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Authors

Newville, Howard

Roley, Jason

Sorensen, James L

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Prescription medication misuse among HIV-infected individuals taking antiretroviral therapy[☆]



Howard Newville, Ph.D.^{a,*}, Jason Roley, B.A.^b, James L. Sorensen, Ph.D.^b

^a Mount Sinai St. Luke's, New York, NY, United States

^b University of California, San Francisco, San Francisco, CA, United States

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ABSTRACT

HIV has become a highly treatable disease due to advances in antiretroviral therapy (ART). Additionally, HIV-infected individuals often take opiates, barbiturates, and benzodiazepines to treat co-occurring conditions, including pain and symptoms of HIV. We sought to examine prescription medication misuse by surveying 295 HIV-infected patients receiving ART. Participants answered questions about their demographics, alcohol and other drug use, psychiatric diagnoses, ART adherence and side effects, and quality of life. Eleven percent of our sample acknowledged prescription medication misuse. In regression analysis, prescription medication misusers were more likely to report any drinking to intoxication (OR = 4.31, 95% CI: 1.35–13.76, $p = 0.013$), reported greater severity of ART side effects (OR = 1.05, 95% CI: 1.01–1.10, $p = 0.041$), and demonstrated poorer cognitive functioning (OR = 0.97, 95% CI: 0.94–0.99, $p = 0.048$) compared to those who did not misuse prescription medications. Special care should be taken by medical providers before prescribing medications that may be abused or diverted. Patients should also be screened for aberrant use, even if not prescribed. ART side effects, cognitive deficits, and alcohol abuse may serve as risk factors or indicators of prescription medication misuse, and should be monitored.

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1. Introduction

Prescription medication misuse, i.e. the use of a prescription medication without a prescription or in a way other than the manner it was prescribed, is a growing problem in public health. Its prevalence has increased dramatically over the past decade (Becker, Tobin, & Fiellin, 2011; Johnston, O'Malley, Bachman, & Schulenberg, 2007; SAMHSA, 2007). According to the White House Office of National Drug Control Policy (ONDCP), prescription medication misuse is the second most prevalent drug problem in the United States (SAMHSA, 2012). In 2008, 36,450 people died in the United States as a result of a drug overdose; 20,044 (55%) of these were attributed to a prescription medication (CDC, 2011). In addition, prescription medication misuse has been associated with other negative outcomes, such as interactions with other prescribed medications (Carr & Cooper, 2000; Treisman & Kaplin, 2002) and increased sex risk behaviors that can transmit HIV (Benotsch, Martin, Koester, Cejka, & Luckman, 2011; Kelly & Parsons, 2010).

HIV-infected individuals often present with conditions that are associated with prescription medication misuse. Pain, a common comorbidity in HIV-infected patients, is associated with misuse of prescription medications (Ives et al., 2006; Tsao, Plankey, & Young,

2012; Tsao, Stein, & Dobalian, 2007; Turk, Swanson, & Gatchel, 2008; Vijayaraghavan, Penko, Bangsberg, Miaskowski, & Kushel, 2013). Prescription medication misuse has been associated with greater psychiatric symptomatology, especially depressive, anxiety, and somatic symptoms (Benotsch, Koester et al., 2013; Benotsch, Zimmerman et al., 2013; Tsao et al., 2012), and a higher likelihood of meeting criteria for a psychiatric disorder (Blanco et al., 2013; Novak, Herman-Stahl, Flannery, & Zimmerman, 2009; Schepis & Hakes, 2011). Research has also found the presence of a substance use disorder, injection drug use (IDU) (Martinez, D'Amico, Kral, & Bluthenthal, 2012), and regular illicit drug use (Tetrault et al., 2008) are associated with prescription medication misuse. Other factors associated with prescription medication misuse include male gender (Huang et al., 2006), younger age (Blanco et al., 2013; Boyd, Teter, West, Morales, & McCabe, 2009; Johnston et al., 2007; SAMHSA, 2007), white ethnicity (Blanco et al., 2013), non-heterosexual sexual orientation (Kecejevic et al., 2012), being unmarried (Huang et al., 2006), and having less education (Wasan et al., 2007); these factors are also associated with new HIV infections in the United States (Prejean et al., 2011).

Despite these comorbidities, little is known about prescription medication misuse among the HIV population, although initial research suggests that rates are high. In one examination of HIV-infected individuals, 37% reported prescription opioid misuse in the 90 days prior to the interview (Hansen et al., 2011). Another study found that HIV-infected men who have sex with men (MSM) were more likely to misuse prescription medications than HIV-negative

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* Corresponding author.

MSM (Kelly & Parsons, 2010). Further analyses within the HIV Cost and Services Utilization Study (HCSUS) found that individuals with a history of illicit drug use were more likely to report prescription medication misuse (Tsao et al., 2007). A recent study found that misuse of prescription opioids was associated with less than 90% adherence to antiretroviral therapy (ART) (Jeevanjee et al., 2014). Further examination of prescription medication misuse in HIV-infected individuals on ART, including non-opioid medications, is needed.

Understanding factors associated with the prescription medication misuse represents the first step in addressing this issue in HIV-infected patients, which can help clinicians balance the need to provide relief for legitimate symptoms with the risks for abuse and addiction. In this study, we evaluated self-reported prescription medication misuse in a community sample of HIV-infected patients prescribed ART, based on substance use, psychiatric, and quality of life indicators.

2. Methods

2.1. Study subjects

To be eligible, individuals were (a) HIV-infected, (b) at least 18 years of age, (c) prescribed HAART at the time of the interview, and (d) able to complete the assessment in English.

2.2. Procedures

Participants were recruited from the Positive Health Program (PHP), the HIV primary care clinic at San Francisco General Hospital Medical Center (SFGH). PHP is a collaborative effort between the San Francisco Department of Public Health and the University of California, San Francisco (UCSF) Department of Medicine's Medical Service, which provides primary care and interdisciplinary services to approximately 3500 HIV-infected individuals. This study was approved by the UCSF Institutional Review Board. Recruitment took place between March and May 2012.

Research assistants approached potential participants in the clinic waiting room about participating in a survey. Interested patients were taken to a private room where they were administered a one-page screener to determine eligibility. Eligible individuals who agreed to participate provided informed consent and were told that their answers are confidential and will not be provided to their medical providers. Participants gave consent for research assistants to access their medical records after the interview.

Participants responded to the survey questions, which were administered on a laptop computer with Audio Computer-Assisted Self-Interview (ACASI) technology. Assessments conducted with ACASI software result in higher self-reported rates of "undesirable" behaviors than face-to-face interviews (Gross et al., 2000; Metzger et al., 2000). Subjects were paid \$10 for completing the questionnaire. After the survey was completed, research assistants used a chart review tool to collect information on CD4 T cell count, viral load, psychiatric and medical diagnoses from the participants' medical record.

2.3. Measures

2.3.1. Demographics

We collected data on demographic variables that have been associated with prescription medication misuse in previous studies. These variables include age, gender, sexual orientation, race/ethnicity, and education (Blanco, Rafful, Wall, Jin, Kerridge & Schwartz, 2013; Blanco et al., 2013; Boyd et al., 2009; Huang et al., 2006; Johnston et al., 2007; Kecojevic et al., 2012; SAMHSA, 2007; Wasan et al., 2007). We asked participants if they identified as "male", "female", or "transgender", and then dichotomized gender into "male" vs. "non-male". Similarly, we asked participants if they identified as gay, lesbian, bisexual, or heterosexual, and then dichotomized participants into

"heterosexual" vs. "gay, lesbian, or bisexual". Race/ethnicity was dichotomized into "white" vs. "non-white", and education was collapsed into three groups: those who did not complete high school, those who graduated from high school or obtained a GED, and those who attended college. Participants also answered when they were initially diagnosed with HIV and whether or not they had ever received a psychiatric diagnosis. This was later confirmed through chart review. We also obtained the most recent CD4 + T cell counts and viral load, if within 1 month of the interview, from the chart review.

2.3.2. Addiction Severity Index Lite (ASI-Lite; McLellan, Cacciola, & Zanis, 1997)

The ASI-Lite is a widely used structured clinical interview in the drug abuse field. It assesses 'severity' of alcohol, drug, medical, psychiatric, family-social, employment, and legal problems from both the clinician's and patient's perspective. The measure is shorter in duration than the full ASI, yet demonstrates reliability and validity (Cacciola, Alterman, McLellan, Lin, & Lynch, 2007). For the current study, only the Alcohol and Drug sections were administered. We assessed each whether or not the participant endorsed use of alcohol to intoxication, methadone, heroin, other opiates/analgesics, crack/cocaine, amphetamines, and sedatives/hypnotics/tranquilizers over the past 30 days. Additional questions were included to ask about whether the use of methadone, opiates/analgesics, or sedatives/hypnotics/tranquilizers were by prescription. If the participant acknowledged using one of these substances, we asked if they had a prescription. If they responded yes, we asked whether or not they used the drug as prescribed. If they acknowledged use of methadone, opiates/analgesics, or sedatives/hypnotics/tranquilizers without a prescription or in a manner other than the way the drug was prescribed, we coded them as "prescription medication misusers". This approach has been used in previous research (Huang et al., 2006).

2.3.3. Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996)

The BDI-II is a 21-item instrument widely used to measure depression based on the symptoms of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 1994)*. Scores range from 0 through 63. The BDI-II demonstrates excellent reliability and internal consistency (Dozois, Dobson, & Ahnberg, 1998).

2.3.4. Visual analogue scale (VAS) for ART adherence

Participants indicated on VAS to what percent, between 0 and 100%, they have adhered to their ART regimen over the past 30 days. A 30 day time frame maintains variability in results. This method has demonstrated significant correlations with unannounced pill counts and viral load (Giordano, Guzman, Clark, Charlebois, & Bangsberg, 2004), and in the current study, demonstrated fair to moderate agreement with viral load among substance using participants (Newville & Sorensen, 2013).

2.3.5. ART side effects

Participants were asked the extent to which they experienced 18 common side effects of their ART regimens. These side effects included pain, nausea, fatigue, dizziness, difficulty remembering things, and insomnia. Participants were asked the extent to which each of these side effects bothered them on a five-point Likert scale, ranging from "not at all" to "extremely". Scores were summed to create a total score for the measure, ranging from 0 to 72, with higher scores representing greater side effect severity. This measure has been used in previous research (Arnsten et al., 2002; Berg et al., 2004).

2.3.6. Medical Outcomes Study HIV Health Survey (MOS-HIV; Wu, Revicki, Jacobson, & Malitz, 1997)

The Medical Outcomes Study HIV Health Survey (MOS-HIV) is a 35-item scale that measures health-related quality of life. The MOS-HIV provides scale scores for general health perceptions, physical functioning, role functioning, pain, social functioning, mental

health, energy, health distress, cognitive functioning, quality of life, and health transition. Each scale is scored on a 0–100 scale, with higher scores indicating better health.

2.4. Data analysis

We first presented demographic information (age, gender, sexual orientation, race/ethnicity, education, duration of HIV disease), as well as information on CD4+ T-cell count (cells/mm³), viral load (copies/mL), psychiatric diagnoses, substance use, depressive symptomatology, ART adherence and side effects, and quality of life. We identified the participants who acknowledged prescription medication misuse in the past month (use of methadone, other opiates/analgesics, barbiturates, and/or sedatives/hypnotics/tranquilizers without a prescription or in a manner other than as prescribed). We compared participants who reported prescription medication misuse to those who did not on demographics, alcohol and other drug use, psychiatric diagnoses, ART adherence and side effects, and quality of life in bivariate analyses. Chi-square tests were used for categorical variables (sexual orientation, white race, education, psychiatric diagnoses, illicit drug use, any alcohol use to intoxication). T-tests were used for normally distributed continuous variables (age, duration of HIV infection, quality of life). Mann–Whitney U tests were used for non-normally distributed continuous variables (depression, ART adherence and side effects). All variables that were significantly associated with prescription medication misuse in bivariate analysis were entered into a logistic regression, where prescription medication misuse was the outcome variable. Due to multicollinearity among substance use variables, the use of heroin, crack/cocaine, and/or amphetamines was condensed into one variable for the regression analysis. Missing data were minimal (4%), appeared to be at random, and cases were removed from regression analysis using listwise deletion. All analyses were run using SPSS Version 20, with the cutoff for significance set at $p = 0.05$ for all analyses.

3. Results

3.1. Patient characteristics

A total of 295 participants completed the survey. Their mean age was 47.5 years ($SD = 9.7$). The gender breakdown was 200 (68%) male, 76 (26%) female and 19 (6%) transgender. A majority of the sample (182; 62%) was gay, lesbian, or bisexual. A plurality (127; 43%) of the sample identified as black or African American, while 114 (39%) identified as Caucasian, and 26 (9%) identified as Hispanic. Only 26 (9%) reported that they were married. A quarter (69; 23%) did not finish high school, while 105 (36%) had a high school diploma or GED, and 127 (43%) had attended college. Participants had been diagnosed with HIV for an average of 13.9 years ($SD = 11.5$), and had mean CD4+ T cell counts (cells/mm³) of 492.4 ($SD = 293.1$) and mean viral load (copies/mL) of 12,252.9 ($SD = 54,502.0$). Regarding the lifetime presence of a psychiatric diagnosis, 190 (64%) had been diagnosed with a depressive disorder, 95 (32%) with substance abuse or dependence, 91 (31%) with an anxiety disorder, 17 (6%) with schizophrenia, 9 (3%) with post-traumatic stress disorder, and 6 (2%) with an eating disorder.

In the most recent 30 days, 120 (41%) reported using alcohol to intoxication, while 115 (39%) reported any use of heroin, crack/cocaine, or amphetamines. Specifically, 29 (10%) reported using heroin, 64 (22%) reported using crack/cocaine, and 57 (22%) reported using amphetamines. In total, 32 (11%) reported past month misuse of prescription medications. Of these, 13 (41%) reported misusing opiates/analgesics, 12 (38%) reported misusing sedatives, hypnotics, or tranquilizer, 6 reported misusing methadone, and 6 (19%) reported misusing barbiturates. No participants reported misusing methadone. In total, 8 (25%) reported misusing a prescription medication that they were

prescribed, while 24 (75%) reported using a prescription medication that they were not prescribed.

The mean depression score was 16.2 ($SD = 13.2$). ART adherence was 83.5% ($SD = 22.1$), while ART side effect severity was 12.4 ($SD = 11.7$). Quality of life scores ranged from a low of 39.0 ($SD = 45.1$) for role functioning, to 63.7 ($SD = 30.8$) for health distress (Table 1).

3.2. Bivariate analysis

Participants with and without self-reported misuse of prescription medications in the past month did not differ from each other on age, gender, sexual orientation, race/ethnicity, education, marital status, ART adherence, or self-reported psychiatric disorders. They also did not differ on duration of HIV disease, CD4+ T cell count, or viral load (Table 1).

Substance use was associated with the misuse of prescription medications. Those who reported misuse of prescription medications were more likely to report any drinking to intoxication ($\chi^2 = 10.32$, $p < 0.001$) and the use of heroin, crack/cocaine, or amphetamines ($\chi^2 = 10.74$, $p < 0.001$), as well as for heroin ($\chi^2 = 20.58$, $p < 0.001$), crack/cocaine ($\chi^2 = 12.06$, $p = 0.001$), and amphetamines ($\chi^2 = 5.02$, $p = 0.025$) individually. Greater depressive symptomatology ($Z = -2.63$, $p = 0.009$) was also associated with reporting prescription medication misuse. Among quality of life indices, individuals reporting prescription medication misuse had poorer general health perceptions ($t = 2.90$, $p = 0.004$), cognitive functioning ($t = 3.15$, $p = 0.002$), quality of life ($t = 2.50$, $p = 0.013$), and greater health distress ($t = 2.29$, $p = 0.023$) than those not reporting prescription medication misuse. In addition, ART side effect severity ($Z = -2.90$, $p = 0.004$) was associated with the misuse of prescription medications in bivariate analyses (Table 1).

3.3. Multivariable analysis

The variables that were significantly associated with prescription medication misuse in bivariate analyses (any drinking to intoxication, any use of heroin, crack/cocaine, or amphetamines, depressive symptomatology, ART side effects, general health perceptions, cognitive functioning, health distress, and quality of life) were included in a logistic regression, where prescription medication misuse was the outcome variable. As age, gender, sexual orientation, race/ethnicity, education, marital status, ART adherence, and self-reported psychiatric disorders were not significantly associated with prescription medication misuse, they were not included in the model.

The results of the regression are presented in Table 2. The use of alcohol to intoxication (odds ratio [OR] = 4.31, 95% CI: 1.35–13.76, $p = 0.013$), greater ART side effect severity (OR = 1.05, 95% CI: 1.01–1.10, $p = 0.041$), and decreased cognitive functioning (OR = 0.97, 95% CI: 0.94–0.99, $p = 0.048$) remained significant predictors of prescription medication misuse when controlling for the other variables.

4. Discussion

Individuals with HIV experience many known risk factors associated with the misuse of prescription medications, including the use of alcohol and illicit substances, psychiatric illnesses, and physical pain. As they are often prescribed psychotropic medications to aid with insomnia, provide analgesia, and as substitution therapy, a consideration of the improper use of these medications among the HIV-infected is critical. In this study, 11% of the sample reported misusing prescription medications in the past 30 days. For comparison, a study of IDU, most of whom did not have HIV, found that 17% acknowledged misusing prescription medications in the past 6 months (Martinez et al., 2012), while 24% of respondents of a national survey reported lifetime prescription opioid misuse (McCabe, West, Morales, Cranford, & Boyd, 2007), and 37% of a community-based HIV sample

Table 1
Sample demographics and descriptive information.

	Total sample (N = 295)	Prescription medication misuse		Statistic	p
		Yes (n = 32)	No (n = 263)		
Age, M (SD)	47.5 (9.7)	47.7 (10.7)	47.4 (9.5)	t = 0.25	NS
Male gender, n (%)	200 (67.8)	19 (59.4)	181 (68.8)	$\chi^2 = 1.31$	NS
Married, n (%)	26 (8.8)	2 (6.3)	24 (9.1)	$\chi^2 = 0.31$	NS
Gay, lesbian, or bisexual, n (%)	182 (61.7)	18 (56.3)	164 (62.4)	$\chi^2 = 0.54$	NS
White, non-Hispanic, n (%)	114 (38.6)	14 (43.8)	100 (38.0)	$\chi^2 = 0.40$	NS
Education, n (%)					
Less than high school	69 (23.4)	10 (31.3)	59 (22.4)	$\chi^2 = 2.18$	NS
High school or GED	105 (35.6)	8 (25.0)	97 (36.9)		
Any college	127 (43.1)	15 (46.9)	112 (42.6)		
Years living with HIV	13.9 (11.5)	12.3 (10.4)	14.2 (11.6)	t = 0.66	NS
CD4 + T cell count (cells/mm ³), M (SD)	492.4 (293.1)	505.8 (262.4)	490.9 (296.8)	Z = 0.34	NS
Viral load (copies/ml), M (SD)	12,252.9 (54,502)	12,328.5 (28,960.1)	12,244.5 (56,690.0)	Z = 0.99	NS
Psychiatric diagnoses, n (%)					
Depressive disorder	190 (64.4)	21 (65.6)	169 (64.3)	$\chi^2 = 1.47$	NS
Substance use disorder	95 (32.2)	12 (37.5)	83 (31.6)	$\chi^2 = 2.91$	NS
Anxiety disorder	91 (30.8)	9 (28.1)	82 (31.1)	$\chi^2 = 0.02$	NS
Schizophrenia	17 (5.8)	1 (3.1)	16 (6.1)	$\chi^2 = 0.29$	NS
Post-traumatic stress disorder	9 (3.1)	1 (3.1)	8 (3.0)	$\chi^2 = 0.01$	NS
Eating disorder	6 (2.0)	1 (3.1)	5 (1.9)	$\chi^2 = 0.36$	NS
Substance use, n (%)					
Any alcohol use (to intoxication)	120 (40.7)	20 (62.5)	100 (38.0)	$\chi^2 = 10.32$	0.003
Any heroin use	29 (9.8)	10 (31.2)	19 (7.2)	$\chi^2 = 20.58$	<0.001
Any crack/cocaine use	64 (21.7)	14 (43.8)	50 (19.0)	$\chi^2 = 12.06$	0.001
Any amphetamine use	69 (23.4)	12 (37.5)	57 (21.7)	$\chi^2 = 5.02$	0.025
Depression, M (SD)	16.2 (13.2)	23.0 (14.9)	15.4 (12.7)	Z = 2.63	0.009
ART adherence, M (SD)	83.5% (22.1)	78.8% (23.3)	84.1% (22.0)	Z = -1.68	NS
ART side effects, M (SD)	12.4 (11.7)	20.0 (14.9)	11.4 (10.9)	Z = 2.90	0.004
Quality of life, M (SD)					
General health perceptions	58.7 (22.6)	46.3 (20.9)	60.2 (22.4)	t = 2.90	0.004
Physical health	53.2 (29.7)	44.4 (26.6)	54.2 (29.9)	t = 0.95	NS
Role functioning	39.0 (45.1)	35.0 (45.8)	39.5 (45.1)	t = 0.52	NS
Social functioning	58.3 (33.7)	51.6 (32.2)	59.1 (33.8)	t = 1.17	NS
Cognitive functioning	65.9 (27.4)	51.2 (23.7)	67.6 (27.4)	t = 3.15	0.002
Pain	56.3 (30.0)	53.4 (30.1)	56.9 (30.1)	t = 0.57	NS
Mental health	60.1 (22.4)	53.0 (19.3)	60.9 (22.6)	t = 1.78	NS
Energy/fatigue	50.3 (22.1)	44.0 (16.0)	51.1 (22.6)	t = 1.69	NS
Health distress	63.7 (30.8)	51.7 (30.7)	65.1 (30.5)	t = 2.29	0.023
Quality of life	61.5 (24.9)	50.8 (30.4)	62.7 (23.9)	t = 2.50	0.013
Health transitions	62.3 (26.5)	59.2 (33.1)	62.7 (25.7)	t = 0.69	NS

reported aberrant prescription opioids over the past 90 days (Hansen et al., 2011). In a survey of providers, 12% reported that their patients were addicted to prescription opioids (Lum et al., 2011). In our study, we found that alcohol use to intoxication, ART side effects, and cognitive functioning emerged as key issues to focus on in assessing the prescription medication misuse of HIV-infected patients prescribed ART.

Among subjects in our study, the use of alcohol to intoxication was associated with prescription medication misuse. Heavy drinking behavior has been associated with prescription medication misuse in other populations (McCabe, Cranford, & Boyd, 2006; McCabe, Cranford, Morales, & Young, 2006). Previous literature in HIV populations documents that alcohol use is associated with increased risky sexual behavior, medication non-adherence, and may be related to accelerated HIV disease progression (Hahn & Samet, 2010). Given

the intersection between prescription medication misuse, alcohol use disorders, and ART non-adherence, our findings suggest that patients abusing prescription medications are at an increased risk for ART resistance and HIV disease progression.

The cognitive functioning of HIV-infected patients is an important consideration. ART is associated with neuropsychiatric side effects, including sleep disturbances, behavioral changes, mood disturbances, anxiety, cognitive disorders, hallucinations, and dizziness (Hawkins et al., 2005; Lochet et al., 2003; Reust, 2011). Substance abuse has been associated with poor cognitive functioning (Rapeli, Fabritius, Kalska, & Alho, 2011), and opioids and benzodiazepines can cause decreases in cognitive functioning (Barker, Greenwood, Jackson, & Crowe, 2004; Ersek, Cherrier, Overman, & Irving, 2004). The combination of ART with opiate or benzodiazepine medications can have synergistic effects to decrease cognitive functioning (Carr & Cooper, 2000; Treisman & Kaplin, 2002). As the cognitive functioning of HIV-infected patients on ART may already be impaired, caution should be taken when prescribing medications that may exacerbate this condition.

ART side effects may cause prescription medication misuse. Participants misusing prescription medications may have been attempting to self-medicate symptoms of HIV or ART medication side effects, including those relating to neuropsychiatric symptoms associated with decreased cognitive functioning. Low doses of benzodiazepines can ameliorate neurological side effects of ART medications (Max & Sherer, 2000). In some cases of prescription medication misuse, the individual may be displaying pseudoaddiction, where the drug use is an effort to treat undertreated symptoms,

Table 2
Logistic regression analysis with prescription medication misuse.

Variable	Odds ratio	95% CI	p
Any drinking to intoxication	4.31	1.35–13.76	0.013
Any heroin, crack/cocaine, and/or amphetamine use	2.11	0.64–9.45	NS
Depression	0.99	0.94–1.05	NS
Medication side effects	1.05	1.01–1.10	0.041
General health perceptions	1.00	0.97–1.03	NS
Cognitive functioning	0.97	0.94–0.99	0.048
Health distress	1.01	0.98–1.05	NS
Quality of life	0.98	0.95–1.01	NS

rather than evidence of a drug use disorder (Tsao et al., 2012). On the other hand, others prescribed opioid or benzodiazepine medications may be abusing or diverting them.

This study has several limitations which should be noted. We utilized a cross-sectional design, and thus these associations should not be construed as causal pathways. Participants were recruited from a single HIV clinic, and thus our results may not be generalizable to other settings. Also, our data collection relies on respondents' self-reports, though we were able to confirm some information through the participants' electronic medical records. Self-reported information may be influenced by biases associated with reporting, such as memory errors. Our method for measuring prescription medication misuse was not validated, although it is similar to the method used in other studies (Huang et al., 2006). Validated methods for assessing prescription medication misuse would greatly improve the field of research. We did not inquire about prescriptions for stimulant medications, or misuse of ART and erectile dysfunction medications, which could also be abused. Also, while we captured ART side effects, we did not ask about side effects to other medications these participants may take. Lastly, the study's relatively small sample size limits the ability to make comparisons between subgroups of prescription medication misusers as well as comparisons with non-users. A noteworthy strength of our study is our use of ACASI technology, which is likely to increase respondents' reporting of socially stigmatized or sensitive drug use behaviors (Gross et al., 2000; Metzger et al., 2000).

As suggested by the American Pain Society and the American Academy of Pain Medicine, clinicians should perform a risk assessment before prescribing medications that could be abused, including opioids and benzodiazepines, in order to minimize the possibility of prescription medication misuse (Chou, Ballantyne, Fanciullo, Fine, & Miaskowski, 2009; Chou, Fanciullo, Fine, Adler et al., 2009; Chou, Fanciullo, Fine, Miaskowski et al., 2009). Clinicians should further assess patients for signs of pseudoaddiction, due to the undertreatment of symptoms. Doctors should also be alert for signs of prescription medication misuse and diversion, such as frequent requests for dose increases, missed appointments, and other forms of treatment non-adherence. If a provider is unsure if abuse or diversion are occurring, drug testing can provide answers. It is important to gauge what other substances the patient is using. Also, a negative test result for a benzodiazepine or opiate if those medication classes are prescribed could indicate that the patient is diverting their prescription medications, or has run out of their medications (Robinson-Papp, Elliott, Simpson, & Morgello, 2012).

Benzodiazepines should not be prescribed for long-term use (Ashton, 2005). In cases of anxiety, a selective serotonin reuptake inhibitor may be a safer choice than a benzodiazepine (Turjanski & Lloyd, 2005). Opioid replacement therapies, including methadone and buprenorphine, can help HIV-infected patients with their addictions to opioid painkillers, while also reducing high risk transmission behaviors, such as IDU, needle sharing, and unprotected sex (Roux et al., 2011). Medication tapering and detoxification, along with adjunctive psychotherapies, can help treat prescription medication misuse (Ashton, 2005; Veilleux, Colvin, Anderson, York, & Heinz, 2010). Prevention and treatment efforts should address drinking behavior as it is an important factor in influencing medication non-adherence. Alcohol use presents a risk for prescription medication misuse in HIV-infected patients as well as the general population.

Despite our limitations, our study provides valuable information on prescription medication misuse in HIV-infected patients prescribed ART. This study supports the idea that caution should be taken in prescribing opioids, benzodiazepines, and other potentially abused medications, especially when the patient is presenting with alcohol and/or other drug use, medication side effects from their ART regimen, and declining cognitive functioning. As many misuse prescription medications that they are not prescribed, any patient suspected of misusing them should be assessed. Future research

should examine health-related outcomes of prescription medication misuse. Promising intervention models will be those that systematically identify, evaluate, and provide the specific needed treatment. As prescription medication misuse remains a major problem, further examinations on misuse of prescriptions and diversion to other users and interventions designed to curtail these behaviors would benefit the public health system.

References

- American Psychiatric Association (1994). *Diagnostic and statistical manual of mental disorders: DSM-IV* (4th ed.) (Washington, DC).
- Arnstien, J. H., Demas, P. A., Grant, R. W., Gourevitch, M. N., Farzadegan, H., Howard, A. A., et al. (2002). Impact of active substance use on antiretroviral therapy adherence and viral suppression in HIV-infected substance users. *Journal of General Internal Medicine*, 17(5), 377–381.
- Ashton, H. (2005). The diagnosis and management of benzodiazepine dependence. *Current Opinion on Psychiatry*, 18, 249–255.
- Barker, M. J., Greenwood, K. M., Jackson, M., & Crowe, S. F. (2004). Cognitive effects of long-term benzodiazepine use: A meta-analysis. *CNS Drugs*, 18(1), 37–48.
- Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *BDI-II, Beck depression inventory: Manual* (2nd ed.). Boston: Harcourt Brace.
- Becker, W. C., Tobin, D. G., & Fiellin, D. A. (2011). Nonmedical use of opioid analgesics obtained directly from physicians: Prevalence and correlates. *Archives of Internal Medicine*, 171(11), 1034–1036, <http://dx.doi.org/10.1001/archinternmed.2011.217>.
- Benotsch, E. G., Koester, S., Martin, A. M., Cejka, A., Luckman, D., & Jeffers, A. J. (2013). Intentional misuse of over-the-counter medications, mental health, and polysubstance use in young adults. *Journal of Community Health*, <http://dx.doi.org/10.1007/s10900-013-9811-9>.
- Benotsch, E. G., Martin, A. M., Koester, S., Cejka, A., & Luckman, D. (2011). Nonmedical use of prescription drugs and HIV risk behavior in gay and bisexual men. *Sexually Transmitted Diseases*, 38(2), 105–110.
- Benotsch, E. G., Zimmerman, R., Cathers, L., McNulty, S., Pierce, J., Heck, T., et al. (2013). Non-medical use of prescription drugs, polysubstance use, and mental health in transgender adults. *Drug and Alcohol Dependence*, 132(1–2), 391–394, <http://dx.doi.org/10.1016/j.drugalcdep.2013.02.027>.
- Berg, K. M., Demas, P. A., Howard, A. A., Schoenbaum, E. E., Gourevitch, M. N., & Arnsten, J. H. (2004). Gender differences in factors associated with adherence to antiretroviral therapy. *Journal of General Internal Medicine*, 19(11), 1111–1117.
- Blanco, C., Rafful, C., Wall, M. M., Jin, C. J., Kerridge, B., & Schwartz, R. P. (2013). The latent structure and predictors of non-medical prescription drug use and prescription drug use disorders: A national study. *Drug and Alcohol Dependence*, 133(2), 473–479, <http://dx.doi.org/10.1016/j.drugalcdep.2013.07.011>.
- Boyd, C. J., Teter, C. J., West, B. T., Morales, M., & McCabe, S. E. (2009). Non-medical use of prescription analgesics: A three-year national longitudinal study. *Journal of Addictive Diseases*, 28(3), 232–242, <http://dx.doi.org/10.1080/10550880903028452>.
- Cacciola, J. S., Alterman, A. I., McLellan, A. T., Lin, Y. T., & Lynch, K. G. (2007). Initial evidence for the reliability and validity of a "Lite" version of the Addiction Severity Index. *Drug and Alcohol Dependence*, 87(2–3), 297–302, <http://dx.doi.org/10.1016/j.drugalcdep.2006.09.002>.
- Carr, A., & Cooper, D. A. (2000). Adverse effects of antiretroviral therapy. *Lancet*, 356(9239), 1423–1430, [http://dx.doi.org/10.1016/s0140-6736\(00\)02854-3](http://dx.doi.org/10.1016/s0140-6736(00)02854-3).
- Centers for Disease Control and Prevention (CDC) (2011). Vital signs: overdoses of prescription opioid pain relievers—United States, 1999–2008. *Morbidity and Mortality Weekly Report*, 60(43), 1487–1492.
- Chou, R., Ballantyne, J. C., Fanciullo, G. J., Fine, P. G., & Miaskowski, C. (2009). Research gaps on use of opioids for chronic noncancer pain: Findings from a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. *Journal of Pain*, 10(2), 147–159, <http://dx.doi.org/10.1016/j.jpain.2008.10.007>.
- Chou, R., Fanciullo, G. J., Fine, P. G., Adler, J. A., Ballantyne, J. C., Davies, P., et al. (2009). Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *Journal of Pain*, 10(2), 113–130, <http://dx.doi.org/10.1016/j.jpain.2008.10.008>.
- Chou, R., Fanciullo, G. J., Fine, P. G., Miaskowski, C., Passik, S. D., & Portenoy, R. K. (2009). Opioids for chronic noncancer pain: Prediction and identification of aberrant drug-related behaviors: A review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. *Journal of Pain*, 10(2), 131–146, <http://dx.doi.org/10.1016/j.jpain.2008.10.009>.
- Dozois, D. J., Dobson, K. S., & Ahnberg, J. L. (1998). A psychometric evaluation of the Beck Depression Inventory-II. *Psychological Assessment*, 10, 83–89.
- Ersek, M., Cherrier, M. M., Overman, S. S., & Irving, G. A. (2004). The cognitive effects of opioids. *Pain Management Nursing*, 5(2), 75–93.
- Giordano, T. P., Guzman, D., Clark, R., Charlebois, E. D., & Bangsberg, D. R. (2004). Measuring adherence to antiretroviral therapy in a diverse population using a visual analogue scale. *HIV Clinical Trials*, 5(2), 74–79.
- Gross, M., Holte, S. E., Marmor, M., Mwatha, A., Koblin, B. A., & Mayer, K. H. (2000). Anal sex among HIV-seronegative women at high risk of HIV exposure. The HIVNET Vaccine Preparedness Study 2 Protocol Team. *Journal of Acquired Immune Deficiency Syndromes*, 24(4), 393–398.
- Hahn, J. A., & Samet, J. H. (2010). Alcohol and HIV disease progression: Weighing the evidence. *Current HIV/AIDS Reports*, 7(4), 226–233, <http://dx.doi.org/10.1007/s11904-010-0060-6>.

- Hansen, L., Penko, J., Guzman, D., Bangsberg, D. R., Miaskowski, C., & Kushel, M. B. (2011). Aberrant behaviors with prescription opioids and problem drug use history in a community-based cohort of HIV-infected individuals. *Journal of Pain and Symptom Management*, 42(6), 893–902, <http://dx.doi.org/10.1016/j.jpainsymman.2011.02.026>.
- Hawkins, T., Geist, C., Young, B., Giblin, A., Mercier, R. C., Thornton, K., et al. (2005). Comparison of neuropsychiatric side effects in an observational cohort of efavirenz- and protease inhibitor-treated patients. *HIV Clinical Trials*, 6(4), 187–196, <http://dx.doi.org/10.1310/92VR-FP24-J8GA-B49Q>.
- Huang, B., Dawson, D. A., Stinson, F. S., Hasin, D. S., Ruan, W. J., Saha, T. D., et al. (2006). Prevalence, correlates, and comorbidity of nonmedical prescription drug use and drug use disorders in the United States: Results of the National Epidemiologic Survey on Alcohol and Related Conditions. *Journal of Clinical Psychiatry*, 67(7), 1062–1073.
- Ives, T. J., Chelminski, P. R., Hammett-Stabler, C. A., Malone, R. M., Perhac, J. S., Potisek, N. M., et al. (2006). Predictors of opioid misuse in patients with chronic pain: A prospective cohort study. *BMC Health Services Research*, 6, 46, <http://dx.doi.org/10.1186/1472-6963-6-46>.
- Jeevanjee, S., Penko, J., Guzman, D., Miaskowski, C., Bangsberg, D. R., & Kushel, M. B. (2014). Opioid analgesic misuse is associated with incomplete antiretroviral adherence in a cohort of HIV-infected indigent adults in San Francisco. *AIDS Behavior*, 18(7), 1352–1358.
- Johnston, L. D., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2007). *Monitoring the future national survey results on drug use, 1975–2006: Volume I, Secondary school students*. Bethesda, MD: National Institute on Drug Abuse (NIH Publication No. 07-6205).
- Kecojevic, A., Wong, C. F., Schragger, S. M., Silva, K., Jackson Bloom, J., Iverson, E., et al. (2012). Initiation into prescription drug misuse: Differences between lesbian, gay, bisexual, transgender (LGBT) and heterosexual high-risk young adults in Los Angeles and New York. *Addictive Behaviors*, 37(11), 1289–1293.
- Kelly, B. C., & Parsons, J. T. (2010). Prevalence and predictors of non-medical prescription drug use among men who have sex with men. *Addictive Behaviors*, 35(4), 312–317, <http://dx.doi.org/10.1016/j.addbeh.2009.11.002>.
- Lochet, P., Peyrière, H., Lotthé, A., Mauboussin, J. M., Delmas, B., & Reynes, J. (2003). Long-term assessment of neuropsychiatric adverse reactions associated with efavirenz. *HIV Medicine*, 4(1), 62–66, <http://dx.doi.org/10.1046/j.1468-1293.2003.00136.x>.
- Lum, P. J., Little, S., Botsko, M., Hersh, D., Thawley, R. E., Egan, J. E., et al. (2011). Opioid-prescribing practices and provider confidence recognizing opioid analgesic abuse in HIV primary care settings. *Journal of Acquired Immune Deficiency Syndromes*, 56 (Suppl. 1), S91–S97, <http://dx.doi.org/10.1097/QAI.0b013e31820a9a82>.
- Martinez, A. N., D'Amico, E. J., Kral, A. H., & Bluthenthal, R. N. (2012). Nonmedical prescription drug use among injection drug users. *Journal of Drug Issues*, 42(3), 216–225.
- Max, B., & Sherer, R. (2000). Management of the adverse effects of antiretroviral therapy and medication adherence. *Clinical Infectious Diseases*, 30(Suppl. 2), S96–S116, <http://dx.doi.org/10.1086/313859>.
- McCabe, S. E., Cranford, J. A., & Boyd, C. J. (2006). The relationship between past-year drinking behaviors and nonmedical use of prescription drugs: Prevalence of co-occurrence in a national sample. *Drug and Alcohol Dependence*, 84(3), 281–288.
- McCabe, S. E., Cranford, J. A., Morales, M., & Young, A. (2006). Simultaneous and concurrent polydrug use of alcohol and prescription drug: Prevalence, correlates, and consequences. *Journal of Studies on Alcohol*, 67(4), 529–537.
- McCabe, S. E., West, B. T., Morales, M., Cranford, J. A., & Boyd, C. J. (2007). Does early onset of non-medical use of prescription drugs predict subsequent prescription drug abuse and dependence? Results from a national study. *Addiction*, 102(12), 1920–1930, <http://dx.doi.org/10.1111/j.1360-0443.2007.02015.x>.
- McLellan, A. T., Cacciola, J. S., & Zanis, D. (1997). *The Addiction Severity Index—“Lite” (ASI-“Lite”)*. Center for the Studies of Addiction, University of Pennsylvania/Philadelphia VA Medical Center.
- Metzger, D. S., Koblin, B., Turner, C., Navaline, H., Valenti, F., Holte, S., et al. (2000). Randomized controlled trial of audio computer-assisted self-interviewing: Utility and acceptability in longitudinal studies. HIVNET Vaccine Preparedness Study Protocol Team. *American Journal of Epidemiology*, 152(2), 99–106.
- Newville, H., & Sorensen, J. L. (2013). The efficacy of a computerized assessment of medication adherence in active substance users. *Journal of the International Association of Providers of AIDS Care*, 12(4), 232–235, <http://dx.doi.org/10.1177/2325957413488206>.
- Novak, S. P., Herman-Stahl, M., Flannery, B., & Zimmerman, M. (2009). Physical pain, common psychiatric and substance use disorders, and the non-medical use of prescription analgesics in the United States. *Drug and Alcohol Dependence*, 100(1–2), 63–70, <http://dx.doi.org/10.1016/j.drugalcdep.2008.09.013>.
- Prejean, J., Song, R., Hernandez, A., Ziebell, R., Green, T., Walker, F., et al. (2011). Estimated HIV incidence in the United States, 2006–2009. *PLoS ONE*, 6(8), e17502, <http://dx.doi.org/10.1371/journal.pone.0017502>.
- Rapeli, P., Fabritius, C., Kalska, H., & Alho, H. (2011). Cognitive functioning in opioid-dependent patients treated with buprenorphine, methadone, and other psychoactive medications: stability and correlates. *BMC Clinical Pharmacology*, 11, 13, <http://dx.doi.org/10.1186/1472-6904-11-13>.
- Reust, C. E. (2011). Common adverse effects of antiretroviral therapy for HIV disease. *American Family Physician*, 83(12), 1443–1451.
- Robinson-Papp, J., Elliott, K., Simpson, D. M., & Morgello, S. (2012). Problematic prescription opioid use in an HIV-infected cohort: The importance of universal toxicology testing. *Journal of Acquired Immune Deficiency Syndromes*, 61(2), 187–193, <http://dx.doi.org/10.1097/QAI.0b013e3182683c98>.
- Roux, P., Carrier, P. M., Cohen, J., Ravau, I., Spire, B., Gossop, M., et al. (2011). Non-medical use of opioids among HIV-infected opioid dependent individuals on opioid maintenance treatment: The need for a more comprehensive approach. *Harm Reduction Journal*, 8, 31.
- SAMHSA (2012). *Mental Health Services Administration (2012) Results from the 2011 National Survey on Drug Use and Health: Summary of national findings. NSDUH series, H-44*. Rockville: Substance Abuse and Mental Health Services Administration (HHS publication no. (SMA) 12-4713).
- Schepis, T. S., & Hakes, J. K. (2011). Non-medical prescription use increases the risk for the onset and recurrence of psychopathology: Results from the National Epidemiological Survey on Alcohol and Related Conditions. *Addiction*, 106(12), 2146–2155, <http://dx.doi.org/10.1111/j.1360-0443.2011.03520.x>.
- Substance Abuse and Mental Health Services Administration (2007). *Results from the 2006 National Survey on Drug Use and Health: National findings. NSDUH Series, H-32*. Rockville, MD: Office of Applied Studies (DHHS Publication No. SMA 07-4293).
- Tetrault, J. M., Desai, R. A., Becker, W. C., Fiellin, D. A., Concato, J., & Sullivan, L. E. (2008). Gender and non-medical use of prescription opioids: Results from a national US survey. *Addiction*, 103(2), 258–268, <http://dx.doi.org/10.1111/j.1360-0443.2007.02056.x>.
- Treisman, G. J., & Kaplin, A. I. (2002). Neurologic & psychiatric complications in HIV & antiretroviral drugs. *AIDS*, 16, 1201–1215.
- Tsao, J. C., Plankey, M. W., & Young, M. A. (2012). Pain, psychological symptoms and prescription drug misuse in HIV: A literature review. *Journal of Pain and Symptom Management*, 5(2), 111–118.
- Tsao, J. C., Stein, J. A., & Dobalian, A. (2007). Pain, problem drug use history, and aberrant analgesic use behaviors in persons living with HIV. *Pain*, 133(1–3), 128–137, <http://dx.doi.org/10.1016/j.pain.2007.03.016>.
- Turjanski, N., & Lloyd, G. G. (2005). Psychiatric side-effects of medications: Recent developments. *Advances in Psychiatric Treatment*, 11, 58–70, <http://dx.doi.org/10.1192/apt.11.1.58>.
- Turk, D. C., Swanson, K. S., & Gatchel, R. J. (2008). Predicting opioid misuse by chronic pain patients: A systematic review and literature synthesis. *Clinical Journal of Pain*, 24(6), 497–508, <http://dx.doi.org/10.1097/AJP.0b013e31816b1070>.
- Veilleux, J. C., Colvin, P. J., Anderson, J., York, C., & Heinz, A. J. (2010). A review of opioid dependence treatment: Pharmacological and psychosocial interventions to treat opioid addiction. *Clinical Psychology Review*, 30(2), 155–166.
- Vijayaraghavan, M., Penko, J., Bangsberg, D. R., Miaskowski, C., & Kushel, M. B. (2013). Opioid analgesic misuse in a community-based cohort of HIV-infected indigent adults. *JAMA Internal Medicine*, 173(3), 235–237, <http://dx.doi.org/10.1001/jamainternmed.2013.1576>.
- Wasan, A. D., Butler, S. F., Budman, S. H., Benoit, C., Fernandez, K., & Jamison, R. N. (2007). Psychiatric history and psychologic adjustment as risk factors for aberrant drug-related behavior among patients with chronic pain. *Clinical Journal of Pain*, 23(4), 307–315, <http://dx.doi.org/10.1097/AJP.0b013e3180330dc5>.
- Wu, A. W., Revicki, D. A., Jacobson, D., & Malitz, F. E. (1997). Evidence for reliability, validity and usefulness of the Medical Outcomes Study HIV Health Survey (MOS-HIV). *Quality of Life Research*, 6(6), 481–493.