

Adherence to antipsychotic medication among homeless adults in Vancouver, Canada: a 15-year retrospective cohort study

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Abstract

Purpose The purpose of this study was to investigate the level of adherence to antipsychotic prescription medication in a well-defined homeless cohort over a 15-year period. We hypothesized that adherence would be well below the recommended threshold for clinical effectiveness (80 %), and that it would be strongly associated with modifiable risk factors in the social environment in which homeless people live.

Method Linked baseline data (including comprehensive population-level administrative prescription records) were examined in a subpopulation of participants from two pragmatic-randomized trials that investigated Housing First for homeless and mentally ill adults. Adherence to antipsychotic medication was operationalized using the medication possession ratio. Multivariable logistic regression was used to estimate effect sizes between socio-demographic, homelessness-related and illness factors, and medication possession ratio.

Results Among the 290 participants who met inclusion criteria for the current analysis, adherence to antipsychotic

prescription was significantly associated with: history of psychiatric hospitalization; receipt of primary medical services; long-acting injectable antipsychotic formulations; and duration of homelessness. Mean medication possession ratio in the pre-randomization period was 0.41. Socio-demographic characteristics previously correlated with antipsychotic non-adherence were not significantly related to medication possession ratio.

Conclusions This is the first study to quantify the very low level of adherence to antipsychotic medication among homeless people over an extended observation period of 15 years. Each of the four factors found to be significantly associated with adherence presents opportunities for intervention. Strategies to end homelessness for this population may represent the greatest opportunity to improve adherence to antipsychotic medication.

Keywords Antipsychotic · Adherence · Homelessness · Medication possession ratio · Serious mental illness

Introduction

Poor adherence to antipsychotic pharmacotherapy limits its effectiveness in naturalistic/real world conditions, leading to increased risk of relapse, hospitalization and suicide [1], arrest, violence and victimization [2], and greater overall public costs [3]. A systematic review in 2015 found adherence rates in treated samples ranging from 47 to 95 % [4], noting that this wide variability may be partially attributable to heterogeneity in study measures. It is also likely that widespread marketing and use of off-label antipsychotic prescription [5] further widen inconsistencies in reported adherence, although recent research indicates that this trend may be declining [6]. Previous studies have

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defined acceptable adherence to antipsychotic drugs as taking medication 80 % of the time for which it is prescribed [7], a threshold which is frequently used in health research [8] and health economics literature [9].

Antipsychotic medication adherence among the homeless

Psychotic disorders are particularly overrepresented among homeless people [10], a subpopulation with numerous challenges related to medication adherence generally [11]. More specifically, homelessness has been shown to be predictive of poor adherence to psychotropic medication [12] and to antipsychotics in particular [13]. One recent study examined psychotropic prescriptions dispensed to US veterans with serious mental disorders [14]. Results indicated that homeless veterans received significantly fewer prescriptions than those who were housed. This study had important limitations, however (e.g., lack of validated diagnostic instrument) and may not be representative of civilians receiving public services.

Current antipsychotic treatment guidelines provide little information on working with homeless populations. Although ‘depot’ or long-acting injectable antipsychotic formulations may provide a means to increase adherence and reduce healthcare expenditure [15], meta-analyses [16, 17] and randomized controlled trials [18, 19] based on outpatient samples have reported inconsistent findings. It has been recommended that more effectiveness research is required to evaluate long-acting injectable antipsychotics in real world settings [20]. To date, research examining their use among homeless people is limited to one uncontrolled two and a half year trial involving 30 individuals, the majority of whom discontinued therapy after the study [21].

Risk factors for non-adherence to antipsychotics

Among outpatient samples in the existing literature, patient-level characteristics, such as age and ethnicity [22], symptom severity [23], and side effects [24], have been correlates of poor adherence to antipsychotic medication, although some of these associations were inconsistent between studies [25]. A growing body of research indicates that several modifiable risk factors may also be related to non-adherence with antipsychotic prescriptions in non-homeless populations, including living alone [26], complexity of dosing regimen [27], concurrent substance use [28], duration of untreated psychosis [29], poor illness insight, and negative attitudes to antipsychotic medication [4]. Little is known about the role of these or other potentially modifiable risk factors among patients who are homeless. To the best of our knowledge, this study is the

first epidemiological analysis of antipsychotic prescription adherence using comprehensive administrative prescription records in a well-defined homeless cohort. We aimed to examine adherence to antipsychotics over a 15-year period and identify correlates of higher vs lower levels of medication adherence.

We hypothesized that antipsychotic adherence within our homeless cohort would be below the indicated level of 80 %, and that adherence to antipsychotics in this sample would be associated with modifiable risk factors, including: prescription of long-acting injectable formulations; access to health and hospitalization services; duration of homelessness; and substance use.

Methods

Ethics statement

This study underwent institutional review, and was approved by the Research Ethics Boards at Simon Fraser University and the University of British Columbia. The study sample was recruited for two experimental trials: ISRCTN57595077 (Vancouver At Home study: Housing First plus Assertive Community Treatment vs congregate housing plus supports vs treatment as usual); and ISRCTN66721740 (Vancouver At Home study: Housing First plus Intensive Case Management vs treatment as usual). Participants were asked to provide separate informed consent for researchers to receive an extract of comprehensive prescription details and other health service encounters. Study protocols for both trials included the collection of self-reported information related to socio-demographics, medical, and homelessness histories. This study investigated events in the pre-recruitment period exclusively. Further details of the Vancouver At Home protocol, including measures and procedures not included in this study, have been published separately [30].

Recruitment and eligibility

Recruitment of participants (between October 2009 and June 2011) was conducted in collaboration with community agencies serving individuals who are homeless and mentally ill in Vancouver. Eligible participants were Canadian citizens, at least 19 years of age, who met criteria for homelessness or precarious housing and current mental disorder status, as described in detail previously [30].

Further inclusion criteria specific to this study included participant consent for researchers to receive administrative data and linkability of health records. To generate a stable estimate of antipsychotic medication adherence in the sample, we limited participants to those whose first

antipsychotic prescription was recorded at least 1-year prior to their recruitment date. For descriptive purposes, comparative analysis was conducted between eligible participants and those who were excluded.

Outcome variable

Patient-specific medication details were drawn from a province-wide database (BC PharmaNet¹) that records every prescription dispensed in British Columbia. PharmaNet was implemented in 1995 to support improvements in patient safety and clinical effectiveness, and has previously been shown to accurately reflect medication adherence for most patients [31]. These data are sufficiently detailed to calculate long-term adherence to prescription medications for residents of British Columbia.

Adherence to antipsychotic prescription was operationalized using the medication possession ratio (MPR), which represents the percentage of time that a given patient was dispensed prescribed medication (i.e., number of days of medication supplied within refill interval divided by the total number of days in refill interval). The MPR has been used to evaluate patient adherence with long-term medications [32], and has been validated as a predictor of patient outcomes [33], including psychiatric hospital admission among patients diagnosed with schizophrenia [22, 34].

In this study, the observation period used to assess adherence to antipsychotic medication consisted of the length of time from the date of each participant's first antipsychotic prescription (ranging from January 1, 1996² to 1-year prior to recruitment) and ending on the date of recruitment. Accordingly, observation periods varied among participants from a minimum of 1 to >15 years. Previous analyses of adherence measures have recommended using observation periods longer than 9 months to improve the stability of measurement [32]. The MPR was calculated using the number of days for which antipsychotics were prescribed as the numerator, and the total observation period as the denominator. Recently published treatment guidelines recommend continuous antipsychotic prescription for 1–2 years following a first episode of psychosis, and indefinite prescription where clinically indicated [35]. Our participants' cumulative experiences of long-standing homelessness, substance use, frequent involvement with the justice system and other hardships rendered prolonged remission extremely challenging and unlikely. Accordingly, we assumed that continuous

prescription of antipsychotic medication was indicated for members of the cohort.

Consequently, our MPR sample distribution was dichotomized into 'lower' and 'higher' levels of antipsychotic adherence (using the rounded median value), and analyzed as a categorical variable. Our selection of a binary measurement was influenced by the non-normality of the MPR data, and facilitates comparison with existing studies that use binary adherence measures [8, 36, 37].

Independent variables

The following socio-demographic variables were self-reported at baseline and incorporated in the present analyses: age, gender, ethnicity, education, and marriage status. Information about chronic health conditions, blood-borne infectious diseases, and lifetime duration of homelessness was also self-reported (see [30] for a list of questionnaires used to elicit these details). Participant age was treated as a continuous variable in the analysis. Ethnicity was collapsed to three groups: White Aboriginal (Inuit, Metis, First Nations Status, First Nations Non-Status, Indigenous from outside Canada) and other (Asian, Black, Latin American, Indian-Caribbean, Middle Eastern or other category). Education level was defined as highest level of formal education obtained at the time of recruitment and was analyzed by dichotomizing into complete/incomplete high school. Lifetime duration of homelessness was dichotomized using the median value and analyzed categorically. All antipsychotic medication details (including long-acting formulations) and all service use encounters (substance use related, non-psychiatric health services and hospital admissions) were drawn from provincial administrative data extending from roughly 15 years prior to recruitment (variability due to the staggered nature of study recruitment). To assess the impact of inconstant observation time on MPR, first, recorded antipsychotic prescription was categorized into three groups: less than 5, 5–10 years, and more than 10 years (prior to recruitment). There was no duplication between administrative and self-reported data.

Residents of British Columbia are covered by the provincial medical services plan (MSP), which documents billing data for all medically required outpatient medical services, maternity care, and diagnostic X-ray and laboratory services. Provincial MSP records based on the International Classification of Diseases (ICD) 9th Revision were examined for mental disorders diagnosed prior to randomization. All disorders within the ICD range of 290–319 (mental disorders) were included, in addition to 50B (anxiety/depression). Substance use disorders were identified using the three-digit codes of 291, 292, 303, 304, and 305. Non-substance related mental disorders consisted of all other codes within the range identified. ICD-9 codes and

¹ See: <http://www2.gov.bc.ca/gov/content/health/health-drug-coverage/pharmacare-for-bc-residents/pharmanet>.

² PharmaNet introduced a Maximum Days' Supply policy in 1996.

descriptions for mental disorders are provided in Table A of Supplementary Materials.

Psychiatric diagnoses leading to acute hospital admission were derived from the province-wide database that includes clinical, demographic, and administrative data for hospital admissions for the province. Psychiatric diagnoses were identified using ICD 10th Revision Canadian Adaptation codes for mental disorders following the convention used in British Columbia hospitals (i.e., F00–F99). ICD-10 codes and descriptions for mental disorders are provided in Table B of Supplementary Materials. Although secondary diagnoses are listed in the database, we chose the primary diagnosis to identify psychiatric hospitalizations. Services related to substance use disorders and psychiatric hospital admissions were analyzed as continuous measures, while non-psychiatric services were analyzed as a categorical variable using 100 and 300 as cutoff values.

Statistical analysis

Continuous variables (e.g., age, number of services) were presented using descriptive statistics (i.e., mean with standard deviation, or median with inter-quartile range, as appropriate). Categorical variables (e.g., gender and ethnic status) were presented using counts (n) and proportions (%). Independent sample t tests were used to compare continuous variables, and Pearson Chi-square test was used to compare categorical variables between groups (e.g., MPR lower vs higher). Due to the dichotomous nature of the outcome variable, binary logistic regression analyses were conducted to examine the relationship between MPR and predictor variables (using ‘higher’ MPR as the reference group). The effects of independent variables on MPR were examined in both univariate and multivariable analyses.

Variables used in multivariable regression models were selected a priori for their potential association with MPR. These included age, gender, ethnicity, education, marital status, duration of homelessness, duration of antipsychotic prescription, history of long-acting formulations, previous psychiatric hospital admission, substance use treatment, receipt of primary medical services (i.e., non-psychiatric or substance use related) medical services, and diagnosed blood-borne infectious diseases and chronic medical conditions. All variables found to be significant in bivariate models ($p \leq 0.05$) were included in the model building process. Socio-demographic variables and co-morbid conditions were included in multivariable models, regardless of significance in bivariate models. Effect sizes are presented as crude and adjusted odds ratios with 95 % confidence intervals. All reported p values were two-sided. IBM SPSS Statistics (version 22) was used to conduct all analyses [38].

Results

Of 497 individuals recruited between October 2009 to June 2011, 433 (87 %) provided consent for access to their administrative records, and had linkable, comprehensive files from the British Columbia Ministry of Health. 290 participants (58 %) had been prescribed an antipsychotic drug at least 1-year prior to the date of recruitment and were included in our analyses.

The eligible sample consisted predominantly of men, with a mean age of 41.5 years, who identified ethnically as White (see Table 1). Most participants reported not having completed high school, and over two-thirds were single and/or never married. Nearly, half of the patients described experiencing over 3 years of homelessness in their lifetime, and were first homeless at roughly 30 years of age. Concurrent chronic conditions were common among participants (details are listed in Table C of Supplementary Materials) and nearly one-third disclosed having a blood-borne infectious disease (HIV, Hep. B or C). The eligible sample did not differ significantly from the ineligible sample on any of these variables.

The vast majority of participants had been diagnosed with schizophrenia. A much smaller proportion was diagnosed with bipolar disorder, or neither bipolar disorder nor schizophrenia (see Table 2). Throughout the observation period (i.e., from the first recorded antipsychotic prescription³ until randomization), antipsychotic medications were prescribed spanning an average of nearly 7.5 years, while they were dispensed for an average of approximately 3.2 years. Approximately, half of participants were dispensed their medications ≤ 40 % of the time for which they were prescribed. Only 12 % of participants met or exceeded the clinically indicated threshold of 0.80 prior to recruitment. Median MPR was rounded to 0.40 and used as a cutoff between higher and lower levels.

Nearly, two-thirds of the sample received their first recorded antipsychotic prescription at least 5 years prior to recruitment, and for one-third, the first recorded antipsychotic prescription was more than 10 years prior to recruitment. Over one-third of participants had a history of long-acting injectable antipsychotic prescription. For further detail, please refer to Table D in Supplementary Materials, which presents the frequency of each antipsychotic drug (typical and atypical) prescribed during the study period.

Membership in the lower MPR group was significantly associated with: younger age of first homelessness ($p = 0.020$); longer lifetime duration of homelessness ($p \leq 0.001$); shorter history of antipsychotic prescription

³ Beginning January 1, 1996.

Table 1 Socio-demographic characteristics of Vancouver At Home participants at time of recruitment

| Variable | Entire recruited sample (<i>n</i> = 497) <i>n</i> (%) / mean (SD) | Sample with administrative data (<i>n</i> = 433) ^a <i>n</i> (%) / mean (SD) | Eligible sample ^b (<i>n</i> = 290) <i>n</i> (%) / mean (SD) | Ineligible sample ^c (<i>n</i> = 207) <i>n</i> (%) / mean (SD) | <i>p</i> value ^d |
|---|---|--|--|--|-----------------------------|
| Age at recruitment (in years) | 40.8 (11.0) | 40.8 (11.0) | 41.5 (10.8) | 40.0 (11.3) | 0.134 |
| Age of first homelessness (in years) | 30.3 (13.3) | 30.1 (13.4) | 30.5 (13.6) | 30.0 (13.0) | 0.690 |
| Women | 134 (27) | 112 (26) | 82 (28) | 52 (25) | 0.445 |
| Ethnicity | | | | | |
| Aboriginal | 77 (16) | 70 (16) | 36 (12) | 41 (20) | 0.071 |
| White | 280 (56) | 235 (54) | 167 (58) | 113 (55) | |
| Other | 140 (28) | 128 (30) | 87 (30) | 53 (26) | |
| Incomplete high school | 280 (57) | 247 (57) | 171 (59) | 109 (53) | 0.153 |
| Single/never married | 343 (70) | 293 (68) | 202 (70) | 141 (68) | 0.645 |
| Lifetime duration of homelessness (over 3 years) ^e | 234 (48) | 199 (46) | 132 (46) | 102 (50) | 0.484 |
| Blood-borne infectious disease (HIV; hepatitis B/C) | 157 (32) | 139 (32) | 95 (33) | 62 (31) | 0.585 |
| Chronic medical conditions (3 or more) | 344 (69) | 305 (70) | 202 (70) | 142 (69) | 0.801 |

SD standard deviation

^a Of 497 participants, 433 provided consent to access of administrative health data and were linkable to health records. 64 did not consent or were not linkable to health records. No significant ($p < 0.05$) differences were observed between these two groups ($n = 433$ vs $n = 64$)

^b Among these 433 cases, 290 received an antipsychotic prescription at least 1-year prior to recruitment

^c Of 207 participants, 60 did not consent to access of administrative health data, and four provided consent but were not linkable to health records. The remaining 143 had no history of antipsychotic prescription ($n = 90$) prior to recruitment or received their first antipsychotic prescription 1-year prior to recruitment ($n = 53$)

^d *p* values are based on comparisons between eligible participants and non-eligible participants in the entire sample

^e Median values (36 months) as a cutoff

($p = 0.001$); fewer long-acting injectable prescriptions ($p \leq 0.001$); fewer psychiatric hospitalizations ($p \leq 0.001$); and diagnosis of a blood-borne infectious disease ($P = 0.003$) (see Table 3).

Crude and adjusted odds ratios and 95 % confidence intervals are reported for each comparison. In the adjusted model, participants who reported being homeless longer than 3 years were twice as likely to have a low MPR. Receipt of relatively fewer non-psychiatric health services (≤ 100) in the 5 years prior to recruitment was also positively correlated with a lower MPR. Diagnosis of a blood-borne infectious disease more than doubled the odds of having an MPR below 0.40. Conversely, participants with a history of long-acting injectable prescriptions and those hospitalized for psychiatric reasons in the 5 years prior to recruitment were less likely to have a lower MPR. Each of these five variables was significant ($p < 0.05$). None of the other variables included in the table exhibited a significant relationship with MPR in the adjusted model.

Discussion

In the 15 years prior to recruitment, adherence to antipsychotic medication among Vancouver At Home participants was 0.41, and well below the indicated minimum MPR of 0.80. Higher adherence was significantly associated with: history of psychiatric hospitalization; receipt of primary medical services; long-acting injectable antipsychotic prescription; duration of homelessness; and diagnosed blood-borne infectious disease. These results present potential opportunities to improve adherence through clinical and social interventions.

The study sample was characterized by chronic medical conditions, co-occurring substance use and longstanding homelessness. Participants also presented with socio-demographic features previously correlated with poor adherence to antipsychotic medication (i.e., <45 years of age and non-white ethnicity [22]; low levels of educational attainment and living alone [23]). However, none of the latter variables were significant in the current study.

Table 2 Medication possession ratio (MPR) and related characteristics among eligible Vancouver At Home participants ($n = 290$)

| Variables | |
|---|-------------------|
| Number of days antipsychotics dispensed prior to recruitment | |
| Mean (SD) | 1177 (1207) |
| Median (IQR) | 764 (248, 1856) |
| Number of days between first observed antipsychotic dispensed and recruitment | |
| Mean (SD) | 2732 (1617) |
| Median (IQR) | 2582 (1245, 4240) |
| MPR prior to recruitment | |
| Mean (SD) | 0.41 (0.29) |
| Median (IQR) | 0.38 (0.15, 0.64) |
| MPR prior to recruitment ^a , n (%) | |
| <0.40 | 150 (52) |
| \geq 0.40 | 140 (48) |
| MPR prior to recruitment, n (%) | |
| <0.10 | 59 (20) |
| 0.10–0.19 | 36 (12) |
| 0.20–0.29 | 29 (10) |
| 0.30–0.39 | 26 (9) |
| 0.40–0.49 | 26 (9) |
| 0.50–0.59 | 32 (11) |
| 0.60–0.69 | 21 (7) |
| 0.70–0.79 | 26 (9) |
| 0.80–0.89 | 23 (8) |
| \geq 0.90 | 12 (4) |
| History of long-acting injectable antipsychotic prescription prior to recruitment, n (%) | 107 (37) |
| First recorded antipsychotic prescription prior to recruitment | |
| Fewer than 5 years | 109 (38) |
| 5–10 years | 84 (29) |
| Over 10 years | 97 (33) |
| History of severe mental disorders (schizophrenia or bipolar disorder) 10 years prior to recruitment, n (%) | |
| Neither bipolar disorder nor schizophrenia | 52 (18) |
| Only bipolar disorder | 32 (11) |
| Schizophrenia | 206 (71) |

IQR interquartile range, SD standard deviation

^a Dichotomized using rounded median value

Hospitalization [1] and psychiatric hospitalization in particular [39] have been previously associated with subsequent non-adherence to antipsychotics among outpatients with schizophrenia. Our finding that psychiatric-related hospitalization was significantly associated with higher subsequent adherence among homeless patients is thus noteworthy, (albeit correlational), and consistent with a recent analysis involving homeless US veterans [14]. Hospitalization may provide the opportunity to establish important connections with service providers and community supports during a period of uninterrupted antipsychotic use, and the potential development of community

treatment orders, resulting in higher MPRs. Similar improvements in community stabilization may be attainable without hospital admission. For instance, participation in assertive community treatment programs was recently shown to be associated with higher levels of antipsychotic adherence among veterans with schizophrenia [40]. It is equally possible, however, that US Veterans and homeless citizens in Canada are uniquely able to access health benefits, and that these findings may not necessarily be generalizable to other contexts.

We found that long-acting injectable prescription was significantly associated with higher adherence to

Table 3 Associations between socio-demographic, homelessness-related, and illness factors with lower medication possession ratio (MPR) (<0.40; $n = 150$ vs ≥ 0.40 ; $n = 140$)

| Variables | Lower MPR (<0.40); ($n = 150$) Mean (SD)/ N (%) | Higher MPR (≥ 0.40); ($n = 140$) Mean (SD)/ N (%) | Crude odds ratio; 95 % confidence interval | Adjusted odds ratio; 95 % confidence interval |
|--|---|--|--|---|
| Age at recruitment (years) | 40.9 (10.5) | 42.1 (11.2) | 0.99 (0.97, 1.01) | 1.00 (0.96, 1.04) |
| Age of first homelessness (years) | 28.7 (13.1) | 32.4 (13.8) | 0.98 (0.96, 1.00)* | 0.99 (0.96, 1.02) |
| Women | 45 (30) | 37 (26) | 1.22 (0.73, 2.03) | 1.55 (0.83, 2.92) |
| Aboriginal | 21 (14) | 15 (11) | 1.36 (0.67, 2.75) | 0.78 (0.29, 2.06) |
| White | 81 (54) | 86 (61) | 0.74 (0.46, 1.18) | 0.57 (0.30, 1.08) |
| Incomplete high school | 90 (60) | 81 (59) | 1.06 (0.66, 1.69) | 0.82 (0.46, 1.48) |
| Single marital status | 101 (68) | 101 (73) | 0.81 (0.49, 1.35) | 0.78 (0.39, 1.54) |
| Lifetime duration of homelessness ^a (>3 years) | 84 (57) | 48 (35) | 2.43 (1.51, 3.93)* | 2.00 (1.07, 3.74)* |
| First recorded antipsychotic prescription prior to recruitment | | | | |
| <5 years | 71 (47) | 38 (27) | Reference | Reference |
| 5–10 years | 39 (26) | 45 (32) | 0.46 (0.26, 0.83)* | 0.61 (0.30, 1.23) |
| >10 years | 40 (27) | 57 (41) | 0.38 (0.21, 0.66)* | 0.76 (0.35, 1.66) |
| History of long-acting injectable antipsychotic prescription prior to recruitment | 34 (23) | 73 (52) | 0.27 (0.16, 0.45)* | 0.32 (0.16, 0.65)* |
| Primary ^b health services ^c (number in last 5 years prior to recruitment) | | | | |
| Low (≤ 100) | 75 (50) | 55 (39) | 1.53 (0.80, 2.90) | 3.31 (1.31, 8.37)* |
| Medium (101–300) | 50 (33) | 57 (41) | 0.98 (0.51, 1.90) | 1.68 (0.70, 4.01) |
| High (>300) | 25 (17) | 28 (20) | Reference | Reference |
| Substance use-related services (number in last 5 years prior to recruitment) | 21.9 (50.2) | 20.9 (51.3) | 1.00 (1.00, 1.01) | 1.00 (0.99, 1.01) |
| Psychiatric (including substance use-related) hospitalizations (number in last 5 years prior to recruitment) | 2.9 (4.6) | 5.8 (6.8) | 0.91 (0.86, 0.95)* | 0.95 (0.89, 1.00)* |
| Blood-borne infectious disease (HIV; hepatitis B/C) | 61 (41) | 34 (24) | 2.16 (1.30, 3.58)* | 2.45 (1.27, 4.72)* |
| Chronic medical conditions (3 or more) | 111 (74) | 91 (65) | 1.53 (0.93, 2.54) | 1.14 (0.60, 2.15) |

SD standard deviation

* $p \leq 0.05$

^a Median values (36 months) as a cutoff

^b Refers to non-psychiatric and non-substance related health services

^c The values 100 (45th percentile) and 300 (81st percentile) were used as cutoff point to dichotomize into low, medium, and high service use groups

antipsychotic regimens. This is important, given the recent call for pragmatic study designs to accurately demonstrate the advantages of injectable vs oral antipsychotics in naturalistic settings [20]. Long-acting injectables are reportedly underused [41], and particularly in Canada [42] where rates of use among outpatients are 6.3 % nationally and 12.5 % in British Columbia [43]. At 38 %, the prevalence of long-acting injectable prescriptions in our sample of homeless, mentally ill adults was considerably higher. This may be due, in part, to physician recognition that homeless patients face considerable barriers to medication adherence—even in the context of

full prescription coverage⁴—and/or that symptoms experienced by our homeless cohort were relatively severe. In the case of the latter, the significant association between receipt of long-acting injectable formulations and higher MPR may well be a function of confounding by indication. Further research is indicated to assess the potential contribution of long-acting injectables toward increased

⁴ Residents of British Columbia who are diagnosed with mental illness who demonstrate clinical and financial need are eligible for the provincial no-charge psychiatric medication plan. Income assistance recipients are also eligible for 100 % coverage of eligible prescription costs.

MPR among homeless people. Our results identified a significant relationship between lower rates of primary care engagement and lower antipsychotic MPRs. Efforts to bolster engagement of homeless mentally ill patients in community-based medical care may contribute to greater medication adherence.

Half of participants in our study cohort had received medical treatment for substance use disorder in the 5 years prior to recruitment. Previous studies have demonstrated a strong association between substance use and suboptimal adherence to antipsychotic medication [25, 28]. Contrary to these findings, substance use disorder was not significantly associated with antipsychotic adherence in the current analysis and, perhaps, overshadowed by the impact of homelessness, which introduces a range of difficulties that may account for low rates of antipsychotic adherence. In other words, it is possible that the added burden of substance use (which has been found to be predictive of low-adherence in non-homeless samples) was not significant here because of the burden imposed by homelessness itself. This interpretation is consistent with our finding that longer lifetime duration of homelessness was associated with low adherence to antipsychotic medication.

Diagnosis of blood-borne infectious disease was significantly associated with lower adherence to antipsychotic regimens. This finding is in keeping with previously published research from the parent study demonstrating a significant association between blood-borne infectious disease status and relatively low engagement with health services [44]. Better engagement of this subpopulation is needed for both treatment and prevention.

Finally, participants who reported being homeless longer than 3 years were more than twice as likely to be classified in the lower MPR group, suggesting that housing stability may be an important factor influencing antipsychotic adherence. Reciprocally, homelessness has been identified as a secondary consequence of non-adherence [45]. Plausibly, homelessness and poor adherence to antipsychotic medication contribute to a vicious circle perpetuating poor outcomes among the homeless and mentally ill.

Research conducted in the context of universal health care coverage found that when medications were publicly provided, socio-demographic factors (which were significant correlates of non-adherence in other—mostly American—studies) were no longer significantly related to antipsychotic adherence [29]. Economic factors may, therefore, play a key and even deciding role in determining the availability and regular use of medication. However, among homeless individuals, the removal of financial barriers to medication (as in our study) may be necessary but not sufficient to increase adherence. Our results indicate that despite 100 % drug coverage and abundant

pharmacies available to dispense antipsychotic medications, adherence was nevertheless very low. The provision of safe and stable housing may be crucial to long-term adherence, bringing structural supports, including storage, safety, and the opportunity to maintain a routine.

Our findings indicate that adherence to antipsychotic prescriptions among homeless individuals is significantly influenced by several potentially modifiable risk factors. Targeted action aimed at increasing engagement with primary health care providers, coordination of community-based care and supports, and greater use of long-acting injectable formulations may be beneficial. In addition to these clinically focused interventions, strategies to end homelessness for this population may represent the greatest opportunity to improve adherence to antipsychotic medication.

Some limitations of this study should be considered. Our design did not include all potential correlates of antipsychotic adherence (e.g., level of cognitive deficit), and our analysis was not able to account for potential (albeit unlikely) periods of remission during the period of observation. Furthermore, our use of ICD codes did not provide us with measures of symptom severity, and due to our assumption that continuous prescription of antipsychotics would be indicated for all members of the cohort, our analysis is potentially limited by any off-label antipsychotic use that may have been prescribed among the 18 % of participants who had not been diagnosed with either schizophrenia or bipolar disorder.

Moreover, while the MPR is a useful measure of adherence to prescribed medication, it likely reflects the upper limit of medication ingestion. Although BC PharmaNet data have previously been shown to accurately reflect medication adherence [31], results of the existing validation studies based on general outpatient samples may not generalize to homeless individuals. It is, therefore, possible that actual adherence within our homeless sample was overestimated using pharmacy-based measures. Furthermore, due to the non-normality of the MPR data and the small cell values in each MPR group, we analyzed this outcome variable using a binary measure, resulting in some loss of power and precision.

Both homelessness variables included in our analyses (i.e., age at first homelessness and duration of homelessness) were based on participant self-report and are subject to recall and/or reporting bias. However, recent analyses examining the accuracy of self-reported service use (i.e., health, justice, and income assistance) among members of the Vancouver At Home cohort revealed high levels of concordance between administrative records and self-report spanning up to 5 years [46]. Our analyses are also subject to possible exclusions and/or classification and coding errors associated with the creation of administrative databases. Furthermore, the correlational nature of our analyses does not address causal

relationships between homelessness, other risk factors, and adherence to antipsychotic medication regimens. As previously suggested, the significant association found between long-acting injectable formulations and higher MPR may reflect confounding by indication, and needs to be further examined.

To the best of our knowledge, this study is the first epidemiological analysis of antipsychotic prescription adherence using comprehensive administrative prescription records within a homeless cohort. It is also among the first analyses to examine correlates of adherence to prescription medication among homeless people. Strengths of this research include use of a sample selected on the basis of longstanding homelessness and serious mental illness, and the linkage of population-level data spanning a 15-year observation period in the context of comprehensive drug coverage.

Antipsychotic medication is an essential component in the treatment of serious mental illness. Our findings suggest that homeless individuals may be at risk for particularly low rates of adherence to prescribed antipsychotic regimens spanning many years, and thus to worsening illness. Our results indicate that important correlates of antipsychotic adherence among homeless people are modifiable, and may be effectively addressed using targeted and coordinated community-based care and supports. Research is needed to prospectively investigate the impact of interventions to improve adherence to antipsychotic medication among homeless people with serious mental illness.

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Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest. All authors declare that the submitted work has not been published before, and that the work is not under consideration for publication elsewhere.

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