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# High-intensity cannabis use is associated with retention in opioid agonist treatment: a longitudinal analysis

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## Abstract

**Background and Aims:** Cannabis use is common among people on opioid agonist treatment (OAT), causing concern for some care providers. However, there is limited and conflicting evidence on the impact of cannabis use on OAT outcomes. Given the critical role of retention in OAT in reducing opioid-related morbidity and mortality, we aimed to estimate the association of at least daily cannabis use on the likelihood of retention in treatment among people initiating OAT. As a secondary aim we tested the impacts of less frequent cannabis use.

**Design:** Data were drawn from two community-recruited prospective cohorts of people who use illicit drugs (PWUD). Participants were followed for a median of 81 months (interquartile range: 37–130).

**Setting:** Vancouver, Canada.

**Participants:** 820 PWUD (58% men, 59% of Caucasian ethnicity, 32% HIV-positive) initiating OAT between December 1996 and May 2016. The proportion of women was higher among HIV-negative participants, with no other significant differences.

**Measurements:** The primary outcome was retention in OAT, defined as remaining in OAT (methadone or buprenorphine/naloxone-based) for two consecutive six-month follow-up periods. The primary explanatory variable was cannabis use (at least daily versus less than daily) during the same six-month period. Confounders assessed included: socio-demographic characteristics, substance use patterns and social-structural exposures.

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**Competing interests:** The University of British Columbia has received unstructured funding from NG Biomed, Ltd., an applicant to the Canadian federal government for a licence to produce medical cannabis, to support M-JM.

**Findings:** In adjusted analysis, at least daily cannabis use was positively associated with retention in OAT (Adjusted Odds Ratio = 1.21, 95% Confidence Interval: 1.04–1.41). Our secondary analysis showed that compared with non-cannabis users, at least daily users had increased odds of retention in OAT (AOR = 1.20, 95% CI: 1.02 – 1.43), but not less than daily users (AOR = 1.00, 95% CI: 0.87 – 1.14).

**Conclusions:** Among people who use illicit drugs initiating opioid agonist treatment in Vancouver, at least daily cannabis use was associated with approximately 21% greater odds of retention in treatment compared with less than daily consumption.

### Keywords

cannabis; opioid agonist treatment; opioid use disorder; methadone; buprenorphine; cannabinoid

## Introduction

Globally, it is estimated that there were approximately 15.5 million individuals with an opioid use disorder (OUD) in 2010, an increase of five million people from 1990 (1), and the burden of disease continue to rise (2). Particularly, the substantial rise in the non-medical use of prescription opioids and heroin in the past decade, alongside the increasing contamination of the illicit drug supply with powerful synthetic analogues such as illicitly manufactured fentanyl, has resulted in an escalating crisis of opioid-related morbidity and mortality in many settings (2–4). Nowhere is this more clear than North America, where fatal opioid overdose is now a leading cause of death (3, 5).

Untreated OUD is increasingly recognized as one of the major drivers of the opioid overdose emergency (6–8). Unfortunately, despite effective therapies, such as buprenorphine/naloxone and methadone (i.e., opioid agonist treatment [OAT]), coverage of OAT programs remains low in many settings (9). Additionally, among those who access OAT, only a minority are retained on treatment, with some studies documenting six-month retention rates as low as 20% (10, 11). This is concerning as discontinuation from OAT has been associated with increased mortality risk (7). Therefore, there is an urgent public health need to identify barriers and facilitators to OAT uptake and retention.

Accumulating evidence supports the use of cannabis-based therapies for a number of health conditions (12). Among potential medical uses of cannabis, preclinical-, clinical- and population-level data suggest a potential role for cannabis/cannabinoids as substitutes for opioids for pain management, with studies documenting associations between cannabis use or medical and adult-use cannabis laws with significant reductions in opioid analgesic use and related harms (e.g., fatal overdose) (13–20).

Considerably less attention has been paid, though, to the potential therapeutic use of cannabis in the context of the treatment of OUD, for example as an adjunct therapy to OAT (13). Although pre-clinical data indicate that some cannabinoids may reduce opioid withdrawal, craving, and other symptoms common among OUD populations (16, 21), evidence from human studies is equivocal, with studies showing beneficial, negative or no impact of cannabis use on OAT outcomes (22–26). Despite this limited and conflicting

evidence, many OAT programs require abstinence from cannabis and other drugs as a sign of stability (e.g., to be eligible for take-home dosing privileges) (23, 24, 27). Given the urgent need to identify novel effective strategies to address the ongoing opioid crisis in North America, and in the context of increasing availability of cannabis (through both medical and adult-use laws) it is critical to better understand the impacts of cannabis use on OAT outcomes—including its potential therapeutic potential. Therefore, the aim of the present study was to (1) estimate the relationship between at least daily cannabis use and retention in treatment among people initiating OAT in Vancouver, Canada, a setting with *de facto* decriminalization of cannabis use (28). As a secondary aim we tested the impacts of less frequent cannabis use. Although the utility of retention in treatment as outcome measure for other substance use disorders has been questioned (29, 30), we decided to focus on retention in OAT given its consistent association with decreased all-cause and overdose mortality risk (7), and other beneficial outcomes in the context of OUD (10).

## Methods

### Design and sample

In light of recent findings from this research group on the cannabis decriminalization and outcomes from HIV treatment (28), as well as possible links between cannabis use and the use of other substances (31), we developed the current study to estimate the effect of cannabis use on engagement in OAT. The study hypothesis and analytic approach were developed by two authors (ES and M-JM) in consultation with study statisticians (SL and HS). The planning of the analysis preceded looking at the data.

We used data from two harmonized and ongoing prospective community-recruited cohorts of adult PWUD in Vancouver, Canada, a setting with low-barrier OAT, to investigate the longitudinal relationship between cannabis use and retention in OAT. The analytic sample was restricted to participants who initiated or re-initiated OAT (i.e., methadone or buprenorphine/naloxone maintenance therapy) after recruitment into the cohorts, and had at least one follow-up visit after OAT initiation between December 1, 1996 and May 31, 2016. We decided to restrict the study sample to only incident OAT starts to avoid biasing the results with the inclusion of participants who have been long stabilized in OAT. Participants with missing responses to the main outcome (i.e., retention in OAT) or main explanatory variable of interest (i.e., frequency of cannabis use) were also excluded. We considered baseline as the first observation in which enrolment in an OAT program was reported.

### Study setting

British Columbia (BC)’s OAT program was established in 1996, with a low-threshold model that resulted in a rapid expansion of enrollment from less than 3,000 clients in 1996 to more than 19,000 in 2016 (32–34). Specifically, under this model, OAT pharmacotherapies are typically prescribed by primary care physicians and dispensed through community-based pharmacies, health care facilities and correctional institutions. Medical care and pharmacotherapies are fully publicly funded for low-income residents, while individuals not eligible for this benefit have to pay a proportion of the cost of medications either through private or work insurance plans or out-of-pocket (33).

During the study period, methadone was the most accessible OAT in BC. Buprenorphine/naloxone was introduced in the provincial drug formulary in 2010, but until 2015 it was only covered for individuals with previous unsuccessful attempts or contraindications to methadone (32). By 2016, still over 80% of individuals on OAT in the province were receiving methadone (32).

## Data sources and procedures

The Vancouver Injection Drug Users Study (VIDUS) and the AIDS Care Cohort to Evaluate exposure to Survival Services (ACCESS) are sister cohorts of PWUD in Vancouver. VIDUS consists of HIV-negative adults (i.e., ≥ 18 years old) who injected drugs in the month prior to enrolment; and ACCESS of HIV-positive adults who used illicit drugs (other than or in addition to cannabis) in the previous month. Since December 1996 more than 2,500 PWUD have been enrolled through snowball sampling and extensive street outreach in the greater Vancouver region.

Study procedures for both cohorts are harmonized to allow for pooled analyses and have been described in detail previously (35, 36). In brief, after providing informed consent, at baseline and semi-annually thereafter, participants complete a semi-structured interviewer-administered questionnaire, undergo HIV and hepatitis C (HCV) testing and HIV clinical monitoring as appropriate. The questionnaire elicits information on socio-demographics, drug use patterns, healthcare utilization, and other relevant social-structural exposures. Participants receive a $30 honorarium at each study visit. The VIDUS and ACCESS studies have received approval by the University of British Columbia/Providence Health Care Research Ethics Board.

## Measures

Our main outcome of interest was retention in OAT. At each semi-annual visit, participants are asked if they are in any kind of drug or alcohol treatment; and for those replying “yes” they are asked to further specify the type of treatment. Retention in OAT was defined as a self-report of being on methadone or buprenorphine/naloxone-based treatment in the current and immediately previous follow-up interview, approximately a six-month retention interval. In the event of missing information for the immediately previous interview (e.g., if the participant had missed the previous study visit) a participant was considered as not retained in OAT. The primary explanatory variable was the frequency of cannabis use in the six-month period prior to the interview, assessed with the following question: “In the last six months, how often have you used marijuana?”. Possible response options included: no use, less than once a month, 1–3 times a month, about once a week, 2–3 times a week, and ≥ daily. We chose to dichotomize cannabis exposure at ≥ daily vs. < daily to be consistent with the measure employed in previous analyses of OAT outcomes (37, 38), as well as because daily use might more likely reflect self-medication use (26). Of note, measurements of cannabis use and involvement in OAT were asked in different parts of the interview.

We also considered covariates that, based on a review of prior literature, were hypothesized to potentially confound the relationship between cannabis use and retention on OAT (39). These included socio-demographic characteristics, such as age (per year older), sex (male

vs. female), ethnicity (Caucasian vs. non-Caucasian) and educational attainment (≥ high school diploma vs. < high school diploma); substance use patterns, including illicit substance (e.g. ≥ daily vs. < daily heroin injection, cocaine injection, prescription opioid use, crack use) and alcohol use (>4 vs. ≤4 drinks/day); and social-structural exposures (e.g., homelessness, incarceration). Socio-demographic variables were time-fixed at baseline, while substance use-related and social-structural exposures were time-updated, and refer to the six-month period prior to the interview.

### Statistical analyses

As a first step, we examined characteristics of study participants stratified by ≥ daily cannabis use at baseline. Categorical variables were analyzed using the Pearson's chi-squared test (or Fisher's exact test in the presence of small cell counts) and continuous variables were analyzed using the Wilcoxon rank sum test. Next, we estimated the bivariable relationships between the primary explanatory variable (i.e., daily cannabis use) and all other covariates with retention on OAT. We used generalized linear mixed-effects modeling with a logit-link function to account for repeated measurements from the same participants over time. Finally, to estimate the independent effect of ≥ daily cannabis use on retention on OAT, we fit a multivariable model using an *a priori* model fitting approach described by Maldonado and Greenland (40), that we have used extensively in previous research (41, 42). Starting with a full model containing our primary explanatory variable, and covariates that were associated with the outcome in bivariable analyses at a p-value <0.10, we constructed reduced models in a stepwise manner, removing the covariate that resulted in the smallest relative coefficient change for cannabis use. This iterative process was continued until the minimum relative change exceeded 5%. The remaining variables were considered as confounders in the multivariable analysis. In addition, variables representing calendar year of the interview and cohort membership (i.e., HIV serostatus) were forced into the multivariable model to control for cohort effect and possible heterogeneity across cohorts.

To test the robustness of our analyses we conducted two sensitivity analyses. First, to further investigate the hypothesized causal relationship between time-varying cannabis use and retention in OAT, we replicated the analysis using another statistical approach. Specifically, we built marginal structural models with inverse probability of treatment weights (IPTWs). This statistical approach allows for the handling of time-varying variables that are simultaneously confounders of the outcome of interest and are also affected by previous treatment, and can also adjust for the non-random assignment of the treatment (43). Second, to further explore a potential dose-response of cannabis use on OAT retention, we conducted a sub-analysis using a three-level cannabis use variable: no use, <daily use, ≥daily use. All analyses were conducted using R studio (Version 3.2.4) (44), and all p-values were two-sided.

## Results

Between December 1, 1996 and May 31, 2016, 2,679 individuals were recruited into the ACCESS and VIDUS cohorts, of whom 636 (23.7%) reported being in an OAT program at their first study visit. Of the 938 (35.0% of the parent cohorts) participants who reported

initiating or reinitiating OAT during follow-up, 118 (12.6%) were excluded (68 had no additional follow-up interview and 50 had missing data for the outcome and/or primary explanatory variable), resulting in a final analytic sample of 820 participants (87.4% of eligible participants). Characteristics of included and excluded participants, as well as those ineligible (participants on OAT at the time of recruitment into the cohorts) are presented in the supplementary material (Table S1). Of note, compared to include participants, those excluded were more likely to be homeless (36.4% vs. 22.8%, p=0.001, but less likely to inject heroin on a daily basis (33.1% vs. 43.9%, p= 0.024) than those included. Ineligible participants were older, more likely to be of Caucasian ethnicity (72.2% vs. 59.4%, p<0.001), less likely to report daily heroin injection (25.3% vs. 43.9%, p<0.001), as well as less likely have been recently incarcerated (11.2% vs. 23.7%, p<0.001). No other significant differences were found, including on frequency of cannabis use.

The median observation period per participant was 81 months (interquartile range [IQR]: 37–130), resulting in a total of 9,284 person years of follow-up. Just over half of participants initiated OAT between 1996–2005 (n=433, 52.8%), and almost all started methadone (n=815, 99.4%). Overall, 6-month, 12-month and 18-month OAT retention rates were 52.6%, 38.5%, and 31.5%, respectively. Of these, the majority started methadone maintenance treatment. Baseline characteristics of the study sample, stratified by ≥ daily cannabis use, are presented in Table 1. The median age of the study sample was 38 years (IQR 30–45), 474 (57.8%) were male, and 264 (32.2%) were HIV-positive. The proportion of women was higher among HIV-negative participants, with no other significant differences between the two cohorts. At the time of OAT initiation, 360 (43.9%) participants reported daily heroin injection, 65 (7.9%) daily prescription opioid use, and approximately half (398, 48.5%) cannabis use, of whom 139 (17.0% of the study sample) were daily cannabis users. As shown in Table 1, frequent cannabis users at baseline were more likely to be younger and male, and less likely to have been recently incarcerated (all p<0.05). Over the study period, the mean proportion of participants reporting daily cannabis use was 17.6% (95% CI 16.0–19.1). Additionally, of a total of 10,850 observations, 5,767 (53.2%) were characterized by retention in OAT, and 2,007 (18.5%) by ≥ daily cannabis use.

As indicated in Table 2, in unadjusted analysis, ≥ daily cannabis users had increased odds of being retained on OAT (Odds Ratio = 1.20, 95% Confidence Interval [CI]: 1.03–1.39). The positive association between ≥ daily cannabis use and retention on OAT remained after adjusting for potential confounders (Adjusted Odds Ratio [AOR] = 1.21, 95% CI: 1.04 – 1.41).

A sensitivity analysis using marginal structural modelling resulted in a positive and significant association between ≥ daily cannabis use and retention in OAT, with an effect measure larger than the main analysis (AOR = 1.42, 95% CI: 1.23 – 1.63). The second sensitivity analysis using a three-level cannabis use variable indicated that compared to non-cannabis users, ≥ daily users had increased odds of retention in OAT (AOR = 1.20, 95% CI: 1.02 – 1.43), but not < daily users (AOR = 1.00, 95% CI: 0.87 – 1.14).

## Discussion

The present study found that individuals initiating OAT were approximately 21% more likely to be retained in treatment at six months if they reported ≥ daily use of cannabis. This finding persisted after adjustment for a range of confounders, including high-intensity concurrent use of other substances and relevant social-structural exposures (e.g., homelessness).

To our knowledge, this is the first study to find a positive correlation between high-intensity cannabis use and retention in treatment among people initiating OAT. Four previous studies have examined the potential impacts of cannabis use on OAT retention, primarily examining methadone maintenance treatment. Three found no association (23, 24, 45), and two a negative effect (26, 46). A possible explanation for these mixed findings may relate to differences in programmatic requirements for OAT related to cannabis use (e.g., elimination of carry privileges if cannabis use is documented), which in turn may lead to treatment drop-out. Alternatively, the discrepancy in findings between our study and others may reflect differences in study populations and details about the cannabis used, which can vary widely in potency and composition (e.g., ratio of major cannabinoids), as well as to how cannabis use was measured. In particular, while all of the previous studies evaluating cannabis use as a potential predictor of retention in OAT assessed in-treatment rates of cannabis use, our study is the first to specifically investigate the time-varying relationship between periods of cannabis use and retention in OAT. For example, a recent study conducted in Ontario, Canada, found that among patients initiating methadone maintenance therapy, heavy cannabis use during the first year of OAT was associated with higher risk of treatment drop-out (26). However, the definition of heavy use (>75% of available urines positive for THC) in this study was limited as the number of urine samples could be as low as five, did not consider frequency of use (e.g., THC can remain detectable in urine for long periods of time) nor its temporal relationship with discontinuation of treatment. Interestingly, prior research in the context of naltrexone-based treatment for OUD did find a positive association between intermittent cannabis use and retention in treatment (22, 47). The reasons as to why our results are more congruent with findings in the context of antagonist-based for OUD remain unclear, and deserve further evaluation.

Accumulating preclinical and clinical data lend support to a potential therapeutic role of cannabinoids cannabis in the context of OUD treatment. For example, a number of experimental animal studies have demonstrated that THC, the main psychoactive component of cannabis, may be effective in decreasing the severity of opioid withdrawal symptoms (16, 48, 49). This potential of THC for the treatment of acute opioid withdrawal has subsequently been suggested in small clinical trials using dronabinol (i.e., oral capsules of synthetic THC) (22, 50). However, some concerns regarding dose-related side effects, including cardiovascular and psychoactive effects, also arose in these studies which may limit the clinical utility of dronabinol in this context (50, 51). In rat models, cannabidiol (CBD, a non-intoxicating phytocannabinoid) has also been found to attenuate withdrawal symptoms (52) and cue-induced heroin-seeking behavior, with long lasting effects (21, 53). In line with findings from animal studies, preliminary data in humans also suggest that CBD may be effective in reducing cue-induced heroin craving, and anxiety among opioid-dependent

individuals, with protracted effects of up to seven days (25). Importantly, human studies have also indicated a good safety profile and tolerability of CBD (54), even when co-administered with low doses of opioids (e.g., fentanyl) (55). In addition, CBD has also shown promising anxiolytic and antipsychotic properties, which may be relevant in the context of OUD (56). Collectively, these findings provide a rationale to further explore cannabinoids, and in particular CBD or CBD/THC combinations, as an adjunctive treatment to OAT to potentially help manage cravings or other common symptoms among people with OUD and therefore optimize treatment outcomes (13, 53).

Finally, the use of cannabis as a substitute for other potentially more harmful substances, such as crack cocaine or alcohol, may further contribute to explain higher odds of OAT retention among daily cannabis users in the present study. For example, a previous study conducted in Vancouver found significant declines in crack use among those self-medicating with cannabis (31). Studies among medical cannabis patients also suggest a potential harm reduction role of cannabis in the context of problematic alcohol use (57, 58).

This study has limitations. First, the study sample was not randomly selected, and therefore findings from this study may not be generalizable to individuals starting OAT in Vancouver or other settings. Similarly, given that the majority of study participants were enrolled in methadone maintenance therapy, results for the buprenorphine/naloxone context should be taken with caution. It could be the case that cannabis may be more effective in mitigating side effects or pain management in the context of methadone maintenance therapy, but not for buprenorphine/naloxone. As buprenorphine/naloxone becomes a preferred first-line treatment option for OUD in Canada and elsewhere, future research should seek to confirm whether the beneficial effect of daily cannabis use on treatment retention is also observed when only buprenorphine/naloxone clients are considered. Second, since we used observational data, where the exposure of interest (i.e., daily cannabis use) was not randomly assigned we cannot exclude the possibility that the observed positive association between ≥daily cannabis use and retention in OAT is the result of unmeasured confounding. However, this beneficial effect of cannabis persisted after the adjustment for a range of behavioral and structural confounders, and resulted in an even larger effect when using marginal structural modelling. In addition, we have no reason to believe that differential reporting of OAT status based on cannabis use likely occurred. Third, our main outcome measure and explanatory variable relied on self-reported data, which may be prone to responses biases. However, previous research has indicated PWUD's reports of drug use and addiction treatment to be reliable (59, 60). Fourth, the definition of our outcome measure (retention in OAT) was based on participant's reports at two-time points, and therefore it may not be representative of engagement with OAT during the entire period between these two points. Finally, our survey instrument did not collect information on the type and composition of cannabis used, mode of administration, or purpose of use. Therefore, we cannot attribute the observed association to a specific cannabinoid(s), dose, mode of administration, or intended therapeutic use of cannabis. Further research to describe the composition of cannabis used, in particular the ratio of THC to CBD and presence of other cannabinoids, as well as dosing strategies, is ongoing and could illuminate potential patterns of therapeutic use. The imminent legalization and regulation of the production, sale, and use

of non-medical cannabis by adults in Canada will offer an unprecedented opportunity to investigate these aspects of cannabis use in much greater depth.

In summary, this longitudinal study found that periods of ≥ daily cannabis use were associated with being retained in OAT among individuals starting OAT in Vancouver, Canada. Given the well-known mortality risk reduction benefit of sustained engagement in OAT, findings from the present study alongside prior research evidence support the urgent need for clinical research to evaluate the therapeutic potential of cannabinoids as adjunctive treatment to OAT to address the escalating opioid-overdose epidemic.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1.**

Baseline characteristics of 820 people who use drugs and initiated opioid agonist treatment during follow-up, stratified by ≥ daily cannabis use, Vancouver, Canada (1996-2016)

| Characteristic | Total, n (%) (*N* = 820) | ≥Daily cannabis use, n (%)* | | *p* - value |
|---|---|---|---|---|
| | | Yes (*n* = 139) | No (*n* = 681) | |
| **Socio-demographics** | | | | |
| Age (med, IQR) | 38 (30–45) | 35 (29–42) | 39 (31–46) | 0.006† |
| Male gender | 474 (57.8) | 93 (67.0) | 381 (56.0) | 0.017 |
| Caucasian ethnicity | 487 (59.4) | 89 (64.0) | 398 (58.4) | 0.222 |
| ≥High school education | 542 (66.1) | 93 (66.9) | 449 (65.9) | 0.998 |
| HIV positive | 264 (32.2) | 46 (33.1) | 218 (32.1) | 0.804 |
| **Substance use-related factors*** | | | | |
| ≥Daily heroin injection | 360 (43.9) | 57 (41.0) | 303 (44.5) | 0.426 |
| ≥Daily prescription opioid use | 65 (7.9) | 15 (10.8) | 50 (7.3) | 0.175 |
| ≥Daily cocaine injection | 160 (19.5) | 29 (20.9) | 131 (19.2) | 0.659 |
| ≥Daily crack use | 228 (27.8) | 45 (32.3) | 183 (26.9) | 0.170 |
| Heavy alcohol use | 332 (40.5) | 62 (44.6) | 270 (39.6) | 0.284 |
| **Social-structural factors*** | | | | |
| Homeless | 187 (22.8) | 27 (19.4) | 160 (23.5) | 0.293 |
| Incarceration | 194 (23.7) | 23 (16.5) | 171 (25.5) | 0.030 |
| **Calendar year of OAT initiation** | | | | |
| 1996-2000 | 201 (24.5) | 15 (10.8) | 186 (27.3) | |
| 2001-2005 | 232 (28.3) | 59 (42.5) | 173 (25.4) | |
| 2006-2010 | 218 (26.6) | 27 (19.4) | 191 (28.1) | |
| 2011-2016 | 169 (20.6) | 38 (27.3) | 131 (19.2) | |

OAT, opioid agonist therapy

*Refers to the 6-month period prior to OAT initiation

†Wilcoxon rank sum test

**Table 2.**

Unadjusted and adjusted generalized linear mixed-effects analyses of the association between ≥daily cannabis use and retention in opioid agonist treatment, Vancouver, Canada (1996-2016)

| | Unadjusted | | Adjusted‡ | |
|---|---|---|---|---|
| **Variable** | **Odds Ratio (95% CI)** | ***p* - value** | **Odds Ratio (95% CI)** | ***p* - value** |
| **Primary variable of interest** | | | | |
| ≥Daily cannabis use * | 1.20 (1.03 – 1.39) | 0.016 | 1.21 (1.04 – 1.41) | 0.014 |
| **Covariates** | | | | |
| Age (per year older) | 1.08 (1.07 – 1.09) | <0.001† | 1.05 (1.04 – 1.06) | <0.001 |
| Male gender | 0.96 (0.77 – 1.21) | 0.755 | | |
| Caucasian ethnicity | 1.37 (1.09 – 1.73) | 0.007† | | |
| ≥High school education | 0.93 (0.80 – 1.10) | 0.411 | | |
| HIV positive | 1.62 (1.30 – 2.03) | <0.001† | | |
| ≥Daily heroin injection * | 0.22 (0.19 – 0.25) | <0.001† | 0.25 (0.22 – 0.29) | <0.001 |
| ≥Daily prescription opioid use * | 0.33 (0.27 – 0.42) | <0.001† | 0.37 (0.29 – 0.47) | <0.001 |
| ≥Daily cocaine injection * | 0.64 (0.55 – 0.75) | <0.001† | | |
| ≥Daily crack use * | 0.90 (0.80 – 1.02) | 0.098† | | |
| Heavy alcohol use * | 1.11 (0.99 – 1.24) | 0.062† | 1.13 (1.00 – 1.26) | 0.047 |
| Homeless * | 0.50 (0.43 – 0.57) | <0.001† | | |
| Incarceration * | 0.48 (0.41 – 0.55) | <0.001† | | |
| Calendar-year of OAT initiation | 0.96 (0.94 – 0.98) | <0.001† | | |

OAT, opioid agonist therapy

Level of heterogeneity between cohorts: p=0.0268

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

†p<0.10 in the unadjusted analyses and considered for inclusion in the multivariable model

‡Only the variables included in the final multivariable confounder model are presented in this column