

Linking Depressive Symptoms to Viral Nonsuppression Among Women With HIV Through Adherence Self-Efficacy and ART Adherence

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Background: Depression plays a key role in suboptimal HIV outcomes, possibly mediated by adherence self-efficacy beliefs and antiretroviral treatment (ART) adherence behavior. Applying social-cognitive theory, we examined a longitudinal sequential path model of the association between depressive symptoms and viral nonsuppression in women with HIV (WWH) through these mediating mechanisms.

Methods: This was an observational longitudinal study using data from the Women's Adherence and Visit Engagement substudy of the Women's Interagency HIV Study. WWH (N = 375) completed measures of depressive symptoms, adherence self-efficacy, and ART adherence. Viral load was measured through blood draw. We examined a longitudinal sequential path model spanning 3 time points at least 6 months apart between 2015 and 2017. Indirect effects were assessed of depressive symptoms at time 1 (T₁) on viral nonsuppression at T₃ through adherence self-efficacy at T₂ and ART adherence at T₃. Covariates included age, income, recreational drug use, race, and months on ART.

Results: Depressive symptoms were associated with subsequent viral nonsuppression through its association with adherence self-efficacy and ART adherence [indirect effect: adjusted odds ratio = 1.004, 95% confidence interval: (1.001 to 1.008)]. Months on ART and recreational drug use were also significantly associated with viral nonsuppression at T₃.

Conclusions: Our findings support depressive symptoms' association with adherence self-efficacy that in turn lead to suboptimal ART adherence and ultimately to viral nonsuppression for WWH. Tailoring of interventions aimed at addressing depressive symptoms, substance use, and adherence self-efficacy among WWH is needed to help close the gap between ART prescription and viral suppression on the HIV care continuum.

Key Words: depression, self-efficacy, adherence, viral load, women, HIV

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INTRODUCTION

Women with HIV (WWH) tend to have poorer antiretroviral treatment (ART) adherence and viral suppression relative to men living with HIV.^{1–3} WWH are also heavily burdened by depressive symptoms, with estimates that WWH have 3.5 times the prevalence of major depressive disorder compared with women in the general population.⁴ Depressive symptoms may be the most prominent risk factor for suboptimal HIV health outcomes. Indeed, depressive symptoms, even at subclinical levels, are consistently linked to suboptimal ART adherence.^{5–7} Addressing HIV-related health outcomes without effectively diagnosing and treating depressive symptoms is likely to be ineffective.^{8,9} Addressing both depressive symptoms and adherence behavior may be necessary, and understanding the mechanisms through which depressive symptoms impact adherence behavior is important.¹⁰ Moreover, linking these mechanisms to viral load is relevant to understanding the impact of depressive symptoms on the HIV care continuum.¹¹

According to social-cognitive theory (SCT), self-efficacy is a person's belief in their ability to control their behavior and habits.^{12,13} Applied to ART adherence, self-efficacy implies a person's belief in their ability to take ART medications as prescribed or ART adherence behavior.¹⁴ SCT also addresses the role of negative emotional states and thought patterns that create disconnections between previous knowledge and skills and behavior. Depressive symptoms may interfere with self-efficacy through their impact on cognitive, behavioral, affective, and interpersonal processes such as motivation, decision-making, problem-solving, support seeking, and hopefulness. Informed by SCT, the current study examined the longitudinal relationship between depressive symptoms and viral nonsuppression among WWH through the proposed mechanisms of adherence self-efficacy and ART adherence. To do so, we tested a serial mediation model of these variables on the outcome of HIV viral nonsuppression.

METHODS

Participants included WWH in the Women's Adherence and Visit Engagement (WAVE) substudy of the Women's Interagency HIV Study (WIHS).¹⁵ WAVE includes women from WIHS study sites located in San Francisco, CA; Atlanta, GA; and Birmingham, AL/Jackson, MS. WAVE participants completed interviewer-assisted measures between April 2016 and April 2017. WAVE data were merged with WIHS core study measures occurring at biannual study visits occurring between October 2015 and October 2017.

Measures

Depressive symptoms were measured as part of the WIHS core study using the 20-item Center for Epidemiologic Studies Depression Scale (CES-D),¹⁶ which assesses a range of cognitive, affective, interpersonal, and vegetative symptoms of depression. Participants responded how often each symptom occurred over the past 2 weeks from 0 (rarely or none of the time) to 3 (most or almost all of the time). The

CES-D has been widely used in medical populations including people with HIV.^{17–19} It demonstrated good internal consistency among WWH in the WAVE study ($\alpha = 0.90$). For this study, we used the CES-D measure collected between October 2015 and March 2016 in WIHS for our “time 1” (T_1) predictor variable.

The HIV Treatment Adherence Self-Efficacy Scale¹⁴ includes 12 items assessing participants' confidence in their ability to adhere to their ART plan. WWH were presented with the question stem: “In the past month, how confident have you been that you can.” An example item is “stick to your treatment schedule even when you are not feeling well?” Participants then responded to each item on a 10-point scale from 1 (cannot do it at all) to 10 (certain I can do it). Higher scores indicate greater adherence self-efficacy, and the measure has very good internal consistency in the present sample ($\alpha = 0.94$). This measure was collected as part of the WAVE study between April 2016 and April 2017, representing “time 2” (T_2) for this study.

ART adherence is assessed in WIHS core study measures with a 3-item self-report measure assessing number of days ART was missed, frequency of taking ART, and rating how well participants took their ART as prescribed in the past 30 days.²⁰ Responses across the 3 items were linearly transformed on a 0–100 scale, with higher scores representing better adherence. Internal consistency across items was good in the present sample ($\alpha = 0.87$). Owing to the negative skew of the adherence measure, responses were dichotomized such that 0 represented less than 95% adherence or suboptimal adherence and 1 represented greater than or equal to 95% adherence or optimal adherence²¹ for a sensitivity analysis. For this study, this measure was used at “time 3” (T_3) and was collected between April 2017 and October 2017.

Viral load was collected through blood draw as part of the WIHS core study. Viral load values were dichotomized as 0 (viral suppression, <20 copies/mL) and 1 (viral nonsuppression, >20 copies/mL). Because participants were asked about their adherence in the past 30 days at T_3 , we used the corresponding viral load value collected at T_3 .

Analysis

Data were analyzed using SPSS, version 24. Descriptive and bivariate correlation analyses were used to characterize the sample and relevant study variables. Path analysis was conducted using the PROCESS macro for SPSS.²² The primary study analysis used a longitudinal serial mediation path model to examine the associations between continuous depressive symptoms (T_1), continuous adherence self-efficacy (T_2), continuous ART adherence (T_3), and dichotomous viral nonsuppression (T_3). The sensitivity analysis with dichotomous ART adherence at T_3 was estimated in AMOS for SPSS²³ that can handle dichotomous mediators. We assessed whether adherence self-efficacy and ART adherence mediated the association between depressive symptoms and viral load. This model estimated 2 additional simple indirect effects: (1) the indirect effect of depressive symptoms on viral nonsuppression through adherence self-efficacy and (2) the indirect effect of depressive symptoms on viral nonsuppression through ART adherence.

This approach to estimating indirect effects does not require the total effect (the association controlling for covariates without any mediators in the model) to be statistically significant in order for an indirect effect to be present.^{24,25} Bootstrapping with 2000 resamples was used to estimate 95% confidence intervals (CIs).^{26,27} Covariates included age, income, dichotomous recreational drug use in the past 6 months (0 = no and 1 = yes), dichotomous race (0 = white vs. 1 = nonwhite), and amount of time on antiretroviral therapy (months) as of T₁. Associations between variables and indirect effects are presented as adjusted odds ratios with bootstrap 95% CIs.

RESULTS

Of the 460 women enrolled in the WAVE study, a total of 19 (4%) reported not starting an ART regimen during the observation period and were excluded from this analysis. Of the 441 remaining women, 375 (85%) had complete data across all 3 time points. Sample characteristics (N = 375) and bivariate correlations are described in Table 1.

Path coefficients from our hypothesized serial mediation model are presented in Figure 1, and the indirect path is indicated in bold. There was a positive indirect effect of depressive symptoms at T₁ on viral nonsuppression at T₃ first through adherence self-efficacy at T₂ and then through ART adherence at T₃, adjusted odds ratio (aOR) = 1.004, 95% CI: (1.001 to 1.008). Comparison of indirect effects showed a nonsignificant simple indirect effect of depressive symptoms on viral nonsuppression through adherence self-efficacy and a nonsignificant simple indirect effect of depressive

symptoms on viral nonsuppression through ART adherence. The only covariates that were significantly associated with viral nonsuppression at T₃ in the final model were months on ART [aOR = 1.008, 95% CI: (1.004 to 1.012)] and recreational drug use [aOR = 2.910, 95% CI: (1.742 to 4.860)].

In a sensitivity analysis using a 95% threshold for ART adherence, the indirect effect of depression on viral nonsuppression was very similar to the continuous model, aOR = 1.005, 95% CI: (1.002 to 1.010).

DISCUSSION

We explored the relationship between depressive symptoms and viral nonsuppression over a period of 2 years in a geographically diverse sample of WWH using a social cognitive theory-derived path model. We specifically explored this association through the mediating mechanisms of adherence self-efficacy and ART adherence behavior. Our findings confirmed our hypothesis that depressive symptoms interfere with WWH's adherence self-efficacy—or beliefs in their ability to take their ART as prescribed. Diminished self-efficacy in turn translated to lower ART adherence behavior, which was then associated with the biologic outcome of viral nonsuppression.

These findings support regular depressive symptom monitoring in HIV care for WWH, especially considering it is the most prevalent comorbidity for people with HIV across age groups.²⁸ In this study, taking ART for a longer period was associated with both greater depressive symptoms and

TABLE 1. Description of Demographic Characteristics and Study Variables for 375 Women With HIV

Demographic/Health Variable	n (%) or M ± SD, Range	Bivariate Correlations			
		Depressive Symptoms	Adherence Self-Efficacy	ART Adherence‡	Viral Nonsuppression
Age	48.5 ± 9.6, 27–81	−0.20	0.10	0.08	0.13
Months on ART	92.1 ± 69.5, 0–267	0.12	−0.04	0.03	0.25¶
Nonwhite race	331 (88)	−0.04	−0.09	−0.05	−0.03
Annual household income		−0.10	0.06	0.09	−0.03
≤\$18,000	270 (72)				
\$18,001–36,000	73 (19)				
>\$36,001–75,000	32 (9)				
Recreational drug use past 6 months*	115 (31)	0.21¶	−0.15	−0.22¶	0.30¶
Study variable					
T ₁ depressive symptoms†	13.8 ± 11.8, 0–57	—			
T ₂ adherence self-efficacy	8.7 ± 1.6, 1.7–10	−0.28¶	—		
T ₃ ART adherence past 30 d					
Continuous ART adherence‡	87.4 ± 18.2, 0–100	−0.16	0.43¶	—	
≥95% ART adherence	314 (84)	−0.09	0.32¶	0.59¶	−0.25¶
T ₃ viral nonsuppression§	126 (34)	0.15	−0.24¶	−0.30¶	—

*Recreational drug use includes marijuana, hallucinogens, club drugs, methamphetamines, injection drugs, or prescription medications used other than prescribed.

†Center for Epidemiological Studies Depression (CES-D) total score.

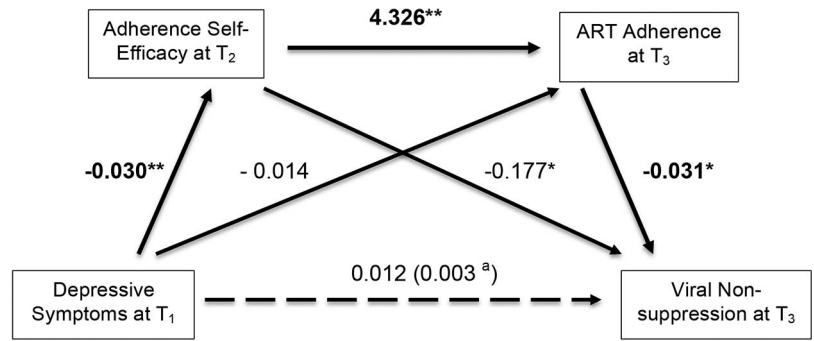
‡Linearly transformed 3-item ART adherence measure.

§>20 copies/mL.

||P < 0.05.

¶P < 0.001.

FIGURE 1. Longitudinal sequential path model depicting associations between depressive symptoms and viral nonsuppression, through adherence self-efficacy and ART adherence among N = 375 WWH. Path coefficients are unstandardized β . Covariates included age, income, recreational drug use, dichotomized race, and months on ART. ^aWhen mediators are present in model (direct effect). * $P < 0.05$; ** $P < 0.001$.



viral nonsuppression. Ongoing support of adherence self-efficacy is important, and addressing only depression or self-efficacy alone will likely be unsuccessful. Indeed, results from a large trial assessing the impact of antidepressant management on depressive symptoms and HIV health outcomes only found improvement in depressive symptoms, but not in ART adherence.²⁹ Other evidence suggests antidepressant treatments including medications and psychotherapy improve ART adherence, but adherence to these treatments may be crucial.^{9,30,31} However, few studies measure adherence to antidepressant treatment and/or psychotherapy and HIV care providers may not routinely follow-up with patients on their depression care.³² Overall, interventions intended to improve adherence self-efficacy and ART adherence will not have their intended effect in the context of untreated or undertreated depressive symptoms.

In the present analysis, we found recreational drug use was significantly associated with depression, adherence self-efficacy, adherence, and viral nonsuppression. A recent review of 13 ART adherence interventions for women found that only 2 interventions addressed mental health and 3 addressed substance use in addition to adherence.³³ Additional work is needed to implement interventions that address mental health, substance use, and adherence. Cognitive-Behavioral Therapy for Adherence and Depression (CBT-AD) combines a brief intervention addressing adherence self-efficacy using cognitive-behavioral strategies (Life-Steps) with empirically validated methods to alleviate depressive symptoms.^{34–37} Tailoring interventions such as CBT-AD for WWH and WWH who use substances is warranted. In the previously mentioned review of interventions for adherence in women, only 3 interventions tailored content specific to women.³³ While not developed for the treatment of depression, the Striving Towards EmPowerment and Medication Adherence (STEP-AD)³⁸ is an intervention tailored for black WWH that combines content related to adherence, coping with trauma, discrimination, and sex roles. Such themes could certainly be adapted to address depressive symptoms in WWH in future intervention research. Monitoring and addressing substance use is another important component for future interventions in light of its association with depressive symptoms, adherence self-efficacy, ART adherence, and viral nonsuppression in this study.

The findings presented here should be interpreted in light of some limitations. This sample included WWH participating in a longitudinal cohort study at urban research

centers, and results may not generalize to all WWH in the United States. Another limitation was the use of a self-reported ART adherence measure. Although this measure has shown validity in previous studies,²⁰ it is susceptible to social desirability and recall bias. Third, our study design and hypothesized model assumed a 1-way causal chain of effects over time. The lag in measures over time that spanned 2 years from T₁ to T₃ diluted the effect between depressive symptoms and viral nonsuppression. Furthermore, our model does not account for other variables affecting the relationship between depression and viral nonsuppression that may result in a smaller than expected total effect. As interventions addressing depression and ART adherence are increasingly implemented, changes in these variables should be monitored to assess how decreasing depressive symptoms, for instance, translates to clinically significant changes in adherence self-efficacy and vice versa.

In sum, our findings support that depressive symptoms interfere with self-management processes pertinent to controlling HIV among WWH. Ongoing monitoring and management of depressive symptoms, substance use, and adherence self-efficacy is important, particularly as more women are aging with HIV. Adaptation and evaluation of interventions addressing mental health, substance use, and adherence are needed for WWH.

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