



Published in final edited form as:

Pain. 2005 December 15; 119(1-3): 124–132.

Illness burden mediates the relationship between pain and illicit drug use in persons living with HIV

Tsao Jennie C. I.^a, Aram Dobalian^b, and Judith A. Stein^c

a Pediatric Pain Program, Department of Pediatrics, David Geffen School of Medicine at UCLA, Los Angeles, California.

b VA Greater Los Angeles Healthcare System HSR&D Center of Excellence for the Study of Healthcare Provider Behavior and Department of Health Services, UCLA School of Public Health, Los Angeles, California.

c UCLA Department of Psychology, Los Angeles, California.

Abstract

We investigated predictive and concurrent relationships among reported pain, HIV/AIDS illness burden, and substance use history in 2,267 participants in the longitudinal HIV Cost and Services Utilization Study (HCSUS). Substance use history was classified as screening positive for current illicit drug use (N = 253), past drug use (N = 617), and non-user (N = 1397) at baseline. To control for demographic correlates, age, sex and socioeconomic status (SES) were included as predictors. Covariance structure models indicated greater pain at baseline among participants acknowledging current substance use. Pain at baseline was also directly predicted by greater HIV/AIDS illness burden, lower SES, and older age. At 6 months, pain was directly predicted by prior pain, worse concurrent HIV/AIDS illness burden and female sex. At 12 months, pain was predicted by older age, prior pain, and concurrent HIV/AIDS illness. It was also modestly but significantly predicted by current substance use at baseline. In addition to the direct effects on pain, there were significant indirect effects of demographic and drug use variables on pain mediated through HIV/AIDS illness burden and prior pain. There were significant and positive indirect effects of current and past drug use, greater age, and lower SES on pain at all three time periods. Pain at 6 months and pain at 12 months were also indirectly impacted by previous illness burden. Our results indicate that HIV+ persons who screened positive for current use of a range of illicit substances experienced greater HIV/AIDS illness burden which in turn predicted increased pain.

Keywords

pain; substance use; illicit drug use; HIV; AIDS

1. Introduction

Pain has been characterized as the most significant disability in persons with human immunodeficiency virus (HIV) (Lebovits et al. 1989; Lebovits et al. 1994; Norval 2004). Recent estimates indicate that 67% of HIV+ individuals reported experiencing pain in the previous 4 weeks (Dobalian et al. 2004), suggesting that despite improvements in treatment modalities and increasing awareness among clinicians, pain remains a considerable problem

Contact for correspondence: Jennie C. I. Tsao, PhD, Pediatric Pain Program, Department of Pediatrics, David Geffen School of Medicine at UCLA, 10940 Wilshire Blvd., Suite 1450, Los Angeles, California 90024. Telephone: 310-824-7667, FAX: 310-824-0012, e-mail: jtsao@mednet.ucla.edu.

in persons with HIV. Injection drug use (IDU) accounts for nearly 50% of new HIV infections and is the primary exposure factor in the majority of cases diagnosed in the United States (U.S.) (Centers for Disease Control and Prevention 1997). Whereas pain in HIV+ persons may arise from various sources including the direct effects of the disease on the central or peripheral nervous system, immunosuppression, iatrogenic treatment effects, or various disorders associated with HIV (Hewitt et al. 1997), there may be additional sources of pain in drug dependent individuals with HIV such as withdrawal symptoms or other pre-existing conditions.

HIV patients who are injection drug users (IDUs) are particularly underserved with respect to the use of health services (Shapiro et al. 1999b) and the quality of care for IDUs and drug dependent persons with HIV may be suboptimal. Lack of adequate care may therefore contribute to an increased burden of HIV disease which in turn may result in greater pain. Prior studies in convenience samples however, have yielded mixed findings: some found that IDUs with HIV report more pain than non-IDUs (Fantoni et al. 1997; Martin et al. 1999; Vogl et al. 1999; Del Borgo et al. 2001), whereas others found no differences in reported pain (Breitbart et al. 1996a; Breitbart et al. 1997). In our research with a representative U.S. sample of HIV+ persons, we found that women, but not men, exposed to HIV via IV-drug use reported more pain compared to men who have sex with men (MSM) (Dobalian et al. 2004). However, we did not examine the impact of current vs. past drug use, nor did we investigate use of substances other than IV-drugs. Previous work in this sample has indicated that 12.5% screened positive for drug dependence for at least one illicit drug in the prior year (Bing et al. 2001).

The present study investigated the predictive and concurrent associations among pain, HIV/AIDS illness burden (i.e., clinical category and presence/absence of wasting syndrome), and substance use history in a U.S. national sample using a prospective, longitudinal design. We used structural equation modeling (SEM) to test a conceptual model in which screening positive for current (i.e., in the prior year) and past illicit drug use (i.e., not in the prior year) relative to non-use would predict increased pain and greater disease burden at baseline and at 6 and 12 month follow-ups (see Figure 1). Within the hypothesized model, history of illicit drug use was also posited to predict increased disease burden which would in turn predict greater pain. Thus, illness burden was expected to mediate the association between pain and history of drug use.

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 the 6- and 12-month follow-ups. 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. 1999a). 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 percent). All consent forms and informational materials were reviewed and approved by institutional review boards

(IRBs), including local IRBs. The baseline interviews began in January 1996 and ended in April 1997 (Berry et al. 1999). First follow-up interviews 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 first “6-month” follow-up was 223 days (95% confidence interval [CI], 204-244). The second “12-month” 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 the second follow-up was 416 days (95% CI, 391-441).

2.2 Questionnaire items

Background variables—To control for demographic correlates, 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 was, thus, not included. Demographic data are presented in Table 1.

Drug use—Drug use status reported at baseline was used as a predictor at all three time periods. Drug use at baseline was assessed using screeners developed by the HCSUS consortium [see (Sherbourne et al. 2000; Bing et al. 2001; Burnam et al. 2001)] which were based on the short form of the World Health Organization’s Composite International Diagnostic Interview (Kessler et al. 1998). In the HCSUS sample, the sensitivity and specificity of the CIDI-SF for any psychiatric disorder was 0.80 and 0.76, respectively (Bing et al. 2001), although separate data for diagnosis of drug dependence was not available. To screen for drug use, participants were asked if they had used any substances belonging to at least one of eight categories of illicit drugs in the past year. The categories of illicit drugs (percentage of drug-dependent respondents endorsing use) were: 1) sedatives, sleeping pills or tranquilizers (36.9%); 2) amphetamines or other stimulants (25.9%); 3) analgesics or other prescription painkillers (42.3%); 4) marijuana or hashish (63.2%); 5) cocaine, crack, or free base (63.0%); 6) inhalants other than cocaine (15.4%); 7) LSD or other hallucinogens (5.2%); and 8) heroin (23%). (These percentages sum to more than 100% due to the reported use of multiple substances).

The HCSUS consortium has defined “drug dependence” as reported use of at least one of the above illicit drugs and answering affirmatively to either of the two following queries: 1) using larger amounts to get the same effect, and 2) experiencing any emotional or psychological problems as a result of such use. Although the HCSUS consortium has defined “drug dependence” accordingly, these criteria fall short of meeting the standard diagnostic criteria for drug dependence as specified in the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV) (American Psychiatric Association 1994). The DSM-IV diagnostic criteria for drug dependence include: A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period: (1) tolerance, as defined by either of the following: (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect; (b) markedly diminished effect with continued use of the same amount of the substance; (2) withdrawal, as manifested by either of the following: (a) the characteristic withdrawal syndrome for the substance; (b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms; (3) the substance is often taken in larger amounts or over a longer period than was intended; (4) there is a persistent desire or unsuccessful efforts to cut down or

control substance use; (5) a great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects; (6) important social, occupational, or recreational activities are given up or reduced because of substance use; (7) the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption).

Although prior work has reported findings based on the HCSUS consortium criteria for “drug dependence” (Sherbourne et al. 2000; Bing et al. 2001; Burnam et al. 2001; Turner et al. 2001; Galvan et al. 2003), the HCSUS did not conduct formal diagnostic interviews to determine if participants met full DSM-IV diagnostic criteria for drug dependence. Given that we were unable to confirm diagnosis of drug dependence or drug withdrawal symptoms in the present sample (e.g., via formal diagnostic interviews, or urine toxicology screening, requiring a period of abstinence, or administering antagonist agents), and to avoid overstating the results of this study, respondents who screened positive for current and past “drug dependence” according to the HCSUS consortium criteria are referred to more accurately as being current or past illicit drug users. Thus, 11% of respondents who screened positive for current “drug dependence” according to the HCSUS criteria were classified as current illicit drug users; 27% of respondents who screened positive for past “drug dependence” according to HCSUS criteria were classified as past illicit drug users. The remaining participants reported never having been “drug dependent” according to HCSUS criteria and were classified as non-users.

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 et al. 1988; 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.

HIV/AIDS Illness was measured by the same items at each of the three time periods. It was a latent variable indicated by 2 items: 1) The respondent’s clinical category based upon AIDS diagnoses: 1 = asymptomatic/PGL (persistent generalized lymphadenopathy); 2 = symptomatic; 3 = AIDS indicator condition; and 2) Whether the respondent had wasting syndrome (1 = no; 2 = yes). CD4 count was not included because prior work indicated no relationship between CD4 and pain in HIV+ individuals (Breitbart et al. 1996a; Dobalian et al. 2004).

2.3 Statistical analysis

Latent variable structural equation modeling (SEM) was performed using EQS 6 (Bentler 2005). The comparative fit index (CFI), maximum likelihood chi-square values (ML χ^2), and the Root Mean Square Error of Approximation (RMSEA) were used as indicators of fit (Hu and Bentler 1999; Bentler 2005). 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 2005). Because the sample was very large, we expected a significant chi-square value. Chi-square is sensitive to sample size. 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 demographics were correlated with no imputation of causality or temporal ordering. This analysis assessed the adequacy of the proposed factor structure (measurement model) and the relationships among the latent and measured variables.

Once the factor structure was confirmed, we tested a predictive longitudinal path model in which the background demographics and the illicit drug use variables predicted pain and HIV/AIDS illness at all three time periods (see Figure 1). The stability paths between similar constructs were expected to be very strong. Furthermore, concurrent HIV/AIDS illness was used as a further predictor of pain at all three time periods (e.g., baseline HIV/AIDS illness predicted baseline pain, etc.). All possible paths were included and gradually dropped if they were non-significant. We allowed the error residuals of the same measured variables assessed across time to be freely estimated (e.g., residual of wasting syndrome baseline correlated with residual of wasting syndrome at 6 months). We did not add any non-hypothesized paths or correlations to the model. We also examined the indirect effects of the background variables on later pain and HIV/AIDS illness. They could have exerted an influence through their earlier associations with the baseline constructs.

Because the sample was stratified, a multilevel analysis could have been warranted. A preliminary analysis examined the magnitude of the intraclass correlations of all model variables. 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.

3. Results

3.1 Confirmatory factor analysis

Table 2 presents the factor loadings and other summary statistics for the variables used in the analyses. All measured variables loaded significantly ($p < 0.001$) on their hypothesized latent factors. Fit indices were excellent, especially considering the large sample sizes and larger χ^2 values: ML χ^2 (77, $N = 2267$) = 223.92, CFI = 0.99, RMSEA = 0.029 (confidence interval = .025-.033).

Table 3 reports the correlations among the single-item variables and the latent variables. Significance levels among the variables were very high due in large part to the large sample size. As expected, correlations between similar constructs across time were very high; pain and HIV/AIDS illness were highly correlated at all time periods and across time periods. Current illicit drug use was significantly and positively associated with all of the pain and HIV/AIDS illness latent variables as was past illicit drug use. Higher socioeconomic status was significantly associated with being male, less current and past illicit drug use, greater age, and less pain and HIV/AIDS illness. All of the correlated error residuals of the similar HIV/AIDS illness measured indicators were significantly associated and retained in the path model. Only one association between the residuals of the pain indicators was retained: the one between pain interfering with work at 6 months and at 12 months.

3.2 Path analysis

Figure 1 presents the significant regression paths in the final trimmed longitudinal model. Significant correlations among the background predictors are included as well. The fit indexes of the path model are excellent: Maximum Likelihood χ^2 (106, $N = 2267$) = 268.04, CFI = 0.99, RMSEA = 0.026 (confidence interval = .022-.030).

As expected, there were strong stability paths across time for the pain latent variable and the HIV/AIDS illness latent variable. HIV/AIDS illness significantly predicted reporting of concurrent pain at all three time points. Current illicit drug use predicted pain and HIV/AIDS illness at baseline and also modestly predicted HIV/AIDS illness at 6 months and more pain at 12 months. Past illicit drug use predicted greater HIV/AIDS illness at baseline. Lower SES predicted greater pain and HIV/AIDS illness. Females reported more pain at 6 months but the effect was very small. Older participants reported more pain and HIV/AIDS illness at baseline and more pain at 12 months.

3.3 Indirect effects

We examined whether the indirect effects of the background predictors on pain at baseline, and pain and HIV/AIDS illness at 6 months and 12 months were significant. Significant indirect effects on pain at baseline included current illicit drug use and past illicit drug use ($p \leq .001$), age ($p \leq .01$), and lower SES ($p \leq .05$). We found that pain at 6 months was significantly impacted indirectly by HIV/AIDS illness at baseline, age, current and past illicit drug use, and by lower SES (all $p \leq .001$). Pain at 12 months was indirectly impacted by pain at baseline, HIV/AIDS illness at baseline and 6 months, age, current and past illicit drug use, and lower SES (all $p \leq .001$). HIV/AIDS illness at 6 months was indirectly impacted by current and past illicit drug use ($p \leq .001$), and age and lower SES ($p \leq .05$). HIV/AIDS illness at 12 months was indirectly impacted by HIV/AIDS illness at baseline, current and past illicit drug use ($p \leq .001$), and age and lower SES ($p \leq .05$).

4. Discussion

In this national sample of persons living with HIV, our conceptual model confirmed that screening positive for current and past illicit drug use exerted significant direct and indirect effects on pain and HIV/AIDS illness burden and that these effects persisted across 6 and 12 month follow-ups. Specifically, current drug use directly predicted increased pain at baseline as well as having a small but statistically significant direct effect on pain at 12 months, even after controlling for prior pain. Current drug use also had a significant direct effect on illness burden (i.e., more advanced clinical stage and presence of wasting syndrome) at 6 months. Past drug use had a similar direct effect on illness burden at baseline. In addition, the hypothesized model indicated that the impact of current and past drug use on pain was mediated by greater disease burden. At baseline, both past and current drug use were associated with increased disease burden which in turn predicted greater pain. At 6 and 12 months, there were significant indirect effects of current and past drug use on pain mediated through HIV/AIDS illness burden and prior pain. The conceptual model also revealed that lower SES, female sex and older age were directly and indirectly associated with increased pain and greater illness burden at all three time points.

The current findings support the view that HIV+ persons who report using a broad range of illicit drugs report more pain compared to those who report no longer using such substances and those without a history of drug use. The present results are consistent with prior research indicating increased pain report among IDUs with HIV (Fantoni et al. 1997; Martin et al. 1999; Vogl et al. 1999; Del Borgo et al. 2001). However, our findings are inconsistent with reports that found no differences in pain report in HIV+ IDUs and non-IDUs (Breitbart et al. 1996a; Breitbart et al. 1997). One possibility is that overall, the Breitbart samples had more advanced disease—i.e., roughly 70% met criteria for AIDS, whereas only 36.3% of the HCSUS sample met criteria for AIDS. It may be that at more advanced stages of illness, differences in pain based on drug use history become less salient. Another possibility is that the relationship between pain and drug use was muted in these prior studies since they did not distinguish

between past vs. current substance use; in our model, current drug use had a stronger association with pain compared to past use.

Our findings extend earlier research by revealing the adverse impact of using a broad range of substances including, but not limited to, IV drugs. In our prior work with the HCSUS, we found that women (but not men) exposed to HIV via IV-drug use reported more pain than MSM (Dobalian et al. 2004), although we did not differentiate between current and past drug use. In the present model, the direct impact of female sex on pain was relatively small and it appears that drug use (particularly current use) played a larger role in pain report. As with non-users, pain in HIV+ drug users may derive from various sources related to the direct effects of HIV or its treatment, as well as factors unrelated to HIV disease or its treatment (Hewitt et al. 1997; Del Borgo et al. 2001). However, as discussed by Stein et al. (1997), there may be additional sources of pain in persons with diagnosed drug dependence including prolonged withdrawal symptoms. Psychosocial stressors such as physical/sexual abuse which have been commonly reported in drug dependent persons (Roberts et al. 2003; Reynolds et al. 2005), may lead to lower pain thresholds as has been found among women without HIV (Scarinci et al. 1994). Prior needle use may also contribute to increased pain sensitivity by affecting sensory perception. Alternatively, psychological characteristics of persons who use substances may contribute to increased somatization and hypervigilance to pain. In accord, Vogl et al. (1999) found that HIV+ IDUs reported more symptoms and greater symptom distress than non-IDUs.

Our conceptual model also indicated that screening positive for both past and current illicit drug use were associated with greater HIV/AIDS illness burden, which in turn predicted greater pain; there may be several possible pathways by which this occurs. HIV patients with a history of drug use may suffer from additional health problems [e.g., bacterial infections (Selwyn et al. 1992)] and adverse events (e.g., homelessness) which may then lead to poor health outcomes and increased pain (Riley et al. 2003). The presence of drug use may exacerbate pain due to inadequate attention to preventive care. In addition, there is evidence for the significant undertreatment of pain in HIV+ IDUs (Breitbart et al. 1996b) (although see Larue et al., 1997 discussed below). One study reported that IDUs were 1.8 times more likely to receive inadequate analgesia compared to non-IDUs (Breitbart et al. 1996b). The undertreatment of pain not only promotes needless suffering but may also lead to inappropriate use of illicit drugs for pain relief, resulting in adverse effects on overall health status and health behaviors, which may in turn lead to increased pain. Future studies should examine the extent to which inadequate treatment of pain might contribute to illicit drug use in this population through self-medication.

Consistent with prior research (Dobalian et al. 2004), the present model confirmed a general stability of pain in persons living with HIV over an approximately 12 month period. Illness burden was also highly stable across time and significantly predicted concurrent pain at each time point. We also found persistent direct and indirect effects of demographic characteristics on pain and illness behavior. At baseline, persons of lower SES and who were older reported increased pain compared to those of higher SES and younger, respectively. Women reported modestly but statistically significantly more pain than men at 6 months, and older persons reported greater pain than younger persons at 12 months. Lower SES and older age also indirectly predicted greater pain and increased illness burden at 6 and 12 months. Future studies should examine whether the observed association between lower SES and greater pain relates to undertreatment, differential access to palliative care, or other causes.

Limitations to our findings should be noted. Our study does not identify mechanisms by which drug use leads to more pain or increased illness burden. The HCSUS did not assess pain duration

or other important aspects of pain (e.g., sensory quality of HIV-related pain). Because our focus was on the impact of substance use, our conceptual model did not include the possible role of other psychological disorders. Prior work using the HCSUS found that screening positive for psychological disorder was associated with current drug use (Bing et al. 2001), and such disorders (especially panic disorder) have strong relationships with pain (Tsao et al. 2004). Future studies employing more complex modeling should examine the inter-relationships among pain, psychological disorders, drug use, and health outcomes. Our classification of drug use was based on screeners. Formal diagnostic interviews would likely have yielded more precise data regarding actual diagnoses and it is not known whether all participants that screened positive met full DSM-IV criteria for drug dependence. Our findings are limited to the U.S. population of persons in care for HIV. In contrast to a U.S. study which found that HIV+ IDUs were more likely than non-IDUs to receive inadequate analgesia for pain (Breitbart et al. 1996b), a study conducted in France found that IDUs with HIV (as well as MSM and sicker patients) were actually more likely to receive some type of analgesic than other patients (Larue et al. 1997), suggesting local regulatory climate may affect treatment. Undertreatment of pain among IDUs in the U.S. may relate to fear of criminal prosecution or concern regarding drug-seeking behavior. Additional comparative studies may address this issue. Finally, the HCSUS included only those receiving care for HIV and therefore, certain populations (e.g., those who were unaware they were HIV+) were not represented.

It has been suggested that patients with a history of substance use may over-report pain as part of drug-seeking behavior (O'Connor and Samet 1996). Although drug-seeking behavior cannot be ruled out on the basis of the present results, our findings that current drug-using patients not only reported more pain but also evidenced greater disease burden is consistent with the notion that increased pain in such patients is primarily related to poorer health status. Future research should examine whether adequate treatment of pain among drug dependent persons leads to improved health outcomes. Our findings also indicate the need to investigate whether substance use intervention in drug using HIV patients may help ameliorate pain. The integration of appropriate pain management and substance use treatment may therefore constitute the optimal approach when these conditions are comorbid. Using existing guidelines [e.g., World Health Organization's analgesic ladder; (Breitbart 1998; World Health Organization 1999; Center for Substance Abuse Treatment 2000)] to improve pain management among HIV+ persons who use substances may lead to improved health-related quality of life for this particularly vulnerable population.

Acknowledgements

Support for this research was provided by DA017026 awarded to the first author by the National Institute on Drug Abuse and DA01070 from the National Institute on Drug Abuse awarded to the third author. Dr. Dobalian is supported by a Veterans Administration Health Services Research and Development Merit Review Entry Program award (MRP 03-328). The HIV Cost and Services Utilization Study (HCSUS) was supported by a cooperative agreement (U01HS08578) between RAND and the Agency for Healthcare Research and Quality. Substantial additional support for this agreement was provided by the Health Resources and Services Administration, the National Institute of Mental Health, the National Institute on Drug Abuse, and the Office of Research on Minority Health through the National Institute for Dental Research. Additional support was provided by the Robert Wood Johnson Foundation, Merck and Company, Glaxo-Wellcome, and the National Institute on Aging. The authors thank Gisele Pham for her secretarial and administrative contributions to this research project, and the participants in this study.

References

- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). Washington DC: Author, 1994.
- Bentler P. EQS 6 structural equations program manual. Encino, CA: Multivariate Software, Inc, 2005.
- Berry S, Brown J, Athey L, Keesey J, Tebow J, Webster R, Cotton S. HCSUS Baseline Patient Questionnaire Documentation; 1999.

- Bing EG, Burnam A, Longshore D, Fleishman JA, Sherbourne CD, London AS, Turner BJ, Eggan 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. Psychotropic adjuvant analgesics for pain in cancer and AIDS. *Psychooncology* 1998;7:333–345. [PubMed: 9741072]
- 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.
- 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.
- 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]
- Center for Substance Abuse Treatment. Substance Abuse Treatment for Persons With HIV/AIDS. Treatment Improvement Protocol (TIP) Series, Number 37. DHHS Pub. No. (SMA) 00-3410; 2000.
- Centers for Disease Control and Prevention. HIV AIDS Surveillance Report; 1997.
- 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 JCI, Duncan RP. The role of pain in the use of outpatient services among persons with HIV: Results from a nationally representative survey. *Med Care* 2004;42:129–138. [PubMed: 14734950]
- 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. [PubMed: 9231582]
- 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]
- Galvan FH, Burnam MA, Bing EG. Co-occurring psychiatric symptoms and drug dependence or heavy drinking among HIV-positive people. *J Psychoactive Drugs* 2003;35 (Suppl 1):153–160. [PubMed: 12825758]
- Hays RD, Morales LS. The RAND-36 measure of health-related quality of life. *Ann Med* 2001;33:350–357. [PubMed: 11491194]
- Hewitt DJ, McDonald M, Portenoy RK, Rosenfeld B, Passik S, Breitbart W. Pain syndromes and etiologies in ambulatory AIDS patients. *Pain* 1997;70:117–123. [PubMed: 9150284]
- 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.
- 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;7:171–85.
- 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]
- Lebovits AH, Lefkowitz M, McCarthy D. The prevalence and management of pain in patients with AIDS: a review of 134 cases. *Clin J Pain* 1989;5:245–248. [PubMed: 2520410]
- Lebovits AH, Smith G, Maignan M, Lefkowitz M. Pain in hospitalized patients with AIDS: analgesic and psychotropic medications. *Clin J Pain* 1994;10:156–161. [PubMed: 8075469]

- 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]
- Norval DA. Symptoms and sites of pain experienced by AIDS patients. *S Afr Med J* 2004;94:450–454. [PubMed: 15250459]
- O'Connor PG, Samet JH. The substance-using human immunodeficiency virus patient: approaches to outpatient management. *Am J Med* 1996;101:435–444. [PubMed: 8873515]
- Reynolds M, Mezey G, Chapman M, Wheeler M, Drummond C, Baldacchino A. Co-morbid post-traumatic stress disorder in a substance misusing clinical population. *Drug Alcohol Depend* 2005;77:251–258. [PubMed: 15734225]
- Riley ED, Wu AW, Perry S, Clark RA, Moss AR, Crane J, Bangsberg DR. Depression and drug use impact health status among marginally housed HIV-infected individuals. *AIDS Patient Care STDS* 2003;17:401–406. [PubMed: 13678541]
- Roberts AC, Wechsberg WM, Zule W, Burroughs AR. Contextual factors and other correlates of sexual risk of HIV among African-American crack-abusing women. *Addict Behav* 2003;28:523–536. [PubMed: 12628624]
- Scarinci IC, McDonald-Haile J, Bradley LA, Richter JE. Altered pain perception and psychosocial features among women with gastrointestinal disorders and history of abuse: a preliminary model. *Am J Med* 1994;97:108–118. [PubMed: 8059776]
- Selwyn PA, Alcapes P, Hartel D, Buono D, Schoenbaum EE, Klein RS, Davenny K, Friedland GH. Clinical manifestations and predictors of disease progression in drug users with human immunodeficiency virus infection. *N Engl J Med* 1992;327:1697–1703. [PubMed: 1359411]
- Shapiro M, Berk M, Berry S, Emmons C, Athey L, Hsia D, Leibowitz A, Maida C, M MM, 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* 1999a;34:951–968.
- Shapiro MF, Morton SC, McCaffrey DF, Senterfitt JW, Fleishman JA, Perlman JF, Athey LA, Keesey JW, Goldman DP, Berry SH, Bozzette SA. Variations in the care of HIV-infected adults in the United States: results from the HIV Cost and Services Utilization Study. *JAMA* 1999b;281:2305–2315.
- 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 MD, Wimbush J, Panil N. Pain among drug users completing an inpatient detoxification program. *Subst Abus* 1997;18:113–118.
- Stewart AL, Hays RD, Ware JEJ. The MOS short-form general health survey. Reliability and validity in a patient population. *Med Care* 1988;26:724–735. [PubMed: 3393032]
- Tsao JCI, Dobalian A, Naliboff BD. Panic disorder and pain in a national sample of persons living with HIV. *Pain* 2004;109:172–180. [PubMed: 15082139]
- 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]
- World Health Organization. *Cancer Pain Relief*, 2nd ed. Geneva, Switzerland: World Health Organization; 1999.

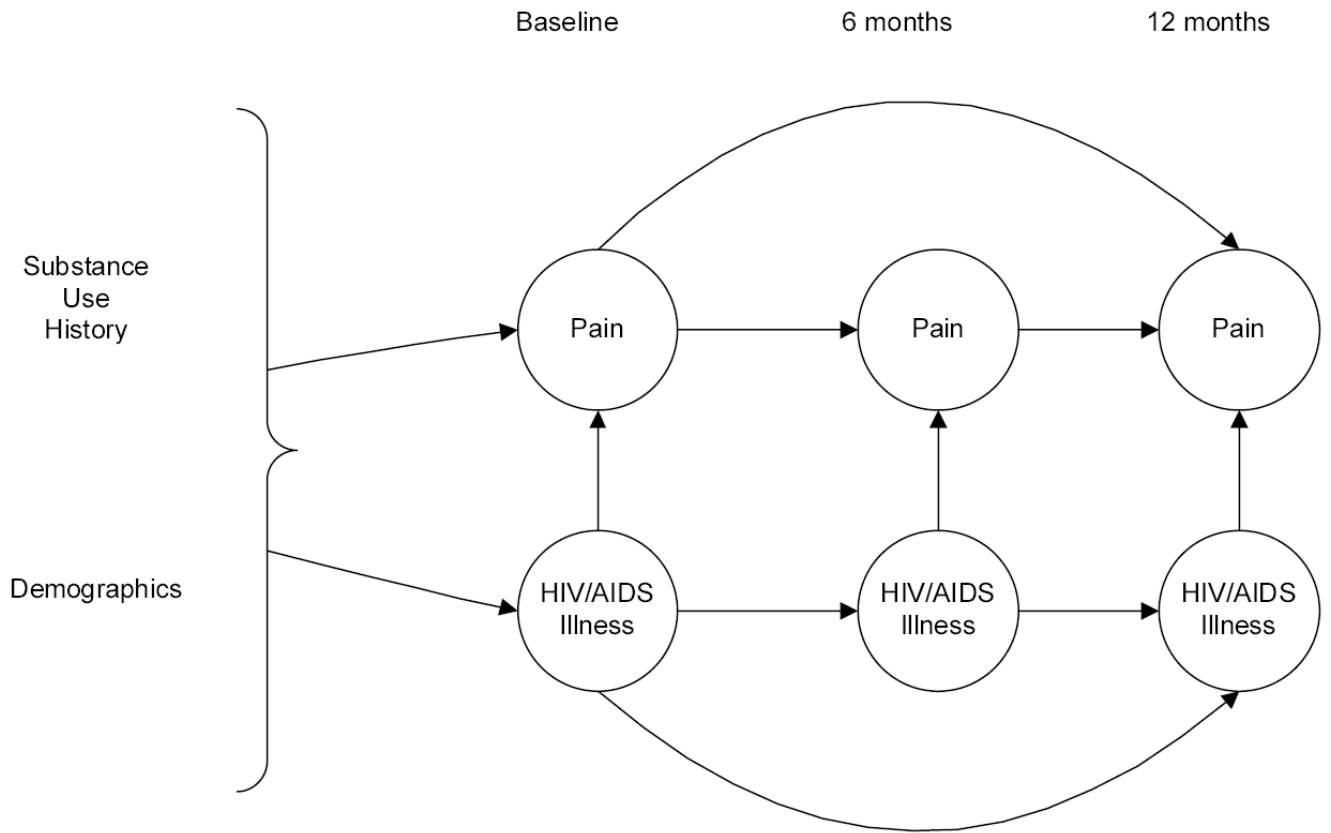


Figure 1. Conceptual model illustrating the hypothesized relationships among substance use history, demographics, pain and illness burden at baseline and 6- and 12-month follow-ups.

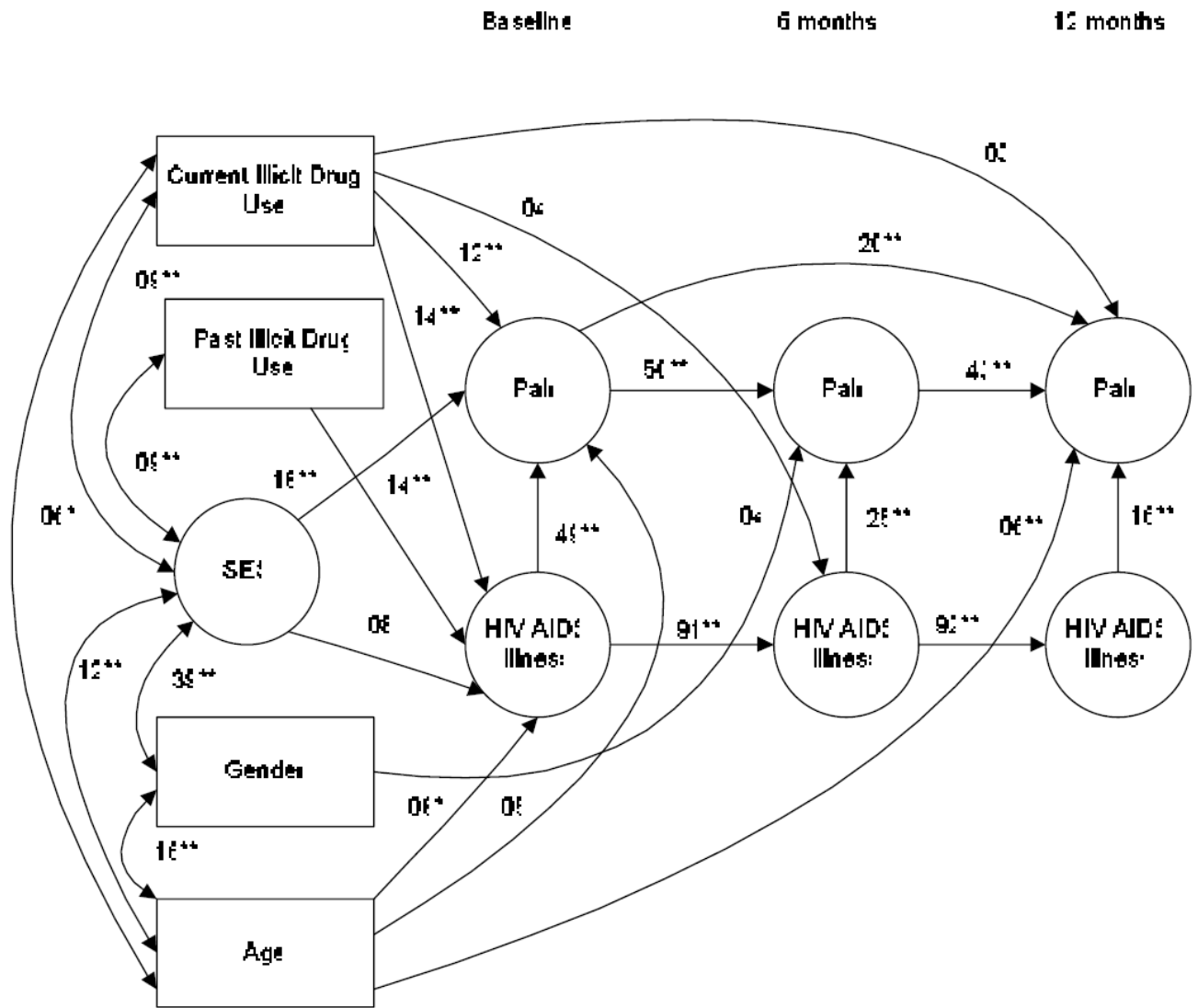


Figure 2. Longitudinal path model for HCSUS participants ($N = 2267$). Latent constructs are in circles, single items are in rectangles; 1-headed arrows depict standardized regression paths, 2-headed arrows represent correlations (standardized covariances). (* = $p \leq .05$, ** = $p \leq .01$, *** = $p \leq .001$).

Table 1
Sociodemographic characteristics of the HCSUS sample.

Variables	Unweighted N = 2267	Weighted % (pop.)	SE
<u>Gender</u>			
Female	664	0.23	0.03
Male	1,603	0.77	0.03
<u>Race/ethnicity</u>			
African American	707	0.32	0.03
Hispanic	326	0.15	0.02
White	1158	0.49	0.03
Other	76	0.03	0.01
<u>Education</u>			
<High School diploma	547	0.25	0.03
High School diploma	627	0.28	0.01
Associate's degree	658	0.28	0.02
BA/BS or more	435	0.20	0.03
<u>Income</u>			
\$0-\$5,000	456	0.20	0.02
\$5,001-\$10,000	567	0.25	0.02
\$10,001-\$25,000	597	0.26	0.01
\$25,001+	647	0.29	0.03
<u>Illicit Drug Use</u>			
Current (prior year)	253	0.11	0.01
Past (before prior year)	617	0.27	0.02
Never	1,397	0.62	0.03

Table 2
Means, standard deviations (SD), and factor loadings of measured variables in the Confirmatory Factor Analysis.

Variable	Mean / SD	Factor loadings*
<u>Single items</u>		
Current illicit drug use	.11 / .31	N. A. **
Past illicit drug use	.27 / .45	N.A.
Sex (1=male)	1.23 / .42	N.A.
Age (years)	38.81 / 8.74	N.A.
<u>Latent variables</u>		
Socioeconomic Status		
Income (1-4)	2.65 / 1.10	.60
Education (1-4)	2.43 / 1.06	.70
Pain - baseline		
Interfere work (1-5)	2.09 / 1.25	.85
Bodily pain (1-6)	2.67 / 1.45	.86
Illness - baseline		
Clinical category (1-3)	2.25 / .63	.53
Wasting syndrome (0-1)	0.14 / .35	.47
Pain - 6 months		
Interfere work	1.92 / 1.14	.85
Bodily pain	2.49 / 1.41	.84
Illness - 6 months		
Clinical category	2.34 / .59	.58
Wasting syndrome	0.12 / .32	.43
Pain - 12 months		
Interfere work	1.99 / 1.20	.90
Bodily pain	2.55 / 1.48	.86
Illness - 12 months		
Clinical category	2.39 / .58	.60
Wasting syndrome	0.12 / .32	.44

* all factor loadings significant, $p \leq .001$;

** N. A. = not applicable

Table 3
Correlations among single-item and latent variables.

Single items	1	2	3	4	5	6	7	8	9	10
1. Current illicit drug use	—									
2. Past illicit drug use	-.21***	—								
3. Sex	.03	-.02	—							
4. Age	-.07***	.02	-.16***	—						
<u>Latent Variables</u>										
5. Socioeconomic Status	-.11***	-.08**	-.40***	.12***	—					
6. Pain - Baseline	.19***	.06**	.04	.05*	-.25***	—				
7. Illness - Baseline	.11***	.11***	-.01	.06*	-.09*	.52***	—			
8. Pain - 6 months	.14***	.07**	.06**	.03	-.20***	.63***	.43***	—		
9. Illness - 6 months	.13***	.07**	-.01	.05	.12***	.46***	.94***	.47***	—	
10. Pain - 12 months	.15***	.06**	.01	.09***	.14***	.55***	.42***	.63**	.43**	—
11. Illness - 12 months	.14***	.08**	-.01	.05	.13***	.44***	.88***	.45***	.92***	.45***