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Canadian Addiction Treatment Centre (CATC) opioid agonist treatment cohort in Ontario, Canada

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ABSTRACT

Purpose The Canadian Addiction Treatment Centre (CATC) cohort was established during a period of increased provision of opioid agonist treatment (OAT), to study patient outcomes and trends related to the treatment of opioid use disorder (OUD) in Canada. The CATC cohort's strengths lie in its unique physician network, shared care model and event-level data, making it valuable for validation and integration studies. The CATC cohort is a valuable resource for examining OAT outcomes, providing insights into substance use trends and the impact of service-level factors.

Participants The CATC cohort comprises 32 246 people who received OAT prescriptions between April 2014 and February 2021, with ongoing tri-annual updates planned until 2027. The cohort includes data from all CATC clinics' electronic medical records and includes demographic information and OAT clinical indicators.

Findings to date This cohort profile describes the demographic and clinical characteristics of patients being treated in a large OAT physician network. As well, we report the longitudinal OAT retention by treatment type during a time of increasing exposure to a contaminated dangerous drug supply. Notable findings also include retention differences between methadone (32% of patients at 1 year) and buprenorphine (20% at 1 year). Previously published research from this cohort indicated that patient-level factors associated with retention include geographic location, concurrent substance use and prior treatment attempts. Service-level factors such as telemedicine delivery and frequency of urine drug screenings also influence retention. Additionally, the cohort identified rising OAT participation and a substantial increase in fentanyl use during the COVID-19 pandemic.

Future plans Future research objectives are the longitudinal evaluation of retention and flexible modelling techniques that account for the changes as patients are treated with OAT. Furthermore, future research aims are the use of conditional models, and linkage with provincial-level administrative datasets.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The Canadian Addiction Treatment Centre cohort is a large observational cohort in Canada designed to retrospectively examine opioid agonist treatment (OAT).
⇒ It is based on a network of OAT physicians that share a common care delivery model and electronic medical record.
⇒ The cohort is structured as event-level data on addiction medicine clinical interactions featuring unique identifiers and opportunities to link the clinical data to provincial administrative datasets for monitoring the integration between acute and community-based services.
⇒ Selection bias is a limitation of observational data, however, matched controls and linked data can be used to mitigate this limitation since patients are seen in routine care.
⇒ Unmeasured factors such as concurrent disorders, homelessness history, mental health diagnoses, psychosocial elements and other unknown and unmeasured factors may confound the link between OAT outcomes and the measured contributing characteristics.
⇒ In this observational real-world study, medication choice was determined by clinical factors and patient preference.
⇒ Differences in patient retention may be influenced by observed and unobserved factors since the medication was not randomly allocated or assigned.

INTRODUCTION

Opioid use and subsequent dependence have led to an increase in opioid-related harms in the last decade.[1–3] This increase in opioid use has resulted in the highest number of opioid poisoning deaths ever recorded in Canada.[4] Canada has experienced approximately 20 opioid-related fatalities per day, a notable increase from 12 per day in 2018 and 8 per day in 2016.[4] Ontario, the largest province in Canada, with 37% (14.2 million out of 38.3 million) of the total Canadian population, has also experienced a rise in opioid-related deaths. These fatalities have been attributed to the contamination of the drug supply with synthetic opioids.[5 6] The annual rate of opioid toxicity incidents in Ontario increased from 5.4 deaths per 100 000 people in September 2019 to 19.6 deaths per 100 000 people in September 2021.[7]

People with opioid use disorder (OUD) are among the most exposed to the contaminated

drug supply. In contrast, opioid agonist treatment (OAT), which includes methadone and buprenorphine/naloxone, is currently the most effective, evidence-based approach for treating OUD.[8–11] OAT effectively reduces cravings and withdrawal symptoms enabling patients to achieve physical, mental and emotional stability.[9] Prolonged and sustained engagement with OAT is associated with a reduced likelihood of overdoses, mortality and infections such as hepatitis C virus (HCV) and HIV.[12–14] Consequently, OAT is associated with lowered healthcare costs and improved overall quality of life.[9 15 16] Nevertheless, re-initiation following treatment discontinuation is common among OAT patients, resulting in fluctuations in opioid tolerance and an elevated risk of overdose and mortality.[17] Since people with OUD on OAT have a statistically significantly lower risk of mortality compared with people with OUD off OAT,[6] retention on OAT is one of the important[6] interventions providing a crucial protective mechanism for mortality risk during a public health opioid overdose crisis.[6 18 19]

In a Canadian population with universal single-payer healthcare coverage, we have created a cohort of patients with a history of OAT. This data collection was started in collaboration with the Canadian Addiction Treatment Centre (CATC), the largest multisite physician practice organisation dedicated to addressing OUD in Canada. The primary research aim was to measure trends over time in the quality of care and patient outcomes. The CATC offers OAT at 70 clinics across Ontario, until 2021, and a 2024 cohort update will add new clinical sites in British Columbia and New Brunswick. These clinics adhere to standardised policies, ensuring consistency among physicians delivering OAT.[20] The CATC has established a shared standardised electronic medical record (EMR) and a set of uniform practices. This comprehensive database provides a platform for the assessment of specialised addiction treatment within a network of care providers.

COHORT DESCRIPTION

The cohort contains 32 246 people who received at least one prescription for OAT, defined as having filled a prescription for buprenorphine/naloxone or methadone, from April 2014 to February 2021. Tri-annual updates are scheduled to continue until 2027. The study used medical records from all patients who received OAT at any CATC location in Ontario. Ontario operates a single-payer healthcare system that offers residents identical healthcare benefits through the Ontario Health Insurance Plan.[21] Moreover, residents have universal, cost-free access to care associated with OAT, which is funded by public insurance, but medications are not universally covered in Ontario.[21] CATC provides care to patients with substance use disorders including pharmacological therapy, primary healthcare, harm reduction and counselling at select clinics. Standardised practices, policies and operational procedures are followed across all clinics within the organisation including urine drug screening (UDS), HCV screening and treatment and OAT. CATC treatment centres also provide naloxone training and kit distribution, and an on-site pharmacy for observed dosing at select locations.[20] The study was created and designed by a multidisciplinary group of researchers at the Northern Ontario School of Medicine University in collaboration with the Canadian Addiction Treatment Centre, partnering and various stakeholders including physicians, nurses, healthcare systems, policymakers, governmental agencies and professional societies. Our research team has a data-sharing agreement with the CATC, from whom we receive the data. The patients provided informed consent to participate in the research cohort at their baseline. Patients who did not consent to inclusion in the research cohort were excluded from the data abstraction. Participant data were de-identified and, aggregated for analysis to remove direct patient health information. All research findings are reported with minimum cell sizes of 9, to mitigate the risk of re-identification.

What has been measured?

Patient demographics

Individual patient variables were measured at cohort baseline entry and clinical variables were measured at cohort entry and subsequent follow-up. Individual patient variables include age, sex (male or female or X), location of residence, index of remoteness and the Ontario Marginalisation Index. The Ontario Marginalisation Index is a continuous composite measure derived from the patient postal code. It is scored on a scale from 0 to 5, representing four domains of marginalisation, including economic, ethnic-racial-ethnic-racial, age-based and social marginalisation. Higher values, approaching 5, indicate a higher level of marginalisation and are based on scores from these four domains:

1. Households and dwellings: includes indicators that measure types and density of residential accommodations, and certain family structure characteristics, such as per cent living alone and per cent dwellings not owned.[22]
2. Material resources: includes indicators that measure access to, and attainment of basic material needs, such as per cent unemployment and per cent without a high school degree.
3. Age and labour force: includes indicators to describe the percentage of seniors (aged 65+ years), the dependency ratio (the ratio of seniors and children to the population aged 15–64 years) and the percentage not participating in the labour force.
4. Racialised and newcomer populations: includes indicators to describe per cent recent immigrants and per cent who self-identify as a 'visible minority' (as defined by Statistics Canada)[22] and Local Health Integration Network (LHIN).[23]

The Ontario Marginalisation Index is publicly available data in Ontario.[22] We linked these data within the CATC cohort to measure the social determinants of health among an OUD population receiving OAT.

Geographic variations were measured using LHINs, which are regional health authorities responsible for the regional administration of public healthcare services in Ontario. Ontario had 14 LHINs that administered hospital-based and community-based services to all residents within their geographical boundaries, northern geographic indicators were defined as patient residence in LHIN 13 or 14[23] (online supplemental file 1). From the postal code of residence, an index of remoteness was calculated using the 2021 census values, the index of remoteness is an approximate percentile score with 0 being the most urban and 100 being the most remote.[24]

OAT clinical indicators

Key measures of longitudinal follow-up of OAT indicators include OAT medication (methadone or buprenorphine/naloxone), dosing, carry level and UDS results for cocaine, fentanyl, cannabis and all opioids other than fentanyl and the patient's OAT medication. UDS time points and frequency are set by a computer-generated variable ratio. The variable-ratio increases the frequency of tests based on increased patient drug use, decreased treatment compliance and less time in treatment. In Ontario, UDS is integrated into contingency management, with the lowest frequency of urine testing observed in both stable patients, to monitor their ongoing stability, and unstable patients, who undergo less frequent testing due to their severe disease state. Additional UDS can be requested depending on clinical judgement. UDS results are obtained using the FaStep Assay (Trimedic Supply Network, Concord, Ontario, Canada) with results for assays detecting amphetamine or methamphetamine combined for amphetamine-type stimulant results and assays detecting morphine or oxycodone combined with other opioid results. Results for methadone, buprenorphine, fentanyl, cannabis, benzodiazepines and cocaine are based on specific assays detecting methadone metabolite, buprenorphine, fentanyl, delta-9-tetrahydrocannabinol, diazepam or structurally similar benzodiazepines and cocaine metabolite, respectively. The longitudinal follow-up allows for the measurement of OAT services over time, providing critical time-to-event data for patient outcomes with validity and reliability.

Our cohort includes blood work results for HCV detection and concurrent HCV treatment. Additional holdings include data on naloxone kit distribution and referral sources. A combination of these indicators can measure the association of integrated care and harm reduction initiatives in CATC clinics among a real-world clinical population living in geographically and socioeconomically diverse regions. Together, these data allow for a robust examination of OAT treatment from a network of physicians committed to evidence-based addiction treatment delivered through integrated medical, pharmacy and support services.

Patient characteristics

The cohort represents 47.6% of patients receiving OAT in Ontario (32 246/67 646) (figure 1, online supplemental file 2). Cohort demographics, drug use and treatment characteristics of the cohort are detailed in table 1, revealing the average age of patients was 36.3 years, and the cohort was 61.4% male patients (19 805/32 246). The mean remoteness index score was 0.16 indicating that 84% of the Ontario population is more remote than people in the cohort.[24] The mean Ontario Marginalisation Index

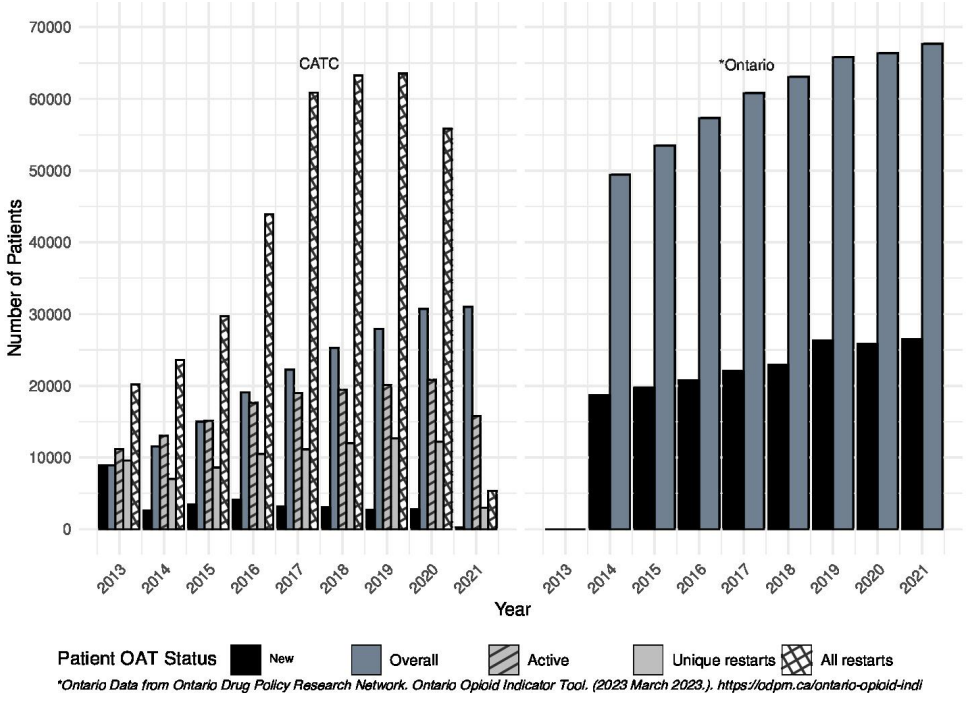

Figure 1 Number of treated patients in CATC and the province of Ontario grouped by treatment status. CATC, Canadian Addiction Treatment Centre; OAT, opioid agonist treatment.

Table 1 Demographic, drug use and treatment characteristics at cohort entry*

Variable	Values
Age, mean (Q1–Q3)	36.3 (28–43)
Sex n (%)	
Male	19 806 (61.4)
Female	12 403 (38.5)
X	26 (0.08)
Follow-up time, mean (Q1–Q3)	3.1 (0.7–5.2)
Time in treatment, mean (Q1–Q3)	2.2 (0.3–3.4)
Remoteness index, mean (Q1–Q3)	0.16 (0.08–0.25)
Ontario Marginalisation Index, mean (Q1–Q3)	
Housing and dwellings	4.1 (3–5)
Material resources	3.5 (3–4)
Age and labour force	2.4 (1–3)
Racialised and newcomer populations	4.4 (4–5)
Geographical location, n (%)	
Northern Ontario	5943 (18.4)
Southern Ontario	21 556 (78.4)
Starting medication, n (%)	
Methadone	25 056 (77.7)
Buprenorphine	7190 (22.3)
Positive urine drug screen tests*, n (%)	
Fentanyl	130 273 (13)
Other opioids	869 011 (7.6)
Amphetamines and methamphetamines	256 155 (14.6)
Cocaine	1 084 336 (22.4)
Cannabis	262 691 (53.7)
Take-home dose days*, mean (range)	2.5 (range 0–7 days)
Number of HCV tests completed*	68 722
Number of positive HCV-antibody tests*	12 530
Number of positive HCV RNA tests*	12 170
Number of patients treated for HCV*	2102
Referral source* n (%)	
Community programme	9308 (28.9)
Hospital	143 (0.4)
Corrections	294 (0.9)
Self/Family/Friend	8301 (24.7)
Walk-in	2835 (8.8)
Primary care	203 (0.6)
Other	11 160 (34.6)

*Asterisk iIndicate which characteristics were measured at weekly intervals for the entire follow-up. All characteristics without asterisks are measured at cohort entry.
HCV, hepatitis C virus; Q, quartile; X, sex other than male or female.

component score was 4.1 for households and dwellings, 3.5 for material resources, 2.4 for age and labour force and 4.4 for racialised and newcomer populations with values closer to 5 indicating a higher level of marginalisation or social vulnerability[22] (figure 2).

The average time in treatment was 2.2 years with methadone as the most common starting medication for patients in the cohort, methadone: 77.7% (25 045/32 246) and buprenorphine/naloxone: 22.3% (7186/32 246). UDS indicated that 53.7% of tests were positive for cannabis, 22.4% of tests were positive for cocaine, 22.4% were positive for amphetamine or methamphetamine and 14.6% were positive for fentanyl. Data showed a mean per-patient carry level of 2.5 take-home doses and 4.5 observed doses, ranging from 0 to 7 doses of OAT per week.

From 2014 to 2021, 3964 nasal naloxone kits were distributed, 1772 injection kits were distributed, 70 529 HCV tests were conducted and 37.62% (26 534) were positive. During the first visit, all patients are tested for HCV and retested annually if risks persist or based on clinical judgement. When stratified by referral source, 28.87% (9308) of patients were referred to CATC by community programmes including narcotics anonymous, community support services, needle exchange programmes, etc; 0.4% (143) were referred from hospital, 0.9% (294) from corrections facilities and 0.6% (203) from primary care; 24.74% (8301) were self, family or friend referrals with 34.61% (11,160) with no specified referral source listed.

Follow-up

This cohort provides a longitudinal perspective on OAT usage in a clinical cohort. The data spans from 1 April 2014 to 28 February 2021. Study follow-up is observational, and patients are considered lost to follow-up if they discontinue treatment. The cut-off period was determined based on studies conducted in British Columbia,[3] and all newly initiated studies use available follow-up windows to observe patients irrespective of gaps. The median patient-years in treatment in the cohort was 1.2 years, and the median years of patient follow-up was 2.5 years, measured from the initial OAT contact to the conclusion of the study follow-up. The cohort is scheduled to undergo tri-annual updates as new data become available.

Patient and public involvement

No patients were involved, however, the cohort was created with the CATC. We are currently developing an advisory group to provide feedback on future studies.

FINDINGS TO DATE

Since 2017, CATC cohort data have resulted in a total of 16 publications[5 25–38] and has provided valuable clinical insights.

Treatment retention

The first cohort-based studies examined treatment retention, defined as an OAT interruption of 5 days without methadone or 6 days without buprenorphine (figure 3). Multiple studies provide evidence that patients who

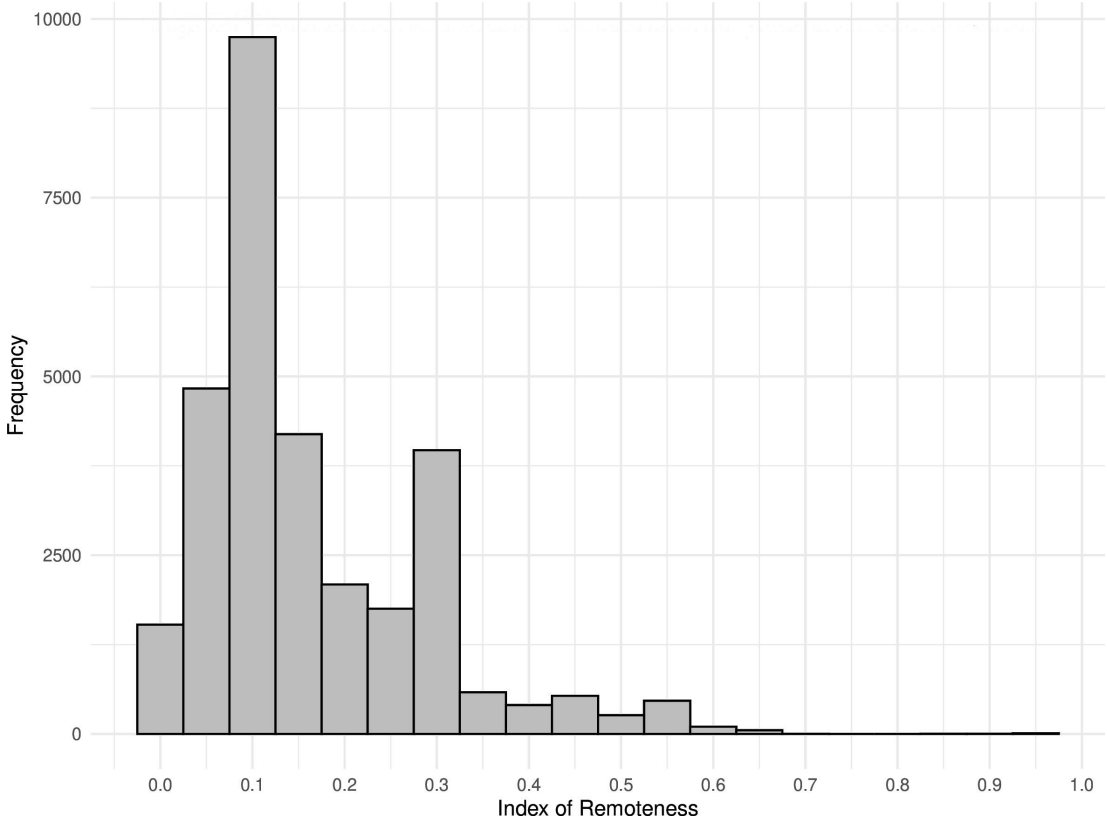

Figure 2 Distribution of index of remoteness for patients in Canadian Addiction Treatment Centre cohort.

remained in treatment for 1 year experience improved outcomes including lowered mortality risk, increased psychosocial functioning, reduced interaction with the criminal justice system, decreased soft tissue, HCV and HIV infections and decreased acute health service utilisation.[9 39 40] Existing studies measure the association of patient-level and service-level factors on initial retention on the first OAT prescription within CATC. Future research objectives include longitudinally evaluating retention rates and flexible modelling techniques that

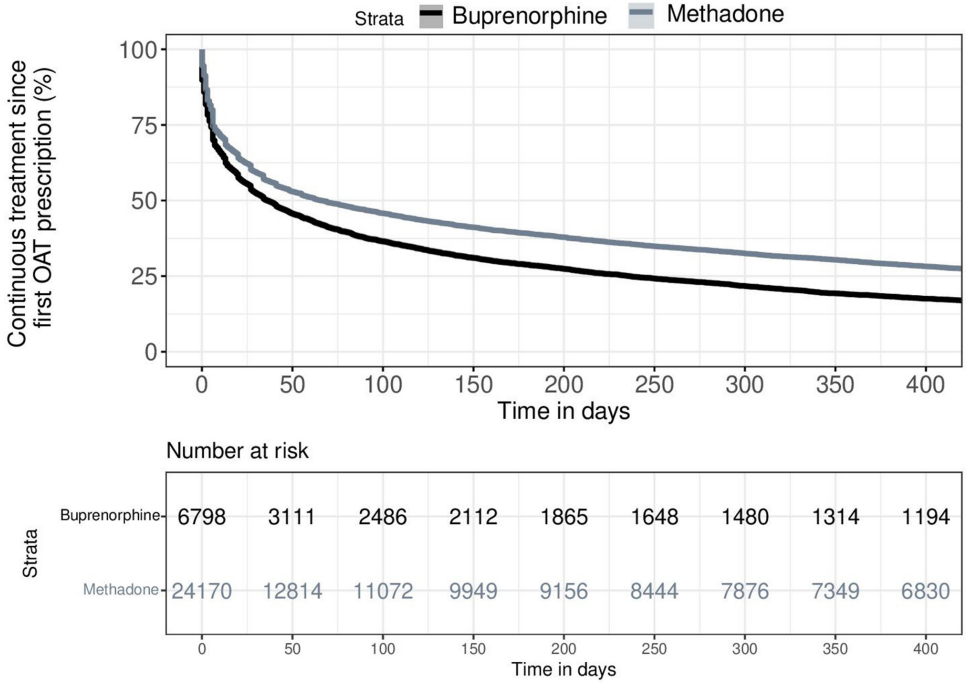

Figure 3 Time to treatment discontinuation grouped by methadone and buprenorphine medication. OAT, opioid agonist treatment.

account for the frequent changes in OAT. Additionally, future research aims to use conditional models and link them with provincial-level administrative datasets to gain additional insight into patient care.

Patient-level factors associated with first-time retention in OAT

Our previous study has identified factors associated with OAT retention and the positive outcomes associated with increased retention in treatment. Our findings indicate that patients residing in northern rural and northern urban regions in Ontario have 1.31 times higher likelihood of 1-year treatment retention compared with those residing in southern urban regions (adjusted OR (aOR) 1.31, 95% CI 1.09 to 1.58).[7 38] Additionally, patients were 1.149 times more likely to drop out of treatment if they had benzodiazepine-positive urine samples (adjusted HR (aHR) 1.149, 95% CI 1.02 to 1.29)[30]; OAT patients with baseline cannabis use and heavy cannabis use were at increased risk of dropout (1.39 and 1.48 times more likely, respectively)[31]; compared with those with no amphetamine-type stimulant use, the number of days retained in OAT treatment for people who use amphetamine-type stimulant was reduced (aHR 1.19, 95% CI 1.07 to 1.17)[34] and people who used cocaine at baseline were 1.24 times more likely to drop out of treatment than baseline non-users (aHR 1.124, 95% CI 1.03 to 1.23).[32] Furthermore, our previous studies highlighted several factors associated with patients' retention in treatment including the number of prior treatment attempts, a higher frequency of average monthly UDS and a lower proportion of positive UDS results for substances other than opioids.[35 36]

Service-level factors associated with first-time retention in OAT

We also identified service-level factors associated with OAT retention. Previous studies have shown that providing OAT by telemedicine is comparable to in-person care in terms of treatment retention.[28] We also observed significant associations between the frequency of UDS and 1-year treatment retention in OAT. Specifically, the aOR for biweekly UDS=3.20 (95% CI 2.75 to 3.75), for weekly UDS (aOR 6.86, 95% CI 5.88 to 8.00) and for more than weekly UDS (aOR 8.03, 95% CI 6.87 to 9.38), with the monthly or less group serving as the reference.[35]

We found an association between onsite pharmacies in OAT clinics on treatment retention in methadone maintenance therapy compared with community (offsite) pharmacies.[33] Among the 3743 patients included in our analysis, those filling methadone prescriptions from onsite pharmacies exhibited a significantly higher likelihood of remaining in treatment for at least 1 year. Specifically, patients using onsite pharmacies were 0.23 times as likely to withdraw from treatment before 1 year (n=2605; aHR 0.23, 95% CI 0.21 to 0.25) compared with the community (offsite) pharmacy group (n=1138). Furthermore, the retention rate at 1 year for patients using onsite pharmacies was 57.3% compared with 11.9% for the community (offsite) pharmacy group.

TRENDS IN OAT AND SUBSTANCE USE

We identified trends in OAT use and substance use behaviours over time. We observed an increase in the number of patients participating in OAT from 2014 to 2020.[36] Furthermore, our findings revealed a statistically significant 108% increase in fentanyl use among OAT patients in Ontario during the COVID-19 pandemic. Additionally, we found that rural residence is associated with a higher percentage of positive UDS results for fentanyl.[5]

STRENGTHS AND LIMITATIONS OF THIS STUDY

The CATC cohort is based on a network of OAT physicians that share a common care delivery model and EMR which is unique in Canada. Due to the nature of the network of physicians and data capture, CATC has been used as a validation cohort for other jurisdictions. Another strength of this cohort is the event-level data on addiction medicine clinical interactions. Using unique identifiers like health card numbers, we can link the clinical data to provincial administrative datasets enabling us to monitor the integration between acute and community-based services which is not possible with provincial health administrative datasets alone.

Some limitations require consideration. Since patients must receive an OAT prescription to enter the cohort, there is potential for selection bias and channel bias because we do not have access to data for patients not in OAT. This means that treatment choice may systematically covary with other factors. Data linkage could address this by providing a control group of age-sex-clinical non-OAT receiving controls. Another limitation is unmeasured confounders that could modify the association between patient retention and their characteristics, for example, factors like concurrent disorders, history of homelessness, mental health diagnoses, death or other psychosocial factors. [20,26] Since this cohort was observational, the choice of starting medication was based on clinical characteristics and patient preference at the time of treatment initiation, and it was not randomly assigned or allocated. Therefore, differences in retention correlated with starting medication may reflect differences in observed and unobserved confounders including selection or channel bias because the patient characteristics for whom methadone was chosen could be systematically different from patients prescribed buprenorphine/naloxone.

COLLABORATION

Requests must have approval from all database stewards and appropriate research ethics board approval including compliance with Provincial and National privacy laws. Requests will be approved by Dr David Marsh and the

CATC. Inquiries can be sent by email to dmarsh@nosm.ca.

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Contributors KAM oversaw the project, helped to interpret the findings, prepared and revised the final manuscript. MT designed the analytical strategy and helped to interpret the findings, prepared and revised the final manuscript. DM plays a supervisory role in the design and interpretation analysis and DM revised the final manuscript. DM acts as the guarantor for this manuscript.

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Competing interests DM previously held the position of Chief Medical Director at CATC ending in June 2022, and maintains the role of OAT provider. DM had no ownership stake in the CATC as a stipendiary employee. We do not foresee any conflict of interest as findings will be made freely available to the public and the CATC, and neither the Universities nor CATC can prevent publication and dissemination of knowledge. The authors have no conflicts declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the 'Methods' section for further details.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study was approved by Laurentian University Research and Ethics Board (#6020852). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Privacy restricts data sharing on a public repository. Requests for statistical code and anonymised data may be made to the corresponding author. There are data generated from this study that have not been presented because it has been previously published .[5 27–40] Data are available on reasonable request. Privacy restricts data sharing on a public repository. Requests for statistical code and anonymised data may be made to the corresponding author.

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