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Methadone use among HIV-positive injection drug users in a Canadian setting

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Abstract

We examined methadone maintenance therapy (MMT) use among HIV-positive injection drug users (IDU) in Vancouver. Among 353 participants, 199 (56.3%) were on MMT at baseline, and 48 initiated MMT during follow-up. Female gender (adjusted odds ratio [AOR] = 1.73, 95% CI: 1.14 – 2.62) and antiretroviral therapy use (AOR = 2.04, 95% CI: 1.46 – 2.86) were positively associated with MMT use, while frequent heroin injection (AOR = 0.34, 95% CI: 0.23–0.50), public injection (AOR = 0.76, 95% CI: 0.59 – 0.97), syringe borrowing (AOR = 0.54, 95% CI: 0.32 – 0.90), and non-fatal overdose (AOR = 0.58, 95% CI: 0.36 – 0.92) were negatively associated with MMT use. The rate of discontinuation of MMT was 12.46 (95% CI: 8.28 – 18.00) per 100 person years. Frequent heroin use (adjusted hazards ratio = 4.49, 95%CI: 1.81 – 11.13) was positively associated with subsequent discontinuation of MMT. These findings demonstrate the benefits of MMT among HIV-positive IDU and the need to improve access to and retention in MMT.

Keywords

methadone; injection drug use; HIV

INTRODUCTION

Opiate addiction continues to be associated with many adverse health and social harms, including infectious disease transmission, fatal overdose, elevated health care costs, public disorder and crime (American Society of Addiction Medicine, 1994; Wall et al., 2000; Wood et al., 2005). Community-based addiction treatment programs continue to be commonly applied methods used to reduce the harms of opiate addiction (Wood et al., 2007). Methadone maintenance treatment (MMT) is among the most effective treatments for opiate dependence and has been successfully implemented in both developed and developing countries (Corsi, Kwiatkowski, & Booth, 2009; Davstad, Stenbacka, Leifman, & Romelsjo, 2009; Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003; Lawrinson et al., 2008). Methadone, a synthetic opiate agonist, has been shown to be effective in reducing

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withdrawal symptoms and the impulse to continue injecting opiates (Dole et al., 1969; Goldstein, 1991; Greenstein, Fudala, & O'Brien, 1997; Senay & Uchtenhagen, 1990).

In recent years, the benefits of MMT use among HIV-positive injection drug users (IDU) have received increasing interest. For example, MMT has been shown to increase access and adherence to antiretroviral drug treatment (ART) among IDU (Clarke, Keenan, Ryan, Barry, & Mulcahy, 2002; Spire, Lucas, & Carrieri, 2007). In a study involving IDU co-infected with HIV and hepatitis C who were receiving antiretroviral therapy, MMT was also associated with improved likelihood of virological suppression and CD4 cell count response (Palepu et al., 2006). These findings are consistent with a small number of other studies, most cross-sectional, demonstrating an impact of MMT on HIV-related outcomes (Spire, Lucas, & Carrieri, 2007; Roux et al., 2008).

A large body of literature exists examining the impact of MMT among IDU. However, there are few longitudinal investigations of MMT among HIV-positive IDU, and the vast majority of studies have been restricted to either samples of IDU in MMT or on ART. Consequently, the use of MMT within the broader community of HIV-positive IDU has not been well characterized. Therefore, we sought to longitudinally investigate MMT use among HIV-positive IDU participating in a community-recruited cohort in Vancouver, Canada.

METHODS

The AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS) is a prospective study of HIV-positive IDU based out of Vancouver, Canada. The ACCESS cohort was populated through snowball sampling and extensive street outreach methods in the city's Downtown Eastside. Individuals were eligible for ACCESS if they were aged 18 years or older, HIV-seropositive, had used injection drugs, and provided written informed consent. Evidence of recent injection drug use was confirmed via inspection of needle tracks. At baseline and at every 6-month follow-up, participants answer a standardized interviewer-administered questionnaire and provide blood samples for serologic analysis. In the present study, cohort participants were eligible if they reported heroin or MMT use at baseline or at any time during the study period spanning from December 2005 to May 2008.

The local setting is unique in that there is a province-wide centralized antiretroviral dispensation program and HIV/AIDS laboratory, which enables a complete prospective profile of all patient CD4 cell count determinations and plasma HIV-1 RNA levels, as well as a complete prospective profile of antiretroviral therapy use among cohort participants. This includes the specific antiretroviral agents prescribed, including dose, as well as a validated measure of patient adherence derived from prescription refill compliance. The universal healthcare system and centralized antiretroviral dispensary provides free HIV/AIDS care and antiretroviral therapy to all HIV-infected individuals in the province and enables the examination of HIV-related outcomes in a setting where financial barriers to health care and HIV treatment are largely eliminated. The study has been approved by the Providence Health Care/University of British Columbia Research Ethics Board. Plasma HIV-1 RNA was measured using the Roche Amplicor Monitor assay (Roche Molecular Systems, Mississauga, Canada).

The primary outcome of interest was self-reporting current enrollment in MMT. Explanatory variables of interest in our analyses included: age (above the median vs. below the median); gender (female vs. male); Aboriginal ethnicity (yes vs. no); residence in the Downtown Eastside (DTES), Vancouver's HIV epicenter (yes vs. no); homelessness (yes vs. no); frequent heroin injection (yes vs. no); frequent cocaine injection (yes vs. no); frequent methamphetamine use (yes vs. no); frequent crack use (yes vs. no); public injection (yes vs.

no); syringe borrowing (yes vs. no); syringe lending (yes vs. no); sex work involvement (yes vs. no); recent non-fatal overdose (yes vs. no); recent incarceration (yes vs. no); CD4 count (> 200 copies/uL vs. < 200 copies/uL); and being on ART (yes vs. no). All behavioral variables referred to the 6-month period prior to the interview. If more than one CD4 count sample had been taken within the last 6 months, then the mean of those samples would be used. If a sample had not been taken within the last 6 months, then the first available sample prior to the interview was used.

We began by analyzing univariate relationships between the potential explanatory variables and MMT use at baseline using a Pearson's chi-square. Next, we identified factors associated with MMT use during follow-up. Here, since serial measures were available for each subject, we used generalized estimating equations (GEE) for binary outcomes with logit link for the analysis of correlated data to determine which factors were independently associated with using MMT in the prior 6 months throughout the 24-month follow-up period. These methods provided standard errors adjusted by multiple observations per person using an exchangeable correlation structure. Therefore, data from every participant follow-up visit was considered in this analysis. For instance, an individual participant may have gone off and on MMT during follow-up, and this approach serves to examine behaviors and characteristics that correlated with times on versus off MMT within individuals and between individuals. This approach has been used successfully in previous studies examining correlates of drug treatment access in prospective cohort studies of IDU (Kerr et al., 2007; Shah et al., 2000a). We fitted a multivariate GEE model using an *a priori* defined model building protocol to include all variables that were statistically significant at $p < 0.05$ in univariate analyses. As a subanalysis, to examine predictors of time to discontinuation of MMT, we conducted univariate and multivariate Cox regression analyses that incorporated the same set of independent variables considered in our GEE analyses focused on MMT use. However, we examined potential predictor variables from the follow-up period occurring 6 months prior to a reported discontinuation of MMT as a means of identifying predictors (rather than consequences) of MMT discontinuation. For these analyses, we also considered methadone dose (per 100 ml) as a potential predictor of MMT discontinuation. We fit our multivariate Cox regression model using an *a priori* defined model building protocol to include all variables that were statistically significant at $p < 0.05$ in univariate analyses. All statistical procedures were performed using SAS software (SAS, Cary, NC, USA). All p-values are two-sided.

RESULTS

Of the 353 IDU eligible for the present analysis, 138 (39.1%) were female and 131 (37.1%) reported Aboriginal ancestry. The median age at baseline was 40.8 years. At baseline, 199 (56.4%) participants were enrolled in MMT and an additional 49 participants initiated MMT during follow-up. Of the individuals who ever used MMT at some point during follow-up, the rate of discontinuation of MMT was 12.46 (95%CI: 8.28 – 18.00) per 100 person years.

As shown in Table 1, baseline factors positively associated with MMT use included age above the median (odds ratio [OR] = 1.55, 95% confidence interval [CI]: 1.01–2.36) and being on ART (OR = 3.57 95% CI: 2.23–5.72), while homelessness (OR = 0.29, 95% CI: 0.17–0.49), frequent heroin injection (OR = 0.17, 95% CI: 0.10–0.28), public injection (OR = 0.38, 95% CI: 0.25–0.59), syringe borrowing (OR= 0.35, 95% CI: 0.17–0.72), non-fatal overdose (OR = 0.47, 95% CI: 0.23–0.97) were negatively associated with MMT use.

The results from the univariate GEE analyses are displayed in Table 2. As shown here, MMT use was positively associated with being on ART (OR = 2.11 95% CI: 1.55–2.88), while frequent heroin injection (OR = 0.33, 95% CI: 0.23–0.46), public injection (OR =

0.61, 95% CI: 0.48–0.76), syringe borrowing (OR = 0.56, 95% CI: 0.37–0.85), non-fatal overdose (OR = 0.58, 95% CI: 0.40–0.86) were negatively associated with being on MMT.

In the multivariate GEE analysis, also shown in Table 2, factors independently and positively associated with accessing MMT included female gender (adjusted odds ratio [AOR] = 1.73, 95% CI: 1.14–2.62) and being on ART (AOR = 2.04, 95% CI: 1.46–2.86). Factors independently and negatively associated with MMT use included: frequent heroin injection (AOR = 0.34, 95% CI: 0.23–0.50); public injection (AOR = 0.76, 95% CI: 0.59–0.97); syringe borrowing (AOR = 0.54, 95% CI: 0.32–0.90); non-fatal overdose (AOR = 0.58, 95% CI: 0.36–0.92). In subanalyses using univariate Cox regression, frequent heroin use was associated with MMT discontinuation (Hazard Ratio [HR] = 6.07, 95%CI: 2.81 – 13.01). Factors negatively associated with MMT discontinuation in univariate analyses included age above the median (HR = 1.55, 95% CI: 1.01 – 2.36), frequent heroin injection (HR = 6.07, 95%CI: 2.81 – 13.10), and methadone dose per 100ml (HR = 0.34, 95%CI: 0.14 – 0.79). In multivariate Cox regression analyses, frequent heroin use (adjusted hazards ratio [AHR] = 4.49, 95%CI: 1.81 – 11.13) was the only factor that remained associated with time to MMT discontinuation.

DISCUSSION

In the present analysis, MMT had been accessed by approximately 56% of opioid-using HIV-positive IDU at baseline, as well as another 13% during follow-up, and was independently associated with a reduction in a range of health-related harms, including reduced heroin injection, public injection, syringe borrowing, and non-fatal overdose. The rate of discontinuation of MMT was 12.46 (8.28 – 18.00) per 100 person years.

The results have indicated a moderate amount of MMT use among HIV-positive IDU; however, the rate of discontinuation of MMT is of concern given that provincial guidelines in British Columbia favor long-term treatment (> 2 years) and given previous findings indicating better outcomes for individuals exposed to continuous treatment (Condelli & Dunteman, 1993; Kerr, Marsh, Li, Montaner, & Wood, 2005). In our analysis, individuals engaged in frequent heroin injection were more likely to subsequently discontinue MMT, and suggest that efforts should be made to promote retention in treatment among those at risk of premature discontinuation of MMT, including those engaging in higher intensity drug use behavior.

Female gender was a strong predictor of MMT use in this study, with our results suggesting that women are more than 1.5 times more likely than men to be accessing MMT. These findings are consistent with previous studies (Shah et al., 2000b; Wood et al., 2005) which have recognized that females are more likely to start MMT than males. However, further research is necessary to unpack the relationship between gender and MMT and identify ways of refining methods to attract male IDU to initiate MMT.

It is also of interest to note that no association existed between Aboriginal ethnicity and MMT. Indeed, previous studies examining addiction treatment, including MMT, have observed that Aboriginal IDU have lower rates of addiction treatment access (Craib et al., 2003; Wood et al., 2005; Wood et al., 2007; Wood et al., 2008). It appears that recent efforts to expand MMT access have resulted in an increased access to MMT among Aboriginal IDU (Marsh & Fair, 2006). Given the ongoing burden of HIV/AIDS among Aboriginal IDU (Wood et al., 2008), lower rates of ART access within this population (Wood et al., 2006), and the identified impacts of MMT use, these results are encouraging.

Non-fatal overdose, syringe borrowing, frequent heroin injection, and public injection were all negatively associated with MMT use. These findings are consistent with other studies

that illustrate how MMT use can protect against an array of drug-related risks and harms, including the risk for injection-related infections that arises from injecting within unhygienic environments (e.g., public alleyways) (Kerr et al., 2004). Indeed, HIV-positive IDU are believed to have a heightened susceptibility to bacterial infections due to compromised immunity and, again, these results are very encouraging (Palepu, 2001). Among participants eligible for ART, individuals on MMT were more than twice as likely to have accessed ART. These results are similar to other studies demonstrating higher rates of ART access and adherence among IDU on MMT (Roux et al., 2008; Lucas et al., 2007).

There are several limitations to this study. First, the study sample was not selected at random; this might limit the ability to generalize these findings to other groups of HIV-positive IDU. Also, the possibility of social desirability influencing responses to questions about some behaviors exist, which could potentially affect some variables (e.g., public injection) (Des Jarlais et al., 1999). However, we can think of no reason why differential reporting by MMT status would occur. Finally, accessing MMT was self-reported by all participants. However, the results from the study have generated strong relationships which are similar to results documented in past studies (Ball & Ross, 1991).

In summary, we observed a high rate of uptake of MMT among HIV-positive IDU in this study, although some discontinuation of MMT, predicted by more intensive heroin injection, was also observed. MMT use was associated with a reduced likelihood of frequent heroin injection, syringe borrowing, non-fatal overdose, and public injection. Further, MMT use was positively associated with access to ART. These findings provide further confirmation of the positive benefits of MMT, although efforts should seek to ensure higher rates of access to and continuation of MMT in this setting.

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Table 1

Baseline analyses of factors associated with MMT use among HIV-positive IDU (n = 353)

Characteristic	Yes n (%)(n = 199)	No n (%)(n = 154)	Odds Ratio (95% CI)	*p*-value
Age				
> median (40.8 years)	105 (53.0)	65 (42.2)	1.55 (1.01–2.36)	0.044
< median (40.8 years)	93 (47.0)	89 (57.8)		
Gender				
female	83 (41.7)	55 (35.7)	1.29 (0.83–1.99)	0.252
male	116 (58.3)	99 (64.3)		
Aboriginal ancestry				
yes	69 (34.7)	62 (40.3)	0.79 (0.51–1.22)	0.281
no	130 (65.3)	92 (59.7)		
DTES residence				
yes	138 (69.3)	113 (73.4)	0.82 (0.51–1.31)	0.408
no	61 (30.7)	41 (26.6)		
Homelessness				
yes	27 (13.6)	54 (35.1)	0.29 (0.17–0.49)	< 0.001
no	172 (86.4)	100 (64.9)		
Frequent heroin injection*				
yes	28 (14.1)	76 (49.4)	0.17 (0.10–0.28)	< 0.001
no	171 (85.9)	78 (50.6)		
Frequent cocaine injection*				
yes	20 (10.1)	23 (14.9)	0.64 (0.34–1.21)	0.164
no	179 (89.9)	131 (85.1)		
Frequent methamphetamine use*				
yes	4 (2.00)	8 (5.20)	0.37 (0.11–1.27)	0.102
no	195 (98.0)	146 (94.8)		
Frequent crack use*				
yes	90 (45.2)	81 (52.6)	0.74 (0.49–1.13)	0.169
no	109 (54.8)	73 (47.4)		
Public injection*				
yes	65 (32.7)	86 (55.8)	0.38 (0.25–0.59)	< 0.001
no	134 (67.3)	68 (44.2)		
Syringe borrowing*				
yes	12 (6.00)	24 (15.6)	0.35 (0.17–0.72)	0.003
no	187 (94.0)	130 (84.4)		
Syringe lending*				
yes	8 (4.00)	8 (5.20)	0.76 (0.28–2.08)	0.599
no	191 (96.0)	146 (94.8)		
Sex work involvement*				
yes	37 (18.6)	23 (14.9)	1.30 (0.74–2.30)	0.364

Characteristic	Yes n (%)(n = 199)	No n (%)(n = 154)	Odds Ratio (95% CI)	*p*-value
no	162 (81.4)	131 (85.1)		
Recent incarceration*				
yes	38 (19.1)	33 (21.4)	0.87 (0.51–1.46)	0.588
no	161 (80.9)	121 (78.6)		
Non-fatal overdose*				
yes	13 (6.50)	20 (13.0)	0.47 (0.23–0.97)	0.039
no	186 (93.5)	134 (87.0)		
CD4 count*				
> 200 copies/μL	53 (26.6)	33 (21.4)	1.33 (0.81–2.19)	0.259
≤ 200 copies/μL	146 (73.4)	121 (78.6)		
On ART*				
yes	119 (66.1)	47 (35.3)	3.57 (2.23–5.72)	< 0.001
no	61 (33.9)	86 (64.7)		

* Refers to the 6-month period prior to the interview

Table 2

Univariate and multivariate GEE analyses of factors associated with MMT use among HIV-positive IDU (n = 353)

	Unadjusted		Adjusted	
Characteristic	**Odds Ratio (95% CI)**	***p* - value**	**Odds Ratio (95% CI)**	***p* - value**
Age[*]				
(> median (40.8 years) vs. < median)	1.42 (1.00–2.01)	0.048	0.99 (0.68–1.46)	0.973
Gender[†]				
(female vs. male)	1.19 (0.82–1.76)	0.354	1.73 (1.14–2.62)	0.010
Aboriginal ethnicity[‡]				
(Aboriginal vs. other)	0.91 (0.62–1.33)	0.621	0.79 (0.52–1.20)	0.269
DTES residence				
(yes vs. no)	0.76 (0.57–1.04)	0.084		
Homelessness				
(yes vs. no)	0.74 (0.55–1.00)	0.051	0.79 (0.56–1.10)	0.164
Frequent heroin injection[*]				
(yes vs. no)	0.33 (0.23–0.46)	< 0.001	0.34 (0.23–0.50)	< 0.001
Frequent cocaine injection[*]				
(yes vs. no)	0.83 (0.57–1.20)	0.313	1.42 (0.92–2.21)	0.115
Frequent crack use[*]				
(yes vs. no)	0.85 (0.69–1.05)	0.122	1.10 (0.86–1.40)	0.463
Frequent methamphetamine use[*]				
(yes vs. no)	0.60 (0.29–1.24)	0.166		
Public injection[*]				
(yes vs. no)	0.61 (0.48–0.76)	< 0.001	0.76 (0.59–0.97)	0.031
Syringe borrowing[*]				
(yes vs. no)	0.56 (0.37–0.85)	0.006	0.54 (0.32–0.90)	0.019
Syringe lending[*]				
(yes vs. no)	0.69 (0.36–1.32)	0.259		
Sex work involvement[*]				
(yes vs. no)	1.15 (0.84–1.55)	0.383		
Recent incarceration[*]				
(yes vs. no)	0.97 (0.74–1.27)	0.383		
Non-fatal overdose[*]				
(yes vs. no)	0.58 (0.40–0.86)	0.006	0.58 (0.36–0.92)	0.021
CD4 count				
(> 200 copies/μL vs. ≤ 200 copies/μL)	1.26 (0.94–1.74)	0.126	1.21 (0.87–1.69)	0.260
On ART[*]				
(yes vs. no)	2.11 (1.55–2.88)	< 0.001	2.04 (1.46–2.86)	< 0.001

[*] Refers to the 6-month period prior to the interview