



Published in final edited form as:

AIDS Behav. 2020 December ; 24(12): 3482–3490. doi:10.1007/s10461-020-02919-w.

Internalized HIV Stigma and Pain among Women with HIV in the United States: The Mediating Role of Depressive Symptoms

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No conflicts of interest were reported by the authors of this paper.

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Abstract

Pain is common in women with HIV, though little research has focused on psychosocial experiences contributing to pain in this population. In the present study we examined whether internalized HIV stigma predicts pain, and whether depressive symptoms mediate this relationship among women with HIV. Data were drawn from the Women's Interagency HIV Study (WIHS), for 1,364 women with HIV who completed three study visits between 2015 and 2016. We used a sequential longitudinal design to assess the relationship between internalized HIV stigma at time 1 on pain at time 3 through depressive symptoms at time 2. Analyses revealed internalized HIV stigma was prospectively associated with greater pain, $B = 5.30$, 95%CI [2.84, 7.60]. The indirect effect through depressive symptoms supported mediation, $B = 3.68$, 95%CI [2.69, 4.79]. Depression is a modifiable risk factor that can be addressed to improve pain prevention and intervention for women with HIV.

Keywords

HIV; internalized stigma; pain; depression; women; WIHS

INTRODUCTION

Advancements in antiretroviral therapy (ART) shifted the focus among medical professionals from addressing acute immunodeficiency concerns among people with HIV to treating inflammation and comorbid medical conditions (1, 2). Pain is a common, yet relatively understudied comorbidity among people with HIV (3, 4). Compared to the general population with an estimated pain prevalence of 20–30%, people with HIV are disproportionately impacted by pain with estimated prevalence between 39% and 85% (5–7). Some research suggests women with HIV are more likely to experience more severe pain compared to men with HIV, and to under-report their pain (7–9). A recent study within the Women's Interagency HIV Study (WIHS) cohort found approximately half of the women in the cohort reported pain in the past week (10). When the investigators compared pain

experiences of HIV-positive and HIV-negative women matched on socioeconomic and behavioral risk characteristics they found minimal differences between groups in their experience of pain (10). These findings suggest women with HIV do not necessarily experience more pain due to HIV infection or its treatment, but rather due to other etiological factors such as aging, or social and behavioral influences.

Sociodemographic factors and conditions such as psychiatric illness, substance use, psychological distress, and stigma may contribute to pain among women with HIV (11, 12), but few of these pathways have been explored empirically. The negative consequences of pain that complicate care and quality of life for people with HIV include impaired mobility, missed healthcare visits, poorer ART adherence, and reduced CD4 cell counts (13–16). Understanding mechanisms that attenuate or exacerbate pain may inform interventions to improve pain outcomes, reduce comorbidity, and enhance health-related quality of life.

Researchers who have synthesized the empirical HIV-pain literature support a biopsychosocial approach (12, 17, 18). Social processes contribute to pain; and there is a substantial body of work on the neural connections of social rejection and pain in the general population (19–22). Negative social experiences, like HIV stigma, can impact pain experiences for people with HIV. HIV stigma – defined as the social devaluation and discrediting of people with HIV – is a significant barrier to improving the health and wellbeing of people with HIV (23–25). However, as of 2018 only two cross-sectional studies examined the associations between stigma and pain (18). A more recent preliminary cross-sectional analysis conducted by Wadley and colleagues in a clinic-based cohort in South Africa found a positive relationship between perceived HIV stigma and pain severity (26). Perceived HIV stigma can lead to internalized HIV stigma and affect mental and physical health among people with HIV (27, 28). Internalized HIV stigma is the extent to which individuals apply negative beliefs and attitudes about HIV to themselves (29, 30). Thus, extending from Wadley and colleagues' preliminary findings (26), internalized stigma may have implications for the experience of pain. Internalized HIV stigma is associated with greater psychological distress (31), negative emotional states (30), and depressive symptoms (29, 32, 33). There is strong empirical support for the relationship between internalized HIV stigma and depressive symptoms that have downstream effects on health outcomes (27, 30, 34–36). Therefore, depression may play a role in the relationship between internalized stigma and pain.

Psychological processes, like depression, contribute to pain. Depressive symptoms and pain are linked as they often co-occur, exacerbate one another, and share biological pathways (37–39). One explanation for the common depression-pain comorbidity is the gate-control theory of pain, whereby depression serves to widen the gate for pain-related signals reaching the central nervous system (40, 41). Indeed, depression is one of the extenuating factors that contributes to acute pain persisting into chronic pain (42). People with depressive symptoms often present with medically unexplained physical pain and report more severe pain and more pain-related interference – wherein pain prevents normal functioning in work and other daily activities (18, 43). A recent systematic review and meta-analysis found similar associations between depression and pain among people with HIV that were consistent with these associations reported in the broader pain literature (18).

In the present longitudinal study, we sought to better understand how internalized HIV stigma impacts pain in women with HIV and whether depressive symptoms mediate this relationship. We first examined whether internalized HIV stigma predicts pain in a geographically diverse cohort of women with HIV in the United States (U.S.). Our analyses and hypotheses were derived from the biopsychosocial model of pain in HIV (12). While this model was developed for chronic pain in people with HIV, we wanted to know how internalized HIV stigma and depressive symptoms relate to acute experiences of pain and pain-related interference for women with HIV. Evidence suggests that depressive symptoms mediate the relationship of internalized HIV stigma on health-related outcomes such as ART adherence and viral load (34). We therefore hypothesized that internalized HIV stigma would predict pain, and that depressive symptoms would mediate this relationship. We used a longitudinal sequential mediation model over a time period of one year to test our hypotheses.

METHODS

Participants and Procedures

Participants were women with HIV enrolled in WIHS, a multisite prospective cohort study investigating HIV disease progression, comorbid health conditions, and the psychosocial and behavioral impact of HIV among women in the United States (44). Women were included from 10 WIHS sites located in Bronx, NY; Brooklyn, NY; Washington DC; San Francisco, CA; Chicago, IL; Chapel Hill, NC; Atlanta, GA; Miami, FL; Birmingham, AL; and Jackson, MS. During semiannual study visits, women participated in physical examinations and interviewer-assisted assessments of psychosocial and behavioral information. The current analysis includes data from three separate study visits that occurred approximately six months apart between 2015 and 2016. All study procedures were approved by Institutional Review Boards at each WIHS site and all participants provided written informed consent prior to participation.

Measures

Demographic and Health Information—Participants reported their demographic information including their age, race and ethnicity (White non-Hispanic, Black non-Hispanic, Hispanic/Latina, or ‘Other’ inclusive of American Indian, Alaskan Native, Asian, Native Hawaiian, Pacific Islander, and multiple races/ethnicities). Participants reported their approximate household income (1: \leq \$6,000; 2: \$6,001–12,000; 3: \$12,001–18,000; 4: \$18,001–24,000; 5: \$24,001–30,000; 6: \$30,001–36,000; 7: \$36,001–75,000; 8: $>$ 75,000). Participants also reported whether or not they used drugs (marijuana/hash, crack or cocaine, heroin, non-prescribed methadone, methamphetamines, amphetamines, hallucinogens, club drugs, tranquilizers, narcotics) recreationally since their last study visit (in the past six months). Plasma viral load was measured at each study visit via blood draw and dichotomized as suppressed ($<$ 20 copies/mL) or unsuppressed ($>$ 20 copies/mL).

Internalized HIV Stigma—The seven-item negative self-image subscale of the HIV Stigma Scale (45, 46) was used to assess internalized HIV stigma. Participants responded to items (e.g., “Having HIV/AIDS makes me feel that I’m a bad person.”) on a scale from 1:

strongly disagree, to 4: *strongly agree*. Higher scores indicate greater internalized HIV stigma. This stigma measure is given once per year (every other study visit) in WIHS. Scale reliability for the internalized HIV stigma scale was good in this sample (Cronbach's $\alpha=0.87$ at Time 1 [T1]).

Depressive Symptoms—Depressive symptoms were measured by the Center for Epidemiological Studies Depression Scale (CES-D; 47). The CES-D measures cognitive, affective, interpersonal, and vegetative symptoms of depression experienced during the past week. Participants responded to each item on the following scale: 0: *Rarely or none of the time (less than 1 day)*; to 3: *Most or all of the time (5–7 days)*. Higher scores on the scale indicate greater symptoms of depression. The CES-D has been widely used in health populations including people with HIV. Because the CES-D measures somatic symptoms that may overlap with potential symptoms of HIV and/or pain, we computed the CESD-11 total score (48) that omits the somatic symptom items for a sensitivity analysis. Depressive symptoms were assessed every six months (every visit) in WIHS. Reliability scores were high for the CES-D: Cronbach's $\alpha=0.91$ for the CES-D total score, and $\alpha=0.87$ for the CESD-11 at Time 2 [T2].

Bodily Pain—Pain experienced in the *past 4 weeks* was assessed using two items from the Medical Outcomes Study Short Form Health Survey (SF-36; 49): 1) “How much bodily pain have you had during the past 4 weeks?”; and 2) “During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?” Both items were answered on a 5-point Likert-type scale from 1: *None/Not at all*, to 5: *Very severe/Extremely*. The mean of both items was calculated to create a composite score of acute bodily pain and pain-related interference. Mean scores were transformed to a 0 to 100 scale with 0 indicating no bodily pain or pain-related interference, and 100 indicating very severe bodily pain and extreme pain-related interference. This scoring was reversed from the typical interpretation of SF-36 scores to enhance interpretability along with the other metrics in this study where higher scores indicate more symptoms. Bodily pain was assessed yearly (every other visit) in WIHS.

Statistical Analysis

Descriptive analyses were first conducted to characterize the sample using SPSS version 25. Mediation analyses were done using structural equation modeling in Mplus (50) using maximum likelihood estimation. The following covariates collected at T1 were included in the models: age, months on ART, race (0: White, 1: Black/African American, 2: Hispanic and Other), income, recreational drug use (0: No, 1: Yes), and viral suppression (0: suppressed, 1: non-suppressed). Internalized HIV stigma at T1 was the independent variable. Pain was the outcome at Time 3 (T3). The indirect effect of internalized HIV stigma on pain through depressive symptoms at T2 was assessed with bootstrapping using 5,000 re-samples to derive the percentile-corrected 95% confidence interval (51). Mediation is present when 95% confidence interval for the indirect effect does not contain 0. Unstandardized beta coefficients and 95% confidence intervals are presented to promote interpretation based on the metrics used in the study. A sensitivity analysis was conducted with the somatic symptom items removed from the total CES-D score. An additional sensitivity analysis was

done to determine if depression mediated the relationship between internalized stigma and pain given baseline pain by controlling for pain at T1. In these analyses, missing data were addressed via full-information maximum likelihood estimation (FIML) under the conditionally missing at random (MAR) assumption.

RESULTS

Sample Description

The sample included 1,364 women with HIV who completed study visits every 6 months between 2015 and 2016. Study-related demographic and health variables are described in Table I. Briefly, participants' mean age was 49 years (SD: 9, Range 26–78 years). The majority (74%) identified their race/ethnicity as Black, non-Hispanic. Participants were largely socio-economically disadvantaged, reporting a median household income in the range of \$6,000–12,000. They reported taking ART an average of 126 months (SD: 83 months, Range: 0–277 months). Most women reported no recreational drug use (77%), and most had suppressed viral loads (71%). At T1, participants reported a mean of 1.8 ± 0.7 (range 1–4) on the internalized HIV stigma scale. At time 2, they reported a mean CES-D score of 11.4 ± 11.1 (Range: 0–57). At time 3, participants reported a mean pain score of 28 ± 27 (Range 0–100).

Longitudinal Sequential Mediation Analysis

Results of the longitudinal sequential mediation model are shown in Figure 1, with model coefficients fully described in Table II. Internalized HIV stigma at T1 was associated with greater pain one year later at T3, $B = 5.30$, 95% CI [2.84, 7.60]), as shown as the total effect in the path diagram. When depressive symptoms at T2 were added to the model, the direct effect of internalized HIV stigma was no longer statistically significant, $B = 1.62$, 95% CI [–0.88, 4.08]. The indirect effect of internalized HIV stigma on pain, indicated that depressive symptoms account for the association between internalized HIV stigma and later pain ($B = 3.68$, 95% CI [2.69, 4.79]). Model covariates were significantly associated with pain at T3, including a positive association with age, a negative association with income, and a positive association with recreational drug use at T1.

Sensitivity Analyses

Our analysis using the CES-D cognitive, affective, and interpersonal items only (CESD-11), omitting the somatic symptoms showed little change in the estimates. The direct effect of internalized HIV stigma on pain was attenuated when CESD-11 was added to the model, $B = 2.00$, 95% CI: [–0.47, 4.46]. The indirect effect of internalized HIV stigma at T1 on pain at T3, through cognitive and affective symptoms of depression was above 0, $B = 3.26$, 95% CI: [2.28, 4.28], again supporting mediation.

In the second sensitivity analysis we controlled for pain at T1 and found that internalized HIV stigma was associated with later pain (Total effect: $B=2.51$, 95% CI: [0.46, 4.50]). When the CES-D total score was included in the model, the direct effect was attenuated and non-significant ($B=1.03$, 95% CI: [–1.11, 3.08]). The confidence interval for the indirect

effect of internalized HIV stigma on pain at T3 was above zero even when controlling for pain at T1 (Indirect effect: $B=1.03$, 95% CI: [0.82, 2.23]).

DISCUSSION

Data from a large cohort of women with HIV in the U.S. support a longitudinal association between internalized HIV stigma and acute bodily pain that is mediated by depressive symptoms. This mediated effect of depressive symptoms is present with or without the somatic domain of depression. Taken together with previous conceptual and empirical work (12, 18, 26), these findings support the hypothesis that the internalization of negative social attitudes toward HIV increases depressive symptoms, which then leads to subsequent reports of bodily pain.

The negative impact of pain is well described in the literature and has a variety of social, clinical, and economic implications – most notably affecting quality of life, disability, substance use, and mortality (52–54). Pain in women with HIV can have a complex etiology, including the influences of social and psychological factors. Women may be more likely to discuss complaints regarding physical pain as opposed to bringing up difficulties with depression or stigma with a healthcare provider (10). Thus, pain emerges as a clinical focus while other modifiable factors could be targeted to enhance the treatment of pain in women with HIV.

Internalized HIV stigma has few empirically supported interventions, but it may be most amenable to community-level efforts aiming to normalize the experience of people with HIV (55). Individual-level interventions for internalized HIV stigma do not directly address the social and structural determinants of internalized stigma, and can place the responsibility for coping with negative social attitudes on the individual who is experiencing stigma (56). Additional research is needed to refine and evaluate internalized stigma interventions to meet the needs of women with HIV who may also be experiencing depression and pain.

Unlike stigma, depressive symptoms are often screened for in HIV primary care settings, representing an important opportunity for psychoeducation and intervention. Pharmacologic treatments for depression can directly address pain conditions. Tricyclic antidepressants and anticonvulsant medications are considered first-line treatment for neuropathic pain (57). Serotonin and norepinephrine reuptake inhibitors (SNRIs) are also effective for improving depressive symptoms and pain (58). In spite of the potential effectiveness of antidepressants, opioid medications are a common treatment approach for pain in women with HIV. In a previous study among women in WIHS who reported experiencing pain, nearly two thirds received a prescription for opioid medications (10). Opioid medications were the second most commonly prescribed medications behind non-steroidal anti-inflammatory drugs. While opioid medications have their place in relieving pain for some conditions, there is little evidence of efficacy for long-term use of opioids (59). Opioids also carry significant risks for depression (60), addiction and overdose (61, 62). Based on the results of the present study, a broader repertoire for addressing psychosocial factors in pain among women with HIV is needed.

Psychosocial approaches to treating depression may enhance pain self-management and can be tailored to address underlying causes of depression such as HIV-related stigma. Cognitive behavioral approaches are applied to the experience of pain and have been adapted in existing psychosocial pain interventions. For instance, cognitive behavioral therapy for chronic pain (CBT-CP) integrates cognitive strategies, behavioral activation, and support seeking that are effective skills for improvement in both depression and pain symptoms (63). Merlin's Skills TO Manage Pain (STOMP) intervention is a behavioral intervention specifically designed for people with HIV and chronic pain (64). STOMP uses peer leaders to model pain self-management skills while bolstering social support that may also have implications for depression.

While internalized stigma related to HIV was this study's focus, women with HIV may face other intersecting forms of stigma in their daily lives (65) that can be assessed for their associations with mental health and pain. For instance, a recent investigation supported a compounding influence of HIV-related stigma and pain-related stigma on depressive symptoms (5). Research focusing on the prevalence, impact, and mechanisms of pain in people with HIV is especially important in the development of intervention efforts to prevent chronic pain conditions that may confer additional social stigma.

The results of this study should be interpreted in light of some limitations. First, women in the WIHS cohort are part of an interval study taking place at academic medical centers and may not represent the general population of women with HIV in the U.S. Second, women in this study were not included on the basis of a diagnosed pain condition. Our measure of pain included two self-reported items that examined symptoms experienced in the past week. Future research may differentiate women based on diagnosis of acute versus chronic pain to measure these associations in clinical samples. Third, the measure of recreational drug use in this study assessed any use of different types of drugs over the previous six months. Drug use emerged as a significant covariate in our analyses and warrants a more focused investigation into types and frequency of use in relation to pain. Fourth, the observation period for this study was only one year. However, our longitudinal mediation model adds to the existing literature on HIV stigma and pain that is cross-sectional. Future investigations may explore the bidirectional effects with more waves of data with this evidence of a mediated association between internalized HIV stigma and pain. In spite of these limitations, the findings presented here have implications for better understanding depressive symptoms as a mechanism linking HIV-related stigma with pain in women with HIV.

Our findings suggest that the internalization of negative social attitudes related to HIV "hurts", with internalized HIV stigma predicting pain one year later among women with HIV. Depressive symptoms can help explain this relationship based on the results of this mediation analysis. Tailored approaches to addressing pain prevention and intervention that consider stigma, depression, and other contextual factors experienced by women with HIV are critically needed.

Acknowledgements

CONFLICTS OF INTEREST AND SOURCES OF FUNDING

Data in this manuscript were collected by the Women's Interagency HIV Study (WIHS). WIHS (Principal Investigators): UAB-MS WIHS (Mirjam-Colette Kempf and Deborah Konkle-Parker), U01-AI-103401; Atlanta WIHS (Ighowwerha Ofotokun, Anandi Sheth, and Gina Wingood), U01-AI-103408; Bronx WIHS (Kathryn Anastos and Anjali Sharma), U01-AI-035004; Brooklyn WIHS (Deborah Gustafson and Tracey Wilson), U01-AI-031834; Chicago WIHS (Mardge Cohen and Audrey French), U01-AI-034993; Metropolitan Washington WIHS (Seble Kassaye and Daniel Merenstein), U01-AI-034994; Miami WIHS (Maria Alcaide, Margaret Fischl, and Deborah Jones), U01-AI-103397; UNC WIHS (Adaora Adimora), U01-AI-103390; Connie Wofsy Women's HIV Study, Northern California (Bradley Aouizerat and Phyllis Tien), U01-AI-034989; WIHS Data Management and Analysis Center (Stephen Gange and Elizabeth Golub), U01-AI-042590; Southern California WIHS (Joel Milam), U01-HD-032632 (WIHS I – WIHS IV). The WIHS is funded primarily by the National Institute of Allergy and Infectious Diseases (NIAID), with additional co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the National Cancer Institute (NCI), the National Institute on Drug Abuse (NIDA), and the National Institute on Mental Health (NIMH). Targeted supplemental funding for specific projects is also provided by the National Institute of Dental and Craniofacial Research (NIDCR), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Deafness and other Communication Disorders (NIDCD), and the NIH Office of Research on Women's Health. WIHS data collection is also supported by U11-TR000004 (UCSF CTSA), P30-AI-050409 (Atlanta CFAR), P30-AI-050410 (UNC CFAR), and P30-AI-027767 (UAB CFAR). Additional support for software was provided by the National Institute on Minority Health and Health Disparities under Award Number U54MD000502. This research was also supported by K12HL143958, an NIH funded grant made possible through the NHLBI. The contents of this publication are solely the responsibility of the authors and do not represent the official views of the National Institutes of Health (NIH).

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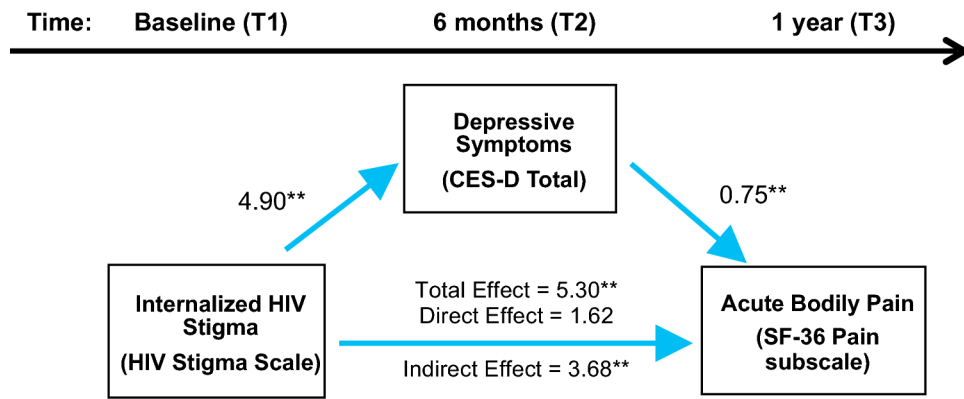


Figure 1.

Longitudinal mediation model showing internalized HIV stigma predicting bodily pain one year later, mediated by depressive symptoms at 6 months. Covariates include age, race, income, recreational drug use, months on ART, and viral load suppression measured at baseline.

CES-D: Center for Epidemiological Studies Depression Scale; SF-36: Short Form Health Survey

** $p < 0.001$, * $p < 0.05$

Table 1.

Description of demographic and health information for women with HIV (N=1,364).

Baseline (T1) Demographic/Health Variable	N (%) for categorical variables or M (SD, range) for continuous variables
Age	49 (9, 26–78)
Race	
White, Non-Hispanic	126 (9%)
Black/African American, Non-Hispanic	1012 (74%)
Hispanic or Other Race	227 (17%)
Household Income < \$18,000	892 (65%)
Recreational Drug Use *	314 (23%)
Months on ART	126 (83, 0–277)
Viral Load Suppression (<20 copies/mL)	973 (71%)
Study variables	M (SD, range)
T1: Internalized HIV Stigma	1.8 (0.7, 1–4)
T2: Depressive Symptoms (CES-D Total)	11.4 (11.1, 0–57)
T3: Pain (SF-36 pain subscale)[†]	28.0 (27.5, 1–100)

Note: Time 1 (T1), T2, T3 coincide with WIHS study visits occurring every 6 months.

* Self-reported use of marijuana/hash, crack or cocaine, heroin, illicit methadone, methamphetamines, amphetamines, hallucinogens, club drugs, tranquilizers, narcotics in the past 6 months.

[†] Reverse scored such that higher scores represent greater pain severity and interference.

CES-D: Center for Epidemiological Studies Depression Scale; SF-36: Short Form Health Survey; ART: antiretroviral therapy.

Table II.

Results of mediation analysis (N=1364).

Variables	Outcomes									
	Depressive Symptoms (CES-D)					Pain (SF-36 pain subscale)				
	Coefficient B	SE	Standardized β	<i>p</i>	Unstandardized 95% CI	Coefficient B	SE	Standardized β	<i>p</i>	Unstandardized 95% CI
Internalized HIV Stigma	4.90	0.47	0.29	<.001	3.98, 5.82	1.62 *	1.27	0.04	.20	-0.88, 4.08
Depressive Symptoms	---	---	---	---	---	0.75	0.08	0.31	<.001	0.60, 0.90
Total Effect *	---	---	---	---	---	5.30	1.21	0.13	<.001	2.84, 7.60
Indirect Effect	---	---	---	---	---	3.68	0.53	0.09	<.001	2.69, 4.79
Covariates										
Age	0.07	<0.01	0.05	.05	0, 0.13	0.53	0.08	0.17	<.001	0.37, 0.68
Race (0: White)	-0.40	0.59	-0.02	.50	-1.53, 0.78	-2.08	1.43	-0.04	.15	-4.87, 0.78
Income	-0.92	0.14	-0.17	<.001	-1.20, -0.64	-1.04	0.35	-0.08	.003	-1.75, -0.35
Recreational Drug Use (0: None)	4.18	0.73	0.15	<.001	2.77, 5.59	4.32	1.82	0.07	.017	0.87, 8.05
Months on ART	0.01	<0.01	0.04	0.14	-0.00, 0.01	<0.01	0.01	0.01	.71	-0.02, 0.02
Viral Load (0: Suppressed)	1.01	0.68	0.04	0.13	0.28, 2.38	-1.03	1.68	-0.02	.54	-4.30, 2.29

Notes: Results were estimated using Mplus 8.3 using full-information maximum likelihood estimation (FIML) with confidence intervals estimated via the percentile-corrected bootstrap based on 5,000 replicate samples.

* Direct effect of internalized HIV stigma on pain with depressive symptoms in the model. The Total Effect is the relationship between internalized HIV stigma and pain without controlling for depressive symptoms.

CES-D: Center for Epidemiological Studies Depression Scale; SF-36: Short Form Health Survey; ART: antiretroviral therapy.