Characterizing longitudinal health state transitions among heroin, cocaine, and methamphetamine users

B. Nosyk [a,b,c], L. Li [c], E. Evans [c], D. Huang [c], J. Min [a], T. Kerr [a,d], M.L. Brecht [c], Y.I. Hser [c,*]

[a] BC Centre for Excellence in HIV/AIDS, Vancouver, British Columbia V6Z 2C7, Canada
[b] Faculty of Health Sciences, Simon Fraser University, Burnaby, British Columbia V5A 1S6, Canada
[c] UCLA Integrated Substance Abuse Programs, Los Angeles, CA 90025, USA
[d] Division of AIDS, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia V5Z 1M9, Canada

A R T I C L E   I N F O

A B S T R A C T

Aims: Characterize longitudinal patterns of drug use careers and identify determinants of drug use frequency across cohorts of primary heroin, methamphetamine (MA) and cocaine users.
Design: Pooled analysis of prospective cohort studies.
Settings: Illicit drug users recruited from community, criminal justice and drug treatment settings in California, USA.
Participants: We used longitudinal data on from five observational cohort studies featuring primary users of heroin ($N = 629$), cocaine ($N = 694$) and methamphetamine ($N = 474$). The mean duration of follow-up was 20.9 years.
Measurements: Monthly longitudinal data was arranged according to five health states (incarceration, drug treatment, abstinence, non-daily and daily use). We fitted proportional hazards (PH) frailty models to determine independent differences in successive episode durations. We then executed multi-state Markov (MSM) models to estimate probabilities of transitioning between health states, and the determinants of these transitions.
Findings: Across primary drug use types, PH frailty models demonstrated durations of daily use diminished in successive episodes over time. MSM models revealed primary stimulant users had more erratic longitudinal patterns of drug use, transitioning more rapidly between periods of treatment, abstinence, non-daily and daily use. MA users exhibited relatively longer durations of high-frequency use. Criminal engagement had a destabilizing effect on health state durations across drug types. Longer incarceration histories were associated with delayed transitions toward cessation.
Conclusions: PH frailty and MSM modeling techniques provided complementary information on longitudinal patterns of drug abuse. This information can inform clinical practice and policy, and otherwise be used in health economic simulation models, designed to inform resource allocation decisions.

Published by Elsevier Ireland Ltd.

1. Introduction

Drug dependence has been characterized as a chronic relapsing disorder (McLellan, 2002; McLellan et al., 2000). Longitudinal studies have characterized drug users as following a recurrent pattern of frequent use, treatment, abstinence and relapse that are of varying duration and acuity (Brecht et al., 2008; Boeri et al., 2011; Dennis et al., 2005; Galai et al., 2003; Genberg et al., 2011; Grella and Lovinger, 2011; Hser et al., 2008a,b; Juon et al., 2011; Scott et al., 2005). Few opioid users are able to abstain from illicit drug use for sustained periods (Bell et al., 2006; Bovasso and Cacciola, 2003; Dobler-Mikola et al., 2005; Galai et al., 2003; Termorshuizen et al., 2005a,b). Instead, switching between periods of treatment and relapse is evident, with relapse typically occurring within five or fewer years of drug use cessation (Termorshuizen et al., 2005a,b).

Trajectories of drug use progression and outcome vary by primary drug of abuse. Prior research has revealed that episodes of high frequency use and incarceration occur more frequently among users of heroin and methamphetamine than cocaine, and patterns of persistent high frequency use occur more frequently for heroin use relative to cocaine or methamphetamine (MA) use (Hser et al., 2008a,b). These prior longitudinal analyses used finite mixture

* Corresponding author at: UCLA Integrated Substance Abuse Programs, 11075 Santa Monica Boulevard, Suite 200, Los Angeles, CA 90025, USA.
Tel.: +1 310 267 5388; fax: +1 310 473 7885.
E-mail address: yhser@ucla.edu (Y.I. Hser).

Table 1
Description of prospective cohort studies from which the study populations were drawn.

Project name	Population	% male	Mean age (SD) at baseline	Race/ethnicity	Primary drug type	Time-points (years of data collection)	Sample size used for this analysis
Natural History of Narcotics Addiction – 33 Year Follow-Up of Heroin Users (CAP)	Male opioid users treated by the California Civil Addict Program (CAP)	100	25.4 (5.8)	36.5% White; 55.6% Hispanic; 7.9% African American	Heroin	Baseline (1964) 12 years (1974) 25 years (1986) 35 years (1997)	472
A 12 Year Follow Up of a Cocaine Dependent Sample (CTE)	Male military veterans treated for cocaine dependence	100	35.0 (6.4)	24.7% White; 6.9% Hispanic; 67.5% African American; <1% Asian/other	Cocaine	Baseline (1988–1989) 1 year (1989–1990) 2 years (1990–1991) 12 years (2002–2003)	319
Methamphetamine Abuse: Natural History, Treatment Effect (Meth)	Methamphetamine users recruited from drug treatment and non-drug treatment settings	57	32.6	47.1% White; 29.7% Hispanic; 16.6% African American; 6.6% Asian/other	Methamphetamine	Baseline (1995–1997) 3 years (1998–1999) 5.5 years (1999–2002)	350
Drug Treatment Process (TXPR)	Drug users recruited from drug treatment settings in Los Angeles County	46	35.7 (9.6)	41.4% White; 18.5% Hispanic; 32.3% African American; 7.9% Asian/other	Heroin, cocaine, methamphetamine	Baseline (1995) 1 year (1996)	391
Treatment Utilization and Effectiveness Project (TUE)	Drug users, respectively, recruited from drug treatment and non-drug treatment settings in Los Angeles County	65	32.2 (8.9)	19.4% White; 25.6% Hispanic; 51.8% African American; 3.2% Asian/other	Heroin, cocaine, methamphetamine	Baseline (1993) 1 year (1994) 2 years (1995) 3 years (1996)	265

modeling to provide qualitative descriptions of latent trajectories of drug use; focused on periods in which diseases have been symptomatic; or analyzed the time to failure (adverse event, death) from drug treatment initiation, without considering the order and duration of preceding events. Given the inherent limitations of these types of analyses, the dynamic sequences of transitions between health states and their durations, particularly in light of prior events, remain unclear. Few studies have considered the overall dynamic pattern of events as they unfold over an individual's lifetime (Nosyk et al., 2009, 2013; Termorshuizen et al., 2005a,b). A more nuanced understanding of the longitudinal patterns of drug abuse afforded by emerging statistical methods can help inform both policy and clinical practice for chronic drug users.

According to international guidelines and evidence-based standards (Sculpher et al., 2006; Weinstein et al., 2003), health economic evaluations in substance abuse have estimated costs and health outcomes over an extended duration to reflect continued availability and long-term or recurrent use of drug treatment (Nosyk et al., 2012; Zaric et al., 2000; Zarkin et al., 2005). A key input for these models is an empirical basis on the dynamics of transitions from one health state to another. Estimates can be used to develop simulation models that can ultimately provide a sound basis for resource allocation decisions.

Our objectives are to identify, by primary drug type (heroin, methamphetamine (MA), and cocaine), the probability and determinants of transitions between successive durations of drug use, treatment, and incarceration in the process toward drug use cessation. We draw upon a recurrent events framework and apply two complementary forms of analysis, Proportional Hazards (PH) frailty modeling and multi-state Markov (MSM) modeling. MSM modeling can capture inherent competing risks, however this framework cannot easily incorporate patient histories. For instance, accounting for differences in durations of successive episodes of a given health state requires explicit modeling of each successive entry into the health state (i.e., treatment$_{episode\ 1}$, treatment$_{episode\ 2}$, ..., treatment$_{episode\ N}$), with the resulting high level of dimensionality making estimation infeasible. PH frailty modeling, on the other hand, can reveal differences in durations of successive episodes

and can handle time-dependency, but it cannot adequately characterize the competing risks of transitioning to multiple different states. Contrasting these methodologies can provide complementary insights into longitudinal drug use careers and, subsequently, yield a better understanding of how these methodological strengths and limitations impact simulation modeling of disease processes.

2. Methods

2.1. Study population

This analysis employed data on adult drug users combined from non-overlapping samples from five studies that collected longitudinal information using the Natural History Interview (described below and in Table 1). All studies were conducted in California. Following our prior work with this sample (Brecht et al., 2008; Evans et al., 2013; Hser et al., 2008a,b), we selected from each study those subjects who reported a primary drug problem of heroin, cocaine, or methamphetamine use. Projects included: (1) 33-year heroin follow-up study (Hser et al., 2001); cocaine treatment evaluation (Hser et al., 2006), methamphetamine natural history study (Brecht et al., 2004), treatment process study (Hser et al., 2004), and treatment utilization and effectiveness study (Hser et al., 2003). Studies included subjects recruited from drug treatment and non-drug treatment (e.g., emergency rooms, sexually transmitted disease clinics, jails) settings. Written informed consent was obtained. Use of these data for the current analysis was reviewed and approved by the University of California Los Angeles Institutional Review Board.

2.2. Study design

The Natural History Interview (NHI), from which the variables for this analysis were derived, was used in all five studies. The NHI was adapted from instruments designed by Nurco et al. (1975) and has been used with various drug-abusing populations. The NHI 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 et al., 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 0.86 and 0.90 (Anglin et al., 1993; Chou et al., 1996; Hser et al., 1992). A comparison of drug use obtained using Addiction Severity Index