior AIDS diagnosis	
No	556 (64)
Yes	202 (23)
Not reported	106 (12)
Disclosure of HIV status	
Full (i.e. to all friends and family)	41 (5)
Partial (i.e. to some friends or family)	617 (71)
None, to no one	162 (19)
No response/ not reported/ unknown	44 (5)
Coinfections, comorbidities and medical history	
Hepatitis B co-infection	
Negative	297 (34)
Positive	34 (4)
Not tested	533 (62)
Hepatitis C co-infection	
Negative	410 (47)
Positive	30 (3)
Not tested	424 (49)
History of STIs in the past 5 years	
No	413 (48)
Yes	263 (30)
Not reported/unknown	188 (22)
Current chronic comorbid condition	
No	352 (41)
Yes	150 (17)
Not reported/unknown	362 (42)
Previous mental health diagnosis	
No	639 (74)
Yes	67 (8)
Not reported/unknown	158 (18)
Family history of mental health diagnoses	
No	739 (86)
Yes	34 (4)
Not reported/unknown	91 (10)

Table 1 (continued)

	Total patients (%)
Traumatic events or stressors experienced in the past 5 years (multiple answers allowed)	
None	389 (45)
Unknown	46 (5)
Sexual assault or abuse	32 (4)
Physical assault or abuse	33 (4)
Physical pain or injury e.g. car accident, burns, dog attack	63 (7)
Major surgery or life-threatening illness	75 (9)
Natural disaster e.g. hurricane, flood, fire or earthquake	36 (4)
War or political violence (civil war, terrorism, refugee)	14 (2)
Death of family member, partner or friend	168 (19)
Divorce or separation from a partner	37 (4)
Unemployment, redundancy or significant financial concerns	190 (22)
Home relocation	90 (10)
Arrest or prison stay	14 (2)
Other	33 (4)
Not reported	24 (3)

ART antiretroviral therapy, *STIs* sexually transmitted infections, *MSM* men who have sex with men, *NRTI* nucleoside reverse transcriptase inhibitors, *NNRTI* non-NRTI, *PI* protease inhibitors, *INSTI* integrase inhibitors, *USD* US dollars

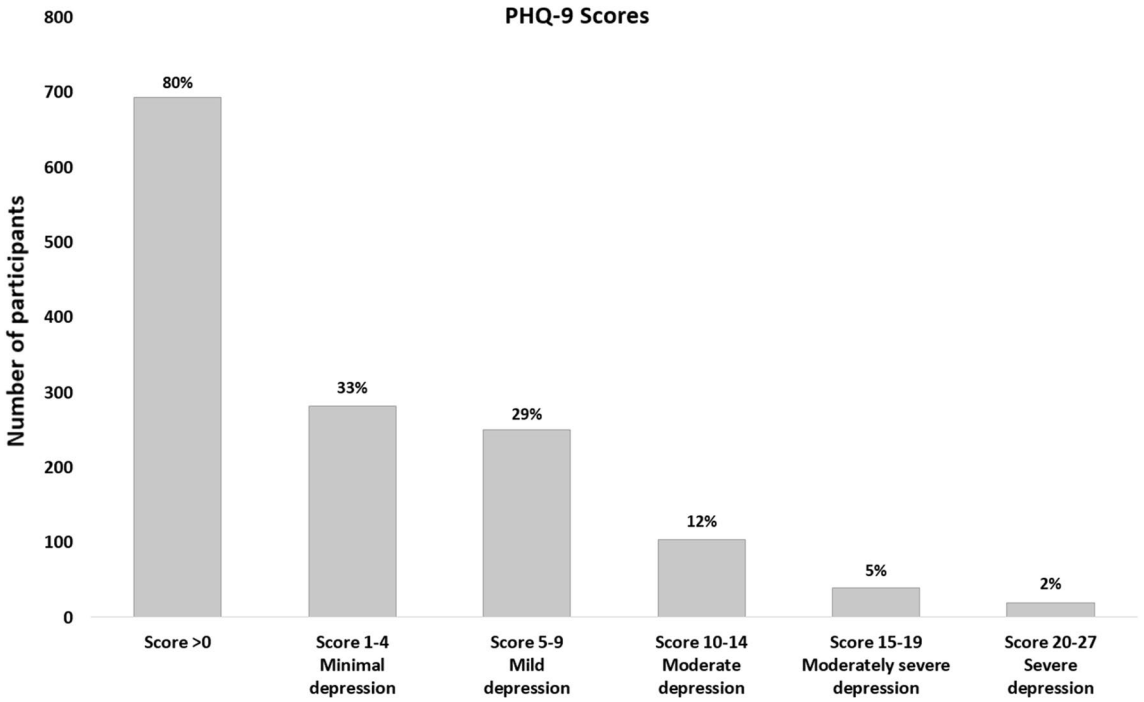

Fig. 1 PHQ-9 scores and severity classification of study participants (N = 864)

were less likely to report moderate-to-high risk substance use (Table 4). Those who had partially (aOR = 0.30, 95% CI 0.14–0.63, p = 0.002) or not disclosed their HIV status to others (aOR = 0.33, 95% CI 0.15–0.74, p = 0.007) compared to those who had fully disclosed, and participants from upper-middle and lower-middle income countries (aOR = 0.60, 95% CI 0.43–0.82, p = 0.001) compared to those from high-income countries, were less likely to report moderate-to-high

Table 2 Factors associated with moderate-to-severe depressive symptoms by PHQ-9

	Total patients	Number with moderate to severe depression	Univariate			Multivariate		
			OR	95% CI	p	aOR	95% CI	p
Total	864	161						
Age at study assessment (years)					< 0.001			< 0.001
≤ 30	203	55	1			1		
31–40	270	57	0.72	(0.47, 1.10)	0.131	0.81	(0.51, 1.28)	0.358
41–50	255	31	0.37	(0.23, 0.61)	< 0.001	0.39	(0.23, 0.66)	< 0.001
> 50	136	18	0.41	(0.23, 0.74)	0.003	0.40	(0.21, 0.75)	0.004
Sex								
Male	758	149	1					
Female	106	12	0.52	(0.28, 0.98)	0.042			
Employment					< 0.001			
No	180	49	2.41	(1.59, 3.66)	< 0.001			
Full time	499	67	1					
Part time	123	34	2.46	(1.54, 3.95)	< 0.001			
Not reported/unknown	62	11						
Household income (USD) per month					< 0.001			< 0.001
≤ $500	212	59	1			1		
$501-$2000	258	40	0.48	(0.30, 0.75)	0.001	0.52	(0.31, 0.87)	0.013
> $2000	257	28	0.32	(0.19, 0.52)	< 0.001	0.31	(0.16, 0.58)	< 0.001
Not reported/unknown	137	34						
Highest education level								
No education	4	0	N/A					
Primary to high school	277	52	1.01	(0.70, 1.45)	0.975			
College to university	562	105	1					
Not reported/unknown	21	4						
HIV mode of exposure					0.031			
Heterosexual contact	276	48	1					
MSM	460	78	0.97	(0.65, 1.44)	0.880			
Injecting drug use	15	6	3.17	(1.08, 9.31)	0.036			
Other/Unknown	113	29	1.64	(0.97, 2.77)	0.065			
Year of ART initiation					0.066			
< 2010	236	31	1					
2010–2012	115	18	1.23	(0.65, 2.30)	0.524			
2013–2015	189	41	1.83	(1.10, 3.06)	0.021			
2016–2020	313	69	1.87	(1.18, 2.97)	0.008			
No ART/unknown	11	2	1.47	(0.30, 7.12)	0.633			
Viral load at study assessment (copies/mL)					0.016			
< 50	535	82	1					
50–399	37	7	1.29	(0.55, 3.03)	0.561			
400–999	4	1	1.84	(0.19, 17.92)	0.599			
≥ 1000	49	14	2.21	(1.14, 4.29)	0.019			
Not tested	239	57						
CD4 at study assessment (cells/μL)					< 0.001			
≤ 200	73	23	1					

Table 2 (continued)

	Total patients	Number with moderate to severe depression	Univariate			Multivariate		
			OR	95% CI	p	aOR	95% CI	p
201–350	94	21	0.63	(0.31, 1.25)	0.184			
351–500	123	21	0.45	(0.23, 0.88)	0.021			
> 500	319	43	0.34	(0.19, 0.61)	< 0.001			
Not tested	255	53						
Current ART					0.035			
NRTI + NNRTI	455	88	1					
NRTI + PI	55	14	1.42	(0.74, 2.73)	0.286			
INSTI	320	48	0.74	(0.50, 1.08)	0.119			
Other	11	2	0.93	(0.20, 4.37)	0.923			
None/unknown	23	9	2.68	(1.12, 6.39)	0.026			
ART adverse events in the previous year								
No	603	88	1					
Yes	93	15	1.13	(0.62, 2.04)	0.698			
Not reported/unknown	168	58						
ART adherence in the previous year								
≥ 95	566	80	1			1		
< 95	58	16	2.31	(1.24, 4.31)	0.008	2.41	(1.23, 4.75)	0.011
Not reported/unknown	240	65						
Prior AIDS diagnosis								
No	556	85	1					
Yes	202	37	1.24	(0.81, 1.90)	0.316			
Not reported	106	39						
HIV disclosure status					0.173			
Full	41	9	1					
Partial	617	122	0.88	(0.41, 1.88)	0.735			
None, to no one	162	22	0.56	(0.24, 1.33)	0.187			
No response/not reported/unknown	44	8						
Hepatitis B co-infection								
Negative	297	36	1					
Positive	34	3	0.70	(0.20, 2.41)	0.574			
Not tested	533	122						
Hepatitis C co-infection								
Negative	410	46	1					
Positive	30	3	0.88	(0.26, 3.01)	0.838			
Not tested	424	112						
History of STIs in the past 5 years								
No	413	58	1					
Yes	263	43	1.20	(0.78, 1.84)	0.413			
Not reported/unknown	188	60						
Current chronic comorbid condition								
No	352	58	1					
Yes	150	32	1.37	(0.85, 2.22)	0.195			
Not reported/unknown	362	71						
Previous mental health diagnosis								
No	639	83	1			1		
Yes	67	25	3.99	(2.31, 6.88)	< 0.001	2.97	(1.65, 5.32)	< 0.001

Table 2 (continued)

	Total patients	Number with moderate to severe depression	Univariate			Multivariate		
			OR	95% CI	p	aOR	95% CI	p
Not reported/unknown	158	53						
Family history of mental health diagnoses								
No	739	125	1					
Yes	34	9	1.77	(0.81, 3.88)	0.155			
Not reported/unknown	91	27						
Previous stressors								
No	369	32	1			1		
Yes	437	116	3.81	(2.50, 5.79)	< 0.001	3.05	(1.95, 4.75)	< 0.001
Not reported/unknown	58	13						
Moderate to high risk substance use								
No	439	68	1					
Yes	425	93	1.53	(1.08, 2.16)	0.016			
World Bank country income grouping								
High	334	52	1			1		
Upper-middle and lower-middle	530	109	1.40	(0.98, 2.02)	0.067	0.82	(0.49, 1.36)	0.435

Not reported values were included in the analysis as a separate category but were excluded from test for heterogeneity

Global p-value for age, viral load, CD4, household income were test for trend

OR odds ratio, *aOR* adjusted odds ratio, *CI* confidence interval, *ART* antiretroviral therapy, *STIs* sexually transmitted infections, *MSM* men who have sex with men, *NRTI* nucleoside reverse transcriptase inhibitors, *NNRTI* non-NRTI, *PI* protease inhibitors, *INSTI* integrase inhibitors

Table 3 ASSIST screening of recent and lifetime substance use, and risk-level

Substance	Total patients used substance in last 3 months (%)	Total patients ever used substance (%)	Total patients with lower risk (%)	Total patients with moderate risk (%)	Total patients with high risk (%)
Tobacco	282 (51)	407 (60)	123 (30)	252 (62)	32 (8)
Alcohol	443 (80)	597 (88)	376 (63)	184 (31)	37 (6)
Cannabis	40 (7)	130 (19)	101 (78)	29 (22)	0 (0)
Cocaine	7 (1)	36 (5)	31 (86)	5 (14)	0 (0)
Amphetamines	69 (12)	151 (22)	75 (50)	66 (44)	10 (7)
Inhalants	14 (3)	33 (5)	19 (58)	13 (39)	1 (3)
Sedatives	62 (11)	101 (15)	47 (47)	50 (50)	4 (4)
Hallucinogens	7 (1)	43 (6)	39 (91)	4 (9)	0 (0)
Opioids	2 (0)	21 (3)	17 (81)	4 (19)	0 (0)
Other	4 (1)	14 (2)	9 (64)	5 (36)	0 (0)
Total patients	553	681	447	398	69

A participant may take multiple substances and the total patients at the bottom of each column is the count of individual patients. Percentages are column percentages for recent and lifetime substance use columns. Percentages are row percentages for risk-level columns

risk substance use. Participants in part-time employment (aOR = 2.07, 95% CI 1.34–3.19, p = 0.001) compared to full time, and those reporting previous stressors (aOR = 1.63, 95% CI 1.21–2.20, p = 0.001) compared to none, and suboptimal ART adherence (< 95%) in the previous year (aOR = 2.90, 95% CI 1.55–5.40, p = 0.001) compared to adherence ≥ 95% were more likely to report moderate-to-high risk substance use. Moderate-to-severe depression was not found to be associated with moderate-to-high risk substance use.

Table 4 Factors associated with moderate to high risk substance use

	Total patients	Number with moderate to high risk substance use	Univariate			Multivariate		
			OR	95% CI	p	aOR	95% CI	p
Total	864	425						
Age at study assessment (years)					0.002			0.008
≤ 30	203	107	1			1		
31–40	270	152	1.16	(0.80, 1.67)	0.438	1.24	(0.84, 1.82)	0.279
41–50	255	112	0.70	(0.49, 1.02)	0.062	0.78	(0.52, 1.16)	0.213
> 50	136	54	0.59	(0.38, 0.92)	0.019	0.60	(0.37, 0.96)	0.033
Sex								
Male	758	398	1			1		
Female	106	27	0.31	(0.20, 0.49)	< 0.001	0.38	(0.23, 0.61)	< 0.001
HIV mode of exposure					0.096			
Heterosexual contact	276	119	1					
MSM	460	238	1.41	(1.05, 1.91)	0.024			
Injecting drug use	15	9	1.98	(0.69, 5.71)	0.207			
Other/Unknown	113	59	1.44	(0.93, 2.24)	0.103			
Viral load at study assessment (copies/mL)					0.982			
< 50	535	256	1					
50–399	37	16	0.83	(0.42, 1.63)	0.588			
400–999	4	0	N/A					
≥ 1000	49	25	1.14	(0.63, 2.04)	0.671			
Not tested	239	128						
CD4 at study assessment (cells/μL)					0.179			
≤ 200	73	29	1					
201–350	94	49	1.65	(0.89, 3.07)	0.112			
351–500	123	54	1.19	(0.66, 2.14)	0.567			
> 500	319	163	1.59	(0.94, 2.66)	0.081			
Not tested	255	130						
Current ART					0.270			
NRTI + NNRTI	455	214	1					
NRTI + PI	55	28	1.17	(0.67, 2.04)	0.587			
INSTI	320	163	1.17	(0.88, 1.56)	0.284			
Other	11	9	5.07	(1.08, 23.71)	0.039			
None/unknown	23	11	1.03	(0.45, 2.39)	0.941			
Hepatitis B co-infection								
Negative	297	132	1					
Positive	34	8	0.38	(0.17, 0.88)	0.023			
Not tested	533	285						
Hepatitis C co-infection								
Negative	410	169	1					
Positive	30	13	1.09	(0.52, 2.30)	0.821			
Not tested	424	243						
Prior AIDS diagnosis								
No	556	268	1					
Yes	202	100	1.05	(0.76, 1.45)	0.751			
Not reported	106	57						
Household income (USD) per month					0.012			
≤ $500	212	95	1					
$501–$2000	258	112	0.94	(0.66, 1.36)	0.761			

Table 4 (continued)

	Total patients	Number with moderate to high risk substance use	Univariate			Multivariate		
			OR	95% CI	p	aOR	95% CI	p
> $2000	257	144	1.57	(1.09, 2.26)	0.016			
Not reported/unknown	137	74						
Employment					< 0.001			< 0.001
No	180	78	0.87	(0.61, 1.22)	0.411	0.76	(0.52, 1.12)	0.168
Full time	499	234	1			1		
Part time	123	79	2.03	(1.35, 3.06)	0.001	2.07	(1.34, 3.19)	0.001
Not reported/unknown	62	34						
Highest education level					0.579			
No education	4	1	0.34	(0.03, 3.25)	0.346			
Primary to high school	277	133	0.93	(0.70, 1.24)	0.622			
College to university	562	280	1					
Not reported/unknown	21	11						
HIV disclosure status					0.025			0.007
Full	41	29	1			1		
Partial	617	302	0.40	(0.20, 0.79)	0.009	0.30	(0.14, 0.63)	0.002
None, to no one	162	76	0.37	(0.17, 0.77)	0.008	0.33	(0.15, 0.74)	0.007
No response/not reported/unknown	44	18						
Previous stressors								
No	369	156	1			1		
Yes	437	238	1.63	(1.23, 2.16)	0.001	1.63	(1.21, 2.20)	0.001
Not reported/unknown	58	31						
Current chronic comorbid condition								
No	352	191	1					
Yes	150	76	0.87	(0.59, 1.27)	0.460			
Not reported/unknown	362	158						
Previous mental health diagnosis								
No	639	297	1					
Yes	67	39	1.60	(0.96, 2.67)	0.069			
Not reported/unknown	158	89						
Family history of mental health diagnoses								
No	739	349	1					
Yes	34	23	2.34	(1.12, 4.86)	0.023			
Not reported/unknown	91	53						
History of STIs in the past 5 years								
No	413	167	1					
Yes	263	153	2.05	(1.50, 2.80)	< 0.001			
Not reported/unknown	188	105						
Year of ART initiation					0.045			
< 2010	236	97	1					
2010–2012	115	61	1.62	(1.03, 2.54)	0.035			
2013–2015	189	93	1.39	(0.94, 2.04)	0.095			
2016–2020	313	169	1.68	(1.20, 2.37)	0.003			
No ART/unknown	11	5	1.19	(0.35, 4.02)	0.775			
ART adverse events in the previous year								
No	603	290	1					
Yes	93	41	0.85	(0.55, 1.32)	0.472			
Not reported/unknown	168	94						

Table 4 (continued)

	Total patients	Number with moderate to high risk substance use	Univariate			Multivariate		
			OR	95% CI	p	aOR	95% CI	p
ART adherence in the previous year								
≥ 95	566	259	1			1		
< 95	58	41	2.86	(1.59, 5.15)	< 0.001	2.90	(1.55, 5.40)	0.001
Not reported/unknown	240	125						
Moderate to severe depression								
No	703	332	1					
Yes	161	93	1.53	(1.08, 2.16)	0.016			
World Bank country income grouping								
High	334	187	1			1		
Upper-middle and lower-middle	530	238	0.64	(0.49, 0.84)	0.002	0.60	(0.43, 0.82)	0.001

Not reported values were included in the analysis as a separate category but were excluded from test for heterogeneity

Global p-value forage, viral load, CD4, household income were test for trend

OR odds ratio, *aOR* adjusted odds ratio, *CI* confidence interval, *ART* antiretroviral therapy, *STIs* sexually transmitted infections, *MSM* men who have sex with men, *NRTI* nucleoside reverse transcriptase inhibitors, *NNRTI* non-NRTI, *PI* protease inhibitors, *INSTI* integrase inhibitors

Discussion

In this cross-sectional study of 864 adult PLHIV in care at five HIV clinical sites in five countries in the Asia–Pacific region, 19% had moderate-to-severe depressive symptoms, 19% had suicidal thoughts, 80% ever used at least one substance, and 64% used at least one substance in the past three months. Alcohol, tobacco, amphetamine, sedative, and cannabis use was common, as was moderate-to-high risk substance use. Moderate-to-severe depressive symptoms and moderate-to-high risk substance use were both associated with younger age, previous stressors, and previous suboptimal ART adherence. Neither was associated with mean CD4 cell count or VL < 1000 copies/mL. We found no association between moderate-to-high risk substance use and moderate-to-severe depressive symptoms.

Rates and risk factors for depressive symptoms in our cohort are consistent with those documented in similar adult PLHIV cohorts in the region, for example a study of predominantly male adult PLHIV in Southern India, screened using PHQ-9, found that 23% had moderate-to-severe depressive symptoms [26] and a meta-analysis of PLHIV in sub-Saharan Africa found a 14% prevalence of depressive symptoms among PLHIV on ART based on a PHQ-9 cut-off score of ≥ 10 [27]. The same analysis found depressive symptoms were associated with lower personal income, and an analysis of adult PLHIV in East Africa found both stressful life events and low personal income were associated with depression [28]. Rates of suicidal thoughts in our cohort appear higher than those documented elsewhere. A recent study of adult PLHIV in Indonesia identified *lifetime* suicidal ideation in 23% [29], and a survey of adult PLHIV in Nigeria found a 12-month prevalence rate for suicidal ideation of 2.9% [30]. These differences are likely explained by differences in screening instruments used, and differences in key sociodemographic characteristics often linked to mental health status, such as sex, age, marital status, and income and education levels.

The high rates of alcohol and tobacco use found in our cohort are consistent with those observed in other adult PLHIV cohorts in the region. Studies among HIV-positive adults in Nepal and India found a prevalence of alcohol use disorder of 25.7 and 12.8% [31, 32]. Recent tobacco use among adult men-who-have-sex-with-men (MSM) living with HIV in Taiwan was just under 50% [33]. Amphetamine use in our adult PLHIV cohort are consistent with those reported in populations at risk of HIV infection in the region, with rates of 7% reported among Cambodian female sex workers [34] and 30% among MSM in Vietnam [35]. Although the substantial proportions of sedative users in our cohort have not been widely documented elsewhere in the region, a study in Taiwan did find that PLHIV had an increased risk of sedative use compared to those without HIV, after adjusting for demographic data and psychiatric comorbidities [36]. Factors associated with moderate-to-high risk substance use are also consistent with those identified in cohorts elsewhere. Meta-analyses have found higher prevalence of both alcohol use disorders and current smoking among male PLHIV than female PLHIV, and a higher prevalence of alcohol use disorders among PLHIV in developed countries than those in developing countries [37, 38].

Our finding that those with suboptimal adherence in the previous year were more likely to experience moderate-to-severe depressive symptoms and report moderate-to-high

risk substance use adds to the substantial body of evidence from this region linking mental health issues, substance use and poorer adherence across different adult PLHIV populations [20, 32, 39–43]. Our finding that mean CD4 cell count and viral load < 1000 copies/mL were not risk factors for moderate-to-high risk substance use or moderate-to-severe depressive symptoms, adds to the insubstantial and conflicting regional evidence of associations between mental health or substance use and HIV clinical or treatment outcomes. In a systematic review published in 2018, none of the three Asia–Pacific studies included identified mental health disorders or substance use to be a predictor of poor retention in HIV care for adults living with HIV [14]. However, an analysis of adult PLHIV in South Korea did find patients with depression were more likely to frequently miss clinical appointments and have a higher cumulative time lost to follow-up per month compared to patients without depression [44]. Among HIV-positive heterosexual men and MSM in Thailand, non-injection substance use was associated with a lower likelihood of having an undetectable viral load [45], but a study of predominantly male adult PLHIV in care at community and hospital-based ART clinics in Vietnam found no association between mental health symptoms and virologic suppression [46].

Despite a high burden of depression and substance use, and the potential for negative impacts on HIV clinical outcomes, there remain substantial gaps in access to mental health and substance use related care for adult PLHIV in the region, and fragmented integration of related services within HIV clinical settings. In a global analysis, only 43% of 28 HIV clinical Asia–Pacific sites screened for depression and 39% for substance use disorders, rates of screening that were among the lowest of any region [47]. We feel the relatively low screening rates for depression and substance use in HIV clinical settings in the region are likely reflective of a general lack of resources dedicated to addressing mental health and substance use issues across all settings and populations in the region, and related to this, limited capacity of health care workers and health systems to support the delivery of such services [22]. The same global analysis reported on-site management of substance use disorders in 57%, and another global analysis noted substantial gaps persist in the integration of substance use services into HIV care settings, particularly in resource-constrained settings [48]. A study in Malaysia published in 2020, found that over 80% of adult PLHIV with prevalent psychiatric symptoms had not previously been recognized clinically, and that only 32% of participants with severe mental health symptoms received a psychiatric referral [49]. This limited integration is in spite of growing regional evidence of the effectiveness of non-pharmacological mental health and substance use interventions among adult PLHIV populations, including telephone-based behavioral therapy [50], group coping interventions [51], group rational-emotive-behavior-based therapy [52], brief cognitive behavioral therapy interventions [53], and home-based social support [54].

Further integration of mental health and substance use services within HIV clinical settings in the region is exacerbated by a lack of local research on optimal integration models and strategies. In recent systematic reviews of interventions and approaches to integrating HIV, mental health or substance use services, none or very few of the eligible articles were from the Asia–Pacific region [55, 56]. The limited research on approaches to integrating HIV, mental health and substance use services in the region are likely related to a lack of implementation research capacities in the region, and the relatively recent emergence of implementation research as a priority research discipline in the region. Indeed, the importance of implementation research to inform the integration, adaptation or scale-up of mental health or substance use services within HIV care in Asian or resource-limited settings is increasingly being highlighted [48, 57, 58].

It is worth noting that our study had a number of limitations. As a cross-sectional study, it can say nothing of trends in mental health or substance use disorders, or incidence levels. Study methodology did not support assessment of causal relationships between depression, substance use and HIV clinical and treatment outcomes. Because study participants were only recruited from adult PLHIV in routine care, those with more severe mental health or substance use issues may have dropped out of care, raising the potential for sampling bias. Formal validation of translated mental health and substance use screening tools was not conducted among the study population. Despite these limitations, we feel the study provides an informative picture of the mental health and substance use burden, risks and impacts among adults living with HIV in the region in the pre-COVID-19 pandemic period.

Conclusions

The high prevalence of mild to severe depressive symptoms, suicidal ideation, and substance use, and their association with suboptimal ART adherence, in our adult PLHIV cohort highlight the need to improve access to and integration of mental health and substance use screening and management in HIV clinical settings in the Asia–Pacific region. Enhanced linkages to specialist mental health care for further assessment or interventions, should also be considered in the context of HIV clinical settings. It is important that service integration is localised to address local mental health and substance use issues, particularly depression, suicidality, tobacco, alcohol, amphetamine and sedative use. Further implementation research would inform optimal approaches

to integrating mental health and substance use services within HIV care in the region.

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Data Availability Study data available on request.

Code Availability Codes available on request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical Approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the following institutional research ethics committees: Research Ethics Committee (Kowloon Central / Kowloon East), Hospital Authority IRB, Hong Kong SAR; Research Institute for Tropical Medicine (RITM) Institutional Review Board, Muntinlupa City, the Philippines; Severance Hospital Yonsei University College of Medicine Institutional Review Board, Seoul, South Korea; Institutional Review Board Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; Medical Research Ethics Committee, University Malaya Medical Centre, Kuala Lumpur, Malaysia; Human Research Ethics Committee (HREC), The University of New South Wales, UNSW Sydney, NSW, Australia; and Advarra, Inc. Institutional Review Board, Maryland, U.S.A.

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