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# Longitudinal predictors of injection cessation and subsequent relapse among a cohort of injection drug users in Baltimore, MD, 1988–2000

Nina G. Shah<sup>a,\*</sup>, Noya Galai<sup>b</sup>, David D. Celentano<sup>b</sup>, David Vlahov<sup>c</sup>, Steffanie A. Strathdee<sup>d</sup>

<sup>a</sup> Epidemiology and Response Division, New Mexico Department of Health, 1190 St. Francis Drive, P.O. Box 26110, Santa Fe, NM 87502-6110, USA b Department of Epidemiology, Bloomberg School of Public Health, The Johns Hopkins University, 615 North Wolfe Street, Baltimore, MD 21205, USA

Received 25 May 2005; received in revised form 3 November 2005; accepted 7 November 2005

#### **Abstract**

*Objective:* To determine predictors of injection drug use cessation and subsequent relapse among a cohort of injection drug users (IDUs). *Methods:* IDUs in Baltimore, MD were recruited through community outreach in 1988–1989. Among IDUs with at least three follow-up visits, parametric survival models for time to injection cessation (≥6 months) and subsequent relapse were constructed.

Results: Of 1327 IDUs, 94.8% were African American, 77.2% were male, median age was 34 years, and 37.7% were HIV-infected. Among 936 (70.5%) subjects who ceased injection, median time from baseline to cessation was 4.0 years. Three-quarters subsequently resumed injection drug use, among whom median time to relapse was 1.0 year. Factors independently associated with a shorter time to cessation were: age <30 years, stable housing, HIV seropositivity, methadone maintenance treatment, detoxification, abstinence from cigarettes and alcohol, injecting less than daily, not injecting heroin and cocaine together, and not having an IDU sex partner. Factors independently associated with shorter time to injection relapse were male gender, homelessness, HIV seropositivity, use of alcohol, cigarettes, non-injection cocaine, sexual abstinence and having a longer time to the first cessation.

Conclusions: This study provides strong support for targeting cessation efforts among young IDUs and severely dependent, unstably housed, and HIV-infected individuals.

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Keywords: Injection drug use; Cessation; Relapse; Methadone maintenance; HIV infection; Homelessness

#### 1. Introduction

Injection drug use is associated with considerable social, economic and medical consequences. Drug-related societal and economic costs are attributable to losses in productivity due to drug-related morbidity, premature mortality and crime (Harwood et al., 1999). Injection drug users (IDUs) experience increased risk of developing endocarditis, cellulitis and abscesses, and acquiring blood borne infections such as human immunodeficiency virus (HIV) and hepatitis C (HCV) through needle sharing. In Baltimore, MD, a prospective study of IDUs found that within 1 year of initiating injection the prevalence

of HIV, HBV and HCV was 14%, 50% and 65%, respectively (Garfein et al., 1996).

Although several studies have shown that IDUs are capable of reducing their frequency of needle sharing, in settings where HIV infection is prevalent, low levels of risk behaviors can give rise to HIV incidence rates as high as 3–4% per year (van Ameijden and Coutinho, 1998). These observations underscore the need to consider strategies to encourage cessation of injection as the primary goal of harm reduction a major public health priority (Langendam et al., 2000; Stimson et al., 1996).

For opioid-dependent persons, opiate agonist therapies such as methadone maintenance (National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction, 1998; van Ameijden and Coutinho, 2001; Sullivan et al., 2005), buprenorphine (Raisch et al., 2002) and heroin-assisted treat-

<sup>&</sup>lt;sup>c</sup> Center for Urban Epidemiologic Studies, New York Academy of Medicine, 1216 Fifth Avenue, New York, NY 10029, USA

<sup>&</sup>lt;sup>d</sup> University of California San Diego School of Medicine, Division of International Health and Cross Cultural Medicine, 9500 Gilman Drive, Mailstop 0622, San Diego, CA 92093, USA

<sup>\*</sup> Corresponding author. Tel.: +1 505 476 3607; fax: +1 505 827 0013. E-mail address: nina.shah@state.nm.us (N.G. Shah).

ment (Rehm et al., 2001) have been found to significantly reduce drug use. However, in countries such as the US, drug users experience considerable barriers accessing drug treatment, including the lack of third party reimbursement and lengthy waiting times for limited existing drug treatment slots (Shah et al., 2000; Lewis, 1999). Among populations of IDUs in North America, only 18–36% are estimated to be receiving some form of drug treatment at any given time (Joseph et al., 2000).

Relapse is a major characteristic of drug dependence and remains a primary problem in treating drug abuse. Individuals need to be engaged in drug treatment for an adequate length of time in order to reap the greatest benefits (Goldstein et al., 2000; Hartel and Schoenbaum, 1998). However, half of those admitted to methadone maintenance treatment (MMT) programs in the US leave within a year for a variety of reasons (Simpson et al., 1997). Generally, drug users who are retained in MMT for only a short time experience higher relapse rates than those who spend a longer time engaged in treatment (Simpson, 1981; Toumbourou et al., 1998). Many IDUs require multiple attempts at drug treatment before becoming drug-free (Raisch et al., 2002; Bammer et al., 2000).

The relapsing and remitting nature of drug dependence is a major issue in the study of the natural history of drug use (Galai et al., 2003). Few empirical investigations have described predictors of time to injection cessation and relapse to injection among well-characterized samples of out-of-treatment IDUs. In the present study, we sought to examine predictors of time to first injection cessation and, given cessation, to identify predictors associated with time to subsequent relapse to injection. These findings may help identify appropriate interventions and support systems to reduce the negative health and social consequences of injection drug use.

# 2. Methods

# 2.1. Population

The rationale, design and methods of the AIDS link to intravenous experiences (ALIVE) cohort study have been described previously (Vlahov et al., 1991; Anthony et al., 1991). Briefly, subjects were eligible to participate if they were at least 18 years old, were AIDS-free at enrollment and had injected illicit drugs within the past 10 years. Over 80% of subjects reported having been recruited by another study participant or friend, rather than referral by a drug treatment program, public health program or trained street outreach worker. A total of 2946 IDUs were enrolled into the ALIVE Study, though the present study was restricted to 1327 participants who were active injectors at baseline and had at least three follow-up visits, to permit study of factors associated with injection cessation and subsequent relapse to injection drug use. That is, a minimum of three visits after enrollment was needed for the participant to be "at risk" for one cessation and one relapse. Recruitment began in 1988-1989 and follow-up for this analysis continued through December 2000. Study visits were scheduled every 6 months with ongoing effort to minimize loss to follow-up using mail and phone reminders and street tracking.

### 2.2. Data collection

At study entry and semi-annually thereafter, participants underwent venipuncture for HIV antibody testing and completed an interviewer-administered questionnaire on sociode-mographic characteristics, risk behaviors for HIV infection, health status indicators, and health service utilization. Sociode-mographic variables of interest included gender, age, ethnicity, employment, education, recent homelessness and history of incarceration. Drug use and sexual risk behaviors referred to the previous 6 months and included frequency of injection, needle sharing, overdose, shooting gallery attendance, non-injection drug use, number and type of sexual partners, trading sex for money or drugs, and unprotected sex. Data on hospital admissions, drug treatment and HIV-related symptoms were also collected at each assessment.

The baseline questionnaire had a number of unique questions regarding the initiation of injection drug use, including age of first injection and how long it took to reach the highest frequency (peak) of use. Based on this information, the variable "time to peak drug use" was created. The outcome of injection cessation was defined as the first self-report of not having injected drugs within the prior 6 months. Relapse was defined as the first self-report of injection following cessation. Note that the exact time of relapse within the prior 6-month interval was not known and thus the event time for analysis was the date of the first report of relapse to injection. Thus, the variability for injection cessation was within a window of 6–12 months, and the time window for relapse was 1 day to less than 6 months.

## 2.3. Statistical analyses

Characteristics of the study sample were described using medians and inter-quartile range for continuous variables and frequencies for categorical variables. The population included in the present analysis was compared to those excluded by simple  $\chi^2$ -tests for categorical variables and t-tests or non-parametric tests for continuous variables.

Two separate survival analyses were performed: time from enrollment (where all participants reported injecting) to first cessation of drug injection was assessed; then, time from cessation to first relapse to injection was assessed among those who reported cessation and had at least one visit following cessation.

Factors affecting time to outcome (cessation or relapse) were evaluated using parametric survival models, assuming a log-normal distribution (accelerated failure time) (Hosmer and Lemeshow, 1999). In the accelerated failure time model, the effect of a covariate is expressed as either accelerating (shortening) or decelerating (lengthening) time to the event of interest. The log-normal survival models assume that the hazard function has a log-normal shape with two parameters (mean and dispersion) which are estimated from the data. The use of parametric survival models allows a convenient calculation of the predicted survival curve for any specific combination of explanatory variables as well as the underlying hazard. Further, covariate effects are shown as time ratios (TR), rather than hazard ratios, and hence have an interpretation on the time scale. For example,

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