BMJ Open

Evaluating the association between urine drug screening frequency and retention in opioid agonist treatment in Ontario, Canada

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-060857
Article Type:	Original research
Date Submitted by the Author:	06-Jan-2022
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Keywords:	Substance misuse < PSYCHIATRY, PUBLIC HEALTH, EPIDEMIOLOGY

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Title: Evaluating the association between urine drug screening frequency and retention in opioid agonist treatment in Ontario, Canada

Running Title: Urine drug screen frequency and OAT retention

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word count: 2,216

ABSTRACT

Objective: The objective of this study was to evaluate how urine drug screening frequency is associated with treatment retention in opioid agonist treatment (OAT).

Methods: Data for this retrospective cohort study of 55,921 adults in OAT 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 urine drug screening 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 urine drug screens per month (weekly or more UDS). Significant associations were observed between urine drug screening 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 urine drug screening (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 urine drug screening and one-year treatment retention in OAT. Therefore, these findings put into question the recent changes in OAT guidelines recommending urine drug screening only be conducted monthly. More research is needed to strengthen the evidence base for urine drug screening frequency in OAT.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- There is the possibility of data entry and reporting errors associated with using administrative-level data.
- The data is collected for physician remuneration and funding therefore, its initial intention is not for research.
- 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.
- 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).

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 is associated with 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 under project number 6009752. 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 Figure 1.

Patient and Public Involvement

There was no patient and public involvement involved in the design, conduct, reporting or dissemination of our research.

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

Figure 2 shows that 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.

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

d = standardized difference
**statistically significant*

	Urine Drug Test Frequency							
	Monthly or less		**Bi-Weekly**		**Weekly**		**More than weekly**	
	n=6,252 (11.20)	*d*	*n=9,495 (16.98)*	*d*	*n= 24,948 (44.61)*	*d*	*n =15,226 (27.23)*	*d*
Sex		0.02		0.03		0.09		0.12*
Female	2,268 (36.28)		3,217 (33.88)		8,217 (32.94)		5,992 (39.35)	
Male	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*
15 to 24	720 (11.20)		1,064 (11.21)		4,716 (18.90)		3,741 (24.57)	
25 to 34	1,358 (21.72)		2,656 (27.97)		9,086 (36.42)		5,906 (38.79)	
35 to 44	1,186 (18.967)		2,249 (23.69)		5,573 (22.34)		3,087 (20.27)	
45 to 54	1,415 (22.63)		2,277 (23.98)		4,161 (16.68)		1,947 (12.79)	
55 to 64	887 (14.19)		1,004 (10.57)		1,289 (5.17)		505 (3.32)	
65+	686 (10.97)		245 (2.58)		123 (0.49)		40 (0.26)	
Geography		0.11*		0.29*		0.22*		0.45*
Northern Rural	366 (5.85)		239 (2.52)		828 (3.32)		1,400 (9.19)	
Northern Urban	445 (7.12)		441 (4.64)		1,753 (7.03)		2,655 (17.44)	
Southern Rural	457 (7.31)		672 (7.08)		2,107 (8.45)		1,462 (9.60)	
Southern Urban	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*
1 (lowest)	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

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).

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

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

**reference group*
UDS - Urine drug screening
OR – Odds Ratio
aOR - Adjusted Odds Ratio
95% CI – 95% confidence interval

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.

LIST OF 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

OUD Opioid Use Disorder

RPDB Registered Persons Database

SAS Statistical Analytics Software

DECLARATIONS

Acknowledgments

We thank IC/ES Data Analytic Services, more specifically Ryan Ng for his assistance with data extraction and database set up. We also thank Frank Vojtesek for efforts with database management, cleaning and organization.

Funding

This research was partially supported by the NOAMA Clinical Innovation Grant AFP Innovation Fund - Project #C-21-08.

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.

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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 under project ID number 6009752.

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.

Acknowledgements

We thank members of the Marsh research lab for their continued support and feedback. We also thank ICES, ICES North and Data Analytic Services (DAS) for their continued support.

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Figure 1: Flow Chart Outlining Data Build Including Linkages.

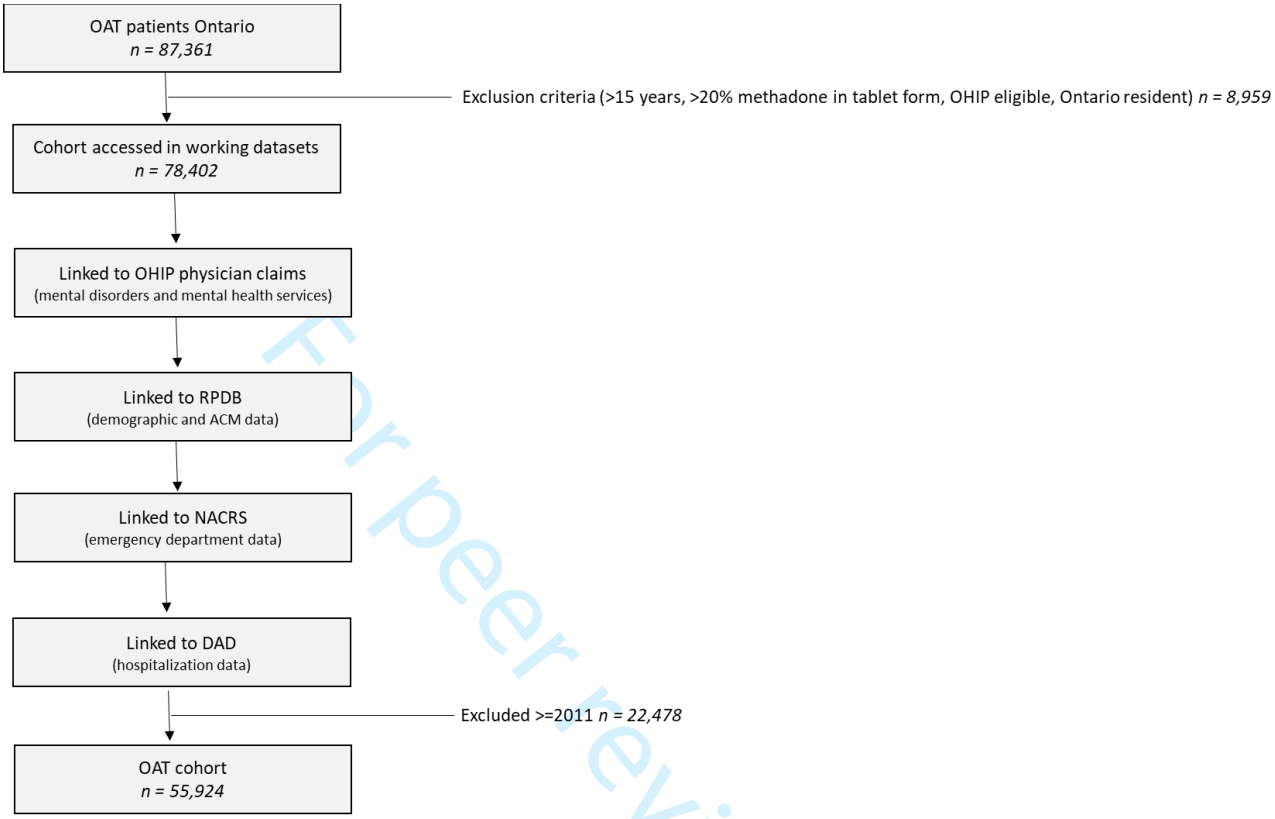
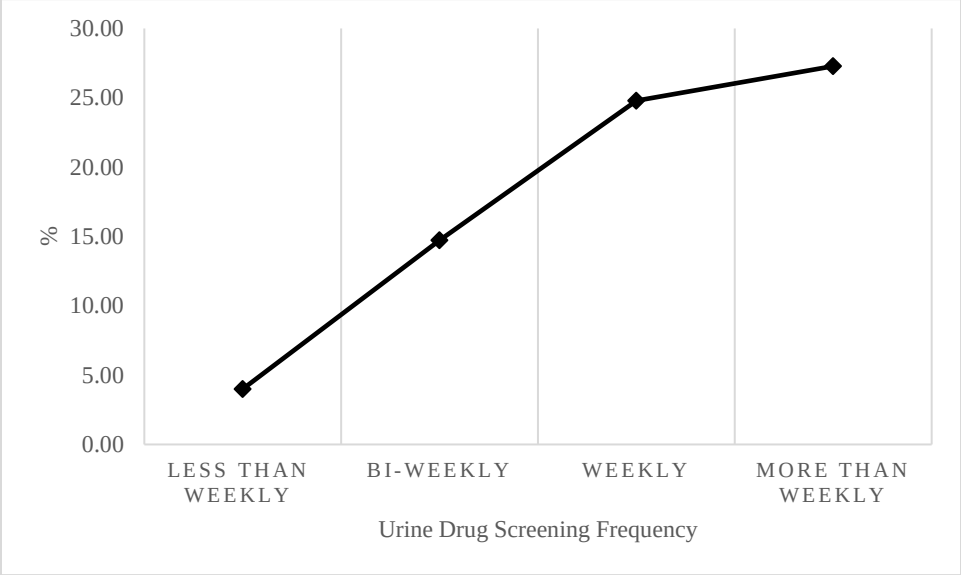


Figure 2: Proportion of individuals retained for one year by UDS frequency groups



	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	**page 2 -** ABSTRACT, , *"Data for this retrospective cohort…"*	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	**page 2-** ABSTRACT, , in-text reference: *"were derived from administrative data sources …" and* **page 2-** ABSTRACT, in-text reference: *"…in Ontario, Canada…"* **page 2-** ABSTRACT, in-text reference: *"All patient information was linked anonymously across databases using encrypted ten-*

					digit health card numbers."
Introduction,					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	**page 4 to 5 -** INTRODUCTION,		
Objectives	3	State specific objectives, including any pre-specified hypotheses	**page 5-** INTRODUCTION, in-text reference: *"...the goal of this study was to evaluate how UDS frequency impacts treatment retention in OAT in Ontario."*		
Methods					
Study Design	4	Present key elements of study design early in the paper	**page 5 -** METHODS, in-text reference: *"Data for this retrospective cohort study..."*		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	**page 5 to 6 -** METHODS		
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of	**Page 6 -** METHODS, in-text reference: "*We*	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to	**Page 6 and Figure 1 -** METHODS,

		selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	*excluded all patients…"* *n/a*	identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	**Page 6,** in-text reference: "*The Ontario Drug Benefit…"* *n/a* **Figure 1**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	**Page 7 -** METHODS,	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	**Page 7 -** METHODS,
Data sources/ measurement	8	For each variable of interest, give sources of data and	**Page 6 -** METHODS		

		details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			
Bias	9	Describe any efforts to address potential sources of bias	*n/a*		
Study size	10	Explain how the study size was arrived at	**Figure 1**		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	**Page 7 and 8-** MEHTODS		
Statistical methods	12	(a)Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed	**Page 8-** MEHTODS, in-text reference: "*Descriptive statistics were calculated…"* *n/a* **page 6 -** METHODS, in-text reference: *"…and those with missing…"*		

		(d) *Cohort study* - If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses			
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	**Page 5-** METHODS, **"***These data were obtained…"* **page 6 -** METHODS, in-text reference: *"…and those with missing…"*
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	**page 5 and 6 -** METHODS, in-text reference: "*Patient-level…"*
Results					
Participants	13	(a)Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed	**Figure 1**	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality,	**Figure 1**

		eligible, included in the study, completing follow-up, and analysed) (b)Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	
Descriptive data	14	(a)Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest	**Page 8-** RESULTS, in-text reference: *"There were significant differences between…"* **page 6 -** METHODS, in-text reference: *"…and those with missing…"*		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	**Page 9 and 10 -** RESULTS, in-text reference: *"As shown in Table 2…"*		

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	RESULTS, page 5, in-text reference: *"As shown in Table 2…"* and Table 2		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	*n/a*		
Discussion					
Key results	18	Summarise key results with reference to study objectives	**Page 10 and 11 -** DISCUSSION, in-text reference: *"The study sought to evaluate…"*		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	**Page 12 -** DISCUSSION, in-text reference: *"Some limitations in the current study…"*	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	**Page 12 -** DISCUSSION, in-text reference: *"Some limitations in the current study…"*
Interpretation	20	Give a cautious overall interpretation of results	**Page 12 an 13 -** CONCLUSION,		

		considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results	**Page 12 and 13 -** CONCLUSION		

BMJ Open

Evaluating the association between urine drug screening frequency and retention in opioid agonist treatment in Ontario, Canada

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-060857.R1
Article Type:	Original research
Date Submitted by the Author:	13-Jul-2022
Complete List of Authors:	Morin, Kristen; Northern Ontario School of Medicine Dabous, John; Northern Ontario School of Medicine - East Campus Vojtesek, Frank; Northern Ontario School of Medicine - East Campus Marsh, David; Northern Ontario School of Medicine,
Primary Subject Heading:	Addiction
Secondary Subject Heading:	Epidemiology, Health services research, Public health
Keywords:	Substance misuse < PSYCHIATRY, PUBLIC HEALTH, EPIDEMIOLOGY

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Title: Evaluating the association between urine drug screening frequency and retention in opioid agonist treatment in Ontario, Canada

Running Title: Urine drug screen frequency and OAT retention

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word count: 2,939

ABSTRACT

Objective: The objective of this study was to evaluate how urine drug screening frequency is associated with treatment retention in opioid agonist treatment (OAT).

Methods: Data for this retrospective cohort study of 55,921 adults in OAT 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 urine drug screening 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 urine drug screens per month (weekly or more UDS). Significant associations were observed between urine drug screening 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 urine drug screening (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 urine drug screening and one-year treatment retention in OAT. Therefore, these findings put into question the recent changes in OAT guidelines recommending urine drug screening only be conducted monthly. There are limitations associated with the use of administrative data, potential unmeasured confounding. Therefore, more research is needed to strengthen the evidence base for urine drug screening frequency in OAT.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- There is the possibility of data entry and reporting errors associated with using administrative-level data.
- The data is collected for physician remuneration and funding therefore, its initial intention is not for research.
- There is potential for unmeasured confounding, including confounding related to other substance use (1-3), social and interpersonal factors (4-7) and clinical characteristics (8, 9) 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.
- 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 (10).

INTRODUCTION

An epidemic of opioid use disorder (OUD) and deaths related to opioid poisoning has emerged across Canada in last decade (1-5). Fortunately, 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, 6-9). 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 (10). Additionally, treatment discontinuation and cycling are very common (7, 8); and changes in opioid tolerance while on OAT (11)are contributing factors that lead to an exceptionally high risk of overdose mortality following discontinuation (2, 12-14). Sustained engagement in OAT, ideally for one year or more (15-17), is thus critical to realizing the protective benefits of this vital tool to address the opioid overdose crisis.

Patients in Ontario typically start treatment in a specialized addiction clinic for observed daily dosing for both methadone and buprenorphine/naloxone. Patients can receive increasing number of take home doses, based on the assessment of the physician in determining their level of functional stability (cessation of other opioid use, reduced problematic use of other substances, stable housing, stable physical and mental health, along with other factors.). Increasing or decreasing numbers of take home doses are linked to urine screening (UDS) results and frequency in an explicit contingency management schedule such that patients who are in the process of gradually increasing their level of stability, and thus number of weekly take home

doses, will have more frequent urine testing (18, 19).These take-home privileges are increased based on appointment attendance and consistently negative UDS 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. Within this general context there is scope for some variability in how this approach is applied by individual physicians. Some physicians place less emphasis on this contingency management approach or rely less on urine testing to determine which patients receive increased numbers of take home doses. Some physicians may also be concerned that frequent UDS acts as a deterrent to treatment retention which counteracts the effectiveness of contingency management in reducing other drug use and improving retention.

The cost of UDS billing has been the source of debate in Ontario (17, 18), resulting in recent UDS billing fee cuts (20) and recommendations for less frequent screening (21). 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 (22). In Ontario, there has been some variability in physician practice in terms of frequency of UDS and application of contingency management practices with respect to linking carry doses to drug-free urines. The study is meant to look at whether this variability impacts

patient outcomes and in particular whether more frequent testing represents a barrier to 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 (23). 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 (24-26). The Laurentian University Research Ethics Board provided ethical approval for this study under project number 6009752. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used to write this manuscript (27).

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 (28, 29). Studies have demonstrated that multiple treatment attempts are correlated with a higher

likelihood of positive outcomes (30-32). 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 Figure 1.

Patient and Public Involvement

There was no patient and public involvement involved in the design, conduct, reporting or dissemination of our research.

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). We defined patients with mental disorders group using OHIP database diagnostic codes. The following codes are outlined in Appendix A.

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 (15, 17, 33-37). 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 (15, 33, 36). 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 (38).

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 (39).

RESULTS

Figure 2 shows that 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.

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

	Urine Drug Test Frequency							
	Monthly or less		**Bi-Weekly**		**Weekly**		**More than weekly**	
	n=6,252 (11.20)	*d*	*n=9,495 (16.98)*	*d*	*n= 24,948 (44.61)*	*d*	*n =15,226 (27.23)*	*d*
Sex		0.02		0.03		0.09		0.12*
Female	2,268 (36.28)		3,217 (33.88)		8,217 (32.94)		5,992 (39.35)	
Male	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*
15 to 24	720 (11.20)		1,064 (11.21)		4,716 (18.90)		3,741 (24.57)	
25 to 34	1,358 (21.72)		2,656 (27.97)		9,086 (36.42)		5,906 (38.79)	
35 to 44	1,186 (18.967)		2,249 (23.69)		5,573 (22.34)		3,087 (20.27)	
45 to 54	1,415 (22.63)		2,277 (23.98)		4,161 (16.68)		1,947 (12.79)	
55 to 64	887 (14.19)		1,004 (10.57)		1,289 (5.17)		505 (3.32)	
65+	686 (10.97)		245 (2.58)		123 (0.49)		40 (0.26)	
Geography		0.11*		0.29*		0.22*		0.45*
Northern Rural	366 (5.85)		239 (2.52)		828 (3.32)		1,400 (9.19)	
Northern Urban	445 (7.12)		441 (4.64)		1,753 (7.03)		2,655 (17.44)	
Southern Rural	457 (7.31)		672 (7.08)		2,107 (8.45)		1,462 (9.60)	

Southern								
Urban	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*
1 (lowest)	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

d = standardized difference
**statistically significant*

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).

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

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

**reference group*
UDS - Urine drug screening
OR – Odds Ratio
aOR - Adjusted Odds Ratio
95% CI – 95% confidence interval

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. UDS frequency can vary based on patient drug use, treatment compliance, time in treatment, some physician discretion. Since in Ontario UDS is part of contingency management, the lowest frequency of urine testing would typically be seen in two groups of patients. First, less frequent testing is done for those patients who are chronically unstable (most often due to sustained use of other drugs, homelessness, or ineffectively treated mental health problems or a combination of these) and thus have the frequency or urine testing reduced as they are not engaged in demonstrating increasing levels of stability. Secondly, those patients who have demonstrated sustained periods of stability, including cessation of problematic use of other substances, will have observed dosing and urine testing less frequently and sufficient only to monitor for continued stability.

In our data we found that younger patients and those living in northern rural areas had more frequent UDS tests. This observation is likely reflective of physician and patient factors which may account for the higher frequency of urine testing in the Northern Ontario patient group. The physicians practicing in this geographic area may place more emphasis on adherence to the

contingency management schedule in determining frequency of both UDS and take home doses. Alternatively, given the longer distances between patients and providers (35), the patients in this area may be more motivated to engage in the process of increased UDS in the short-term in order to obtain less frequent testing and higher frequency take home doses in the long-term. It is worth noting that our repeated observation in earlier papers (34, 35, 40) of higher treatment retention in the northern Ontario geographic area and the higher frequency of testing in this geographic area demonstrated in this paper is consistent with the overall relationship between UDS frequency and retention reported here.

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 (15, 33). 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 (41). 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 (36, 42, 43), social and interpersonal factors (44-47), the lack of patient descriptors that assess addiction severity and clinical characteristics (48, 49) due to our study only having access to routinely collected data. Finally, in this study, methadone and buprenorphine/naloxone patients were grouped due to low frequency of buprenorphine/naloxone prescriptions during our study period. 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 (50).

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.

FIGURE LEGEND

Figure 1: Flow Chart Outlining Data Build Including Linkages

Figure 2: Proportion of individuals retained for one year by UDS frequency groups

LIST OF 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

OUD Opioid Use Disorder

RPDB Registered Persons Database

SAS Statistical Analytics Software

DECLARATIONS

Acknowledgments

We thank IC/ES Data Analytic Services, more specifically Ryan Ng for his assistance with data extraction and database set up. We also thank Frank Vojtesek for efforts with database management, cleaning and organization.

Funding

This research was partially supported by the NOAMA Clinical Innovation Grant AFP Innovation Fund - Project #C-21-08.

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.

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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 under project ID number 6009752.

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.

Acknowledgements

We thank members of the Marsh research lab for their continued support and feedback. We also thank ICES, ICES North and Data Analytic Services (DAS) for their continued support.

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Figure 1: Flow Chart Outlining Data Build Including Linkages.

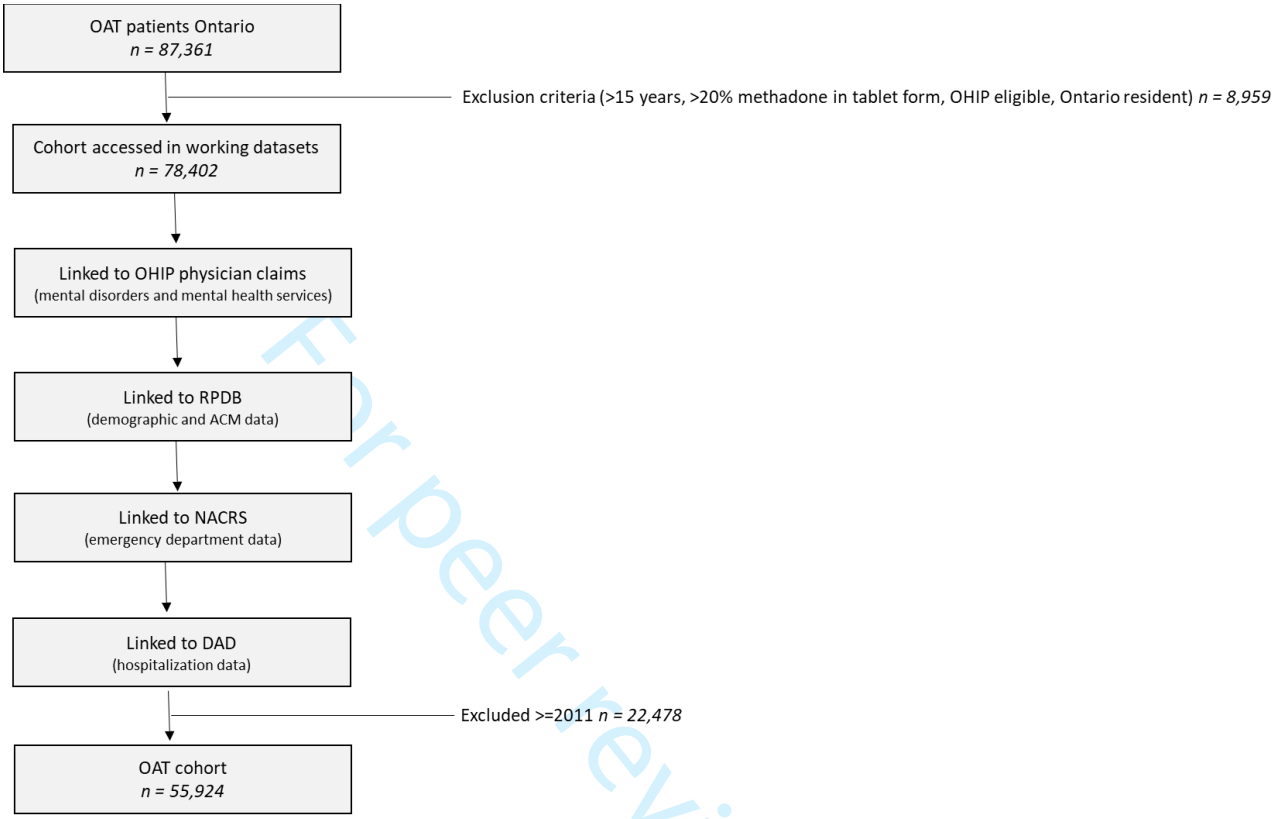
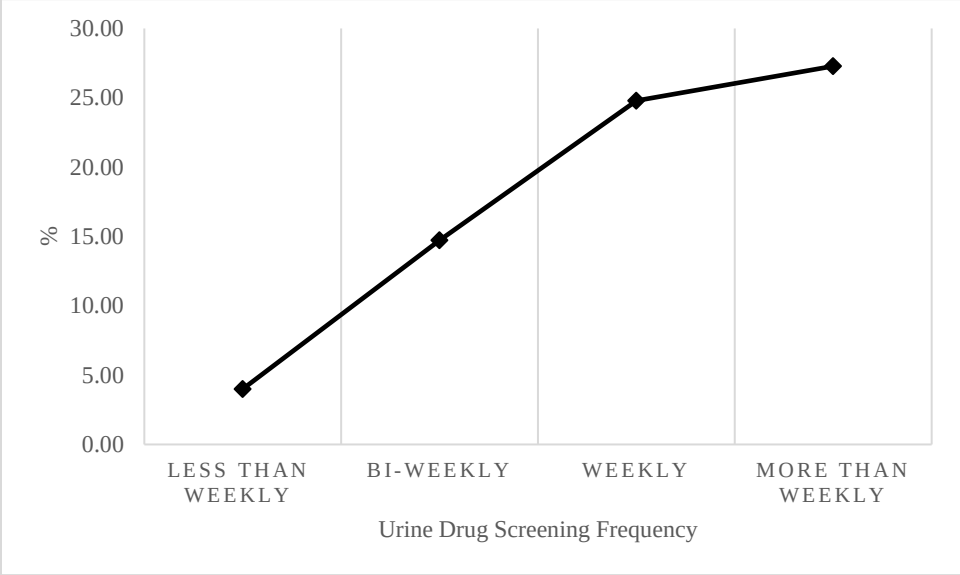


Figure 2: Proportion of individuals retained for one year by UDS frequency groups



Appendix D- Definition and ICD 9 and ICD10 codes for Mental Health Conditions

Definition Mental Health Conditions			
Mental Health Conditions	**ICD-10 Codes (DX10CODE1)**	**ICD-9 Codes**	Go Back
Neurodevelopmental Disorders	**F90 Attention-deficit hyperactivity disorders Includes:** attention deficit disorder with hyperactivity attention deficit syndrome with hyperactivity **F90.0 Attention-deficit hyperactivity disorder, predominantly inattentive type** **F90.1 Attention-deficit hyperactivity disorder, predominantly hyperactive type** **F90.2 Attention-deficit hyperactivity disorder, combined type** **F90.8 Attention-deficit hyperactivity disorder, other type** **F90.9 Attention-deficit hyperactivity disorder, unspecified type** Attention-deficit hyperactivity disorder of childhood or adolescence NOS Attention-deficit hyperactivity disorder NOS	**314.0**	**ATTENTION DEFICIT DIS***
		314.00	Attention-Deficit/Hyperactivity Disorder, Predominantly Inattentive Type
		314.01	Attention-Deficit/Hyperactivity Disorder, Combined Type or Attention-Deficit/Hyperactivity Disorder Predominantly Hyperactive-Impulsive Type
		314.9	Attention-Deficit/Hyperactivity Disorder NOS
Schizophrenia Spectrum and Related Disorders	**Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders (F20-F29)** **F20 Schizophrenia** **F20.0 Paranoid schizophrenia** Paraphrenic schizophrenia **F20.1 Disorganized schizophrenia** Hebephrenic schizophrenia Hebephrenia **F20.2 Catatonic schizophrenia** Schizophrenic catalepsy Schizophrenic catatonia Schizophrenic flexibilitas cerea **F20.3 Undifferentiated schizophrenia** Atypical schizophrenia **F20.5 Residual schizophrenia** Restzustand (schizophrenic) Schizophrenic residual state **F20.8 Other schizophrenia** **F20.81 Schizophreniform disorder** Schizophreniform psychosis NOS **F20.89 Other schizophrenia** Cenesthopathic schizophrenia Simple schizophrenia **F20.9 Schizophrenia, unspecified** **F21 Schizotypal disorder** Borderline schizophrenia Latent schizophrenia Latent schizophrenic reaction Prepsychotic schizophrenia Prodromal schizophrenia Pseudoneurotic schizophrenia Pseudopsychopathic schizophrenia Schizotypal personality disorder **F22 Delusional disorders** Delusional dysmorphophobia Involutional paranoid state Paranoia Paranoia querulans Paranoid psychosis Paranoid state Paraphrenia (late) Sensitiver Beziehungswahn **F23 Brief psychotic disorder** Paranoid reaction	**295**	**SCHIZOPHRENIC DISORDERS***
		295.0	SIMPLE SCHIZOPHRENIA*
		295.00	SIMPLE SCHIZOPHREN-UNSPECIFIED
		295.01	SIMPL SCHIZOPHREN-SUBCHR
		295.02	SIMPLE SCHIZOPHREN-CHR
		295.03	SIMP SCHIZ-SUBCHR/EXACER
		295.04	SIMPL SCHIZO-CHR/EXACERB
		295.05	SIMPL SCHIZOPHREN-REMISS
		295.1	HEBEPHRENIA*
		295.10	Schizophrenia, Disorganized Type
		295.11	HEBEPHRENIA-SUBCHRONIC
		295.12	HEBEPHRENIA-CHRONIC
		295.13	HEBEPHREN-SUBCHR/EXACERB
		295.14	HEBEPHRENIA-CHR/EXACERB
		295.15	HEBEPHRENIA-REMISSION
		295.2	CATATONIC SCHIZOPHRENIA*
		295.20	Schizophrenia, Catatonic Type
		295.21	CATATONIA-SUBCHRONIC
		295.22	CATATONIA-CHRONIC
		295.23	CATATONIA-SUBCHR/EXACERB
		295.24	CATATONIA-CHR/EXACERB
		295.25	CATATONIA-REMISSION
		295.3	PARANOID SCHIZOPHRENIA*
		295.30	Schizophrenia, Paranoid Type
		295.31	PARANOID SCHIZO-SUBCHR
		295.32	PARANOID SCHIZO-CHRONIC
		295.33	PARAN SCHIZO-SUBCHR/EXAC
		295.34	PARAN SCHIZO-CHR/EXACERB
		295.35	PARANOID SCHIZO-REMISS
		295.4	AC SCHIZOPHRENIC EPISODE*
		295.40	Schizophreniform Disorder
		295.41	AC SCHIZOPHRENIA-SUBCHR
		295.42	AC SCHIZOPHRENIA-CHR
		295.43	AC SCHIZO-SUBCHR/EXACERB
		295.44	AC SCHIZOPHR-CHR/EXACERB
		295.45	AC SCHIZOPHRENIA-REMISS
		295.5	LATENT SCHIZOPHRENIA*
		295.50	LATENT SCHIZOPHREN-UNSP
		295.51	LAT SCHIZOPHREN-SUBCHR
		295.52	LATENT SCHIZOPHREN-CHR
		295.53	LAT SCHIZO-SUBCHR/EXACER
		295.54	LATENT SCHIZO-CHR/EXACER
		295.55	LAT SCHIZOPHREN-REMISS

	Psychogenic paranoid psychosis	295.6 RESIDUAL SCHIZOPHRENIA*
	F24 Shared psychotic disorder	295.60 Schizophrenia, Residual Type
	Folie à deux	295.61 RESID SCHIZOPHREN-SUBCHR
	Induced paranoid disorder	295.62 RESIDUAL SCHIZOPHREN-CHR
	Induced psychotic disorder	295.63 RESID SCHIZO-SUBCHR/EXAC
	F25 Schizoaffective disorders	295.64 RESID SCHIZO-CHR/EXACERB
	F25.0 Schizoaffective disorder, bipolar type	295.65 RESID SCHIZOPHREN-REMISS
	Cyclic schizophrenia	295.7 SCHIZOAFFECTIVE TYPE*
	Schizoaffective disorder, manic type	295.70 Schizoaffective Disorder
	Schizoaffective disorder, mixed type	295.71 SCHIZOAFFECTIVE-SUBCHR
	Schizoaffective psychosis, bipolar type	295.72 SCHIZOAFFECTIVE-CHRONIC
	Schizophreniform psychosis, manic type	295.73 SCHIZOAFF-SUBCHR/EXACER
	F25.1 Schizoaffective disorder, depressive type	295.74 SCHIZOAFFECT-CHR/EXACER
	Schizoaffective psychosis, depressive type	295.75 SCHIZOAFFECTIVE-REMISS
	Schizophreniform psychosis, depressive type	295.8 SCHIZOPHRENIA NEC*
	F25.8 Other schizoaffective disorders	295.80 SCHIZOPHRENIA NEC-UNSPEC
	F25.9 Schizoaffective disorder, unspecified	295.81 SCHIZOPHRENIA NEC-SUBCHR
	Schizoaffective psychosis NOS	295.82 SCHIZOPHRENIA NEC-CHR
	F28 Other psychotic disorder not due to a substance or known physiological condition	295.83 SCHIZO NEC-SUBCHR/EXACER
		295.84 SCHIZO NEC-CHR/EXACERB
	Chronic hallucinatory psychosis	295.85 SCHIZOPHRENIA NEC-REMISS
	F29 Unspecified psychosis not due to a substance or known physiological condition	295.9 SCHIZOPHRENIA NOS*
		295.90 Schizophrenia Undifferentiated Type
	Psychosis NOS	295.91 SCHIZOPHRENIA NOS-SUBCHR
		295.92 SCHIZOPHRENIA NOS-CHR
		295.93 SCHIZO NOS-SUBCHR/EXACER
		295.94 SCHIZO NOS-CHR/EXACERB
		295.95 SCHIZOPHRENIA NOS-REMISS
		297.1 Delusional Disorder
		297.3 Shared Psychotic Disorder
		298.0 REACT DEPRESS PSYCHOSIS
		298.1 EXCITATIV TYPE PSYCHOSIS
		298.2 REACTIVE CONFUSION
		298.3 ACUTE PARANOID REACTION
		298.4 PSYCHOGEN PARANOID PSYCH
		298.8 Brief Psychotic Disorder
		298.9 Psychotic Disorder NOS
Bipolar and Related Disorders	**F30 –F31 Manic episode**	296.00 Bipolar I Disorder, Single Manic Episode, Unspecified
	Includes:	
	bipolar disorder, single manic episode	296.01 Bipolar I Disorder, Single Manic Episode, Mild
	mixed affective episode	
	F30.1 Manic episode without psychotic symptoms	296.02 Bipolar I Disorder, Single Manic Episode, Moderate
	F30.10 Manic episode without psychotic symptoms, unspecified	296.03 Bipolar I Disorder, Single Manic Episode, Severe Without Psychotic Features
	F30.11 Manic episode without psychotic symptoms, mild	296.04 Bipolar I Disorder, Single Manic Episode, Severe With Psychotic Features
	F30.12 Manic episode without psychotic symptoms, moderate	296.05 Bipolar I Disorder, Single Manic Episode, In Partial Remission
	F30.13 Manic episode, severe, without psychotic symptoms	296.06 Bipolar I Disorder, Single Manic Episode, In Full Remission
	F30.2 Manic episode, severe with psychotic symptoms	296.1 MANIC, RECURRENT EPISODE*
	Manic stupor	296.10 RECUR MANIC DIS-UNSPEC
	Mania with mood-congruent psychotic symptoms	296.11 RECUR MANIC DIS-MILD
	Mania with mood-incongruent psychotic symptoms	296.12 RECUR MANIC DIS-MOD
	F30.3 Manic episode in partial remission	296.13 RECUR MANIC DIS-SEVERE
	F30.4 Manic episode in full remission	296.14 RECUR MANIC-SEV W PSYCHO
	F30.8 Other manic episodes	296.15 RECUR MANIC-PART REMISS
	Hypomania	296.16 RECUR MANIC-FULL REMISS
	F30.9 Manic episode, unspecified	296.4 BIPOLAR AFFECTIVE, MANIC*
	Mania NOS	296.40 Bipolar I Disorder, Most Recent Episode Hypomanic or Manic, Unspecified
	F31 Bipolar disorder	
	Includes:	296.41 Bipolar I Disorder, Most Recent Episode Manic, Mild
	manic-depressive illness	
	manic-depressive psychosis	296.42 Bipolar I Disorder, Most Recent Episode Manic, Moderate
	manic-depressive reaction	
	F31.0 Bipolar disorder, current episode hypomanic	296.43 Bipolar I Disorder, Most Recent Episode Manic, Severe Without Psychotic Features
	F31.1 Bipolar disorder, current episode manic without psychotic features	296.44 Bipolar I Disorder, Most Recent Episode Manic, Severe With Psychotic Features

	F31.10 Bipolar disorder, current episode manic without psychotic features, unspecified **F31.11 Bipolar disorder, current episode manic without psychotic features, mild** **F31.12 Bipolar disorder, current episode manic without psychotic features, moderate** **F31.13 Bipolar disorder, current episode manic without psychotic features, severe** **F31.2 Bipolar disorder, current episode manic severe with psychotic features** Bipolar disorder, current episode manic with mood-congruent psychotic symptoms Bipolar disorder, current episode manic with mood-incongruent psychotic symptoms F31.3 **Bipolar disorder, current episode depressed, mild or moderate severity** **F31.30 Bipolar disorder, current episode depressed, mild or moderate severity, unspecified** **F31.31 Bipolar disorder, current episode depressed, mild** **F31.32 Bipolar disorder, current episode depressed, moderate** **F31.4 Bipolar disorder, current episode depressed, severe, without psychotic features** **F31.5 Bipolar disorder, current episode depressed, severe, with psychotic features** Bipolar disorder, current episode depressed with mood-incongruent psychotic symptoms Bipolar disorder, current episode depressed with mood-congruent psychotic symptoms **F31.6 Bipolar disorder, current episode mixed** **F31.60 Bipolar disorder, current episode mixed, unspecified** **F31.61 Bipolar disorder, current episode mixed, mild** **F31.62 Bipolar disorder, current episode mixed, moderate** **F31.63 Bipolar disorder, current episode mixed, severe, without psychotic features** **F31.64 Bipolar disorder, current episode mixed, severe, with psychotic features** Bipolar disorder, current episode mixed with mood-congruent psychotic symptoms Bipolar disorder, current episode mixed with mood-incongruent psychotic symptoms **F31.7 Bipolar disorder, currently in remission** **F31.70 Bipolar disorder, currently in remission, most recent episode unspecified** **F31.71 Bipolar disorder, in partial remission, most recent episode hypomanic** **F31.72 Bipolar disorder, in full remission, most recent episode hypomanic** **F31.73 Bipolar disorder, in partial remission, most recent episode manic** **F31.74 Bipolar disorder, in full remission, most recent episode manic** **F31.75 Bipolar disorder, in partial remission, most recent episode depressed** **F31.76 Bipolar disorder, in full remission, most recent episode depressed** **F31.77 Bipolar disorder, in partial remission, most recent episode mixed** **F31.78 Bipolar disorder, in full remission, most recent episode mixed** **F31.8 Other bipolar disorders** **F31.81 Bipolar II disorder** **F31.89 Other bipolar disorder** Recurrent manic episodes NOS **F31.9 Bipolar disorder, unspecified**	296.45 Bipolar I Disorder, Most Recent Episode Manic, In Partial Remission 296.46 Bipolar I Disorder, Most Recent Episode Manic, In Full Remission 296.5 BIPOLAR AFFECT, DEPRESS* 296.50 Bipolar I Disorder, Most Recent Episode Depressed, Unspecified 296.51 Bipolar I Disorder, Most Recent Episode Depressed, Mild 296.52 Bipolar I Disorder, Most Recent Episode Depressed, Moderate 296.53 Bipolar I Disorder, Most Recent Episode Depressed, Severe Without Psychotic Features 296.54 Bipolar I Disorder, Most Recent Episode Depressed, Severe With Psychotic Features 296.55 Bipolar I Disorder, Most Recent Episode Depressed, In Partial Remission 296.56 Bipolar I Disorder, Most Recent Episode Depressed, In Full Remission 296.6 BIPOLAR AFFECTIVE, MIXED* 296.60 Bipolar I Disorder, Most Recent Episode Mixed, Unspecified 296.61 Bipolar I Disorder, Most Recent Episode Mixed, Mild 296.62 Bipolar I Disorder, Most Recent Episode Mixed, Moderate 296.63 Bipolar I Disorder, Most Recent Episode Mixed, Severe Without Psychotic Features 296.64 Bipolar I Disorder, Most Recent Episode Mixed, Severe With Psychotic Features 296.65 Bipolar I Disorder, Most Recent Episode Mixed, In Partial Remission 296.66 Bipolar I Disorder, Most Recent Episode Mixed, In Full Remission 296.7 Bipolar I Disorder, Most Recent Episode Unspecified 296.8 MANIC-DEPRESSIVE NEC/NOS* 296.80 Bipolar Disorder NOS 296.81 ATYPICAL MANIC DISORDER 296.82 ATYPICAL DEPRESSIVE DIS 296.89 Bipolar II Disorder

Depressive Disorders	**F32 Major depressive disorder, single episode** **Includes:** single episode of agitated depression single episode of depressive reaction single episode of major depression single episode of psychogenic depression single episode of reactive depression single episode of vital depression **F32.0 Major depressive disorder, single episode, mild** **F32.1 Major depressive disorder, single episode, moderate** **F32.2 Major depressive disorder, single episode, severe without psychotic features** **F32.3Major depressive disorder, single episode, severe with psychotic features** Single episode of major depression with mood-congruent psychotic symptoms Single episode of major depression with mood-incongruent psychotic symptoms Single episode of major depression with psychotic symptoms Single episode of psychogenic depressive psychosis Single episode of psychotic depression Single episode of reactive depressive psychosis **F32.4 Major depressive disorder, single episode, in partial remission** **F32.5 Major depressive disorder, single episode, in full remission** **F32.8 Other depressive episodes** Atypical depression Post-schizophrenic depression Single episode of 'masked' depression NOS **F32.9 Major depressive disorder, single episode, unspecified** Depression NOS Depressive disorder NOS Major depression NOS **F33 Major depressive disorder, recurrent** **Includes:** recurrent episodes of depressive reaction recurrent episodes of endogenous depression recurrent episodes of major depression recurrent episodes of psychogenic depression recurrent episodes of reactive depression recurrent episodes of seasonal depressive disorder recurrent episodes of vital depression **F33.0 Major depressive disorder, recurrent, mild** **F33.1 Major depressive disorder, recurrent, moderate** **F33.2 Major depressive disorder, recurrent severe without psychotic features** **F33.3 Major depressive disorder, recurrent, severe with psychotic symptoms** Endogenous depression with psychotic symptoms Recurrent severe episodes of major depression with mood-congruent psychotic symptoms Recurrent severe episodes of major depression with mood-incongruent psychotic symptoms Recurrent severe episodes of major depression with psychotic symptoms Recurrent severe episodes of psychogenic depressive psychosis Recurrent severe episodes of psychotic depression Recurrent severe episodes of reactive depressive psychosis **F33.4 Major depressive disorder, recurrent, in remission** **F33.40 Major depressive disorder, recurrent, in remission, unspecified**	296.2 DEPR PSYCH, SINGL EPISOD* 296.20 Major Depressive Disorder, Single Episode, Unspecified 296.21 Major Depressive Disorder, Single Episode, Mild 296.22 Major Depressive Disorder, Single Episode, Moderate 296.23 Major Depressive Disorder, Single Episode, Severe Without Psychotic Features 296.24 Major Depressive Disorder, Single Episode, Severe With Psychotic Features 296.25 Major Depressive Disorder, Single Episode, In Partial Remission 296.26 Major Depressive Disorder, Single Episode, In Full Remission 296.3 DEPR PSYCH, RECUR EPISOD* 296.30 Major Depressive Disorder, Recurrent, Unspecified 296.31 Major Depressive Disorder, Recurrent, Mild 296.32 Major Depressive Disorder, Recurrent, Moderate 296.33 Major Depressive Disorder, Recurrent, Severe Without Psychotic Features 296.34 Major Depressive Disorder, Recurrent, Severe With Psychotic Features 296.35 Major Depressive Disorder, Recurrent, In Partial Remission 296.36 Major Depressive Disorder, Recurrent, In Full Remission 296.90 Mood Disorder NOS 300.4 Dysthymic Disorder 311 Depressive Disorder NOS

	F33.41 Major depressive disorder, recurrent, in partial remission **F33.42 Major depressive disorder, recurrent, in full remission** **F33.8 Other recurrent depressive disorders** **F33.9 Major depressive disorder, recurrent, unspecified** Monopolar depression NOS **F34 Persistent mood [affective] disorders** **F34.0 Cyclothymic disorder** Affective personality disorder Cycloid personality Cyclothymia Cyclothymic personality **F34.1 Dysthymic disorder** Depressive neurosis Depressive personality disorder Dysthymia Neurotic depression Persistent anxiety depression **F34.8 Other persistent mood [affective] disorders** **F34.9 Persistent mood [affective] disorder, unspecified** **F39 Unspecified mood [affective] disorder** Affective psychosis NOS		
Anxiety Disorders	**F40 Phobic anxiety disorders** **F40.0 Agoraphobia** **F40.00 Agoraphobia, unspecified** **F40.01 Agoraphobia with panic disorder** Panic disorder with agoraphobia **F40.02 Agoraphobia without panic disorder** **F40.1 Social phobias** Anthropophobia Social anxiety disorder of childhood **F40.10 Social phobia, unspecified** **F40.11 Social phobia, generalized** **F41.0 Panic disorder [episodic paroxysmal anxiety] without agoraphobia** Panic attack Panic state **F41.1Generalized anxiety disorder** Anxiety neurosis Anxiety reaction Anxiety state Overanxious disorder **F41.3Other mixed anxiety disorders** **F41.8 Other specified anxiety disorders** Anxiety depression (mild or not persistent) Anxiety hysteria Mixed anxiety and depressive disorder **F41.9 Anxiety disorder, unspecified** Anxiety NOS	300.0 300.00 300.01 300.02 300.09 300.2 300.20 300.21 300.22 Disorder 300.23	ANXIETY STATES* Anxiety Disorder NOS Panic Disorder Without Agoraphobia Generalized Anxiety Disorder ANXIETY STATE NEC PHOBIC DISORDERS* PHOBIA NOS Panic Disorder With Agoraphobia Agoraphobia Without History of Panic Social Phobia
Obsessive-Compulsive and Related Disorders	**F42 Obsessive-compulsive disorder** Anancastic neurosis Obsessive-compulsive neurosis	300.3 312.39	Obsessive-Compulsive Disorder Trichotillomania
Trauma and Stressor-Related Disorders	F43 **Reaction to severe stress, and adjustment disorders** **F43.0 Acute stress reaction** Acute crisis reaction Acute reaction to stress Combat and operational stress reaction Combat fatigue Crisis state Psychic shock **F43.1 Post-traumatic stress disorder (PTSD)** Traumatic neurosis **F43.10 Post-traumatic stress disorder, unspecified** **F43. 11 Post-traumatic stress disorder, acute** **F43.12 Post-traumatic stress disorder, chronic**	**308** **309** 308 308.0 308.1 308.2 308.3 308.4 308.9 309 309.0 Mood	**Acute reaction to stress** **Adjustment reaction** ACUTE REACTION TO STRESS* STRESS REACT, EMOTIONAL STRESS REACTION, FUGUE STRESS REACT, PSYCHOMOT Acute Stress Disorder STRESS REACT, MIXED DIS ACUTE STRESS REACT NOS ADJUSTMENT REACTION* Adjustment Disorder With Depressed

	F43.2 Adjustment disorders Culture shock Grief reaction Hospitalism in children **F43.20 Adjustment disorder, unspecified** **F43.21 Adjustment disorder with depressed mood** **F43.22 Adjustment disorder with anxiety** **F43.23 Adjustment disorder with mixed anxiety and depressed mood** **F43.24 Adjustment disorder with disturbance of conduct** **F43.25 Adjustment disorder with mixed disturbance of emotions and conduct** **F43.29 Adjustment disorder with other symptoms** **F43.8 Other reactions to severe stress** **F43.9 Reaction to severe stress, unspecified**	309.1 PROLONG DEPRESSIVE REACT 309.2 ADJUST REACT/OTH EMOTION* 309.21 Separation Anxiety Disorder 309.22 EMANCIPATION DISORDER 309.23 ACADEMIC/WORK INHIBITION 309.24 Adjustment Disorder With Anxiety 309.28 Adjustment Disorder With Mixed Anxiety and Depressed Mood 309.29 ADJ REACT-EMOTION NEC 309.3 Adjustment Disorder With Disturbance of Conduct 309.4 Adjustment Disorder With Mixed Disturbance of Emotions and Conduct 309.8 OTHER ADJUST REACTION* **309.81 Posttraumatic Stress Disorder** 309.82 ADJUST REACT-PHYS SYMPT 309.83 ADJUST REACT-WITHDRAWAL 309.89 ADJUSTMENT REACTION NEC 309.9 Adjustment Disorder Unspecified
Feeding and Eating Disorders	**F50 Eating disorders** **F50.00Anorexia nervosa** F50.01**Anorexia nervosa, unspecified** **F50.02 Anorexia nervosa, restricting type** **F50.03 Anorexia nervosa, binge eating/purging type** **F50.2 Bulimia nervosa** Bulimia NOS Hyperorexia nervosa **F50.9 Eating disorder, unspecified** Atypical anorexia nervosa Atypical bulimia nervosa	307.1 Anorexia Nervosa 307.5 EATING DISORDERS NEC/NOS* 307.50 Eating Disorder NOS 307.51 Bulimia Nervosa
Gender Dysphoria	**F64 Gender identity disorders** **F64.1 Gender identity disorder in adolescence and adulthood** Dual role transvestism Transsexualism **F64.2 Gender identity disorder of childhood** **F64.8 Other gender identity disorders** **F64.9 Gender identity disorder, unspecified** Gender-role disorder NOS	302.5 TRANS-SEXUALISM* 302.50 TRANS-SEXUALISM NOS 302.51 TRANS-SEXUALISM, ASEXUAL 302.52 TRANS-SEXUAL, HOMOSEXUAL 302.53 TRANS-SEX, HETEROSEXUAL 302.6 Gender Identity Disorder in Children or Gender Identity Disorder NOS 302.85 Gender Identity Disorder in Adolescents or Adults
Disruptive, Impulse-Control, and Conduct Disorders	**Behavioral and emotional disorders with onset usually occurring in childhood and adolescence (F90-F98)** Codes within categories F90-F98 may be used regardless of the age of a patient. These disorders generally have onset within the childhood or adolescent years, but may continue throughout life or not be diagnosed until adulthood **F91 Conduct disorders** **F91.0 Conduct disorder confined to family context** **F91.1 Conduct disorder, childhood-onset type** Unsocialized conduct disorder Conduct disorder, solitary aggressive type Unsocialized aggressive disorder **F91.2 Conduct disorder, adolescent-onset type** Socialized conduct disorder Conduct disorder, group type **F91.3 Oppositional defiant disorder** **F91.8 Other conduct disorders** **F91.9 Conduct disorder, unspecified** Behavioral disorder NOS Conduct disorder NOS Disruptive behavior disorder NOS **F63 Impulse disorders** **Excludes2:** habitual excessive use of alcohol or psychoactive substances (F10-F19) impulse disorders involving sexual behavior (F65.-) **F63.0 Pathological gambling** Compulsive gambling	312 Disturbance of conduct, not elsewhere classified 312.3 IMPULSE CONTROL DIS NEC* 312.30 Impulse-Control Disorder NOS 312.81 Conduct Disorder, Childhood-Onset Type 312.82 Conduct Disorder, Adolescent-Onset Type 312.89 Conduct Disorder, Unspecified Onset 312.9 Disruptive Behavior Disorder NOS 312.20 SOCIAL CONDUCT DIS-UNSP 312.21 SOCIAL CONDUCT DIS-MILD 312.22 SOCIAL CONDUCT DIS-MOD 312.23 SOCIAL CONDUCT DIS-SEV 312.3 IMPULSE CONTROL DIS NEC* 312.30 Impulse-Control Disorder NOS 312.31 Pathological Gambling 312.32 Kleptomania 312.33 Pyromania 312.34 Intermittent Explosive Disorder 312.35 ISOLATED EXPLOSIVE DIS 313.81 Oppositional Defiant Disorder

	F63.1 Pyromania Pathological fire-setting **F63.2 Kleptomania** Pathological stealing **F63.3 Trichotillomania** Hair plucking **F63.8 Other impulse disorders** **F63.81 Intermittent explosive disorder** **F63.89 Other impulse disorders** **F63.9 Impulse disorder, unspecified** Impulse control disorder NOS	
Personality Disorders	**F60** **F60.1 Schizoid personality disorder** **F60.2 Antisocial personality disorder** Amoral personality (disorder) Asocial personality (disorder) Dissocial personality disorder Psychopathic personality (disorder) Sociopathic personality (disorder) **F60.3 Borderline personality disorder** Aggressive personality (disorder) Emotionally unstable personality disorder Explosive personality (disorder) **F60.4 Histrionic personality disorder** Hysterical personality (disorder) Psychoinfantile personality (disorder) **F60.5 Obsessive-compulsive personality disorder** Anankastic personality (disorder) Compulsive personality (disorder) Obsessional personality (disorder) obsessive-compulsive disorder (F42) **F60.6 Avoidant personality disorder** Anxious personality disorder **F60.7 Dependent personality disorder** Asthenic personality (disorder) Inadequate personality (disorder) Passive personality (disorder) **F60.8 Other specific personality disorders** **F60.81 Narcissistic personality disorder** **F60.89 Other specific personality disorders** Eccentric personality disorder 'Haltlose' type personality disorder Immature personality disorder Passive-aggressive personality disorder Psychoneurotic personality disorder Self-defeating personality disorder **F60.9 Personality disorder, unspecified** Character disorder NOS Character neurosis NOS Pathological personality NOS	**301 PERSONALITY DISORDERS*** 301.0 Paranoid Personality Disorder 301.1 AFFECTIVE PERSONALITY* 301.10 AFFECTIV PERSONALITY NOS 301.11 CHRONIC HYPOMANIC PERSON 301.12 CHR DEPRESSIVE PERSON 301.13 Cyclothymic Disorder 301.2 SCHIZOID PERSONALITY* 301.20 Schizoid Personality Disorder 301.21 INTROVERTED PERSONALITY 301.22 Schizotypal Personality Disorder 301.3 EXPLOSIVE PERSONALITY 301.4 Obsessive-Compulsive Personality Disorder 301.50 Histrionic Personality Disorder 301.51 CHR FACTITIOUS ILLNESS 301.59 HISTRIONIC PERSON NEC 301.6 Dependent Personality Disorder 301.7 Antisocial Personality Disorder 301.8 OTHER PERSONALITY DIS* 301.81 Narcissistic Personality Disorder 301.82 Avoidant Personality Disorder 301.83 Borderline Personality Disorder 301.84 PASSIVE-AGGRESSIV PERSON 301.89 PERSONALITY DISORDER NEC 301.9 Personality Disorder NOS
Substance Use Disorders	**F10-F19**	**303 Alcohol dependence syndrome**

304 Drug dependence
305 Nondependent abuse of drugs

303 ALCOHOL DEPENDENCE SYNDR*
303.0 AC ALCOHOL INTOXICATION*
303.00 Alcohol Intoxication
303.01 AC ALCOHOL INTOX-CONTIN
303.02 AC ALCOHOL INTOX-EPISOD
303.03 AC ALCOHOL INTOX-REMISS
303.9 ALCOHOL DEPEND NEC/NOS*
303.90 Alcohol Dependence
303.91 ALCOH DEP NEC/NOS-CONTIN
303.92 ALCOH DEP NEC/NOS-EPISOD
303.93 ALCOH DEP NEC/NOS-REMISS
304 DRUG DEPENDENCE*
304.0 OPIOID TYPE DEPENDENCE*
304.00 Opioid Dependence
304.01 OPIOID DEPEND-CONTIN
304.02 OPIOID DEPENDENCE-EPISOD
304.03 OPIOID DEPENDENCE-REMISS
304.1 BARBITURATE DEPENDENCE*
304.10 Sedative, Hypnotic, or Anxiolytic Dependence
304.11 BARBITURAT DEPEND-CONTIN
304.12 BARBITURAT DEPEND-EPISOD
304.13 BARBITURAT DEPEND-REMISS
304.2 COCAINE DEPENDENCE*
304.20 Cocaine Dependence
304.21 COCAINE DEPEND-CONTIN
304.22 COCAINE DEPEND-EPISODIC
304.23 COCAINE DEPEND-REMISS
304.3 CANNABIS DEPENDENCE*
304.30 Cannabis Dependence
304.31 CANNABIS DEPEND-CONTIN
304.32 CANNABIS DEPEND-EPISODIC
304.33 CANNABIS DEPEND-REMISS
304.4 AMPHETAMINE DEPENDENCE*
304.40 Amphetamine Dependence
304.41 AMPHETAMIN DEPEND-CONTIN
304.42 AMPHETAMIN DEPEND-EPISOD
304.43 AMPHETAMIN DEPEND-REMISS
304.5 HALLUCINOGEN DEPENDENCE*
304.50 Hallucinogen Dependence
304.51 HALLUCINOGEN DEP-CONTIN
304.52 HALLUCINOGEN DEP-EPISOD
304.53 HALLUCINOGEN DEP-REMISS
304.6 DRUG DEPENDENCE NEC*
304.60 Inhalant Dependence or Phencyclidine Dependence
304.61 DRUG DEPEND NEC-CONTIN
304.62 DRUG DEPEND NEC-EPISODIC
304.63 DRUG DEPEND NEC-IN REM
304.7 OPIOID/OTHER DRUG DEPEND*
304.70 OPIOID/OTHER DEP-UNSPEC
304.71 OPIOID/OTHER DEP-CONTIN
304.72 OPIOID/OTHER DEP-EPISOD
304.73 OPIOID/OTHER DEP-REMISS
304.8 COMB DRUG DEPENDENCE NEC*
304.80 Polysubstance Dependence
304.81 COMB DRUG DEP NEC-CONTIN
304.82 COMB DRUG DEP NEC-EPISOD
304.83 COMB DRUG DEP NEC-REMISS
304.9 DRUG DEPENDENCE NOS*
304.90 Other (or Unknown) Substance Dependence
304.91 DRUG DEPEND NOS-CONTIN
304.92 DRUG DEPEND NOS-EPISODIC
304.93 DRUG DEPEND NOS-REMISS

305	NONDEPENDENT DRUG ABUSE*
305.0	ALCOHOL ABUSE*
305.00	Alcohol Abuse
305.01	ALCOHOL ABUSE-CONTINUOUS
305.02	ALCOHOL ABUSE-EPISODIC
305.03	ALCOHOL ABUSE-IN REMISS
305.1	Nicotine Dependence
305.2	CANNABIS ABUSE*
305.20	Cannabis Abuse
305.21	CANNABIS ABUSE-CONTIN
305.22	CANNABIS ABUSE-EPISODIC
305.23	CANNABIS ABUSE-IN REMISS
305.3	HALLUCINOGEN ABUSE*
305.30	Hallucinogen Abuse
305.31	HALLUCINOG ABUSE-CONTIN
305.32	HALLUCINOG ABUSE-EPISOD
305.33	HALLUCINOG ABUSE-REMISS
305.4	BARBITURATE ABUSE*
305.40	Sedative, Hypnotic, or Anxiolytic Abuse
305.41	BARBITURATE ABUSE-CONTIN
305.42	BARBITURATE ABUSE-EPISOD
305.43	BARBITURATE ABUSE-REMISS
305.5	OPIOID ABUSE*
305.50	Opioid Abuse
305.51	OPIOID ABUSE-CONTINUOUS
305.52	OPIOID ABUSE-EPISODIC
305.53	OPIOID ABUSE-IN REMISS
305.6	COCAINE ABUSE*
305.60	Cocaine Abuse
305.61	COCAINE ABUSE-CONTINUOUS
305.62	COCAINE ABUSE-EPISODIC
305.63	COCAINE ABUSE-IN REMISS
305.7	AMPHETAMINE ABUSE*
305.70	Amphetamine Abuse
305.71	AMPHETAMINE ABUSE-CONTIN
305.72	AMPHETAMINE ABUSE-EPISOD
305.73	AMPHETAMINE ABUSE-REMISS
305.8	ANTIDEPRESSANT ABUSE*
305.80	ANTIDEPRESS ABUSE-UNSPEC
305.81	ANTIDEPRESS ABUSE-CONTIN
305.82	ANTIDEPRESS ABUSE-EPISOD
305.83	ANTIDEPRESS ABUSE-REMISS
305.9	DRUG ABUSE NEC/NOS*
305.90	Phencyclidine Abuse, Inhalant Abuse, Other (or Unknown) Substance Abuse
305.91	DRUG ABUSE NEC-CONTIN
305.92	DRUG ABUSE NEC-EPISODIC
305.93	DRUG ABUSE NEC-IN REMISS
291.3	Alcohol-Induced Psychotic Disorder, With Hallucinations
291.4	PATHOLOGIC ALCOHOL INTOX
291.5	Alcohol-Induced Psychotic Disorder, With Delusions
291.8	ALCOHOLIC PSYCHOSIS NEC*
291.81	Alcohol Withdrawal
291.82	Alcohol-Induced Sleep Disorder
291.89	Alcohol-Induced Mood Disorder; Alcohol-Induced Sexual Dysfunction; Alcohol-Induced Sleep Disorder; Alcohol-Induced Anxiety Disorder
291.9	Alcohol-Related Disorder NOS
292	DRUG PSYCHOSES*
292.0	Amphetamine, Cocaine, Nicotine, Opioid, or Other (or Unknown)] Withdrawal; Sedative, Hypnotic or Anxiolytic Withdrawal
292.1	DRUG PARANOID/HALLUCINOS*
292.11	Amphetamine, Cannabis, Cocaine, Hallucinogen, Inhalant, Opioid, Phencyclidine, or Other (or Unknown) Substance-Induced Psychotic

Disorder, With Delusions; Sedative, Hypnotic or Anxiolytic-Induced Psychotic Disorder, With Delusions

292.12 Amphetamine, Cannabis, Cocaine, Hallucinogen, Inhalant, Opioid, Phencyclidine, or Other (or Unknown)] Substance-Induced Psychotic Disorder, With Hallucinations; Sedative-, Hypnotic- or Anxiolytic-Induced Psychotic Disorder, With Hallucinations

292.2 PATHOLOGIC DRUG INTOX

292.8 OTHER DRUG MENTAL DIS*

292.81 Amphetamine, Cannabis, Cocaine, Hallucinogen, Inhalant, Opioid, Phencyclidine, or Other (or Unknown)] Substance Intoxication Delirium; Sedative, Hypnotic or Anxiolytic Intoxication or Withdrawal Delirium

292.82 Inhalant or Other (or Unknown) Substance-Induced Persisting Dementia; Sedative-, Hypnotic- or Anxiolytic-Induced Persisting Dementia

292.83 Other (or Unknown)] Substance-Induced Persisting Amnestic Disorder; Sedative-, Hypnotic- or Anxiolytic-Induced Persisting Amnestic Disorder

292.84 Amphetamine, Cocaine, Hallucinogen, Inhalant, Opioid, Phencyclidine, or Other (or Unknown) Substance-Induced Mood Disorder; Sedative-, Hypnotic- or Anxiolytic-Induced Mood Disorder

292.85 Amphetamine, Caffeine, Cocaine, Opioid, or Other (or Unknown) Substance-Induced Sleep Disorder, Sedative-, Hypnotic- or Anxiolytic-Induced Sleep Disorder

292.89 Substance-Induced Anxiety Disorder, Sexual Disfunction, Sleep Disorder, or Intoxication (Refer to the DSM-IV-TR); Hallucinogen Persisting Perception Disorder

292.9 Amphetamine, Caffeine, Cannabis, Cocaine, Hallucinogen, Inhalant, Nicotine, Opioid, Phencyclidine, or Other (or Unknown) Substance-Related Disorder NOS; Sedative-, Hypnotic- or Anxiolytic-Related Disorder NOS

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	**page 2 -** ABSTRACT, , *"Data for this retrospective cohort…"*	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	**page 2-** ABSTRACT, , in-text reference: *"were derived from administrative data sources …" and* **page 2-** ABSTRACT, in-text reference: *"…in Ontario, Canada…"* **page 2-** ABSTRACT, in-text reference: *"All patient information was linked anonymously across databases using encrypted ten-*

					digit health card numbers."
Introduction,					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	**page 4 to 5 -** INTRODUCTION,		
Objectives	3	State specific objectives, including any pre-specified hypotheses	**page 5-** INTRODUCTION, in-text reference: *"...the goal of this study was to evaluate how UDS frequency impacts treatment retention in OAT in Ontario."*		
Methods					
Study Design	4	Present key elements of study design early in the paper	**page 5 -** METHODS, in-text reference: *"Data for this retrospective cohort study..."*		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	**page 5 to 6 -** METHODS		
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of	**Page 6 -** METHODS, in-text reference: "*We*	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to	**Page 6 and Figure 1 -** METHODS,

		selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	*excluded all patients…"* *n/a*	identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	**Page 6,** in-text reference: "*The Ontario Drug Benefit…"* *n/a* **Figure 1**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	**Page 7 -** METHODS,	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	**Page 7 -** METHODS,
Data sources/ measurement	8	For each variable of interest, give sources of data and	**Page 6 -** METHODS		

		details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			
Bias	9	Describe any efforts to address potential sources of bias	*n/a*		
Study size	10	Explain how the study size was arrived at	**Figure 1**		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	**Page 7 and 8-** MEHTODS		
Statistical methods	12	(a)Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed	**Page 8-** MEHTODS, in-text reference: "*Descriptive statistics were calculated…"* *n/a* **page 6 -** METHODS, in-text reference: *"…and those with missing…"*		

		(d) *Cohort study* - If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses			
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	**Page 5-** METHODS, **"***These data were obtained…"* **page 6 -** METHODS, in-text reference: *"…and those with missing…"*
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	**page 5 and 6 -** METHODS, in-text reference: "*Patient-level…"*
Results					
Participants	13	(a)Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed	**Figure 1**	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality,	**Figure 1**

		eligible, included in the study, completing follow-up, and analysed) (b)Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	
Descriptive data	14	(a)Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest	**Page 8-** RESULTS, in-text reference: *"There were significant differences between…"* **page 6 -** METHODS, in-text reference: *"…and those with missing…"*		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	**Page 9 and 10 -** RESULTS, in-text reference: *"As shown in Table 2…"*		

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	RESULTS, page 5, in-text reference: *"As shown in Table 2…"* and Table 2		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	*n/a*		
Discussion					
Key results	18	Summarise key results with reference to study objectives	**Page 10 and 11 -** DISCUSSION, in-text reference: *"The study sought to evaluate…"*		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	**Page 12 -** DISCUSSION, in-text reference: *"Some limitations in the current study…"*	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	**Page 12 -** DISCUSSION, in-text reference: *"Some limitations in the current study…"*
Interpretation	20	Give a cautious overall interpretation of results	**Page 12 an 13 -** CONCLUSION,		

		considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results	**Page 12 and 13 -** CONCLUSION		

BMJ Open

Evaluating the association between urine drug screening frequency and retention in opioid agonist treatment in Ontario, Canada: A Retrospective Cohort Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-060857.R2
Article Type:	Original research
Date Submitted by the Author:	14-Sep-2022
Complete List of Authors:	Morin, Kristen; Northern Ontario School of Medicine Dabous, John; Northern Ontario School of Medicine - East Campus Vojtesek, Frank; Northern Ontario School of Medicine - East Campus Marsh, David; Northern Ontario School of Medicine,
Primary Subject Heading:	Addiction
Secondary Subject Heading:	Epidemiology, Health services research, Public health
Keywords:	Substance misuse < PSYCHIATRY, PUBLIC HEALTH, EPIDEMIOLOGY

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Title: Evaluating the association between urine drug screening frequency and retention in opioid agonist treatment in Ontario, Canada: A Retrospective Cohort Study

Running Title: Urine drug screen frequency and OAT retention

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word count: 3,132

ABSTRACT

Objective: The objective of this study was to evaluate how urine drug screening frequency is associated with retention in opioid agonist treatment (OAT).

Methods: Data for this retrospective cohort study of 55,921 adults in OAT in Ontario, Canada, were derived from administrative sources between January 1, 2011, and December 31, 2015. All patient information was linked anonymously across databases using encrypted health card numbers. Descriptive statistics were calculated for comparing urine drug screening frequency groups 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 (aOR) 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 urine drug screens per month (weekly or more UDS). Significant associations were observed between urine drug screening 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 urine drug screening (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 an association between weekly urine drug screening and one-year treatment retention in OAT. There is an active discussion within Canada about the utility of urine drug screening. The lack of evidence for the impact of UDS on retention has left it open to some to argue they simply provide a barrier to patient engagement. Therefore it is timely of this study to demonstrate that more frequent urine testing is not associated with a reduction in treatment retention.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- There is the possibility of data entry and reporting errors associated with using administrative-level data.
- There is potential for unmeasured confounding, including confounding related to poly-substance use, social and interpersonal factors and clinical characteristics due to our study only having access to routinely collected data.
- In this study, analyze OAT (methadone and buprenorphine/naloxone) therefore, we did not adjust for medication type which has been shown to potentially impact retention.

- 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.
- This study cannot determine whether the requirement for UDS is a barrier to potential patients ever engaging in care, however the high level of treatment engagement in Ontario compared to other jurisdictions weighs against this being a substantial factor from a public health perspective

INTRODUCTION

An epidemic of opioid use disorder (OUD) and deaths related to opioid poisoning has emerged across Canada in last decade (1-5). Fortunately, 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, 6-9). 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 (10). Additionally, treatment discontinuation and cycling are very common (7, 8); and changes in opioid tolerance while on OAT (11) are contributing factors that lead to an exceptionally high risk of overdose mortality following discontinuation (2, 12-14). Sustained engagement in OAT, ideally for one year or more (15-17), is thus critical to realizing the protective benefits of this vital tool to address the opioid overdose crisis.

Patients in Ontario typically start treatment in a specialized addiction clinic for observed daily dosing for both methadone and buprenorphine/naloxone. Patients can receive increasing number of take home doses, based on the assessment of the physician in determining their level of functional stability (cessation of other opioid use, reduced problematic use of other substances, stable housing, stable physical and mental health, along with other factors.). Increasing or decreasing numbers of take home doses are linked to urine screening (UDS) results and frequency in an explicit contingency management schedule such that patients who are in the process of gradually increasing their level of stability, and thus number of weekly take home doses, will have

more frequent urine testing (18, 19). These take-home privileges are increased based on appointment attendance and consistently negative UDS 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. Within this general context there is scope for some variability in how this approach is applied by individual physicians. Some physicians place less emphasis on this contingency management approach or rely less on UDS to determine which patients receive increased numbers of take home doses. Some physicians may also be concerned that frequent UDS acts as a deterrent to treatment retention which counteracts the effectiveness of contingency management in reducing other drug use and improving retention. It is important to note that not all UDS collection events are associated with a physician appointment. Many patients are attending the clinic more often than weekly and can leave samples during the visit to receive medication. So the frequency of urine collection does not add an additional burden to reintegration over and above the burden of supervised ingestion of medication.

The cost of UDS billing has been the source of debate in Ontario (17, 18), resulting in recent UDS billing fee cuts (20) and recommendations for less frequent screening (21). 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 (22). In Ontario, there has been some variability in physician practice in terms of frequency of UDS and application of contingency management practices with respect to linking carry doses to drug-free urines. The study is meant to look at whether this variability impacts patient outcomes and in particular whether more frequent testing represents a barrier to 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 (23). 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 (24-26). The Laurentian University Research Ethics Board provided ethical approval for this study under project number 6009752. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used to write this manuscript (27).

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 (28, 29). Studies have demonstrated that multiple treatment attempts are correlated with a higher likelihood of positive outcomes (30-32). 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 Figure 1.

Patient and Public Involvement

There was no patient and public involvement involved in the design, conduct, reporting or dissemination of our research.

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). We defined patients with mental disorders group using OHIP database diagnostic codes. The following codes are outlined in Appendix A.

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 (15, 17, 33-37). 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 (15, 33, 36). 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 (38).

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 (39).

RESULTS

Figure 2 shows that 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.

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

	Urine Drug Test Frequency							
	Monthly or less		**Bi-Weekly**		**Weekly**		**More than weekly**	
	n=6,252 (11.20)	*d*	*n=9,495 (16.98)*	*d*	*n= 24,948 (44.61)*	*d*	*n =15,226 (27.23)*	*d*
Sex		0.02		0.03		0.09		0.12*
Female	2,268 (36.28)		3,217 (33.88)		8,217 (32.94)		5,992 (39.35)	
Male	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*
15 to 24	720 (11.20)		1,064 (11.21)		4,716 (18.90)		3,741 (24.57)	
25 to 34	1,358 (21.72)		2,656 (27.97)		9,086 (36.42)		5,906 (38.79)	
35 to 44	1,186 (18.967)		2,249 (23.69)		5,573 (22.34)		3,087 (20.27)	
45 to 54	1,415 (22.63)		2,277 (23.98)		4,161 (16.68)		1,947 (12.79)	

55 to 64	887 (14.19)		1,004 (10.57)		1,289 (5.17)		505 (3.32)	
65+	686 (10.97)		245 (2.58)		123 (0.49)		40 (0.26)	
Geography		0.11*		0.29*		0.22*		0.45*
Northern Rural	366 (5.85)		239 (2.52)		828 (3.32)		1,400 (9.19)	
Northern Urban	445 (7.12)		441 (4.64)		1,753 (7.03)		2,655 (17.44)	
Southern Rural	457 (7.31)		672 (7.08)		2,107 (8.45)		1,462 (9.60)	
Southern Urban	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*
1 (lowest)	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

d = standardized difference
**statistically significant*

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).

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

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

**reference group*
UDS - Urine drug screening
OR – Odds Ratio
aOR - Adjusted Odds Ratio
95% CI – 95% confidence interval

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. UDS frequency can vary based on patient drug use, treatment compliance, time in treatment, some physician discretion. Since in Ontario UDS is part of contingency management, the lowest frequency of urine testing would typically be seen in two groups of patients. First, less frequent testing is done for those patients who are chronically unstable (most often due to sustained use of other drugs, homelessness, or ineffectively treated mental health problems or a combination of these) and thus have the frequency or urine testing reduced as they are not engaged in demonstrating increasing levels of stability. Secondly, those patients who have demonstrated sustained periods of stability, including cessation of problematic use of other substances, will have observed dosing and urine testing less frequently and sufficient only to monitor for continued stability.

In our data we found that younger patients and those living in northern rural areas had more frequent UDS tests. This observation is likely reflective of physician and patient factors which may account for the higher frequency of urine testing in the Northern Ontario patient group. The physicians practicing in this geographic area may place more emphasis on adherence to the contingency management schedule in determining frequency of both UDS and take home doses. Alternatively, given the longer distances between patients and providers (35), the patients in this area may be more motivated to engage in the process of increased UDS in the short-term in order to obtain less frequent testing and higher frequency take home doses in the long-term. It is worth noting that our repeated observation in earlier papers (34, 35, 40) of higher treatment retention in the northern Ontario geographic area and the higher frequency of testing in this geographic area demonstrated in this paper is consistent with the overall relationship between UDS frequency and retention reported here.

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 (15, 33). 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 (41). 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, we acknowledge that this study cannot determine whether the requirement for UDS is a barrier to potential patients ever engaging in care. However the high level of treatment engagement in Ontario compared to other jurisdictions (for example US where the large majority of those with OUD have never been prescribed OAT) (42) weighs against this being a substantial factor from a public health perspective. Second, there is the possibility of data entry and reporting errors associated with using administrative-level data. Third, the data is collected for physician remuneration and funding therefore, its initial intention is not for research. Fourth, although we considered various factors associated with treatment retention, there is potential for unmeasured confounding, including confounding related to other substance use (36, 43, 44), social and interpersonal factors (45-48), the lack of patient descriptors that assess addiction severity and clinical characteristics (49, 50) due to our study only having access to routinely collected data. Fifth, in this study, methadone and buprenorphine/naloxone patients were grouped due to low frequency of buprenorphine/naloxone

prescriptions during our study period. 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 (51).

CONCLUSION

In summary, our study identified a significant association between the frequency of UDS and one-year treatment retention in OAT. There is an active discussion within Canada about the utility of UDS with some practitioners arguing that they should not be collected at all, or very rarely while others collect them frequently and tie them to increased take home doses under contingency management. The lack of evidence for the impact of UDS on retention has left it open to some to argue they simply provide a barrier to patient engagement. Therefore, it is timely of this study to demonstrate that more frequent urine testing is not associated with a reduction in treatment retention. 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.

FIGURE LEGEND

Figure 1: Flow Chart Outlining Data Build Including Linkages

Figure 2: Proportion of individuals retained for one year by UDS frequency groups

LIST OF 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

OUD Opioid Use Disorder

RPDB Registered Persons Database

SAS Statistical Analytics Software

DECLARATIONS

Acknowledgments

We thank IC/ES Data Analytic Services, more specifically Ryan Ng for his assistance with data extraction and database set up.

Funding

This research was partially supported by the Northern Ontario Academic Medicine Association Clinical Innovation Grant AFP Innovation Fund - Project #A-21-10.

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

Frank Vojtesek participated in database management, cleaning and organization, 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 under project ID number 6009752.

Availability of data and material

Data may be obtained from a third party and are not publicly available

Acknowledgements

We thank members of the Marsh research lab for their continued support and feedback. We also thank ICES, ICES North and Data Analytic Services (DAS) for their continued support.

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Figure 1: Flow Chart Outlining Data Build Including Linkages.

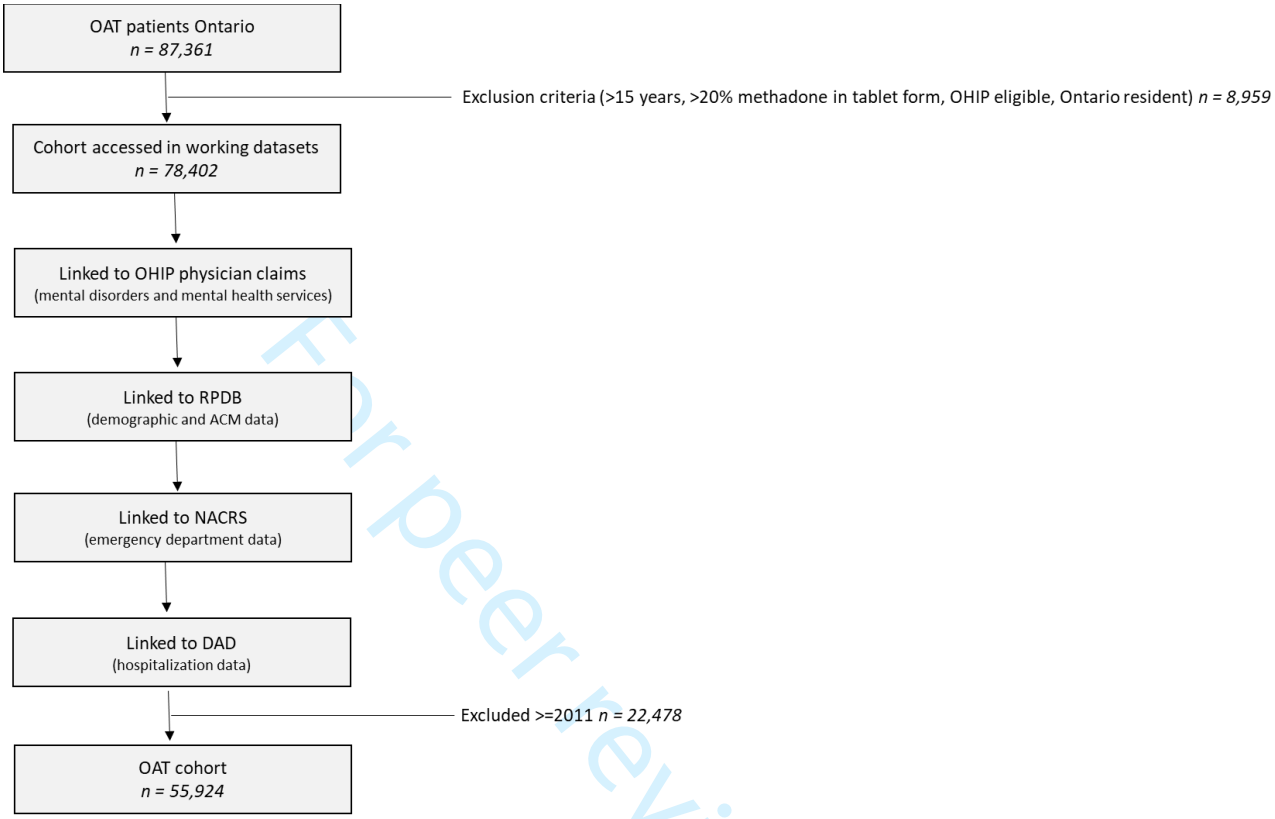
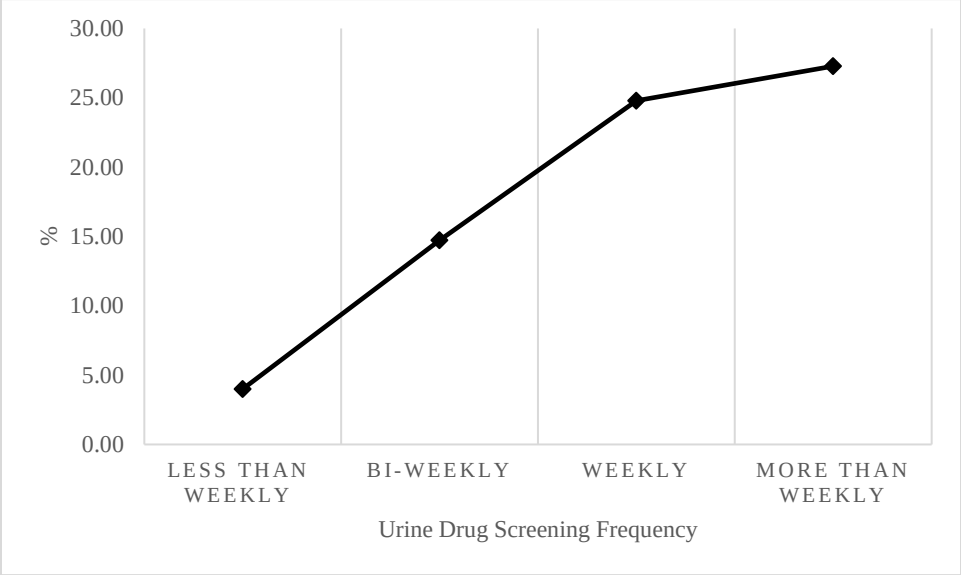


Figure 2: Proportion of individuals retained for one year by UDS frequency groups



Appendix A- Definition and ICD 9 and ICD10 codes for Mental Health Conditions

Definition Mental Health Conditions			
Mental Health Conditions	**ICD-10 Codes (DX10CODE1)**	**ICD-9 Codes**	Go Back
Neurodevelopmental Disorders	**F90 Attention-deficit hyperactivity disorders Includes:** attention deficit disorder with hyperactivity attention deficit syndrome with hyperactivity **F90.0 Attention-deficit hyperactivity disorder, predominantly inattentive type** **F90.1 Attention-deficit hyperactivity disorder, predominantly hyperactive type** **F90.2 Attention-deficit hyperactivity disorder, combined type** **F90.8 Attention-deficit hyperactivity disorder, other type** **F90.9 Attention-deficit hyperactivity disorder, unspecified type** Attention-deficit hyperactivity disorder of childhood or adolescence NOS Attention-deficit hyperactivity disorder NOS	**314.0**	**ATTENTION DEFICIT DIS***
		314.00	Attention-Deficit/Hyperactivity Disorder, Predominantly Inattentive Type
		314.01	Attention-Deficit/Hyperactivity Disorder, Combined Type or Attention-Deficit/Hyperactivity Disorder Predominantly Hyperactive-Impulsive Type
		314.9	Attention-Deficit/Hyperactivity Disorder NOS
Schizophrenia Spectrum and Related Disorders	**Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders (F20-F29)** **F20 Schizophrenia** **F20.0 Paranoid schizophrenia** Paraphrenic schizophrenia **F20.1 Disorganized schizophrenia** Hebephrenic schizophrenia Hebephrenia **F20.2 Catatonic schizophrenia** Schizophrenic catalepsy Schizophrenic catatonia Schizophrenic flexibilitas cerea **F20.3 Undifferentiated schizophrenia** Atypical schizophrenia **F20.5 Residual schizophrenia** Restzustand (schizophrenic) Schizophrenic residual state **F20.8 Other schizophrenia** **F20.81 Schizophreniform disorder** Schizophreniform psychosis NOS **F20.89 Other schizophrenia** Cenesthopathic schizophrenia Simple schizophrenia **F20.9 Schizophrenia, unspecified** **F21 Schizotypal disorder** Borderline schizophrenia Latent schizophrenia Latent schizophrenic reaction Prepsychotic schizophrenia Prodromal schizophrenia Pseudoneurotic schizophrenia Pseudopsychopathic schizophrenia Schizotypal personality disorder **F22 Delusional disorders** Delusional dysmorphophobia Involutional paranoid state Paranoia Paranoia querulans Paranoid psychosis Paranoid state Paraphrenia (late) Sensitiver Beziehungswahn **F23 Brief psychotic disorder** Paranoid reaction	**295**	**SCHIZOPHRENIC DISORDERS***
		295.0	SIMPLE SCHIZOPHRENIA*
		295.00	SIMPLE SCHIZOPHREN-UNSPECIFIED
		295.01	SIMPL SCHIZOPHREN-SUBCHR
		295.02	SIMPLE SCHIZOPHREN-CHR
		295.03	SIMP SCHIZ-SUBCHR/EXACER
		295.04	SIMPL SCHIZO-CHR/EXACERB
		295.05	SIMPL SCHIZOPHREN-REMISS
		295.1	HEBEPHRENIA*
		295.10	Schizophrenia, Disorganized Type
		295.11	HEBEPHRENIA-SUBCHRONIC
		295.12	HEBEPHRENIA-CHRONIC
		295.13	HEBEPHREN-SUBCHR/EXACERB
		295.14	HEBEPHRENIA-CHR/EXACERB
		295.15	HEBEPHRENIA-REMISSION
		295.2	CATATONIC SCHIZOPHRENIA*
		295.20	Schizophrenia, Catatonic Type
		295.21	CATATONIA-SUBCHRONIC
		295.22	CATATONIA-CHRONIC
		295.23	CATATONIA-SUBCHR/EXACERB
		295.24	CATATONIA-CHR/EXACERB
		295.25	CATATONIA-REMISSION
		295.3	PARANOID SCHIZOPHRENIA*
		295.30	Schizophrenia, Paranoid Type
		295.31	PARANOID SCHIZO-SUBCHR
		295.32	PARANOID SCHIZO-CHRONIC
		295.33	PARAN SCHIZO-SUBCHR/EXAC
		295.34	PARAN SCHIZO-CHR/EXACERB
		295.35	PARANOID SCHIZO-REMISS
		295.4	AC SCHIZOPHRENIC EPISODE*
		295.40	Schizophreniform Disorder
		295.41	AC SCHIZOPHRENIA-SUBCHR
		295.42	AC SCHIZOPHRENIA-CHR
		295.43	AC SCHIZO-SUBCHR/EXACERB
		295.44	AC SCHIZOPHR-CHR/EXACERB
		295.45	AC SCHIZOPHRENIA-REMISS
		295.5	LATENT SCHIZOPHRENIA*
		295.50	LATENT SCHIZOPHREN-UNSP
		295.51	LAT SCHIZOPHREN-SUBCHR
		295.52	LATENT SCHIZOPHREN-CHR
		295.53	LAT SCHIZO-SUBCHR/EXACER
		295.54	LATENT SCHIZO-CHR/EXACER
		295.55	LAT SCHIZOPHREN-REMISS

	Psychogenic paranoid psychosis	295.6 RESIDUAL SCHIZOPHRENIA*
	F24 Shared psychotic disorder	295.60 Schizophrenia, Residual Type
	Folie à deux	295.61 RESID SCHIZOPHREN-SUBCHR
	Induced paranoid disorder	295.62 RESIDUAL SCHIZOPHREN-CHR
	Induced psychotic disorder	295.63 RESID SCHIZO-SUBCHR/EXAC
	F25 Schizoaffective disorders	295.64 RESID SCHIZO-CHR/EXACERB
	F25.0 Schizoaffective disorder, bipolar type	295.65 RESID SCHIZOPHREN-REMISS
	Cyclic schizophrenia	295.7 SCHIZOAFFECTIVE TYPE*
	Schizoaffective disorder, manic type	295.70 Schizoaffective Disorder
	Schizoaffective disorder, mixed type	295.71 SCHIZOAFFECTIVE-SUBCHR
	Schizoaffective psychosis, bipolar type	295.72 SCHIZOAFFECTIVE-CHRONIC
	Schizophreniform psychosis, manic type	295.73 SCHIZOAFF-SUBCHR/EXACER
	F25.1 Schizoaffective disorder, depressive type	295.74 SCHIZOAFFECT-CHR/EXACER
	Schizoaffective psychosis, depressive type	295.75 SCHIZOAFFECTIVE-REMISS
	Schizophreniform psychosis, depressive type	295.8 SCHIZOPHRENIA NEC*
	F25.8 Other schizoaffective disorders	295.80 SCHIZOPHRENIA NEC-UNSPEC
	F25.9 Schizoaffective disorder, unspecified	295.81 SCHIZOPHRENIA NEC-SUBCHR
	Schizoaffective psychosis NOS	295.82 SCHIZOPHRENIA NEC-CHR
	F28 Other psychotic disorder not due to a substance or known physiological condition	295.83 SCHIZO NEC-SUBCHR/EXACER
		295.84 SCHIZO NEC-CHR/EXACERB
	Chronic hallucinatory psychosis	295.85 SCHIZOPHRENIA NEC-REMISS
	F29 Unspecified psychosis not due to a substance or known physiological condition	295.9 SCHIZOPHRENIA NOS*
		295.90 Schizophrenia Undifferentiated Type
	Psychosis NOS	295.91 SCHIZOPHRENIA NOS-SUBCHR
		295.92 SCHIZOPHRENIA NOS-CHR
		295.93 SCHIZO NOS-SUBCHR/EXACER
		295.94 SCHIZO NOS-CHR/EXACERB
		295.95 SCHIZOPHRENIA NOS-REMISS
		297.1 Delusional Disorder
		297.3 Shared Psychotic Disorder
		298.0 REACT DEPRESS PSYCHOSIS
		298.1 EXCITATIV TYPE PSYCHOSIS
		298.2 REACTIVE CONFUSION
		298.3 ACUTE PARANOID REACTION
		298.4 PSYCHOGEN PARANOID PSYCH
		298.8 Brief Psychotic Disorder
		298.9 Psychotic Disorder NOS
Bipolar and Related Disorders	**F30 –F31 Manic episode**	296.00 Bipolar I Disorder, Single Manic Episode, Unspecified
	Includes:	
	bipolar disorder, single manic episode	296.01 Bipolar I Disorder, Single Manic Episode, Mild
	mixed affective episode	
	F30.1 Manic episode without psychotic symptoms	296.02 Bipolar I Disorder, Single Manic Episode, Moderate
	F30.10 Manic episode without psychotic symptoms, unspecified	296.03 Bipolar I Disorder, Single Manic Episode, Severe Without Psychotic Features
	F30.11 Manic episode without psychotic symptoms, mild	296.04 Bipolar I Disorder, Single Manic Episode, Severe With Psychotic Features
	F30.12 Manic episode without psychotic symptoms, moderate	296.05 Bipolar I Disorder, Single Manic Episode, In Partial Remission
	F30.13 Manic episode, severe, without psychotic symptoms	296.06 Bipolar I Disorder, Single Manic Episode, In Full Remission
	F30.2 Manic episode, severe with psychotic symptoms	296.1 MANIC, RECURRENT EPISODE*
	Manic stupor	296.10 RECUR MANIC DIS-UNSPEC
	Mania with mood-congruent psychotic symptoms	296.11 RECUR MANIC DIS-MILD
	Mania with mood-incongruent psychotic symptoms	296.12 RECUR MANIC DIS-MOD
	F30.3 Manic episode in partial remission	296.13 RECUR MANIC DIS-SEVERE
	F30.4 Manic episode in full remission	296.14 RECUR MANIC-SEV W PSYCHO
	F30.8 Other manic episodes	296.15 RECUR MANIC-PART REMISS
	Hypomania	296.16 RECUR MANIC-FULL REMISS
	F30.9 Manic episode, unspecified	296.4 BIPOLAR AFFECTIVE, MANIC*
	Mania NOS	296.40 Bipolar I Disorder, Most Recent Episode Hypomanic or Manic, Unspecified
	F31 Bipolar disorder	
	Includes:	296.41 Bipolar I Disorder, Most Recent Episode Manic, Mild
	manic-depressive illness	
	manic-depressive psychosis	296.42 Bipolar I Disorder, Most Recent Episode Manic, Moderate
	manic-depressive reaction	
	F31.0 Bipolar disorder, current episode hypomanic	296.43 Bipolar I Disorder, Most Recent Episode Manic, Severe Without Psychotic Features
	F31.1 Bipolar disorder, current episode manic without psychotic features	296.44 Bipolar I Disorder, Most Recent Episode Manic, Severe With Psychotic Features

	F31.10 Bipolar disorder, current episode manic without psychotic features, unspecified **F31.11 Bipolar disorder, current episode manic without psychotic features, mild** **F31.12 Bipolar disorder, current episode manic without psychotic features, moderate** **F31.13 Bipolar disorder, current episode manic without psychotic features, severe** **F31.2 Bipolar disorder, current episode manic severe with psychotic features** Bipolar disorder, current episode manic with mood-congruent psychotic symptoms Bipolar disorder, current episode manic with mood-incongruent psychotic symptoms F31.3 **Bipolar disorder, current episode depressed, mild or moderate severity** **F31.30 Bipolar disorder, current episode depressed, mild or moderate severity, unspecified** **F31.31 Bipolar disorder, current episode depressed, mild** **F31.32 Bipolar disorder, current episode depressed, moderate** **F31.4 Bipolar disorder, current episode depressed, severe, without psychotic features** **F31.5 Bipolar disorder, current episode depressed, severe, with psychotic features** Bipolar disorder, current episode depressed with mood-incongruent psychotic symptoms Bipolar disorder, current episode depressed with mood-congruent psychotic symptoms **F31.6 Bipolar disorder, current episode mixed** **F31.60 Bipolar disorder, current episode mixed, unspecified** **F31.61 Bipolar disorder, current episode mixed, mild** **F31.62 Bipolar disorder, current episode mixed, moderate** **F31.63 Bipolar disorder, current episode mixed, severe, without psychotic features** **F31.64 Bipolar disorder, current episode mixed, severe, with psychotic features** Bipolar disorder, current episode mixed with mood-congruent psychotic symptoms Bipolar disorder, current episode mixed with mood-incongruent psychotic symptoms **F31.7 Bipolar disorder, currently in remission** **F31.70 Bipolar disorder, currently in remission, most recent episode unspecified** **F31.71 Bipolar disorder, in partial remission, most recent episode hypomanic** **F31.72 Bipolar disorder, in full remission, most recent episode hypomanic** **F31.73 Bipolar disorder, in partial remission, most recent episode manic** **F31.74 Bipolar disorder, in full remission, most recent episode manic** **F31.75 Bipolar disorder, in partial remission, most recent episode depressed** **F31.76 Bipolar disorder, in full remission, most recent episode depressed** **F31.77 Bipolar disorder, in partial remission, most recent episode mixed** **F31.78 Bipolar disorder, in full remission, most recent episode mixed** **F31.8 Other bipolar disorders** **F31.81 Bipolar II disorder** **F31.89 Other bipolar disorder** Recurrent manic episodes NOS **F31.9 Bipolar disorder, unspecified**	296.45 Bipolar I Disorder, Most Recent Episode Manic, In Partial Remission 296.46 Bipolar I Disorder, Most Recent Episode Manic, In Full Remission 296.5 BIPOLAR AFFECT, DEPRESS* 296.50 Bipolar I Disorder, Most Recent Episode Depressed, Unspecified 296.51 Bipolar I Disorder, Most Recent Episode Depressed, Mild 296.52 Bipolar I Disorder, Most Recent Episode Depressed, Moderate 296.53 Bipolar I Disorder, Most Recent Episode Depressed, Severe Without Psychotic Features 296.54 Bipolar I Disorder, Most Recent Episode Depressed, Severe With Psychotic Features 296.55 Bipolar I Disorder, Most Recent Episode Depressed, In Partial Remission 296.56 Bipolar I Disorder, Most Recent Episode Depressed, In Full Remission 296.6 BIPOLAR AFFECTIVE, MIXED* 296.60 Bipolar I Disorder, Most Recent Episode Mixed, Unspecified 296.61 Bipolar I Disorder, Most Recent Episode Mixed, Mild 296.62 Bipolar I Disorder, Most Recent Episode Mixed, Moderate 296.63 Bipolar I Disorder, Most Recent Episode Mixed, Severe Without Psychotic Features 296.64 Bipolar I Disorder, Most Recent Episode Mixed, Severe With Psychotic Features 296.65 Bipolar I Disorder, Most Recent Episode Mixed, In Partial Remission 296.66 Bipolar I Disorder, Most Recent Episode Mixed, In Full Remission 296.7 Bipolar I Disorder, Most Recent Episode Unspecified 296.8 MANIC-DEPRESSIVE NEC/NOS* 296.80 Bipolar Disorder NOS 296.81 ATYPICAL MANIC DISORDER 296.82 ATYPICAL DEPRESSIVE DIS 296.89 Bipolar II Disorder

Depressive Disorders	**F32 Major depressive disorder, single episode** **Includes:** single episode of agitated depression single episode of depressive reaction single episode of major depression single episode of psychogenic depression single episode of reactive depression single episode of vital depression **F32.0 Major depressive disorder, single episode, mild** **F32.1 Major depressive disorder, single episode, moderate** **F32.2 Major depressive disorder, single episode, severe without psychotic features** **F32.3Major depressive disorder, single episode, severe with psychotic features** Single episode of major depression with mood-congruent psychotic symptoms Single episode of major depression with mood-incongruent psychotic symptoms Single episode of major depression with psychotic symptoms Single episode of psychogenic depressive psychosis Single episode of psychotic depression Single episode of reactive depressive psychosis **F32.4 Major depressive disorder, single episode, in partial remission** **F32.5 Major depressive disorder, single episode, in full remission** **F32.8 Other depressive episodes** Atypical depression Post-schizophrenic depression Single episode of 'masked' depression NOS **F32.9 Major depressive disorder, single episode, unspecified** Depression NOS Depressive disorder NOS Major depression NOS **F33 Major depressive disorder, recurrent** **Includes:** recurrent episodes of depressive reaction recurrent episodes of endogenous depression recurrent episodes of major depression recurrent episodes of psychogenic depression recurrent episodes of reactive depression recurrent episodes of seasonal depressive disorder recurrent episodes of vital depression **F33.0 Major depressive disorder, recurrent, mild** **F33.1 Major depressive disorder, recurrent, moderate** **F33.2 Major depressive disorder, recurrent severe without psychotic features** **F33.3 Major depressive disorder, recurrent, severe with psychotic symptoms** Endogenous depression with psychotic symptoms Recurrent severe episodes of major depression with mood-congruent psychotic symptoms Recurrent severe episodes of major depression with mood-incongruent psychotic symptoms Recurrent severe episodes of major depression with psychotic symptoms Recurrent severe episodes of psychogenic depressive psychosis Recurrent severe episodes of psychotic depression Recurrent severe episodes of reactive depressive psychosis **F33.4 Major depressive disorder, recurrent, in remission** **F33.40 Major depressive disorder, recurrent, in remission, unspecified**	296.2 DEPR PSYCH, SINGL EPISOD* 296.20 Major Depressive Disorder, Single Episode, Unspecified 296.21 Major Depressive Disorder, Single Episode, Mild 296.22 Major Depressive Disorder, Single Episode, Moderate 296.23 Major Depressive Disorder, Single Episode, Severe Without Psychotic Features 296.24 Major Depressive Disorder, Single Episode, Severe With Psychotic Features 296.25 Major Depressive Disorder, Single Episode, In Partial Remission 296.26 Major Depressive Disorder, Single Episode, In Full Remission 296.3 DEPR PSYCH, RECUR EPISOD* 296.30 Major Depressive Disorder, Recurrent, Unspecified 296.31 Major Depressive Disorder, Recurrent, Mild 296.32 Major Depressive Disorder, Recurrent, Moderate 296.33 Major Depressive Disorder, Recurrent, Severe Without Psychotic Features 296.34 Major Depressive Disorder, Recurrent, Severe With Psychotic Features 296.35 Major Depressive Disorder, Recurrent, In Partial Remission 296.36 Major Depressive Disorder, Recurrent, In Full Remission 296.90 Mood Disorder NOS 300.4 Dysthymic Disorder 311 Depressive Disorder NOS

	F33.41 Major depressive disorder, recurrent, in partial remission **F33.42 Major depressive disorder, recurrent, in full remission** **F33.8 Other recurrent depressive disorders** **F33.9 Major depressive disorder, recurrent, unspecified** Monopolar depression NOS **F34 Persistent mood [affective] disorders** **F34.0 Cyclothymic disorder** Affective personality disorder Cycloid personality Cyclothymia Cyclothymic personality **F34.1 Dysthymic disorder** Depressive neurosis Depressive personality disorder Dysthymia Neurotic depression Persistent anxiety depression **F34.8 Other persistent mood [affective] disorders** **F34.9 Persistent mood [affective] disorder, unspecified** **F39 Unspecified mood [affective] disorder** Affective psychosis NOS		
Anxiety Disorders	**F40 Phobic anxiety disorders** **F40.0 Agoraphobia** **F40.00 Agoraphobia, unspecified** **F40.01 Agoraphobia with panic disorder** Panic disorder with agoraphobia **F40.02 Agoraphobia without panic disorder** **F40.1 Social phobias** Anthropophobia Social anxiety disorder of childhood **F40.10 Social phobia, unspecified** **F40.11 Social phobia, generalized** **F41.0 Panic disorder [episodic paroxysmal anxiety] without agoraphobia** Panic attack Panic state **F41.1Generalized anxiety disorder** Anxiety neurosis Anxiety reaction Anxiety state Overanxious disorder **F41.3Other mixed anxiety disorders** **F41.8 Other specified anxiety disorders** Anxiety depression (mild or not persistent) Anxiety hysteria Mixed anxiety and depressive disorder **F41.9 Anxiety disorder, unspecified** Anxiety NOS	300.0 300.00 300.01 300.02 300.09 300.2 300.20 300.21 300.22 Disorder 300.23	ANXIETY STATES* Anxiety Disorder NOS Panic Disorder Without Agoraphobia Generalized Anxiety Disorder ANXIETY STATE NEC PHOBIC DISORDERS* PHOBIA NOS Panic Disorder With Agoraphobia Agoraphobia Without History of Panic Social Phobia
Obsessive-Compulsive and Related Disorders	**F42 Obsessive-compulsive disorder** Anancastic neurosis Obsessive-compulsive neurosis	300.3 312.39	Obsessive-Compulsive Disorder Trichotillomania
Trauma and Stressor-Related Disorders	F43 **Reaction to severe stress, and adjustment disorders** **F43.0 Acute stress reaction** Acute crisis reaction Acute reaction to stress Combat and operational stress reaction Combat fatigue Crisis state Psychic shock **F43.1 Post-traumatic stress disorder (PTSD)** Traumatic neurosis **F43.10 Post-traumatic stress disorder, unspecified** **F43. 11 Post-traumatic stress disorder, acute** **F43.12 Post-traumatic stress disorder, chronic**	**308** **309** 308 308.0 308.1 308.2 308.3 308.4 308.9 309 309.0 Mood	**Acute reaction to stress** **Adjustment reaction** ACUTE REACTION TO STRESS* STRESS REACT, EMOTIONAL STRESS REACTION, FUGUE STRESS REACT, PSYCHOMOT Acute Stress Disorder STRESS REACT, MIXED DIS ACUTE STRESS REACT NOS ADJUSTMENT REACTION* Adjustment Disorder With Depressed

	F43.2 Adjustment disorders Culture shock Grief reaction Hospitalism in children **F43.20 Adjustment disorder, unspecified** **F43.21 Adjustment disorder with depressed mood** **F43.22 Adjustment disorder with anxiety** **F43.23 Adjustment disorder with mixed anxiety and depressed mood** **F43.24 Adjustment disorder with disturbance of conduct** **F43.25 Adjustment disorder with mixed disturbance of emotions and conduct** **F43.29 Adjustment disorder with other symptoms** **F43.8 Other reactions to severe stress** **F43.9 Reaction to severe stress, unspecified**	309.1 PROLONG DEPRESSIVE REACT 309.2 ADJUST REACT/OTH EMOTION* 309.21 Separation Anxiety Disorder 309.22 EMANCIPATION DISORDER 309.23 ACADEMIC/WORK INHIBITION 309.24 Adjustment Disorder With Anxiety 309.28 Adjustment Disorder With Mixed Anxiety and Depressed Mood 309.29 ADJ REACT-EMOTION NEC 309.3 Adjustment Disorder With Disturbance of Conduct 309.4 Adjustment Disorder With Mixed Disturbance of Emotions and Conduct 309.8 OTHER ADJUST REACTION* **309.81 Posttraumatic Stress Disorder** 309.82 ADJUST REACT-PHYS SYMPT 309.83 ADJUST REACT-WITHDRAWAL 309.89 ADJUSTMENT REACTION NEC 309.9 Adjustment Disorder Unspecified
Feeding and Eating Disorders	**F50 Eating disorders** **F50.00Anorexia nervosa** F50.01**Anorexia nervosa, unspecified** **F50.02 Anorexia nervosa, restricting type** **F50.03 Anorexia nervosa, binge eating/purging type** **F50.2 Bulimia nervosa** Bulimia NOS Hyperorexia nervosa **F50.9 Eating disorder, unspecified** Atypical anorexia nervosa Atypical bulimia nervosa	307.1 Anorexia Nervosa 307.5 EATING DISORDERS NEC/NOS* 307.50 Eating Disorder NOS 307.51 Bulimia Nervosa
Gender Dysphoria	**F64 Gender identity disorders** **F64.1 Gender identity disorder in adolescence and adulthood** Dual role transvestism Transsexualism **F64.2 Gender identity disorder of childhood** **F64.8 Other gender identity disorders** **F64.9 Gender identity disorder, unspecified** Gender-role disorder NOS	302.5 TRANS-SEXUALISM* 302.50 TRANS-SEXUALISM NOS 302.51 TRANS-SEXUALISM, ASEXUAL 302.52 TRANS-SEXUAL, HOMOSEXUAL 302.53 TRANS-SEX, HETEROSEXUAL 302.6 Gender Identity Disorder in Children or Gender Identity Disorder NOS 302.85 Gender Identity Disorder in Adolescents or Adults
Disruptive, Impulse-Control, and Conduct Disorders	**Behavioral and emotional disorders with onset usually occurring in childhood and adolescence (F90-F98)** Codes within categories F90-F98 may be used regardless of the age of a patient. These disorders generally have onset within the childhood or adolescent years, but may continue throughout life or not be diagnosed until adulthood **F91 Conduct disorders** **F91.0 Conduct disorder confined to family context** **F91.1 Conduct disorder, childhood-onset type** Unsocialized conduct disorder Conduct disorder, solitary aggressive type Unsocialized aggressive disorder **F91.2 Conduct disorder, adolescent-onset type** Socialized conduct disorder Conduct disorder, group type **F91.3 Oppositional defiant disorder** **F91.8 Other conduct disorders** **F91.9 Conduct disorder, unspecified** Behavioral disorder NOS Conduct disorder NOS Disruptive behavior disorder NOS **F63 Impulse disorders** **Excludes2:** habitual excessive use of alcohol or psychoactive substances (F10-F19) impulse disorders involving sexual behavior (F65.-) **F63.0 Pathological gambling** Compulsive gambling	312 Disturbance of conduct, not elsewhere classified 312.3 IMPULSE CONTROL DIS NEC* 312.30 Impulse-Control Disorder NOS 312.81 Conduct Disorder, Childhood-Onset Type 312.82 Conduct Disorder, Adolescent-Onset Type 312.89 Conduct Disorder, Unspecified Onset 312.9 Disruptive Behavior Disorder NOS 312.20 SOCIAL CONDUCT DIS-UNSP 312.21 SOCIAL CONDUCT DIS-MILD 312.22 SOCIAL CONDUCT DIS-MOD 312.23 SOCIAL CONDUCT DIS-SEV 312.3 IMPULSE CONTROL DIS NEC* 312.30 Impulse-Control Disorder NOS 312.31 Pathological Gambling 312.32 Kleptomania 312.33 Pyromania 312.34 Intermittent Explosive Disorder 312.35 ISOLATED EXPLOSIVE DIS 313.81 Oppositional Defiant Disorder

	F63.1 Pyromania Pathological fire-setting **F63.2 Kleptomania** Pathological stealing **F63.3 Trichotillomania** Hair plucking **F63.8 Other impulse disorders** **F63.81 Intermittent explosive disorder** **F63.89 Other impulse disorders** **F63.9 Impulse disorder, unspecified** Impulse control disorder NOS	
Personality Disorders	**F60** **F60.1 Schizoid personality disorder** **F60.2 Antisocial personality disorder** Amoral personality (disorder) Asocial personality (disorder) Dissocial personality disorder Psychopathic personality (disorder) Sociopathic personality (disorder) **F60.3 Borderline personality disorder** Aggressive personality (disorder) Emotionally unstable personality disorder Explosive personality (disorder) **F60.4 Histrionic personality disorder** Hysterical personality (disorder) Psychoinfantile personality (disorder) **F60.5 Obsessive-compulsive personality disorder** Anankastic personality (disorder) Compulsive personality (disorder) Obsessional personality (disorder) obsessive-compulsive disorder (F42) **F60.6 Avoidant personality disorder** Anxious personality disorder **F60.7 Dependent personality disorder** Asthenic personality (disorder) Inadequate personality (disorder) Passive personality (disorder) **F60.8 Other specific personality disorders** **F60.81 Narcissistic personality disorder** **F60.89 Other specific personality disorders** Eccentric personality disorder 'Haltlose' type personality disorder Immature personality disorder Passive-aggressive personality disorder Psychoneurotic personality disorder Self-defeating personality disorder **F60.9 Personality disorder, unspecified** Character disorder NOS Character neurosis NOS Pathological personality NOS	**301 PERSONALITY DISORDERS*** 301.0 Paranoid Personality Disorder 301.1 AFFECTIVE PERSONALITY* 301.10 AFFECTIV PERSONALITY NOS 301.11 CHRONIC HYPOMANIC PERSON 301.12 CHR DEPRESSIVE PERSON 301.13 Cyclothymic Disorder 301.2 SCHIZOID PERSONALITY* 301.20 Schizoid Personality Disorder 301.21 INTROVERTED PERSONALITY 301.22 Schizotypal Personality Disorder 301.3 EXPLOSIVE PERSONALITY 301.4 Obsessive-Compulsive Personality Disorder 301.50 Histrionic Personality Disorder 301.51 CHR FACTITIOUS ILLNESS 301.59 HISTRIONIC PERSON NEC 301.6 Dependent Personality Disorder 301.7 Antisocial Personality Disorder 301.8 OTHER PERSONALITY DIS* 301.81 Narcissistic Personality Disorder 301.82 Avoidant Personality Disorder 301.83 Borderline Personality Disorder 301.84 PASSIVE-AGGRESSIV PERSON 301.89 PERSONALITY DISORDER NEC 301.9 Personality Disorder NOS
Substance Use Disorders	**F10-F19**	**303 Alcohol dependence syndrome**

304 Drug dependence
305 Nondependent abuse of drugs

303 ALCOHOL DEPENDENCE SYNDR*
303.0 AC ALCOHOL INTOXICATION*
303.00 Alcohol Intoxication
303.01 AC ALCOHOL INTOX-CONTIN
303.02 AC ALCOHOL INTOX-EPISOD
303.03 AC ALCOHOL INTOX-REMISS
303.9 ALCOHOL DEPEND NEC/NOS*
303.90 Alcohol Dependence
303.91 ALCOH DEP NEC/NOS-CONTIN
303.92 ALCOH DEP NEC/NOS-EPISOD
303.93 ALCOH DEP NEC/NOS-REMISS
304 DRUG DEPENDENCE*
304.0 OPIOID TYPE DEPENDENCE*
304.00 Opioid Dependence
304.01 OPIOID DEPEND-CONTIN
304.02 OPIOID DEPENDENCE-EPISOD
304.03 OPIOID DEPENDENCE-REMISS
304.1 BARBITURATE DEPENDENCE*
304.10 Sedative, Hypnotic, or Anxiolytic Dependence
304.11 BARBITURAT DEPEND-CONTIN
304.12 BARBITURAT DEPEND-EPISOD
304.13 BARBITURAT DEPEND-REMISS
304.2 COCAINE DEPENDENCE*
304.20 Cocaine Dependence
304.21 COCAINE DEPEND-CONTIN
304.22 COCAINE DEPEND-EPISODIC
304.23 COCAINE DEPEND-REMISS
304.3 CANNABIS DEPENDENCE*
304.30 Cannabis Dependence
304.31 CANNABIS DEPEND-CONTIN
304.32 CANNABIS DEPEND-EPISODIC
304.33 CANNABIS DEPEND-REMISS
304.4 AMPHETAMINE DEPENDENCE*
304.40 Amphetamine Dependence
304.41 AMPHETAMIN DEPEND-CONTIN
304.42 AMPHETAMIN DEPEND-EPISOD
304.43 AMPHETAMIN DEPEND-REMISS
304.5 HALLUCINOGEN DEPENDENCE*
304.50 Hallucinogen Dependence
304.51 HALLUCINOGEN DEP-CONTIN
304.52 HALLUCINOGEN DEP-EPISOD
304.53 HALLUCINOGEN DEP-REMISS
304.6 DRUG DEPENDENCE NEC*
304.60 Inhalant Dependence or Phencyclidine Dependence
304.61 DRUG DEPEND NEC-CONTIN
304.62 DRUG DEPEND NEC-EPISODIC
304.63 DRUG DEPEND NEC-IN REM
304.7 OPIOID/OTHER DRUG DEPEND*
304.70 OPIOID/OTHER DEP-UNSPEC
304.71 OPIOID/OTHER DEP-CONTIN
304.72 OPIOID/OTHER DEP-EPISOD
304.73 OPIOID/OTHER DEP-REMISS
304.8 COMB DRUG DEPENDENCE NEC*
304.80 Polysubstance Dependence
304.81 COMB DRUG DEP NEC-CONTIN
304.82 COMB DRUG DEP NEC-EPISOD
304.83 COMB DRUG DEP NEC-REMISS
304.9 DRUG DEPENDENCE NOS*
304.90 Other (or Unknown) Substance Dependence
304.91 DRUG DEPEND NOS-CONTIN
304.92 DRUG DEPEND NOS-EPISODIC
304.93 DRUG DEPEND NOS-REMISS

305	NONDEPENDENT DRUG ABUSE*
305.0	ALCOHOL ABUSE*
305.00	Alcohol Abuse
305.01	ALCOHOL ABUSE-CONTINUOUS
305.02	ALCOHOL ABUSE-EPISODIC
305.03	ALCOHOL ABUSE-IN REMISS
305.1	Nicotine Dependence
305.2	CANNABIS ABUSE*
305.20	Cannabis Abuse
305.21	CANNABIS ABUSE-CONTIN
305.22	CANNABIS ABUSE-EPISODIC
305.23	CANNABIS ABUSE-IN REMISS
305.3	HALLUCINOGEN ABUSE*
305.30	Hallucinogen Abuse
305.31	HALLUCINOG ABUSE-CONTIN
305.32	HALLUCINOG ABUSE-EPISOD
305.33	HALLUCINOG ABUSE-REMISS
305.4	BARBITURATE ABUSE*
305.40	Sedative, Hypnotic, or Anxiolytic Abuse
305.41	BARBITURATE ABUSE-CONTIN
305.42	BARBITURATE ABUSE-EPISOD
305.43	BARBITURATE ABUSE-REMISS
305.5	OPIOID ABUSE*
305.50	Opioid Abuse
305.51	OPIOID ABUSE-CONTINUOUS
305.52	OPIOID ABUSE-EPISODIC
305.53	OPIOID ABUSE-IN REMISS
305.6	COCAINE ABUSE*
305.60	Cocaine Abuse
305.61	COCAINE ABUSE-CONTINUOUS
305.62	COCAINE ABUSE-EPISODIC
305.63	COCAINE ABUSE-IN REMISS
305.7	AMPHETAMINE ABUSE*
305.70	Amphetamine Abuse
305.71	AMPHETAMINE ABUSE-CONTIN
305.72	AMPHETAMINE ABUSE-EPISOD
305.73	AMPHETAMINE ABUSE-REMISS
305.8	ANTIDEPRESSANT ABUSE*
305.80	ANTIDEPRESS ABUSE-UNSPEC
305.81	ANTIDEPRESS ABUSE-CONTIN
305.82	ANTIDEPRESS ABUSE-EPISOD
305.83	ANTIDEPRESS ABUSE-REMISS
305.9	DRUG ABUSE NEC/NOS*
305.90	Phencyclidine Abuse, Inhalant Abuse, Other (or Unknown) Substance Abuse
305.91	DRUG ABUSE NEC-CONTIN
305.92	DRUG ABUSE NEC-EPISODIC
305.93	DRUG ABUSE NEC-IN REMISS
291.3	Alcohol-Induced Psychotic Disorder, With Hallucinations
291.4	PATHOLOGIC ALCOHOL INTOX
291.5	Alcohol-Induced Psychotic Disorder, With Delusions
291.8	ALCOHOLIC PSYCHOSIS NEC*
291.81	Alcohol Withdrawal
291.82	Alcohol-Induced Sleep Disorder
291.89	Alcohol-Induced Mood Disorder; Alcohol-Induced Sexual Dysfunction; Alcohol-Induced Sleep Disorder; Alcohol-Induced Anxiety Disorder
291.9	Alcohol-Related Disorder NOS
292	DRUG PSYCHOSES*
292.0	Amphetamine, Cocaine, Nicotine, Opioid, or Other (or Unknown)] Withdrawal; Sedative, Hypnotic or Anxiolytic Withdrawal
292.1	DRUG PARANOID/HALLUCINOS*
292.11	Amphetamine, Cannabis, Cocaine, Hallucinogen, Inhalant, Opioid, Phencyclidine, or Other (or Unknown) Substance-Induced Psychotic

	Disorder, With Delusions; Sedative, Hypnotic or Anxiolytic-Induced Psychotic Disorder, With Delusions
	292.12 Amphetamine, Cannabis, Cocaine, Hallucinogen, Inhalant, Opioid, Phencyclidine, or Other (or Unknown)] Substance-Induced Psychotic Disorder, With Hallucinations; Sedative-, Hypnotic- or Anxiolytic-Induced Psychotic Disorder, With Hallucinations
	292.2 PATHOLOGIC DRUG INTOX
	292.8 OTHER DRUG MENTAL DIS*
	292.81 Amphetamine, Cannabis, Cocaine, Hallucinogen, Inhalant, Opioid, Phencyclidine, or Other (or Unknown)] Substance Intoxication Delirium; Sedative, Hypnotic or Anxiolytic Intoxication or Withdrawal Delirium
	292.82 Inhalant or Other (or Unknown) Substance-Induced Persisting Dementia; Sedative-, Hypnotic- or Anxiolytic-Induced Persisting Dementia
	292.83 Other (or Unknown)] Substance-Induced Persisting Amnestic Disorder; Sedative-, Hypnotic- or Anxiolytic-Induced Persisting Amnestic Disorder
	292.84 Amphetamine, Cocaine, Hallucinogen, Inhalant, Opioid, Phencyclidine, or Other (or Unknown) Substance-Induced Mood Disorder; Sedative-, Hypnotic- or Anxiolytic-Induced Mood Disorder
	292.85 Amphetamine, Caffeine, Cocaine, Opioid, or Other (or Unknown) Substance-Induced Sleep Disorder, Sedative-, Hypnotic- or Anxiolytic-Induced Sleep Disorder
	292.89 Substance-Induced Anxiety Disorder, Sexual Disfunction, Sleep Disorder, or Intoxication (Refer to the DSM-IV-TR); Hallucinogen Persisting Perception Disorder
	292.9 Amphetamine, Caffeine, Cannabis, Cocaine, Hallucinogen, Inhalant, Nicotine, Opioid, Phencyclidine, or Other (or Unknown) Substance-Related Disorder NOS; Sedative-, Hypnotic- or Anxiolytic-Related Disorder NOS

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	**page 2 -** ABSTRACT, , *"Data for this retrospective cohort…"*	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	**page 2-** ABSTRACT, , in-text reference: *"were derived from administrative data sources …" and* **page 2-** ABSTRACT, in-text reference: *"…in Ontario, Canada…"* **page 2-** ABSTRACT, in-text reference: *"All patient information was linked anonymously across databases using encrypted ten-*

					digit health card numbers."
Introduction,					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	**page 4 to 5 -** INTRODUCTION,		
Objectives	3	State specific objectives, including any pre-specified hypotheses	**page 5-** INTRODUCTION, in-text reference: *"...the goal of this study was to evaluate how UDS frequency impacts treatment retention in OAT in Ontario."*		
Methods					
Study Design	4	Present key elements of study design early in the paper	**page 5 -** METHODS, in-text reference: *"Data for this retrospective cohort study..."*		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	**page 5 to 6 -** METHODS		
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of	**Page 6 -** METHODS, in-text reference: "*We*	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to	**Page 6 and Figure 1 -** METHODS,

		selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	*excluded all patients…"* *n/a*	identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	**Page 6,** in-text reference: "*The Ontario Drug Benefit…"* *n/a* **Figure 1**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	**Page 7 -** METHODS,	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	**Page 7 -** METHODS,
Data sources/ measurement	8	For each variable of interest, give sources of data and	**Page 6 -** METHODS		

		details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			
Bias	9	Describe any efforts to address potential sources of bias	*n/a*		
Study size	10	Explain how the study size was arrived at	**Figure 1**		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	**Page 7 and 8-** MEHTODS		
Statistical methods	12	(a)Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed	**Page 8-** MEHTODS, in-text reference: "*Descriptive statistics were calculated…"* *n/a* **page 6 -** METHODS, in-text reference: *"…and those with missing…"*		

		(d) *Cohort study* - If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses			
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	**Page 5-** METHODS, **"***These data were obtained…"* **page 6 -** METHODS, in-text reference: *"…and those with missing…"*
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	**page 5 and 6 -** METHODS, in-text reference: "*Patient-level…"*
Results					
Participants	13	(a)Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed	**Figure 1**	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality,	**Figure 1**

		eligible, included in the study, completing follow-up, and analysed) (b)Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	
Descriptive data	14	(a)Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest	**Page 8-** RESULTS, in-text reference: *"There were significant differences between…"* **page 6 -** METHODS, in-text reference: *"…and those with missing…"*		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	**Page 9 and 10 -** RESULTS, in-text reference: *"As shown in Table 2…"*		

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	RESULTS, page 5, in-text reference: *"As shown in Table 2…"* and Table 2		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	*n/a*		
Discussion					
Key results	18	Summarise key results with reference to study objectives	**Page 10 and 11 -** DISCUSSION, in-text reference: *"The study sought to evaluate…"*		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	**Page 12 -** DISCUSSION, in-text reference: *"Some limitations in the current study…"*	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	**Page 12 -** DISCUSSION, in-text reference: *"Some limitations in the current study…"*
Interpretation	20	Give a cautious overall interpretation of results	**Page 12 an 13 -** CONCLUSION,		

		considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results	**Page 12 and 13 -** CONCLUSION		