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Frequent Occurrence of Pain and Prescription Opioid Use for Treatment of Pain among Women with and at Risk for HIV Infection

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INTRODUCTION

Despite the successes of potent antiretroviral therapies in reducing the mortality and morbidity of HIV infection, pain remains a frequently reported problem among HIV+ patients. Estimates of the prevalence of pain among HIV+ adults vary widely, ranging from 25% to 80%, suggesting that pain may be more common in this population than the 20–30% reported among general populations of American adults.[1–7] Many studies report that pain is

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associated with various psychosocial outcomes including: reduced health-related quality of life (HRQOL), functional impairments, psychological distress, and increased use of healthcare for HIV+ persons.[4, 8, 9–14] Despite its high prevalence and negative health consequences, pain is often underestimated and undertreated in HIV+ patients, particularly among women, those with less education, or intravenous drug use.[1, 8, 15–18] Additionally, because women living with HIV have an increased prevalence of conditions associated with opioid analgesic misuse, such as dependency on drugs or alcohol and psychiatric disorders, this population is at particular risk for adverse outcome of opioid therapies.[18–21]

Some studies have shown that HIV+ women report greater pain than do HIV+ men,[1, 22, 23] while others have not found sex differences in the prevalence of pain in HIV+ populations.[24–26] In a nationally representative sample of HIV+ adults receiving care in the United States, 67% of respondents reported experiencing pain in the previous 4 weeks, with the greatest pain severity reported among women who injected drugs and individuals who were unemployed and less educated.[8] However many studies of pain among HIV+ persons have been limited to men,[2, 27] or focus on those with advanced HIV disease/AIDS,[1–4, 22, 24, 25] prior to the general availability of effective antiretroviral therapy,[1, 2, 19, 21, 22] or lack of an HIV-uninfected comparison group.[1–6, 8, 22–30] We therefore sought to compare the occurrence of pain, pain severity, and pain interference between HIV+ and HIV− participants of the Women's Interagency HIV Study (WIHS). We also sought to characterize the types of pain treatments used and the extent to which these treatments provided pain relief in this cohort of predominantly racial and ethnic minority women with or at-risk for HIV infection.

METHODS

Study Population

The WIHS is a multicenter prospective cohort study established in 1994 to investigate the natural and treated history of HIV disease progression in women with similar risk and sociodemographic characteristics. A total of 2843 HIV+ and 975 HIV− women were enrolled during either 1994–95, or 2001–02, and in 2011–12 at six sites (Bronx/Manhattan, NY; Brooklyn, NY; Chicago, IL; Los Angeles, CA; San Francisco; CA and Washington DC). In 2014–15, the WIHS closed its Los Angeles site and added four southern U.S. sites: Atlanta GA, Chapel Hill NC, Miami FL, and Birmingham AL/Jackson MI; of these southern sites, only data from the Atlanta site was available and included at the time of the current analyses. WIHS methods and baseline cohort characteristics have been described previously.[31, 32]

At semi-annual visits, participants complete interviewer-administered questionnaires which provide data on demographics, clinical characteristics, and medical history including antiretroviral therapy (ART) usage, undergo targeted physical examinations, and provide biologic specimens.[33] Variables examined in this study included HIV acquisition risk category [injection drug use (IDU), heterosexual exposure, transfusion/other]; year of WIHS enrollment (1994–95, 2001–02, or 2011–14); age; race [White (including Hispanic and non-Hispanic), Black (including Hispanic and non-Hispanic) and Other (predominantly women who self-identified as Hispanic but not White or Black)]; ever and current illicit drug use

(cocaine, crack, or heroin); current cannabis use; any history of injection drug use; alcohol use < or ≥ 7 drinks/week; tobacco use (current, past, or never); annual income of $12,000 or less; educational attainment (less than high school, completed high school, some college, or completed 4 years of college or more); depressive symptom score defined as Center for Epidemiology Studies Depression score (CES-D) of ≥16;[34] history of a clinical AIDS defining illness (ADI, excludes CD4 depletion category); hepatitis C virus (HCV) infection determined by positive serology with viremia at enrollment; diabetes mellitus as previously defined in WIHS;[35] current and nadir CD4+ cell count; log10 HIV-1 RNA viral load at the study visit; self-reported current and cumulative duration of ART use; and extent of adherence to prescribed antiretroviral regimen.

Starting at either visit 37 or 39 (October 1, 2012 to March 31, 2013) WIHS participants were asked to complete a brief pain inventory short form (BPI-SF). This cross-sectional analysis includes all WIHS participants who had completed the BPI-SF at least once, at either visit 37 or 39, which is referred to as the index visit. The WIHS protocol was approved by the institutional review boards at each study site and all participants provided written informed consent.

Additional Details on Pain Measures

Pain Assessment—The BPI-SF is a validated tool used in numerous diseases, including osteoarthritis,[36] peripheral neuropathy,[37] low back pain,[38] cancer,[39, 40] and HIV.[1, 15] The BPI-SF is 9-item tool measuring pain intensity and interference on function in the past week, and the amount of pain relief experienced with pain medication use. Participants rated their pain intensity “at its worst”, “at its least”, and “on average” for pain in the past week, as well as for pain they have “right now” using on a 0–10 scale for each. Participants reported the medications or treatments they received for pain, and rated the percentage of reduction in pain intensity achieved with medications or treatment, on a scale of 0–100%, shown in 10% increments. To ascertain self-evaluation of “pain interference”, participants were instructed to indicate how much, during the past week, pain interfered with their daily function in each of 7 domains, ranging from no interference (0) to 10 (complete interference): (a) general activity, (b) mood, (c) walking ability, (d) normal work, (e) relations with other people, (f) sleep, and (g) enjoyment of life. Overall pain interference was calculated by averaging scores across these seven domains. Participants who reported pain were also asked to note the anatomic site where the pain was most severe, using an anatomic diagram.

Use of Prescription Pain Medications

The Use of Pain Prescription Medication survey was abbreviated from the 2010 National Survey of Drug Use and Health Survey and administered to each participant who reported pain in the prior week on the BPI.[41] This survey collects self-reported data on ever use of medications received specifically for treatment of pain and then categorizes medication class as: non-steroidal anti-inflammatory drugs (NSAIDS), steroids, antidepressants, anticonvulsants/anti-epileptics, topical anesthetics, opioids, cannabis, sleeping medications, sedatives/anxiolytics, muscle relaxants, migraine medications, and stimulants. Participants are instructed to include only those medications they have taken specifically for pain and not to include mediations taken for other reasons. Participants were also queried on the source of

their pain medication: over the counter, prescribed by a doctor, or other source (including spouse/long-term partner, family, friend, co-worker, internet, or drug dealer/stranger); participants could report multiple sources of medications.

Laboratory Methods

Plasma HIV-1 RNA was measured by isothermal nucleic acid sequence-based amplification (NASBA/Nuclisens; Organon Teknika Corp., Durham, NC, USA) with a lower limit of detection (LLD) of 80 copies/ml prior to October 1, 2008 and then by COBAS Taqman HIV-1 assay with LLD of 48 or 20 copies/mL, based on assay kit detection performance. Lymphocyte subsets were quantified using standard flow cytometric methods in laboratories participating in the NIH/NIAID Flow Cytometry Quality Assessment Program.[42] HCV RNA was measured on frozen repository specimens for all women who tested HCV antibody-positive at WIHS enrollment using either the COBAS Amplicor Monitor 2.0 assay or the COBAS Taqman assay (Roche Diagnostics, Branchburg, NJ, USA).[43]

Statistical Analyses

Participant characteristics were compared by HIV status using Chi-square tests for categorical variables, and t-test and Wilcoxon rank sum tests for continuous variables. Linear regression models adjusting for race, age, and WIHS site examined differences in pain severity for; worst, least, average, and current pain as well as for differences in pain interference for each domain by HIV status. Since many women reported that their pain did not interfere with relationships with other people, this pain interference domain was dichotomized into any vs. none, and logistic regression compared odds of any pain interference with their relationships with other people between HIV+ and HIV− women, adjusting for race, age, and WIHS study site. Logistic regression adjusting for race, age and WIHS site was also used to calculate odds ratios for use of each medication class among women reporting treatment for pain in the prior week for HIV+ vs. HIV− women. Year of study enrollment was not included in multivariable models due to collinearity with WIHS site and age; however including enrollment year in models did not qualitatively alter the point estimates (data not shown). All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Participant Characteristics

Demographic and clinical characteristics of HIV+ and HIV− women who contributed data to this study are summarized in Table 1. The median age was 48 years for HIV+ women and 47 years for uninfected women, and income and education level were similar between HIV+ and HIV− women. HIV+ women were more likely to have active hepatitis C virus infection as evidenced by viremia and to report depressive symptoms (CESD score ≥16), but were less likely to report current tobacco use, heavy alcohol use (≥ 7 drinks per week), and current use of cannabis or “heroin, crack, and/or cocaine” when compared with HIV− women (Table 1).

Characteristics of Pain in the WIHS cohort

Overall, half of the WIHS cohort reported having had “any pain” within the past 7 days, with similar proportions reporting pain by HIV status (50% HIV+ vs. 49% HIV−, p=0.70). Self-reported levels of pain severity were similar between HIV+ and HIV− women, including pain at its worst, at its least, average pain, and current pain (Table 2). On a scale of 0–10, unadjusted mean rating of participants’ average pain was 5.38 ± 2.24 for HIV+ vs. 5.25 ± 2.49 for HIV− women, and after adjusting for race, age, WIHS site, enrollment year, HCV, CESD, diabetes mellitus, alcohol use, and current cocaine, crack, or heroin use the difference between average pain level for HIV+ and HIV− was not statistically or clinically significant 0.10, p=0.55 (Table 2). The unadjusted level of most severe pain was 7.45 ± 2.09 for HIV+ vs. 7.51 ± 2.08 for HIV− women, and adjusted differences in the worst pain level between HIV+ and HIV− women remained nonsignificant (Table 2).

When comparing the effects of pain by HIV status, we found that HIV+ and HIV− women had similar experiences with pain interference associated with their general activity, walking ability, normal work (including both work outside the home and housework), relationships with other people, and sleep (Table 2). Notably, after adjusting for race, age, WIHS site, enrollment year, HCV, CESD, diabetes mellitus, alcohol use, and current cocaine, crack, or heroin use, HIV+ women reported less pain interference with their mood and enjoyment of life than did HIV− women (Table 2).

When comparing receipt of treatment for current pain by HIV status, and the extent to which these treatments provided pain relief, we found no differences in the proportion of women receiving treatment for their pain; although only slightly more than half of women with pain in the past week reported using medication for treatment of their pain (58% HIV+ vs. 56% HIV−, p =0.52). HIV+ and HIV− women reported similar pain relief from the treatments they used. Among women receiving treatment for pain, HIV+ women reported a 66% reduction in pain level, compared with 62% among HIV− women in unadjusted analyses (p= 0.11); adjusted differences in mean percent pain reduction was 5.35% greater for HIV+ women compared to HIV− women (p=0.04) (Table 2).

Use of Pain Medication among WIHS Participants with Self-reported Pain

Classification of pain medications used among HIV+ and HIV− women, as well as source of medications (over the counter, prescribed by doctor, or other) are shown in Table 3. The five pain medication classes most frequently used were NSAIDS (90% HIV+ vs. 96% HIV−, p=0.006), followed by opioids (65% HIV+ vs. 67% HIV−, p=0.53), topical anesthetics (46% HIV+ vs. 56% HIV−, p=.004), muscle relaxants (23% HIV+ vs. 14% HIV−, p=0.008), and anticonvulsants (23% HIV+ vs. 14% HIV−, p=0.002). While the proportion of women reporting cannabis use for pain did not statistically differ by HIV status (16% HIV+ vs. 19% HIV−, p=0.26), HIV+ women used prescribed cannabis more often than HIV− women, (55% HIV+ vs. 32% HIV−, p= 0.001). Opioids were very commonly used for treatment of pain in both groups, and almost all opioid users reported physician prescriptions as a source (99% HIV+ vs. 95% HIV−, p=0.004). Notably, because participants could report multiple sources of medications, 8% of HIV+ and 14% of HIV− women also reported other sources of opioids for pain (such as friend, family, dealer, etc.) (p=0.01). In adjusted analyses, HIV+

women remained significantly less likely to take NSAIDS (AOR 0.41; 95% CI: 0.22–0.77), topical anesthetics (AOR 0.58; 95% CI: 0.43–0.79), or muscle relaxants (AOR 0.61; 95% CI: 0.44–0.85) for pain, and more likely to take anticonvulsants (AOR 1.66; 95% CI: 1.12–2.46) compared to HIV− women (Table 3).

DISCUSSION

This is the first large scale study on the experience and treatment of pain in HIV+ women and HIV− women with similar socioeconomic and behavioral risk profiles, particularly among racial and ethnic minority women who have substantial medical and substance use histories. Half of the participants reported pain in the prior week; however this observed occurrence of pain is similar to that reported in other studies of HIV+ patients,[1–6, 27–30] and is no greater among HIV+ women than among HIV− women with similar risk characteristics. General characteristics of pain reported by women did not differ by HIV status, including the overall occurrence of pain, severity of pain, and proportion of women using medications to treat pain. Only slightly over half of all women reported receiving pharmacotherapy for current pain, whether prescribed by their doctor, purchased over-the-counter, or obtained from other sources.

Differences in the impact of pain in domains of function (pain interference) by HIV status, if any, were minimal. HIV+ women reported less pain interference with mood, enjoyment of life, and relationships with others when compared to HIV− women, despite having similar levels of pain severity, in addition to greater reduction in pain with treatment; these differences were nevertheless small. Perhaps most notable was the degree to which pain severity, treatment, and report of pain interference were similar between HIV+ and HIV− women. These findings might suggest that in the current era of antiretroviral therapy, pain syndromes observed among HIV+ individuals are less likely directly related to HIV infection or its therapies. Distal symmetric polyneuropathy, the most common form of HIV−associated peripheral neuropathy, may result from untreated HIV infection, but more commonly from exposure to specific NRTIs that are no longer used in the United States (e.g. didanosine, zalcitabine, and stavudine).[44] Use of newer antiretroviral agents, that are less toxic, more potent, and less likely to result in painful neuropathic syndromes, may have led to a reduction in pain experienced among HIV-infected persons, or the etiology of pain may have shifted towards co-morbidities related to aging, obesity, or perhaps more likely, related to other sociodemographic factors associated with pain that are more prevalent among seropositive individuals.

Although participants used a wide range of types of medication for pain, a striking two-thirds of women with pain on pharmacotherapy were treated with opioids. The vast majority of women using opioids for treatment of pain reported prescription opioid use, while 8% of HIV+ women and 14% of HIV− women also reported non-prescribed opioid use. The high occurrence of opioid use for treatment of pain among this sample of middle-aged women reflects the national trends towards an overall increase in the use of prescription opioids for treatment of pain in the general U.S. population. As the number of per capita opioid prescriptions has increased, there has been a parallel and marked increase in the opioid-related mortality rate in the U.S.[45–49] Prospective evaluation of increased opioid prescription

and opioid-related mortality in relation to newer prescription patterns and in contemporary cohorts of HIV-infected persons may be warranted. Moreover, although pain is commonly reported in both HIV-infected and uninfected women in the WIHS, many participants are not ideal candidates for opioid prescribing; thus effective pain management, including use of both opioid and non-opioid based regimens, may be challenging in this population. Further investigation into provider decision-making surrounding opioid prescribing, as well as effective strategies to help mitigate opioid prescribing in at-risk populations is needed. Additionally, future research should further characterize patterns of opioid use among racial and ethnic minority women with pain, including duration of opioid use, and the effects of opioid management of pain including the risks and benefits of opioid use for acute and chronic pain in women with or at risk for HIV infection.

A sizeable and similar number of HIV+ and HIV− women also reported use of cannabis for the treatment of pain, with the majority of HIV+ women using cannabis reporting medical, physician-prescribed use. Of note, we did not find differences in the frequency of cannabis use by HIV status, but rather differences in the way in which cannabis was obtained. Unsurprisingly, HIV+ women were more likely to obtain cannabis via prescription than were HIV− women, as HIV/AIDS is one of the medical conditions that allows patients to qualify for medical cannabis programs. Given the changing national landscape of medical cannabis use for chronic disease management, understanding how medical cannabis use not only affects pain, but also opioid and other analgesic prescription patterns is imperative, particularly among HIV+ populations.

Our study has several limitations. We do not have data on the etiology or type of pain (such as neuropathic, musculoskeletal, inflammatory, or mechanical), nor can we distinguish between acute or chronic pain, as the BPI assesses pain in the prior week only. Medication use, including type and source of pain medication, is based on self-report. Although all participants are instructed to include only those medications they have taken specifically for pain, it is possible that some participants may inadvertently report medications prescribed for indications other than pain. Non-pharmacologic treatments for pain such as physical therapy, mindfulness, massage, or acupuncture were not assessed. Although we have adjusted for depressive symptoms in analyses, assessments for other mental illnesses are not performed in the WIHS. We are also unable to assess the prevalence of opioid misuse in the WIHS cohort. Because our study is cross sectional, we are unable to assess changes in pain characteristics or clinical consequences of pain or its treatment over time. Future studies should prospectively investigate the relationships between pain and HIV-related outcomes, such as adherence to antiretroviral therapy, virologic suppression and retention in care, as well as non-HIV outcomes, such as physical function, disability, and health care utilization, including the effects of opioid treatment for pain on these outcomes.

Our study contributes substantially to the scientific literature on the experience of pain in HIV+ and HIV− women, including the effects of pain on daily functioning, and characterization of pain treatment in racial and ethnic minority women, in whom there is a paucity of data. In the WIHS cohort, in which the vast majority of HIV+ women are receiving antiretroviral therapy and have high CD4+ cell counts, pain is frequently reported and treated regardless of HIV serostatus or CD4+ cell count, and a large proportion of both

HIV+ and HIV− women report use of opioids for pain management. Further research is needed to understand factors associated with prescribing of opioid vs. non-opioid based regimens for pain management, as well as the relation of medicinal and non-medicinal cannabis use for pain control, either alone or in combination with other analgesics. Lastly, among HIV+ women, additional research is needed to better characterize pain etiology in the era of newer HIV medications, and the extent to which pain itself, treatment of pain, and type of pain treatment may impact HIV disease outcomes.

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Table 1

Participant Characteristics

Characteristic	HIV+ (N=1393)	HIV− (N=587)	P value
Age, year, median (IQR)	48.0 (43.0–54.0)	47.0 (39.0–53.0)	<0.0001
WIHS Site, n (%)			0.14
Bronx	243 (17.4%)	125 (21.3%)	
Brooklyn	253 (18.2%)	98 (16.7%)	
Chicago	225 (16.2%)	78 (13.3%)	
Los Angeles	225 (16.2%)	84 (14.3%)	
Washington DC	216 (15.5%)	89 (15.2%)	
San Francisco	219 (15.7%)	104 (17.7%)	
Atlanta	12 (0.9%)	9 (1.5%)	
Race/Ethnicity, n (%)			0.01
Black	862 (61.9%)	399 (68.0%)	
White	292 (21.0%)	90 (15.3%)	
Hispanic/Other	239 (17.2%)	98 (16.7%)	
Education level, n (%)			0.40
Less than High School	529 (38.0%)	203 (34.7%)	
Completed High School	406 (29.2%)	189 (32.3%)	
Some College	347 (24.9%)	151 (25.8%)	
Completed 4 years of college or more	110 (7.9%)	42 (7.2%)	
Annual income < $12,000	716 (51.8%)	281 (48.0%)	0.13
Study enrollment period			<0.0001
1994–1995	694 (49.8%)	244 (41.6%)	
2001–2002	447 (32.1%	252 (42.9%)	
2011–2014	252 (18.1%)	91 (15.5%)	
Tobacco use, n (%)			<0.0001
Current	490 (35.2%)	275 (46.9%)	
Former	451 (32.4%)	180 (30.7%)	
Never	452 (32.5%)	132 (22.5%)	
Alcohol use ≥ 7 drinks/week, n (%)	137 (9.8%)	105 (17.9%)	<0.0001
Current heroin, cocaine, or crack use, n (%)	88 (6.3%)	67 (11.4%)	0.0001
Current cannabis use, n (%)	243 (17.5%)	157 (26.8%)	<0.0001
History of injection drug use ever, n (%)	310 (22.3%)	135 (23.0%)	0.72
CESD ≥ 16 (%)	419 (30.2%)	149 (25.5%)	0.04
Hepatitis C Virus positive, n (%)	200 (14.4%)	59 (10.1%)	0.009

Characteristic	HIV+ (N=1393)	HIV− (N=587)	P value
Diabetes Mellitus, n (%)	278 (20.0%)	136 (23.2%)	0.11
Report of any pain within 7 days, n (%)	699 (50.2%)	289 (49.2%)	0.70
Ever AIDS, n (%)	553 (39.7%)	N/A	N/A
Current CD4+ count, cells/μL, median (IQR)	566 (380–771)	N/A	N/A
Nadir CD4+ count, cells/μL, median (IQR)	231 (116–375)	N/A	N/A
Current $\log_{10}$ HIV RNA, copies/mL, median (IQR)	1.30 (1.30–2.26)	N/A	N/A
Current ART use, n (%)	1241 (89.2%)	N/A	N/A

Abbreviations: CESD = Centers for Epidemiologic Studies – Depression Scale score; IQR = interquartile range; ART= antiretroviral therapy.

Table 2

Pain Characteristics among WIHS Participants with Self-reported Pain

Pain Characteristic	HIV+ (N=699)	HIV− (N=289)	P value[1]	Adjusted[2] Difference HIV+ minus HIV − (95% CI)	P value
Pain severity (0 to 10)					
Pain at its worst, Mean ± SD	7.45 ± 2.09	7.51 ± 2.08	0.74	−0.04 (−0.33, 0.25)	0.78
Paint at its least, Mean ± SD	3.65 ± 2.29	3.35 ± 2.25	0.05	0.37 (0.06, 0.69)	0.02
Average pain level, Mean ± SD	5.38 ± 2.24	5.25 ± 2.49	0.45	0.10 (−0.22, 0.41)	0.55
Current pain level, Mean ± SD	3.69 ± 2.91	3.51 ± 3.03	0.29	0.15 (−0.25, 0.55)	0.46
Pain interference Level (0 to 10)					
General activity, Mean ± SD	4.72 ± 3.31	4.90 ± 3.41	0.50	−0.35 (−0.80, 0.10)	0.13
Mood, Mean ± SD	4.30 ± 3.30	4.84 ± 3.47	0.03	−0.63 (−1.06, −0.19)	0.005
Walking ability, Mean ± SD	4.74 ± 3.47	5.00 ± 3.50	0.29	−0.39 (−0.86, 0.08)	0.10
Normal work, Mean ±SD	4.56 ± 3.39	4.70 ± 3.61	0.58	−0.27 (−0.74, 0.19)	0.25
Relations with other people, any interference vs. none, n (%)	360 (51.6%) vs. 337 (48.4%)	153 (52.9%) vs. 136 (47.1%)	0.71	[3] AOR 0.86 (0.63, 1.17)	0.34
Sleep, Mean ± SD	4.51 ± 3.57	4.60 ± 3.71	0.52	−0.16 (−0.64, 0.32)	0.52
Enjoyment of life, Mean ± SD	3.78 ± 3.54	4.18 ± 3.72	0.13	−0.53 (−0.99, −0.06)	0.03
Receipt of treatment for pain, n (%)			0.52	1.01 (0.75, 1.36)	0.96
Yes	385 (57.8%)	151 (55.5%)			
No	281 (42.2%)	121 (44.5%)			
Missing	33 (4.7%)	17 (5.9%)			
Percentage pain reduction with treatment (0–100), Mean ± SD	65.7 ± 27.5	61.7 ± 26.8	0.11	5.35 (0.23, 10.46)	0.04

[1] Chi-Square test for categorical variables and Wilcoxon test for continuous variable without missing category

[2] Linear regression adjusted for race, age, WIHS site, enrollment year, HCV, CESD, diabetes mellitus, alcohol use, and current cocaine, crack, or heroin use

[3] Logistic regression adjusted for race, age, WIHS site, enrollment year, HCV, CESD, diabetes mellitus, alcohol use, and current cocaine, crack, or heroin use; reference is HIV-uninfected

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Table 3

Current Use of Pain Medication among WIHS Participants with Self-reported Pain

Medication Type Used and Source	HIV+ (N=699)	HIV− (N=289)	P value	Adjusted[1] Odds Ratio: HIV+ vs. HIV− (95% CI)	P value
Non-steroidal Anti-inflammatory Drugs(NSAIDS)	628 (89.8%)	276 (95.5%)	0.006	0.41 (0.22, 0.77)	0.006
Over the counter, n (%)	482 (76.8%)	226 (81.9%)			
Prescribed by a doctor, n (%)	363 (57.8%)	147 (53.3%)			
Steroids	63 (9.0%)	26 (9.0%)	0.98	0.97 (0.58, 1.63)	0.92
Anticonvulsants	162 (23.2%)	41 (14.2%)	0.002	1.66 (1.12, 2.46)	0.01
Topical Anesthetics	323 (46.2%)	163 (56.4%)	0.004	0.58 (0.43, 0.79)	0.0004
Over the counter, n (%)	267 (82.7%)	142 (87.1%)			
Prescribed by a doctor, n (%)	74 (22.9%)	25 (15.3%)			
Other source, n (%)	27 (8.4%)	12 (7.4%)			
Opioids	455 (65.1%)	194 (67.1%)	0.53	0.86 (0.63, 1.18)	0.36
Prescribed by a doctor, n (%)	449 (98.7%)	184 (94.8%)			
Other source, n (%)	36 (7.9%)	28 (14.4%)			
Cannabis	110 (15.7%)	54 (18.7%)	0.26	0.90 (0.60, 1.35)	0.62
Prescribed by a doctor, n (%)	60 (54.5%)	17 (31.5%)			
Other source, n (%)	67 (60.9%)	41 (75.9%)			
Sleeping Medications	31 (4.4%)	17 (5.9%)	0.34	0.76 (0.40, 1.45)	0.40
Over the counter, n (%)	2 (6.5%)	2 (11.8%)			
Prescribed by a doctor, n (%)	30 (96.8%)	15 (88.2%)			
Other source, n (%)	0	0			
Sedative or Anxiety Medication	56 (8.0%)	30 (10.4%)	0.23	0.75 (0.45, 1.25)	0.27
Prescribed by a doctor, n (%)	53 (94.6%)	26 (86.7%)			
Other source, n (%)	5 (8.9%)	5 (16.7%)			
Muscle Relaxants	161 (23.0%)	90 (31.1%)	0.008	0.61 (0.44, 0.85)	0.003

Medication Type Used and Source	HIV+ (N=699)	HIV− (N=289)	P value	Adjusted[1] Odds Ratio: HIV+ vs. HIV− (95% CI)	P value
Over the counter, n (%)	4 (2.5%)	0			
Prescribed by a doctor, n (%)	155 (96.3%)	81 (90.0%)			
Other source, n (%)	5 (3.1%)	13 (14.4%)			
Migraine Medications	121 (17.3%)	53 (18.3%)	0.70	0.92 (0.63, 1.35)	0.67
Over the counter, n (%)	39 (32.2%)	28 (52.8%)			
Prescribed by a doctor, n (%)	96 (79.3%)	37 (69.8%)			
Other source, n (%)	7 (5.8%)	6 (11.3%)			
Stimulants	7 (1.0%)	3 (1.0%)	0.96	1.58 (0.29, 8.60)	0.60
Over the counter, n (%)	0	0			
Prescribed by a doctor, n (%)	6 (85.7%)	2 (66.7%)			
Other source, n (%)	1 (14.3%)	1 (33.3%)			

[1]Logistic regression for use of medication class (yes/no) adjusted for race, age, WIHS site, enrollment year, HCV, CESD, diabetes mellitus, alcohol use, and current cocaine, crack, or heroin use; reference is HIV-uninfected