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The mediating role of pain in substance use and depressive symptoms among Multicenter AIDS Cohort Study (MACS) participants

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Abstract

Pain in HIV frequently co-occurs with substance use and depression. The complex associations among patient characteristics, pain, depression, and drug use in HIV suggests a role for testing models that can account for relationships simultaneously, control for HIV status and also test for mediation. Using structural equation modeling (SEM), the current study examined associations among pain, sociodemographics, illicit drug use and depressive symptoms in 921 HIV seropositive and 1,019 HIV seronegative men from the Multicenter AIDS Cohort Study (MACS), an ongoing prospective study of the natural history of HIV infection among gay/bisexual men. Longitudinal repeated measures data collected over a 6 year period were analyzed using predictive path models in which sociodemographics, HIV status and CD4+ cell counts predicted pain which in turn predicted depressive symptoms and illicit drug use. The path models did not differ substantially between HIV seropositive and seronegative men. Analyses using the total sample indicated that pain served both as a mediator and as a predictor of more use of cannabis, cocaine and heroin, as well as more depressive symptoms. HIV seropositive status predicted more use of inhaled nitrites. In this cohort, having lower CD4+ cell counts (predicted by HIV status), being African-American, less educated, and older were all associated with more pain which in turn was associated with more illicit drug use and more depressive symptoms. The results underscore the

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Pain partially mediated the association between sociodemographic/clinical characteristics and illicit drug use/depressive symptoms in a longitudinal cohort of HIV seropositive and HIV seronegative men.

need for adequate pain management, particularly among vulnerable subgroups of HIV seropositive and HIV seronegative men to reduce the risk of drug use and depression.

Keywords

substance use; depression; HIV; pain; drug use

1. Introduction

Pain is a common occurrence among persons living with HIV—67% of a nationally representative sample of HIV seropositive persons in the United States (US) reported experiencing pain in the past month [16]. Investigation of the correlates of pain in HIV has highlighted the frequent co-occurrence of pain with both psychological problems and illicit drug use [17,18,55]. Pain in HIV seropositive persons is exacerbated when there is a coexisting psychological disorder [22,47,52,57], particularly depression [22,32,33]. Injection drug use (IDU) [15,23,37,60], as well as use of other illicit drugs (not just IDU) have also been associated with increased pain in HIV [58]. Efforts to identify which patients are more vulnerable to pain as well as depression and substance use, have indicated some common clinical and sociodemographic characteristics. For example, more advanced HIV disease has been associated with both increased pain [2,7,8 16,22,28,50,51], and with higher rates of depression (e.g., [38; 21]). Similarly, lower socioeconomic status (SES) has been linked with more pain [58; 41] and also with increased illicit drug use [58] in HIV seropositive persons.

These findings suggest that the observed relationships among clinical/sociodemographic characteristics, pain, depression, and drug use in HIV may be part of a more complex sequence of effects. Yet, previous research has rarely employed models that go beyond simple correlational designs. The goal of a mediational model is to clarify the mechanism through which an initial variable (e.g., SES) affects an outcome (e.g., drug use) via a third explanatory or mediator variable [36]. We propose a conceptual model in which pain acts as a mediator between clinical/sociodemographic characteristics and depressive symptoms/ drug use (see Figure 1). Our mediational model tests whether certain patients are more vulnerable to pain, and whether pain in turn leads to depressive symptoms and drug use. If confirmed, our model may assist in the targeting of pain interventions to patient subgroups with the aim of reducing pain, depression and drug use.

In order to disentangle the associations among the variables in terms of the impact of HIV-positivity on these behaviors, we also tested the proposed model in a control group of HIV seronegative persons. Few prior studies have examined whether the strength of such relationships is altered or moderated by HIV status. HIV status therefore functioned as a moderator variable in our analyses. Inclusion of an HIV seronegative control group may also provide information on the mediating role of pain in non-HIV infected populations (e.g., persons suffering from other health conditions). We used structural equation modeling (SEM) to test our conceptual model in a longitudinal sample of HIV seropositive and seronegative gay/bisexual men enrolled in the Multicenter AIDS Cohort Study (MACS). We hypothesized that HIV seropositivity as well as key clinical and sociodemographic characteristics would predict more pain which would in turn be associated with more depressive symptoms and more drug use.

2. Method

2.1 Participants and procedures

Participants were enrolled in the Multicenter AIDS Cohort Study (MACS), an ongoing prospective study of the natural and treated histories of HIV infection among homosexual and bisexual men in the United States. A total of 6972 men were recruited (4954 in 1984–1985, 668 in 1987–1991, and 1350 in 2001–2003) at four centers: Baltimore/Washington DC; Chicago; Los Angeles; and Pittsburgh. The study design has been described in more detail previously [19,31]. MACS study protocols were approved by the institutional review boards of each of the participating centers, their community partners, and community advisory boards. Informed consent was obtained from all participants.

This study used longitudinal repeated measures data from the MACS and included 1940 recent participants available in the last 12 waves of data collection (1019 HIV− men, 921 HIV+ men). MACS participants return every 6 months for detailed interviews, physical examinations, and collection of blood for laboratory testing and storage in a central repository. The interview includes questions about medical conditions, medical treatments, emotional distress, and various health-related behaviors including illicit drug use (defined below) and pain perceptions. Because of the voluminous quantity of measures in this study, pertinent variables from the 12 study visits (April 1, 2003-March 31, 2009) were combined by twos to yield 6 contiguous study visit means used in the current study. If systematic change over time was detected, we planned to use a latent growth modeling approach. However, because no significant change was detected by latent growth models over the time period among the variables selected for this study (see means reported in Table 1), we used the individual repeated measures as indicators of over-arching latent variables which we felt could better capture the underlying long-term relations among the constructs in the model [14].

2.2 Measures

Single item demographic variables—Age, education and ethnicity were included as baseline demographic correlates and predictors. Following the recommendations of Edwards et al [20], we use the term “ethnicity” to describe groups of participants in this study. According to Edwards et al., ethnicity is based on distinguishing behaviors, culture, history, experience, ancestry, and beliefs. Consequently, ethnicity includes what is usually called “race”, as well as characteristics that are of social, psychological, cultural, and political nature. Age was reported in years (the average age for the whole sample was 45.9 years at the start of the first assessment point of this current study). Education was assessed categorically on a 1–7 scale: 1 = 8th grade or less, 2 = 9, 10, or 11th grade, 3 = 12th grade, 4 = At least one year college, but no degree; 5 = Four years of college/got degree, 6 = Some graduate work; 7 = Post-graduate degree. White or Black ethnicity were coded as separate yes/no variables (1 = yes; 0 = no); all other ethnic groups (Hispanics, Asians/Pacific Islanders, Native Americans) were used as the reference group. The sample was 64% White, 25% Black, and 11% Other.

CD4+ Cell Count—T-lymphocyte subset levels were quantified at each study visit using standardized flow cytometry [25,49].

Pain—The bodily pain scale of the Short-Form 36 (SF-36), a widely used and psychometrically verified instrument [27,54], assessed self-reported pain. A latent variable for Pain was indicated by the mean of responses to the 2 scale items: 1) “During the *past four weeks*, how much did pain interfere with your normal work (including work outside the house and housework)?” Responses ranged from “Not at all” = 1, to “extremely” = 5; 2)

How much bodily pain have you had during the *past four weeks*? Responses ranged from "none" = 1 to "very severe" = 6. Thus, there were 6 repeated measures indicators for Pain (mean of the two items at assessment waves 1 and 2, up to assessment waves 11 and 12). Coefficient alpha for the 2 scales = .93, which indicated that combining the responses was acceptable.

Depressive Symptoms—Depressive symptoms were assessed with the Center for Epidemiological Studies Depression (CES-D) scale [45]. The 20-item self-report instrument is designed to measure depressive symptomatology in the general population. Each item measures the frequency of a symptom during the past week on a 4-point response scale from 0 to 3 ranging from "Rarely or none of the time (Less than 1 day)" to "Most of the time (5–7 days). Examples of CES-D items are "I felt depressed," and "I felt fearful." The scale was summed; higher scores indicate more depressive symptoms.

Illicit Drug Use—Drug use was considered illicit if the drugs appeared on the US Drug Enforcement Administration (DEA) list of controlled substances. In the current study, illicit drug use included cannabis (marijuana), heroin, cocaine, including its base form known in the US as crack cocaine, and inhaled nitrites (i.e., butyl or isopropyl nitrites inhaled for recreational purposes; also known as "poppers"). The following drugs are referred to using their vernacular form: marijuana, crack cocaine, heroin. The frequency of participants' use of illicit drugs since their last study visit was assessed on a 0–4 scale as follows: 0 = None, 1 = Daily, 2 = Weekly, 3 = Monthly, 4 = Less often. Items were rescaled so that responses ranged from 0 = none to 4 = daily.

2.3 Statistical analysis

Confirmatory Factor Analysis—Latent variable structural equation modeling (SEM) was performed using the EQS SEM program [4]. The robust comparative fit index (RCFI), and Satorra-Bentler robust chi-square values (S-B χ^2), were used as indicators of fit [4,29] due to the very high multivariate kurtosis in the data set (normalized estimate = 945.12). The RCFI compares the improvement of fit of a hypothesized model to a model of complete independence among the measured variables. The RCFI ranges between 0 and 1; values greater than or equal to .95 indicate a good fit [4,29]. As an additional indicator of fit, we also report the Root Mean Square Error of Approximation (RMSEA). The RMSEA is a measure of fit per degrees of freedom, controlling for sample size; values less than .06 indicate a relatively good fit between the hypothesized model and the observed data [29].

An initial confirmatory factor analysis (CFA) was performed for the entire sample and also separately for each group of men (HIV seropositive and HIV seronegative) with each hypothesized latent construct indicated by its measured indicators. All latent constructs, and the single-item variables were correlated with no imputation of causality or temporal ordering in the CFA. This analysis assessed the adequacy of the proposed factor structure and the relations among the latent and measured variables. This analysis was used in the next stage which compared the HIV-seropositive men and the HIV-seronegative men with multi-sample models. This analysis tested whether the entire sample related similarly to the items and could be used in a single path analysis or, alternatively, needed to be evaluated in two separate path analyses assessing the impact of reported pain on drug use and depressive symptoms. If relations were substantially different, then 2 path models would be warranted. To improve fit, we allowed a few correlated error residuals (auto-correlations only) between the same substances over time if they were suggested by the LaGrange Multiplier (LM) Test [12]. Because associations among the latent variables of Crack Cocaine Use, Other Cocaine Use, and Heroin Use were very high, a second-order factor was hypothesized to account for the substantial relationship among those items [4]. This alternative formulation was tested in

the analysis and found to be superior to keeping the primary latent variables separate in terms of overall model fit. This second-order factor is labeled using the vernacular term, “Hard Drug Use.” Thus, Crack Cocaine Use, Other Cocaine Use, and Heroin Use are referred to collectively as Hard Drug Use, as these drugs are listed as Schedule I and II controlled substances in the US by the DEA indicating high abuse potential. In the analyses, Crack Cocaine Use, Other Cocaine Use, and Heroin Use constitute first order latent variable indicators of the second order factor of Hard Drug Use. Marijuana and Inhaled Nitrites Use were kept as separate latent variables in the analyses.

Multisample models—Covariance structure analysis has become the method of choice for assessing the comparability of measures in different groups through the testing of measurement invariance with varying and successive degrees of stringency across groups [53,62]. Using this methodology, one can specify an *a priori* factor model in two groups and test it for various degrees of invariance using structural modeling. Furthermore, structured means models can be used to assess the equivalency of the latent means of the factors across the groups [4]. Establishing factorial invariance does not necessarily mean that different groups will report the same mean scores on a particular measurement instrument. Even if factor structures are similar across different groups, one group may report significantly higher means than the other group [26,53]. For instance, we would expect CD4+ counts to be substantially higher among the men who are HIV seronegative.

We contrasted the two groups on their factor structures, covariances among the constructs, and also on their latent means. We began by specifying an initial baseline model with no constraints that was used for comparison purposes. We then tested a model in which their factor structures were constrained to equality. Subsequently, we constrained the covariances among the latent variables to equality and tested whether they were significantly different in the two groups. These constrained covariances (correlations) would test whether there are differential associations between reported pain and use of various illicit drugs among the HIV seropositive and HIV seronegative men. In addition, following the test that constrained the measurement model (factor structure) to equality, we assessed differences in latent construct means. The tenability of the successively more stringent set of constraints was assessed with the goodness-of-fit indexes described above, χ^2 difference tests, and results from the LM test [12], which in this context identifies constraints that are untenable.

Path model

A predictive path model was tested for the entire sample and for each group separately in which baseline characteristics of age, ethnicity, education, and CD4+ cell counts across the 6 assessment periods predicted Pain which in turn would be associated with Depressive Symptoms, and use of Marijuana, Hard Drugs, and Inhaled Nitrites. This initial model was testing full mediation by the Pain latent variable to assess the amount of variance Pain alone could account for in the outcome variables. Because other variables in the model were expected to impact the outcomes as well (e.g., age, Black ethnicity, etc.), supplementary relationships between the baseline characteristics and the outcome variables were added based on suggestions from the LM test once the contribution of Pain was assessed. Non-significant paths were dropped until only significant paths remained. In the combined sample, HIV status was added as a predictor of CD4+ cell counts and a correlate of the other predictors.

3. Results

3.1 Confirmatory factor analyses

All measured variables loaded significantly ($p < 0.001$) on their hypothesized latent factors. Fit of the model for the total sample was very good: S-B χ^2 (1266, $N = 1940$) = 2439.24, RCFI = 0.96, RMSEA = 0.024 (90% confidence interval = .023–.026). Fit indexes were good for each separate group as well: HIV+ men: S-B χ^2 (1221, $N = 921$) = 1854.09, RCFI = 0.95, RMSEA = 0.026 (90% confidence interval = .023–.028). HIV- men: S-B χ^2 (1221, $N = 1019$) = 1599.61, RCFI = 0.97, RMSEA = 0.019 (90% confidence interval = .017–.022). Degrees of freedom are higher for the total sample because an additional variable representing HIV+ or negative status was included in that analysis. Table 1 reports summary statistics for the measured variables and factor loadings of the latent variables for each group.

Table 2 reports correlations among all variables in the model stratified by HIV status. Of note, the main variable of interest, Pain, was highly associated with more Depressive Symptoms, and more modestly but significantly with Hard Drug Use in both samples. Pain was significantly associated with Marijuana Use among the HIV seropositive men (.11, $p \leq .01$) but not among the HIV seronegative men. Pain was unrelated to CD4+ cell count among HIV seronegative men (.00) but a lower CD4+ cell count was significantly associated with more pain among HIV seropositive men (−.12, $p \leq .001$). More pain was reported among older HIV seronegative men and among Black HIV- men. Less education was associated with more pain in both samples (−.09 for negatives, −.14 for positives). In addition, being Black was associated with more Hard Drug Use; being White was associated with more Inhaled Nitrites Use, being Black with less Inhaled Nitrites Use.

3.2 Multiple group analyses

Constrained factor structure—The unconstrained multisample model served as the baseline (S-B χ^2 (2442) = 3422.81, RCFI = 0.96). When the factor structures were constrained to equality, there was no significant decrement in fit in terms of the chi-square difference between the two models (adjusted χ^2-square difference (42 *df*) = 31.15). Thus, we were able to assume equal factor structures for the two groups and to proceed to the next level of stringency by constraining the covariances (correlations) between the constructs to equality.

Constrained covariances—The more constrained model in which the covariances among the latent variables and also with the single item variables were constrained to equality across the groups also did not have a significant increase in its chi-square value (adjusted χ^2-difference (87 *df*) = 81.70). However, some individual covariances differed significantly in the two groups ($p \leq .01$). Because we were interested in substantive differences between the groups even if the overall difference between the two groups was non-significant, we report the significant differences in Table 2 (see bold-face, italicized correlations). Most significant differences were associations with sociodemographics rather than differences among the latent variables. Depressive Symptoms had a lower association with Black ethnicity among HIV seropositive men than among HIV seronegative men (.09 vs. .21); being Black was less associated with Hard Drug Use among HIV seropositive men (.39 vs. .50) although overall, Black ethnicity was substantially associated with more Hard Drug Use in both groups than in Whites. White HIV seropositive men had higher associations with Inhaled Nitrites Use than White HIV seronegative men (.32 vs. .16). Hard Drug Use was less negatively associated with age among HIV seropositive men than among HIV seronegative men (−.12 vs. −.21). White HIV seronegative men reported less use of Hard Drugs than White HIV seropositive men (−.45 vs. −.30). There were some significant

age differences in the racial distributions of the 2 samples as well. Of most substantive interest, there were no significant group differences concerning the associations with pain, although as reported below and in Table 1, HIV seropositive men reported more pain than HIV seronegative men.

Latent means comparisons—Table 1 reports the results of the latent means comparisons. There were significant differences between the latent means of the two groups in almost all of the variables. Not surprisingly, the HIV seronegative men had significantly higher CD4+ cell count. The HIV seropositive men reported more pain, more marijuana use, more crack cocaine use, more other cocaine use, more depressive symptoms, more inhaled nitrites use, and, overall, more hard drug use. There were no differences in heroin use, which was infrequently reported in both groups. Single-item sociodemographics were also contrasted in this analysis. The HIV seropositive men were proportionally more likely to be Black, less educated, and younger.

3.3 Path model

The separate group path models were highly similar. We thus for simplicity and ease of reporting present one path model that combined both groups and also includes their HIV status as a further predictor and correlate. The fully mediated initial path model that only had Pain as a predictor of the outcomes had an acceptable fit: S-B χ^2 (1290, N = 1940) = 2527.57, RCFI = .96, RMSEA = 0.025 (90% confidence interval = .023–.026). Although Pain was a significant predictor of the outcomes, it explained only 1% of the variance in Marijuana Use, 2% of Hard Drug Use, and less than 1% of Inhaled Nitrites Use. It explained 27% of the variance in Depressive Symptoms. After model modification in which non-significant paths and covariances were dropped and other significant paths were added based on suggestions from the LM test (i.e., paths from age, Black ethnicity, education, and CD+4 cell count to the outcomes), the fit indexes improved: S-B χ^2 (1288, N = 1940) = 2290.08, RCFI = 0.96, RMSEA = 0.022 (90% confidence interval = .021–.024). Figure 2 depicts the results of the path analysis with only significant paths included. This model explained 4% of the variance in Marijuana Use, 33% of the variance in Depressive Symptoms, 24% of the variance in Hard Drug Use, and 6% of the variance in Inhaled Nitrites Use; HIV seropositivity predicted a lower CD4+ count and a higher CD4+ cell count predicted less Pain. Being older, Black and less educated predicted more Pain. Pain was associated with more Marijuana Use, more Hard Drug Use, and considerably more Depressive Symptoms. In this model, in addition to its substantial associations with the other baseline characteristics (see Figure 2), being HIV seropositive predicted more use of Inhaled Nitrites. Black ethnicity predicted more Hard Drug Use; White ethnicity predicted more use of Inhaled Nitrites and fewer Depressive Symptoms. Age predicted fewer Depressive Symptoms. Less education was associated with more Marijuana and Hard Drug Use.

There were several significant indirect effects including a significant effect of HIV seropositivity on Pain, mediated through CD4+ cell count ($p \leq .001$). In addition, a lower CD4+ cell count had a significant effect on more Marijuana and Hard Drug Use ($p \leq .05$), and greater Depressive Symptoms ($p \leq .001$) mediated through Pain. Positive HIV status had significant indirect effects on Marijuana Use and Hard Drug Use ($p \leq .05$), and on Depression ($p \leq .001$) mediated through its effect on a low CD4+ cell count which in turn predicted more Pain.

4. Discussion

Consistent with the hypothesized conceptual model, our results demonstrated that in a large sample of HIV+ and HIV- gay/bisexual men enrolled in the MACS, pain served as a

mediator between key clinical/sociodemographic characteristics and both depressive symptoms and illicit drug use (see Figure 2). Overall, having a lower CD4+ cell count, being older, being Black, and having less education predicted more pain which in turn was associated with more marijuana use, more hard drug use (i.e., use of crack cocaine, other cocaine and heroin), and more depressive symptoms. The final model predicted 33% of the variance in depressive symptoms and 34% of the variance in drug use (combined across all drug categories). Being HIV seropositive predicted a lower CD4+ cell count and more use of inhaled nitrites. The predictive path models we tested indicated that the pattern of associations among the study variables were similar across HIV status. Our latent means comparisons indicated however, that relative to HIV seronegative men, HIV seropositive men reported more pain and more depressive symptoms, as well as more use of a variety of drugs (i.e., marijuana, crack cocaine use, cocaine use, inhaled nitrites) (see Table 1). Our results derive from longitudinal data from four study sites representing major population centers in the US that comprise the MACS. A further strength of this analysis is our use of repeated measures data extended over 6 years which gives us additional confidence in the robustness of our results.

Our findings are consistent with prior work in a US national sample of HIV seropositive individuals which indicated that use of a broad range of illicit drugs (not just IDU) predicted worse illness burden (i.e., lower CD4+ cell count and presence of wasting syndrome) which in turn predicted more pain. This earlier study also found that lower SES and older age predicted more pain, which is consistent with the present results. Our findings are also in line with Miaskowski et al who recently reported that in a community sample of indigent persons living with HIV, both lower education and depression were associated with more severe pain [41]. Additionally, the current findings support previous work in HIV seropositive samples showing strong relationships between pain and depressive symptoms [22,32,33,57] as well as between pain and illicit drug use [15,23,37,60,58].

However, some prior studies did not find associations between pain and IDU [8,9]. Miaskowski et al found no relationship between pain severity and use of a range of illicit drugs; they posited that high overall rates of substance use in their sample of indigent persons made it difficult to detect significant differences [41]. In the present analyses, the amount of variance in drug use explained by pain alone (i.e., without the clinical/sociodemographic variables) was relatively small. One possible reason is that we did not include use of opioid or other prescription drugs as the MACS did not assess the use of these substances during the study visits we analyzed. Earlier, we found strong links between pain and aberrant use of prescription analgesics in a different sample of HIV-infected persons particularly among individuals with a history of problematic illicit drug [58]. Given the recent and growing problem of prescription drug misuse, future work may test whether the present model also applies to use of such medications. It should also be noted that in the current analyses, pain was not associated with use of inhaled nitrites. It may be that use of this recreational drug is more prevalent among higher functioning persons who are not experiencing significant pain.

There are several possible pathways by which pain may increase the risk of depressive symptoms and drug use (see [3] for additional discussion of pain and depression comorbidity). Pain and pain-related disability may lead to disruptions in physical, social, and occupational activities which may in turn lead to social isolation, loss of independence and a subsequent increase in depressive symptoms. Such considerations may be especially relevant for gay/bisexual men, who along with lesbian women are at higher risk of mood and anxiety disorders compared to the general population [6]. Gay men also report greater illicit drug use compared to heterosexual men in the US [13,30], and persistent pain may lead to the use of illicit drugs for pain relief among these men. One study found that nearly

one-third of HIV-infected persons reported using marijuana to manage pain and other symptoms [61]. Another investigation found that among HIV-infected patients with peripheral neuropathy, 15% reported using marijuana and 7% reported using street drugs to manage their symptoms [42].

Sociodemographics played a large role in the associations with HIV status as well as the dependent variables (i.e., depressive symptoms and drug use). Many of the strong and substantial mean differences between HIV-infected and HIV-uninfected participants were apparently due more to the sociodemographic correlates of HIV status rather than to HIV status itself. In the current analyses, participants who were HIV seropositive reported more pain than the HIV seronegative men but pain was not significantly and independently predicted by being HIV seropositive once demographic correlates and the association with CD4+ cell count were included. The meaning of being a HIV seropositive participant in the MACS in large part reflects the demographic differences between the two groups – i.e., compared to the HIV seronegative participants, the HIV seropositive participants were more likely to be Black, more poorly educated, and younger. These socioeconomic disparities have been shown to have severe implications for decreased survival and quality of life among HIV-infected individuals [5,39].

Our finding that Blacks reported more pain compared to Whites is consistent with earlier research in an HIV seropositive sample [8], as well as data in the general population indicating more severe pain among ethnic minorities vs. Whites [40,44,46]. However, some investigations in HIV-infected samples have revealed that Blacks reported *less* pain than Whites [2,16]; others have found no ethnic differences in pain [48,55; 41]. Differences in pain assessment, sample characteristics, and/or stage of HIV disease may account for the divergent results. Our finding that lower education was linked with more pain is consistent with previous work in a US national sample of HIV seropositive people [16,58], as well as research in the general population [24,43,44,55], although an investigation of HIV–infected individuals with comorbid psychological and substance use disorders revealed no differences in pain based on education [55]. The latter finding may be due to restricted range of educational levels in this selected subgroup.

Several limitations to our findings should be mentioned. Because the MACS is comprised of men, we could not test for sex differences. Although we previously found in a US national sample of HIV seroprevalent individuals that after controlling for age and SES, women reported more pain than men regardless of ethnicity, mode of HIV transmission or prior drug use history [56], others have found no sex differences in pain in HIV [2,11,15,16,34,35,55,48]. Differences in sociodemographic characteristics may be partially responsible for sex differences in pain, particularly among ethnic minority women in the US where the seroprevalence is highest [59], and most existing research among HIV seroprevalent samples has not taken this consideration into account. Additionally, the MACS assessment does not differentiate between recreational vs. medically prescribed marijuana use. Other associations in the data could have been tested including path models that used a different directionality. For example, an alternative model might have tested whether depression mediated the association between pain and illicit drug use. However, our interest centered on implications of the mediating effect of pain on substance use and depressive symptoms in these high-risk samples.

The findings underscore the need for pain assessment and treatment aimed at older, less educated, Black gay/bisexual men as such individuals may be more vulnerable to pain. Among HIV-infected men such efforts should target those with more advanced HIV disease. Research in HIV-uninfected populations has found substantial disparities in the quality of pain management for ethnic minorities compared to Whites [1], and less utilization of care

for pain among persons of low SES [40]. Early research indicated substantial undertreatment of pain among HIV-infected persons, particularly the less educated and IV-drug users [9,10], but there is a dearth of recent research in this area. The current findings point to the continued need to assess and adequately treat pain in gay/bisexual men with, or at risk for HIV, as doing so may reduce the likelihood of drug use and depressive symptoms in these vulnerable populations.

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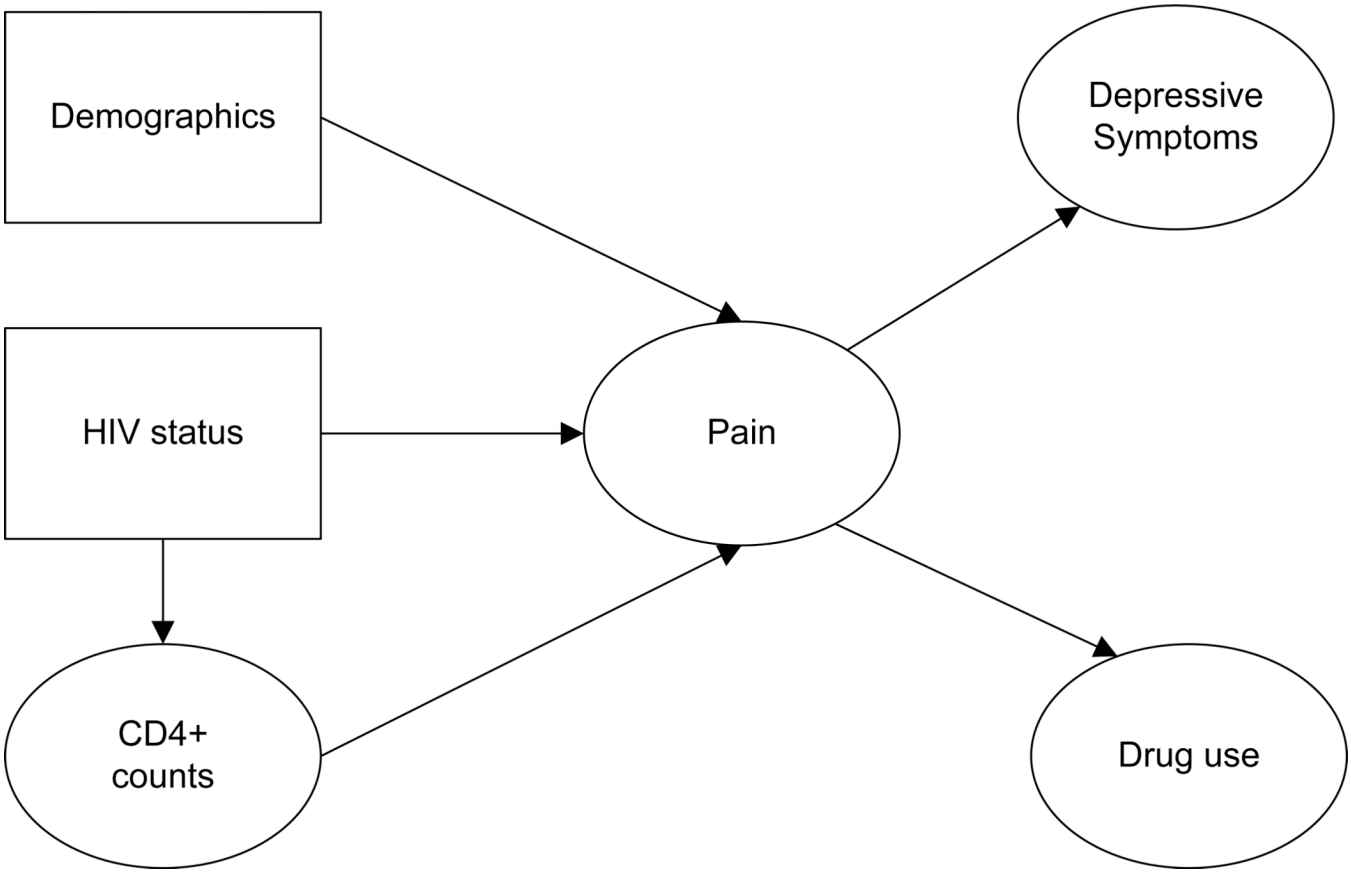

Figure 1.
Hypothesized path model for MACS participants

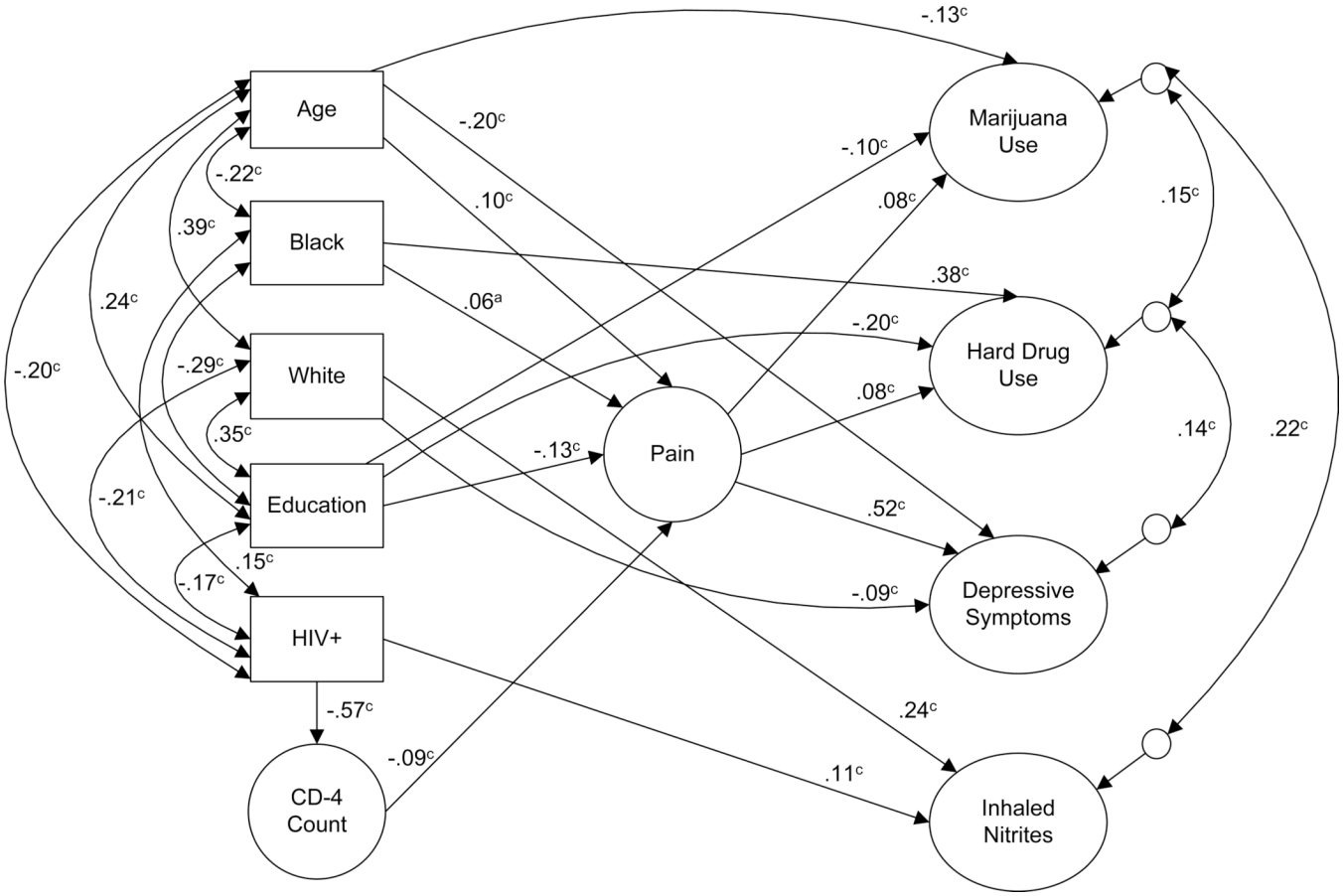

Figure 2.

Path model for MACS participants (N = 1940). Latent constructs are in circles, single items are in rectangles; 1-headed arrows depict standardized regression paths, 2-headed arrows represent correlations (standardized covariances) and correlations among residuals of dependent

Table 1

Summary statistics and factor loadings of variables in Confirmatory Factor Analyses for HIV seropositive and HIVseronegative men.

	HIV+ N = 921		HIV− N = 1019	
Variable	**Mean / SD**	**FL***	**Mean / SD**	**FL**
CD4+ Count**				
Time 1	566.61/278.01	.82	942.49/297.58	.89
Time 2	574.98/285.79	.89	959.34/302.61	.92
Time 3	562.47/278.49	.94	943.43/302.90	.93
Time 4	572.99/281.93	.95	945.40/306.35	.94
Time 5	575.82/270.88	.91	936.72/314.92	.92
Time 6	595.70/278.23	.85	942.89/313.39	.90
Pain***				
Time 1	1.90/0.96	.76	1.78/0.81	.79
Time 2	1.95/0.99	.79	1.78/0.81	.81
Time 3	1.91/0.98	.73	1.81/0.91	.77
Time 4	1.93/1.04	.77	1.83/0.92	.76
Time 5	1.92/1.00	.77	1.82/0.93	.77
Time 6	1.95/1.01	.69	1.82/0.87	.73
Marijuana Use***				
Time 1	0.84/1.29	.85	0.66/1.16	.87
Time 2	0.84/1.30	.88	0.65/1.15	.89
Time 3	0.85/1.28	.90	0.63/1.15	.90
Time 4	0.81/1.31	.91	0.59/1.14	.89
Time 5	0.83/1.33	.88	0.59/1.16	.90
Time 6	0.81/1.32	.85	0.61/1.16	.87
Crack Cocaine***				
Time 1	0.30/0.80	.70	0.16/0.59	.73
Time 2	0.28/0.80	.80	0.17/0.65	.82
Time 3	0.28/0.79	.77	0.16/0.63	.84
Time 4	0.26/0.79	.86	0.14/0.56	.82
Time 5	0.24/0.75	.84	0.15/0.61	.82
Time 6	0.21/0.72	.70	0. 14/0.59	.75
Other Cocaine***				
Time 1	0.19/0.64	.60	0.08/0.38	.64
Time 2	0.16/0.59	.63	0.10/0.44	.64
Time 3	0.15/0.57	.65	0.09/0.42	.63
Time 4	0.12/0.50	.67	0.08/0.41	.60
Time 5	0.11/0.48	.63	0.06/0.36	.56
Time 6	0.11/0.48	.50	0.07/0.36	.54
Heroin				

	HIV+ N = 921		HIV− N = 1019	
Variable	**Mean / SD**	**FL***	**Mean / SD**	**FL**
Time 1	0.07/0.46	.80	0.05/0.39	.74
Time 2	0.07/0.43	.85	0.06/0.40	.68
Time 3	0.06/0.44	.72	0.05/0.37	.89
Time 4	0.05/0.40	.90	0.04/0.31	.83
Time 5	0.04/0.35	.63	0.03/0.27	.75
Time 6	0.03/0.32	.67	0.04/0.34	.58
Depressive Symptoms ***				
Time 1	11.85/10.91	.82	9.87/9.90	.84
Time 2	11.17/10.36	.86	9.35/9.69	.88
Time 3	10.72/10.12	.89	9.11/9.60	.87
Time 4	10.97/9.64	.87	9.88/10.05	.88
Time 5	10.73/10.01	.85	9.16/9.53	.88
Time 6	10.99/9.72	.82	9.49/9.35	.82
Inhaled Nitrites ***				
Time 1	0.62/1.06	.80	0.48/0.97	.84
Time 2	0.62/1.06	.87	0.49/0.98	.88
Time 3	0.62/1.07	.87	0.49/0.98	.91
Time 4	0.60/1.07	.88	0.49/1.02	.91
Time 5	0.57/1.03	.86	0.44/0.95	.91
Time 6	0.57/1.03	.82	0.44/0.95	.86
Demographics				
Age (years)**	43.9/8.6	---	47.8/10.2	---
Black (%)***	31.3	---	18.7	---
White (%)**	53.8	---	73.8	---
Education (1–7)**	5.0/1.5	---	5.5/1.4	---
Hard Drug Use Second Order Factor***				
Crack	---	.86	---	.89
Other Cocaine	---	.73	---	.69
Heroin	---	.52	---	.44

* = Factor loading,

** = significantly higher for HIV- men,

*** = significantly higher for HIV+ men.

Table 2

Correlations among model variables. Correlations for HIV+ men below diagonal, HIV− men above diagonal.

Variables	Age	Black	White	Education	CD4+ count	Pain	Marijuana	Hard Drug Use	Depressive Symptoms	Inhaled Nitrites
1. Age	—	***−.24*** ***	***.33*** ***	.19***	−.02	.11**	−.19***	***−.21*** ***	−.18***	.03
2. Black	***−.15*** ***	—	−.81***	−.31***	.06	.12**	.10**	***.50*** ***	***.21*** ***	−.15***
3. White	***.40*** ***	−.73***	—	.34***	.03	−.07	−.08*	***−.45*** ***	−.20***	***.16*** ***
4. Education	.24***	−.23***	.31***	—	−.06	−.09*	−.14***	−.38***	−.22***	.15***
5. CD4+ count	.04	−.07*	.09*	.09*	—	.00	.11**	.06	−.01	.06
6. Pain	.01	.04	−.02	−.14***	−.12***	—	.04	.18**	.47***	−.06
7. Marijuana	−.10**	.04	−.01	−.08*	−.02	.11**	—	.29***	.09*	.17***
8. Hard Drug Use	***−.12*** ***	***.39*** ***	***−.30*** ***	−.27***	−.12**	.08*	.13***	—	.29***	−.07*
9. Depressive Symptoms	−.24***	***.09*** *	−.18***	−.16***	−.14***	.53***	.07	.21***	—	−.01
10. **Inhaled Nitrites**	.10**	−.25***	***.32*** ***	.14***	.08*	−.06	.21***	−.07	−.05	—

* p ≤ .05;

** p ≤ .01;

*** p ≤ .001. Bold-face italicized type indicates a significant difference, $p = \leq .01$