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Pain, problem drug use history, and aberrant analgesic use behaviors in persons living with HIV

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Abstract

Little is known about the relationship between pain and aberrant use of prescription analgesics in persons living with HIV. We examined the predictive and concurrent associations among pain, aberrant use of opioids, and problem drug use history in a nationally representative longitudinal sample of 2267 HIV+ persons. Covariance structure analyses tested a conceptual model wherein HIV + patients with a history of problematic drug use ($n = 870$), compared to those without such history ($n = 1397$), were hypothesized to report more pain and aberrant opioid use, as well as use of opioids specifically for pain at baseline and 6 and 12 month follow-ups, after controlling for key sociodemographic characteristics. In support of the hypothesized model, patients with a history of problematic drug use reported more pain, and were more likely to report aberrant use of prescription analgesics, as well as use of such medications specifically for pain, compared to patients without such history. We also found a trend toward greater stability of aberrant opioid use over time in problem drug users compared with non-problem users suggesting a persistent pattern of inappropriate medication use in the former group. Our findings suggest that even though HIV+ persons with a history of problematic drug use report on-going patterns of using prescription analgesics specifically for pain, these patients continued to experience persistently higher levels of pain, relative to non-problem users. Among non-problem users, pain was not linked to aberrant use of opioids, but was linked to the use of such medications specifically for pain.

Keywords

pain; opioids; substance abuse; problem drug use; HIV; AIDS

1. Introduction

Drug abuse behaviors constitute the primary exposure factor for Human Immunodeficiency Virus (HIV) infection in the United States (U.S) (National Institute on Drug Abuse 2004). Pain

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management for these medically ill patients within the context of drug abuse presents a particular challenge. In a U.S national sample, we previously found that HIV+ persons with problem drug use history experienced greater HIV illness burden which in turn predicted increased pain (Tsao et al. 2005). We did not however, examine the use of prescription pain medications in this prior investigation. Recently, Passik et al. (2006) found that HIV patients with a history of substance abuse reported over twice as many aberrant analgesic use behaviors than cancer patients without a history of substance abuse. However, a comparison group of non-drug-abusing HIV patients was not included making it difficult to draw conclusions regarding the specific risk posed by a positive drug abuse history for opiate misuse in HIV.

Research in non-HIV populations suggests that among individuals with chronic, nonmalignant pain, previous substance abuse is associated with an increased likelihood of opiate misuse (Schofferman 1993; Dunbar and Katz 1996; Michna et al. 2004; Schieffer et al. 2005). Although analogous investigations have not been conducted in HIV samples, it is likely that HIV patients with a problem drug use history would similarly evidence greater misuse of opiates than their non-problem-drug-using counterparts. There is evidence of substantial undertreatment of pain in HIV+ patients (Rosenfeld et al. 1996), particularly among those with a history of substance abuse (Breitbart et al. 1996b; Breitbart et al. 1997; Larue et al. 1997). It is possible that undertreatment of pain in this population may lead to drug seeking behaviors. These aberrant behaviors may thus represent a form of “pseudoaddiction,” which resolves when pain is effectively treated (Weissman and Haddox 1989). HIV patients have also expressed willingness to engage in aberrant behaviors or excuse them in others if pain management is inadequate (Passik et al. 2000). Existing studies have not examined the use of opiates specifically for pain in HIV patients, taking into account previous substance abuse. In light of our prior findings that HIV patients with problem drug use history reported increased pain compared to non-problem users (Tsao et al. 2005), it is reasonable to expect that problem drug users would be more likely to evidence increased use of opiates specifically for pain than the non-problem group.

The present study used structural equation modeling (SEM) to test the predictive and concurrent associations among pain, aberrant use of prescription analgesics, the use of these medications specifically for pain, and history of problem drug use in a representative U.S. sample using a prospective, longitudinal design. We hypothesized that HIV+ patients with a history of problematic drug use would be more likely to report aberrant use of opiates as well as use of prescription analgesics specifically for pain compared to those without a problem drug history at baseline and 6 and 12 month follow-ups, taking into account pain and controlling for key sociodemographic variables.

2. Methods

2.1 Participants

This study consisted of 2267 participants in the longitudinal HIV Cost and Services Utilization Study (HCSUS) who were assessed at baseline, and at approximately 6-month (Time 2) and 12-month (Time 3) follow-ups. The baseline interviews began in January 1996 and ended in April 1997 (Berry et al. 1999). First follow-up interviews (labeled Time 2 in this study) were conducted from December 1996 to July 1997 and were conducted with 2,466 respondents (86.1% of baseline). The mean time from baseline to the Time 2 follow-up was 223 days (95% confidence interval [CI], 204–244). The second (Time 3) follow-up interviews were conducted from August 1997 to January 1998 with 2,267 persons (84.5% of baseline). The mean time from baseline to Time 3 follow-up was 416 days (95% CI, 391–441).

The majority of participants were male (77%) and their mean age was 39 years; 31% were African-American, 51% were white, 14% were Hispanic, and the remainder (4%) were from

other ethnic groups. The HCSUS is a nationally representative probability sample of HIV-positive persons at least 18 years of age receiving care in the continental United States. The reference population was limited to persons who were known to be HIV+ and who made at least one visit for regular or ongoing care to a non-military, non-prison medical provider other than an emergency department between January 5 and February 29, 1996. Additional details of the design are available elsewhere (Frankel et al. 1999; Shapiro et al. 1999). The HCSUS selected subjects using a three-stage sampling design in which first metropolitan areas and clusters of rural counties, then medical providers, and finally patients were sampled (Lam and Liu 1996). Of 4,042 sampled eligible subjects, interviews were completed by 2,864 (71%). All consent forms and informational materials were reviewed and approved by the appropriate institutional review boards (IRBs), including local IRBs.

Drug Problem History—Those participants who answered “yes” to the following two questions were classified as drug problem history patients; all others were classified as non-drug problem history patients : 1) they ever had to use much larger amounts of illicit drugs than usual to get the same effect or that the same amount had less effect on them than before; and/or 2) that they ever had any emotional or psychological problems from using drugs such as feeling uninterested in things, feeling depressed, suspicious of people, paranoid, or having strange ideas. These items were developed by the HCSUS consortium (Sherbourne et al. 2000; Bing et al. 2001; Burnam et al. 2001) based on the short form of the World Health Organization’s Composite International Diagnostic Interview (CIDI-SF)(Kessler et al. 1998). In the general population, the sensitivity and specificity of the CIDI-SF for diagnosis of drug dependence was 0.77 and 0.99, respectively (Kessler et al. 1998). Although separate data for diagnosis of drug dependence was not available, the sensitivity and specificity of the CIDI-SF for any psychiatric disorder in the HCSUS sample was 0.80 and 0.76, respectively (Bing et al. 2001). There were 870 in the drug problem history group and 1397 who reported no such problems.

2.2 Questionnaire items

Background variables—Detailed information on the demographic characteristics of the sample is available elsewhere (Dobalian et al. 2004; Tsao et al. 2005). To control for baseline demographic correlates in the present study, age, sex and socioeconomic status (SES) were included as predictors. Age was reported in years. Males were assigned a “1”, females a “2.” Socioeconomic status was constructed as a latent variable indicated by education and income. Yearly income was assessed as follows: 1 = \$0 to 5,000; 2 = \$5,001 to \$10,000; 3 = \$10,001 to \$25,000; 4 = >\$25,000 (range: 0–\$75,001+). Education was assessed as follows: 1 = some high school; 2 = high school graduate; 3 = some college; 4 = college graduate or more. Ethnicity (e.g., African-American, or White) was tested as a further control but was not significantly associated with any other variable in the analysis and thus was not included. Demographic data for age and gender are presented in Table 1.

Pain was assessed at all three time periods using the bodily pain scale of the Short-Form 36 (SF-36), a widely used and psychometrically sound instrument (Stewart and Ware 1992; Ware and Sherbourne 1992; Hays and Morales 2001) It was constructed as a latent variable indicated by 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.

Aberrant use of prescription analgesics was assessed at the first two time periods (baseline and Time 2) with the yes/no item: “In the past 12 months have you used analgesics or other prescription painkillers without a doctor’s prescription, in larger amounts than prescribed, or

for a longer period than prescribed. This does not include normal use of aspirin, Tylenol without codeine, etc., but does include use of Tylenol with Codeine and other prescription painkillers like Demerol, Darvon, Darvocet, Percodan, Percoset, Codeine, Morphine, Methadone, and Fentanyl.” At Time 3, they were asked the same question but it referred to the past 30 days rather than the past 12 months. We used this item to avoid an overlap with the prior assessment. We expected this number to be smaller due to the shorter time frame.

Pain-specific use of prescription pain medicine was assessed at baseline with the question: “Over the last 6 months, have you taken any prescription drugs for pain.” At the two follow-up points (Time 2 and Time 3) respondents were asked “since we last interviewed you, have you taken any prescription drugs for pain?”

Established measures of opiate misuse have been developed in chronic pain patients; the utility of these measures in HIV+ patients is unknown. However, given the dearth of research in the HIV population, the use of the current items provided reasonable initial estimates for the constructs of interest. Future validation studies including established measures of aberrant analgesic use in HIV are required.

2.3 Statistical analysis

Because the sample was stratified, a multilevel analysis could have been warranted. A preliminary analysis examined the magnitude of the intraclass correlations of the variables included in the model. They were found to be small and non-significant. To insure the representativeness of the sample over time, weighted data were used in the analyses.

2.3.1 Confirmatory structural equation models—Latent variable structural equation modeling (SEM) was performed using EQS 6 (Bentler 2006). The comparative fit index (CFI), maximum likelihood chi-square values ($ML \chi^2$), and the Root Mean Square Error of Approximation (RMSEA) were used as indicators of fit (Hu and Bentler 1999; Bentler 2006). The CFI compares the improvement of fit of a hypothesized model to a model of complete independence among the measured variables. The CFI ranges between 0 and 1; values greater than or equal to .95 indicate a good fit (Bentler 2006). 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 (Hu and Bentler 1999). An initial confirmatory factor analysis (CFA) was performed with each hypothesized latent construct predicting its measured indicators. All latent constructs, and the single-item variables were correlated with no imputation of causality or temporal ordering. This analysis assessed the adequacy of the proposed factor structure and the relationships among the latent and measured variables.

2.3.2 Multi-sample 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 degrees of stringency across groups (Yin and Fan 2003; Stein et al. 2006). 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 (Bentler 2006). Establishing factorial invariance alone 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, there may be a tendency to score higher or lower in a particular group (Handelsman et al. 2005; Stein et al. 2006).

In the multisample models in this study, 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 is used for comparison purposes. We then tested

a model in which their factor structures were constrained to equality. We then constrained the covariances among the latent variables to equality and tested whether they were significantly different in the two groups. 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 Lagrange Multiplier test (Chou and Bentler 1990), which in this context identifies constraints that are untenable.

2.3.3 Path analysis—Once the factor structure was confirmed in each group, we tested separate predictive longitudinal path models in which gender, age, baseline pain, and prescription analgesic usage patterns (i.e., aberrant and pain-specific use) at baseline predicted pain and prescription analgesic usage patterns at the following two time periods (Time 2 and Time 3). The stability paths between similar constructs were expected to be strong. All possible paths were initially included and gradually dropped if they were non-significant.

3. Results

3.1 Confirmatory factor analysis

Table 1 presents the factor loadings and other summary statistics for the variables used in the analyses for each group. All measured variables loaded significantly ($p < 0.001$) on their hypothesized latent factors. Fit indexes were excellent in both groups: Drug Problem History group: $ML \chi^2 (43, N = 870) = 71.82$, CFI = 0.99, RMSEA = 0.028 (90% confidence interval = .016–.039). No Drug Problem History group: $ML \chi^2 (43, N = 1397) = 53.66$, CFI = 0.99, RMSEA = 0.013 (90% confidence interval = .000–.024). As shown in Table 1, at baseline, 35% of the No Drug Problem History group and 46% of the Drug Problem History group reported taking opiates specifically for pain; 9% of the No Drug Problem History group and 23% of the Drug Problem History group reported aberrant opiate use. At Time 2, 32% of the No Drug Problem History group and 43% of the Drug Problem History group reported taking opiates specifically for pain; 9% of the No Drug Problem History group and 18% of the Drug Problem History group reported aberrant opiate use. At Time 3, 30% of the No Drug Problem History group and 37% of the Drug Problem History group reported taking opiates specifically for pain; 3% of the No Drug Problem History group and 7% of the Drug Problem History group reported aberrant opiate use. Note that reported aberrant analgesic use was low at follow-up 2 (Time 3) probably due to the fact that those numbers reflect 30-day use rather than the 12 month use reported at baseline and follow-up 1 (Time 2).

Table 2 reports the correlations among the single-item variables and latent variables in each group. The Drug Problem History group is below the diagonal. Significance levels among the variables were high due in part to the large sample sizes. Because of the effect of stability, correlations between the same constructs across time were particularly high (e.g., the correlation between Pain at baseline and Pain at Time 2 = .61, .59 for the Drug Problem group and the Non-Drug Problem group respectively). When comparing analogous correlations across the groups, some substantial differences were noted. For instance, at baseline, Pain and aberrant use of prescription analgesics were significantly associated for the Drug Problem group (.18) but were non-significant in the Non-Drug Problem group (.01). Other notable differences include the relationship between aberrant and pain-specific use of prescription analgesics at baseline (.21 vs. .07), and Pain and pain-specific use of prescription analgesics Time 3 (.39 vs. .54) for the Drug Problem and Non-Drug Problem groups respectively. The multiple group analysis reported below tested whether any apparent differences between the correlations were statistically significant once the factor structures were held to equality.

3.2 Multiple group analyses

3.2.1. Constrained factor structure—An unconstrained multisample model served as the baseline ($ML \chi^2(86) = 125.47$, CFI = 0.99, RMSEA = 0.014). 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 ($\chi^2(94) = 132.42$, CFI = 0.99, RMSEA = 0.013, chi-square difference = 6.95/8 *df*, non-significant). 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.

3.2.2. Constrained covariances—The more constrained model in which the covariances among the latent variables and single item variables were constrained to equality across the groups had a significant increase in its chi-square value ($\chi^2(159) = 287.04$, CFI = 0.99, RMSEA = 0.019). The χ^2 -difference was 161.57/73 *df*. This significant result was not surprising given the several noticeable group differences reported in Table 2 and supports our hypothesis of substantive differences between the two groups in their use of prescription analgesics. Table 3 reports the differences between the two groups that were significant as indicated by the largest chi-square values reported by the LM test (A critical value of 3.84/1 *df* ($p \leq .05$) was used.) Each chi-square value indicates the improvement in fit (i.e., decrease in model overall chi-square) that would be obtained if that constraint were to be dropped from the model. Some differences look relatively small which may be due to the large sample sizes.

The largest significant difference was a univariate chi-square of 35.22 indicating that the correlation between pain and pain-specific use of opiates at Time 3 was considerably different in the two groups (.39, .54 for Drug History vs. the Non-Drug History groups). The next largest univariate chi-square was 13.25 for the greater stability of aberrant use of prescription analgesics at baseline and at Time 2 for the Drug History group (.35, vs. .20).

3.2.3 Latent means model—Table 4 reports the *z*-scores of the latent mean differences analysis for the two groups. There were substantial differences between the two groups in all of the variables. The Drug History group reported more pain at all time periods, and an increased likelihood of aberrant and pain-specific use of prescription analgesics at all time periods. The non-Drug History group reported a higher SES. All *z*-scores comparing the latent means are large and highly significant ($p < .001$).

3.2.4 Path analysis—Figures 1 and 2 present the significant regression paths in the final trimmed longitudinal models. Significant correlations among the background predictors are included as well. The fit indexes of the trimmed path models are excellent: Drug Problem History group: $ML \chi^2(74, N = 870) = 116.21$, CFI = 0.99, RMSEA = 0.026 (90% confidence interval = .016-.034). No Drug Problem History group: Maximum Likelihood $\chi^2(72, N = 1397) = 88.00$, CFI = 0.99, RMSEA = 0.013 (90% confidence interval = .000-.021).

As expected, there were strong stability paths across time for the Pain latent variable and there were significant paths between the analgesic use variables as well (e.g., the stability path for aberrant analgesic use from baseline to Time 2 was .32 in the Drug Problem History group and .18 in the No Drug Problem History group; see Figures 1 and 2). In most cases, relationships in the path models were relatively similar across the two groups. However, in the drug problem group, baseline pain predicted both aberrant and pain-specific analgesic use at Time 2 whereas among those without drug problem histories, baseline pain only predicted pain-specific use of analgesics at Time 2. These differences were not as notable at Time 3. It should be noted that aberrant analgesic use was only assessed for the last 30 days at Time 3 and this may have made a difference in the strength of some of the relationships. Of note, similar to what was found in the CFA model, there was a substantial association between pain at baseline and aberrant use

of analgesics at baseline in the drug problem group that was not present in the non-problem group.

4. Discussion

Our findings in a representative sample of persons living with HIV confirmed that patients with a history of problem drug use report more pain, and were more likely to engage in aberrant use of prescription analgesics, as well as use of these medications specifically for pain, compared to patients without such history, after controlling for key sociodemographic characteristics. These differences in pain and opiate use between drug users and non-users persisted over a period of approximately 1 year. Moreover, our analyses revealed that pain at baseline more strongly predicted both aberrant and pain-specific opioid use approximately 6 months later in problem drug users compared to non-problem users. These findings suggest that even though problem users reported persistent patterns of opiate use specifically for pain, they *continued* to experience higher levels of pain, relative to non-problem users. Among non-problem users, pain was not linked to aberrant use of opioids, but was linked to their pain-specific use. We also found a trend toward greater stability of aberrant analgesic use over time in problem drug users compared with non-problem users suggesting a persistent pattern of inappropriate opioid use in the former group.

The present findings agree with previous work among non-HIV patients in which prior substance abuse emerged as one of the strongest risk factors for opiate misuse (Schofferman 1993; Dunbar and Katz 1996; Michna et al. 2004). Schieffer et al. (2005) in the largest study to date reported that chronic pain patients with a history of substance abuse evidenced higher rates of medication misuse compared to those without such history despite equivalent levels of prescribed opiates and similar self-ratings of medication effectiveness. Lusher et al. (2006) found that among patients with sickle cell disease, physiological dependence and illicit drug use were associated with true addiction to opiates (i.e., a primary neurobiological disease characterized by compulsive use despite harm and craving) (Heit 2001; Savage et al. 2003) whereas disputes with staff about analgesics were associated with risk of pseudoaddiction (i.e., aberrant behaviors that resolve once pain is adequately treated).

In the current study, we were not able to determine whether aberrant opiate use was due to true addiction or pseudoaddiction since the latter may only be discerned through clinical intervention and observation (Savage et al. 2003). Nevertheless, if pseudoaddiction were present, we would expect that both pain and aberrant opiate use would improve over time whereas pain-specific use would remain stable. Additional analyses in the present sample indicated that pain, as well as aberrant and pain-specific opiate use all declined significantly over time in both groups. Thus, the extent to which the current data support the presence of pseudoaddiction in HIV+ patients with and without a history of problem drug use remains unclear. The relative contribution of true addiction vs. pseudoaddiction to aberrant analgesic use in HIV+ patients should be investigated in further research.

Our findings suggested a closer relationship between pain-specific opioid use and pain levels among non-problem-drug users, compared to problem users. One interpretation is that non-problem users take opioids in a manner more consistent with and appropriate to their level of pain than those with a problem drug history who may use opioids more indiscriminately. Numerous studies have reported substantial undertreatment of pain in substance-abusing HIV+ patients (e.g., Larue et al., 1997). Breitbart and colleagues (1996b) found that 84% of HIV+ patients received inadequate analgesia, and Passik et al. (2006) more recently reported that 32.9% of HIV+ patients compared to only 8% of cancer patients received inadequate analgesia. Although we were unable to assess the adequacy of analgesia, the finding that problem users reported greater pain than non-problem users over roughly 1 year despite being more likely to

use opiates specifically for pain supports the notion of undertreatment in the former group of patients. Future studies may examine the degree to which undertreatment of pain leads to greater aberrant opiate use in the HIV population.

Passik et al. (2006) found that among HIV+ patients, low percentage of pain relief was related to specific aberrant behaviors. However, the total number of aberrant behaviors did not differ based on level of pain relief, leading the authors to suggest that factors other than pain may primarily drive aberrant behaviors. In our study, pain was linked to aberrant opiate use only in the drug problem group and *not* in the non-problem group. Moreover, the associations between pain and aberrant opioid use were stronger in problem users compared to non-problem users at baseline and roughly 6 months later. In the non-problem group, only demographic variables (younger age, male gender) predicted aberrant opioid use. Notably, demographic characteristics in both groups were similar (percentage of women was 22.8% (problem) vs. 22.9% (non-problem); mean age was roughly 39 years in both groups). The only exception was that the problem group was of lower SES than the non-problem group. Somewhat unexpectedly, higher SES was linked to increased aberrant analgesic use in problem users, perhaps due to greater availability of resources to obtain opioids. In this medically ill sample, rates of aberrant analgesic use behaviors in the non-problem group were relatively low compared to those reported in chronic pain samples, likely due to a more extensive history of opiate use in the latter group.

Our findings are consistent with prior work demonstrating that HIV+ patients who are injection drug users (IDUs) report more pain than non-IDUs (Fantoni et al. 1997; Martin et al. 1999; Vogl et al. 1999; Del Borgo et al. 2001), although null findings have also been reported (Breitbart et al. 1996a; Breitbart et al. 1997). Previously, we found that patients with problematic drug use history experienced greater HIV/AIDS illness burden, which in turn predicted greater pain (Tsao et al. 2005). Preliminary analyses for the current study revealed that whereas illness burden was related to pain-specific use of opioids in problem drug-users, illness burden was not related to aberrant analgesic use in either the problem or non-problem group. Taken together, our findings suggest that HIV+ patients with a problematic drug history, compared to those without such history, experience increased disease burden, leading to more pain that persists regardless of greater continued use of opiates specifically for pain.

Recently, Kaplan et al. (2000) found that HIV+ patients with a history of substance abuse required twice as much morphine to achieve pain relief compared to those without such history. The former group had used heroin and thus the greater opioid analgesic requirement may have reflected differences in underlying neurophysiology. In support, Pud et al. (2006) reported that chronic opioid addicts evidenced lower pain tolerance to the cold pressor task relative to controls, suggesting opioid-induced hyperalgesia in the former group. Nevertheless, Kaplan et al. posited several other possible reasons for the inadequate treatment of HIV+ drug users with pain. Not only do such patients present treatment difficulties during medical care, they may be negatively stereotyped by staff who fear re-initiating addictive behaviors, leading to mutual mistrust between staff and patients. Legal or regulatory policies may interfere with the appropriate prescription of controlled substances to treat pain, particularly among patients with substance abuse histories. Finally, confusion exists regarding terms such as “addiction” and guidelines for opioid administration among clinicians. Breitbart et al. (1999) found that lack of knowledge and concerns regarding addiction were among the most frequently endorsed barriers to pain management by clinicians treating patients with HIV.

Caveats to our findings should be noted. Opiate use at the second follow-up was assessed for the past 30 days vs. 12 months at baseline and first follow-up. Nevertheless, the assessment of opiate use was dichotomous at each timepoint rather than continuous suggesting that the second follow-up assessment provided a reasonable (if not equivalent) indicator of opiate use. The

items used to assess aberrant and pain-specific medication use were not derived from established measures (e.g., SOAPP; Butler et al., 2004) and therefore lacked specificity. Indeed, the two medication use variables were significantly correlated in both the problem and non-problem groups although the magnitude of these relationships was not substantial when compared to the stability paths for pain and opioid use. In addition, the two opioid use variables were more strongly linked in the problem group compared to the non-problem group, supporting our hypothesized model. Our models did not include the use of adjuvant medications (e.g., antidepressants) that are frequently used for pain, nor were we able to characterize the source of pain medications (e.g., legitimately prescribed vs. illicitly obtained). Finally, we did not include measures of psychological distress although previous research has revealed significant associations among pain, psychological well-being (Rosenfeld et al. 1996; Tsao et al. 2004), and aberrant opioid use (Passik et al. 2006) in HIV+ patients. Future studies should examine how pain, drug use history, and psychological distress interact to initiate and/or maintain aberrant analgesic use behaviors in persons living with HIV.

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Reference List

- Bentler, PM. EQS 6 Structural Equations Program Manual. Encino, CA: Multivariate Software, Inc; 2006.
- Berry S, Brown J, Athey L, Keesey J, Tebow J, Webster R, Cotton S. HCSUS Baseline Patient Questionnaire Documentation.
- Bing EG, Burnam A, Longshore D, Fleishman JA, Sherbourne CD, London AS, Turner BJ, Eggen F, Beckman R, Vitiello B, Morton SC, Orlando M, Bozzette SA, Ortiz-Barron L, Shapiro M. Psychiatric Disorders and drug use among human immunodeficiency virus-infected adults in the United States. *Arch Gen Psychiatry* 2001;58:721–728. [PubMed: 11483137]
- Breitbart W, Kaim M, Rosenfeld B. Clinicians' perceptions of barriers to pain management in AIDS. *J Pain Symptom Manage* 1999;18:203–212. [PubMed: 10517042]
- Breitbart W, McDonald MV, Rosenfeld B, Passik SD, Hewitt D, Thaler H, Portenoy RK. Pain in ambulatory AIDS patients. I: Pain characteristics and medical correlates. *Pain* 1996a;68:315–321. [PubMed: 9121820]
- Breitbart W, Rosenfeld B, Passik S, Kaim M, Funesti-Esch J, Stein K. A comparison of pain report and adequacy of analgesic therapy in ambulatory AIDS patients with and without a history of substance abuse. *Pain* 1997;72:235–243. [PubMed: 9272808]
- Breitbart W, Rosenfeld BD, Passik SD, McDonald MV, Thaler H, Portenoy RK. The undertreatment of pain in ambulatory AIDS patients. *Pain* 1996b;65:243–249. [PubMed: 8826513]
- Burnam MA, Bing EG, Morton SC, Sherbourne C, Fleishman JA, London AS, Vitiello B, Stein M, Bozzette SA, Shapiro MF. Use of mental health and substance abuse treatment services among adults with HIV in the United States. *Arch Gen Psychiatry* 2001;58:729–736. [PubMed: 11483138]
- Butler SF, Budman SH, Fernandez K, Jamison RN. Validation of a screener and opioid assessment measure for patients with chronic pain. *Pain* 2004;112:65–75. [PubMed: 15494186]
- Chou C-P, Bentler PM. Model modification in covariance structure modeling: A comparison among likelihood ratio, Lagrange Multiplier, and Wald tests. *Multivariate Behavioral Research* 1990;25:115–136.

- Del Borgo C, Izzi I, Chiarotti F, Del Forno A, Moscati AM, Cornacchione E, Fantoni M. Multidimensional aspects of pain in HIV-infected individuals. *AIDS Patient Care STDS* 2001;15:95–102. [PubMed: 11224935]
- Dobalian A, Tsao JC, Duncan RP. Pain and the use of outpatient services among persons with HIV: results from a nationally representative survey. *Med Care* 2004;42:129–138. [PubMed: 14734950]
- Dunbar SA, Katz NP. Chronic opioid therapy for nonmalignant pain in patients with a history of substance abuse: report of 20 cases. *J Pain Symptom Manage* 1996;11:163–171. [PubMed: 8851374]
- Fantoni M, Ricci F, Del Borgo C, Izzi I, Damiano F, Moscati AM, Marasca G, Bevilacqua N, Del Forno A. Multicentre study on the prevalence of symptoms and symptomatic treatment in HIV infection. *J Palliat Care* 1997;13:9–13.
- Frankel M, Shapiro M, Duan N, Morton S, Berry S, Brown J, Burnam M, Cohn S, Goldman D, McCaffrey D, Smith S, Clair PS, Tebow J, Bozzette S. National probability samples in studies of low-prevalence diseases. Part II: Designing and implementing the HIV cost and services utilization study sample. *Health Serv Res* 1999;34:969–992. [PubMed: 10591268]
- Handelsman L, Stein JA, Grella C. Contrasting predictors of readiness for substance abuse treatment in adults and adolescents: A latent variable analysis of DATOS and DATOS-A participants. *Drug Alcohol Depend* 2005;80:63–81. [PubMed: 15894434]
- Hays RD, Morales LS. The RAND-36 measure of health-related quality of life. *Ann Med* 2001;33:350–357. [PubMed: 11491194]
- Heit HA. The truth about pain management: the difference between a pain patient and an addicted patient. *Eur J Pain* 2001;5(Suppl A):27–29. [PubMed: 11798214]
- Hu L, Bentler P. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling* 1999;6:1–55.
- Kaplan R, Slywka J, Slagle S, Ries K. A titrated morphine analgesic regimen comparing substance users and non-users with AIDS-related pain. *J Pain Symptom Manage* 2000;19:265–273. [PubMed: 10799793]
- Kessler R, Andrews G, Mroczek DBU, Wittchen H. The World Health Organization Composite International Diagnostic Interview Short-Form (CIDI-SF). *Int J Methods Psychiatr Res* 1998;7:171–185.
- Lam N, Liu K. Use of Space-filling Curves in Generating a National Rural Sampling Frame for HIV/AIDS Research. *The Professional Geographer* 1996;48:321–332.
- Larue F, Fontaine A, Colleau SM. Underestimation and undertreatment of pain in HIV disease: multicentre study. *BMJ* 1997;314:23–28. [PubMed: 9001475]
- Lusher J, Elander J, Bevan D, Telfer P, Burton B. Analgesic addiction and pseudoaddiction in painful chronic illness. *Clin J Pain* 2006;22:316–324. [PubMed: 16514333]
- Martin C, Pehrsson P, Osterberg A, Sonnerborg A, Hansson P. Pain in ambulatory HIV-infected patients with and without intravenous drug use. *Eur J Pain* 1999;3:157–164. [PubMed: 10700345]
- Michna E, Ross EL, Hynes WL, Nedeljkovic SS, Soumekh S, Janfaza D, Palombi D, Jamison RN. Predicting aberrant drug behavior in patients treated for chronic pain: importance of abuse history. *J Pain Symptom Manage* 2004;28:250–258. [PubMed: 15336337]
- National Institute on Drug Abuse. NIDA InfoFacts: Drug Abuse and AIDS. 2004. Available at <http://www.nid.nih.gov/infofacts/DrugAbuse.html>
- Passik S, Kirsh KL, McDonald MV, Ahn S, Russak SM, Martin L, Rosenfeld B, Breitbart W, Portenoy RK. A pilot survey of aberrant drug-taking attitudes and behaviors in samples of cancer and AIDS patients. *J Pain Symptom Manage* 2000;19:274–286. [PubMed: 10799794]
- Passik SD, Kirsh KL, Donaghy KB, Portenoy RK. Pain and aberrant drug-related behaviors in medically ill patients with and without histories of substance abuse. *Clin J Pain* 2006;22:173–181. [PubMed: 16428952]
- Pud D, Cohen D, Lawental E, Eisenberg E. Opioids and abnormal pain perception: New evidence from a study of chronic opioid addicts and healthy subjects. *Drug Alcohol Depend* 2006;82:218–223. [PubMed: 16229972]
- Rosenfeld B, Breitbart W, McDonald MV, Passik SD, Thaler H, Portenoy RK. Pain in ambulatory AIDS patients. II: Impact of pain on psychological functioning and quality of life. *Pain* 1996;68:323–328. [PubMed: 9121821]

- Savage SR, Joranson DE, Covington EC, Schnoll SH, Heit HA, Gilson AM. Definitions related to the medical use of opioids: evolution towards universal agreement. *J Pain Symptom Manage* 2003;26:655–667. [PubMed: 12850648]
- Schieffer BM, Pham Q, Labus J, Baria A, Van Vort W, Davis P, Davis F, Naliboff BD. Pain medication beliefs and medication misuse in chronic pain. *J Pain* 2005;6:620–629. [PubMed: 16139781]
- Schofferman J. Long-term use of opioid analgesics for the treatment of chronic pain of nonmalignant origin. *J Pain Symptom Manage* 1993;8:279–288. [PubMed: 7525744]
- Shapiro M, Berk M, Berry S, Emmons C, Athey L, Hsia D, Leibowitz A, Maida C, Marcus M, Perlman J, Schur C, Schuster M, Senterfitt J, Bozzette S. National probability samples in studies of low-prevalence diseases. Part I: Perspectives and lessons from the HIV cost and services utilization study. *Health Serv Res* 1999;34:951–968. [PubMed: 10591267]
- Sherbourne CD, Hays RD, Fleishman JA, Vitiello B, Magruder KM, Bing EG, McCaffrey DF, Burnam A, Longshore D, Eggen F, Bozzette SA, Shapiro MF. Impact of psychiatric conditions on health-related quality of life in persons with HIV infection. *Am J Psychiatry* 2000;157:258–254.
- Stein JA, Lee JW, Jones PS. Assessing cross-cultural differences through the use of multiple group invariance analysis. *J Pers Assess* 2006;87:249–258. [PubMed: 17134332]
- Stewart, AL.; Ware, JE. Measuring functioning and well-being: the medical outcomes study approach. Durham: Duke University Press; 1992.
- Tsao JC, Dobalian A, Naliboff BD. Panic disorder and pain in a national sample of persons living with HIV. *Pain* 2004;109:172–180. [PubMed: 15082139]
- Tsao JC, Dobalian A, Stein JA. Illness burden mediates the relationship between pain and illicit drug use in persons living with HIV. *Pain* 2005;119:124–132. [PubMed: 16297562]
- Vogl D, Rosenfeld B, Breitbart W, Thaler H, Passik S, McDonald M, Portenoy RK. Symptom prevalence, characteristics, and distress in AIDS outpatients. *J Pain Symptom Manage* 1999;18:253–262. [PubMed: 10534965]
- Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473–483. [PubMed: 1593914]
- Weissman DE, Haddox JD. Opioid pseudoaddiction—an iatrogenic syndrome. *Pain* 1989;36:363–366. [PubMed: 2710565]
- Yin P, Fan X. Assessing the factor structure invariance of self-concept measurement across ethnic and gender groups: Findings from a national sample. *Educ Psychol Measurement* 2003;63:296–318.

Figure 1.

Longitudinal path model for HCSUS participants with history of problem drug use ($N = 870$). Latent constructs are in circles, single items are in rectangles; 1-headed arrows depict standardized regression paths, 2-headed arrows represent correlations (standardized covariances). (* = $p \leq .05$, ** = $p \leq .01$, *** = $p \leq .001$.)

Figure 2.

Longitudinal path model for HCSUS participants without a history of problem drug use ($N = 1397$). Latent constructs are in circles, single items are in rectangles; 1-headed arrows depict standardized regression paths, 2-headed arrows represent correlations (standardized covariances). (* = $p \leq .05$, ** = $p \leq .01$, *** = $p \leq .001$).

Table 1

Summary statistics and factor loadings of variables in confirmatory factor analysis.

Variable	Non-Drug Problem History N = 1397		Drug Problem History N = 870	
	Mean / SD	FL *	Mean / SD	FL
Baseline				
Gender (1 = male)	1.23 / .42	NA **	1.23 / .42	NA
Age (years)	39.00 / 9.3	NA	38.50 / 7.7	NA
Aberrant Analgesic Use - Range = (0–1)	.09 / .28	NA	.23 / .41	NA
Pain-specific Analgesic Use - (0–1)	.35 / .48	NA	.46 / .50	NA
Socioeconomic Status				
Income (1–4)	2.72 / 1.11	.58	2.53 / 1.07	.64
Education (1–4)	2.51 / 1.07	.70	2.30 / 1.03	.70
Pain				
Interfere work (1–5)	1.95 (1.21)	.85	2.33 (1.28)	.86
Bodily pain (1–6)	2.50 (1.42)	.86	2.92 (1.46)	.85
Time 2 Follow-up				
Aberrant Analgesic Use	.09 / .29	NA	.18 / .38	NA
Pain-specific Analgesic Use	.32 / .47	NA	.43 / .50	NA
Pain				
Interfere work	1.81 / 1.10	.86	2.10 / 1.17	.84
Bodily pain	2.34 / 1.39	.84	2.72 / 1.41	.82
Time 3 Follow-up				
Aberrant Analgesic Use	.03 / .16	NA	.07 / .25	NA
Pain Specific Analgesic Use	.30 / .46	NA	.37 / .48	NA
Pain				
Interfere work	1.87 / 1.16	.89	2.20 / 1.24	.89
Bodily pain	2.40 / 1.44	.85	2.81 / 1.50	.88

* All factor loadings (FL) significant at $p < .001$.

** NA = Not applicable

Table 2
Correlations among model constructs; people with drug problem histories below diagonal.

Baseline	1	2	3	4	5	6	7	8	9	10	11	12
1. Pain	—	.01	.45 ^c	-.22 ^c	.59 ^c	.02	.31 ^c	.51 ^c	.04	.29 ^c	.02	.01
2. Aberrant Use	.18 ^c	—	.07 ^a	.11 ^b	.03	.20 ^c	.01	.08 ^a	.21 ^c	-.02	-.10 ^c	-.08 ^b
3. Pain-specific Use	.43 ^c	.21 ^c	—	-.11 ^b	.32 ^c	.07 ^a	.42 ^c	.33 ^c	.05	.32 ^c	-.01	.00
4. SES	-.25 ^c	.06	-.14	—	-.22 ^c	.07	-.06	-.11 ^b	.05	.03	.12 ^b	-.41 ^c
Time 2												
5. Pain	.61 ^c	.19 ^c	.32 ^c	-.15 ^b	—	.09 ^a	.45 ^c	.64 ^c	.05	.36 ^c	.00	.03
6. Aberrant Use	.09 ^a	.35 ^c	.09 ^b	.08	.18 ^c	—	.10 ^b	.12 ^c	.19 ^c	.08 ^b	-.06 ^a	-.09 ^c
7. Pain-specific Use	.37 ^c	.16 ^c	.49 ^c	-.09 ^a	.47 ^c	.12 ^b	—	.35 ^c	.09 ^b	.39 ^c	-.04	-.01
Time 3												
8. Pain	.55 ^c	.13 ^c	.31 ^c	-.16 ^c	.61 ^c	.13 ^c	.34 ^c	—	.13 ^c	.54 ^c	.10 ^b	-.02
9. Aberrant Use	.01	.13 ^c	.10 ^b	.09 ^a	.06	.21 ^c	.06	.11 ^b	—	.08 ^b	-.07 ^b	-.05 ^a
10. Pain-specific Use	.33 ^c	.12	.35 ^c	-.10 ^a	.40 ^c	.10 ^b	.45 ^c	.39 ^c	.11 ^b	—	.02	-.05
Demographics												
11. Age	.10 ^a	-.09 ^a	-.01	.13 ^b	.07 ^a	-.16 ^c	-.02	.10 ^a	-.03	.10 ^a	—	-.16 ^c
12. Gender	.09 ^a	-.01	.07 ^a	-.38 ^c	.12 ^b	-.05	.11 ^b	.06	-.02	-.01	-.16 ^c	—

^a = $p \leq .05$,

^b = $p \leq .01$,

^c = $p \leq .001$.

Table 3
Significantly different covariances among latent and single-item variables

Covariance between:	Correlation (Standardized covariance)		Univariate χ^2
	Drug History	Non-Drug History	
Pain Time 3, Pain-specific Use Time 3	.39	.54	35.22
Aberrant Use baseline, Aberrant Use Time 2	.35	.20	13.25
SES, Pain-specific Use Time 3	-.10	.03	9.91
Aberrant Use baseline, Aberrant Use Time 3	.13	.21	6.95
Age, Pain-specific Use Time 3	.10	.02	6.87
Aberrant Use baseline, Pain Time 3	.13	.08	5.64
Aberrant Use baseline, Pain-specific Use Time 3	.12	-.02	4.95
SES, Pain Time 2	-.15	-.22	4.88
Pain Baseline, Aberrant Use baseline	.18	.01	4.80
Age, Pain-specific Use Time 2	-.16	-.06	4.29
Pain-specific Use Baseline, Aberrant Use Time 3	.10	.05	3.97

Note: All covariances significantly different at $p \leq .05$

Table 4
Tests of Latent Mean Differences between Drug Problem History and Non-Drug Problem History groups

Latent Variables	Z-score mean differences ^a
Pain - Baseline	-.7.50 ^b
Aberrant Analgesic Use baseline	-8.63 ^b
Pain-specific Analgesic Use baseline	-4.93 ^b
SES	5.32 ^b
Pain – Time 2	-6.71 ^b
Aberrant Analgesic Use -Time 2	-5.61 ^b
Pain-specific Analgesic Use -Time 2	-4.83 ^b
Pain – Time 3	-6.94 ^b
Aberrant Analgesic Use - Time 3	-3.94 ^b
Pain-specific Analgesic Use – Time 3	-3.91 ^b

^a Negative Z-score indicates higher score for Drug Problem History group.

^b $p \leq .001$.