Pain, Mood, and Substance Abuse in HIV: Implications for Clinic Visit Utilization, Antiretroviral Therapy Adherence, and Virologic Failure

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Background: Cooccurring pain, mood disorders, and substance abuse are common in HIV-infected patients. Our objective was to investigate the relationship between pain, alone and in the context of mood disorders and substance abuse, on clinic utilization, antiretroviral therapy adherence, and virologic suppression.

Methods: Pain, mood disorders, and substance abuse were assessed at the first visit. No-show and urgent visits were measured over a 1-year period. Models were adjusted for age, race, sex, insurance status, $CD4^+$ T-lymphocyte count, and HIV risk factor.

Results: Among 1521 participants, 509 (34%) reported pain, 239 (16%) had pain alone, 189 (13%) had pain and a mood disorder, and 30 (2%) had pain and substance abuse. In univariate models, participants with pain, mood disorders, and substance abuse had higher odds of a no-show visit than those without these conditions [odds ratio (OR), 1.4; 95% confidence interval (CI), 1.1–1.8; OR, 1.5; 95% CI, 1.2–1.9; OR, 2.0; 95% CI, 1.4–2.8, respectively]. In the multivariable model, pain increased the odds of a no-show visit only in participants without substance abuse (OR, 1.5; 95% CI, 1.1–1.9) and pain reduced the odds of a no-show visit in participants with substance abuse (OR, 0.5; 95% CI, 0.2–0.9; *P* for interaction = 0.0022).

Conclusions: In this study, pain increased the odds of no-show visits but only for participants without substance abuse. Because pain, mood disorders, and substance abuse are highly prevalent in HIV-infected patients, our findings have implications for HIV treatment success. Interventions that incorporate pain management may be important for improving health outcomes in patients living with HIV infection.

Key Words: HIV, pain, psychiatric illness, substance abuse, ART adherence, health care utilization

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INTRODUCTION

Clinically significant pain is common in patients with HIV infection. In a recent study of 154 ambulatory HIV-infected patients, 49% reported pain, of whom 51% had moderate-to-severe pain.[1] Other studies in HIV-infected patients have estimated pain prevalence to be between 39% and 55%.[2–7] Mood disorders and substance abuse are also common in patients with HIV infection. Prevalence estimates are as high as 41% for depression, 21% for anxiety, and 21% for substance abuse,[8–13] higher than that observed in the general population.[14,15] Moreover, patients with pain often experience mood disorders, especially depression and anxiety, and substance abuse.[16] However, studies describing the cooccurrence of pain and mood disorders or substance abuse among persons living with HIV infection are lacking.

In the modern treatment era, patients with HIV infection who consistently take antiretroviral therapy (ART) can achieve sustained virologic suppression and a near-normal life expectancy.[17] Thus, regular and consistent attendance at HIV primary care appointments (adherence to HIV primary care, or conversely, missed visits)[18,19] and consistent administration of ART (adherence to ART)[20–26] are of considerable importance across the HIV treatment cascade.[27,28] Adherence to HIV primary care visits has been associated with lower mortality,[18] and ART adherence has been associated with lower rates of virologic resistance,[20] improved virologic outcomes,[21,23] slower progression to AIDS, and improved survival.[9,13,24,26,29–35] Notably, patients with mood disorders and substance abuse have twice the odds of poor adherence to ART than those without these conditions,[29,36–38] and those with active substance abuse are half as likely to be adherent to HIV clinic visits.[39]

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Despite the high prevalence of pain in HIV-infected patients, the impact of pain, alone and in the context of mood disorders and substance abuse, on clinic visit utilization (including no-show and urgent visits), adherence to ART, and ultimately, virologic failure has not been well studied. Our objective was to test the hypothesis that pain is negatively related to these outcomes and that these effects are accentuated by mood disorders and substance abuse.

METHODS

Study Participants

The University of Alabama at Birmingham (UAB) 1917 Clinic Cohort is an ongoing prospective HIV clinical cohort protocol established in 1992 that has been described in detail previously (www.uabcliniccohort.org).[40] The cohort includes 1976 patients actively engaged in primary HIV medical care at the UAB 1917 HIV/AIDS Clinic. Of these patients, 1705 have provided informed consent to complete electronic Patient Reported Outcome (PRO) questionnaires.[40] PROs are standardized, validated, self-administered questionnaires that are integrated into routine clinical care. They are administered electronically to participants using touch-screen computers at primary care visits every 4–6 months at UAB.[40,41] Implemented in April 2008, the PRO assessment includes instruments that span a variety of domains including mood disorders, substance abuse, and quality of life, which includes the assessment of pain. The Cohort and this study were approved by the Institutional Review Board of UAB.

Data were captured prospectively during the study period, between April 2008 and June 2011. Inclusion criteria for this study included HIV infection, speaking and reading English, age $\geq$19 years at the date of the first completed PRO questionnaire during the study period, and having at least 1-year of follow-up until the end of the study period or death. Data from PRO questionnaires, the administrative scheduling system, the 1917 Clinic electronic medical record, and the 1917 Clinic Cohort electronic database were used to obtain values for independent variables, outcome variables, and covariates.

Independent Variables

Pain, mood disorders, and substance abuse were the principal independent variables of interest and were measured at the first visit during the study period during which a PRO questionnaire was completed, referred to as the index visit. Pain was measured using the EuroQOL, which includes a single question about pain "today." Participants' responses to this question were dichotomized as moderate/extreme discomfort versus no pain/discomfort.[42] A mood disorder was defined as the presence of depression, anxiety, or both. Participants with moderate, moderately severe, and severe depressive symptoms (Patient Health Questionnaire [PHQ]-9, $>$10) were considered to be depressed.[43,44] Participants with anxiety symptoms and panic syndrome (PHQ-A, $>$1) were considered to have anxiety.[45] Substance abuse was measured using the ASSIST questionnaire and categorized as current or prior/never.[46]

Outcome Variables

We studied 4 outcomes: (1) no-show visits, (2) urgent visits, (3) adherence to ART, and (4) virologic suppression. No-shows and urgent care visits were measured over a 1-year observation period after the index visit, and adherence and virologic suppression were measured at the index visit. ART adherence was measured using the Adult AIDS Clinical Trials Group questionnaire among participants who reported being on ART.[47] Based on recent guidelines that suggest patients should be asked to recall their adherence over a relatively short time frame,[48] evidence that suggests adherence in the low 90% range can adversely affect outcomes,[26,49] and prior studies that have used this approach,[50] participants who reported missing ART medications within the past 2 weeks were considered to have suboptimal adherence. Virologic failure was defined as an HIV viral load $\geq$200 copies per milliliter among participants who reported being on ART, in accordance with current guidelines.[51] Standard of care at the site included HIV primary care visits scheduled every 3–6 months. Urgent care visits are available on weekdays to patients with any pressing medical issue and are scheduled by a triage nurse. Having at least 1 no-show visit over 1 year has been associated with increased mortality in multiple settings.[18,52,53] Consistent with prior studies,[54] no-show visits were defined as scheduled HIV primary care visits the patient did not attend and did not call ahead to cancel. Individuals having any no-show primary HIV provider or having any urgent care visits for the year were considered to have met these dichotomized end points.

Covariates

Covariates were selected from a list of numerous potential covariates, including age, race, sex, insurance status, $CD4^+$ T-lymphocyte count, HIV transmission risk factor, and body mass index. Only body mass index was not consistently associated with our outcomes of interest; therefore, we included the remainder of the covariates in our models.

Statistical Analyses

Separate univariate and multivariable logistic regression models were built for each outcome. We first analyzed the main effects of pain, mood, and substance abuse on outcomes. Then, we evaluated the 2- and 3-way interactions between pain, mood, and substance abuse. These interaction terms formally assess whether the effect of pain, mood, and substance differ in the presence of the other. When the P value for the interaction was $<$0.2, we reviewed the consistency of the point estimates of the main effects and interaction models to determine whether the results should be stratified. When the P value for the interaction was $>$0.2 or when the point estimates were similar, we only considered the main effects.

Based on prior analyses from this cohort demonstrating interactions between race and sex (reference here), we stratified

race and sex into 4-categories: non-white female, non-white male, white female, white male.

RESULTS

As of the index date, participants had a median age of 44 years and were predominantly male, uninsured or had public insurance, had CD4$^+$ T-lymphocyte counts >350 cells per milliliter, and were virologically suppressed (Table 1). Pain was common, occurring in 34% of participants. Mood disorders occurred in 25% of participants, and substance abuse occurred in 10%. Pain, mood disorders, and substance abuse commonly cooccurred. In addition, of the of the 376 patients who reported moderate or extreme pain at the first PRO in the study period and who had a subsequent pain value in the study period, 255 (67.8%) again reported moderate or extreme pain.

No-Show Visits

In univariate models, participants with pain, mood disorders, and substance abuse had higher odds of a no-show visit than those without these conditions [odds ratio (OR), 1.4; 95% confidence interval (CI), 1.1–1.8; OR, 1.5; 95% CI, 1.2–1.9; OR, 2.0; 95% CI, 1.4–2.8, respectively]. There was a significant interaction between pain and substance abuse. In the multivariable model, pain increased the odds of a no-show visit only in participants without substance abuse (OR, 1.5; 95% CI, 1.1–1.9) and pain reduced the odds of a no-show visit in participants with substance abuse (OR, 0.5; 95% CI, 0.2–0.9, P for interaction = 0.0022). Similarly, substance abuse increased the odds of a no-show visit only in participants without pain (OR, 3.1; 95% CI, 1.8–5.3); for participants with pain, substance abuse had no impact on the odds of a no-show visit (OR, 0.9; 95% CI, 0.6–1.6, P value for interaction=0.0022). In the multivariable model, being a non-white female, non-white male, or white female, lack of insurance or public insurance, and a CD4 count of <200 or 200–350 cells per milliliter were also associated with higher odds of having at least 1 no-show. In contrast, increasing age was inversely associated with having a no-show (Table 2).

Urgent Visits

Participants with mood disorders had higher odds of an urgent visit than those without mood disorders (unadjusted OR, 1.8; 95% CI, 1.4–2.4; adjusted OR, 1.6; 95% CI, 1.2–2.2). The relationship between pain and having an urgent visit was present in the unadjusted model (OR, 1.6; 95% CI, 1.2–2.0) but only marginal in the adjusted model (OR, 1.3; 95% CI, 1.0–1.7). Substance abuse was not related to urgent visits in either the adjusted or unadjusted model. There was no evidence of interactions between pain, mood disorders, and substance abuse. In the multivariable model, having public insurance or a CD4 count of 200–350 cells per cubic millimeter were also associated with having an urgent visit (Table 3).

ART Adherence

Participants with mood disorders and substance abuse had higher odds of suboptimal ART adherence than those without these disorders (unadjusted OR, 2.1; 95% CI, 1.6–2.9 and adjusted OR, 2.2; 95% CI, 1.5–3.2; adjusted OR, 3.1; 95% CI, 2.0–4.8 and adjusted OR, 2.8; 95% CI, 1.7–4.6, respectively). The relationship between pain and adherence was small in the unadjusted model (OR, 1.4;

TABLE 1. Characteristics of 1521 HIV-Infected Patients Seen for Outpatient Medical Care at the UAB HIV Clinic, April 2008–June 2011

Characteristic	Sample (N = 1521)
Age, yr	43.7 (36.0–50.0)
Sex × race/ethnicity, n (%)	
Non-white female	244 (16.1)
Non-white male	548 (36.2)
White female	96 (6.4)
White male	624 (41.3)
Health insurance, n (%)	
Uninsured	468 (30.9)
Public	454 (29.9)
Private	594 (39.2)
CD4$^+$ T-lymphocyte count (cells/mL)	445 (270–648)
<200, n (%)	259 (17.1)
200–350, n (%)	289 (19.1)
>350, n (%)	963 (63.7)
HIV transmission risk factor, n (%)	
Injection drug use	141 (9.3)
Men who have sex with men	835 (54.9)
Other/unknown	15 (1.0)
Heterosexual	530 (34.9)
Pain, n (%)	509 (33.9)
Mood, n (%)	383 (25.2)
Substance abuse, n (%)	153 (10.1)
Pain-mood-substance categories, n (%)	
Only pain	239 (16.0)
Only mood	115 (7.7)
Only substance abuse	47 (3.2)
Pain and mood	189 (12.7)
Pain and substance	30 (2.0)
Mood and substance	24 (1.6)
Pain, mood, and substance	46 (3.1)
None	800 (53.7)
Outcome variables, n (%)	
≥1 no-show visit	624 (41.0)
≥1 urgent visit	390 (25.6)
Skip ART past 2 weeks (adherence)	220 (19.0)
HIV RNA ≥200 copies/mL	309 (37.2)

Data are presented as medians and interquartile ranges or frequencies (column percent). Age and health insurance measured at the index visit. HIV RNA and CD4$^+$ T-lymphocyte count measurements were the value closest to the index visit, with a window of −210 to +14 days. No-show and urgent visits were measured over 1-year period after index visit. Missing data: race/sex, 9; insurance status, 5; CD4$^+$ T-lymphocyte count, 10; pain, 21; substance abuse, 11; adherence, 10 (plus 353 not on ART); HIV RNA ≥200 copies/mL, 18 (plus 353 not on ART).

TABLE 2. No-Show Visits

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Pain	**1.4 (1.1–1.8)**	—
With substance abuse*	—	**0.5 (0.2–0.9)**
Without substance abuse†	—	**1.5 (1.1–1.9)**
Mood disorder	**1.5 (1.2–1.9)**	1.3 (1.0–1.7)
Substance abuse	**2.0 (1.4–2.8)**	—
With pain‡	—	0.9 (0.6–1.6)
Without pain§	—	**3.1 (1.8–5.3)**
Age (per 10 years)	**0.7 (0.6–0.8)**	**0.7 (0.6–0.8)**
Sex and race/ethnicity		
Non-white female	**2.4 (1.7–3.2)**	**2.4 (1.6–3.7)**
Non-white male	**2.6 (2.1–3.3)**	**2.2 (1.7–2.9)**
White female	**2.0 (1.3–3.2)**	**1.8 (1.0–3.1)**
White male	1.0	1.0
Health insurance		
None	**2.5 (1.9–3.2)**	**1.6 (1.2–2.1)**
Public	**2.5 (1.9–3.2)**	**2.0 (1.5–2.7)**
Private	1.0	1.0
Baseline $CD4^+$ T lymphocyte count (cells/mL)		
<200	**2.2 (1.7–2.9)**	**1.7 (1.2–2.3)**
200–350	**1.6 (1.2–2.1)**	**1.6 (1.2–2.1)**
>350	1.0	1.0
HIV transmission risk factor		
Intravenous drug use	1.2 (0.8–1.7)	1.3 (0.9–2.1)
Men who have sex with men	**0.7 (0.6–0.9)**	1.0 (0.7–1.4)
Other/unknown	**5.0 (1.4–17.9)**	2.6 (0.7–9.8)
Heterosexual	1.0	1.0

Event: At least 1 HIV primary care no-show visit during the year following the index visit. Bolded results are statistically significant. Adjusted model contains all variables shown here.

*n = 76/147 (51.7%) (among participants with substance abuse, proportion with pain).

†n = 428/1343 (31.9%) (among participants without substance abuse, proportion with pain).

‡n = 76/504 (15.1%) (among participants with pain, proportion with substance abuse).

§n = 71/986 (7.2%) (among participants without pain, proportion with substance abuse).

TABLE 3. Urgent Visit Utilization

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Pain	**1.6 (1.2–2.0)**	1.3 (1.0–1.7)
Mood disorder	**1.8 (1.4–2.4)**	**1.6 (1.2–2.2)**
Substance abuse	1.4 (1.0–2.0)	1.1 (0.7–1.6)
Age (per 10 years)	1.0 (0.9–1.1)	1.0 (0.8–1.1)
Sex and race/ethnicity		
Non-white female	1.2 (0.8–1.6)	1.4 (0.9–2.1)
Non-white male	0.9 (0.7–1.1)	0.9 (0.7–1.3)
White female	1.0 (0.6–1.6)	0.8 (0.5–1.5)
White male	1.0	1.0
Health insurance		
None	**1.4 (1.0–1.8)**	1.2 (0.9–1.7)
Public	**1.6 (1.2–2.2)**	**1.4 (1.0–1.9)**
Private	1.0	1.0
Baseline CD4+ T lymphocyte count (cells/mL)		
<200	1.4 (1.0–1.9)	1.3 (1.0–1.8)
200–350	**1.6 (1.2–2.2)**	**1.7 (1.2–2.3)**
>350	1.0	1.0
HIV transmission risk factor		
Intravenous drug use	**1.7 (1.1–2.5)**	1.5 (0.9–2.4)
Men who have sex with men	1.0 (0.8–1.3)	1.1 (0.7–1.5)
Other/unknown	0.2 (0.03–1.7)	0.2 (0.02–1.3)
Heterosexual	—	—

Event: At least 1 urgent visit during the year after the index visit. Bolded results are statistically significant. Adjusted model contains all variables shown here.

95% CI, 1.1–1.9 and absent in the adjusted model OR, 1.2; 95% CI, 0.8–1.7). There was no evidence of interaction between pain, mood disorders, and substance abuse. In the multivariable model, being a non-white female, non-white male, or white female was also associated with suboptimal ART adherence (Table 4).

Virologic Failure (Viral Load ≥ 200 Copies/mL)

There was no relationship between pain, mood, and substance abuse and virologic failure (unadjusted OR, 1.2; 95% CI, 0.9–1.5 and adjusted OR, 1.1; 95% CI, 0.8–1.5; unadjusted OR, 1.2; 95% CI, 0.9–1.7 and adjusted OR, 1.1; 95% CI, 0.8–1.6; unadjusted OR, 1.4; 95% CI, 0.9–2.1 and adjusted OR, 1.1; 95% CI, 0.7–1.8). There was no evidence of interaction between pain, mood disorders, and substance abuse. In the multivariable model, being a non-white male, having a $CD4^+$ T-cell count <200 cells per cubic millimeter, and having a $CD4^+$ T-cell count between 200 and 350 cells per cubic millimeter were associated with virologic failure (Table 5).

DISCUSSION

In our study, pain increased the odds of no-show visits but only for participants without substance abuse. In the subset of participants with substance abuse, who are traditionally difficult to retain in HIV primary care, pain actually appeared to be protective against no-show visits. By affecting no-show visits, an important step in the HIV treatment cascade, pain has important implications for individual and public health outcomes. No shows are a marker of retention in HIV primary care,[54] and the importance of retention in HIV primary care has been increasingly recognized. Retention is prominently featured in recent HIV guidelines[48] and in the US National HIV/AIDS Strategy.[55]

There are numerous potential explanations for our findings about the relationship of pain to no-show visits. In patients without substance abuse, pain increases the risk of a no-show. We hypothesized that pain would negatively affect no-show visits, as patients with pain may feel too sick to come to an HIV primary care visit or prioritize HIV primary care lower than pain relief, which they can achieve outside the context of an HIV primary care visit. However, we found the opposite: patients with substance abuse are actually more likely to attend an HIV primary care visit if

TABLE 4. Adherence to Antiretroviral Therapy

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Pain	**1.4 (1.1–1.9)**	1.2 (0.8–1.7)
Mood disorder	**2.1 (1.6–2.9)**	**2.2 (1.5–3.2)**
Substance abuse	**3.1 (2.0–4.8)**	**2.8 (1.7–4.6)**
Age (per 10 years)	0.9 (0.8–1.0)	0.9 (0.8–1.1)
Sex and race/ethnicity		
Non-white female	**2.3 (1.5–3.5)**	**2.4 (1.4–4.3)**
Non-white male	**1.7 (1.2–2.4)**	**1.9 (1.3–2.8)**
White female	**0.3 (0.1–1.0)**	**0.3 (0.1–1.0)**
White male	1.0	1.0
Health insurance		
None	1.3 (0.9–1.8)	1.0 (0.7–1.5)
Public	1.1 (0.8–1.6)	0.9 (0.6–1.3)
Private	1.0	1.0
Baseline $CD4^+$ T lymphocyte count (cells/mL)		
<200	1.4 (1.0–2.1)	1.1 (0.7–1.6)
200–350	1.0 (0.7–1.5)	1.0 (0.7–1.5)
>350	1.0	1.0
HIV transmission risk factor		
Intravenous drug use	0.6 (0.3–1.0)	0.6 (0.3–1.1)
Men who have sex with men	0.8 (0.6–1.1)	0.9 (0.5–1.4)
Other/unknown	0.7 (0.2–3.3)	0.4 (0.1–2.0)
Heterosexual	1.0	1.0

TABLE 5. Virologic Failure

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Pain	1.2 (0.9–1.5)	1.1 (0.8–1.5)
Mood disorder	1.2 (0.9–1.7)	1.1 (0.8–1.6)
Substance abuse	1.4 (0.9–2.1)	1.1 (0.7–1.8)
Age (per 10 years)	**0.9 (0.8–1.0)**	0.9 (0.8–1.1)
Sex and race/ethnicity		
Non-white female	1.0 (0.7–1.6)	1.2 (0.7–2.0)
Non-white male	**1.6 (1.2–2.2)**	**1.4 (1.0–2.0)**
White female	0.9 (0.5–1.7)	1.0 (0.5–2.0)
White male	1.0	1.0
Health insurance		
None	1.2 (0.9–1.7)	0.9 (0.6–1.2)
Public	1.3 (1.0–1.8)	1.1 (0.8–1.5)
Private	1.0	1.0
Baseline CD4+ T lymphocyte count (cells/mL)		
<200	**3.7 (2.6–5.2)**	**3.3 (2.3–4.8)**
200–350	**1.8 (1.3–2.5)**	**1.8 (1.3–2.5)**
>350	1.0	1.0
HIV transmission risk factor		
Intravenous drug use	0.8 (0.5–1.4)	0.9 (0.5–1.6)
Men who have sex with men	1.0 (0.8–1.4)	1.1 (0.8–1.7)
Other/unknown	2.7 (0.9–8.6)	1.9 (0.5–6.3)
Heterosexual	1.0	1.0

Event: Failure to suppress virus (viral load ≥ 200) at the index visit. Bolded results are statistically significant. Adjusted model contains all variables shown here. Models are based on the subset of patients who reported being on ART (n = 1168).

they have pain. It is possible that patients with substance abuse may have more severe and difficult to control pain, as prior substance use may be associated with increased pain severity.[56] As a result, patients with a history of substance abuse may be more likely to keep their HIV primary care appointments because they plan to seek help for their pain from their HIV primary care provider. If opioids are prescribed for pain, this may necessitate a clinic visit, as many opioid prescriptions cannot be called into pharmacies. The mechanism behind these complex associations between pain, substance abuse, and no-show visits should be investigated, as it has potential to be used in retention interventions for patients with pain, with and without substance abuse. Such interventions would likely require multidisciplinary and multifaceted components to address patients' pain and substance abuse.

It is unclear whether the pain patients report in this study is acute or chronic. Although we did not specifically ask participants about chronic pain, we found that of the 376 patients who reported moderate or extreme pain at the first PRO in the study period and who had a subsequent pain value in the study period, 255 (67.8%) again reported moderate or extreme pain. This suggests that these patients may have chronic pain. The strongest evidence for effective chronic pain management comes from interdisciplinary approaches that incorporate physical rehabilitation and psychological therapies, in addition to pharmacologic management.[57] Recent evidence suggests that HIV primary care providers often use opioids to manage chronic pain[58] and often feel uncomfortable and inadequately trained to do so.[59] HIV providers and clinics need to be able to access additional resources, either within their clinic or in the larger local community, to address the pain needs of their patients.

This study is one of many studies that confirm the high prevalence of pain among patients with HIV.[1–4] In addition, this study is the first to examine pain's downstream effects. Many other conditions, such as the metabolic syndrome and renal disease, are prevalent in patients with HIV, have negative downstream effects, and as a result, have been identified as important targets of early treatment.[51] We posit that pain's protective effect against no-show visits also makes it an important target for investigation. The effect of treating pain, in particular in patients with substance abuse, is unclear. As pain is protective against no shows, it is possible that improving patients' pain could result in more no-shows. This does not undermine the need to treat pain, but rather, draws attention to the importance of doing so in a way that does not have unintended consequences. Research into evidence-based approaches to pain management in patients with HIV is lacking.

Consistent with prior results, we also found that mood disorders and substance abuse were associated with worse outcomes. Mood disorders were associated with higher odds of an urgent visit, both mood disorders and substance abuse were associated with higher odds of suboptimal adherence, and substance abuse was associated with higher odds of no-show visits in participants without pain. Development of pain-based interventions must explore the substantial impact

of mood disorders and substance abuse and consider the importance of these conditions as part of the intervention. Furthermore, in our multivariable analyses, younger age, being non-white, no insurance or public insurance, and lower CD4 counts were associated with worse outcomes. This is consistent with prior findings regarding retention[18] and adherence[60] in HIV-infected patients, highlighting the importance of these behaviors as contributors to health care disparities in HIV outcomes.

This study has limitations. The EuroQOL questionnaire assessed pain "today" and did not distinguish between acute pain, such as pain related to recent injury, and chronic pain, which is defined as persistent pain that lasts longer than 3 months.[61–64] Future prospective studies should capture data to differentiate and specifically evaluate the role of chronic pain in HIV-related outcomes. In addition, this study does not address issues of causality or the mechanisms by which pain, mood disorders, and substance abuse affect outcomes. Future studies using quantitative and qualitative means should explore the mechanisms by which these associations occur. These studies may provide insight into how to develop interventions to improve engagement in HIV primary care in patients with HIV and pain.

Because pain, mood disorders, and substance abuse are highly prevalent in HIV-infected patients, our findings have implications for HIV treatment success. Our findings suggest that interventions that incorporate pain management should be investigated, as they may be important for improving health outcomes in patients living with HIV infection.

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