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Predictors of timely opioid agonist treatment initiation among veterans with and without HIV

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ABSTRACT

Background: Opioid use disorder (OUD) is prevalent among people with HIV (PWH). Opioid agonist therapy (OAT) is the most effective treatment for OUD and is associated with improved health outcomes, but is often not initiated. To inform clinical practice, we identified factors predictive of OAT initiation among patients with and without HIV.

Methods: We identified 19,698 new clinical encounters of OUD between 2000 and 2012 in the Veterans Aging Cohort Study (VACS), a national observational cohort of PWH and matched uninfected controls. Mixed effects models examined factors predictive of OAT initiation within 30-days of a new OUD clinical encounter.

Results: 4.9% of both PWH and uninfected patients initiated OAT within 30 days of a new OUD clinical encounter. In adjusted models, participants with a psychiatric diagnosis (aOR = 0.54, 95% CI 0.47 – 0.62), PWH (aOR = 0.79, 95% CI 0.68–0.92), and rural residence (aOR = 0.56, 95% CI 0.39-0.78) had a lower likelihood of any OAT initiation, while African-American patients (aOR = 1.60, 95% CI 1.34–1.92), those with an alcohol related diagnosis (aOR = 1.76, 95% CI 1.48–2.08), diagnosis year 2005–2008 relative to 2000–2004 (aOR = 1.24, 95% CI 1.05–1.45), and patients with HCV (aOR = 1.50, 95% CI 1.27–1.77) had a greater likelihood of initiating any OAT within 30 days. Predictive factors were similar in the total sample and PWH only models.

Conclusions: PWH were less likely to receive timely OAT initiation than demographically similar uninfected patients. Given the health benefits of such treatment, the low rate of OAT initiation warrants focused efforts in both PWH and uninfected populations.

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1. Introduction

Within the U.S., diagnoses of opioid use disorder (OUD) and the adverse events associated with the disorder, including overdose death, have reached crisis levels (Kolodny et al., 2015). OUD is prevalent among people living with HIV (PWH) as injection drug use is a major risk-factor for HIV transmission (Weiss et al., 2011). Left untreated, OUD is associated with poor HIV outcomes in multiple populations (Altice et al., 2011; Chitsaz et al., 2013; Lima et al., 2014), including veterans (Korthuis et al., 2012). In contrast, OUD treated with the opioid agonist therapies (OAT) methadone or buprenorphine is associated with positive HIV disease management and other health outcomes (Roux et al., 2009; Altice et al., 2011; Fiellin et al., 2011). Buprenorphine treatment is associated with decreased opioid use, increased rates of antiretroviral therapy (ART) and improved CD4 counts (Altice et al., 2011; Fiellin et al., 2011), while methadone treatment facilitates initiation of ART and improves ART adherence among people who inject drugs (Roux et al., 2008; Uhlmann et al., 2010). More generally, strong evidence shows OAT to be a clinically effective means of decreasing the use of illicit opioids and HIV risk behaviors, such as needle sharing, among PWH diagnosed with OUD (Marsch, 1998; Fiellin et al., 2011; Edelman et al., 2014).

Veterans use illicit substances at rates roughly equivalent to those of a comparable civilian population, with 4.4% of both Veterans and comparable non-Veterans reporting past-month illicit substance use (Wagner et al., 2007). In 2010, .79% of VA patients received a diagnosis of OUD (Oliva et al., 2013). Among a VA patient population, research has examined sociodemographic and clinical characteristics associated with the likelihood of receiving OAT for OUD, as well as the type of pharmacotherapy prescribed. Patient-level factors associated with a decreased likelihood of receiving OAT include female gender, African-American race/ethnicity, older age, the absence of a mental health diagnosis, rural residence, homeless status and disability due to military service (Oliva et al., 2012; Finlay et al., 2016). Further, older age, urban residence and African-American race/ethnicity are associated with lower likelihood of receiving buprenorphine relative to methadone (Manhapra et al., 2016). Although the VA is the largest single provider of HIV care in the US (Backus et al., 2015), research has not examined the role of HIV status in predicting use of OAT among a Veteran population. Thus, in a national sample of Veterans with and without HIV, we sought to examine the prevalence of and factors associated with OAT initiation and the impact of HIV status to inform future policy and practice interventions to promote OAT. We specifically investigate predictors of OAT *initiation* because timely initiation of treatment following a new OUD clinical encounter—an opportunity for treatment engagement– is an important indicator of the quality of SUD treatment and is associated with improved long-term treatment outcomes (Harris et al., 2010; Paddock et al., 2017).

2. Methods

2.1. Sample and data source

We utilized the Veteran Aging Cohort Study (VACS) for our analyses (Justice et al., 2006). VACS is a national observational cohort study of all PWH receiving care within the VA Health Care System identified from 1996 to 2012 (n = 47,805 and 1:2 matched uninfected patients (n = 99,060). HIV status is determined by ICD-9-CM codes 042-044 (AIDS) and V08 (asymptomatic HIV and diagnosis related groups (DRG) codes 4888-490) (Fultz et al., 2006). Matching was based on age, race/ethnicity, gender, geographic region (Veterans Integrated Systems Network), and fiscal year. VACS is composed of national, electronic medical records obtained from the Corporate Data Warehouse and Pharmacy Benefits Management databases, and includes ICD-9 codes1, pharmacy and laboratory data, and clinical health measures. The study protocol was approved by the University of Pittsburgh, VA Pittsburgh Healthcare System, and VA Connecticut Healthcare System Institutional Review Boards.

2.1.1. Analytic sample

Within VACS, we identified patients with one or more new OUD clinical encounters across the period 2000-2012. A new OUD clinical encounter was defined as an inpatient or outpatient encounter with a primary or secondary opioid abuse or dependence diagnosis (ICD-9-CM codes 304.0×, 305.5×, and 304.7×) following a break in care with no ICD-9 code for OUD and no OAT for five or more months (Watkins et al., 2011). For this longitudinal cohort study, we used a five-month break-in-care to ensure the identified OUD clinical encounter constituted a new opportunity for treatment (Watkins et al., 2011).

2.2. Measures

We examined initiation of any OAT (defined as either methadone or buprenorphine) within 30 days of a new OUD clinical encounter. Methadone treatment was identified via methadone maintenance clinic "stopcodes," while buprenorphine prescriptions were identified through national VA prescription fill/refill data. Buprenorphine prescriptions include buprenorphine/naloxone combinations, but exclude buprenorphine transdermal patch, which is used to treat pain. The definition of initiation as occurring within 30 days of a new OUD clinical encounter, and opportunity for treatment, is adapted from the Washington Circle alcohol or drug performance measures for substance use treatment (McCorry et al., 2000; Garnick et al., 2002), in which initiation is defined as any *non-pharmacologic* treatment received within 14 days of a new SUD diagnosis (Mattke et al., 2017). Here, we focus exclusively on the provision of *pharmacologic* treatment (e.g., OAT) and expand the time window defined as "initiation" to 30-days following a new OUD clinical encounter (Bernstein and D'Onofrio, 2017). This expanded time-window is based on authors' clinical knowledge of standard care processes within VA clinics, and is a more realistic reflection of the time-frame within which OAT is initiated following identification of a new OUD clinical encounter. Extended-release injectable naltrexone is not included in these analyses as it was first made widely available within VA "i.e., on formulary" in 2014 (Wyse et al., 2018).

As secondary outcomes, we also evaluated rapid and delayed initiation of OAT. We define *rapid* initiation as OAT received within 14-days of a new clinical encounter (consistent with the Washington Circle initiation time-frame) (Garnick et al., 2002), and *delayed* initiation as that received within 6-months or 1-year of a new encounter.

2.2.1. Covariates

Potential predictive factors of OAT initiation included age, gender, race/ethnicity, HIV status, CD4 count, viral load (VL), Hepatitis C viral infection (HCV), urban versus rural residence, alcohol related diagnosis, non-opioid substance use diagnoses, multi-substance use diagnosis (defined as 2 or more non-opioid drug use diagnoses), psychiatric diagnoses (defined as *non-SUD* psychiatric diagnoses including depression, anxiety, bipolar disorder, post-traumatic stress disorder and schizophrenia), and year of new OUD clinical encounter. Values for CD4 and VL were selected at the time-point closest to the date of new encounter in the year prior to the index OUD encounter. Comorbid substance use and psychiatric diagnoses were included if patients had ever received a diagnosis prior to the clinical encounter date. Age at start of clinical encounter was categorized as < 50, 50–64, and 65 years and older. Rurality was defined using rural-urban commuting area (RUCA) codes, which are based on the zip code of the patient's residence. The year of new clinical encounter diagnosis was defined by

three categories, representing early, middle and later years of OAT availability, a baseline of 2000–2004, 2005–2008, and 2009-2012. In analyses utilizing just PWH, HIV was stratified into patients with viral load suppressed (VL < 500 copies/mL), and viral load detectable (VL > 500 copies/mL). Use of ART was determined by pharmacy fill/refill prior to the OUD encounter.

2.3. Analysis

We used Chi-square tests to compare socio-demographic and clinical characteristics across PWH and uninfected groups. Next, we constructed mixed effects multivariate logistic regression models examining factors predictive of initiation of any OAT within the 30-day, 14-day, 6-month, and 1-year windows following the new OUD clinical encounter. We used clustered standard errors to account for correlated data given multiple clinical encounters per patient.

We then created a second set of models restricted only to the PWH patients to identify differences in predictive factors between the PWH patients and the full sample. All models utilized covariates included in the prior models, but additionally included an indicator for virologic suppression. We report the adjusted odds ratio with a 95% confidence interval.

Finally, we conducted sensitivity analyses. First, we ran each of the models using just the first OUD encounter for each patient (i.e., excluding multiple clinical encounters). Second, we ran the PWH models, first including CD4 > / < 200 cells/mm^3 and then ART (yes/no) in place of VL. Stata version 14.2 was used to conduct all analyses (Stata Corp 015, 2019).

3. Results

3.1. Participants

Of the n = 146,865 patients who were included in the sample from 2000 to 2012, n = 10,165 (7%) contributed at least one new OUD clinical encounter including 4,107 PWH and 6,058 uninfected (Table 1). Overall, patients were predominantly African-American males residing in urban areas. Nearly two-thirds were diagnosed with a psychiatric comorbidity, more than half had an alcohol related diagnosis, more than half had multi-substance use diagnoses and just over half had a history of homelessness. Among PWH, most had a CD4 count of greater than 200 cells/mm3, and had received ART. Compared to uninfected patients, PWH were more likely to receive services in an urban setting, have a diagnosis of HCV, and less likely to have a diagnosed psychiatric disorder or alcohol related diagnosis.

3.2. OUD clinical encounters

Among the n = 10,165 participants who contributed at least one OUD clinical encounter, 43% contributed multiple encounters for a total of 19,698 new OUD encounters. Participants were followed for 12.1 months on average, with PWH evidencing a shorter follow-up period (mean [M] = 11.8 months, standard deviation [SD] = 3.9 months) than uninfected patients (M = 12.4, SD = 3.7). The mean number of new OUD clinical encounters per participant was 1.94 (SD = 1.5) with no differences between PWH and uninfected participants (p = 1.0). Although only 1332 participants (13.1%) had 4 or more new OUD encounters, they accounted for 35% of the total clinical encounters.

3.3. Bivariate comparisons of OAT initiation

Just 4.9% of overall sample initiated any form of OAT within 30 days of a new OUD clinical encounter, and results did not differ by HIV status (p = 0.329). (Table 1).

In secondary analyses, to determine whether the time window for initiation substantially altered our conclusions, we examined likelihood of initiating OAT within 14 days, 6 months and one year of a new OUD clinical encounter. We found that 3.5% of participants initiated any OAT within 14 days, 8.5% initiated OAT within 6 months and 10.2% initiated OAT within 1 year. Chi square also revealed no differences by HIV status for these alternate time-frames. Of those who initiated OAT, 25% did so within 3 days and 52% within 30 days.

3.4. Multivariate analyses for OAT initiation – total sample

In the adjusted mixed effects logistic regression model for initiation of any OAT within 30 days (n = 19,698 OUD treatment clinical encounters, Table 2), participants with a psychiatric diagnosis (adjusted odds ratio [aOR] = 0.54, 95% confidence interval [CI] 0.47 – 0.62), PWH (aOR = 0.79, 95% CI 0.68-0.92) and rural residence (aOR = 0.56, 95% CI 0.39-0.78) had a lower likelihood of any OAT initiation, while African-American patients (aOR = 1.60, 95% CI 1.34–1.92), those with an alcohol related diagnosis (aOR = 1.76, 95% CI 1.48–2.08), diagnosis

Table 1
Baseline characteristics of participants with at least one Opioid Use Disorder (OUD) diagnosis from 2000 to 2012, stratified by HIV status (N = 10,165).

	PWH (n = 4107)	Uninfected (n = 6058)	P-value
Age, *mean years (SD)*	50.6 (7.0)	50.6 (7.1)	0.59
Race/Ethnicity, *n (%)*			< 0.01
White	1,110 (27.0)	1,774 (29.3)	
African-American	2, 548 (62.0)	3,723 (60.0)	
Latino/other	449 (11.0)	561 (9.3)	
Male gender, *n (%)*	4,019 (97.9)	5,965 (98.5)	0.023
Residence, *n (%)*			
Urban	3,595 (87.5)	5,299 (87.5)	< 0.001
History of Homelessness, *n (%)*	2,088 (50.7)	3,046 (50.1)	.5
Hepatitis C, *n (%)*	3,306 (80.3)	3,224 (53.0)	< .001
Psychiatric diagnoses, *n (%)*			
Depression	2,022 (49.2)	2,972 (49.1)	0.863
Anxiety	801(19.5)	1,304 (21.5)	0.014
PTSD	822 (20.0)	1,635 (27.0)	< 0.001
Bipolar Disorder	642 (15.6)	1,216 (20.0)	< 0.001
Schizophrenia	491 (12.0)	876 (14.5)	< 0.001
Any psychiatric comorbidity, *n (%)*	2,549 (62.1)	3,975 (65.6)	< 0.001
Alcohol related diagnosis, *n (%)*	2,485 (60.5)	4,022 (66.4)	< 0.001
Non-opioid drug use diagnosis, *n (%)*			
Cocaine	2,529 (61.6)	3,493 (57.7)	< 0.001
Stimulant	204 (5.0)	345 (5.7)	0.111
Sedative-Hypnotic	242 (5.9)	485 (8.0)	< 0.001
Cannabis	978 (23.8)	1,776 (29.3)	< 0.001
Hallucinogen	34 (0.8)	79 (1.3)	0.025
Multi-substance use,* *n (%)*	2,313 (56.3)	3,535 (58.4)	0.042
HIV-Related, *n (%)*+		–	–
Virologic suppression	1,568(38.2)	–	–
CD4 > 200 cells/mm^3	2,190 (53.3)	–	–
Antiretroviral therapy receipt	2, 709 (66.0)	–	–
OAT Initiation Within**			
14 days	136 (3.3%)	224 (3.7%)	0.304
30 days	190 (4.6%)	306 (5.1%)	0.329
6 months	329 (8.1%)	521 (8.8%)	0.244
1 year	382 (9.7%)	599 (10.5%)	0.231

Abbreviations: PWH-people living with HIV, SD-standard deviation, HIV-human immunodeficiency virus, PTSD-post-traumatic stress disorder, OAT-opioid agonist therapy. ICD-9-CM, V08 (asymptomatic HIV), and diagnosis related group (DRG) codes identified diagnoses and HIV status.

* defined as 2+ non-opioid drug use diagnoses.

** The denominators for initiation within 14 days, 30 days, 6 months and 1-year are 10,184, 10,165, 9,960 and 9,666 respectively.

+ Missing data accounts for differences in the denominator of HIV-related variables.

Table 2
Factors associated with OAT Initiation within 30 days of new OUD episode, mixed effects multivariate logistic regression (n = 19, 698).

	Any OAT (methadone or buprenorphine)	P-value
	AOR (95% CI)	
Age (ref = < 50 years old)		
50-64	0.99 (0.85-1.15)	0.869
65+	0.79 (0.46-1.37)	0.405
Race/Ethnicity (ref = white)		
African-American	1.60 (1.34-1.92)	0.000
Latino/Other	1.30 (0.98-1.73)	0.064
PWH	0.79 (0.68-0.92)	0.002
Psychiatric diagnosis (ref = none)	0.54 (0.47-0.62)	0.000
Year of episode (ref = 2000-2004)		
2005-2008	1.24 (1.05-1.45)	0.009
2009-2012	1.03 (0.86-1.23)	0.767
Rural location (ref = urban)	0.56 (0.39-0.78)	0.001
Alcohol related diagnosis (ref = no)	1.76 (1.48-2.08)	0.000
Multi-substance use[+] (ref = no)	0.87 (0.75-1.02)	0.082
Hepatitis C	1.50 (1.27-1.77)	0.000

ˆ Reference group is HIV-uninfected.
Abbreviations: AOR-adjusted odds ratio, CI-confidence interval.
[+] Multi-substance use defined as 2+ non-opioid drug use diagnoses.

year 2005–2008, relative to 2000–2004, (aOR = 1.24, 95% CI 1.05–1.45) and patients with HCV (aOR = 1.50, 95% CI 1.27–1.77) had a greater likelihood of initiating any OAT within 30 days. (Table 2)

3.4.1. Secondary outcomes

OAT Initiation within 14 Days, 6 Months and 1 Year. While most predictors of initiation within 14-days of a new OUD clinical encounter did not differ significantly from that of the 30-day model, HIV status was not significant (p = .07) in this model. Additionally, multi-substance use was associated with a lower likelihood of initiating any OAT (aOR = 0.75, 95% CI 0.63-0.90) within 14 days. In the model examining predictors of initiation within a 6-month period, patients of older age (OR = 0.54, 95% CI 0.33-0.89) had a lower likelihood of initiating any OAT within six months. All other results mirrored those of the 30-day model. There were no significant differences between the model predicting initiation within 1-year and that predicting initiation within six-months of the new OUD encounter.

3.4.2. Sensitivity analyses

In sensitivity analyses, we ran multivariate analyses utilizing the initial OUD clinical encounter for each participant (i.e., rather than including multiple clinical encounters/patient) to assess whether predictors of initiation within 30-days would remain unchanged. Some differences did emerge. Specifically, HIV status, year of diagnosis and rural residence were not significant in this model, although in each case the direction remained unchanged. Further, those with multi-substance use had a lower likelihood of initiating OUD within 30 days in this model (aOR = 0.73, CI 0.58-0.91). In a separate analysis, we ran the model including an interaction for HIV and race, and found no effect.

3.5. Multivariate analyses for OAT initiation – restricted to the PWH sample

Next, we ran adjusted mixed effects logistic regression models for OAT initiation at 30 days utilizing just the PWH sample (n = 8112 OUD treatment clinical encounters). (Table 3) Akin to the full sample, participants with a non-SUD psychiatric diagnosis (aOR = 0.57, 95% CI 0.46-0.72) were less likely to initiate any OAT within 30 days of diagnosis, while African-American patients (aOR = 1.95, 95% CI 1.45–2.61), those with an alcohol related diagnosis (aOR = 2.00, 95% CI 1.52–2.63) and HCV diagnosis (aOR = 1.82, 95% CI 1.27–2.62) were more likely to initiate. Unlike the full sample, rural residence and year of new OUD clinical encounter were not associated with OAT initiation in this model. Virologic suppression was not predictive of initiation.

We also ran the model incorporating alternative indicators of HIV control, first CD4 count and then ART. While CD4 count was not associated with initiation of any OAT within 30 days, ART was positively associated with initiation (aOR = 1.27, 95% CI 1.01–1.60).

4. Discussion

We identified low rates of OAT initiation within 30 days of a new OUD clinical encounter among both PWH and uninfected patients receiving care within the VA health care system. Even one year following the new OUD clinical encounter, rates of initiation of any OAT remained low. Further, multivariate analyses identified a lower likelihood of initiation of any OAT within 30-days among PWH, patients with a psychiatric diagnosis, and those of rural residence. Examining predictors of initiation within alternate time-frames, in the model utilizing a 14-day window, HIV status was not significantly associated with initiation, while multi-substance use was associated with a lower likelihood of initiation. In models utilizing 6-month and 1-year windows for initiation, findings were generally consistent with those identified in the main model, with the exception of older age, which was associated with a lower likelihood of initiating any OAT. In analyses restricted to PWH, predictors of timely initiation identified were, again, largely consistent with those identified in analyses utilizing the full sample.

The low rates of timely initiation of OAT are of concern given the importance of OAT initiation for HIV and other health outcomes (Altice et al., 2011; Fiellin et al., 2011). Findings suggest that VA clinics (both primary care as well as infectious disease) should evaluate their care processes surrounding OAT initiation following a new OUD clinical encounter and identify barriers to timely OAT initiation. Prior research has found that, within the VA, buprenorphine is prescribed largely by psychiatrists, rather than primary care clinicians, as is common outside the VA (Gordon et al., 2011; Oliva et al., 2013). Thus, lack of timely initiation may point to a time-lag between diagnosis in the primary care/infectious disease setting and patients' ability to schedule and be seen in a new clinical setting. As others have noted, expanding buprenorphine prescribing in non-specialty SUD settings would likely greatly enhance buprenorphine availability for VA patients (Wyse et al., 2018). The VA capacity to provide methadone has declined in recent decades, and VA currently operates just 32 methadone clinics across the nation (Wyse et al., 2018), which may influence lack of timely initiation as well. Qualitative research is needed to illuminate the system, provider

Table 3
Adjusted Odds Ratios (AOR) of OAT Initiation within 30 days among PWH veterans (n = 8,112 new OUD episodes).

	Any OAT	P-value
	AOR (95% CI)	
Age (ref = < 50 years old)		
50-64	1.02 (0.80-1.31)	0.848
65+	0.68 (0.30-1.53)	0.350
Race/Ethnicity (ref = white)		
African-American	1.95 (1.45-2.61)***	0.000
Latino/Other	1.20 (0.75-1.93)	0.440
HIV viral load detectable (ref = suppressed)	1.00 (0.78-1.29)	0.976
Psychiatric diagnosis (ref = none)	0.57 (0.46-0.72)***	0.000
Year of episode (ref = 2000-2004)		
2005-2008	1.02 (0.79-1.30)	0.899
2009-2012	0.89 (0.66-1.18)	0.412
Rural location (ref = urban)	0.84 (0.51-1.39)	0.494
Alcohol related diagnosis	2.00 (1.52-2.63)***	0.000
Multi-substance use[+]	0.79 (0.62-1.02)	0.068
Hepatitis C	1.82 (1.27-2.62)***	0.001

Abbreviations: AOR-adjusted odds ratio, CI-confidence interval.
[+] Multi-substance use defined as 2+ non-opioid drug use diagnoses.

and patient barriers to timely OAT initiation among vulnerable patients, which could inform the design of new clinical approaches. VA should also consider targeted patient outreach and engagement efforts in the month following a new OUD clinical encounter, whether through the use of peer navigators, community health workers or clinical staff.

In addition to low rates of initiation overall, multivariate analyses identified sociodemographic and clinical factors associated with timely OAT initiation. Specifically, a lower likelihood of timely initiation of OAT was identified among patients with HIV, patients with a psychiatric diagnosis and those of rural residence. The finding regarding PWH is quite important, given the known benefits of OAT treatment for PWH, and suggests that infectious disease clinics may need to enhance their clinical capacity to prescribe buprenorphine, either by encouraging existing staff to undertake buprenorphine waiver training, or by hiring additional staff to meet this pressing need. The consistent finding that patients with comorbid psychiatric disorders are less likely to receive timely OAT could reflect clinician concern regarding adherence or diversion among these patients. If this is the case, educational initiatives such as academic detailing campaigns emphasizing the effectiveness of OAT for patients with psychiatric disorders comorbid with OUD may be in order (Nunes et al., 2004; Gerra et al., 2006; Lingford-Hughes et al., 2012). The fact that rurality was strongly associated with a lower likelihood of OAT initiation is aligned with substantial prior research. Opioid treatment programs tend to be located in large, urban areas, and buprenorphine providers are underrepresented in rural settings (Rosenblatt et al., 2015). Continuing to build capacity to serve rural Veterans through VA's Telehealth and VideoConnect programs should remain a high priority. Adoption of extended-release buprenorphine and the buprenorphine implant, which delivers continuous medication for 1 and 6 months, respectively, may also make OAT more accessible to rural patients in the future. The medication-specific association between year of diagnosis and timely initiation likely reflects changes in medication availability within VA over time, with methadone availability declining as buprenorphine capacity expanded. The higher likelihood of timely OAT initiation among African-American patients we identified is somewhat surprising, given past research finding African American patients are less likely to receive OAT within VA (Manhapra et al., 2016). This finding may reflect facility-level differences we were unable to account for in our models, such as presence of an opioid treatment program on site. Finally, the reason for the higher likelihood of timely initiation in OAT treatment among patients with HCV is unclear.

An important motivation for this study was to identify the role of HIV status in the likelihood of receiving timely OAT. An examination of predictors of timely initiation among just PWH revealed no difference in the likelihood of initiating any OAT by virologic suppression, however, sensitivity analyses found patients on ART were more likely to initiate any OAT at 30 days. This may be explained by the fact that patients receiving ART are actively engaged in care, presenting opportunities for referral to treatment and/or initiation of OAT. These findings call for more detailed longitudinal analyses that examine whether viral load improves after initiation of OAT and/or during periods on OAT versus not on OAT.

4.1. Limitations

There are several limitations to our study. To define a new OUD clinical encounter, we required a "break in care" of five months in which patients had no clinical encounters with an OUD diagnosis or OAT medication (Watkins et al., 2011). This may have been too stringent a definition of a new OUD encounter given the relapsing-remitting nature of OUD. Our primary outcome was OAT receipt within 30 days of a new OUD clinical encounter, while prior work has examined receipt of any OAT within one year of a new OUD diagnosis (Finlay et al., 2016), or one year of a current OUD diagnosis, whether new or ongoing (Oliva et al., 2012). Our measures of OAT initiation reflect our knowledge of standard care processes for OAT initiation, but may not be directly comparable to other research on this topic. The lack of a consistent approach for measuring and reporting on the quality of SUD treatment remains an unresolved issue in this field (Pincus et al., 2011). Another limitation is posed by the time period (2000–2012) captured within this study, including years in which buprenorphine was not widely available within VA. Extended release injectable naltrexone prescribed for OUD was also not included in these analyses, as it was first added to the VA formulary in 2014 (Wyse et al., 2018). Finally, we did not have facility-level data in our database and analysis. There is significant heterogeneity in rates of OAT across VA facilities, ranging from 1% to 68% (Finlay et al., 2016). VA facilities that include on-site methadone or office-based buprenorphine have higher rates of OAT than facilities that lack on-site services (Oliva et al., 2012). Our data also may not capture all treatment patients receive outside of the VA context (i.e., in care paid for, but not administered by, the VA). In future work, we hope to incorporate care received outside of the VA and include facility characteristics from the VA's Drug and Alcohol Program Survey to better understand how facility factors are associated with timely OAT receipt.

4.2. Conclusion

We found low rates of OAT initiation after a diagnosis of OUD within the context of a new clinical encounter in a cohort of PWH and uninfected veterans. Importantly, PWH were less likely than uninfected patients to receive timely OAT. Efforts to expand OAT initiation among this population are essential, and likely to have significant implications for HIV care, and patient health and well-being.

Contributors

Authors Wyse and Robbins drafted the article, McGinnis and Skanderson conducted analyses, and all authors contributed revision, feedback and final article approval.

Conflict of interest

No conflicts declared.

Role of funding source

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2019.01.038.

References

Altice, F.L., Bruce, R.D., Lucas, G.M., Lum, P.J., Korthuis, P.T., Flanigan, T.P., Cunningham, C.O., Sullivan, L.E., Vergara-Rodriguez, P., Fiellin, D.A., Cajina, A., Botsko, M., Nandi, V., Gourevitch, M.N., Finkelstein, R., BHIVES Collaborative, 2011, Altice, F.L., Bruce, R.D., Lucas, G.M., Lum, P.J., Korthuis, P.T., Flanigan, T.P., Cunningham, C.O., Sullivan, L.E., Vergara-Rodriguez, P., Fiellin, D.A., Cajina, A., Botsko, M., Nandi, V., Gourevitch, M.N., Finkelstein, R., BHIVES Collaborative, 2011. HIV treatment outcomes among HIV-infected, opioid-dependent patients receiving buprenorphine/naloxone treatment within HIV clinical care settings: results from a multisite study. J. Acquir. Immune Defic. Syndr. 56, S22–32.

Backus, L., Czarnogorski, M., Yip, G., Thomas, B.P., Torres, M., Bell, T., Ross, D., 2015.

HIV care continuum applied to the US Department of Veterans Affairs: HIV virologic outcomes in an integrated health care system. J. Acquir. Immune Defic. Syndr. 69, 474–480.
Bernstein, S.L., D'Onofrio, G., 2017. Screening, treatment initiation, and referral for substance use disorders. Addict. Sci. Clin. Pract. 12, 18.
Chitsaz, E., Meyer, J.P., Krishnan, A., Springer, S.A., Marcus, R., Zaller, N., Jordan, A.O., Lincoln, T., Flanigan, T.P., Porterfield, J., 2013. Contribution of substance use disorders on HIV treatment outcomes and antiretroviral medication adherence among HIV-infected persons entering jail. AIDS Behav. 17, 118–127.
Edelman, E.J., Chantarat, T., Caffrey, S., Chaudhry, A., O'Connor, P.G., Weiss, L., Fiellin, D.A., Fiellin, L.E., 2014. The impact of buprenorphine/naloxone treatment on HIV risk behaviors among HIV-infected, opioid-dependent patients. Drug Alcohol Depend. 139, 79–85.
Fiellin, D.A., Weiss, L., Botsko, M., Egan, J.E., Altice, F.L., Bazerman, L.B., Chaudhry, A., Cunningham, C.O., Gourevitch, M.N., Lum, P.J., Sullivan, L.E., Schottenfeld, R.S., O'Connor, P.G., BHIVES Collaborative, 2011a, Fiellin, D.A., Weiss, L., Botsko, M., Egan, J.E., Altice, F.L., Bazerman, L.B., Chaudhry, A., Cunningham, C.O., Gourevitch, M.N., Lum, P.J., Sullivan, L.E., Schottenfeld, R.S., O'Connor, P.G., B.H.I.V.E.S. Collaborative, 2011. Drug treatment outcomes among HIV-infected opioid-dependent patients receiving buprenorphine/naloxone. J. Acquir. Immune Defic. Syndr. 56 (Suppl 1), S33–8.
Finlay, A.K., Harris, A.H., Rosenthal, J., Blue-Howells, J., Clark, S., McGuire, J., Timko, C., Frayne, S.M., Smelson, D., Oliva, E., 2016. Receipt of pharmacotherapy for opioid use disorder by justice-involved US Veterans Health Administration patients. Drug Alcohol Depend. 160, 222–226.
Fultz, S.L., Skanderson, M., Mole, L.A., Gandhi, N., Bryant, K., Crystal, S., Justice, A.C., 2006. Development and verification of a "virtual" cohort using the National VA Health Information System. Med. Care 44, S25–30.
Garnick, D.W., Lee, M.T., Chalk, M., Gastfriend, D., Horgan, C.M., McCorry, F., McLellan, A.T., Merrick, E.L., 2002. Establishing the feasibility of performance measures for alcohol and other drugs. J. Subst. Abuse Treat. 23, 375–385.
Gerra, G., Leonardi, C., D'amore, A., Strepparola, G., Fagetti, R., Assi, C., Zaimovic, A., Lucchini, A., 2006. Buprenorphine treatment outcome in dually diagnosed heroin dependent patients: A retrospective study. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 30, 265–272.
Gordon, A.J., Kavanagh, G., Krumm, M., Ramgopal, R., Paidisetty, S., Aghevli, M., Goodman, F., Trafton, J., Liberto, J., 2011. Facilitators and barriers in implementing buprenorphine in the Veterans Health Administration. Psychol. Addict. Behav. 25, 215.
Harris, A.H., Humphreys, K., Bowe, T., Tiet, Q., Finney, J.W., 2010. Does meeting the HEDIS substance abuse treatment engagement criterion predict patient outcomes? J. Behav. Health Serv. Res. 37, 25–39.
Justice, A.C., Dombrowski, E., Conigliaro, J., Fultz, S.L., Gibson, D., Madenwald, T., Goulet, J., Simberkoff, M., Butt, A.A., Rimland, D., Rodriguez-Barradas, M.C., Gibert, C.L., Oursler, K.A., Brown, S., Leaf, D.A., Goetz, M.B., Bryant, K., 2006. Veterans aging cohort study (VACS): overview and description. Med. Care 44, S13.
Kolodny, A., Courtwright, D.T., Hwang, C.S., Kreiner, P., Eadie, J.L., Clark, T.W., Alexander, G.C., 2015. The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. Annu. Rev. Public Health 36, 559–574.
Korthuis, P.T., Fiellin, D.A., McGinnis, K.A., Skanderson, M., Justice, A.C., Gordon, A.J., Doebler, D.A., Asch, S.M., Fiellin, L.E., Bryant, K., Gibert, C.L., Crystal, S., Goetz, M.B., Rimland, D., Rodriguez-Barradas, M.C., Kraemer, K.L., 2012. Unhealthy alcohol and illicit drug use are associated with decreased quality of HIV care. J. Acquir. Immune Defic. Syndr. 61, 171–178.
Lima, V.D., Kerr, T., Wood, E., Kozai, T., Salters, K.A., Hogg, R.S., Montaner, J.S., 2014. The effect of history of injection drug use and alcoholism on HIV disease progression. AIDS Care 26, 123–129.
Lingford-Hughes, A.R., Welch, S., Peters, L., Nutt, D., 2012. BAP updated guidelines: evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from BAP. Psychopharmacology 26, 899–952.
Manhapra, A., Quinones, L., Rosenheck, R., 2016. Characteristics of veterans receiving buprenorphine vs. methadone for opioid use disorder nationally in the Veterans Health Administration. Drug Alcohol Depend. 160, 82–89.
Marsch, L.A., 1998. The efficacy of methadone maintenance interventions in reducing illicit opiate use, HIV risk behavior and criminality: a meta-analysis. Addiction 93, 515–532.
Mattke, S., Predmore, Z., Sloss, E., Wilks, A., Watkins, K.E., 2017. Evidence for misspecification of a nationally used quality measure for substance use treatment. J. Healthc. Qual. 40, 228–235.
McCorry, F., Garnick, D.W., Bartlett, J., Cotter, F., Chalk, M., Babor, T., Falcon, S., Gastfriend, D.R., Gelber, S., Harrison, P.A., 2000. Developing performance measures for alcohol and other drug services in managed care plans. Comm. J. Qual. Improv. 26, 633–643.
Nunes, E.V., Sullivan, M.A., Levin, F.R., 2004. Treatment of depression in patients with opiate dependence. Biol. Psychiatry 56, 793–802.
Oliva, E.M., Harris, A.H., Trafton, J.A., Gordon, A.J., 2012. Receipt of opioid agonist treatment in the Veterans Health Administration: facility and patient factors. Drug Alcohol Depend. 122, 241–246.
Oliva, E.M., Trafton, J.A., Harris, A.H., Gordon, A.J., 2013. Trends in opioid agonist therapy in the Veterans Health Administration: is supply keeping up with demand? Am. J. Drug Alcohol Abuse 39, 103–107.
Paddock, S.M., Hepner, K.A., Hudson, T., Ounpraseuth, S., Schrader, A.M., Sullivan, G., Watkins, K.E., 2017. Association between process based quality indicators and mortality for patients with substance use disorders. J. Stud. Alcohol Drugs 78, 588–596.
Pincus, H.A., Spaeth-Rublee, B., Watkins, K.E., 2011. The case for measuring quality in mental health and substance abuse care. Health Aff. 30, 730–736.
Rosenblatt, R.A., Andrilla, C.H., Catlin, M., Larson, E.H., 2015. Geographic and specialty distribution of US physicians trained to treat opioid use disorder. Ann. Fam. Med. 13, 23–26.
Roux, P., Carrieri, M.P., Villes, V., Dellamonica, P., Poizot-Martin, I., Ravaux, I., Spire, B., 2008. The impact of methadone or buprenorphine treatment and ongoing injection on highly active antiretroviral therapy (HAART) adherence: evidence from the MANIF2000 cohort study. Addiction 103, 1828–1836.
Roux, P., Carrieri, M.P., Cohen, J., Ravaux, I., Poizot-Martin, I., Dellamonica, P., Spire, B., 2009. Retention in opioid substitution treatment: a major predictor of long-term virological success for HIV-infected injection drug users receiving antiretroviral treatment. Clin. Infect. Dis. 49, 1433–1440.
Stata Corp 015, 2019. Stata Statistical Software. StataCorp LP, College Station, TX.
Uhlmann, S., Milloy, M., Kerr, T., Zhang, R., Guillemi, S., Marsh, D., Hogg, R.S., Montaner, J.S., Wood, E., 2010. Methadone maintenance therapy promotes initiation of antiretroviral therapy among injection drug users. Addiction 105, 907–913.
Wagner, T.H., Harris, K.M., Federman, B., Dai, L., Luna, Y., Humphreys, K., 2007. Prevalence of substance use disorders among veterans and comparable nonveterans from the National Survey on Drug Use and Health. Psychol. Serv. 4, 149.
Watkins, K.E., Pincus, H.A., Paddock, S., Smith, B., Woodroffe, A., Farmer, C., Sorbero, M.E., Horvitz-Lennon, M., Mannle Jr., T., Hepner, K.A., 2011. Care for veterans with mental and substance use disorders: good performance, but room to improve on many measures. Health Aff. 30, 2194–2203.
Weiss, L., Egan, J.E., Botsko, M., Netherland, J., Fiellin, D.A., Finkelstein, R., 2011. The BHIVES collaborative: organization and evaluation of a multisite demonstration of integrated buprenorphine/naloxone and HIV treatment. J. Acquir. Immune Defic. Syndr. 56, S7–S13.
Wyse, J.J., Gordon, A.J., Dobscha, S.K., Morasco, B.J., Tiffany, E., Drexler, K., Sandbrink, F., Lovejoy, T.I., 2018. Medications for opioid use disorder in the Department of Veterans Affairs (VA) Health Care System: historical perspective, lessons learned and next steps. Subst. Abus. 39, 139–144.