Evaluating the Impact of Urine Drug Screen Frequency on Retention in Opioid Agonist Treatment in Ontario, Canada

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Research

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Abstract

Objective

The objective of this study was to evaluate how UDS frequency impacts treatment retention in OAT.

Methods

Data for this retrospective cohort study of 55,921 adults with OUD in Ontario, Canada, were derived from administrative data sources between January 1, 2011, and December 31, 2015. All patient information was linked anonymously across databases using encrypted ten-digit health card numbers. Descriptive statistics were calculated for comparing urine drug screening frequency groups (less than monthly, monthly, bi-weekly and, weekly) using standardized differences (d) where d less than 10% indicated a statistically significant difference. A logistic regression model was then used to calculate odds ratios for the association between UDS frequency and one-year treatment retention adjusting for baseline covariates, including sex, age, location of residence, income quintile, mental disorders, HIV status and deep tissue infections.

Results

Over 70 percent of the cohort had four or more UDS per month (weekly or more UDS). Significant associations were observed between UDS frequency and one-year treatment retention in OAT bi-weekly (adjusted Odds Ratio (aOR) = 3.20, 95% confidence interval (CI) 2.75-3.75); weekly UDS (aOR = 6.86, 95% CI, 5.88-8.00) and; more than weekly (aOR = 8.03, 95% CI, 6.87-9.38) using the monthly or less groups as the reference.

Conclusion

This study identified a significant association between weekly UDS and one-year treatment retention in OAT. Therefore, these findings put into question the recent changes in OAT guidelines recommending UDS only be conducted monthly. More research is needed to strengthen the evidence base for UDS frequency in OAT.

Introduction

Several studies have documented an unprecedented burden of disease due to opioid use in recent years (1–5). The rate of opioid-related deaths has increased dramatically in the United States and Canada. In Canada, between January and June 2018, there were 2066 opioid-related deaths, with fentanyl or fentanyl analogues detected in 72.0% of cases (6). Similar rates have been reported in the United States, and in 2020, opioid overdose was the leading cause of accidental death (7).

Fortunately, opioid use disorder (OUD) is treatable with Opioid Agonist Treatment (OAT), including methadone and buprenorphine/naloxone. Research has shown that OAT is the most effective treatment

to reduce mortality and hospitalization rates, decrease the use of opioids and other substances, lower the transmission of HIV, hepatitis C and other infectious diseases, and improve unemployment rates and other social factors. (2, 8–11). Despite its known benefits, uptake and effective use of OAT by general practitioners is relatively low. Little training is given to medical professionals about the complexity and continuum of care necessary for the successful treatment of individuals with OUD (12). Additionally, treatment discontinuation and cycling are very common (7, 8); and changes in opioid tolerance while on OAT lead to an exceptionally high risk of overdose mortality following discontinuation (2, 13–15). Sustained engagement in OAT, ideally for one year or more (16–18), is thus critical to realizing the protective benefits of this vital tool to address the opioid overdose crisis.

Most patients in Ontario will start treatment in a specialized addiction clinic for observed daily dosing. Urine Drug Screening (UDS) is used to detect drug use and monitor adherence to OAT (19, 20). UDS is part of a contingency management strategy that includes increasing the number of methadone or buprenorphine/naloxone doses that a patient can take home. These take-home privileges are increased based on appointment attendance and consistently negative urine screens for opioids, cocaine, stimulants, and other substances. In Ontario, patients enrolled in OAT at specialized addiction clinics will achieve six take-home doses after at least eight months of negative UDS, which is equivalent to visiting the clinic once per week for a UDS and assessment.

The cost of UDS billing has been the source of debate in Ontario (17, 18), resulting in recent UDS billing fee cuts (21) and recommendations for less frequent screening (22). Ideal UDS frequency is therefore critical to treat OUD effectively in a specialized OAT setting. However, a recent review conducted by McEachern et al. concluded that there is a critical gap in peer-reviewed evidence regarding UDS frequency and health outcomes for individuals in OAT. Despite this lack of evidence, the OAT guidelines in Ontario have been recently replaced with new national guidelines which recommend drug screening only once per month, even when a much higher frequency of UDS is currently being conducted. Furthermore, federal and provincial guidelines are inconsistent. They often rely on expert opinion and politically driven reasons rather than peer-reviewed evidence (23). Therefore, the goal of this study was to evaluate how UDS frequency impacts treatment retention in OAT in Ontario.

Methods

Study Design and setting

Data for this retrospective cohort study of 55,921 adults with OUD in Ontario were derived from three databases that routinely collect publically funded health care services between January 1, 2011, and December 31, 2015. These data were obtained through the Data Analytics Services (DAS) department at ICES. ICES is a not-for-profit research organization that gathers population-based health and social data from Ontario's publicly funded health services to generate knowledge (24). The study data were accessed remotely using a secure server. Patient-level information was linked anonymously across databases using encrypted ten-digit health card numbers. The linking protocol is used routinely for health system

research in Ontario (25–27). The Laurentian University Research Ethics Board provided ethical approval for this study. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used to write this manuscript (28).

The Ontario Drug Benefit Plan database using drug identification numbers and the Ontario Health Insurance Plan (OHIP) database physician billing codes including OAT monthly management codes (K682, K683, and K684), visit/consultation codes (A680 and A957) and, point of care testing codes (G040, G041, G042 or G043) were used to define the primary study cohort. All patients who initiated OAT for the first time within the study time frame in Ontario were included. First-time OAT was defined as no previous history of treatment in the year before the first treatment episode. It is common for OAT patients to cycle between treatment and relapse (29, 30). Studies have demonstrated that multiple treatment attempts are correlated with a higher likelihood of positive outcomes (31–33). We chose only to include first-time OAT patients to eliminate bias related to numerous treatment attempts.

We excluded all patients under 15 years old, patients who were not eligible for OHIP, non-Ontario residents, and those with missing age, gender, and postal codes used for identification and linking across databases. We then combined patients identified from ODB, patients identified from OHIP, and patients identified in both databases to create the primary study cohort. See Fig. 1.

Study variables

Baseline statistics were used to describe the study population and included age groups (18 to 34, 35 to 64, 65+), sex (male vs female), income quintile (1 – highest, 2, 3, 4, 5), and location of residence, missing $n = 3$ (northern/rural, northern/urban, southern/rural, southern/urban), all extracted from the RPDB database. Comorbidity variables included: HIV status (positive vs negative), Deep tissue infections (yes vs no), mental health conditions (yes vs no).

UDS frequency

UDS billing information, including the following OHIP fee codes: G040, G041, G042, G043, were extracted from the OHIP database. Patients were assigned to one of four groups: Less than once in 30 days, bi-weekly (> 1 to ≤ 3 in 30 days), weekly (> 3 to ≤ 5 in 30 days) more than weekly (> 5 in 30 days). The classification of groups was decided based on the distribution of the means of the UDS in 30 days.

One-year treatment retention

One-year treatment retention is a common measure used in several studies as a positive treatment outcome (16, 18, 34–38). After their first treatment episode, all patients were followed to a maximum follow-up date of December 31, 2016. Continuous OAT (one-year treatment retention) was assessed based on prescription refill data (from the Ontario Drug Benefit database). The thirty-day cut-off was chosen based on this interval has been well-established in this field of research (16, 34, 37). The database used for medication dispensing in this study might not capture doses administered in a hospital or provincial correctional setting. However, in Ontario, patients will typically continue to receive

methadone or buprenorphine in these settings. Since most hospital admissions or provincial incarcerations are less than 30 days, this approach allows the analysis to be conducted without misinterpreting such events as treatment interruption.

Statistical Analysis

Descriptive statistics were calculated for all UDS groups and used standardized differences (d) where d less than 10% indicated a clinically relevant difference. Standardized differences are not affected by sample size. Therefore, standard differences can be used to compare the balance in measured variables between exposure groups in the study (39).

A logistic regression model was then used to calculate odds ratios for the association between UDS frequency and one-year treatment retention. We adjusted for baseline covariates in the models, including sex, age, location of residence, income quintile, mental disorders, HIV status and deep tissue infections. All data were analyzed using SAS Version 9.4 (40).

Results

Between January 2011 and December 2015, a total of 55,921 individuals were included in the study. Of these, 6,252 (11.20%) had UDS monthly or less, 9,495 (16.98%) had bi-weekly UDS, 24,948 (44.61%) had weekly UDS, and 15,226 (27.23%) had UDS six or more times in 30 days.

There were significant differences between the UDS frequency groups. Notably, we observed that the proportion of younger patients (aged 15 to 34) increased and that the proportion of older patients (55 to 65+) decreased with increased UDS frequency. Similarly, the proportion of northern rural patients increased, and the proportion of southern rural patients decreased with higher UDS frequency. Other demographic characteristics at OAT initiation are shown in Table 1.

As shown in Table 2, a logistic regression model was conducted to determine the association between UDS frequency and one-year treatment retention. A total of 250 (4.00%) of patients who were retained for one year had less than one UDS in 30 days, 1,398 (14.72%) had bi-weekly UDS, 6,185 (24.79%) had weekly UDS, and 4,153 (27.28%) had more than weekly UDS. UDS frequency was positively associated with one-year treatment retention within our cohort. Compared to patients who had less than monthly UDS, bi-weekly UDS was associated with an increase in one-year treatment retention (adjusted Odds Ratio (aOR) = 3.20, 95% confidence interval (CI) 2.75–3.75); weekly UDS was associated with an increase in one-year treatment retention (aOR = 6.86, 95% CI, 5.88–8.00) and; more than weekly UDS was associated with an increase in one-year treatment retention (aOR = 8.03, 95% CI, 6.87–9.38).

Discussion

The study sought to evaluate the relationship between the frequency of UDS tests and one-year retention in OAT. Drawing on longitudinal data from publically funded health administrative data in Ontario,

Canada, it was observed that more frequent UDS tests are associated with a significantly increased likelihood of one-year treatment retention in OAT.

We found a certain degree of heterogeneity in the UDS frequency groups. Specifically, younger patients and those living in northern rural areas had more frequent UDS tests. This observation is likely reflective of the lack of stability observed in younger patients do to less time in treatment. In Ontario, after a period of stabilization, OAT physicians can allocate take-home doses, leading to less frequent UDS, which is mainly dependent on the patient's progress with treatment (5). Patients in Northern and rural regions of Ontario are subject to several barriers in accessing care, increasing their likelihood of delaying accessing services. For example, northern patients may have difficulty enrolling in treatment due to the well-documented lack of resources, including primary care physicians. They may also have to travel long distances to access health service providers who can provide observed dosing (41–43).

In this study, when evaluating one-year treatment retention as the primary outcome, we accounted for variations in UDS frequency by adjusting for baseline patient characteristics. Compared to monthly UDS, increased frequency of urine screening was associated with a higher likelihood of one-year treatment retention in OAT. Importantly, we observed that the more frequent the UDS, the stronger the association was with one-year treatment retention. Research has shown that one-year treatment is correlated with various positive health outcomes for OAT patients, including reduced rates of drug use, hospitalization, criminal activity, and mortality (16, 34). Therefore, it is often used as a marker for a positive treatment outcome.

In our review of the literature, we found that only one other study has examined the impact of UDS frequency on OAT patient outcomes. Our search was consistent with a recent critical review of the literature by McEachern et al., which only identified one full-text report that met their search criteria studies focusing on individuals with substance use disorders and comparing UDS frequency to evaluate health outcomes. The other study evaluating UDS frequency was a three-arm randomized open-label trial (N = 53) by Chutuape et al.. The main intervention was random weekly or monthly testing, which was associated with higher retention rates over time, compared to no urine testing or contingency management (44). Although there is minimal research on UDS frequency and OAT outcomes, our study and the other study by Chutuape et al. were consistent in demonstrating the positive effect of more frequent UDS on retention. Additional research is required to continue to add to this evidence base to provide clinicians with clearer, consistent guidelines on UDS frequency across Canada.

Some limitations in the current study require consideration. First, there is the possibility of data entry and reporting errors associated with using administrative-level data. Second, the data is collected for physician remuneration and funding therefore, its initial intention is not for research. Third, although we considered various factors associated with treatment retention, there is potential for unmeasured confounding, including confounding related to other substance use (37, 45, 46), social and interpersonal factors (47–50) and clinical characteristics (51, 52) due to our study only having access to routinely collected data. Finally, in this study, methadone and buprenorphine/naloxone patients were grouped.

Research has shown that OAT medication type can impact retention. Therefore further study is needed to compare UDS frequency between methadone and buprenorphine/naloxone patients. Finally, some expert opinions have suggested that routine use of urine toxicology testing reinforces a power dynamic and invites shame, stigma and judgment. We were not able to account for such factors in our analysis (53).

Conclusion

In summary, our study identified a significant association between the frequency of UDS and one-year treatment retention in OAT. Given the evidence regarding the benefits of frequent UDS, our findings put into question the recent changes in OAT guidelines recommending UDS only be conducted monthly. The results can be generalized to any other locations with similar OAT regulations. This study adds to previous research showing the association between UDS frequency and positive OAT treatment outcomes, and more research is needed to strengthen the evidence base for UDS frequency in OAT.

Abbreviations

ACM All-Cause Mortality

aOR Adjusted Odds Ratio

CI Confidence Interval

CIHI Canadian Institute for Health Information

d Standardized Differences

DAD Discharge Abstract Database

HIV Human Immunodeficiency Virus

ICES Institute for Clinical Evaluative Sciences

LHIN Local Health Integration Network

NACRS National Ambulatory Care Reporting System

OAT Opioid Agonist Treatment

ODB Ontario Drug Benefit Plan

OHIP Ontario Health Insurance Plan

OR Odds Ratio

ODU Opioid Use Disorder

RPDB Registered Persons Database

SAS Statistical Analytics Software

Declarations

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Authors' contributions

Kristen A. Morin participated in the conceptualization, design, data analysis, writing and preparation of the article in question.

John R. Dabous participated in the conceptualization, data analysis, and final revision of the article in question

Dr. David C. Marsh is the corresponding author. He played a leadership role in planning of this study as part of a larger research project. He also has contributed to the interpretation of results and final review of the article in question.

Authors' information

KA Morin is a postdoctoral fellow at the Northern Ontario School of Medicine. JR Dabous is a PhD Candidate in the School of Rural and Northern Health at Laurentian University. DC Marsh maintains the following roles: Chief Medical Canadian Addiction Treatment Center, opioid agonist therapy provider, and Associate Dean of Community Engagement and Associate Dean of Research, Research Innovation and International Relations Professor, Clinical Sciences at the Northern Ontario School of Medicine. He is a well-established physician and researcher in the addiction medicine field.

Competing interest statement

Dr. David Marsh maintains the following roles: Chief Medical Director at CATC (Canadian Addiction Treatment Center), opioid agonist therapy provider. Dr. Marsh has no ownership stake in the CATC as a stipendiary employee. We do not foresee any conflict of interest as data will be made freely available to

the public and the CATC, and the Universities have no ability to prevent publication and dissemination of knowledge. The authors have no conflicts declared.

Consent for publication

All authors have given consent for publication. Universities have no ability to prevent publication and dissemination of knowledge.

Ethics approval and consent to participate

The Laurentian University Research Ethics Board provided ethical approval for this study.

Availability of data and material

All relevant data are within the manuscript and its Supporting Information files. The data were made available through ICES Data Analytic Services (DAS). Raw data cannot be shared under conditions set by ICES policy.

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Tables

Table 1: Summary statistics of individuals with OUD by UDS frequency group

d = standardized difference

**statistically significant*

Table 2: Urine Drug Screening Frequency and One-year Treatment Retention

Urine Drug Test Frequency

	Monthly or less		Bi-Weekly		Weekly		More than weekly	
	<i>n</i> =6,252 (11.20)	<i>d</i>	<i>n</i> =9,495 (16.98)	<i>d</i>	<i>n</i> = 24,948 (44.61)	<i>d</i>	<i>n</i> =15,226 (27.23)	<i>d</i>
Sex		0.02		0.03		0.09		0.12*
<i>Female</i>	2,268 (36.28)		3,217 (33.88)		8,217 (32.94)		5,992 (39.35)	
<i>Male</i>	3,984 (63.72)		6,278 (66.12)		16,731 (67.06)		9,234 (60.65)	
Age		0.64*		0.36*		0.24*		0.40*
<i>15 to 24</i>	720 (11.20)		1,064 (11.21)		4,716 (18.90)		3,741 (24.57)	
<i>25 to 34</i>	1,358 (21.72)		2,656 (27.97)		9,086 (36.42)		5,906 (38.79)	
<i>35 to 44</i>	1,186 (18.967)		2,249 (23.69)		5,573 (22.34)		3,087 (20.27)	
<i>45 to 54</i>	1,415 (22.63)		2,277 (23.98)		4,161 (16.68)		1,947 (12.79)	
<i>55 to 64</i>	887 (14.19)		1,004 (10.57)		1,289 (5.17)		505 (3.32)	
<i>65+</i>	686 (10.97)		245 (2.58)		123 (0.49)		40 (0.26)	
Geography		0.11*		0.29*		0.22*		0.45*
<i>Northern Rural</i>	366 (5.85)		239 (2.52)		828 (3.32)		1,400 (9.19)	
<i>Northern Urban</i>	445 (7.12)		441 (4.64)		1,753 (7.03)		2,655 (17.44)	
<i>Southern Rural</i>	457 (7.31)		672 (7.08)		2,107 (8.45)		1,462 (9.60)	
<i>Southern Urban</i>	4,984 (79.72)		8,143 (85.76)		20,260 (81.21)		9,709 (63.77)	
Income		0.10		0.11*		0.05		0.15*
<i>1 (lowest)</i>	1,999 (31.97)		2,847 (29.98)		8,293 (33.24)		5,953 (39.10)	

2	1,348 (21.56)		2,206 (23.23)		5,644 (22.62)		3,301 (21.68)	
3	1,089 (17.42)		1,777 (18.72)		4,586 (18.38)		2,520 (16.55)	
4	956 (15.29)		1,497 (15.77)		3,755 (15.05)		1,884 (12.37)	
5	860 (13.76)		1,168 (12.30)		2,670 (10.70)		1,568 (10.30)	
Mental Health	5,544 (88.68)	0.06	8,426 (88.74)	0.06	21,472 (86.07)	0.05	13,234 (86.92)	0.01
HIV positive	59 (0.94)	0.03	111 (1.17)	0.06	158 (0.63)	0.02	83 (0.55)	0.03
Deep Tissue Infection	344 (5.50)	0.14*	420 (4.42)	0.09	591 (2.37)	0.07	321 (2.11)	0.08
UDS Frequency per Month	Patients (N)	One-year Retention, N (%)	Unadjusted OR	Unadjusted 95% CI	Adjusted OR	Adjusted 95% CI		
Less than monthly	6,252	250 (4.0)						
Bi-weekly	9,495	1,398 (14.72)	3.18	2.71-3.72	3.20	2.75-3.75		
Weekly	24,948	6,185 (24.79)	6.07	5.22-7.05	6.86	5.88-8.00		
More than weekly	15,226	4,153 (27.28)	6.90	5.93-8.03	8.03	6.87-9.38		

*UDS - Urine drug screening

*OR – Odds Ratio

*aOR - Adjusted Odds Ratio

*95% CI – 95% confidence interval

Figures

Figure 1

Flow Chart Outlining Data Sources Including Linkages

Figure 2

Proportion of individuals retained for one year by UDS frequency groups