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Predictors of transition to heroin use among initially non-opioid dependent illicit pharmaceutical opioid users: A natural history study

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ABSTRACT

Background: Increases in illicit pharmaceutical opioid (PO) use have been associated with risk for transition to heroin use. We identify predictors of transition to heroin use among young, illicit PO users with no history of opioid dependence or heroin use at baseline.
Methods: Respondent-driven sampling recruited 383 participants; 362 returned for at least one biannual structured interview over 36 months. Cox regression was used to test for associations between lagged predictors and hazard of transition to heroin use. Potential predictors were based on those suggested in the literature. We also computed population attributable risk (PAR) and the rate of heroin transition.
Results: Over 36 months, 27 (7.5%) participants initiated heroin use; all were white, and the rate of heroin initiation was 2.8% per year (95% CI = 1.9%–4.1%). Mean length of PO at first reported heroin use was 6.2 years (SD = 1.9). Lifetime PO dependence (AHR = 2.39, 95% CI = 1.07–5.48; PAR = 32%, 95% CI = −2% to 64%), early age of PO initiation (AHR = 3.08, 95%; CI = 1.26–7.47; PAR = 30%, 95% CI = 2%–59%), using illicit POs to get high but not to self-medicate a health problem (AHR = 4.83, 95% CI = 2.11–11.0; PAR = 38%, 95% CI = 12%–65%), and ever using PO non-orally most often (AHR = 6.57, 95% CI = 2.81–17.2; PAR = 63%, 95% CI = 31%–86%) were significant predictors.
Conclusion: This is one of the first prospective studies to test observations from previous cross-sectional and retrospective research on the relationship between illicit PO use and heroin initiation among young, initially non-opioid dependent PO users. The results provide insights into targets for the design of urgently needed prevention interventions.

1. Introduction

Over the past decade, the non-medical use of pharmaceutical opioids emerged as one of the fastest growing forms of drug abuse in the United States with young adults showing rates higher than other age groups (Johnston et al., 2010; Substance Abuse and Mental Health Services Administration (SAMHSA, 2010). Increases in illicit pharmaceutical opioid (PO) use resulted in escalating accidental overdose death rates (Paulozzi et al., 2006) and increasing prevalence of opioid abuse and dependence disorders (McCabe et al., 2008). Prior research with an Appalachian sample of illicit drug users demonstrated that PO use, in particular illicit use of OxyContin (pre-abuse deterrent formulation), was related to a high risk of transition to injection (Young and Havens, 2011).

Growing evidence also suggests that illicit PO use has expanded pathways to heroin initiation and contributed to the heroin epidemic in the United States. Qualitative and cross-sectional quantitative studies conducted in different regions of the country, including Ohio as early as 2002 (Siegal et al., 2003a), Washington (Peavy et al., 2012), California, New York and Pennsylvania (Lankenau et al., 2012; Mars et al., 2014), were among the first to describe a trend of illicit PO users becoming opioid dependent and transitioning to heroin use. Analysis of data from the U.S. National Survey of Drug Use and Health (NSDUH) indicated that between 2002–2004 and 2008–2010, heroin use increased substantially among non-medical users of pharmaceutical opioids but remained unchanged among non-users (Jones, 2013). Martins et al. (2015) also found a significant relationship between illicit PO use and heroin use in the years 2008–2011 NSDUH cohort, compared to the 2002–005 period. Another NSDUH-based study found that the inci-

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dence rate of heroin initiation was approximately 19 times greater among prior illicit PO users than among non-users (Muhuri et al., 2013). Data on drug overdose hospitalizations and mortality rates demonstrated significant increases in heroin-related overdoses and reductions in PO-related overdose rates over the past few years (Unick et al., 2013; Dasgupta et al., 2014; Lee et al., 2014; Rudd et al., 2014). Similar trends were identified in Ohio, with overdose death data showing large increases in heroin-related deaths and leveling off of PO-related deaths in 2012 (Massatti et al., 2014). In Ohio, like other areas of the country, these increases appear to be linked to implementation of stricter pharmaceutical opioid prescription policies and guidelines (Massatti et al., 2014) and the introduction of an abuse-deterrent formulation of extended-release oxycodone (ADF OxyContin; Cicero and Ellis, 2015).

Although there is mounting evidence of the "intertwined" epidemics of illicit PO and heroin use, there is a lack of prospective studies designed to identify the factors associated with heroin initiation among illicit PO users. This study reports the findings of a 36-month natural history study of young adult illicit PO users who, at baseline, were not opioid dependent and had no history of heroin use or illicit injection. We examine associations between selected predictors and time to first heroin use using a time-to-event analysis. Potential predictors were selected mostly based on prior retrospective research findings suggesting associations between heroin initiation and: PO dependence (e.g., Jones, 2013; Jones et al., 2015; Lankenau et al., 2012; Mars et al., 2014); frequency of PO use (Jones, 2013; Jones et al., 2015; Muhuri et al., 2013; Cicero and Ellis, 2015); route of administration (ROA; McCabe et al., 2007a; Kirsh et al., 2012; Young et al., 2010); non-medical use of OxyContin (high abuse liability; Hays, 2004; Ternes and O'Brien, 1990; Siegal et al., 2003a,b; Martins et al., 2009; Cicero and Ellis, 2015; Young and Havens, 2011); and the introduction of ADF OxyContin (Cicero and Ellis, 2015).

2. Methods

2.1. Sample recruitment

Between April, 2009 and May, 2010, we recruited 383 eligible participants in the Columbus, Ohio, area using respondent-driven sampling (RDS; Heckathorn, 1997, 2002). We limited referrals to three eligible participants and compensated referrers $15 for each person presenting at the project office (Wang et al., 2005, 2007). Daniulaityte et al. (2012) provide more details on sample recruitment.

Located in Franklin County, with a population over one million, Columbus is the Ohio state capitol, with a population of 787,033 people, 61% of whom are white, 28% African American, and 11% of other ethnicity (United States Census Bureau, 2010). Like much of Ohio, the Columbus area has experienced dramatic increases in the PO/heroin epidemics that began fomenting as early as 2002 when OxyContin was first identified as a potential new risk factor for heroin initiation (Siegal et al., 2003a,b). In Franklin County, unintentional drug overdose deaths increased 41.7% from 139 in 2009 to 197 in 2013 (Ohio Department of Health, 2014). In 2013, heroin was present in 46.6% of overdose deaths and POs in 34.4% (Ohio Department of Health, 2014).

2.2. Eligibility

Eligibility criteria included: (1) age 18–23 years (to recruit those in emerging adulthood when the risk of drug and drug-related behaviors peaks (Arnett, 2000; Bachman et al., 1996); (2) self-reporting non-medical PO use on five or more occasions in the previous 90 days (to recruit active PO users); (3) expressing intentions to use illicit POs again (to capture active PO users); (4) residence in the Columbus, OH, area; (5) identifying opioids s/he reported having used on a pill card similar to that used in the NSDUH (Caviness et al., 2006), but without drug names listed (to verify reported illicit PO use); (6) no lifetime opioid dependence as ascertained with the DSM-IV Checklist (Forman et al., 2004; Hudziak et al., 1993); (7) no self-reported history of heroin use or history of drug injection as verified by visual inspection of arms for injection track marks; (8) no pending criminal charges (to minimize loss to follow-up); and (9) not involved in formal substance abuse treatment in the past 30 days (to avoid recruiting participants in active recovery who would be different from active users not wishing to stop drug use).

2.3. Data collection

Baseline and follow-up structured questionnaires (conducted every six months for 36 months) were administered by trained interviewers in private offices following completion of an informed consent. Participants were compensated $50 for completing a 1.5–2.5 h baseline interview. Compensation for follow-up interviews was $40 for briefer semi-annual interviews and $50 for longer, annual follow-up interviews. All protocols were approved by the Wright State University IRB.

The final 36-month follow-up interview was conducted in May 2013, and retention rates were excellent. Of the 383 participants interviewed at baseline, 89.8% returned at 6 months; 88.5% at 12 months; 86.7% at 18 months, 83.3% at 24 months; 78.6% at 30 months; and 73.4% at 36 months.

2.4. Outcome and predictors

The outcome in this time-to-event analysis was time from initiation of illicit PO use to heroin initiation. Age of initiation of illicit PO use was self-reported as a whole number, and initiation of heroin use was self-reported as using heroin for the first time since the most recent follow-up interview. The outcome was computed as the difference between the age at the first interview where heroin use was reported and the age of initiation of illicit PO use.

Frequency of illicit PO use was ascertained through an author-generated item previously employed (Carlson et al., 2005; Falck et al., 2005; Siegal et al., 1998): "During the past six months, how often did you use non-prescribed pain pills (e.g., Vicodin, Percocet)?" Seven response options ranged from "never/none" to "daily" and were collapsed to $\leq$1, about 2, and $\geq$3 days per week. The predictor, "frequency of pain pill use," represents the maximum reported value since the baseline interview.

At baseline and follow-up interviews, lifetime use (yes/no) of other drugs (alcohol, marijuana, sedatives ("non-prescribed tranquilizers like Xanax, Ativan, Valium")), cocaine, non-prescribed stimulants ('like Ritalin, Adderall, Concerta"), MDMA, and LSD were ascertained using the questions "Have you ever used [drug]?" and "Since your last interview, have you used [drug]?" Use of immediate-release oxycodone was ascertained via the question: "Have you ever (since your last interview) used Percocet, Percodan, Tylox, or other drugs containing immediate-release oxycodone?" Use of OxyContin was assessed by asking a similar question. Use of ADF OxyContin was added as a distinct question in November, 2010, roughly coinciding with the availability of the reformulation in December, 2010 (Cicero and Ellis, 2015).

Lifetime opioid dependence was assessed using the DSM-IV checklist (Forman et al., 2004; Hudziak et al., 1993). The computerized version of the Diagnostic Interview Schedule (CDIS) was used to ascertain lifetime dependence on other drugs, and lifetime psychiatric comorbidity (ASPD, depression, GAD, mania, or PTSD; Robins et al., 1999). The only drugs with greater than mini-