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# Alternate Routes of Administration and Risk for HIV Among Prescription Opioid Abusers

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**ABSTRACT.** Route of administration is an important contributor to the adverse health consequences of prescription medication abuse. The current study examines characteristics associated with non-oral routes of administration among a large sample of prescription opioid abusers and explores needle-related human immunodeficiency virus (HIV) risk behaviors as well. In the study, 791 opioid abusers completed a one-time structured interview, including complete histories of illicit and prescription drug abuse and route of drug administration. The most common method of pill use was oral (91%), followed by intranasal (53.1%), injection (23.8%), and smoking (14.5%). The youngest prescription opioid abusers, ages 18–24, displayed significantly higher odds of using alternate routes of administration and of reusing nonsterile needles for injection. HIV prevention programming should be developed for young prescription opioid injectors.

**KEYWORDS.** Prescription opioid abuse, route of administration, HIV

### **INTRODUCTION**

As the well-documented epidemic of prescription drug abuse in the United States continues to evolve, <sup>1-3</sup> route of drug administration is emerging as an important contributor to the adverse health consequences associated with prescription medication abuse. <sup>4-6</sup> In this regard, recent data indicate that non-oral routes of prescription drug ingestion are not uncommon in samples of high school and college students, rural drug abusers, and urban street drug users <sup>7-10</sup> and are associated with greater drug problem severity, including dependence and overdose. <sup>6</sup>

Because altered routes of administration provide faster drug delivery and onset, the reinforcing effects are often intensified, 11 thereby increasing the vulnerability to addiction. Although there are some early indications that young prescription drug abusers seeking treatment are more likely to use alternate routes of administration and to display greater problem severity than their older counterparts, 12 few studies have systematically examined route of administration among large, diverse samples of prescription drug abusers. Moreover, there is general recognition that prescription drug injection increases risk for human immunodeficiency virus (HIV) and hepatitis infection through the use of non-sterile equipment,<sup>2</sup> yet studies examining risky needle use practices among prescription drug injectors are not apparent in

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the literature. The current study examines the characteristics associated with alternate routes of drug administration among large samples of treatment and street-based prescription opioid abusers in South Florida and explores the scope of needle risk behaviors among a subsample of prescription drug injectors to examine risk for HIV and other blood-borne infections.

#### **METHODS**

#### **Participants**

Eligible participants were individuals 18 years or older who reported abuse of psychoactive prescription drugs at least 5 times in the past 90 days (or 90 days prior to treatment entry, where applicable). In addition, participants met criteria for membership in one of five subpopulations: (1) methadone clients (n = 201), who were enrolled in a methadone maintenance treatment program; (2) street drug users (n = 106), who reported current illicit drug use; (3) public treatment clients (n = 147), who were enrolled in a publicly funded or subsidized drug treatment facility for fewer than 45 days prior to interview; (4) private treatment clients (n =188), who were enrolled in a substance abuse treatment program, paid for with private insurance or personal funds, for fewer than 45 days prior to interview; and (5) men who have sex with men (n = 149) who reported current illicit stimulant use.

#### **Procedures**

A variety of purposive sampling strategies were used to locate study participants. Print media advertisements and the posting or manual distribution of cards and flyers were largely used to recruit street drug users and men who have sex with men. We also used chain-referral sampling to recruit participants in these subgroups, such that each participant received a \$10 cash incentive per eligible referral that completed an interview, with a maximum of five referrals per participant. Referrals from methadone clinic and drug treatment center staff served as the primary recruitment method for methadone maintenance clients and drug treatment enrollees, and these

treatment facilities also provided space for interviews to be conducted. The study was conducted in the investigators' research field offices or in treatment centers located in Broward, Lee, Miami-Dade, and Palm Beach Counties.

All participants were screened for eligibility by trained research staff prior to participation in a single standardized face-to-face interview. Following informed consent, computer-assisted face-to-face interviews were conducted in private offices and lasted 1.5 to 2 hours. Participants received a \$30 monetary incentive for their participation. All study protocols and instruments were reviewed and approved by the University of Delaware's Institutional Review Board.

#### Measures

The Global Appraisal of Individual Needs (GAIN)<sup>13</sup> was the primary data collection instrument for the study. The GAIN has eight core sections, including demographics, health status, mental health, risk behaviors, and substance use, abuse, and dependence measures based on DSM-IV criteria. Questions were added to the GAIN to increase the range of abused prescription drugs we queried, including hydrocodone, hydromorphone, immediate and extended release oxycodone, morphine, methadone, codeine, as well as alprazolam, diazepam and clonazepam. We also queried abuse of prescription stimulants, antidepressants, and antipsychotics. The assessment instrument captured a complete illicit and non-medical prescription drug history, including the number of days using in the past 90 days. Route of administration for prescription medications was assessed through a series of dichotomous 90-day items querying oral/swallowing, snorting, smoking, injecting, rectal/vaginal, and other administration. Routes of administration were not mutually exclusive.

HIV testing was beyond the scope of the study; therefore, HIV prevalence was captured by self-report using the following item: What was the result of your last HIV test (for which you received the results)? Past year needle risk behaviors were captured by a series of dichotomous items querying needle reuse, reuse of non-sterile needles, and sharing needles with other individuals.

#### Data Analysis

For the analyses presented here, only participants who reported at least one occasion of prescription opioid abuse in the past 90 days and those who had complete data on route of administration items were included (N = 1,070). Because route of administration items were asked jointly for all abused prescription pills, we conducted the analyses in two waves: (1) including all 1,070 prescription opioid abusers (regardless of other prescription medication abuse), and (2) excluding opioid abusers who also reported any abuse of prescription stimulants, antidepressants, or antipsychotics (n = 791). We were unable to exclude opioid abusers who also reported benzodiazepine abuse due to the very high prevalence of benzodiazepine use in the sample. Comparison of the two analyses revealed no substantive differences in the findings; therefore, we present only the findings from the smaller, more focused sample of prescription opioid abusers (n = 791).

Data were analyzed using Predictive Analytics Software (PASW, formerly SPSS) version 18. Descriptive statistics were calculated to describe the sample in terms of demographics, health status, substance use and dependence, and route of prescription drug administration. Bivariate logistic regression models were developed to predict route of administration by demographics, subpopulation, substance-specific abuse, and DSM-IV dependence. Finally, we computed multivariate logistic regression models to examine patterns of past-year risky needle use among the subsample of drug injectors, including age and injection patterns (prescription versus illicit drug injection) as predictors.

#### RESULTS

Sample characteristics are displayed in Table 1. The overall sample was young, with a mean age of 34.5 years. Given study eligibility criteria, substantial proportions reported illicit drug use in the 90 days prior to interview. Past 90-day injection of any drug was reported by 29.7% of participants. The prevalence of prescription benzodiazepine abuse in the past 90 days was

TABLE 1. Characteristics of Prescription Opioid Abusers in South Florida (N = 791)

Variable	No.	%
Demographics		
Age		
18–24	176	22.3
25–34	262	33.1
35–44	169	21.4
45+	184	23.2
Mean	34.5	20.2
Gender (% male)	493	62.3
Ethnicity	400	02.0
Hispanic	125	15.8
African American/Black	146	18.5
White	494	62.5
Other	26	3.2
Subsample	20	0.2
Street drug users	106	13.4
Public treatment clients	147	18.6
Private treatment clients	188	23.8
Methadone maintenance clients	201	25.4
Men who have sex with men	149	18.8
Substance use (past 90 days)	143	10.0
Any drug injection	235	29.7
Cocaine (powder)	445	56.3
Crack cocaine	355	44.9
Heroin	211	26.7
Prescription benzodiazepines	618	78.1
Prescription opioids	010	70.1
Oxycodone (excluding OxyContin)	618	78.1
OxyContin	406	51.3
Hydrocodone	306	38.7
Methadone	168	21.2
Codeine	119	15.0
Hydromorphone	78	9.9
Morphine	65	8.2
Other	81	10.2
Past-year substance dependence	750	94.9
Routes of prescription pill administration	750	34.3
Oral	720	91.0
Snorting	420	53.1
Injecting	188	23.8
Smoking	115	14.5
HIV status (% positive) (n = 738)	77	10.4
111 Status (70 positive) (11 — 700)	11	10.4

Participants for the subcategories Substance use (past 90 days), Prescription opioids, and Routes of prescription pill administration could select more than one option.

78.1%. Among the most commonly abused prescription opioids were immediate-release oxycodone (78.1%), OxyContin (51.3%), hydrocodone (38.7%), and methadone (21.2%). Slightly less than 95% of the sample met DSM-IV criteria for substance dependence.

Oral administration was the most common method of pill use (91%); however, substantial proportions reported alternate routes as well, including intranasal (53.1%), injection (23.8%), and smoking (14.5%). More than 10% of the sample reported being HIV positive.

Bivariate logistic regression models predicting route of pill administration are displayed in Table 2. The odds of oral administration were significantly lower among younger opioid abusers (ages 18-24, 25-34 years) compared with older abusers, significantly lower among Whites compared to African Americans, and significantly lower among all treatmentbased participants compared with street drug users. In terms of substance use, the odds of oral administration were significantly higher among powder cocaine users, benzodiazepine abusers, and codeine abusers compared with non-users of these substances; lower odds of oral administration were observed among heroin users, OxyContin abusers, and hydromorphone abusers.

The odds of intranasal administration were significantly higher among younger opioid abusers (ages 18–24, 25–34, 35–44 years) compared with older abusers, significantly higher among both Whites and Latinos compared to African Americans, and significantly higher among all in-treatment participants compared with street drug users. In terms of substance use, the odds of intranasal pill administration were significantly higher among heroin users and abusers of OxyContin, immediate release oxycodone, methadone, hydromorphone and hydrocodone; lower odds of intranasal administration were observed among crack users and codeine abusers. Past year substance dependence was also associated with increased odds of intranasal pill use.

Smoking of prescription medications was associated with younger age (18–24 years), and the odds of smoking were significantly higher among public and private treatment participants compared with street drug users. Methadone clients had lower odds of smoking as a route of administration compared to street drug users. The odds of smoking were significantly higher among abusers of OxyContin and immediate-release oxycodone.

The odds of injection of prescription pills were significantly higher among all younger opioid abusers (ages 18-24, 25-34, 35-44 years) compared with older abusers, significantly higher among both Whites and Latinos compared to African Americans, and significantly higher among all in-treatment participants compared with street drug users. In terms of substance use, the odds of injection were significantly higher among heroin users and abusers of OxyContin, immediate release oxycodone, methadone, hydromorphone and morphine; lower odds of pill injection were observed among cocaine users and codeine abusers. Pastyear substance dependence was associated with increased odds of pill injection. Benzodiazepine use was not associated with injection or any other non-oral routes of administration.

Multivariate logistic regression models examining past-year injection practices are displayed in Table 3. The youngest age group (18–24) had significantly higher odds of several HIV risk behaviors, including reusing needles, reusing needles without cleaning them, and lending needles, compared with their older counterparts. Compared with injectors of illicit drugs, those also endorsing prescription pill injection were observed to have significantly higher odds of reusing unsterile needles.

#### DISCUSSION

This study is among the first to examine alternative routes of administration in a large and diverse sample of prescription opioid abusers. The prevalence of non-oral routes of administration in our sample far exceeds that documented in several studies<sup>6–8</sup> but is in line with estimates from opioid dependent patients in treatment.<sup>12</sup> Our findings indicate that treatment-based individuals had higher odds of abusing prescription opioids through non-oral routes, as did individuals who met DSM-IV-R criteria for past-year substance dependence, regardless of treatment status. These results are consistent with prior research in suggesting that non-oral routes of drug administration are associated with the development of more serious drug problems.<sup>4</sup>

TABLE 2. Bivariate Logistic Regressions Predicting Route of Administration (South Florida Opioid Abusers N = 791)

Variable	Oral Odds Ratio	12 %56	d	Snorting Odds Ratio	12 %56	ď	Smoking Odds Ratio	95% CI	ď	Injecting Odds Ratio	95% CI	۵
Demographics Age (years)	96	0.48		0 57			200	1011	G	8 30	12/ 16.95	000
25–34	265	.099, .705	800	4.71	3.11, 7.13	8 8	1.87	.977, 3.59	050.	5.53	2.91, 10.55	8 8
35-44	.487	.163, 1.51	.218	2.70	1.72, 4.23	000	.928	.417, 2.07	.855	4.16	2.09, 8.270	8
45+	—Ref—-			-Ref			-Ref			-Ref		
Male gender Ethnicity	1.17	.712, 1.92	.534	.778	.582, 1.04	060	1.23	.810, 1.88	.328	.776	.556, 1.084	.137
Hispanic	.275	.055, 1.39	118	2.02	1.21. 3.35	200	1.19	.582, 2.45	.628	2.97	1.96. 18.12	005
White	102	.025, .424	005	4.47	2.97, 6.71	000	1.30	.737, 2.28	.370	17.3	6.30, 47.62	000
African American	—Ref—-			—Ref			—Ref			—Ref	•	
Subsample												
Public treatment	.084	.011, .645	.017	3.82	2.22, 6.57	000	2.56	1.20, 5.50	.015	3.69	1.63, 8.34	.00
Private treatment	039	.005, .288	90.	7.48	4.37, 12.82	000	3.77	1.83, 7.78	000	6.63	3.04, 14.46	000
Methadone maintenance	.103	.014, .786	.028	4.58	2.73, 7.69	000	295	.104, .837	.022	6.55	3.01, 14.24	00.
Men who have sex with men	1.41	.87, 22.8	808	1.21	.692, 2.10	.510	1.08	.463, 2.49	.867	.881	.336, 2.31	797
Street drug users	—Ref——			-Ref			-Ref			-Ref		
Substance use: 90 days												
Cocaine (powder)	2.11	1.28, 3.48	.003	897		.448	.972	.653, 1.45	.887	99.	.475, .917	.013
Crack cocaine	1.06	.65, 1.73	.829	.742		.038	1.20	.805, 1.78	.374	1.17	.844, 1.63	.345
Heroin	.559	.737, .929	.025	1.84	1.33, 2.54	000	1.13	.726, 1.75	.596	5.52	3.90, 7.92	000
Prescription benzodiazepines	1.96	1.16, 3.30	.012	1.19		.313	1.39	.830, 2.33	.210	1.42	.933, 2.16	.102
Oxycodone	.492	.239, 1.01	.054	2.47	1.74, 3.50	000	2.03	1.15, 3.60	.015	4.45	2.50, 7.90	00
OxyContin	.543	.327, .924	.019	2.45	1.84, 3.26	000	1.64	1.10, 2.46	.016	2.42	1.71, 3.41	00
Hydrocodone	1.45	.858, 2.45	.165	1.37	1.02, 1.82	.034	868	.596, 1.35	909	1.27	.912, 1.77	.156
Methadone	.920	.513, 1.65	.780	2.26	1.58, 3.25	000	.700	.414, 1.18	.183	2.00	1.37, 2.90	000
Codeine	4.35	1.35, 14.1	.014	.667	.451, .988	.043	926.	.560, 1.70	.932	316	.170, .588	000
Hydromorphone	.496	.254, .970	040	2.28	1.37, 3.79	100	1.08	.562, 2.06	.823	80.6	5.44, 15.13	000
Morphine	1.20	.466, 3.09	.706	1.46	.866, 2.45	.157	.812	.377, 1.75	.595	2.87	1.71, 4.83	000
			000				0		(			3

 $\text{CI} = \text{confidence interval}; \, \text{Ref} = \text{reference category}.$  Bolded number indicates significance at p < .05.

TABLE 3. Multivariate Logistic Regressions Predicting Past-Year Needle Risk Among Drug Injectors in South Florida (N = 264)

Madala	Odds	95%	
Variable	ratio	CI	р
Reused a needle			
Age (years)			
18–24	3.118	1.20, 8.11	.020
25–34	1.020	.442, 2.35	.964
35–44	2.811	1.06, 7.49	.039
45+	-Ref-	-	
Past 90-day prescription drug injection <sup>a</sup>	1.844	.992, 3.43	.053
Reused a needle without			
cleaning it			
Age			
18–24	3.204	1.31, 7.83	.011
25-34	1.450	.622, 3.38	.389
35–44	1.792	.723, 4.44	.208
45+	-Ref-	_	
Past 90-day prescription drug injection <sup>a</sup>	2.302	1.30, 4.09	.004
Let someone else use your			
needle after you			
Age			
18–24	2.869	1.18, 6.99	.020
25-34	1.617	.690, 3.79	.269
35–44	1.938	.780, 4.81	.154
45+	-Ref-	-	
Past 90-day prescription drug injection <sup>a</sup>	1.647	.928, 2.92	.088
Used a needle someone else			
used			
Age			
18–24	1.860	.735, 4.71	.190
25-34	1.329	.539, 3.28	.537
35–44	1.314	.500, 3.45	.580
45+	-Ref-	-	
Past 90-day prescription drug injection <sup>a</sup>	1.230	.672, 2.25	.502

CI = confidence interval; Ref = reference category. <sup>a</sup>Reference category is "illicit drug injection only". Bolded number indicate significance at p < .05.

In the current study, we identified race/ethnic differences in the abuse of prescription medications through alternate routes of administration. Compared with African Americans, both Hispanic and White participants had substantially higher odds of snorting and injecting as routes for medication abuse. Abuse by medication tampering would appear to represent a more serious degree of opioid involvement among White par-

ticipants in our study, which resonates with previous research documenting higher prevalence of prescription opioid misuse among whites in the general population, college students, substance abuse treatment clients, and illicit drug users. <sup>1,14–16</sup>

Age appeared to play an important role in route of administration as well. The youngest group of opioid abusers (age 18-24 years) uniformly displayed the highest odds of using nontraditional routes of administration. This finding accords with prior research indicating higher levels of risk taking among younger treatmentbased opioid abusers.<sup>12</sup> Importantly, younger individuals are also less knowledgeable about the risks associated with abuse of prescription opioids by tampering,<sup>4</sup> and therefore may be especially vulnerable to adverse health consequences. Our findings demonstrated that the youngest opioid abusers had higher odds of unsafe needle use behaviors, which presents a substantial risk for exposure to HIV, hepatitis, and other blood-borne infections.

Notably, our study documented that specific opioids were associated with alternate routes of administration, particularly snorting and injecting, whereas other opioids were more typically associated with oral ingestion. Immediate release oxycodone, OxyContin, methadone, morphine, and hydromorphone abuse were each independently associated with higher odds of injection, whereas codeine and hydrocodone were not. Our findings add to the existing literature on substance-specific route of administration.<sup>10</sup> Clearly, route of administration is closely tied with the specific characteristics of the abused medication, including its pharmacokinetic properties and the presence or absence of additional ingredients, such as acetaminophen, which can cause unpleasant and harmful effects if taken by injection.

As an additional point, past 90-day heroin use was also found to be strongly associated with prescription opioid injection among our sample. This appears to represent an additional piece of evidence in support of the notion that the epidemics of heroin and prescription opioid abuse are increasingly intertwined. For some time, abusers have been observed to substitute heroin

for prescription opioids and vice-versa based on availability, affordability, and other considerations, and increasingly it has been noted that prescription opioid abusers are switching to heroin in areas where heroin is less costly or of higher purity. <sup>17,18</sup> As this situation continues to evolve, proactive monitoring of early warning systems for adverse events related to heroin use will be critical.

Our findings should be considered within the context of the study limitations. First, reliance on self-report data carries the potential for bias in reporting that may have affected our prevalence estimates. In addition, measurement of route of prescription drug administration was somewhat restricted, with items not asked at the drug level. This limited our ability to examine prescription opioid abuse exclusively. Nevertheless, we documented that benzodiazepine abuse was not associated with any non-oral routes of administration, and therefore the route of administration data are attributable to prescription opioids. Lastly, because this research was conducted in South Florida, an area noted for its high prevalence of prescription drug abuse and diversion, the findings may not be generalizable to other locations.

Overall, our findings on route of administration among prescription opioid abusers have important implications for forward-looking prevention and intervention strategies. First, the continued development of abuse-deterrent opioid formulations would appear to be warranted, <sup>19</sup> particularly for younger individuals at a high risk for opioid abuse through tampering. From a public health perspective, it is essential that young prescription opioid injectors be targeted for appropriate HIV and hepatitis education and intervention programming, as well as harm reduction initiatives. Given their young age and underrepresentation in populations traditionally considered to be at high risk for HIV, increased exposure to injection-related disease prevention measures should be emphasized.

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