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Factors Associated with High-Frequency Illicit Methadone Use among Rural Appalachian Drug Users

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Abstract

Background—In recent years there has been a sharp increase in the use of illicit methadone as well as methadone-related overdose deaths.

Objective—The purpose of this study is to describe factors associated low- and high-frequency methadone use in a cohort of rural Appalachian drug users.

Methods—Interviews assessing sociodemographics, illicit drug use and drug treatment, psychiatric disorders, health, and sociometric drug network characteristics were conducted with 503 rural drug users between 2008 and 2010. A two-level mixed effects regression model was utilized to differentiate low- (one use per month or less in the past 6 months) versus high-frequency (daily or weekly use in the past 6 months) illicit methadone users.

Results—The lifetime prevalence of illicit methadone use in this population was 94.7% (n=476) and slightly less than half (46.3%) were high-frequency users. In the mixed effects regression model, initiating illicit methadone use at a younger age was associated with high-frequency illicit methadone use. Whereas taking a prescribed medication for a physical problem, undergoing additional weeks of outpatient drug free treatment, daily OxyContin® use in the past month, and having fewer ties and second order connections in the drug network reduced the odds of high-frequency illicit methadone use.

Conclusions—Rates of illicit methadone use and high-frequency illicit methadone use among this sample of rural drug users were considerably higher than those previously reported in the literature. Health practitioners in rural areas should routinely screen for illicit opioid use, including methadone.

Introduction

The synthetic opioid methadone has a 40-year history in opioid replacement therapy, and in recent years, has also been utilized in the treatment of chronic pain. Despite the demonstrated efficacy of methadone in both contexts, methadone-related fatal drug poisonings increased dramatically between 1999 and 2006 (1). Additionally, emergency department visits involving methadone increased 71% from 2004 to 2009 (2). Methadone is also the most commonly implicated prescription drug in overdose deaths in some U.S. states such as Oklahoma (3) and North Carolina (4) and appears to be disproportionately affecting

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rural areas. One recent study found that residents of rural Appalachian Kentucky were more likely to have been hospitalized and fatally overdose on methadone than other residents of Kentucky (5).

In 2009, the lifetime prevalence of illicit methadone use in the U.S. among those age 12 and older was 0.8% and 2.0% among those aged 18 to 25 (6). The *Monitoring the Future Study* reported the prevalence of illicit methadone use among high school seniors to be 1.2% in 2009, a two-fold increase since 1996 (7). Of the few studies examining illicit methadone use in a community-based setting, Ompad and colleagues (2008) found lifetime prevalence rates of 21.5% among non-injectors and 52.6% among injection drug users in New York City (8).

Given the significant variability that exists between geographic areas with regard to prescription opioid misuse and overdose deaths (1), studies focused specifically on illicit methadone use in high-risk areas are needed. This study will be the first to our knowledge to focus on the use of illicit methadone specifically among a sample of rural drug users. Additionally, we will focus on frequency of illicit methadone misuse because high-frequency opioid use has been shown to consistently increase risk of overdose (9–12). Thus, the purpose of this study is to determine both the individual and network-related factors that differentiate low- and high frequency methadone users in rural Appalachia.

Methods

Study Population

Data are from a longitudinal study of social networks and HIV risk among rural Appalachian drug users. Methods for this study are discussed in greater detail elsewhere (13). To be eligible, participants had to be at least 18 years of age, reside in one of Kentucky's Appalachian counties, and report use of prescription opioids, cocaine, heroin, or methamphetamine in the past 30 days. Participants were compensated $50 for their time, and the study was approved by the University of Kentucky's Institutional Review Board (IRB).

Sampling

Participants were recruited using respondent driven sampling (RDS) (14), an approach focused on accessing "hidden" or stigmatized populations. As a primary focus of the larger study was on infectious disease risk behaviors, the initial participants, or *seeds,* were required to have a history of injection drug use. Upon completion of the baseline interview, seeds were given three coupons and asked to recruit drug-using peers (though injection drug use was not required). Seeds were then compensated $10 each time a drug-using peer met eligibility criteria and completed a baseline interview. RDS has been successfully utilized in studies focused on drug use in both urban (15) and rural contexts (16).

Variables and Measures

Baseline interviews were conducted by trained local interviewers using Computer Assisted Personal Interviewing (CAPI) software. Participants indicating they had ever used methadone to get high were classified as illicit methadone users. Variables chosen for analysis were selected *a priori* based on extant literature. In addition to examination of sociodemographic characteristics, we also sought to determine whether methadone users were more likely to have health problems that may necessitate its use as an analgesic using three measures from the Addiction Severity Index (ASI) (17) – use of medications for chronic health conditions, number of days in past 30 experiencing medical problems, and self-reported chronic medical problems. The ASI was also used to examine other illicit drug use as well as drug abuse treatment history and number of days with drug problems, since methadone is primarily used to treat opioid dependence. Items assessing illicit drug use

included lifetime (yes or no), past six-month (none, once or twice, once per month, weekly, daily or more), and past 30-day use (number of days) of the following psychoactive drugs: alcohol, heroin, licit methadone, illicit methadone, OxyContin®, other oxycodone products, benzodiazepines, methamphetamine, cocaine, crack cocaine, and marijuana. Drug use was further dichotomized to daily use, yes/no. Given that substance use and psychiatric disorders are often comorbid, we also examined the relationship between methadone use and DSM-IV disorders. The Mini-International Neuropsychiatric Interview (MINI) 5.0 was used to measure major depressive disorder, generalized anxiety disorder, panic disorder, post-traumatic stress disorder and antisocial personality disorder (18).

Little has been published on methadone use within drug networks. However, we hypothesized that social networks would play a significant role in differentiating high- and low-frequency users. To build the sociometric drug network we utilized a name-generating questionnaire. Briefly, participants were asked the name (first name, last initial) of anyone they had used drugs with in the six months prior to the baseline interview. Once these data were verified and compiled, the drug network variables were calculated (see [13] for a full description). For this specific analysis, we were interested in measures of network position and cohesion. Three measures of network centrality were utilized to identify individuals who are highly connected within the network: *degree centrality* (19) measures how many individuals one is immediately connected to and has been used in several studies focused on disease transmission (20–24); *betweenness centrality* (19) measures how often one lies on paths for others in the network to reach other; and *eigenvector centrality* is akin to degree, but weights by second order connections providing an index of not just who one uses drugs with, but how often the people you use drugs with use drugs with others (25). Previous studies have demonstrated that eigenvector centrality is correlated with disease transmission (21, 26). Each of these measures were normalized by dividing the raw scores by the maximum possible score and then expressed as a percentage. *K*-cores were used to locate participants who were in particularly dense regions of the network (27). *K*-cores have been shown to impact risky health behaviors (26, 28). These four social network measures were all calculated with UCInet version 6.3 (Harvard, MA).

Analytic Plan

Bivariate comparisons of low- (one use per month or less in the past 6 months, n = 243) versus high- (daily or weekly use in the past 6 months, n = 233) frequency illicit methadone users were conducted using chi-square tests for categorical variables and the Wilcoxon rank-sum test for continuous variables. Given that participants were nested within networks, a two-level mixed effects regression model (*xtmelogit*) was utilized to determine the factors independently associated with illicit methadone use. Variables significant at the $p<0.05$ level in unadjusted logistic models were considered for inclusion in the mixed effects model and a manual, stepwise, backward elimination process was used until the most parsimonious model was achieved. STATA, version 11.0 was used for all analyses (College Station, TX).

Results

The lifetime prevalence of illicit methadone use was 94.6% in this sample of rural Appalachian drug users and the prevalence of high-frequency use was 46.3% in the six months prior to the baseline interview. Friends (46.0%) were the most common source of illicit methadone, followed by a dealer (28.8%), family member (12.4%), spouse/partner (8.8%), and doctor/dentist (2.5%).

In unadjusted analyses (Table 1), compared to low-frequency users of illicit methadone, high-frequency users were significantly younger, indicated fewer days with medical problems and were less likely to be taking medication for physical problem. Low-frequency

illicit methadone users were significantly more likely to report daily OxyContin® use compared with high-frequency users. Low-frequency methadone users were also more likely to use with people who were using with multiple others as measured by eigenvector centrality.

Factors independently associated with illicit methadone use are presented in Table 2. Younger age was associated with high-frequency illicit methadone use, even after adjustment for the other variables in the model. Each additional week of outpatient drug-free treatment in the past year reduced the odds of high-frequent illicit methadone use by 11% (Adjusted Odds Ratio [AOR]: 0.89; 95% Confidence Interval [CI]: 0.83–0.97), as did taking prescribed medication for a physical problem (AOR: 0.59; 95% CI: .37–.93). Additionally, daily OxyContin® use in the past 30 days was also associated with reduced odds of high-frequency illicit methadone use. Finally, eigenvector centrality was inversely associated with high-frequency methadone use (AOR: 0.95, 95% CI: 0.91, 0.99). That is, the fewer people one uses drugs with, as well as using with people who tend to use with fewer people, the greater likelihood they will be a high-frequency methadone user.

Discussion

This study is among the first to report on illicit methadone use among rural drug users. The lifetime prevalence of illicit methadone use in this sample of Appalachian drug users was 94.6%, considerably higher than the lifetime rates of 21.8% for non-injection and 52.6% for injection drug users reported among New York City drug users (8). Although illicit methadone use has become a national health concern, these results demonstrate it is particularly problematic in central Appalachia.

Despite the absence of similar rural samples to serve as comparisons, recent studies of methadone-related overdose deaths provide some insight. A comparison of methadone-related overdose deaths to deaths resulting from other opioids found that methadone-related decedents tended to be younger, though decedents did not differ with regard to ingestion of other drugs at the time of death (29). In our study, high-frequency illicit methadone users were significantly younger than low-frequency illicit methadone users.

The increase in illicit methadone use may be driven largely by availability of methadone prescribed for pain, not opioid treatment programs. In an analysis of methadone distribution data, it was found that the increase in distribution of methadone to opioid treatment providers between 2002 and 2007 had been modest, whereas the amount of methadone distributed to physicians, hospitals, and pharmacies more than doubled in a five year period (30). Consequently, the amount of methadone available for diversion has increased substantially.

The current study also found that for each additional week of outpatient drug-free treatment in the past year, the odds of being a high-frequency illicit methadone user was reduced by 11%. Though high-frequency illicit methadone users in this sample reported more daily drug problems than low-frequency illicit methadone users, they completed fewer weeks of outpatient drug treatment in the past year. Previous studies have demonstrated the benefits of increased length of stay in treatment (31–33). This finding highlights the importance of treatment access and retention. Rural drug users are less likely than urban users to receive treatment for drug problems (34). This is at least partly due to access; individuals in need of drug and alcohol treatment who reside in non-metropolitan areas and in the Southern U.S. Census region, both of which characterize this study, tend to be the furthest from such treatment (35). Additionally, one study reported that only 5% of U.S. opioid-replacement

programs reside in non-metropolitan counties (36). Increasing treatment availability in medically underserved areas must remain a national priority.

Studies have described multiple motives for prescription drug misuse (e.g., self-treatment, recreational use) (37, 38). Illicit prescription drug users also have high rates of the physical and psychological symptoms for which misused drugs may be prescribed (39, 40). Results from the present study suggest that high-frequency illicit methadone use may have a self-treatment component. Specifically, illicit methadone users who reported taking a prescribed medication for a physical problem were considerably less likely to be high-frequency illicit methadone users. This finding suggests that high-frequency illicit methadone use may be associated with untreated or undertreated physical problems. In a national sample of individuals entering treatment for prescription opioid problems, over 60% reported chronic pain and over 80% were first introduced to opioids through a legitimate prescription for pain (41). These findings suggest that greater access to healthcare and pain management in particular may help prevent prescription opioid misuse. Additionally, managing patients with comorbid pain and opioid addiction is complex (42) and successful treatment often requires integrated medical and drug treatment (43).

One surprising finding in the current study was that daily OxyContin® use in the past month reduced the odds of high-frequency illicit methadone use. High-frequency illicit methadone use may result from an inability to access OxyContin®, especially now that the old formulation is no longer available. However, this finding may also suggest that high-frequency prescription opioid users in this study have developed a preference for either methadone or OxyContin®, not both.

Finally, position and relationships within the greater drug network also lowered the odds of being a high-frequency methadone user. Specifically, high-frequency methadone users had fewer social ties and those they were tied to also had fewer ties (i.e., “friends of friends” of other drug users in the network) relative to low-frequency users. This suggests that the high-frequency methadone users are more isolated and may have less support. Interestingly, this finding contrasts sharply with high-frequency OxyContin use; in a previous study with this sample, daily OxyContin use was associated in greater social capital (44). The relative isolation of high-frequency illicit methadone use has serious implications for overdose in particular as the risk of fatal overdose is significantly greater among those using alone (45) and those with less social support (46). Given the fewer second order connections among these high-frequency methadone users, it is also less likely that network-based interventions would be effective in diffusing information to other high-frequency methadone users. This is unfortunate, as high-frequency methadone users may benefit most from overdose interventions. Thus, a preliminary form of intervention for high-frequency illicit methadone users may be increasing social support.

This study has three primary limitations. Items used in this analysis were self-reported. It is possible that drug use was underestimated, though this seems unlikely given the high rates of self-reported use for multiple drugs. Additionally, as this analysis is based on data collected at a single time point, the temporal ordering of the reported associations cannot be determined. Finally, the study did not assess motives for misuse, which may limit the ability to explain differences between high- and low-frequency illicit methadone users.

Despite these limitations, rates of illicit methadone use among this rural sample of drug users were considerably higher than those previously reported in the literature. Illicit methadone use, regardless of frequency, is related to other high-risk health behaviors. Health practitioners in rural areas should routinely screen for illicit opioid use, including methadone.

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Table 1

Characteristics of 476 Rural Appalachian Illicit Methadone Users

	Low Frequency Users n=243		High Frequency Users n=233		
	n	**%**	**n**	**%**	**p-value**
Demographics					
Male	140	57.6	131	56.2	0.759
White	229	94.2	221	94.8	0.769
Age, mdn (IQR)	32 (26, 40)		30 (25, 35)		<0.001
Years education, mdn (IQR)	12 (10, 12)		12 (10, 12)		0.326
30-Day Income, mdn (IQR)	$674 ($250, $1243)		$713 ($353, $1276)		0.357
Physical Health					
Chronic medical problems	91	37.4	69	29.6	0.070
Days w/medical problems in past 30, mdn (IQR)	0 (0, 14)		0 (0,4)		0.033
Medication use physical problems	83	34.2	47	20.2	0.001
Daily Substance Use (Past 30 Days)					
Alcohol	9	3.7	9	3.9	0.928
Licit Methadone	3	1.2	3	1.3	0.959
OxyContin	43	17.7	21	9.0	0.006
Other oxycodone	24	9.9	24	10.3	0.878
Benzodiazepines	24	9.9	26	11.2	0.648
Heroin	0	0	0	0	-
Cocaine	0	0	0	0	-
Crack cocaine	0	0	0	0	-
Methamphetamine	0	0	0	0	-
Marijuana	67	27.6	58	24.9	0.507
Drug Treatment					
Daily drug problems	92	37.9	107	45.9	0.075
Weeks in treatment in past year:					
Outpatient drug free, mdn (IQR)	5 (0, 22)		0 (0, 2)		0.051
Methadone, mdn (IQR)	0 (0, 0)		0 (0, 24.75)		0.096
Residential, mdn (IQR)	0 (0, 1)		0 (0, 0.25)		0.904
DSM-IV Disorders					

	Low Frequency Users n=243		High Frequency Users n=233		
	n	**%**	**n**	**%**	**p-value**
Major depressive disorder	67	27.6	58	24.9	0.507
Generalized anxiety disorder	65	26.7	72	30.9	0.317
Post-traumatic stress disorder	31	12.8	39	16.7	0.220
Antisocial personality disorder	84	34.6	71	30.5	0.340
Social Network					
Degree centrality	0.40 (0.20, 0.80)		0.40 (0.20, 0.60)		0.707
Eigenvector centrality	0.04 (0.0001, 1.07)		0.02 (0.0003. 0.20)		0.026
Betweenness	0.014 (0, 1.13)		0.12 (0, 1.00)		0.921
k-coreness	2 (1, 2)		2 (1, 2)		0.618

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Table 2

Mixed Effects Regression Models Comparing Low- and High Frequency Methadone Users (N=476)

	Unadjusted		Adjusted	
	Odds Ratio	**95% CI**	**Odds Ratio**	**95% CI**
Age (quartiles)				
18–25	1.00	-	1.00	-
26–30	0.91	0.53, 1.53	0.98	0.56, 1.71
31–36	0.77	0.46, 1.28	0.79	0.46, 1.36
37+	0.37	0.22, 0.64	0.41	0.23, 0.73
Chronic health problems	0.70	0.48, 1.03	-	-
Days w/medical problems	0.98	0.96, 0.99	-	-
Medication physical problem	0.48	0.32, 0.74	0.59	0.38, 0.94
Daily OxyContin use	0.46	0.26, 0.80	0.44	0.24, 0.79
Weeks in outpt drug free	0.91	0.85, 0.98	0.89	0.83, 0.97
Daily drug problems	1.39	0.97, 2.00	-	-
Eigenvector centrality	0.95	0.91, 0.98	0.95	0.91, 0.99