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Factors associated with methadone maintenance therapy discontinuation among people who inject drugs

Ada Lo[a], Thomas Kerr[a,b], Kanna Hayashi[a,c], M.-J. Milloy[a,b], Ekaterina Nosova[a], Yang Liu[a], Nadia Fairbairn[a,b,*]

[a] British Columbia Centre on Substance Use, British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada
[b] Department of Medicine, University of British Columbia, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada
[c] Faculty of Health Sciences, Simon Fraser University, 8888 University Drive, Burnaby, BC V5A 1S6, Canada

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ABSTRACT

Background: Methadone maintenance therapy (MMT) continues to be a key treatment for opioid use disorder, although premature discontinuation of MMT can increase risk for overdose and other severe harms. We examined sociodemographic characteristics, substance use patterns and social-structural exposures associated with MMT discontinuation among a cohort of people who use drugs (PWUD) in Vancouver, Canada.

Methods: Data were derived from VIDUS and ACCESS, prospective cohorts of PWUD in Vancouver, Canada. The outcome of interest was self-reported discontinuation of MMT within the last six months. Multivariable Generalized Estimating Equations (GEE) were conducted to identify factors independently associated with MMT discontinuation.

Results: Between 2005 and 2015, 1301 PWUD who had accessed MMT were recruited, among whom 288 (22.1%) discontinued MMT at least once during the study period. In multivariable GEE analyses, homelessness (Adjusted Odds Ratio [AOR] = 1.46, 95% Confidence Interval [95% CI]: 1.09–1.95), daily heroin injection (AOR = 5.17, 95% CI: 3.82–6.99), daily prescription opioid use (injection or non-injection) (AOR = 2.18, 95% CI: 1.30–3.67), recent incarceration (AOR = 1.46, 95% CI: 1.01–2.12), and not being on any form of income assistance (AOR = 2.14, 95% CI: 1.33–3.46) were each independently positively associated with MMT discontinuation. Participants with more study visits on methadone (> 50% vs. ≤50% of visits) (AOR = 0.63, 95% CI: 0.47–0.85) and those with higher methadone dose (> 100 mg vs. < 60 mg per day) (AOR = 0.44, 95% CI: 0.31–0.62) were less likely to discontinue MMT.

Discussion and conclusions: Discontinuation of MMT in this urban setting was associated with recent homelessness and incarceration, not accessing social income assistance, as well as daily prescription opioid use and daily heroin injection drug use. These findings underscore a need to reduce potential barriers to MMT retention by providing access to stable housing and preventing treatment interruptions during transitions between community and custodial settings.

1. Introduction

Opioid misuse and addiction are associated with multiple severe health and social harms, including fatal overdose, HIV and hepatitis C infection, and criminal justice involvement (Degenhardt et al., 2017; Rudd, Seth, David, & Scholl, 2016). Opioid agonist treatment, specifically methadone maintenance therapy (MMT), is a cornerstone of treatment for opioid use disorder (OUD) (Stein et al., 2012; World Health Organization, 2015). MMT has been shown to reduce injection drug use, all-cause and overdose mortality, and improve social functioning and quality of life (Salsitz & Wiegand, 2015; Simoens, 2005). Furthermore, MMT supports antiretroviral therapy adherence among HIV-infected individuals (Bach et al., 2015) and has consistently been shown to lower the risk of blood-borne pathogen transmission (Vlahov, Robertson, & Strathdee, 2010). This large body of evidence for MMT has led to its inclusion on the World Health Organization's list of essential medicines since 2005 (WHO Model List of Essential Medicines, 2017).

It is well demonstrated that longer-term (i.e. six months or greater) retention on MMT helps prevent relapse to illicit opioid use (Sees et al.,

* Corresponding author at: B.C. Centre on Substance Use, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, B.C. V6Z 1Y6, Canada.
E-mail address: nfairbairn@cfenet.ubc.ca (N. Fairbairn).

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2000). In addition, it has been shown that individuals who discontinue MMT are at increased risk for fatal overdose (Davoli et al., 2007) and all-cause mortality (Cornish, Macleod, Strang, Vickerman, & Hickman, 2010; Cousins et al., 2016). However, it is estimated that between 46 and 65% of patients who initiate MMT discontinue within the first year and relapse to opioid use (Magura, Nwakeze, & Demsky, 1998; Nosyk, Marsh, Sun, Schechter, & Anis, 2010; Reisinger et al., 2009). Retention on MMT, and prevention of harms associated with relapse to illicit opioid use, therefore remain ongoing challenges.

Though retention on MMT is a critical component of successful treatment for opioid use disorder, factors that predict MMT discontinuation have been less well studied. To help inform strategies that may support MMT retention, we sought to examine the socio-demographic characteristics, substance use patterns, and social-structural exposures associated with MMT discontinuation among people who use drugs (PWUD) in Vancouver, Canada.

2. Material and methods

2.1. Study participants

Data for this study were collected from two prospective cohorts of PWUD in Vancouver, Canada, the Vancouver Injection Drug Users Study (VIDUS) and the AIDS Care Cohort to Evaluate Exposure to Survival Services (ACCESS). These cohorts have been described previously in detail (Bach et al., 2015; Strathdee, 1998; Wood, 2008). In brief, participants in both cohorts have been recruited since May 1996 through street outreach in the Downtown Eastside, an area with a high prevalence of substance use in Vancouver. VIDUS is a cohort of HIV-negative PWUD who are eligible for participation in the study if they are at least 18 years old and have injected illicit drugs at least once in the past month prior to study enrollment. ACCESS is a study of HIV-positive adults who have used illicit drugs in the month prior to study enrollment. VIDUS participants who seroconvert to be HIV-positive are transferred to the ACCESS study.

Both studies collect data and conduct follow-ups in a harmonized manner to facilitate combined analyses. At baseline and every six months thereafter, participants answer an interviewer- and nurse-administered questionnaire pertaining to socio-demographic information, sex- and drug-related risk behaviors, housing conditions, and experiences with the healthcare and criminal justice systems. Participants provide blood samples for serologic HIV testing (or HIV disease monitoring if positive) and HCV testing at each visit. Participants receive $30 CAD as remuneration at each visit and are offered referrals to addiction treatment and other health services. The VIDUS and ACCESS studies have annual approval from the Providence Health Care Research/University of British Columbia Research Ethics Board. Data for these analyses were collected from December 2005 to May 2015.

Participants who reported ever being on MMT during the last six months at any assessment were included in the study. We compared factors associated with being a “MMT continuer” versus a “MMT discontinuer”. “MMT continuers” were defined as those who reported currently being on MMT at the time of study assessment. “MMT discontinuers” were defined as those who reported being on MMT in the last study assessment but reported not currently being on MMT at the time of study assessment. Of note, some participants may have discontinued MMT more than once during the study period. Baseline characteristics of the “MMT discontinuers” were analyzed only for those who reported discontinuing MMT in the last 6 months at the time of baseline study assessment.

2.2. Variables of interest

The primary endpoint in this analysis was self-reported MMT discontinuation in the last six months (yes vs. no) on the administered questionnaire, defined as reporting accessing methadone at one study visit and reporting not being on methadone at a subsequent study visit. Sociodemographic variables included age, sex (male vs. female), ethnicity (White vs. other race or ethnicity), stable relationship status, defined as being legally married, common-law, or having a regular partner (stable vs. other), education (high school or greater vs. less than high school), and HIV status (HIV-positive vs. HIV-negative). Social-structural risk factors included recent incarceration (yes vs. no), homelessness (yes vs. no), and not accessing government income assistance (yes vs. no). Drug use variables considered included crack cocaine smoking (≥daily vs. < daily), heroin injection (≥daily vs. < daily), cocaine injection (≥daily vs. < daily), prescription opioid injection or non-injection use (≥daily vs. < daily), methamphetamine use (≥daily vs. < daily), binge alcohol use (yes vs. no), and binge injection use (yes vs. no). Factors associated with MMT were also considered and included length of time on methadone, defined as the proportion of consecutive follow-ups on MMT relative to the total number of participant follow-ups (> 50% vs. ≤50%), and MMT dose at most recent follow-up prior to MMT discontinuation (or most recent study visit if no MMT discontinuation was reported) (> 60 to ≤100 mg vs. ≤60 mg and > 100 mg vs. ≤60 mg). Records where methadone dosage was missing were removed from analyses. All behaviors referred to activities in the 6 months prior to interview.

2.3. Statistical methods

First, we examined participants' baseline characteristics, stratified by participants who discontinued MMT. For categorical variables, we used Pearson's χ^2 test, and for continuous variables we used Mann-Whitney (Wilcoxon) rank sum test. Second, we examined factors associated with MMT discontinuation in the past six months during study follow-up using Generalized Estimating Equations (GEE) with a logit link function and an exchangeable correlation structure. These methods provide standard errors adjusted by multiple follow-ups per participant using an exchangeable correlation structure for the analysis of correlated data. Therefore, data from every participant follow-up visit were considered in these analyses. As a first step, we used bivariate GEE analyses to determine factors associated with MMT discontinuation. All variables with $p < 0.1$ in bivariate analyses were then entered in the multivariable logistic GEE model. In sub-analyses, among those who reported having discontinued methadone at follow-up, we explored self-reported reasons for methadone discontinuation.

All statistical analyses were performed using R version 3.2.4 (R Foundation for Statistical Computing, Vienna, Austria, 2016. All reported p-values are two-sided and considered significant at $p < 0.05$.

3. Results

From December 2005 to May 2015, 1301 VIDUS and ACCESS participants who accessed MMT were included in the analyses. In total, the study sample consisted of 1301 participants who contributed 9809 observations, of which 121 (1.2%) observations did not include methadone dose and were removed from analysis, leaving a total of 9688 observations. The median number of follow-up assessments was 7 (Interquartile Range [IQR] = 2–12). Among the study sample, 288 (22.1%) participants ever discontinued MMT and 49 (3.8%) discontinued MMT more than once during the study period.

Baseline characteristics of the study sample stratified by MMT discontinuation are presented in Table 1. At study entry, among this sample, 106 (8.1%) participants had discontinued MMT in the past six months. Of those who had discontinued MMT, the median age at baseline was 39 years (IQR = 34–45), 64 (60%) participants were male, and 64 (60%) participants were White.

Bivariate and multivariable GEE analyses of factors associated with MMT discontinuation are presented in Table 2. In bivariable analyses, MMT discontinuation was positively associated with recent homelessness (OR = 2.43, 95% CI: 1.87–3.15), binge alcohol use