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Factors associated with reduced function and quality of life among adult PLWH with depression and substance use in the Asia-Pacific region

Reena Rajasuriar[1], **Chong Meng Li**[1], **Jeremy L Ross**[2], **Awachana Jiamsakul**[3], **Anchalee Avihingsanon**[4], **Man Po Lee**[5], **Rossana Ditangco**[6], **Jun Yong Choi**[7], **Sivaporn Gatechompol**[4], **Iris Chan**[5], **Maria Isabel Echanis Melgar**[6,8], **Jung Ho Kim**[7], **Annette H. Sohn**[2], **Matthew Law**[3] **on behalf of the Substance use, Stigma, Depression and Disability (S2D2) study group of IeDEA Asia-Pacific**

[1]Department of Medicine and Centre of Excellence for Research in AIDS (CERiA), Faculty of Medicine, University Malaya, Kuala Lumpur, Malaysia

[2]TREAT Asia/amfAR – The Foundation for AIDS Research, Bangkok, Thailand

[3]The Kirby Institute, UNSW Sydney, Australia

[4]HIV-NAT/ Thai Red Cross AIDS Research Centre, Bangkok and Center of Excellence in Tuberculosis, Faculty of Medicine, Chulalongkorn University, Thailand

[5]Queen Elizabeth Hospital, Hong Kong SAR

[6]Research Institute for Tropical Medicine, Muntinlupa City, Philippines

[7]Division of Infectious Diseases, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea

[8]Ateneo de Manila University, Quezon City, Philippines

Abstract

Background: Depression and substance use (SU) disorders are prevalent among people living with HIV (PLWH) and impact health outcomes despite successful antiretroviral therapy (ART). We explored quality of life, functional ability and associated factors among PLWH screened positive for depression and/or SU.

Methods: This cross-sectional study recruited adult PLWH during routine follow-up at five HIV clinical sites in the Asia-Pacific region. Participants were screened for depression using PHQ-9 and SU using ASSIST. Quality of life (QoL) was assessed with WHOQOL-HIV BREF and

Corresponding Author: Reena Rajasuriar, Department of Medicine, Faculty of Medicine, University Malaya, 50603 Kuala Lumpur, Malaysia, Phone: +603 7949 6340, reena@um.edu.my.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Awachana Jiamsakul, Sivaporn Gatechompol, Iris Chan, Maria Isabel Echanis Melgar, Jung Ho Kim, and Meng Li Chong. The first draft of the manuscript was written by Reena Rajasuriar and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Competing interest

The authors declare no competing interests.

functional ability with WHODAS 2.0. Factors associated with mean QoL and disability scores were analysed using linear regression.

Results: Of 864 PLWH enrolled, 753 screened positive for depression or SU. The median (interquartile range, IQR) age was 38 (31–47) years and 97% were on ART. Overall mean WHOQOL-HIV BREF and WHODAS scores indicated greater impairment with increasing depressive symptom severity and SU risk. In multivariate analysis, PLWH reporting previous trauma/stress (difference = 2.7, 95% CI 1.5 to 3.9, p<0.001) and past mental health diagnosis (difference =5.0, 95% CI 2.9 to 7.1, p<0.001) were associated with greater disability and poorer QoL scores across multiple domains (p<0.01 for all). Higher CD4 T-cell counts was also associated with better QoL scores and functional ability.

Conclusion: PLWH with depression/SU experienced poorer QoL and function despite routine engagement in HIV care. Efforts to integrate mental health services and interventions addressing disability into HIV management should be prioritised in the region.

Keywords

Quality of life; HIV; functional ability; WHODAS; depression; substance use; Asia

Introduction

Despite well suppressed viral replication on antiretroviral therapy (ART), a significant proportion of people living with HIV (PLWH) continue to experience poor health-related outcomes [1, 2]. Quality of life is the subjective assessment of an individual's well-being, while functionality, assesses an individual's ability to participate and perform daily physical, social and occupational activities. Functional ability is influenced by both extrinsic factors (example stigma experience, social support) and intrinsic factors (frailty, multimorbidity) which in the context of PLWH may be exacerbated [3, 4]. Both measures help chart an individual's overall health status and there is growing consensus for these measures to be included as part of routine HIV management, redefining the focus of HIV care beyond HIV RNA and CD4 T-cell count [5, 6].

A significant comorbidity which contributes to poor quality of life and disability among PLWH are mental health (MH) disorders including substance use (SU) which occur at rates significantly higher than that reported in the general population [7, 8]. Addressing MH and SU issues through the integration of MH into routine HIV care is one of the key priority actions mooted in the Global AIDS Strategy 2021–2026 [9] as it has been shown to improve mental and overall health outcomes among PLWH [10]. However, the adoption of such programs has been slow in the LMIC setting [11]. In the Asia-Pacific region, the provision of MH care assessments for PLWH are among the lowest globally [12] and efforts to improve such services are often met with multiple challenges. These include the lack of trained MH specialists to meet even the basic MH needs of the general population, poor coordination in planning of MH and HIV services which are done almost exclusively of one another and a high-level of stigma in the healthcare setting against people living and at risk of HIV impacting both health-seeking behaviour among PLWH and the willingness of providers to engage in services for PLWH [13, 14].

To date, there is limited data describing the extent of disability and health-related quality of life experienced by PLWH with MH issues undergoing routine HIV care in Asia. This understanding is especially important as health systems in the region work to develop person-centered, integrated care to address the growing MH and SU burden among PLWH. Understanding factors which negatively impact quality of life and functioning in individuals with pre-existing MH issues can help streamline limited MH care resources and facilitate more timely linkage to specialist care. In this multisite-regional study, we aimed to explore the overall functional ability and QoL experienced by PLWH who screened positive for depression/SU during their routine HIV clinic follow-up, describe the specific QoL domains impacted in these individuals and assess individual and HIV/treatment-related factors associated with QoL domains and overall function.

Methods

Study population

The study population included PLWH returning for routine follow-up between July 2019 and June 2020 at five urban HIV treatment centres in Hong Kong SAR, China, Philippines, Malaysia, South Korea and Thailand. All individuals aged 18 years and above with documented HIV infection were eligible to participate.

All participants provided written informed consent and the study protocol was approved by the institutional ethics board at each recruiting centre, the study coordinating centre (TREAT Asia, amfAR/The Foundation for AIDS Research, Thailand) and the data management centre (The Kirby Institute, University of New South Wales, Australia).

Study measurements

All consenting participants answered a standardised study questionnaire which included information on demographic and socio-economic characteristics, HIV disclosure status, recent traumatic events, medical and family MH history. Medical records were also accessed to extract data on HIV-related parameters.

All participants completed a series of self-administered screening tools with study personnel on standby to assist, if needed. Locally validated tools were utilised where available, and if not, study screening tools were professionally translated and reviewed for face validity by investigators with clinical and research experience. Training was conducted virtually for all study staff prior to study initiation to ensure standardised execution of the questionnaires. Site staff also had access to training videos for periodic review. Screening for depression in the past 2 weeks was done using the Patient Health Questionnaire-9 (PHQ-9) and substance use with the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST v3.1).

Additionally, participants were assessed for quality of life and functional ability using the World Health Organisation Quality of Life - HIV (WHOQOL-HIV BREF) and World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2.0), respectively. The WHOQOL-HIV BREF is a 31-item validated tool which assesses an individual’s perception of quality of life (QoL) in six domains; physical, psychological, level of independence, social relationships, environment and spirituality/self-belief as well as an overall rating of

QoL (Question 1, Q1). Items were rated on a 5-point scale with 1 indicating low, negative perception and 5 high, positive perception. Mean scores for each domain were computed with resulting scores ranging between 4 and 20, where higher scores indicated better QoL. The version of WHODAS 2.0 utilised in this study was the short 12-item questionnaire which assesses the overall profile of functioning and disability from a series of questions in the domains of cognition, self-care, getting along, life activities (household and work) and participation. The tool rates level of functioning across a 5-point scale with 1 indicating no disability and 5 indicating extreme disability. A simple scoring approach was used to score functional ability where sums of scores of the 12-items were assigned to each participant (total scores ranging between 12 to 60) with higher scores indicating a greater level of disability.

Statistical analysis

The WHOQOL-HIV BREF and WHODAS 2.0 scores were reported descriptively in all participants and in the sub-population with mild to severe depressive symptoms (PHQ-9 scores ≥5) or those reporting low to high risk use of any substance according to the ASSIST scores of 0–10 (lower risk), 11–26 (moderate risk), and ≥27 (high risk) for alcohol and 0–3 (lower risk), 4–26 (moderate risk), and ≥27 (high risk) for other substances. [15]. We assessed factors associated with mean WHOQOL-HIV BREF scores (Q1 scores and each of the six domain scores) and mean WHODAS 2.0 scores in this sub-population using linear regression. Missing questionnaire responses were imputed using the “hot deck” imputation method where missing values are replaced by random values from the same variable [4].

World Bank country income grouping was adjusted a priori in all analyses to account for heterogeneity across sites. Covariates included were patient characteristics, as well as socio-economic risk factors from the study-specific questionnaire. 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).

Results

A total of 864 participants were recruited, of which 753 (87%) screened positive for either depression or SU. The clinical characteristics and disposition of those screened positive for depression or SU are summarised in Table 1 and Fig S1 (supplementary data), respectively. The median age in participants who screened positive for depression/SU was 38 (interquartile range, IQR 31–47) years and 90% were males. A total of 97% were on antiretroviral therapy (ART). Of those with HIV RNA (n=533) and CD4 T-cell count (n=528) measures available in the prior 6 months, 92% had HIV RNA <1000 copies/ml and the median CD4 T-cell count was 518 (324–725) cells/ul. The majority (53%) reported experiencing a traumatic or stressful event in the past 5 years and 8% had a prior diagnosis of MH. The demographic, socio-behavioural and clinical parameters of participants who

screened positive for depression/SU and those without are summarised in Supplementary table 1.

Functional ability and quality of life scores in PLWH with depression and substance use issues.

The mean overall WHOQOL-HIV BREF score, defined as mean score for Question 1, for the full study cohort was 3.44 (standard deviation (SD) =0.89). For the different sub-population groups, the mean QOL scores were: 3.12 (SD=0.88) for depression sub-group; 3.43 (SD=0.87) for SU sub-group; 3.40 (SD=0.89) for depression or SU sub-group; 3.13 (SD=0.86) for depression and SU sub-group and 3.77 (SD=0.83) for no depression or SU sub-group (Fig 1A). The mean WHODAS 2.0 scores were 20.24 (SD=8.91) for the study cohort; 24.25 (SD=9.31) for the depression sub-group; 20.31 (SD=8.90) for the SU sub-group; 20.78 (SD=9.02) for the depression or SU sub-group; 24.04 (SD=9.38) for the depression and SU sub-group and 16.59 (SD=7.16) for no depression and SU sub-group. Participants screening positive for depression demonstrated greater impairment in mean QoL and WHODAS scores than PLWH screening positive for SU. There was also a clear trend of decline in mean overall QoL scores and a corresponding increase in mean WHODAS 2.0 scores indicating greater disability with increasing severity of depressive symptoms (Fig 1B). These findings indicate a strong, consistent inverse relationship between indicators of health outcomes and MH symptoms. Mean scores for overall QoL and WHODAS 2.0 were varied depending on the type of substance used. Among PLWH reporting moderate to high risk use, alcohol and tobacco users reported lesser functional impairment compared to users of cocaine and opioids (Fig 2). In general, overall mean QoL and WHODAS 2.0 scores displayed a trend of greater impairment among high compared to low risk users for all substances.

Quality of life domains impacted in PLWH with depression/SU and factors associated with QoL domain scores

When assessing each of the WHOQOL HIV-BREF domains, PLWH screened positive for depression/SU had significantly lower mean scores compared to those without depression/SU for all domains except for environment (Fig S2).

In multivariate analysis assessing factors associated with each QoL domain score, aspects encompassing HIV/treatment-related factors, socio-economic factors, psychosocial and physical well-being were all found to be associated with specific domains (Table 2). The majority of factors identified had an overlapping influence on multiple domains. Older age was associated with better QoL scores in the domains of physical health ($p = 0.003$), independence ($p = 0.015$) and spiritual/personal beliefs ($p = 0.028$). Higher CD4 T-cell counts were associated with better QoL in the domains of physical health ($p < 0.001$), psychological health ($p = 0.013$), independence ($p < 0.001$) and environment ($p = 0.009$). Females (compared to males) were associated with better QoL scores in the domains of independence ($p = 0.024$) and social relationship ($p = 0.016$). Individuals experiencing previous traumatic/stressful events in the past 5 years were associated with lower QoL scores in the domains of physical ($p < 0.001$), psychological ($p = 0.004$), independence ($p = 0.029$) and spiritual/personal beliefs ($p = 0.003$). A previous diagnosis of MH or a family

history of MH were associated with lower QoL scores in all domains except physical health and spiritual/personal beliefs.

Socio-economic factors including higher household income and higher education levels were associated with better QoL scores in physical and environmental domains. PLWH residing in the LMIC setting reported better QoL scores in all domains compared to those residing in high-income settings.

Factors associated with functional ability in PLWH screened positive for depression/SU

Factors associated with lower WHODAS 2.0 scores (better functional ability, Table 3) were CD4 T-cell counts >500 cells/μL (difference = −3.0, 95% CI −5.3 to −0.7, p=0.010) compared to CD4 ≤200 cells/μL; currently on INSTI-based regimen (difference = −2.4, 95% CI −4.2 to −0.5, p=0.013) compared to NRTI+NNRTI-regimen; higher household income of $501-$2000 (difference = −2.2, 95% CI −3.8 to −0.5, p=0.010) and >$2000 (difference = −4.0, 95% CI −5.9 to −2.2, p<0.001) compared to ≤$500 per month; and being from upper-middle or lower-middle income countries (difference = −3.6, 95% CI −5.5 to −1.7, p=0.001) compare to high-income countries. The reversed association of country-income grouping in the multivariate model compared to the univariate model could possibly be due to the presence of the Simpson's Paradox where the trend observed in the aggregated data is reversed when the data are separated [16]. Conversely, factors associated with higher WHODAS 2.0 scores (poorer functional ability) were not currently on ART (difference = 4.6, 95% CI 1.0 to 8.2, p=0.013) compared to receiving NRTI+NNRTI-based regimen; having had previous stressors (difference = 2.7, 95% CI 1.4 to 3.9, p<0.001) compared to none; and having had a previous MH disorder (difference = 5.0, 95% CI 2.9 to 7.1, p<0.001) compared to none.

Discussion

To our knowledge, this is the first study to assess functional ability and health-related quality of life among PLWH screened positive for MH issues in the ambulatory care setting in Asia. The majority of PLWH attending routine HIV follow-up screened positive for depression and/or SU, with those positive for depression demonstrating poorer QoL and greater disability compared to those positive for SU. Both QoL and WHODAS scores demonstrated a strong consistent correlation with depressive symptom severity, demonstrating the utility of these patient-reported outcome measures (PROMs) to reflect clinical symptom burden in an out-patient HIV care setting. We found many of the same factors encompassing an individuals' socio-economic and psycho-social environment to independently influence QoL scores across multiple domains, as well as functional ability, highlighting a profile of PLWH with depression/SU issues who may benefit from additional interventions to improve their overall health outcomes. Higher CD4 T-cell counts was associated with both higher QoL scores across multiple domains and better functional ability, underscoring that early ART initiation should be prioritized in all PLWH including those with issues of depression and SU.

Numerous country-specific studies have explored QoL among PLWH in Asia [17–19] but few have offered a regional perspective and none have specifically explored functional

limitations in the context of depression and SU in the region. Mental well-being and mental distress lie along a continuum and most symptoms associated with mental disorders exist on a spectrum, with many present to some degree even in the "normal" population [20]. These symptoms become a disability when it impacts an individual's ability to function. In our study, the overall scores for QoL and functional ability among PLWH in the region were significantly higher compared to the sub-group of PLWH reporting no issues of MH/SU. With close to 50% of PLWH reporting mild or worse depressive symptoms and 80% reporting ever using substance, the higher overall scores potentially reflect the major, insidious role these comorbidities have on health outcomes in PLWH in the region. These findings are also consistent with the lack of MH focus in the majority of HIV programs in the Asia-Pacific region as previously reported [12]. Despite a higher proportion of PLWH screening positive for SU compared to depression, QoL and functional ability scores indicated greater impairment in individuals with depression. Of note the majority screening positive for SU in our cohort were for low to moderate use of alcohol and tobacco and our study did not discern the use of substances for sexual activity which may be episodic and have less impact on daily functioning. Both QoL and functional ability demonstrated a consistent, incremental impairment with greater depressive symptom severity. Prior studies have also suggested that MH symptom severity accounts for a greater variance in perceptions of health and physical functioning above that predicted by HIV-related factors alone [21, 22]. These findings suggest that these PROMs may be used as a proxy for assessing MH in settings where MH stigma is a barrier to screening uptake.

PLWH reporting a stressful event in the past 5 years, a prior MH disorder or a family history of MH were all associated with poorer QoL scores with each factor impacting at least three of the six QoL domains assessed. A history of stressors and a prior history of MH were also associated with greater disability. Of note, a history of MH disorder had the biggest impact in adjusted disability scores (5 points) compared to all the other factors found to independently influence this outcome. The co-occurrence of traumatic stressful events and MH disorders is well described in the literature [23, 24] and people living or at risk of HIV, especially MSM, have reported significantly higher rates than the general population (reviewed in [25]). These same factors have also been associated with increased healthcare utilisation in PLWH and HIV disease progression [22, 26]. Our findings suggest that the cumulative burden of past trauma and MH identify a profile of PLWH who may be more vulnerable to functional deficits and poor quality of life and could potentially benefit from more intense monitoring and MH intervention even when prevalent depressive symptoms or reported SU are mild [21].

Prior studies have found socio-economic factors including lower household income and lower education levels to be associated with poorer QoL domain scores which was consistent with our study [17, 27]. However, we also found PLWH residing in LMIC settings was associated with better QoL scores across all domains and better functional ability compared to those residing in HI settings when controlling for all other significant covariates, a phenomenon which has also been reported in other multi-site studies spanning different socio-economic settings [28, 29]. This could potentially be attributed to an array of inter-setting/country differences which were not measured including lived experiences, perceptions of hardship, access to health resources, social and family support networks,

resilience and health policy among others. For example, PLWH in LMIC settings may be more accepting and able to deal with and normalise their depressive symptoms from years of hardship, leading to it having less impact on their QoL and daily functioning compared to PLWH in HI settings. Social support among PLWH specifically has been shown to influence health outcomes differently across different income and/or culture settings [30, 31]. Individuals from HI/westernised settings tend to value independence more than LMIC settings which value inter-dependence. The influences and interactions of these factors are likely to be complex but could potentially be dissected through further qualitative studies to identify unique country/setting-specific mediators of QoL and disability in PLWH.

We additionally observed a number of HIV and treatment-related factors to positively impact functional ability including CD4 T-cell counts>500 cells/ul and receiving a INSTI-based vs an NNRTI-based regimen while not receiving ART was associated with greater disability, underscoring the extended benefits of initiating treatment early as has been highlighted in other studies [17, 28, 32]. We also found higher CD4 T-cell counts were consistently associated with better QoL scores across multiple domains as described in other studies [17, 33]. The findings of less severe disability in PLWH on INSTI- vs NNRTI-based regimen has not been previously described and we speculate that this could potentially be associated with drug-related effects including disturbances in sleep and concentration which have been reported to be more frequent with NNRTIs compared to INSTIs, even in the setting of stable disease [34].

There were several limitations in this study. First, we did not explore the influence of physical symptom burden especially chronic pain which has been reported to strongly impact outcomes of QoL and disability [35]. This omission could contribute to the variance in the disability and QoL scores measured in this cohort. Second, we cannot exclude the potential influence of cultural differences on the perception of ability or disability that may have influenced responses in the different countries the study was performed as previously described [28]. Third, as this was a cross sectional study design, we cannot infer any causation for the factors identified to be associated with QoL and disability. Finally, we used the 12-item version of WHODAS 2.0 and did not have data to assess specific domains of function with greater detail nor able to determine clinically significant thresholds of disability scores as we lacked normative data for this measure for PLWH in the region. This should be an area for future research.

In conclusion, we found PLWH screened positive for depression and SU to experience poorer quality of life and functional ability compared to those not screening positive, with greater impairment observed among those with more severe depressive symptoms and high risk substance use. PLWH experiencing a prior stressful event, previous diagnosis of MH or a family history of MH were associated with greater disability and poorer quality of life across multiple domains, suggesting a profile of PLWH who may benefit from greater support services during their routine HIV care. Higher CD4 T-cell counts was also associated with better QoL scores across multiple domains suggesting the extended benefits of early treatment even in PLWH with depression and SU issues. Further implementation studies are needed to develop integrated MH and HIV services to address the poor health-

related outcomes associated with the high burden of MH and SU among PLWH in the Asia-Pacific region.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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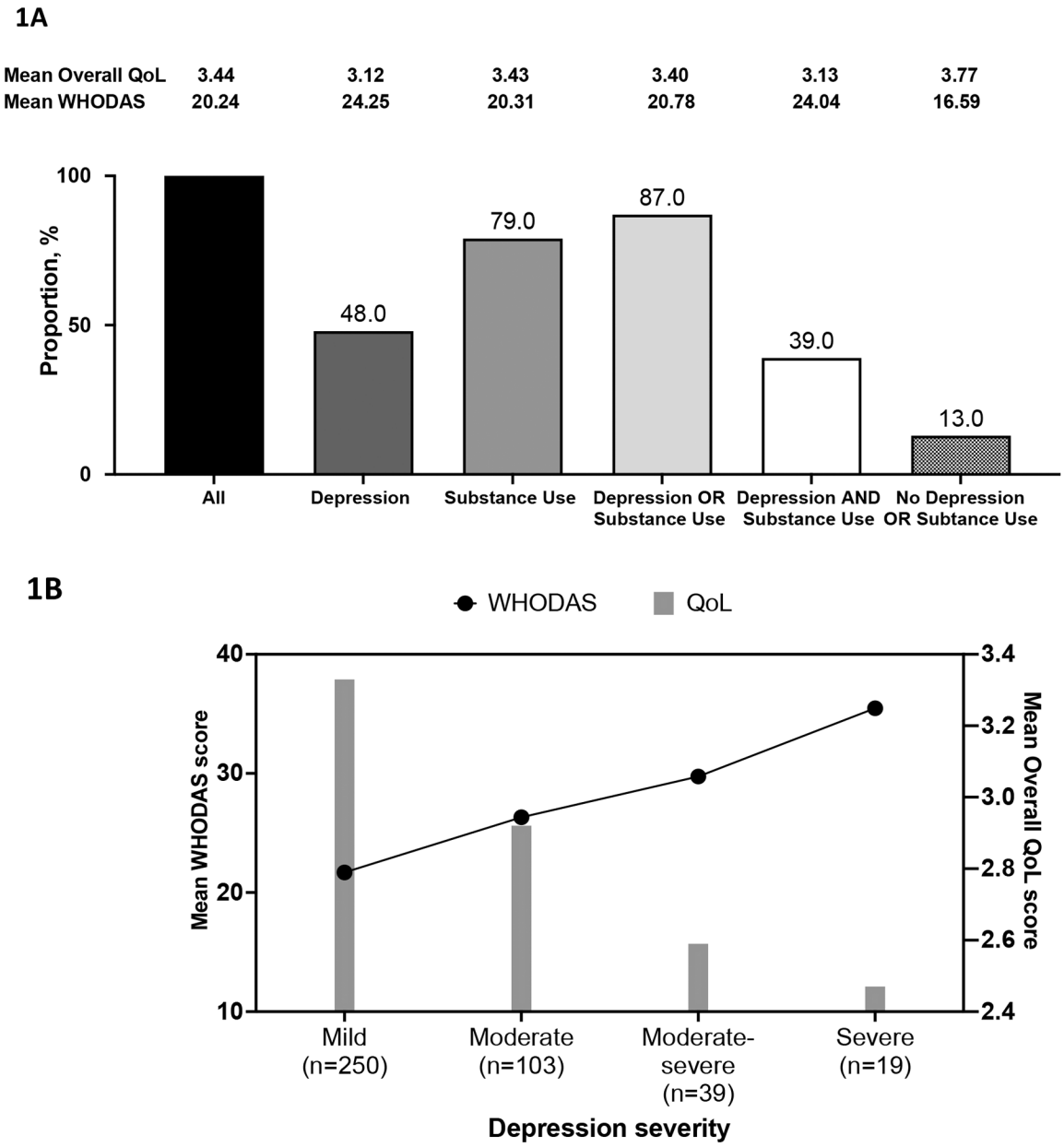

Figure 1: Distribution of PLWH screened positive for depression and/or substance use and mean scores for WHODAS 2.0 and overall Quality of Life (QoL).

(A) Distribution of participants screened positive for depression and/or substance use from all participants recruited in the study (n=864) and corresponding mean WHODAS 2.0 and overall QoL (Q1 of WHOQOL-HIV BREF) scores in each group; **(B)** Trends in mean WHODAS 2.0 (black line) and overall QoL scores (grey bars) by depression symptom severity assessed using the PHQ-9 in PLWH screened positive for depression in the cohort (n=411). The number of participants for each severity group is indicated in the x-axis.

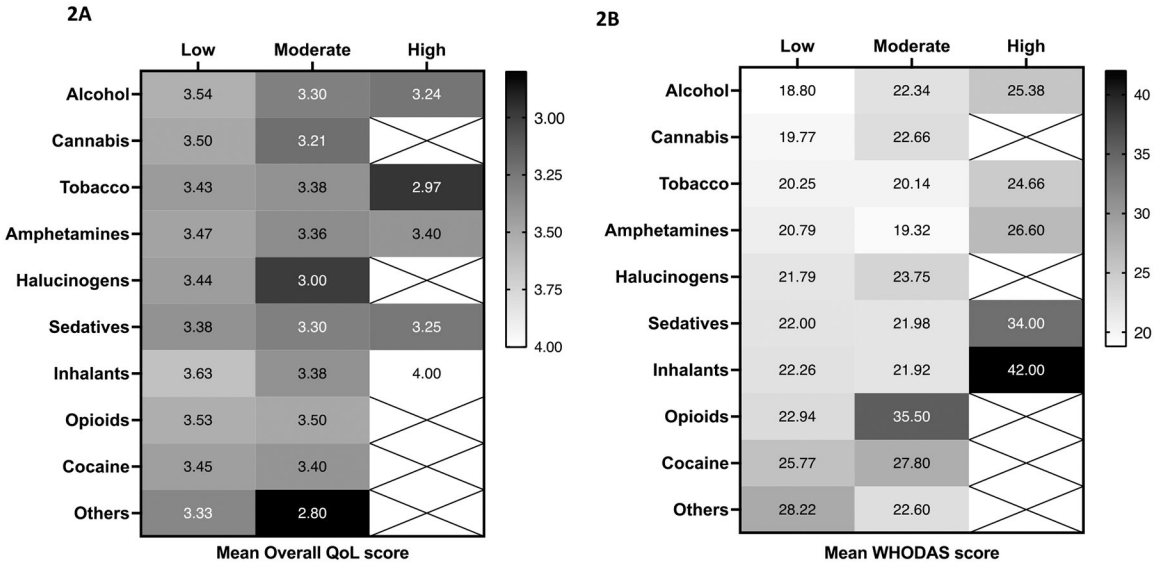

Figure 2: Heat plots describing (A) mean overall QoL and (B) WHODAS 2.0 scores among PLWH screened positive for substance use categorised by type and extent (low, moderate, high) of substance use reported (n=681).

Mean QoL and WHODAS 2.0 scores are displayed in each box for each type of substance (vertical scale) and the extent of its use (low to high-risk) (horizontal scale). Darker shades indicate poorer QoL and greater disability which corresponds with lower mean QoL and higher WHODAS scores, respectively.

Table 1:

Demographic, socio-behavioural and clinical characteristics of participants screened positive for depression or substance use (n=753)

Characteristics	N (%)
Total	753 (100)
Age at survey (years)	Median = 38, IQR (31–47)
≤30	188 (25)
31–40	239 (32)
41–50	216 (29)
>50	110 (15)
Sex	
Male	678 (90)
Female	75 (10)
HIV mode of exposure	
Heterosexual contact	233 (31)
MSM	406 (54)
Injecting drug use	13 (2)
Other/Unknown	101 (13)
Viral load at recruitment (copies/mL)	Median = 33, IQR (19–39)
<50	455 (60)
50–399	32 (4)
400–999	3 (0)
≥1000	43 (6)
Not tested	220 (29)
CD4 count at recruitment (cells/μL)	Median = 518, IQR (324–725)
≤200	63 (8)
201–350	86 (11)
351–500	103 (14)
>500	276 (37)
Not tested	225 (30)
Current ART	
NRTI+NNRTI	387 (51)
NRTI+PI	51 (7)
INSTI	270 (36)
Other	24 (3)
None/unknown	21 (3)
Hepatitis B co-infection	
Negative	250 (33)
Positive	27 (4)
Not tested	476 (63)
Hepatitis C co-infection	
Negative	343 (46)

Characteristics	N (%)
Positive	26 (3)
Not tested	384 (51)
Prior AIDS Diagnosis	
No	476 (63)
Yes	176 (23)
Not reported	101 (13)
House hold income (USD) per month	
≤$500	184 (14)
$501-$2000	215 (29)
>$2000	233 (31)
Not reported/unknown	121 (16)
Employment	
No	159 (21)
Full time	426 (57)
Part time	113 (15)
Not reported/unknown	55 (7)
Highest education level	
No education	3 (0)
Primary to high school	235 (31)
College to university	497 (66)
Not reported/unknown	18 (2)
HIV disclosure status	
Fully	37 (5)
Partially	538 (71)
Not disclosed	140 (19)
Not reported/unknown	38 (5)
Previous stressors	
No	301 (40)
Yes	399 (53)
Not reported/unknown	53 (7)
Family history of mental health disorder	
No	637 (85)
Yes	32 (4)
Not reported/unknown	84 (11)
Comorbidities	
No	302 (40)
Yes	130 (17)
Not reported/unknown	321 (43)
Previous mental health disorder	
No	539 (72)
Yes	61 (8)
Not reported/unknown	153 (20)

Characteristics	N (%)
History of STIs in the past 5 years	
No	339 (45)
Yes	237 (31)
Not reported/unknown	177 (24)
Year of ART initiation	
<2010	199 (26)
2010–2012	98 (13)
2013–2015	160 (21)
2016–2020	286 (38)
No ART/unknown	10 (1)
ART adverse events in the previous year	
No	510 (68)
Yes	80 (11)
Not reported/unknown	163 (22)
ART adherence in the previous year	
≥95	479 (64)
<95	52 (7)
Not reported/unknown	222 (29)
World Bank country income grouping	
High	292 (39)
Upper middle and lower middle	461 (61)

Abbreviations: MSM-men who have sex with men; ART-antiretroviral therapy; NRTI-non-nucleoside reverse transcriptase inhibitors; NNRTI-non-nucleoside reverse transcriptase inhibitors; PI-protease inhibitors; INSTI-integrase strand transfer inhibitors; STIs-sexually transmitted infections.

Table 2:

Findings from multivariate analyses of risk factors associated with each WHOQOL-HIV BREF domain in individuals who screened positive for depression or substance use (n=753)

	Overall		Physical		Psychological		Independence		Social relationships		Environment		Spirituality / personal beliefs	
Variables	**Mean score**	**Diff**	**Mean score**	**Diff**	**Mean score**	**Diff**	**Mean score**	**Diff**	**Mean score**	**Diff**	**Mean score**	**Diff**	**Mean score**	**Diff**
Total	3.4		14.4		13.8		14.9		13.5		13.9		13.6	
Age at survey (years)														
≤30	3.4		13.9	Ref	13.5		14.4	Ref	13.6		13.7		13.3	Ref
31–40	3.4		14.3	+	13.8		14.8	+	13.5		14.0		13.3	+
41–50	3.4		14.7	+	14.3		15.5	+	13.7		14.2		14.0	+
>50	3.2		14.5	+	13.5		14.8	+	13.2		13.4		13.9	+
Sex														
Male	3.4		14.3		13.7		14.8	Ref	13.4	Ref	13.9		13.5	
Female	3.5		15.0		14.7		15.8	+	14.4	+	14.2		14.6	
HIV mode of exposure														
Heterosexual contact	3.3		14.3		14.1		14.9		13.5		13.7		14.1	Ref
MSM	3.5		14.5		13.8		15.1		13.6		14.1		13.3	−
Injecting drug use	3.3		13.8		13.3		14.3		13.1		13.4		11.6	−
Other/Unknown	3.2		14.0		13.3		14.4		13.5		13.5		13.7	−
Viral Load at survey (copies/mL)														
<1000	3.4		14.6		13.8		15.2		13.7		14.0		13.6	
≥1000	3.3		13.2		13.2		13.9		13.0		13.4		13.3	
Not tested	3.5		14.2		14.0		14.5		13.4		13.7		13.6	
CD4 at survey (cells/μL)														
≤200	3.4		12.4	Ref	13.1	Ref	13.3	Ref	13.2		13.4	+	13.4	
201–350	3.2		13.9	+	13.1	+	14.2	+	12.7		13.0	Ref	13.3	
351–500	3.3		14.5	+	13.6	+	14.9	+	13.3		13.9	+	12.9	
>500	3.5		15.0	+	14.1	+	15.7	+	13.9		14.3	+	13.9	
Not tested	3.4		14.3		14.0		14.7		13.6		13.9		13.7	
Current ART														
NRTI+NNRTI	3.5		14.7		14.3		15.1		13.8		14.1		13.8	

Variables	Overall		Physical		Psychological		Independence		Social relationships		Environment		Spirituality / personal beliefs	
	Mean score	Diff	Mean score	Diff	Mean score	Diff	Mean score	Diff	Mean score	Diff	Mean score	Diff	Mean score	Diff
NRTI+PI	3.4		14.5		14.1		14.5		13.3		14.0		13.8	
INSTI	3.3		14.1		13.2		15.1		13.3		13.8		13.2	
Other	3.0		13.7		13.1		14.3		14.0		13.5		14.3	
None/unknown	3.2		12.6		12.6		12.6		12.3		13.0		12.0	
Hepatitis B co-infection														
Negative	3.5		14.7		13.7		15.6		13.6		14.2		13.6	
Positive	3.6		15.8		15.1		16.4		14.7		14.7		14.3	
Not tested	3.3		14.1		13.8		14.5		13.4		13.7		13.5	
Hepatitis C co-infection														
Negative	3.5		15.0		14.3		15.9		14.0		14.4		13.8	
Positive	3.7		15.2		14.4		16.3		15.0		15.2		14.5	
Not tested	3.3		13.7		13.3		14.0		13.0		13.4		13.3	
Prior AIDS Diagnosis														
No	3.4		14.7		13.8		15.4		13.8		14.2		13.4	
Yes	3.4		14.3		13.9		14.7		13.3		13.8		13.7	
Not reported	3.2		12.9		13.6		13.1		12.9		12.8		14.1	
Household income (USD) per month														
≤$500	3.2	Ref	13.7	Ref	13.8		14.0	Ref	13.1		13.2	Ref	13.6	
$501-$2000	3.5	+	15.0	+	14.3		15.4	+	14.1		14.5	+	13.8	
>$2000	3.6	+	14.7	+	13.8		15.7	+	13.7		14.5	+	13.6	
Not reported/unknown	3.1		13.8		13.1		14.0		12.8		12.9		13.3	
Employment														
No	3.1		13.5		13.2		13.8		12.9		13.1		13.5	−
Full time	3.6		14.9		14.2		15.6		13.9		14.4		13.9	Ref
Part time	3.3		13.8		13.4		14.5		13.2		13.4		12.8	−
Not reported/unknown	3.3		14.2		13.4		14.1		13.3		13.7		13.4	
Highest education level														
No education	3.3		17.7		14.7		17.0		13.0	−	13.7	+	14.3	
Primary to high school	3.2		14.1		13.4		14.6		12.9	−	13.3	−	13.2	
College to university	3.5		14.5		14.0		15.1		13.8	Ref	14.2	Ref	13.7	

Variables	Overall		Physical		Psychological		Independence		Social relationships		Environment		Spirituality / personal beliefs	
	Mean score	Diff	Mean score	Diff	Mean score	Diff	Mean score	Diff	Mean score	Diff	Mean score	Diff	Mean score	Diff
Not reported/unknown	3.0		14.3		14.2		14.7		13.5		13.7		14.1	
HIV disclosure status														
Fully	3.4		13.9		14.5		14.1		14.5	Ref	13.9		15.1	Ref
Partially	3.4		14.4		13.7		15.0		13.6	–	13.9		13.6	–
Not disclosed	3.4		14.5		14.1		15.2		12.9	–	13.9		12.9	–
Not reported/unknown	3.2		14.4		13.8		14.5		13.7		13.6		14.1	
Previous stressors														
No	3.6	Ref	15.4	Ref	14.6	Ref	15.8	Ref	14.1		14.5		14.4	Ref
Yes	3.3	–	13.7	–	13.3	–	14.4	–	13.2		13.6		13.1	–
Not reported/unknown	3.2		13.7		13.1		14.1		12.9		13.2		12.8	
Family history of mental health disorder														
No	3.4		14.6		14.1	Ref	15.1		13.7	Ref	14.1	Ref	13.8	
Yes	3.4		13.6		12.4	–	13.8		12.3	–	13.0	–	12.9	
Not reported/unknown	3.1		13.2		12.1		13.9		12.9		13.0		12.4	
Comorbidities														
No	3.3		14.0		13.0		14.8		13.2		13.8		13.2	
Yes	3.4		14.3		13.5		14.6		13.2		13.9		13.2	
Not reported/unknown	3.5		14.7		14.7		15.2		14.0		14.0		14.1	
Previous mental health disorder														
No	3.5	Ref	14.8		14.1	Ref	15.6	Ref	13.8	Ref	14.2		13.7	
Yes	2.9	–	12.9		11.8	–	13.4	–	12.2	–	13.1		12.0	
Not reported/unknown	3.2		13.3		13.7		13.3		13.0		13.0		13.9	
History of STIs in the past 5 years														
No	3.4		14.5		13.8		15.4		13.6		14.1		13.3	
Yes	3.5		14.7		13.8		15.4		13.8		14.3		13.7	
Not reported/unknown	3.3		13.6		13.7		13.6		13.1		13.1		13.9	
Year of ART initiation														
<2010	3.4		14.8		14.2		15.5		13.6		13.9		14.0	
2010–2012	3.5		15.2		14.2		15.8		13.9		14.6		13.6	

Variables	Overall		Physical		Psychological		Independence		Social relationships		Environment		Spirituality / personal beliefs	
	Mean score	**Diff**	**Mean score**	**Diff**	**Mean score**	**Diff**	**Mean score**	**Diff**	**Mean score**	**Diff**	**Mean score**	**Diff**	**Mean score**	**Diff**
2013–2015	3.4		14.4		13.9		14.7		13.6		13.9		13.5	
2016–2020	3.3		13.9		13.4		14.4		13.3		13.7		13.4	
No ART/unknown	3.3		13.0		13.0		13.3		13.9		13.7		12.6	
ART adverse events in the previous year														
No	3.4		14.7		13.9		15.4		13.7		14.1		13.6	
Yes	3.5		14.3		13.9		15.4		13.9		14.5		13.0	
Not reported/unknown	3.2		13.3		13.6		13.3		13.0		13.0		13.9	
ART adherence in the previous year														
≥95	3.5		14.7		13.9		15.5		13.7		14.2		13.6	Ref
<95	3.3		13.9		12.8		14.5		12.8		13.5		12.5	−
Not reported/unknown	3.2		13.7		13.8		13.9		13.3		13.3		13.9	
WHODAS score														
≤17	3.7	Ref	15.9	Ref	15.0	Ref	16.6	Ref	14.7	Ref	15.0	Ref	14.8	Ref
>17	3.1	−	12.8	−	12.6	−	13.3	−	12.3	−	12.8	−	12.3	−
World Bank country income grouping														
High	3.3	Ref	13.9	Ref	12.9	Ref	14.8	Ref	13.0	Ref	13.5	Ref	13.2	Ref
Upper-middle and lower-middle	3.5	+	14.7	+	14.4	+	15.0	+	13.9	+	14.1	+	13.8	+

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.

Abbreviations: Ref-reference group; CI-confidence interval; Diff-difference; MSM-men who have sex with men; ART-antiretroviral therapy; NRTI-non-nucleoside reverse transcriptase inhibitors; NNRTI-non-nucleoside reverse transcriptase inhibitors; PI-protease inhibitors; INSTI-integrase strand transfer inhibitors; STIs-sexually transmitted infections; WHODAS-World Health Organization Disability Assessment Schedule

+ indicates higher mean scores compared to the reference group, − indicates lower mean scores to the reference group.

Bold fonts indicate statistical significance at a level of p<0.05

Refer to Supplementary Table 3 and Supplementary Table 4 for details of differences in mean scores across variable

Table 3:

Multivariate analyses of risk factors associated with WHODAS 2.0 scores in individuals who screened positive for depression or substance use (n=753)

			Univariate analysis		Multivariate analysis	
Variables	**Total patients**	**Mean WHODAS score**	**Difference (95% CI)**	***p***	**Difference (95% CI)**	***p***
Total	753	20.8				
Age at survey (years)				0.766	-	-
≤30	188	21.2	Ref		-	-
31–40	239	20.9	−0.3 (−2.0, 1.4)	0.737	-	-
41–50	216	19.5	−1.7 (−3.5, 0.0)	0.057	-	-
>50	110	22.1	0.8 (−1.3, 2.9)	0.448	-	-
Sex					-	-
Male	678	20.9	Ref		-	-
Female	75	19.7	−1.3 (−3.4, 0.9)	0.255	-	-
HIV mode of exposure				0.002	-	-
Heterosexual contact	233	21.8	Ref		-	-
MSM	406	19.7	−2.1 (−3.6, −0.7)	0.004	-	-
Injecting drug use	13	21.4	−0.4 (−5.4, 4.6)	0.870	-	-
Other/Unknown	101	22.9	1.0 (−1.0, 3.1)	0.325	-	-
Viral Load at survey (copies/mL)					-	-
<1000	490	19.7	Ref		-	-
≥1000	43	22.5	2.8 (0.0, 5.6)	0.046	-	-
Not tested	220	22.9			-	-
CD4 at survey (cells/μL)				<0.001		0.001
≤200	63	25.1	Ref		Ref	
201–350	86	22.2	−2.9 (−5.8, −0.1)	0.045	−1.4 (−4.0, 1.2)	0.284
351–500	103	19.9	−5.2 (−7.9, −2.4)	<0.001	−2.2 (−4.7, 0.4)	0.094
>500	276	18.5	−6.6 (−9.0, −4.2)	<0.001	−3.0 (−5.3, −0.7)	0.010
Not tested	225	22.3				
Current ART				<0.001		0.003
NRTI+NNRTI	387	21.5	Ref		Ref	
NRTI+PI	51	22.0	0.5 (−2.1, 3.0)	0.729	−0.5 (−2.9, 1.8)	0.668
INSTI	270	18.7	−2.8 (−4.2, −1.4)	<0.001	−2.4 (−4.2, −0.5)	0.013
Other	24	22.2	0.6 (−3.0, 4.3)	0.730	1.2 (−2.2, 4.6)	0.487
None	21	28.8	7.3 (3.4, 11.2)	<0.001	4.6 (1.0, 8.2)	0.013
Hepatitis B co-infection				0.609	-	-
Negative	250	17.9	Ref		-	-
Positive	27	17.0	−0.9 (−4.4, 2.6)		-	-
Not tested	476	22.5			-	-
Hepatitis C co-infection				0.318	-	-
Negative	343	17.8	Ref		-	-
Positive	26	16.1	−1.7 (−5.1, 1.7)		-	-

Variables	Total patients	Mean WHODAS score	Univariate analysis Difference (95% CI)	*p*	Multivariate analysis Difference (95% CI)	*p*
Not tested	384	23.8			-	-
Prior AIDS Diagnosis				0.023	-	-
No	476	19.3	Ref		-	-
Yes	176	21.0	1.7 (0.2, 3.2)		-	-
Not reported	101	27.5			-	-
House hold income (USD) per month				<0.001		<0.001
≤$500	184	24.0	Ref		Ref	
$501–$2000	215	19.7	−4.3 (−6.0, −2.6)	<0.001	−2.2 (−3.8, −0.5)	0.010
>$2000	233	17.8	−6.2 (−7.8, −4.5)	<0.001	−4.0 (−5.9, −2.2)	<0.001
Not reported/unknown	121	23.5				
Employment				<0.001	-	-
No	159	24.0	4.9 (3.3, 6.5)		-	-
Full time	426	19.1	Ref		-	-
Part time	113	22.3	3.2 (1.4, 5.1)		-	-
Not reported/unknown	55	21.3			-	-
Highest education level				0.172	-	-
No education	3	15.3	−5.1 (−15.3, 5.2)	0.332	-	-
Primary to high school	235	21.5	1.1 (−0.3, 2.5)	0.118	-	-
College to university	497	20.4	Ref		-	-
Not reported/unknown	18	22.6			-	-
HIV disclosure status				0.062	-	-
Fully	37	24.1	Ref		-	-
Partially	538	20.5	−3.6 (−6.6, −0.6)	0.018	-	-
Not disclosed	140	20.7	−3.4 (−6.7, −0.2)	0.040	-	-
Not reported/unknown	38	21.9			-	-
Previous stressors				<0.001		<0.001
No	301	17.9	Ref		Ref	
Yes	399	22.4	4.5 (3.2, 5.8)		2.7 (1.4, 3.9)	
Not reported/unknown	53	25.0				
Family history of mental health disorder				0.012		<0.001
No	637	20.2	Ref		Ref	
Yes	32	24.3	4.1 (0.9, 7.2)		5.0 (2.9 – 7.1)	
Not reported/unknown	84	24.1			-	-
Comorbidities				0.159	-	-
No	302	19.7	Ref		-	-
Yes	130	21.1	1.3 (−0.5, 3.2)		-	-
Not reported/unknown	321	21.6			-	-
Previous mental health disorder				<0.001	-	-
No	539	18.6	Ref		-	-
Yes	61	24.2	5.6 (3.4, 7.8)		-	-

Variables	Total patients	Mean WHODAS score	Univariate analysis Difference (95% CI)	*p*	Multivariate analysis Difference (95% CI)	*p*
Not reported/unknown	153	27.1			-	-
History of STIs in the past 5 years				0.769	-	-
No	339	19.3	Ref		-	-
Yes	237	19.1	−0.2 (−1.6, 1.2)		-	-
Not reported/unknown	177	25.9			-	-
Year of ART initiation				0.213	-	-
<2010	199	20.2	Ref		-	-
2010–2012	98	19.5	−0.7 (−2.9, 1.4)	0.508	-	-
2013–2015	160	20.9	0.7 (−1.2, 2.6)	0.472	-	-
2016–2020	286	21.4	1.2 (−0.4, 2.9)	0.136	-	-
No ART	10	24.1	3.9 (−1.8, 9.6)	0.183	-	-
ART adverse events in the previous year				0.494	-	-
No	510	18.9	Ref		-	-
Yes	80	19.6	0.7 (−1.3, 2.7)		-	-
Not reported/unknown	163	27.2				
ART adherence in the previous year				0.460	-	-
≥95	479	19.0	Ref		-	-
<95	52	20.0	0.9 (−1.5, 3.4)		-	-
Not reported/unknown	222	24.7			-	-
World Bank country income grouping				0.009		<0.001
High	292	19.7	Ref		Ref	
Upper-middle and lower-middle	461	21.5	1.8 (0.4, 3.1)		−3.6 (−5.5, −1.7)	

Abbreviations: Ref-reference group; CI-confidence interval; MSM-men who have sex with men; ART-antiretroviral therapy; NRTI-non-nucleoside reverse transcriptase inhibitors; NNRTI-non-nucleoside reverse transcriptase inhibitors; PI-protease inhibitors; INSTI-integrase strand transfer inhibitors; STIs-sexually transmitted infections; WHODAS-World Health Organization Disability Assessment Schedule.