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Association between mental disorders and adherence to antiretroviral treatment in health facilities in two Mozambican provinces in 2018: a cross-sectional study

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Abstract

Introduction Lower adherence to antiretroviral treatment (ART) has been found among people with HIV (PWH) who have comorbid mental disorders like depression and alcohol use in Sub-Saharan African. However, there has been less exploration with regards to other mental disorders.

Methods This study assessed the association of multiple mental disorders and adherence to ART based on the data from primary/tertiary health care facilities in Maputo and Nampula, Mozambique. We administered a sociodemographic questionnaire, Mini International Neuropsychiatric Interview (MINI) Plus 4.0.0 adapted for use in Mozambique to assess mental conditions, and a 3-item self-report to measure ART adherence.

Results 395 HIV-positive (self-report) participants on ART, with an average age of 36.7 years (SD=9.8), and 30.4% were male. The most common mental disorders were major depressive disorder (27.34%) followed by psychosis (22.03%), suicidal ideation/behavior (15.44%), and alcohol-use disorder (8.35%). Higher odds of missing at least one dose in the last 30 days (OR= 1.45, 95% CI: 1.01, 2.10) were found in participants with any mental disorder compared to those without a mental disorder. The highest levels of non-adherence were observed among those with drug use disorders and panic disorder.

Conclusions In Mozambique, PWH with any co-occurring mental conditions had a lower probability of ART adherence. Integrating comprehensive mental health assessment and treatment and ART adherence interventions tailored to PWH with co-occurring mental disorders is necessary to attain optimal ART adherence and reach the UNAIDS ART target.

Keywords Mental disorders, ART adherence, HIV/AIDS treatment, Mozambique

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Introduction

The introduction of effective antiretroviral therapy (ART) in 1996 significantly changed the course of the HIV epidemic in high-income countries [1]. Unfortunately, the global effort to include low-income countries in this treatment drive did not succeed until 2001 [2, 3]. Initially, when ART was introduced, 95% adherence to ART was required to achieve maximal viral suppression [4]. Consistent adherence to ART with consequent undetectable HIV viral load increases the life expectancy of people with HIV (PWH) [5] and prevents new HIV infections [6]. The current UNAIDS 95-95-95 global effort to end the HIV epidemic by 2030 emphasizes that 95% of people with HIV know their status, 95% of those knowing their status have access to treatment, and 95% of those under treatment have suppressed viral load [7]. Factors associated with poor adherence to ART in sub-Saharan countries include unavailability of health care services, stigma, and discrimination, mental health problems (e.g., hazardous alcohol use, depression), patients not following the instruction for taking medications, poor understanding of HIV illness, disbelief about HIV and its treatment, poverty, food insecurity, medication side effects, poor patient-provider relationships, and difficulty accessing health services [8–18].

Studies in sub-Saharan Africa and other low-income countries have reported that patients with depression, anxiety, and PTSD symptoms during enrollment in HIV care have shown delayed initiation of ART and negligence to care [19]. Moreover, an association of anxiety, depression, and alcohol use has been found with poor adherence to HIV-treatment [20–24], which in turn leads to high mortality and other poor HIV-related outcomes [23–32].

Studies evaluating the prevalence of mental disorders among PWH in Sub-Saharan Africa, the world's region with the highest prevalence of HIV/AIDS, have reported the high prevalence of depression, hazardous alcohol use, post-traumatic stress disorder, anxiety disorders, psychosis, bipolar disorders, and suicidal ideation [26, 33–39] among HIV patients. However, data regarding the association of poor adherence to ART and comorbid mental disorders besides depression and hazardous alcohol use among PWH, is inconsistent. Some studies from high-income countries have found no association [4, 40, 41] while others reported that depression, anxiety, bipolar disorder, substance use disorder, and suicidal behavior are associated with poor adherence [27, 28, 42]. Noticeably, anxiety was strongly associated with poor adherence to treatment among PWH in six studies from Asia while four from sub-Saharan Africa did not find any association [43]. Among patients with HIV and co-morbidities such as bipolar disorder, nonadherence to psychiatric medication may lead to ART non-adherence with poor outcomes

for both conditions [44]. The assessment of adherence to ART among patients with bipolar disorder is difficult to measure depending on the tool used [44, 45]. Moreover, the few studies available have had the contradictory findings. Wagner et al. in Los Angeles (USA), found high rates of adherence to ART among patients with both serious mental illness and HIV infection [46]. These findings are not in line with those from low-income countries. This could be because of poor knowledge of illness, lack of recognition of medication benefits, and not consistently taking medications. Adrawa et al. also showed an association between alcohol use and non-adherence in community-based ART distribution settings in Uganda, with participants attributing forgetfulness as a major cause of nonadherence [47]. Available data suggest that addressing mental health problems by early screening and interventions at the time of counseling, testing, ART initiation, and follow-up care may be critical for better outcomes for PWH [48–50].

Mozambique is among the countries with the highest prevalence rates of HIV, estimated at 13.2% in 2015 and 12.6% in 2018 among individuals between 15 and 49 years [51, 52]. Although various studies have been conducted in Mozambique which reported rates of adherence to ART [53, 54], to the best of our knowledge none have reported associations between non-adherence to ART and mental health problems.

To promote adherence to ART treatment in low-resource settings, routine screening and treatment for alcohol use disorder [55] and depression [56] are recommended (26; 34). Unfortunately, lay health workers and healthcare professionals who provide HIV/AIDS treatment services often lack the training and skills to identify and treat co-occurring mental disorders in PWH [29]. In Mozambique, similar to most of the low- and middle-income countries (LMICs), screening and treatment for mental conditions have not yet been integrated into HIV care yet. Psychosocial counselors supervised by psychologists are trained to offer ART adherence counseling but not to identify or treat mental disorders [57].

Keeping all this in view, in this study we examined demographic and clinical correlates of adherence to ART among PWH attending two primary health care facilities and one general hospital in the Maputo City metropolitan region, and three health centers in Nampula City. Poorer adherence to ART was hypothesized among PWH with mental disorders than for those without a co-morbid mental illness. To the best of our knowledge, this is the first study to assess if any associations exist between mental disorders in PWH and adherence to antiretroviral treatments in Mozambique.

Methods

Participants and procedures

Adults from 6 primary and tertiary health care facilities in Mozambique who reported being HIV+ (n=409) were included in this study. Participants were recruited from 2 primary healthcare facilities (health centers) and 1 tertiary facility in Maputo (general hospital) between May 16 and Jun 8, 2018, and from 3 primary healthcare facilities in Nampula between Nov 28 to Dec 13, 2018. These health facilities were selected because they have large coverage and provide mental health services. These participants were selected from 1469 adults who had been recruited into a cross-sectional validation study conducted to develop a screening tool for multiple mental disorders – the mental wellness tool (mwTool) [58]. Potential participants were recruited from waiting rooms within these facilities. A member of the research team explained the overall aim of the study. Patients and those accompanying them were considered eligible for the study, if they were 18 years of age or older, to be able to communicate in Portuguese, and provided written consent to participate in the study. We used culturally adapted instruments in Portuguese language administered by trained research assistants (clinical psychologist or senior students of bachelor in clinical psychology), including demographic questions and a diagnostic interview for mental disorders. Research assistants were senior bachelor students in clinical psychology who were trained to administer tablet-based interviews by senior data analysts from the Foundation for Professional Development. All questionnaires and tools used in the study have been either previously validated or translated and adapted using the World Health Organization (WHO) recommended method [59]. Data were collected with tablets using the REDCap electronic data management system. Participants provided written informed consent as approved by the New York State Psychiatric Institute Institutional Review Board (#7479) and the Ethics Council of Eduardo Mondlane University (CIBS FM & HCM/54/2017).

The research assistants administered the sociodemographic questionnaire and then the MINI and mental health screening battery in a randomized order. For participants who were alone or with someone who was not eligible to participate in the study, the research assistant administered the mwTool followed by the MINI to assess the participant's mental health. For participants attending the facility with another participant, research assistants privately asked the items of the mwTool for identification of any mental disorder in regard to their companion's mental health and then administered the complete mwTool and MINI to assess the participant's mental health [58].

Measures

Demographic questions included information regarding age, sex, the reason for attending the hospital (patient, accompanier, or others), marital status, educational level, occupation, and household income. We also recorded information about the study site (Maputo or Nampula) and facility type (primary vs. tertiary care).

Mental Disorders (MD) were assessed using a previously published structured diagnostic interview, the Brazilian version of the Portuguese language Mini-International Neuropsychiatric Interview (MINI) Plus 4.0.0 adapted for use in Mozambique [60, 61]. The following modules were administered and included in the analysis: major depressive disorder, dysthymic disorder, panic disorder, generalized anxiety disorder, post-traumatic stress disorder, somatization disorders, mania, psychotic disorders, alcohol use disorder, drug use disorder, and suicidal instinct.

HIV status and antiretroviral treatment adherence were self-reported. Within the interview, all participants reported on whether they had HIV as part of the assessment for chronic diseases done in the interview. Participants who were HIV-positive were queried about taking ART. Participants on ART were further questioned about the duration of ART and how frequently they go to a medical unit to obtain ART medication. Furthermore, they were asked the following three questions about ART adherence from a 3-item self-report measure for medication adherence, which together forms an *ART adherence composite index* ranging from zero to 100, with scores less than 100 indicating some non-adherence [62]:

1. In the last 30 days, how many days did you miss at least one dose of ART medication?
2. In the last 30 days, how well did you stick to taking the ART medication in the way you were supposed to? Response options: Very poor, Poor, Reasonable, Good, Very Good, Excellent.
3. In the last 30 days, how often did you take your HIV medicine in the way you were supposed to? Response options: Never, Rarely, Sometimes, Habitually, Almost always, Always.

The ART adherence composite index was calculated by linearly transforming responses for the three adherence items to a 0-100 scale with zero representing worst adherence and 100 indicating best adherence as has been done in previous research [62]. Given the zero-inflated distribution, we also dichotomized this variable to indicate optimal (i.e., full) adherence vs. any non-adherence.

Statistical analysis

Bivariate exploratory associations were calculated between ART adherence and (1) socio-demographics and (2) mental disorders using unadjusted logistic regression models among participants who were HIV+ and

responded to the questions about HIV ART adherence (N=395). To control for potential confounders of the association between mental disorders and ART adherence, we reported the adjusted odds ratio and 95% confidence interval controlling for sociodemographic characteristics that were significantly associated with individual indicators of ART adherence and/or hypothesized to be associated with mental disorders and ART adherence based on previous literature (age, gender, marital status, education, occupation, income). Logistic regression model was used to establish the association between any non-adherence (*binary variable*) and specific mental disorders and categories of disorders (common mental disorder, severe mental disorder, moderate/severe suicide risk, and substance use disorder). Among participants who reported any non-adherence based on the composite adherence index, we examined the association between specific mental disorders and categories with the level of non-adherence (*continuous variable ranging from 0 to 100*) in this subgroup. The reference group for each of these models was PWH participants without any mental disorder comorbidities. All models used robust variance estimators to account for clustering within site.

Results

Of the 409 participants who self-reported to be HIV-positive, the analytic sample was restricted to HIV positive participants on ART (n=395, 96.58%). Among these 395 participants, 44.81% met the criteria for at least one mental disorder. The most common mental disorders were: major depressive disorder (27.34%) followed by psychotic disorders (22.03%), any suicidal ideation (15.44%), alcohol use disorder (8.35%), mania (6.84%), generalized anxiety disorder (6.08%), post-traumatic stress disorder (4.05%), panic disorder (3.29%), drug use disorder (1.27%), somatization disorders (0.76%), and dysthymic disorder (0.51%). Most of the PWH participants were recruited from Maputo (73.92%) and in primary healthcare settings (70.89%). The mean age of participants was 36.7 years (SD=9.8). Majority (69.6%) of the participants were females. More than half of the participants were married (58.0%). Most of the participants had less than secondary school education (80.8%), and a mix of occupations and income levels which are represented in Table 1. Relative to participants who reported complete adherence to ART in the past 30 days, those that were not fully adherent were younger in age (OR=0.98, 95% CI: 0.98, 0.99) had a lower odds of being female (OR=0.53, 95% CI: 0.31, 0.90), had a lower odds of having been recruited from Nampula (OR=0.23, 95% CI: 0.14, 0.38), had a higher odds of being single relative to married (OR=1.20, 95% CI: 1.11, 1.29), had a lower odds of a University-level education relative to having not completed primary school (OR=0.71, 95%

CI: 0.57, 0.87), higher odds of having an informal job relative to being unemployed (OR=1.95, 95% CI: 1.29, 2.94), and had higher odds of a salary greater than 2800 Mzn (2801–5000 Mzn: OR=1.52, 95% CI: 1.18, 1.97; 5001–15,000 Mzn: OR=1.71, 95% CI: 1.50, 1.94; >15,000 Mzn: OR=3.13, 95% CI: 2.32, 4.21).

ART adherence and mental disorder

Most of the participants who were on ART reported taking these medications for more than two years (71.1%) and going to the health center monthly to pick up their medication (60.0%), followed by every three months (30.9%) and irregularly (9.1%) (Table 2). Almost three-quarters of the patients (74.68%) reported some non-adherence on at least one of the three questions that comprised the ART composite adherence index in the past 30 days. The presence of a mental disorder was associated with how long participants had been on ART and how often they went to the health centers to pick up ART. In the unadjusted models, a significant number of participants with any mental disorder reported non-adherence (79.66%) defined as any missed doses, less than excellent adherence to medication regimen, or not always taking medication as prescribed relative to those without a mental disorder (70.64%; OR=1.63, 95% CI: 1.03, 2.58). Participants who reported having been on ART between 1 and 2 years displayed lower odds of having a mental disorder relative to those who had been on ART for less than one year (OR=0.59, 95% CI: 0.58, 0.60). Moreover, participants who reported picking up their ART from the health center every three months displayed a lower odds of having a mental disorder comorbidity relative to participants who picked up their ART from the health center monthly (OR=0.79, 95% CI: 0.73, 0.85). When adjusting for sociodemographic characteristics, the association between having a mental disorder and any non-adherence as well as frequency of picking up their ART from the health center were no longer found to be significant. However, the lower odds of having a mental disorder among those who had been on ART for 1–2 years relative to less than a year remained statistically significant (OR=0.63, 95% CI: 0.50, 0.80).

We also assessed the association between ART non-adherence and specific types of mental conditions controlling for sociodemographic characteristics (Table 3). Individuals with any severe mental disorder (OR=2.38, 95% CI: 1.24, 4.56), mania (OR=4.66, 95% CI: 1.03, 21.27), or psychotic disorder (OR=2.33, 95% CI: 1.19, 4.56) displayed greater odds of non-adherence relative to individuals without a mental disorder. Any suicide risk was also associated with an increased odds of non-adherence (OR=1.48, 95% CI: 1.32, 1.65). Other mental disorders also displayed a similar trend, but the difference was not statistically significant. We do not report

Table 1 Sociodemographic correlates of ART adherence among HIV positive participants on ART in Mozambique (n = 395)

	On ART 395 (100.00%)	Complete adherence (past 30-days) 100 (25.32%)	Any non-adherence (past 30-days) 295 (74.68%)	OR	95% CI
Age (yrs); mean (sd)	36.66 (9.82)	38.24 (8.81)	36.12 (10.10)	0.98	0.98, 0.99
% Female; n (Row %)	275 (69.62)	79 (28.73)	196 (71.27)	0.52	0.33, 0.84
Site, n (Row %) ^a					
Maputo	292 (73.92)	51 (17.47)	241 (82.53)	REF	REF
Nampula	103 (26.08)	49 (47.57)	54 (52.43)	0.23	0.14, 0.38
Health facility, n (Row %)					
Primary healthcare	280 (70.89)	72 (25.71)	208 (74.29)	REF	REF
Tertiary healthcare	115 (29.11)	28 (24.35)	97 (75.65)	1.08	0.21, 5.60
Marital status, n (Row %)					
Married/Civil Union	229 (57.97)	59 (25.76)	170 (74.24)	REF	REF
Single	129 (32.66)	29 (22.48)	100 (77.52)	1.20	1.11, 1.29
Widowed, divorced, separated	37 (9.37)	12 (32.43)	25 (67.57)	0.72	0.34, 1.55
Education level, n (Row %)					
Less than primary	92 (23.29)	24 (26.09)	68 (73.91)	REF	REF
Less than secondary/technical	227 (57.47)	58 (25.55)	169 (74.45)	1.03	0.69, 1.53
Secondary/technical	67 (16.96)	15 (22.39)	52 (77.61)	1.22	0.47, 3.16
University or above	9 (2.28)	3 (33.33)	6 (66.67)	0.71	0.57, 0.87
Occupation, n (Row %)					
Unemployed	108 (27.34)	30 (27.78)	78 (72.22)	REF	REF
Formal job	145 (36.71)	42 (28.97)	103 (71.03)	0.94	0.69, 1.30
Informal job	103 (26.08)	17 (16.50)	86 (83.50)	1.95	1.29, 2.94
Full-time student	12 (3.04)	1 (8.33)	11 (91.67)	4.23	0.60, 30.06
Other	27 (6.84)	10 (37.04)	17 (62.96)	0.65	0.37, 1.16
Income (Mzn), n (Row %)					
0 to 2,800 (0–1 minimum salaries)	45 (11.39)	16 (35.56)	29 (64.44)	REF	REF
2801–5000 (1–2 minimum salaries)	124 (31.39)	33 (26.61)	91 (73.39)	1.52	1.18, 1.97
5001–15,000 (2–3 minimum salaries)	90 (22.78)	22 (24.44)	68 (75.56)	1.71	1.50, 1.94
> 15,000 (3 or more minimum salaries)	20 (5.06)	3 (15.00)	17 (85.00)	3.13	2.32, 4.21
Missing	116 (29.37)	26 (22.41)	90 (77.59)	1.91	1.24, 2.93

^aAll models except the association between site and adherence applied a robust variance estimator to account for clustering within site

Table 2 Association between ART adherence and mental disorder among PWH on ART in Mozambique (n = 395)

	No mental disorder comorbidities 218 (55.19%)	Mental disorder comorbidities 177 (44.81%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
How long have you been on ART?				
Less than 1 year	30 (13.76)	32 (18.08)	REF	REF
Between 1–2 years	32 (14.68)	20 (11.30)	0.59 (0.58, 0.60)	0.63 (0.50, 0.80)
More than 2 years	156 (71.56)	125 (70.62)	0.75 (0.51, 1.10)	1.03 (0.85, 1.24)
How often do you go to the health center to pick up your ART medication?				
Monthly	126 (57.80)	111 (62.71)	REF	REF
Every 3 months	72 (33.03)	50 (28.25)	0.79 (0.73, 0.85)	1.02 (0.95, 1.09)
Irregularly	20 (9.17)	16 (9.04)	0.91 (0.52, 1.60)	1.11 (0.71, 1.76)
Adherence to ART medication				
Complete adherence	64 (29.36)	36 (20.34)	REF	REF
Nonadherence	154 (70.64)	141 (79.66)	1.63 (1.03, 2.58)	1.44 (0.98, 2.13)

*Adjusted models controlling for age, sex, marital status, education, occupation, and income

Table 3 Association between specific types of mental disorder and medication adherence in Mozambique

	n (%)	Level of adherence Mean (SD)	Any non-adherence (n = 395) OR (95% CI)	Level of adherence among those without complete adherence (n = 295): Mean Diff (95% CI)
Any mental condition	177 (44.81%)	85.03 (15.23)	1.45 (1.01, 2.10)	-2.54 (-6.83, 1.75)
Common mental disorder	125 (31.65%)	85.95 (14.23)	1.33 (0.86, 2.07)	-2.43 (-6.85, 1.99)
Major depressive disorder	108 (27.34%)	85.71 (14.69)	1.39 (0.58, 3.34)	-2.25 (-9.24, 4.73)
Dysthymic disorder	2 (0.51%)	100 (0.00)	--	--
Panic disorder	13 (3.29%)	77.86 (26.11)	1.54 (1.45, 1.64)	-13.85 (-138.22, 110.52)
Generalized anxiety disorder	24 (6.08%)	84.40 (12.29)	1.43 (0.78, 2.63)	-4.15 (-31.51, 23.19)
Post-traumatic stress disorder	16 (4.05%)	88.54 (6.39)	2.37 (0.55, 10.28)	3.21 (-18.03, 24.44)
Somatization disorders	3 (0.76%)	81.11 (14.70)	--	-1.27 (-32.31, 29.76)
Severe mental disorder	97 (24.56%)	83.54 (15.46)	2.05 (1.14, 3.71)	-2.49 (-14.03, 9.04)
Mania	27 (6.84%)	81.15 (13.73)	4.22 (3.53, 5.03)	-3.32 (-8.46, 1.82)
Psychotic disorders	87 (22.03%)	83.31 (16.07)	1.95 (1.11, 3.41)	-3.00 (-18.85, 12.84)
Any suicide risk (low/med/high)	61 (15.44%)	83.88 (17.09)	1.48 (1.32, 1.65)	-4.79 (-7.94, -1.63)
Substance use disorder	34 (8.61%)	83.01 (14.69)	1.88 (0.34, 10.48)	-2.56 (-10.10, 4.98)
Alcohol use disorder	33 (8.35%)	82.73 (14.83)	1.81 (0.31, 10.73)	-3.09 (-7.75, 1.58)
Drug use disorder	5 (1.27%)	65.33 (23.27)	--	-18.40 (-20.09, -16.72)

Note: the reference group for each of these comparisons included participants without any mental disorders (same reference group for all comparisons). All models account for clustering within site using robust variance estimates and control for age, sex, marital status, education, occupation, and income. The dysthymia, somatization, and drug use disorder logistic models and the dysthymia linear regression model did not converge due to small cell sizes; OR: Odds Ratio; Mean Diff: The mean difference in the level of non-adherence

the parameter estimates from logistic regression models for dysthymia, somatization, and drug use disorders, given the small number of participants meeting these disorders' criteria and the limited variation in adherence.

Among the 295 participants without optimal adherence, we found lower adherence among those with any suicide risk (Mean Diff=-4.79, 95% CI: -7.94, -1.63) and drug use disorder (Mean Diff=-18.40, 95% CI: -20.09, -16.72) relative to individuals without any mental disorder (Table 3; Fig. 1a-b).

Discussion

Our study found that among PWH who were taking ART, almost half (44.81%) of the individuals met the criteria for at least one mental disorder. This finding is consistent with other studies where between 33.4 and 50% of PWH were reported to have any comorbid mental disorder [63, 64].

Most participants in our sample (75%) reported non-adherence to ART in the last 30 days (see Table 1), which is consistent with a previous study in Mozambique reporting that 77–83% of PWH were non-adherent to ART [65]. As in previous studies, we found that younger age was marginally associated with non-adherence to ART [29, 66, 67].

In our study, only severe mental illness, which included mania and psychosis, and suicide risk were associated with non-adherence. This association could be explained by poor insight and judgment, impulsiveness, and disorganization of behavior and thought process, which may impair patients' ability to take a medication daily [68, 69].

However, as suggested by Bogart et al., the use of specialized programs that include access to care management and mental health treatment for patients with severe mental illness may help to narrow the health disparities in this population. They found that following these measures for PWH, there was no difference in the use of ART among patients with severe mental illness when compared with the group without mental illness [70].

In the sub-analysis of participants who did not report complete adherence, suicide risk and drug use disorder were associated with increased levels of non-adherence. Although four studies from sub-Saharan Africa did not find an association between anxiety and poor adherence in PWH, six studies from Asia did describe a strong association, which is similar to our findings [43]. It is possible that taking ART may serve as a reminder of having a chronic and stigmatizing illness, with a subsequent increase in psychological distress and related mental health problems.

We did not find an association between drug use disorders and lower levels of adherence. In contrary to previous studies in sub-Saharan Africa, we did not identify a significant association between alcohol use disorder and ART adherence [71, 72]. Given that the level of non-adherence among participants with alcohol use disorder in our sample were among the highest, we hypothesize that this null finding may be explained, in part, by the analyses being underpowered.

An association between depression and poor adherence has been frequently described in the literature. However, in our sample, MDD was not significantly

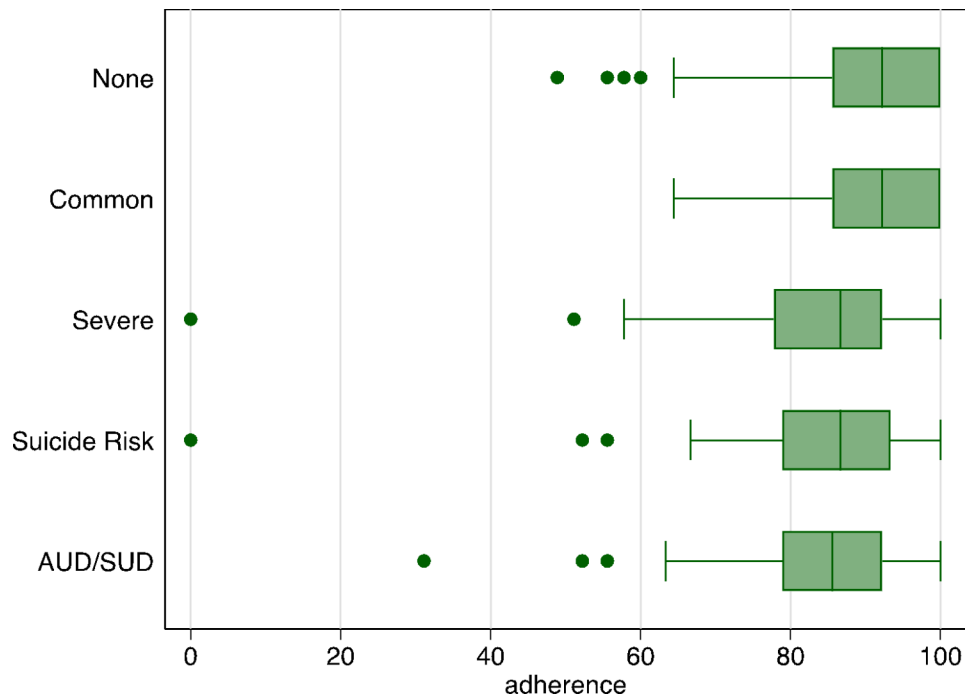


Fig. 1a Distribution in level of medication adherence by mental disorder categories in Mozambique (n = 395)

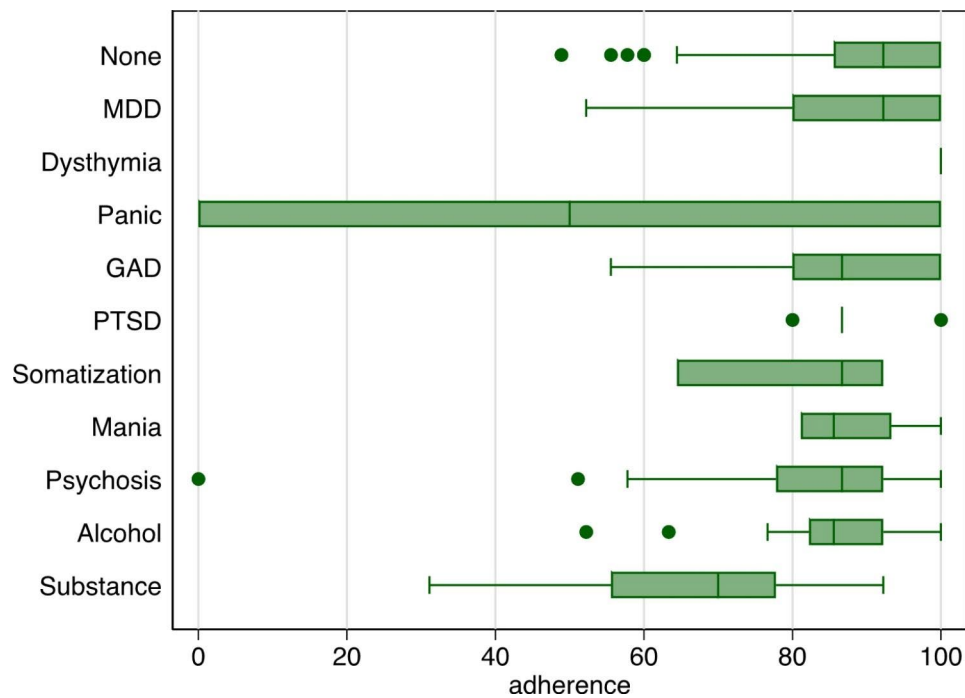


Fig. 1b Distribution in level of medication adherence by mental disorder diagnoses in Mozambique (n = 395)

associated with decreased adherence, similar to a study from Brazil [73]. Of note, our findings showed some discrepancies in the association of poor adherence to ART and comorbid mental disorder, mainly regarding depression with other published data [74–78], but noticeably, there was an association of depressive symptoms with

non-adherence within the past (one) month, although not in the past week. This was in line with a previous study which also did not find any associations between mood and suicidality symptoms and missed doses in the past week or month [77].

As in our study, two cross-sectional studies did not find a statistically significant association between schizophrenia/psychotic disorder and ART adherence, using a self-report measure ACTG (Adult AIDS Clinical Trials Group adherence questionnaire) 3 - days recall and EDMs (electronic drug monitors) to evaluate adherence to ART [79].

This study has some limitations. First, this is a cross-sectional study, and biological markers did not confirm HIV status and ART adherence. We cannot make causal inferences about the direction of the observed relationship between ART adherence and mental conditions, nor are we able to rule out sources of information bias (e.g., reporting bias and recall bias which can arise in self-report questionnaires) and misclassification. Second, we did not obtain information about what specific ART regimens participants were taking and specific adherence to each ART prescribed. Treatment regimens may have affected the results as several antiretrovirals - including efavirenz, which is still commonly used in Mozambique - may cause severe neuropsychiatric side effects, including depression, anxiety, suicidal ideation, psychosis, and mania. This study did not capture all potential confounders of the association between mental conditions and ART adherence, including CD4 levels and ART regimen [66]. Third, this study recruited a convenience sample of PWH in primary and tertiary healthcare facilities and does not represent Mozambique's general population as well as specific populations (e.g., youth and adolescents). The validation study from where our data was obtained was designed to recruit participants with various mental disorders within primary care, HIV care, and mental health clinics. Thus, our findings regarding the proportion of people with mental disorders should not be considered prevalence rates. Fourth, the validity of the MINI to ascertain diagnoses of mental disorders has not been validated within Mozambique. Nor has the adherence tool been used previously in this setting and population. Thus, measurement error may influence some of the study inferences; however, we anticipate that these issues would be non-differential and thus result in conservative estimates of associations within this study. However, previous studies of adherence measures have not found evidence that self-report methodologies are less reliable than more objective measures [80]. Fifth, the number of participants meeting the criteria for some mental disorders in our sample was low, resulting in unstable estimates for some conditions (e.g., drug use disorder, somatization disorders). Given the small sample sizes in subgroups, many of the models may have produced unstable and imprecise estimates. Due to the small sample sizes and the large number of comparisons, these analyses should be interpreted as exploratory. Future research with larger sample sizes is needed to evaluate the relationship

between these low-prevalence mental conditions and ART adherence.

Despite these limitations, this study has several strengths, including using a fully structured diagnostic interview to diagnose most mental disorders resulting in a sample with a breadth of mental conditions and replicating a composite index assessing ART adherence instead of a single-item indicator. Finally, to our knowledge, this is the first study to examine the relationship between ART adherence and its negative association with multiple mental disorders in Mozambique and sub-Saharan Africa, a region with a high burden of HIV/AIDS.

Conclusions

We found that PWH with co-occurring mental disorders displayed a lower odds of being optimally adherent to ART in Mozambique. Our study shows that severe mental disorders among PWH negatively impact ART adherence compared to other disorders. These findings suggest the importance of comprehensive mental health screening to identify and treating these conditions among PWH in HIV care in Mozambique, together with ART adherence interventions in order to achieve the 95-95-95 targets. Future research should study methods to expand current psychosocial support interventions beyond the more common approaches targeting depression and alcohol use disorders. Researchers should consider using valid ART adherence measures and interventions and rigorous, and validated comprehensive mental health assessments [58] with accompanying evidence-based treatments [81] to be implemented through task-shifting approaches integrated within HIV care in Mozambique and throughout the region.

List of Abbreviations

ACTG	Adult AIDS Clinical Trials Group adherence questionnaire
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Treatment
ARV	Antiretroviral
AUD	Alcohol Disorder
AUDIT	Alcohol Use Disorder Tool
ART	Highly Active Antiretroviral Therapy
EDM	Electronic drug monitor
HIV/AIDS	Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome
MDD	Major Depressive Disorder
MD	Mental Disorder
MH	Mental Health
MINI	Plus Mini-International Neuropsychiatric Interview Plus 4.0.0
Mzn	Mozambican New Metical
mwTool	Mental Wellness Tool
PWH	People Living With Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome
sSA	Sub-Saharan Africa

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Authors' contributions

FMM, MCG, LFP drafted the manuscript; MCG did statistical analysis; MLG, JJM, CSD, FC, MFM, MLW reviewed the manuscript; CSD, MAO, MLW designed the protocol. All authors agreed to the final version of the manuscript.

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Data Availability

The data that support the findings of this study are available from Milton Wainberg but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors (Flavio Mandlate and M. Claire Greene) upon reasonable request and with permission of Milton Wainberg.

Declarations

Ethics approval and consent to participate

The study was approved by the New York State Psychiatric Institute Institutional Review Board (#7479) and the Interinstitutional Bioethics Committee Faculty of Medicine Eduardo Mondlane University (CIBS FM & HCM/54/2017). The informed consent has been obtained from all the participants and/ or their Legal guardians. All experiments were performed in accordance with relevant guidelines and regulations (such as the Declaration of Helsinki).

Consent for publication

Not applicable.

Competing interests

Dr. Oquendo receives royalties from the Research Foundation for Mental Hygiene for the Columbia Suicide Severity Rating Scale's commercial use and owns shares in Mantra, Inc. She serves as an advisor to Alkermes and Fundacion Jimenez Diaz (Madrid). Her family owns stock in Bristol Myers Squibb. The other authors declare no competing interests.

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