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Depression mediates the relationship between exposure to stigma and medication adherence among people living with HIV in low-resource setting: a structural equation modeling approach

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Abstract

This study hypothesizes that depression mediates the association between exposure to stigma and medication non-adherence in people living with HIV (PLHIV). We recruited 372 PLHIV from the Stigma, health-related Quality of life, antiretroviral Adherence, and Depression among people living with HIV (SQuAD-HIV) project, a multicenter cross-sectional study conducted between October 2021 and February 2022 among PLHIV attending six ART clinics in two geopolitical regions of northern Nigeria. A structural equation modeling (SEM) framework, utilizing the full information maximum likelihood estimator, was used to elucidate the pathways linking stigma, depression, and ART medication adherence, adjusting for sociodemographic characteristics. The total number of eligible participants analyzed (353) included 32.7% male PLHIV with a mean age (SD) of 39.42 (10.14). Being female was positively associated with adherence (β, 95% CI 0.335, 0.163–0.523, p-value <0.001) but negatively associated with stigma (β, 95% CI -0.334, -0.561 to -0.142, p-value $=0.001$), while urban residence was negatively associated with stigma (β, 95% CI -0.564, -0.804 to -0.340, p-value <0.001). Our analysis also indicated that a higher level of experienced stigma was associated with decreased medication adherence. This association was partially mediated by depression (indirect effect $=(0.256)\ (-0.541)=-0.139$; p-value <0.01). The proportion of the association between stigma and medication adherence explained through mediation by depression was 35.6%. These findings underscore the need for targeted interventions aimed at lowering exposure to stigma among PLHIV to improve medication adherence.

Keywords HIV/AIDS · Stigma · Depression · ART adherence · Nigeria · Africa

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Introduction

HIV/AIDS continues to pose a significant threat to global public health, particularly in sub-Saharan Africa (SSA), which accounts for more than two-thirds of all cases of the disease (HIV and AIDS Fact Sheet_WHO, 2021). Despite the availability of effective medications, the disease is still stigmatized in many parts of the world (Mahajan et al., 2008). One study indicates that more than half of HIV-positive individuals encounter stigma (Lowther et al., 2014). However, although it exists in every country and region, HIV/AIDS-associated stigma is more prevalent in developing nations like Nigeria, where it has led to social ostracization, family breakdown, and human rights violations (Monjok et al., 2009; Onyebuchi-Iwudibia & Brown, 2014).

Stigma is defined as a severely disparaging attribute that causes an individual to have a tarnished identity and status in society (Goffman, 2009). The issue of stigma is particularly relevant to people living with HIV/AIDS (PLHIV) because it has been demonstrated to be a barrier to HIV prevention and therapy and is associated with poor health outcomes (Katz et al., 2013; Monjok et al., 2009; Rueda et al., 2016) Also, previous studies indicate that PLHIV who report experiencing or anticipating higher levels of stigma have an increased propensity for high-risk behavior, such as unsafe sex, and are less likely to disclose their HIV status to others (Mahajan et al., 2008; Yuh et al., 2014), particularly sexual partners, which can have a detrimental impact on compliance with HIV care and prevention (Mahajan et al., 2008; Turan et al., 2017). Furthermore, stigma has consistently been associated with poor adherence to antiretroviral therapy (Katz et al., 2013; Langebeek et al., 2014; Rueda et al., 2016; Sweeney & Vanable, 2016). This association presents a serious threat to the advancement of global efforts to control the pandemic, as an excellent adherence (of greater than 95%) to antiretroviral medications is required to effectively limit viral replication, prevent antiretroviral resistance and treatment failure, as well as reduce morbidity and mortality (Lowther et al., 2014; Rao et al., 2007).

Previous studies have identified some factors that potentially mediate the relationship between HIV-related stigma and poor ART adherence, with psychiatric disorders being one of the major factors identified (Sweeney & Vanable, 2016; Turan et al., 2017). Depression, being the most prevalent psychiatric condition in PLHIV (Nanni et al., 2014), has been recognized to be a long-term predictor of poor clinical outcomes in HIV-infected individuals (Nanni et al., 2014). Also, several studies on PLHIV have demonstrated the presence of a strong relationship between depression and stigma as well as between depressive symptoms and poor HIV drug adherence (Onyebuchi-Iwudibia & Brown, 2014; Rao et al., 2007; Sweeney & Vanable, 2016) Although prior studies have demonstrated that depressive symptoms partially mediate the relationship between HIV-related stigma and HIV treatment adherence (Mitzel et al., 2015; Rao et al., 2012; Turan et al., 2019), in Western countries, no study has been conducted in Sub-Saharan Africa to evaluate the existence or strength of this mediation pathway. Therefore, in this study, we aim to utilize the structural equation modeling (SEM) framework to concurrently examine the link between stigma, depression, and ART adherence among PLHIV attending antiretroviral (ART) clinics as outpatients in two states in Nigeria, the most populous sub-Saharan African nation. We hypothesize that depression mediates the association between stigma and medication (ART) adherence among PLHIV.

Methods

Study design, setting, and participants

The present study is a part of the Stigma, health-related Quality of life, antiretroviral Adherence, and Depression among people living with HIV (SQuAD-HIV) project, a cross-sectional study conducted among people living with HIV attending ART clinics as outpatients in two states, Kano (northwestern Nigeria) and Yobe (northeastern Nigeria). The design, setting, and participants of the SQuAD-HIV study have been previously described (Kabir Sulaiman et al., 2023).

Briefly, participants eligible for the study were PLHIV aged at least 18 years (self-reported and confirmed from the record folder by the interviewer) during the start of the study. Eligible participants were included if they are attending the clinic for follow-up, are currently taking ART, have granted consent to participate, and are not under hospital admission at the time of the study. No remuneration was given for this study.

The Ethics

This study was conducted following the Helsinki Declaration (Association (WMA) WM 2009), and was approved by the research ethics committees of the Kano State Ministry of Health (SHREC/2021/03/2889), the Yobe State Ministry of Health and Human Services (MOH/GEN/747/Vol. 1), and the Yobe State Specialist Hospital, Damaturu (YSS/DTR/GEN/013).

Data collection

Convenience sampling was used to recruit participants for the study between 11th October 2021 and 24th February 2022. Each data collector was assigned a unique Google form link for the study questionnaire and conducted the data collection under the routine watch of a supervisor assigned to each center. Each eligible participant was interviewed in a private room for an average of 60 min. Relevant clinical information of the participants was extracted from their record folders. A total of 372 PLHIV participated in the study. Following response compilation, 19 participants were excluded because their age could not be ascertained (missing age) or because they were younger than 18 years. Therefore, a total of 353 participants were included in this study.

Measures

The SQuAD-HIV registry collects information related to PLHIV, including assessments of stigma, adherence, health-related quality of life, and depression. For this study, we extracted information regarding participants' sociodemographic characteristics (age, sex, level of education attained, marital status, and income), stigma, depression, and adherence to ART.

Stigma

Stigma in the cohort was assessed using eight items derived from the validated 28-item HIV stigma measure, which is reliable in identifying internalized stigma among PLHIV (Sayles et al., 2008). These eight items measure participants' experience of discrimination, stereotyping, and/or prejudice as a result of having HIV, as well as their endorsement or internalization of the negative feelings and beliefs associated with HIV. A five-point Likert scale (none of the time [0], a little of the time [1], some of the time [2], most of the time [3], or all of the time [4]) is common to all the subscale items. The Cronbach's alpha for this eight-item scale, which we termed experienced stigma in our analysis, is 0.90. The questions included in this eight-item scale are as follows: (1) "People blame me for having HIV"; (2) "People think I am a bad person because I have HIV"; (3) "I feel abandoned by family members because I have HIV"; (4) "people treat me as less than human now that I have HIV"; (5) "People avoid me because I have HIV"; (6) "people I am close to are afraid they will catch HIV from me"; (7) "I feel like I am an outsider because I have HIV"; (8) "I feel ashamed to tell other people that I have HIV".

Depressive symptoms

We used the 13-item Beck Depression Inventory short form (BDI-SF) to assess depression among the participants (Furlanetto et al., 2005). Each of the thirteen items is unique and is scored on a four-point Likert scale specific to the item, with 0 and 3 being the least and highest scores, respectively, for each item.

Adherence to ART

A 3-item adherence self-report measure for medication adherence was used to assess adherence to ART among the participants. This scale has been shown to have good validity for measuring non-adherence to both ART and non-ART medications (Wilson et al., 2016). For all three items in the scale, participants were asked with reference to the last 30 days. The first question asked, "How many days did you miss at least one dose of any of your ART drugs?" The responses to this item were reversely scored (negated) during analysis to flow in the direction of the remaining two items of the scale. Item two of the scale asked, "How good a job did you do at taking your ART drug in the way you were supposed to?" The responses to this item were scored on a six-point Likert scale (very poor, poor, fair, good, very good, excellent). The last item asked, "How often did you take your ART drug in the way you were supposed to?" The responses to this item were scored on a six-point Likert scale (never, rarely, sometimes, usually, almost always, always).

Covariates

We included the socio-demographic characteristics (age, sex, place of residence, level of education, employment status, and marital status) of the participants, which are known to have an association with stigma and adherence to medication, as covariates.

Statistical analyses

We report the descriptive statistics of the study variables using mean ± standard deviation (SD) and percentages. Using the correlation matrix, we also computed and reported Pearson's correlation coefficient to assess the linear relationship between all study variables. We initially performed a confirmatory factor analysis (CFA) to test the validity and reliability of the latent constructs. Variables with factor loadings less than 0.5 were deleted from the measurement model (Hair et al., 2006). We then incorporated the measurement model in an SEM (Bollen, 1989) framework, using the full information maximum likelihood (FIML) estimator (Arbuckle, 1996) to evaluate a conceptual framework of the pathways linking stigma,

depression, and medication non-adherence, adjusting for sociodemographic characteristics, including age, sex, level of education, employment status, and marital status. Under the missing at random (MAR) and missing completely at random (MCAR) assumptions, FIML has been shown to produce unbiased estimates and standard errors, which are comparable to the estimates obtained using multiple imputation and better than those obtained using listwise deletion, pairwise deletion, and similar response pattern imputation (Enders, 2001; LM, 2001). Guided by the theoretical plausibility of relationships, we used modification indices to modify and improve the fit of our model (MacCallum et al., 1992; MacLean & Wetherall, 2021; Nachega et al., 2015; Tapp et al., 2011; Whittaker, 2012; Zhang et al., 2023) We used the bootstrapping method with 10,000 resamples to calculate the bias-corrected and accelerated (Bca) 95% confidence intervals (CI) of parameter estimates. We used the goodness-of-fit index (GFI), comparative fit index (CFI), Tucker-Lewis index (TLI), root mean squared error of approximation (RMSEA), and the standardized root mean square residual (SRMR) to assess the fit of our model. Hu and Bentler (1999), we considered GFI, CFI, and TLI values above 0.900, and RMSEA and SRMR values below 0.080 to indicate adequate model fit. All SEM analyses were conducted using the Rosseel (2012) package in R Version 4.3.0. The alpha level of significance for all analyses was set at 0.05.

We hypothesize that depression mediates the association between stigma and medication (ART) adherence among PLHIV. This hypothesis can help us better understand the mechanisms through which behavior impacts health (MacKinnon et al., 2007).

Results

Participants' sociodemographic characteristics

A total of 353 PLHIV with a mean age (SD) of 39.42 (10.14) were included in this study. Most of the participants were female (67.3%), younger than 45 years of age (69.4%), lived in urban settings (71.6%), unemployed (76.9%), and married (66.6%), while only 36.4% of the participants attained at least secondary level of formal education (Table 1).

Correlations among variables

The correlation among measured variables is detailed in Supplemental Material 1 Fig. 1. Experienced stigma was positively correlated with depression ($r = 0.517$, p-value < 0.001), while both experienced stigma ($r = -0.473$, p-value < 0.001) and depression ($r = -0.471$, p-value < 0.001) were negatively correlated with adherence Table 2.

Table 1 Socio-demographic characteristics of the participants

Characteristics	N (%)
Age (years: mean ± SD = 39.42 ± 10.14)	
18–34	119 (33.7)
35–44	126 (35.7)
45–54	73 (20.7)
55–64	31 (8.8)
≥ 65	4 (1.1)
Sex	
Male	115 (32.7)
Female	237 (67.3)
Residence	
Rural	99 (28.4)
Urban	249 (71.6)
Highest level of education	
None	56 (16.0)
Primary	43 (12.3)
Secondary	78 (22.2)
Tertiary	50 (14.2)
Islamic	124 (35.3)
Employment status	
Employed	79 (23.1)
Unemployed	263 (76.9)
Marital status	
Single	26 (7.4)
Married	235 (66.6)
Divorced	34 (9.6)
Widowed	58 (16.4)

Validity and reliability of latent constructs

To ensure that all items retained in our CFA have a substantial effect on the latent constructs, we only retained items with factor loadings greater than 0.5, as widely recommended, in our final CFA model (Table 2) (Arifin & Yusoff, 2016; Hair et al., 2006). All the latent constructs in this study demonstrated an acceptable degree of internal consistency, as the composite reliability (CR) measure for all the latent constructs was > 0.7 (Supplementary Material 2 Table 1). Furthermore, the convergent validity of the latent constructs was measured using the average variance extracted (AVE) measure (Fornell & Larcker, 1981; Segars, 1997). AVE measures the amount of variance captured by a construct relative to the amount of variance due to measurement error. It is recommended that the AVE for a construct should be at least 0.5, as an AVE below 0.5 indicates that the construct does not capture a majority of the variance. However, in situations where the AVE is not substantially lower than 0.5 and the CR of the latent construct is greater than 0.6 (Fornell & Larcker, 1981; Lam, 2012) or the standardized factor loadings of all items are

not significantly lower than 0.5 (Cheung & Wang, 2017), convergent validity can still be concluded. In our analysis, AVE was in the acceptable range (> 0.5) for stigma (0.575) and adherence (0.622); while, the AVE for depression (0.498) was slightly lower than 0.5 (Supplementary Material 2 Table 1). However, since the CR of depression (0.891) was well above 0.6 and the factor loadings of all depression items were greater than 0.5, we concluded that the convergent validity of depression is acceptable. Also, the latent constructs in this analysis exhibited an acceptable degree of discriminant validity, per the Fornell–Larcker criterion (Fornell & Larcker, 1981), since the $\sqrt{AVE}$ for all the latent constructs (Supplementary Material 2 Table 1) were substantially greater than Pearson's correlation coefficient of other related constructs. In essence, the latent constructs considered in this study exhibited good validity and reliability.

Model fit indices

The final model showed a good fit: Chi-square value = 375.17; Degrees of Freedom = 223; p-value < 0.001; Comparative Fit Index (CFI) = 0.960, Tucker-Lewis Index (TLI) = 0.954, Root Mean Square Error of Approximation (RMSEA, 90% CI) = 0.044 (0.036–0.052), Standardized Root Mean Square Residual (SRMR) = 0.044 (Jackson et al., 2009; Joreskog & Sorbom, 1993).

Table 2 Analysis of the validity of constructs

	AVE	Stigma	Depression	Adherence
Stigma	0.575	0.758		
Depression	0.498	0.517	0.706	
Adherence	0.622	−0.473	−0.471	0.789

AVE = Average variance extracted; The bold values along the diagonal represent the $\sqrt{AVE}$ and the numbers below these bold values are estimates of the correlation (Pearson's) between individual constructs

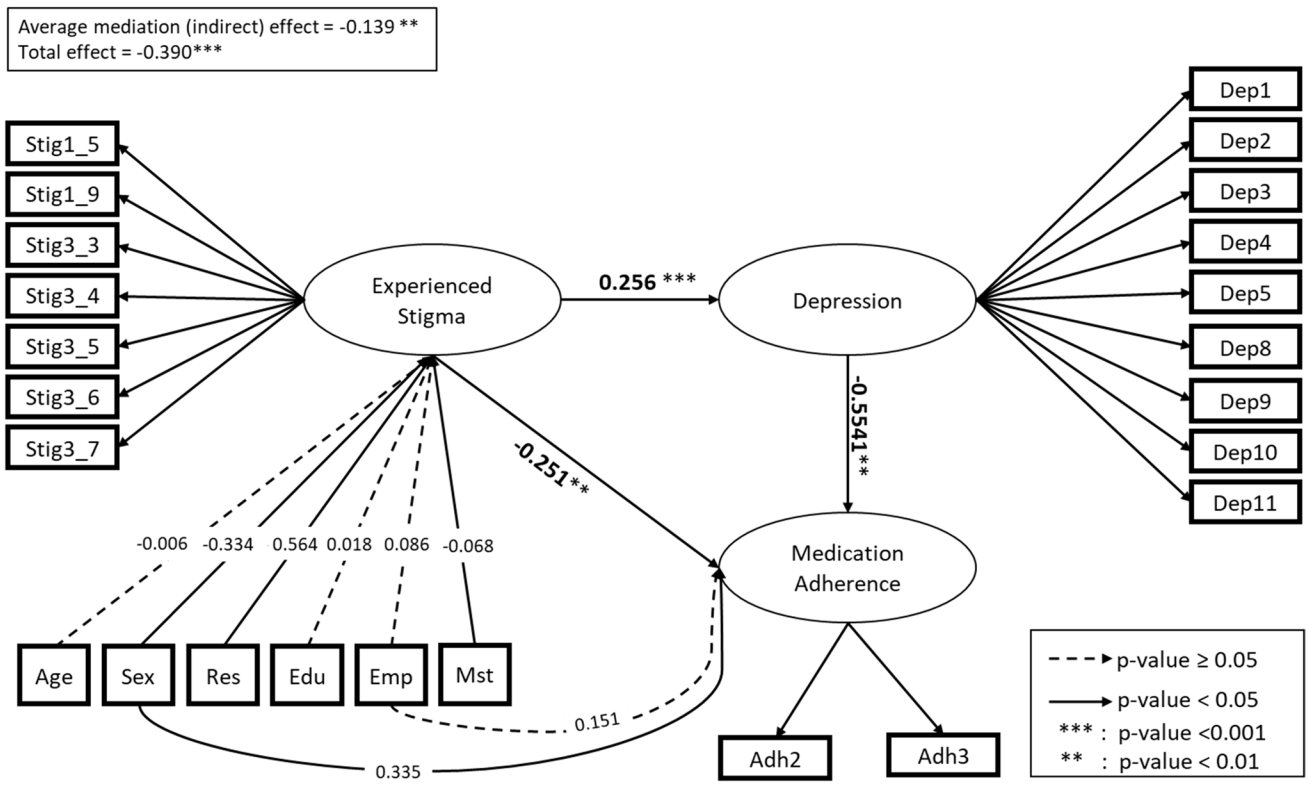

Fig. 1 Path model showing the direct and indirect relationship between stigma and adherence to ART medication. Latent variables are depicted in circles, while observed variables as rectangles. Res = residence, Edu = education, Emp = employment, Mst = marital status, Dep = depression: assessed using the 13-item Beck Depression Inventory short form, BDI-SF. Adh = adherence: assessed using the 3-item adherence self-report measure. Experienced stigma was assessed using items from the 28-item HIV stigma measurement instrument. (stig 1_5: "People blame me for having HIV", stig 1_9: "People think I am a bad person because I have HIV"; stig 3_3: "I feel abandoned by family members because I have HIV"; stig 3_4: "People treat me as less than human now that I have HIV"; stig 3_5: "People avoid me because I have HIV"; stig 3_6: "People I am close to are afraid they will catch HIV from me"; and stig 3_7: "I feel like I am an outsider because I have HIV"

Mediation analysis

Figure 1 presents the graphical depiction of our SEM model. The female sex is positively associated with adherence (β, 95% CI 0.335, 0.163–0.523, p-value < 0.001) but negatively associated with stigma (β, 95% CI −0.334, −0.561 to −0.142, p-value = 0.001), while urban residence is negatively associated with stigma (β, 95% CI −0.564, −0.804 to −0.340, p-value < 0.001). Experienced stigma was positively associated with depression (β, 95% CI 0.256, 0.193–0.343, p-value < 0.001). Depression was, in turn, negatively associated with adherence (β, 95% CI −0.541, −0.846 to 0.292, p-value < 0.001). Also, experienced stigma is directly associated with a lower likelihood of adherence (β, 95% CI −0.251, −0.415 to −0.110, p-value = 0.001). The indirect effect of experienced stigma on adherence, partially mediated through depression, was also statistically significant (β, 95% CI −0.139, −0.215 to −0.079, p-value < 0.001). The total effect of experienced stigma on adherence was also statistically significant (β, 95% CI −0.390, −0.548 to −0.253, p-value < 0.001). Therefore, the indirect association of experienced stigma with adherence, mediated through depression, accounted for 36.2% of the total effect of experienced stigma on adherence. Overall, these findings support our initial hypothesis.

Discussion

In this study, we used an SEM approach to examine the hypothesized mechanism by which depressive symptoms mediate the relationship between exposure to HIV-related stigma and adherence to ART medication among PLHIV in a low-resource setting. Based on our extensive review of the available literature, the present study is the first to use the SEM approach to explain this relationship in Africa (Mitzel et al., 2015; Rao et al., 2012). Our analysis revealed that depression partially mediates the relationship between exposure to HIV-related stigma and adherence to ART, a finding that confirms our hypothesis.

Previous studies have explored the potential mediation effect of depression in the association between stigma and medication adherence; however, these studies were largely conducted in high-income countries (Mitzel et al., 2015; Rao et al., 2012; Turan et al., 2019). Although PLHIV in Africa, a continent that accounts for 7 in 10 global incidences of HIV (de Santos et al., 2014), are at a heightened risk of stigma (HIV & AIDS Fact Sheet_WHO, 2021), no studies were conducted in the African continent to systematically evaluate the mediation effect of depression in the association between stigma and medication adherence.

The findings of this study were consistent with that of two previous studies conducted in the United States by Rao et al. (2012) and Mitzel et al. (2015). Also, a study conducted by Turan et al. (2016) suggested that in addition to depression, loneliness and lack of social support also mediate the effect of HIV-related stigma on adherence to ART among a cohort of women living with HIV in the US. A more recent study reported even stronger evidence of the mediating role of depression in the relationship between HIV-related stigma and antiretroviral therapy adherence using bootstrapping in a longitudinal sample of HIV-infected women in the US (Turan et al., 2019). The results of this study corroborate the findings of these prior studies and also uniquely demonstrate that this association is exhibited among PLHIV in the African continent.

It has been posited that sustained exposure to stigma may predispose PLHIV to experience both physical and mental symptoms of depression including feelings of sadness, pessimism, self-guilt, fatigue, dissatisfaction, anhedonia, indecision, and loss of self-esteem, which in turn increases the propensity for poor adherence to medication and even clinic visit (Shubber et al., 2016; Uthman et al., 2014) Poor adherence to ART among PLHIV has been reported to result in poor outcomes including virologic non-suppression and increased predisposition to opportunistic infection (Altice et al., 2019; Medley et al., 2009; Woldegeorgis et al., 2023). For this reason, many targeted interventions have addressed depression as a vital means of improving medication adherence among PLHIV (Altice et al., 2019; Gonzalez et al., 2011; Medley et al., 2009; Woldegeorgis et al., 2023). Exposure to stigma and higher levels of depression is associated with not only poor medication adherence but also a raised likelihood of suicidal ideation (Zeng et al., 2018). Therefore, the findings of this study highlight the need for interventions targeting stigma reduction strategies among PLHIV, including social marketing, counseling, faith, and problem-solving (Rao et al., 2019). Also, this study highlights the need for healthcare providers to actively assess for and treat depressive symptoms among PLHIV, particularly those with a heightened risk of experiencing stigma. The effectiveness of psychological interventions, including cognitive behavioral therapy (CBT), motivational interviewing, and relaxation in alleviating depressive symptoms has been demonstrated in previous randomized controlled trials conducted among PLHIV (Spaan et al., 2020). Recently, this has led to a growing call on the need to integrate HIV and mental health services of PLHIV globally (Banerjee et al., 2010; Chuah et al., 2017; Haldane et al., 2022; Operario et al., 2022). Future studies should identify effective strategies to mitigate stigma, depression, and medication non-adherence among PLHIV, including the use of a multidisciplinary approach that takes into consideration individual, environmental, social, and contextual factors (Iacob et al., 2017; Rao et al., 2019; Spaan et al., 2020).

Although our findings may not be generalizable to the Nigerian population, the fact that this study was conducted in six ART clinics in two different states belonging to different geopolitical regions (northeast and northwest) of Nigeria adds credence to our findings. Furthermore, the study employed a face-to-face interview, rather than a self-administered questionnaire approach. We want to note that the present study is limited by its cross-sectional design. Therefore, since both exposure and outcome were assessed at the same time, causality may not be established based on the findings of this study. Future longitudinal studies are needed to establish the temporal link between stigma, depression, and adherence. Nonetheless, the findings of this study have elucidated the potential mechanism by which exposure to HIV-related stigma results in poor ART adherence among PLHIV.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest in any form.

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