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Mental health and implications for antiretroviral adherence in a multiethnic Asian cohort

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ABSTRACT

Objectives Research suggests a high prevalence of depression and anxiety in people living with HIV, resulting in negative health outcomes and poorer help-seeking behaviours when undetected. Subsequent disease progression and non-adherence to treatment constitute a significant barrier to HIV treatment. This paper aims to identify the risk factors for the development of psychological distress and non-adherence to antiretroviral medication in people living with HIV.

Methods An HIV outpatient clinical service screened for anxiety and depressive symptoms. As part of a retrospective analysis of the cohort, independent sample t-test and χ^2 test were conducted to examine differences between symptomatic and asymptomatic patients in demographic variables such as mode of transmission and disclosure to family; clinical indicators such as psychiatric history and history of alcohol and substance use; and outcome variables such as current psychological distress and non-adherence. Binary logistic regression was conducted to determine predictors of psychological distress and non-adherence.

Results After adjusting for age, no history of alcohol use and psychiatric history were found to be significant risk factors for psychological distress during the programme. Older patients were less likely to be symptomatic during the programme. After adjusting for age, having received intervention and psychiatric history, significant risk factors for non-adherence to antiretroviral medication were mode of transmission, history of smoking and being symptomatic during the programme.

Conclusion Significant psychological distress occurring early in HIV care predicts future non-adherence to antiretroviral treatment, highlighting the importance of early detection and intervention for psychological distress in people living with HIV. Mental health interventions should be intercalated with treatment adherence interventions to improve HIV treatment outcomes.

INTRODUCTION

Even as the number of new HIV infections has been and is projected to continue decreasing over the years, the number of people living with HIV who have access to treatment is increasing, whereby an estimated 26 million people living with HIV worldwide are on treatment as of June 2020.¹ Out of 1.5 million new HIV infections worldwide in 2020, Singapore saw 261 new infections, with a total of 8879 people diagnosed locally.² This shift has brought into focus the importance of adherence to treatment, given the availability of effective

treatment which allows for good physical health.³ However, multiple studies show that people living with HIV suffer from high rates of psychiatric comorbidity,^{3–5} the presence of which is associated with overall poorer outcomes in HIV treatment.⁵ A potential reason for this is the correlation between psychiatric comorbidity and treatment non-adherence, as demonstrated by a meta-analysis.⁴

Multiple factors have been thought to contribute to psychological distress, including symptom burden, emotional distress from obtaining a positive test result and a heightened sense of HIV-related stigma.⁶ Other contributory factors include increased use of alcohol and drugs.⁷ In a study of 132 outpatients with HIV at an infectious diseases centre in Singapore, 28.8% reported anxiety and 16.7% reported depressive symptoms, approximately fourfold the prevalence found in the general population.⁸ Without timely detection of psychological distress, people living with HIV are at risk of negative health outcomes, lower CD4 cell counts and more advanced HIV disease.³ The presence of psychological distress negatively affects help-seeking behaviour, where patients exhibit poorer adherence to treatment, resulting in high treatment attrition rates.³

There is a complex interplay between HIV and mental health issues, with multiple contributory factors influencing each other. Several studies on patients with HIV found that those who presented with symptoms of depression and anxiety tended to have poorer adherence to medication.^{6,9} In addition to worsening HIV-related health outcomes, untreated psychiatric comorbidity in patients with HIV could also accelerate the spread of HIV through an increase in behaviours such as high-risk drinking, illicit drug use and risky sexual behaviour.^{5,10} Alcohol and substance use is another important factor in the relationship between HIV and mental health. Its use in helping to cope with psychological distress also contributes to negative health outcomes as increased substance use affects adherence.^{7,9}

Despite the diminished quality of life patients with HIV may experience as a result of psychological distress, the stigma associated with mental illness and seeking treatment at mental health institutions often hinders them in seeking help,¹¹ resulting in untreated psychological distress. A systematic review showed that the integration of both HIV and mental health services in a single facility can contribute to the alleviation of associated negative outcomes.¹² Besides increasing patients' access to



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care, the co-location of services improves communication and awareness among service providers. This highlights the importance of an integrated system of HIV and mental health services, the absence of which constitutes an additional significant barrier to HIV treatment.¹³

The Psychological Wellness Programme is a mental health screening service in an urban, tertiary healthcare setting that was introduced in 2010 to facilitate early identification of and appropriate intervention for anxiety and depressive symptoms as part of routine HIV care, with the goal of improving the health outcomes of patients with HIV. This paper aims to identify the risk factors for the development of psychological distress and non-adherence to antiretroviral treatment (ART), and to begin to understand the complex relationship between HIV and these factors. This may prove useful in the design and delivery of services, especially in identifying high-risk groups that may benefit from greater resources.

METHODS

In August 2010, a clinical service was started as a collaboration between the departments of psychiatry and infectious diseases of a 1600-bed tertiary hospital in Singapore, the country's sole provider of HIV care at that time, for proactive screening of anxiety and depressive symptoms in patients with HIV. The HIV clinic, which is sited at an affiliated centre for infectious diseases, provides holistic care for more than 4000 people living with HIV and is the largest and most established HIV care centre in the country. Screening for psychological symptoms was done within the first 6 months of their access to HIV specialist care, with the objective of early detection and intervention to improve patient outcomes. Patients exited from the programme after they had completed two standardised screenings that were between 6 and 12 months apart. Patients were considered dropouts if they did not have a repeat screen within 12 months after the entry screen and were not recontacted for follow-up. Patients were also excluded from the programme if they did not undergo an entry screen within 6 months of their first HIV clinic consult or if they scored less than 7 on the Abbreviated Mental Test.¹⁴ The clinical data collected were then stored in a standing database approved by the relevant ethical review boards.

Outcome measures

Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) is composed of an anxiety subscale and a depression subscale, each subscale comprising seven items that are scored on a scale of 0–3 (maximum score 21 for each subscale).¹⁵ This has been validated in different languages and in various HIV populations.^{16–18} Patients were considered to have clinically significant psychological distress that required intervention if they scored above 7 on either the anxiety or the depression subscale of HADS.¹⁵

Self-reported medication adherence

This was a single question asked during exit (repeat) screening that asked patients how many days in the last 30 days they had missed taking their antiretroviral medications; this number was then subtracted from 30 and converted to a percentage. A 1-month recall period has been shown to be more accurate with significantly less over-reporting than 3-day or 7-day recall periods.¹⁹ It has also been shown to be strongly associated with viral loads.²⁰ We did not have the resources to validate this measure against an objective measure of adherence. Nevertheless, there is sufficient literature showing good correlation with

objective measures²¹ and ability to predict clinical outcomes in the HIV population despite their limitations.²² Moreover, self-reports of non-adherence may have better specificity and sensitivity than self-reports of adherence.²² We defined non-adherence as a self-reported non-adherence level of >5%.²³

Other variables collected

As part of the screening procedure, other variables were recorded. These included demographics (age, gender, educational level, employment status), mode of HIV transmission and disclosure of HIV diagnosis to family. Clinical data included history of psychiatric illness, smoking, use of alcohol, use of illegal substances, first CD4 count (<200 cells/μL or >200 cells/μL) and first viral load obtained at the first HIV clinic consult, as well as presence of medical comorbidities according to the Charlson Comorbidity Index.²⁴ Marital status was not recorded as same-sex marriages are not permitted by law in Singapore. Successful access to interventions for psychological distress based on actualised visits (yes/no) was also recorded during the exit (repeat) screening procedure.

Data were analysed using IBM SPSS Statistics for Windows V.26.0, with statistical significance set at $p < 0.05$. Figure 1 presents the derivation of our study sample. The study sample was divided into two groups for comparison. The first group comprises patients who screened positive on the HADS on at least one of the two screenings conducted according to programme protocol (symptomatic during programme), and the second group consists of those who screened negative on the HADS on both screenings (asymptomatic during programme). Differences in quantitative variables were assessed using the independent samples t-test and categorical variables were compared using the χ^2 test. Binary logistic regression was performed using the variables 'symptomatic during programme' and 'non-adherence' as dependent variables.

RESULTS

Study population

Table 1 presents the comparison of demographic and clinical factors between patients who were symptomatic and asymptomatic during the programme. In clinical practice, patients who screened positive once were no different from those who screened positive twice in terms of intervention workflows following case identification, in keeping with the main programme objective of early detection and intervention. National HIV statistics show that transmission was largely via sexual transmission, further subclassified as heterosexual, homosexual and bisexual contact, with few cases of transmission by intravenous drug use and none due to blood transfusion, transplant or perinatal routes.² For ease of analysis, we grouped the mode of disease transmission into two categories, heterosexual sex versus non-heterosexual sex and others.

A higher proportion of symptomatic patients had psychiatric history ($\chi^2 = 46.9$, $p < 0.001$), history of smoking ($\chi^2 = 3.96$, $p = 0.046$) and history of substance use ($\chi^2 = 4.48$, $p = 0.034$), as compared with asymptomatic patients. Similarly, a significantly greater proportion of symptomatic patients were non-adherent to their antiretroviral medication at the exit screening ($\chi^2 = 11.86$, $p = 0.001$). Conversely, a lower proportion of symptomatic patients than asymptomatic patients had medical conditions comorbid to HIV ($\chi^2 = 6.65$, $p = 0.010$) and had history of alcohol use ($\chi^2 = 5.47$, $p = 0.019$).

Risk factors for psychological distress

A binomial logistic regression was performed to ascertain the effects of various demographic variables and clinical factors

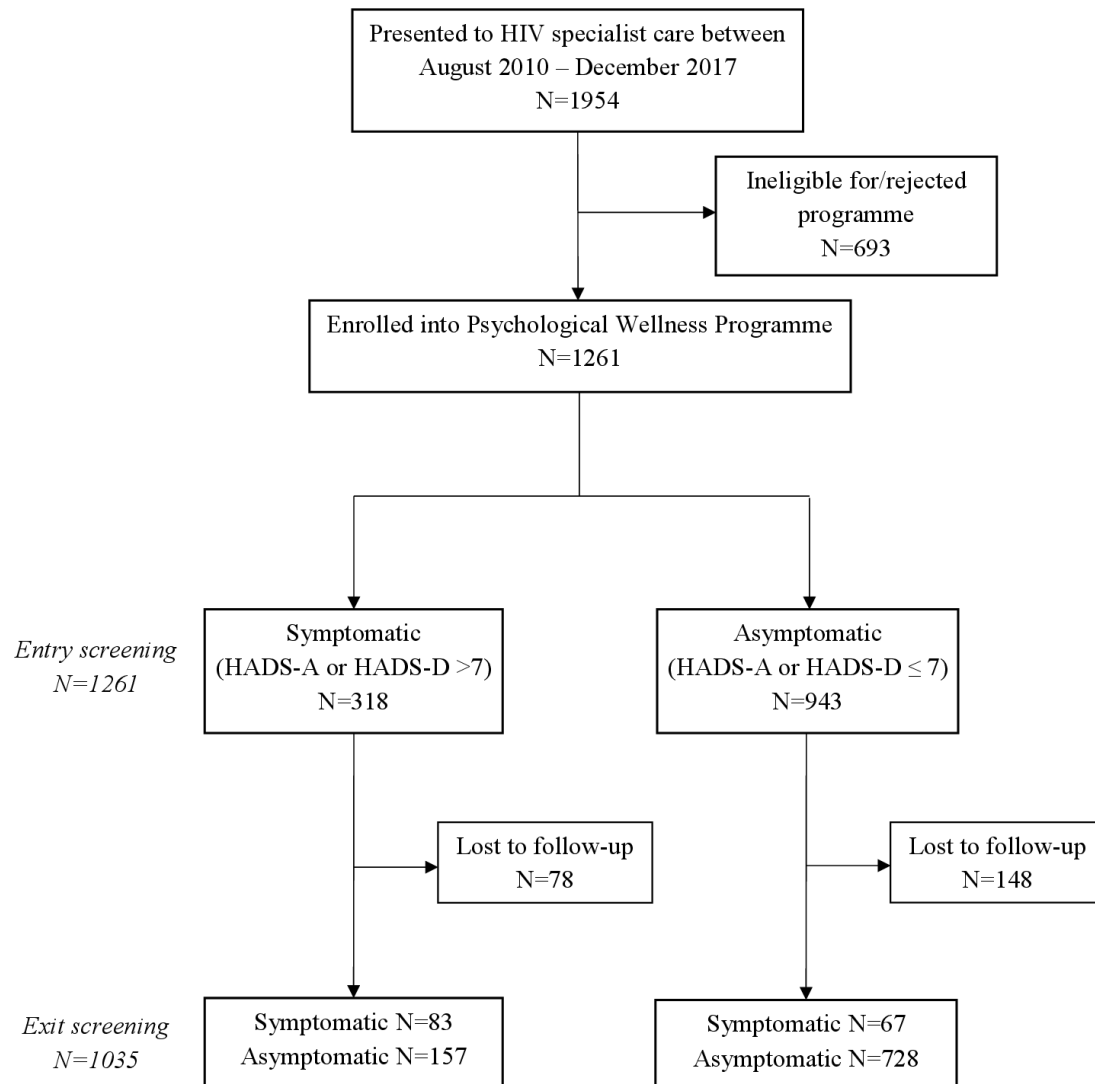


Figure 1 Flow chart of participants enrolled into the Psychological Wellness Programme (August 2010–December 2017). Created by the authors. HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale-Depression.

on the likelihood that patients were symptomatic during the programme (table 2). After adjusting for age, significant risk factors found included psychiatric history and history of alcohol use. Older patients (OR=0.99, 95% CI 0.97 to 1.00, $p=0.022$) and patients with history of alcohol use (OR=0.66, 95% CI 0.49 to 0.90, $p=0.008$) were less likely to report significant psychological distress. Patients with psychiatric history of anxiety and/or depression were more likely to be symptomatic during the programme (OR=3.46, 95% CI 2.27 to 5.27, $p<0.001$).

Risk factors for non-adherence to antiretroviral medication

A binomial regression was performed to determine whether non-adherence to antiretroviral medication could be predicted by demographic variables, clinical factors and being symptomatic during the programme (table 3). After adjusting for age, having received intervention and psychiatric history, significant risk factors found included mode of HIV transmission, history of smoking and presence of psychological distress during the programme. Patients who reported disease transmission through heterosexual contact (OR=1.71, 95% CI 1.10 to 2.67, $p=0.017$), patients with history of smoking (OR=1.56, 95% CI 1.06 to 2.32, $p=0.026$) and patients who were symptomatic

during the programme (OR=2.83, 95% CI 1.69 to 4.75, $p<0.001$) were more likely to report non-adherence to antiretroviral medication.

DISCUSSION

A history of psychiatric illness was associated with the presence of symptoms of psychological distress in this study. Pre-existing psychiatric illness has been associated with a manifold increased risk of HIV acquisition, and it is unsurprising that a high proportion of people living with HIV newly linked to care would also present with concomitant psychological symptoms.²⁵ Despite the absence of a significant association in our study, the relationship between illicit substance use and the presence of symptoms of depression and anxiety has been well reported in the literature.²⁶ We hypothesise that the disclosure of illicit drug use was falsely low due to the strict laws against drug use in our country. Nevertheless, the importance of services integrating general mental health and substance use for people living with HIV should not be undermined by our results.

The association we found between younger age and an increased likelihood of reporting psychological symptoms is likely sociocultural and may include increased stressors from

Table 1 Demographic characteristics of the participants (N=1261)

	Symptomatic during the programme (n=385)	Non-symptomatic during the programme (n=876)	P value
Mean age at entry (SD)	36.8 (11.7)	39.0 (12.5)	0.003**
Gender, n (%)			
Male	356 (30.5)	813 (69.5)	0.83
Female	29 (31.5)	63 (68.5)	
Employment status, n (%)			
Unemployed/retired	130 (34.3)	249 (65.7)	0.057
Employed	255 (28.9)	627 (71.1)	
Education, n (%)			
High school and below	164 (32.4)	342 (67.6)	0.24
Post-high school	221 (29.3)	534 (70.7)	
Disclosure to family, n (%)			
Yes	158 (31.8)	339 (68.2)	0.43
No	227 (29.7)	537 (70.3)	
Mode of transmission, n (%)			
Heterosexual sex	117 (27.9)	303 (72.1)	0.079
Non-heterosexual sex and others	254 (32.8)	521 (67.2)	
Psychiatric history, n (%)			
Yes	63 (60)	42 (40)	<0.001***
No	322 (27.9)	834 (72.1)	
Presence of comorbid conditions, n (%)			
Yes	90 (25.2)	267 (74.8)	0.01*
No	295 (32.6)	609 (67.4)	
First CD4 (cells/μL), n (%)			
≥200	259 (30.9)	580 (69.1)	0.73
<200	126 (29.9)	295 (70.1)	
History of smoking, n (%)			
Yes	172 (33.7)	339 (66.3)	0.046*
No	213 (28.4)	537 (67.6)	
History of alcohol use, n (%)			
Yes	88 (25.6)	256 (74.4)	0.019*
No	297 (32.4)	620 (67.6)	
History of substance use, n (%)			
Yes	57 (38)	93 (62)	0.034*
No	328 (29.5)	783 (70.5)	
Adherence to medication, n (%)			
Not adherent	58 (38.9)	91 (61.1)	0.001**
Adherent	182 (25.1)	543 (74.9)	
HADS positive, n (%)			
At entry screening	318 (25.2)	–	–
At exit screening	150 (11.9)	–	
At both screenings	83 (6.6)	–	
Received intervention, n (%)			
Yes	244 (63.4)	–	–
No	141 (36.6)	–	

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Hosmer and Lemeshow, $\chi^2=5.44$, $df=8$, $p=0.71$.* $P<0.05$, ** $P<0.01$, *** $P<0.001$.

HADS, Hospital Anxiety and Depression Scale.

concealment of HIV status from parents and family members, as is typical in Asian sociocultural context.¹¹ HIV and other STIs remain highly stigmatised and considered deviant in many Asian societies, including Singapore, and disclosure of HIV status has been linked to psychological and emotional stress.²⁷ As our study

Table 2 Predictors of significant psychological distress during the period of surveillance (dependent variable: symptomatic during the programme)

Covariate	OR (95% CI)	P value
Age	0.99 (0.97 to 1.00)	0.022*
Variable		
Education		
Post-high school	(Reference)	
High school and below	1.31 (0.97 to 1.76)	0.74
Employment status		
Unemployed/retired	(Reference)	
Employed	0.89 (0.68 to 1.18)	0.42
Disclosure to family		
Yes	(Reference)	
No	0.91 (0.70 to 1.19)	0.50
Mode of transmission		
Heterosexual sex	(Reference)	
Non-heterosexual sex and others	1.15 (0.84 to 1.57)	0.38
History of anxiety/depression		
No	(Reference)	
Yes	3.46 (2.27 to 5.27)	<0.001***
First CD4 (cells/μL)		
≥200	(Reference)	
<200	1.20 (0.90 to 1.60)	0.23
Presence of comorbid conditions		
No	(Reference)	
Yes	0.77 (0.57 to 1.05)	0.095
History of smoking		
No	(Reference)	
Yes	1.29 (0.98 to 1.69)	0.067
History of alcohol use		
No	(Reference)	
Yes	0.66 (0.49 to 0.90)	0.008**
History of substance use		
No	(Reference)	
Yes	1.31 (0.90 to 1.92)	0.16

Created by the authors.

Hosmer and Lemeshow, $\chi^2=5.44$, $df=8$, $p=0.71$.* $P<0.05$, ** $P<0.01$, *** $P<0.001$.

employed screening for symptoms within the first 6 months of linkage to HIV care, the finding that younger persons were more likely to be symptomatic could also reflect an age-related response to a significant, and likely negative, life event such as a recent diagnosis of HIV. Hence, further studies are required to fully elucidate the relationship between age and psychiatric morbidity in people living with HIV.

It is interesting to note that the mode of sexual transmission was not significantly associated with the likelihood of having psychological symptoms. The pooled prevalence of depression in men who have sex with men (MSM) living with HIV has been estimated to be as high as 43% in a recent meta-analysis.²⁸ Given that consensual sexual relations between same-sex adults remains illegal in Singapore, it is noteworthy that MSM did not report significantly more depressive or anxiety symptoms, and further research would be helpful in further clarifying this, paying particular attention to the group that dropped out after the initial screening. Incomplete data from this group may have contributed to our negative finding.

Adherence to ART is crucial in achieving durable virological suppression and immune reconstitution in people living with HIV and ensuring personal health and well-being, as well

Table 3 Predictors of non-adherence to highly active antiretroviral therapy at exit screening (dependent variable: non-adherence)

Covariate	OR (95% CI)	P value
Age	0.98 (0.97 to 1.00)	0.094
Received intervention		
Yes	(Reference)	
No	2.30 (1.23 to 4.29)	0.009**
History of anxiety/depression		
No	(Reference)	
Yes	1.53 (0.82 to 2.82)	0.18
Variable		
Education		
High school and below	(Reference)	
Post-high school	0.95 (0.61 to 1.47)	0.81
Employment status		
Unemployed/retired	(Reference)	
Employed	0.76 (0.51 to 1.14)	0.18
Disclosure to family		
Yes	(Reference)	
No	1.20 (0.80 to 1.78)	0.38
Mode of transmission		
Non-heterosexual sex and others	(Reference)	
Heterosexual sex	1.71 (1.10 to 2.67)	0.017*
Symptomatic during programme		
No	(Reference)	
Yes	2.83 (1.69 to 4.75)	<0.001***
First CD4 (cells/ μ L)		
≥ 200	(Reference)	
<200	1.45 (0.97 to 2.18)	0.069
Presence of comorbid conditions		
No	(Reference)	
Yes	1.00 (0.66 to 1.52)	1.00
History of smoking		
No	(Reference)	
Yes	1.56 (1.06 to 2.32)	0.026*
History of alcohol use		
No	(Reference)	
Yes	0.90 (0.59 to 1.39)	0.65
History of substance use		
No	(Reference)	
Yes	1.21 (0.70 to 2.08)	0.50

Created by the authors.
Hosmer and Lemeshow, $\chi^2=5.57$, $df=8$, $p=0.70$.
* $P<0.05$, ** $P<0.01$, *** $P<0.001$.

as preventing onward transmission of infection. Adherence to treatment is multifactorial and involves the interplay of health beliefs and health behaviour. Our study found that the presence of significant psychological symptoms in the early phase of accessing care was associated with an increased likelihood of being non-adherent to treatment by self-report, which is consistent with findings in the published literature from different settings.⁹ Rao and colleagues⁶ found that increased levels of experienced HIV-related stigma were associated with more severe depressive symptoms which in turn were associated with poorer ART adherence, further indicating that psychological symptoms may represent a mechanism by which sociocultural phenomena such as HIV stigma may impact treatment adherence and hence HIV control. Conversely, further research is required to verify whether effective intervention of psychiatric symptoms improves ART adherence.

We found that patients who reported disease transmission through heterosexual contact were more likely to be non-adherent to treatment. This was independent of symptoms of psychological distress, which were not significantly different between the heterosexual and MSM groups. Similar findings are reported elsewhere²⁹ and have been attributed to factors such as differences in educational level, knowledge about HIV, as well as perceived efficacy of treatment between the heterosexual and MSM groups. Further research is needed, especially in the local context, to explore possible variations in HIV treatment-related knowledge and attitudes between heterosexual men and MSM.

In our study, a history of smoking was found to be significantly associated with non-adherence to treatment, while substance use was not. These findings are interesting and warrant further study, especially in view of published experience finding positive associations between use of recreational drugs and alcohol and antiretroviral adherence.⁷ Given that the mechanistic pathway for optimal levels of adherence to daily medication requires a high degree of attention to routine as well as insight into the importance of treatment, other pathways may be involved in mediating the lack of significant association between substance use and non-adherence, at least with patients in Singapore. The relationship between smoking tobacco and medication adherence is more complex, with some authors describing no association between smoking status and non-adherence, and others observing poorer adherence to treatment in smokers compared with non-smokers, in concert with other behaviours suggesting lower engagement in health-seeking and health-protective attitudes.³⁰

There are several limitations to our study. We assessed for psychological symptoms at only two time points over a relatively short interval due to the design and demands of the service. We were hence unable to evaluate the longer-term trajectory of psychological distress. As screening was done within the first 6 months of linkage to HIV care, when individuals may also be more distressed due to the recency of HIV diagnosis, we may be overestimating the prevalence of distress in this population. There were relatively high dropout rates from the screening programme, and we are not able to further elucidate differences between those who dropped out and those who completed the planned screenings. Antiretroviral drug adherence was self-reported using only one measure (self-reported doses missed over a 30-day period) without correlation to viral suppression; hence, the effect of psychological symptoms on HIV control cannot be completely described herein.

We believe that our study sample is one of the largest reported in current literature, adding strength to the significance of our findings. Screening at both time points was carried out by a small team of trained professionals, which allowed for consistency in assessment.

CONCLUSION

Significant psychological distress occurring early in the phase of HIV care predicts future non-adherence to ART. This finding lends weight to the premise for early detection and intervention for psychological distress in people living with HIV. Hence, we recommend a model of mental health screening that is integrated with the provision of HIV clinical care similar to what has been implemented in our setting. This screening should take place early in the course of HIV care, and special attention paid to individuals with pre-existing psychiatric illness, history of illicit substance use, and in our setting younger age. Accessing HIV care is difficult enough, so no effort should be spared in

identifying vulnerable subpopulations where mental health issues pose further barriers to consistent engagement with HIV care services. Where these barriers result in a reduced engagement with and retention in HIV care services, the knock-on effect on national HIV control efforts stands to be compromised. Mental health interventions should hence be intercalated with treatment adherence interventions with the aim of improving not merely HIV treatment outcomes, but improving the overall well-being of those living with HIV.

Key messages

- ⇒ High rates of psychiatric comorbidity and treatment non-adherence in HIV are associated with poorer outcomes in HIV treatment.
- ⇒ Psychological distress occurring early in the phase of HIV care predicts future non-adherence to antiretroviral treatment, underlining the importance of early detection and intervention for psychological distress in people living with HIV.
- ⇒ Intercalating mental health interventions with treatment adherence interventions would improve the overall well-being of people living with HIV.

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