



Research paper

Polydrug use and its association with drug treatment outcomes among primary heroin, methamphetamine, and cocaine users



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ABSTRACT

Background: Polydrug use may challenge effective treatment for substance use disorders. We evaluate whether secondary substance use modifies the association between treatment and primary drug use among primary heroin, cocaine and methamphetamine (MA) users.

Methods: Data were obtained from prospective cohort studies on people who use illicit drugs (PWUD) in California, USA. Using repeated monthly data on self-reported secondary substance use (heroin, cocaine, MA, alcohol or marijuana; ≥ 1 day in a month), primary drug use (≥ 1 day in a month), and treatment participation, collected via timeline follow-back, we fitted generalized linear mixed multiple regression models controlling for potential confounders to examine the interactions between treatment and secondary substance use on the odds of primary heroin, cocaine and MA use, respectively.

Results: Included in our study were 587 primary heroin, 444 primary MA, and 501 primary cocaine users, with a median of 32.4, 13.3 and 18.9 years of follow-up, respectively. In the absence of secondary substance use, treatment was strongly associated with decreased odds of primary drug use (adjusted odds ratios (aORs): 0.25, 95% CI: 0.24, 0.27, 0.07 (0.06, 0.08), and 0.07 (0.07, 0.09)) for primary heroin, MA, and cocaine users, respectively. Secondary substance use of any kind moderated these associations (0.82 (0.78, 0.87), 0.25 (0.21, 0.30) and 0.53 (0.45, 0.61), respectively), and these findings were consistent for each type of secondary substance considered. Moreover, we observed different associations in terms of direction and magnitude between secondary substance use and primary drug use during off-treatment periods across substance types.

Conclusion: This study demonstrates secondary substance use moderates the temporal associations between treatment and primary drug use among primary heroin, MA and cocaine users. Disparate patterns of polydrug use require careful measurement and analysis to inform targeted treatment for polydrug users.

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Abbreviations: MA, methamphetamine; CAP, the Civil Addict Program; CTE, the cocaine treatment evaluation study; METH, the methamphetamine natural history study; TXPR, the treatment process study; TUE, the treatment utilization and effectiveness study; NHI, Natural History Interview; GLMM, generalized linear mixed multiple regression model.

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Introduction

Heroin, cocaine, and methamphetamine (MA) have among the highest global burden of disease among illicit drugs (Degenhardt et al., 2013) and are associated with severe public health and social consequences such as mortality, morbidity, and criminality (Hser, Evans, Huang, Brecht, & Li, 2008; UNODC, 2012; Wang et al., 2016). In addition, high levels of polydrug use have been reported among

people who use illicit drugs (PWUD) in a wide variety of treatment and community settings internationally (Ball & Ross, 1991; Booth, Leukefeld, Falck, Wang, & Carlson, 2006; Byqvist, 2006; Darke & Hall, 1995; Ives & Ghelani, 2006; Leri, Bruneau, & Stewart, 2003; Leri et al., 2005). Compared to mono-drug use, polydrug use has been associated with greater psychopathology (Booth et al., 2006; Medina & Shear, 2007; Sumnall et al., 2004); higher levels of risky health behaviors (Patterson, Semple, Zians, & Strathdee, 2005); decreased cognitive functioning (Dillon, Copeland, & Jansen, 2003); poorer treatment engagement (John, Kwiatkowski, & Booth, 2001) and treatment outcomes (Bovasso & Cacciola, 2003; DeMaria, Sterling, & Weinstein, 2000; Williamson, Darke, Ross, & Teesson, 2006b); and increased non-fatal overdoses as well as drug-related deaths (Coffin et al., 2003; Strang et al., 1999).

Treatment for opioid use disorders in the form of non-time limited opioid agonist treatment has been shown to be effective in numerous randomized trials, meta-analyses, and large-scale longitudinal studies (Amato et al., 2005; Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003; Mattick, Kimber, Breen, & Davoli, 2008); however, the evidence for effective treatment of cocaine or MA use disorders is not as clear (Fischer et al., 2015). While psychosocial treatment has shown varying degrees of promise in clinical trials (Courtney & Ray, 2014; Pérez-Mañá, Castells, Vidal, Casas, & Capellà, 2011), the search for pharmacological treatment for cocaine or MA use has yet to produce an effective medication (Brensilver, Heinzerling, & Shoptaw, 2013; Kishi et al., 2013; Minozzi et al., 2015). Development of effective treatment strategies for people who use multiple illicit drugs, or polydrug users, is further challenged by the variety of substances combinations and patterns of use (European Monitoring Centre for Drugs and Drug Addiction, 2009; Ives & Ghelani, 2006). As a consequence, clinical guidelines provide minimal guidance on the management and impact of polydrug use (American Psychiatric Association, 2006; Management of Substance Use Disorders Working Group, 2015; National Institute on Drug Abuse, 2012). For instance, the only suggestion found in treatment guidelines from the US Veterans Health Department and the National Institute on Drug Abuse was to manage multiple substance use disorders according to the recommendations made for each of those individual disorders (Management of Substance Use Disorders Working Group, 2015; National Institute on Drug Abuse, 2012).

Previous studies have mainly evaluated the relationships between cocaine use and treatment outcomes among heroin dependent individuals. For example, prior observational studies have shown that cocaine use was associated with increased heroin use at treatment entry, poorer treatment outcomes including retention, and subsequent relapse into heroin use (Hartel et al., 1995; Sullivan et al., 2010; Termorshuizen, Krol, Prins, & van Ameijden, 2005; Williamson, Darke, Ross, & Teesson, 2006a; Williamson et al., 2006b) among patients receiving opioid agonist treatment. However, there is substantially less evidence regarding polydrug use and treatment outcomes among individuals primarily use cocaine or MA. Furthermore, the majority of PWUD concurrently use alcohol or marijuana (Brecht, Huang, Evans, & Hser, 2008). One review study revealed that alcohol use post-drug treatment increased relapse to drug use, but evidence regarding whether alcohol could become a substitute addiction remained inconclusive (Staiger, Richardson, Long, Carr, & Marlatt, 2013). Evidence on the association between marijuana use and drug treatment outcomes also produced conflicting results, with some demonstrating beneficial effects and others showing an adverse impact (Zielinski et al., 2016).

We take advantage of a unique set of California-based prospective cohort studies, which tracked monthly drug use and treatment receipt for as long as three decades for PWUD characterized by the primary use of heroin, cocaine and MA. We

considered the use of any substance other than the primary drug as secondary substance use, including heroin, cocaine, MA, alcohol and marijuana. Polydrug use was thus defined as self-reported use of any two substances in a given month during study follow-up. We conducted this study to test the hypothesis that secondary substance use would moderate the associations, if treatment was associated with decreased odds of primary drug use. In addition, we examined the relationships between secondary substance use and primary drug use in the absence of treatment to investigate natural polydrug use patterns.

Methods

Study design and subjects

Data were derived from four non-overlapping studies that collected monthly information of adult PWUD in California using the Natural History Interview (NHI): (1) the 33-year Civil Addict Program (CAP) (Hser, Hoffman, Grella, & Anglin, 2001); (2) the cocaine treatment evaluation study (CTE) (Hser et al., 2006); (3) the methamphetamine natural history study (METH) (Brecht, O'Brien, von Mayrhauser, & Anglin, 2004); and (4) the treatment process study (TXPR) (Hser, Huang, Teruya, & Anglin, 2004), with baseline assessments executed in 1964, 1988–1989, 1995–1997, and 1995 respectively, and the last year of follow-up in 1997, 2002–2003, 1999–2002, and 1996 respectively. All studies recruited subjects from treatment settings only, and baseline drug use profiles across studies were previously presented (Nosyk et al., 2014).

We included all participants from the four studies and classified them into primary heroin, cocaine, and MA use categories according to the definitions adopted by the original studies (Brecht et al., 2004; Hser et al., 2001, 2004; Hser, Huang, Teruya, & Douglas Anglin, 2003; Hser et al., 2006). The primary drug use classification was determined at baseline by the drug for which the subject was receiving treatment. Such classification of primary drug use was found to present valid information about drug use patterns over time (Brecht et al., 2008). In the current study, we analyzed participants' drug use histories from their first use of the primary drug. We excluded observations (15.5%) during incarceration because drug use information was not available for all studies during these periods.

Use of these data for the current analysis was reviewed and approved by the University of California Los Angeles Institutional Review Board.

Instruments/measures

All four studies collected information using the NHI, which was adapted from instruments designed by Nurco, Bonito, Lerner, and Balter (1975) and has been used with various drug-using populations. It was designed to collect retrospective longitudinal quantitative data on drug use and related behaviors. The instrument consists of "static" and "dynamic" forms that permit the capture of longitudinal, sequential data on drug use, employment, criminal involvement, treatment, and other behaviors over the life course of research participants (McGlothlin, Anglin, & Wilson, 1977). Using an illustrated time-line, the interviewee notes major life events and then identifies time periods associated with specific behaviors, with periods delineated by changes in behavior. These reported data are translated to longitudinal data of behaviors for each month. The NHI has been shown to have generally high reliability; correlation coefficients of inter-variable relationships, based on 46 variables measured at two interviews 10 years apart, ranged as high as

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