



Characteristics of adherence to methadone maintenance treatment over a 15-year period among homeless adults experiencing mental illness



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ABSTRACT

Background: Methadone maintenance treatment (MMT) has important protective effects related to reduced illicit opioid use, infectious disease transmission, and overdose mortality. Adherence to MMT has not been examined among homeless people. We measured MMT adherence and reported relevant characteristics among homeless adults experiencing mental illness in Vancouver, British Columbia, Canada.

Material and methods: Homeless adults living with mental illness who had received MMT prior to the baseline interview of the Vancouver At Home study ($n = 78$) were included in analyses. The medication possession ratio (MPR) was used to estimate MMT adherence from retrospective administrative pharmacy and public health insurance data collected across 15 years. Independent sample t tests and one-way ANOVA were used to test for significant differences in MMT MPR by participant characteristics.

Results: Mean MMT MPR was 0.47. A large proportion of participants reported blood-borne infectious disease, three or more chronic physical health conditions, and substance use. Being single and never married was associated with significantly lower MMT MPR (0.40 vs. 0.55, $p = 0.036$), while living with schizophrenia, bipolar disorder, or a mood disorder with psychotic features was associated with significantly higher MMT MPR (0.54 vs. 0.37, $p = 0.022$). Daily drug use (excluding alcohol) was associated with significantly lower MMT MPR (0.39 vs. 0.54, $p = 0.051$).

Conclusions: The level of adherence to MMT was very low among homeless adults experiencing mental illness. Efforts are needed to improve adherence to MMT as a means of reducing illicit substance use, preventing overdose deaths, and attenuating infectious disease transmission.

1. Introduction

Methadone maintenance is an established treatment for the management of opioid dependence, and is significantly associated with reductions in illicit opioid use (Gowing, Farrell, Bornemann, Sullivan, & Ali, 2011; Mattick, Breen, Kimber, & Davoli, 2009), injection drug use and equipment-sharing (Gowing et al., 2011), and HIV transmission (Ahamad et al., 2015). A Cochrane review found a non-significant trend of reductions in mortality associated with methadone maintenance treatment (MMT) (Mattick et al., 2009). Moreover, Brugal et al. (2005) reported a seven-fold increased risk of overdose death while not in MMT in a cohort study of heroin users. These findings are especially pertinent given the recent increase in opioid use-related overdose deaths in North American jurisdictions (British Columbia

Coroners Service, 2017; Rudd, Aleshire, Zibbell, & Gladden, 2016). In Vancouver, Canada, the drug use-related overdose death rate more than tripled between 2012 and 2016 (British Columbia Coroners Service, 2017) and has overwhelmed first responders (CTV News, 2016).

Homeless people are particularly vulnerable to substance use-related harms, as inadequate/unstable housing can be a significant structural determinant of risk behaviors (Aidala, Cross, Stall, Harre, & Sumartojo, 2005). Homelessness is independently associated with needle use and sharing (Aidala et al., 2005) as well as nonfatal drug overdose (Fischer et al., 2004). A study from Boston, Massachusetts, reported opioid overdose as a major cause of death among homeless adults (Baggett et al., 2013). MMT thus has strong potential as a treatment and prevention tool among homeless people experiencing opioid dependence.

Abbreviations: MMT, methadone maintenance treatment; MPR, medication possession ratio; VAH, Vancouver At Home; BC, British Columbia; MSP, Medical Services Plan

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Poor adherence to MMT increases the risk of overdose through changes to the central nervous system (Wolff, 2002). However, MMT adherence research is limited (Roux et al., 2014). Existing studies have generally used shorter observation periods ranging from a week to over 2 years (Haskew, Wolff, Dunn, & Bearn, 2008; Raffa et al., 2007; Roux et al., 2014; Shen et al., 2016; Zhao, Holzemer, Tulsy, Johnson, & Dawson Rose, 2014), and, in one case, eight years (Zhou, Li, Wei, Li, & Zhuang, 2017). Longer observation periods may enable more stable estimates of adherence. Moreover, to our knowledge, no studies have reported adherence to MMT among homeless populations.

The current study addresses the aforementioned gaps by being the first to investigate methadone adherence in a well-defined sample of people experiencing both homelessness and mental illness over a period of 15 years using comprehensive pharmacy dispensing data. Our objectives were to identify the prevalence of MMT within the sample, investigate adherence levels over a multi-year period, report characteristics that may differentiate methadone recipients from others in the sample, and identify potential correlates of adherence. Such information is needed to inform MMT programs serving homeless populations and future research, as the level of MMT adherence in this population remains unknown. Cost-effectiveness studies are also important in this area, but at this point, there are very few studies with descriptive details involving MMT among marginalized samples, so an additional goal of the present study was to contribute descriptive information related to cost of MMT, to inform future research.

2. Material and methods

2.1. Data sources and participants

Analysis was based on administrative and self-reported data from participants in the Vancouver At Home (VAH) study. VAH is comprised of two randomized trials of Housing First interventions for homeless adults experiencing mental illness in Vancouver, British Columbia (BC) (Somers et al., 2013). Participants were recruited between October 2009 and June 2011, and met the following inclusion criteria: a minimum age of 19, absolute homelessness or unstable housing, and mental illness. Absolute “homelessness was defined as having no fixed place to sleep or live for more than 7 nights and little likelihood of obtaining accommodation in the coming month” (Somers et al., 2013, p. 3). Unstable “housing was defined as currently residing in marginal accommodation, such as a SRO hotel, and having two or more episodes of [absolute] homelessness (as defined above) during the past 12 months” (Somers et al., 2013, p. 3). Comprehensive diagnostic and prescription data were obtained from BC’s Medical Services Plan (MSP) (Government of British Columbia, 2017a) and BC PharmaNet (Government of British Columbia, 2017c). MSP is the universal health insurance plan in British Columbia (Government of British Columbia, 2017a). PharmaNet is an administrative database containing information related to prescription drug dispensation from all pharmacies in BC (Government of British Columbia, 2017c).

Separate consent was required for 1) participation in VAH and 2) access to administrative records, including MSP and PharmaNet data. The Institutional ethics review board of Simon Fraser University approved the current study. Further details unrelated to the present study have been described separately (Rezansoff, Moniruzzaman, Fazel, Procyshyn, & Somers, 2016; Somers et al., 2013).

Baseline data from VAH and descriptive longitudinal data from MSP and PharmaNet were analyzed. Retrospective PharmaNet data were available from January 1, 1996 to VAH baseline (\approx 15 years). All participants dispensed methadone between January 1, 1996 and baseline were included in analyses. A diagnosis of “drug dependence” occurring at any point during the 15 years preceding VAH baseline was identified from MSP billing data. Drug dependence can be entered into MSP by any community-based health care practitioner qualified to diagnose, using the International Classification of Diseases-9 code of 304.

2.2. MMT adherence and descriptive variables

Methadone treatment in BC is prescribed by MMT-authorized physicians (College of Physicians and Surgeons of British Columbia, 2016). Daily oral methadone is administered at pharmacies, and consumption is observed by pharmacists, unless take-home doses are prescribed (College of Physicians and Surgeons of British Columbia, 2016). MMT is provided at no cost via a provincially sponsored plan (known as BC PharmaCare) to low-income patients (Government of British Columbia, 2017b).

Adherence to methadone was measured using the medication possession ratio (MPR) and derived from administrative prescription data (PharmaNet). MPR is a validated (Steiner, Koepsell, Fihn, & Inui, 1988) and well-established metric for adherence and has been used to measure long-term adherence in homeless mentally ill samples (Rezansoff, Moniruzzaman, Fazel, McCandless, et al., 2016; Rezansoff, Moniruzzaman, Fazel, Procyshyn, et al., 2016). MPR indicates the ratio between the number of days of medication dispensed in a given time interval to the number of days in that interval. Drug costs, dispensing fees, and number of pharmacy transactions were determined separately (per person-year). PharmaCare billings and out-of-pocket patient expenses were also calculated.

Socio-demographic information was collected via questionnaires at recruitment. This also included information related to homelessness, such as age first homeless, lifetime duration of homelessness, and housing status (absolutely homeless or unstably housed). Twenty-nine chronic physical health conditions, diseases, and infections (e.g., HIV) were included in the VAH protocol. Mental disorders were categorized as being in the “less severe cluster” (includes: major depressive episode, post-traumatic stress disorder, and panic disorder) or “severe cluster” (includes: manic or hypomanic episode, mood disorder with psychotic features, and psychotic disorder). In addition to age of first alcohol and drug use, participants were asked if they had engaged in a range of substance use behaviors occurring in the previous month. Instrument details and information regarding methods of administration have been published (Somers et al., 2013).

2.3. Statistical analysis

Percentages were used to present results for each categorical variable. Descriptive statistics were presented for continuous variables.

The observation period used to assess adherence (MPR) consisted of the length of time (in days) between the date of first dispense (any time between January 1, 1996 and the baseline interview) and the date of the baseline interview. Continuous indication for MMT was assumed (Nosyk et al., 2012).

Independent sample *t*-tests (for categorical variables with two levels, such as gender and education) and one-way ANOVA (for categorical variables with more than two levels, such as ethnicity and lifetime duration of homelessness) were conducted to test for differences in MPR between levels of a variety of variables, including socio-demographic, homelessness, physical health, mental disorder, and substance use characteristics. All reported *p* values were two sided. The conventional $p \leq 0.05$ was chosen to determine significance. Due to a small sample size, $p \leq 0.10$ was also used to indicate a significant trend.

3. Results

Baseline interviews for VAH were conducted with 497 participants, and 433 (87.1%) provided consent for researchers to access administrative data (Table 1). PharmaNet records showed that methadone was dispensed to 78 participants (18.0%), of whom all but one had a diagnosis of drug dependence in MSP.

Approximately 40% of participants who received methadone identified as women. The majority were between the ages of 25 and 44 years (66.7%), White (60.3%), had not completed high school (66.7%), and

Table 1
Socio-demographic, physical health, mental disorder, and substance use characteristics of VAH participants at baseline who received methadone.

Variable	Entire sample (n = 497)	Sample with administrative record (n = 433) Mean (SD)/n (%)	Participants with drug dependence (n = 265) Mean (SD)/n (%)	Methadone recipient (n = 78) Mean (SD)/n (%)
Socio-demographics				
Woman	134 (27.2)	112 (26.1)	75 (28.6)	30 (40.3)
Age at randomization				
< 25 years	36 (7.2)	34 (7.9)	17 (6.4)	1 (1.3)
25–44 years	281 (56.6)	242 (55.8)	160 (60.4)	52 (66.7)
> 44 years	180 (36.2)	157 (36.3)	88 (33.2)	25 (32.0)
Ethnicity				
Indigenous	77 (15.5)	70 (16.2)	56 (21.1)	14 (17.9)
White	280 (56.3)	235 (54.2)	148 (55.9)	47 (60.3)
Other	140 (28.2)	128 (29.6)	61 (23.0)	17 (21.8)
Incomplete high school	280 (56.7)	247 (57.4)	166 (62.9)	52 (66.7)
Unemployed	457 (92.3)	398 (92.3)	243 (92.0)	76 (97.4)
Income in past month (< \$800)	234 (47.7)	198 (46.4)	104 (39.7)	31 (40.3)
Single (never married)	343 (69.6)	293 (68.1)	177 (67.6)	44 (57.1)
Homelessness				
Age of first homelessness (\geq 25 years)	277 (56.4)	239 (55.7)	139 (52.9)	40 (51.9)
Lifetime duration of homelessness				
\leq 12 months	134 (27.3)	122 (28.5)	58 (22.1)	10 (12.8)
13–60 months	203 (41.3)	178 (41.6)	115 (43.7)	35 (44.9)
> 60 months	154 (31.4)	128 (29.9)	90 (34.2)	33 (42.3)
Absolutely homeless	388 (78.1)	338 (78.1)	207 (78.1)	63 (80.8)
Physical health				
Hepatitis B	25 (5.0)	24 (5.5)	21 (7.9)	10 (12.8)
Hepatitis C	139 (28.0)	125 (28.9)	106 (40.0)	55 (70.5)
HIV/AIDS	43 (8.7)	39 (9.0)	33 (12.5)	15 (19.2)
Any blood-borne infections (Hepatitis B, C, or HIV)	157 (31.6)	139 (32.1)	114 (43.0)	56 (71.8)
Multiple (\geq 3) chronic health conditions	344 (69.2)	305 (70.4)	200 (75.5)	68 (87.2)
Mental disorders				
Hospitalized for mental illness \geq 2 times in the past 5 years	253 (50.9)	215 (49.7)	131 (49.4)	26 (33.3)
Less severe cluster of mental disorders	264 (53.1)	235 (54.3)	165 (62.3)	58 (74.4)
Severe cluster of mental disorders	363 (73.0)	311 (71.8)	179 (67.5)	46 (59.0)
Substance use behaviors				
Age of first alcohol use (\leq 13 years)	215 (45.6)	185 (44.7)	133 (51.4)	48 (63.2)
Age of first drug use (\leq 13 years)	183 (40.0)	159 (39.5)	111 (43.0)	33 (42.9)
Use of injection drugs in past month	88 (18.0)	76 (17.8)	65 (25.0)	38 (50.0)
Use of alcohol in past month	225 (45.6)	198 (45.9)	130 (49.4)	27 (35.1)
Use of heroin in past month	96 (19.4)	89 (20.6)	77 (29.3)	45 (58.4)
Weekly or daily heroin use in past month	48 (9.7)	46 (10.7)	42 (16.0)	28 (36.4)
Use of benzodiazepine in past month	41 (8.3)	35 (8.1)	30 (11.5)	11 (14.3)
Use of illicit methadone in past month	21 (4.3)	18 (4.2)	16 (6.1)	7 (9.1)
Use of cocaine in past month	83 (16.8)	75 (17.4)	58 (22.1)	23 (29.9)
Use of cocaine-crack base in past month	160 (32.5)	141 (32.8)	121 (46.2)	48 (62.3)
Use of amphetamine in past month	61 (12.4)	51 (11.9)	35 (13.3)	13 (16.9)
Use of cannabis in past month	205 (45.3)	186 (47.4)	15 (6.4)	38 (58.5)
Use of \geq 2 substances in past month (including alcohol)	257 (52.0)	230 (53.4)	173 (65.8)	62 (80.5)
Daily alcohol use in past month	26 (5.3)	22 (5.1)	16 (6.1)	2 (2.6)
Daily drug use (excluding alcohol) in past month	126 (25.5)	118 (27.4)	87 (33.1)	35 (45.5)
Daily hard drug use (excluding alcohol and cannabis) in past month	74 (15.0)	67 (15.5)	56 (21.3)	27 (35.1)

were single (never married) (57.1%). Additional socio-demographic details are presented in Table 1.

Blood-borne infectious disease was prevalent among participants receiving methadone (71.8%), and multiple chronic physical health conditions were very common (87.2%). One third of the sample were hospitalized for mental illness two or more times in the past five years. Almost three-quarters of participants had a mental disorder from the “less severe cluster” (74.4%), whereas 59.0% had one from the “severe cluster”.

In the month before baseline, half of participants had injected drugs, 80.5% used two or more substances (including alcohol), 2.6% used alcohol daily, 45.5% used drugs daily (excluding alcohol), and 35.1% used hard drugs daily (excluding alcohol and cannabis). Specific drugs

used in the previous month, as well as the age of first drug and alcohol use are reported in Table 1.

Mean MMT MPR was 0.47 (SD = 0.33), and while approximately a fifth of participants had an MMT MPR over 0.80, about a quarter had an MMT MPR \leq 0.20 (Table 2). Methadone was dispensed on a mean of 1140 days (SD = 1159 days). A mean of 2379 days (SD = 1543 days) or 6.5 years (SD = 4.2 years) elapsed between date of first dispense and VAH baseline. There were approximately 140 pharmacy transactions per person-year during the observation period, and the associated costs are presented in Table 2.

Comparisons of MMT MPR by participant characteristics are presented in Table 3. A few significant differences were found. Of all socio-demographic variables, marital status was statistically significant;

Table 2
Methadone adherence, service, and cost during the study period (n = 78).

Variable	n (%)
Number of days with methadone	
Mean (SD)	1140 (1159)
Median (IQR)	787 (153, 1666)
Duration of MMT (between randomization and treatment initiation) in days	
Mean (SD)	2379 (1543)
Median (IQR)	2211 (1006, 3611)
Duration of MMT (between randomization and treatment initiation) in years	
Mean (SD)	6.5 (4.2)
Median (IQR)	6.0 (2.8, 9.9)
Medication possession ratio (entire pre-period)	
Mean (SD)	0.47 (0.33)
Medication possession ratio distribution (entire pre-period)	
≤ 0.20	19 (24.4)
0.21–0.40	19 (24.4)
0.41–0.60	11 (14.1)
0.61–0.8	13 (16.7)
> 0.80	16 (20.4)
Pharmacy transactions (#), per person-year (entire pre-period)	140.4
Pharmacy transactions (#), per person-year (past year)	157.3
PharmaCare costs (\$CAD), per person-year (past year)	1714.9
Patient costs (\$CAD), per person-year (past year)	86.2
Drug costs (\$CAD), per person-year (past year)	325.2
Pharmacy fee (\$CAD), per person-year (past year)	1462.6

participants who were single and never married had a lower MPR (0.40 vs. 0.55, $p = 0.036$). Those with a mental disorder from the severe cluster had a significantly higher MMT MPR (0.54 vs. 0.37, $p = 0.022$). With regard to substance use variables, daily drug use (excluding alcohol) was associated with a significantly lower MMT MPR (0.39 vs. 0.54, $p = 0.051$). Weekly or daily heroin use was also associated with a lower MMT MPR, but this was marginally significant (0.38 vs. 0.52, $p = 0.068$), as was MMT MPR among those reporting polysubstance use compared to those who did not (0.44 vs. 0.61, $p = 0.069$).

4. Discussion

Relative to continuous adherence, the level of adherence observed in our sample was very low (mean MPR of 0.47) and may substantially undermine the opportunity to derive therapeutic value from this intervention (Ahamad et al., 2015; Brugal et al., 2005; Gowing et al., 2011; Mattick et al., 2009; Wolff, 2002). In contrast, using a similar adherence measure, Zhou et al. (2017) found that the percentage of “methadone use days” was 76.31% among MMT patients who had accessed community MMT clinics included in their analyses.

Poor adherence to MMT in our sample may be indicative of substance use concurrent with MMT. A previous study found opioid use during MMT to be significantly associated with lower MMT adherence (Raffa et al., 2007). In our sample, reported substance use in the month preceding baseline was very common (e.g., heroin use, polysubstance use, and daily drug use). Further examination of substance use variables revealed that MMT MPR was significantly lower among methadone recipients who reported daily substance use in the month before baseline. Weekly or daily heroin use in the month before baseline was also associated with lower MMT adherence, albeit this finding was marginally significant. Substance use prior to treatment may also predict methadone adherence outcomes. For example, Roux et al. (2014) found cocaine use, harmful alcohol use, and alcohol dependence to each be significantly associated with non-adherence to methadone when used before treatment. Our substance use-related findings may have important implications in the current context of increased opioid use-related overdose deaths (British Columbia Coroners Service, 2017; Rudd et al., 2016). In many jurisdictions, including BC, illicit drug use poses

Table 3
Bivariate comparisons of the methadone medication possession ratio by participant characteristics at baseline (n = 78).

Variable	Medication possession ratio (entire pre-period) (n = 78) Mean (SD)	p value ^a
Socio-demographics		
Gender		
Woman	0.45 (0.32)	0.755
Man	0.48 (0.34)	
Age at randomization		
≤ 44 years	0.45 (0.32)	0.375
> 44 years	0.52 (0.34)	
Ethnicity		
Indigenous	0.43 (0.30)	0.805
White	0.47 (0.34)	
Other	0.51 (0.32)	
Education		
Incomplete high school	0.44 (0.31)	0.296
High school or higher	0.52 (0.35)	
Marital Status		
Single (never married)	0.40 (0.31)	0.036
Other	0.55 (0.32)	
Homelessness		
Age of first homelessness		
< 25	0.46 (0.32)	0.626
≥ 25 years	0.49 (0.33)	
Lifetime duration of homelessness		
≤ 12 months	0.58 (0.28)	0.370
13–60 months	0.48 (0.32)	
> 60 months	0.42 (0.35)	
Housing status		
Absolutely homeless	0.47 (0.34)	0.751
Unstably housed	0.44 (0.28)	
Physical health		
Any blood-borne infections (Hepatitis B, C, or HIV)		
Yes	0.47 (0.32)	0.994
No	0.47 (0.35)	
Multiple (≥ 3) chronic health conditions		
Yes	0.47 (0.33)	0.928
No	0.48 (0.34)	
Mental disorders		
Hospitalized for mental illness ≥ 2 times in the past 5 years		
Yes	0.52 (0.32)	0.303
No	0.44 (0.33)	
Less severe cluster of mental disorders		
Yes	0.46 (0.32)	0.796
No	0.49 (0.36)	
Severe cluster of mental disorders		
Yes	0.54 (0.33)	0.022
No	0.37 (0.30)	
Substance use behaviors		
Use of injection drugs in past month		
Yes	0.50 (0.31)	0.525
No	0.45 (0.35)	
Use of alcohol in past month		
Yes	0.46 (0.35)	0.803
No	0.48 (0.32)	
Use of heroin in past month		
Yes	0.43 (0.31)	0.217
No	0.53 (0.34)	
Weekly or daily heroin use in past month		
Yes	0.38 (0.31)	0.068
No	0.52 (0.33)	
Use of cocaine in past month		
Yes	0.49 (0.33)	0.720
No	0.46 (0.33)	
Use of cocaine-crack base in past month		
Yes	0.45 (0.32)	0.519
No	0.50 (0.34)	

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Table 3 (continued)

Variable	Medication possession ratio (entire pre-period) (n = 78) Mean (SD)	p value ^a
Use of cannabis in past month		
Yes	0.40 (0.33)	0.305
No	0.49 (0.31)	
Use of ≥ 2 substances in past month (including alcohol)		
Yes	0.44 (0.32)	0.069
No	0.61 (0.32)	
Daily drug use (excluding alcohol) in past month		
Yes	0.39 (0.32)	0.051
No	0.54 (0.32)	
Daily hard drug use (excluding alcohol and cannabis) in past month		
Yes	0.41 (0.29)	0.249
No	0.50 (0.34)	

^a Bold indicates a significant difference at $p \leq 0.05$ and italics indicate a significant trend ($p > 0.05$ and $p \leq 0.10$).

an unprecedented risk of overdose death, often attributed to illicit fentanyl (British Columbia Coroners Service, 2017). Our results suggest that despite having received MMT, homeless adults with mental illness were commonly using heroin and multiple illicit substances. Low prescribed MMT dosing may have also affected adherence (Shen et al., 2016) and illicit opioid use (Fareed, Casarella, Amar, Vayalapalli, & Drexler, 2010).

The prevalence of blood-borne infections, and chronic physical health conditions was very high in our sample. Nearly 20% of the sample was living with HIV/AIDS and 87.2% reported three or more chronic physical health conditions. This reflects the vulnerability of participants to chronic health issues in a context of long-term homelessness, serious mental illness, and drug dependence. Homelessness and unstable housing are associated with behaviors that increase risk of blood-borne infections (Aidala et al., 2005). Homelessness and precarious housing also pose barriers to following treatment regimens, as competing priorities involving basic needs can interfere with adherence (Hunter et al., 2015).

In addition to having competing priorities, however, homeless people may also face other barriers to access to health care, such as perceived discrimination, distrusting health practitioners, feeling dehumanized and unwelcomed (Wen, Hudak, & Hwang, 2007), and perceiving office wait times to be long (Lewis, Andersen, & Gelberg, 2003). Mental illness may also make it more difficult to access health care (Hwang et al., 2010), but we found that participants who had a mental illness from the severe cluster of mental disorders had significantly higher MMT adherence. It could be that those living with schizophrenia, bipolar disorder, or a mood disorder with psychotic features are more closely monitored by health and social service providers while in MMT. More research is needed to elucidate this relationship.

Participants who reported being single and never married had significantly lower MMT MPR compared to those who did not. Yang et al. (2013) found that having a good relationship with family was independently and significantly associated with greater MMT retention. Family members may provide support and encouragement for MMT recipients, and this can help inform MMT programs in terms of including family members in the treatment process (Yang et al., 2013).

With regard to cost, dispensing methadone represents a significant public investment. For example, while we found the cost of methadone itself to be \$325.20 per person-year in the year prior to the baseline interview, pharmacy fees entailed a 4.5 times greater cost at \$1462.60 per person-year during the same time-period. Future studies examining cost-effectiveness of MMT among homeless people experiencing mental illness are needed.

Addressing the housing and mental health needs of homeless and

unstably housed MMT patients living with mental illness may be a necessary part of efforts to increase MMT adherence. Appel, Tsemberis, Joseph, Stefancic, and Lambert-Wacey (2012) found higher MMT retention among those receiving supported housing, specifically Housing First. More research is needed to determine whether these findings extend to long-term MMT adherence. VAH demonstrated that 1) homeless adults with mental illness can be housed and supported (Somers et al., 2017) and that 2) scattered-site Housing First was associated with significantly greater antipsychotic medication adherence (Rezansoff, Moniruzzaman, Fazel, McCandless, et al., 2016). The present study is preliminary in nature, and the first to quantify MMT adherence among homeless adults experiencing mental illness. Future research utilizing multivariable models to investigate variables associated with adherence in this population is needed. Alternative opioid maintenance treatments may be better options for some (e.g., injectable diacetylmorphine (Oviedo-Joekes et al., 2009)). It is also important to note that over 20% of our sample had an MMT MPR of over 0.80, considerably higher than the mean. Nevertheless, interventions to increase MMT adherence are needed for homeless and mentally ill methadone patients.

A few limitations should be noted. Prescription information detailing methadone dosage was unavailable. Data related to substance use prior to the month preceding baseline were also unavailable. Insufficient statistical power precluded us from conducting a multivariable analysis to estimate the association between selected variables and MMT MPR. Furthermore, the validity of self-reported data, especially substance use items, may have been compromised (underestimated) by social desirability bias or inaccurate recall. Participants were dispensed methadone within a universal health care system, limiting generalizability to dissimilar contexts. Additionally, we do not know the precise relationship between homelessness status and methadone adherence over the time-period observed for this study. Nevertheless, previous research on this sample has established that participants were profoundly marginalized from early ages, including significant adverse childhood experiences (Patterson, Markey, & Somers, 2012; Patterson, Moniruzzaman, Frankish, & Somers, 2012), as well as family separation (Patterson, Moniruzzaman, & Somers, 2015). Moreover, members of the sample had been homeless for roughly 10 years (Somers et al., 2013) and therefore were likely to have experienced substantial housing instability and marginalization throughout the period of time observed in the present study.

5. Conclusions

This is the first study to investigate MMT adherence among homeless adults living with mental illness, and we found that on average, patients were using methadone less than half the time, despite low threshold access to MMT and publicly funded coverage. Adherence may be even lower among homeless adults experiencing mental illness in other settings without low threshold access to MMT. Chronic homelessness, infectious disease, and substance use were also very common. It remains extremely important to develop and implement interventions that increase MMT adherence among homeless mentally ill adults to decrease illicit opioid use and related harms. These efforts are needed immediately as opioid-related overdose deaths continue to rise, leading to premature mortality and increased demand on health and social resources. Drug use-related overdose deaths in BC have reached crisis levels, and in the month of November 2016, the mean number of people that died each day was over four (Larsen & Zussman, 2016). The number of deaths in 2016 was 922, a 79.7% increase compared to the preceding year (British Columbia Coroners Service, 2017). Housing and adequate supports may be a crucial part of the solution, not only to promote increased adherence to MMT, but also to alleviate physical and psychosocial harms associated with homelessness.

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References

- Ahamad, K., Hayashi, K., Nguyen, P., Dobrer, S., Kerr, T., Schütz, C. G., ... Wood, E. (2015). Low threshold methadone protects against HIV incidence in a Canadian setting: An observational cohort study. *The Lancet HIV*, 2(10), e445–e450.
- Aidala, A., Cross, J. E., Stall, R., Harre, D., & Sumartojo, E. (2005). Housing status and HIV risk behaviors: Implications for prevention and policy. *AIDS and Behavior*, 9(3), 251–265.
- Appel, P. W., Tsemberis, S., Joseph, H., Stefancic, A., & Lambert-Wacey, D. (2012). Housing First for severely mentally ill homeless methadone patients. *Journal of Addictive Diseases*, 31(3), 270–277.
- Baggett, T. P., Hwang, S. W., O'Connell, J. J., Porneala, B. C., Stringfellow, E. J., Orav, E. J., ... Rigotti, N. A. (2013). Mortality among homeless adults in Boston: Shifts in causes of death over a 15-year period. *JAMA Internal Medicine*, 173(3), 189.
- British Columbia Coroners Service (2017). Illicit drug overdose deaths in BC January 1, 2007–February 28, 2017. <http://www2.gov.bc.ca/assets/gov/public-safety-and-emergency-services/death-investigation/statistical/illicit-drug.pdf>, Accessed date: 27 March 2017.
- Brugal, M. T., Domingo-Salvany, A., Puig, R., Barrio, G., García de Olalla, P., & de la Fuente, L. (2005). Evaluating the impact of methadone maintenance programmes on mortality due to overdose and AIDS in a cohort of heroin users in Spain. *Addiction*, 100(7), 981–989.
- College of Physicians and Surgeons of British Columbia (2016). Methadone and buprenorphine: Clinical practice guideline for opioid use disorder. <https://www.cpsbc.ca/files/pdf/MBMT-Clinical-Practice-Guideline.pdf>, Accessed date: 24 January 2017.
- CTV News (2016). Downtown Eastside firefighters struggle with endless fentanyl overdoses. <http://www.ctvnews.ca/health/downtown-eastside-firefighters-struggle-with-endless-fentanyl-overdoses-1.3176176>, Accessed date: 14 February 2017.
- Fareed, A., Casarella, J., Amar, R., Vayalappalli, S., & Drexler, K. (2010). Methadone maintenance dosing guideline for opioid dependence, a literature review. *Journal of Addictive Diseases*, 29(1), 1–14.
- Fischer, B., Brissette, S., Brochu, S., Bruneau, J., El-Guebaly, N., Noël, L., ... Baliunas, D. (2004). Determinants of overdose incidents among illicit opioid users in 5 Canadian cities. *Canadian Medical Association Journal*, 171(3), 235–239.
- Government of British Columbia (2017a). Medical Services Plan of B.C. <http://www2.gov.bc.ca/gov/content/health/health-drug-coverage/msp>, Accessed date: 29 January 2017.
- Government of British Columbia (2017b). PharmaCare for B.C. Residents. <http://www2.gov.bc.ca/gov/content/health/health-drug-coverage/pharmacare-for-bc-residents>, Accessed date: 29 January 2017.
- Government of British Columbia (2017c). PharmaNet. <http://www2.gov.bc.ca/gov/content/health/health-drug-coverage/pharmacare-for-bc-residents/pharmanet>, Accessed date: 29 January 2017.
- Gowing, L., Farrell, M. F., Bornemann, R., Sullivan, L. E., & Ali, R. (2011). Oral substitution treatment of injecting opioid users for prevention of HIV infection. *Cochrane Database of Systematic Reviews*, 8, CD004145.
- Haskew, M., Wolff, K., Dunn, J., & Bearn, J. (2008). Patterns of adherence to oral methadone: Implications for prescribers. *Journal of Substance Abuse Treatment*, 35(2), 109–115.
- Hunter, C. E., Palepu, A., Farrell, S., Gogosis, E., O'Brien, K., & Hwang, S. W. (2015). Barriers to prescription medication adherence among homeless and vulnerably housed adults in three Canadian cities. *Journal of Primary Care & Community Health*, 6(3), 154–161.
- Hwang, S. W., Ueng, J. J. M., Chiu, S., Kiss, A., Tolomiczenko, G., Cowan, L., ... Redelmeier, D. A. (2010). Universal health insurance and health care access for homeless persons. *American Journal of Public Health*, 100(8), 1454–1461.
- Larsen, K., & Zussman, R. (2016). Drug overdose deaths in B.C. reach all-time high in November. <http://www.cbc.ca/news/canada/british-columbia/drug-overdose-bc-november-1.3903256>, Accessed date: 14 February 2017.
- Lewis, J. H., Andersen, R. M., & Gelberg, L. (2003). Health care for homeless women. *Journal of General Internal Medicine*, 18(11), 921–928.
- Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2009). Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database of Systematic Reviews*, 3, CD002209.
- Nosyk, B., Guh, D. P., Bansback, N. J., Oviedo-Joekes, E., Brissette, S., Marsh, D. C., ... Anis, A. H. (2012). Cost-effectiveness of diacetylmorphine versus methadone for chronic opioid dependence refractory to treatment. *Canadian Medical Association*, 184(6), E317–E328.
- Oviedo-Joekes, E., Brissette, S., Marsh, D. C., Lauzon, P., Guh, D., Anis, A., & Schechter, M. T. (2009). Diacetylmorphine versus methadone for the treatment of opioid addiction. *New England Journal of Medicine*, 361(8), 777–786.
- Patterson, M. L., Markey, M. A., & Somers, J. M. (2012). Multiple paths to just ends: Using narrative interviews and timelines to explore health equity and homelessness. *International Journal of Qualitative Methods*, 11(2), 132–151.
- Patterson, M. L., Moniruzzaman, A., Frankish, C. J., & Somers, J. M. (2012). Missed opportunities: Childhood learning disabilities as early indicators of risk among homeless adults with mental illness in Vancouver, British Columbia. *BMJ Open*, 2(6), e001586.
- Patterson, M. L., Moniruzzaman, A., & Somers, J. M. (2015). History of foster care among homeless adults with mental illness in Vancouver, British Columbia: A precursor to trajectories of risk. *BMC Psychiatry*, 15(1), 32.
- Raffa, J. D., Grebely, J., Tossonian, H., Wong, T., Viljoen, M., Khara, M., ... Conway, B. (2007). The impact of ongoing illicit drug use on methadone adherence in illicit drug users receiving treatment for HIV in a directly observed therapy program. *Drug and Alcohol Dependence*, 89(2–3), 306–309.
- Rezansoff, S. N., Moniruzzaman, A., Fazel, S., McCandless, L., Procyshyn, R., & Somers, J. M. (2016). Housing First improves adherence to antipsychotic medication among formerly homeless adults with schizophrenia: Results of a randomized controlled trial. *Schizophrenia Bulletin*, 42(1), 136.
- Rezansoff, S. N., Moniruzzaman, A., Fazel, S., Procyshyn, R., & Somers, J. M. (2016). Adherence to antipsychotic medication among homeless adults in Vancouver, Canada: A 15-year retrospective cohort study. *Social Psychiatry and Psychiatric Epidemiology*, 51(12), 1623–1632.
- Roux, P., Lions, C., Michel, L., Cohen, J., Mora, M., Marcellin, F., ... ANRS Methaville Study Group (2014). Predictors of non-adherence to methadone maintenance treatment in opioid-dependent individuals: Implications for clinicians. *Current Pharmaceutical Design*, 20(25), 4097–4105.
- Rudd, R. A., Aleshire, N., Zibbell, J. E., & Gladden, R. M. (2016). Increases in drug and opioid overdose deaths — United States, 2000–2014. *Morbidity and Mortality Weekly Report*, 64(50–51), 1378–1382.
- Shen, J., Wang, M., Wang, X., Zhang, G., Guo, J., Li, X., & Li, J. (2016). Predictors of poor adherence to methadone maintenance treatment in Yunnan Province, China. *Journal of Addiction Medicine*, 10(1), 40–45.
- Somers, J. M., Moniruzzaman, A., Patterson, M., Currie, L., Rezansoff, S. N., Palepu, A., & Fryer, K. (2017). A randomized trial examining housing first in congregate and scattered site formats. *PLoS One*, 12(1), e0168745.
- Somers, J. M., Patterson, M. L., Moniruzzaman, A., Currie, L., Rezansoff, S. N., Palepu, A., & Fryer, K. (2013). Vancouver At Home: Pragmatic randomized trials investigating Housing First for homeless and mentally ill adults. *Trials*, 14(1), 365.
- Steiner, J. F., Koepsell, T. D., Fihn, S. D., & Inui, T. S. (1988). A general method of compliance assessment using centralized pharmacy records. Description and validation. *Medical Care*, 26(8), 814–823.
- Wen, C. K., Hudak, P. L., & Hwang, S. W. (2007). Homeless people's perceptions of welcome and unwelcome in healthcare encounters. *Journal of General Internal Medicine*, 22(7), 1011–1017.
- Wolff, K. (2002). Characterization of methadone overdose: Clinical considerations and the scientific evidence. *Therapeutic Drug Monitoring*, 24(4), 457–470.
- Yang, F., Lin, P., Li, Y., He, Q., Long, Q., Fu, X., & Luo, Y. (2013). Predictors of retention in community-based methadone maintenance treatment program in Pearl River Delta, China. *Harm Reduction Journal*, 10, 3.
- Zhao, L., Holzemer, W. L., Tulskey, J. P., Johnson, M. O., & Dawson Rose, C. (2014). Effect of methadone dose on maintenance treatment and health consequences among heroin addicts in South China. *Substance Use & Misuse*, 49(1–2), 13–21.
- Zhou, K., Li, H., Wei, X., Li, X., & Zhuang, G. (2017). Medication adherence in patients undergoing methadone maintenance treatment in Xi'an, China. *Journal of Addiction Medicine*, 11(1), 28–33.