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Predictors of initiation of and retention on medications for alcohol use disorder among people living with and without HIV

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Abstract

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Introduction: Infrequent use of and poor retention on evidence-based medications for alcohol use disorder (MAUD) represent a treatment gap, particularly among people living with HIV (PLWH). We examined predictors of MAUD initiation and retention across HIV status.

Methods: From Veterans Aging Cohort Study (VACS) data, we identified new alcohol use disorder (AUD) diagnoses from 1998 to 2015 among 163,339 individuals (50,826 PLWH and 112,573 uninfected, matched by age, sex, and facility). MAUD initiation was defined as a prescription fill for naltrexone, acamprosate or disulfiram within 30 days of a new diagnosis. Among those who initiated, retention was defined as filling medication for ≥80% of days over the following six months. We used multivariable logistic regression to assess patient- and facility-level predictors of AUD medication initiation across HIV status.

Results: Among 10,603 PLWH and 24,424 uninfected individuals with at least one AUD episode, 359 (1.0%) initiated MAUD and 49 (0.14%) were retained. The prevalence of initiation was lower among PLWH than those without HIV (adjusted odds ratio [AOR] 0.66, 95% confidence interval [CI] 0.51–0.85). Older age (for PLWH: AOR 0.78, 95% CI 0.61–0.99; for uninfected: AOR 0.70, 95% CI 0.61–0.80) and black race (for PLWH: AOR 0.63, 95% CI 0.0.49–0.1.00; for uninfected: AOR 0.63, 95% CI 0.48–0.83), were associated with decreased odds of initiation for both groups. The low frequency of retention precluded multivariable analyses for retention.

Conclusions: For PLWH and uninfected individuals, targeted implementation strategies to expand MAUD are needed, particularly for specific subpopulations (e.g. black PLWH).

1. Introduction

Alcohol use and alcohol use disorder (AUD) contribute significantly to health outcomes in the United States (US) and worldwide (G. B. D. Alcohol Collaborators, 2018; Laramee et al., 2015; Murray et al., 2012; Rehm, 2011; Rehm et al., 2009; Roerecke & Rehm, 2013). Recent increases in AUD among women, older adults, racial/ethnic minorities, and economically disadvantaged persons have been termed a public health crisis (Grant et al., 2017). Medications for AUD (MAUD) are effective and widely available (Jonas et al., 2014). Disulfiram, naltrexone (in oral and injectable forms) and acamprosate are approved by the US Food and Drug Administration (FDA) for the treatment of AUD. These medications have been indicated in guidelines as first- or second-line treatments for AUD, including Veterans Affairs/Department of Defense clinical practice guidelines, for over a decade (National Institute on Alcohol Abuse and Alcoholism, 2005; Reus et al., 2018; Substance Abuse and Mental Health Services Administration, 2015; “VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders,” 2015). However, in the United States, fewer than 10% of patients with AUD receive MAUD (Mark, Kassed, Vandivort-Warren, Levit, & Kranzler, 2009), and fewer than 20% of those engaged in treatment programs sustain use of MAUD (Abraham, Knudsen, & Roman, 2011). Among Veterans, 3.4% of those with AUD filled at least one prescription for disulfiram, naltrexone, or acamprosate in 2009 (Harris, Kivlahan, Bowe, & Humphreys, 2010).

Treatment with MAUD may be particularly important for people with comorbid human immunodeficiency virus (HIV), for whom untreated AUD is associated with worse outcomes

along the HIV care continuum and increased risk of morbidity (Braithwaite & Bryant, 2010; Edelman, Williams, & Marshall, 2018; Freiberg & Kraemer, 2010; Freiberg et al., 2010; Korthuis et al., 2012; Lim et al., 2014; Rentsch et al., 2018; Williams, McGinnis, et al., 2018). Further, people living with HIV (PLWH) may experience mortality and physiologic injury at lower levels of alcohol consumption compared to those not infected (Justice et al., 2016), and "feel a buzz" upon lower levels of alcohol consumption (McGinnis et al., 2016). The low use of MAUD, therefore, represents an important and modifiable treatment gap, particularly among PLWH, for whom these medications are safe and effective (Edelman et al., 2018; Springer et al., 2018; Springer, Di Paola, Barbour, Azar, & Altice, 2018; Tetrault et al., 2012).

Little is known about the predictors of initiation of and retention on MAUD. Previous analyses identified overall low use of the medications across Veterans Health Affairs (VHA) facilities (Harris et al., 2010), racial/ethnic disparities in the receipt of medications (Williams, Gupta, et al., 2017), and increased use following market entry of FDA-approved MAUD (Mark et al., 2009). Williams and colleagues compared the receipt of evidence-based alcohol-related care across HIV status in a national sample of US Veterans and demonstrated that HIV infection was associated with a 35% decreased odds of receiving MAUD after adjustment for other factors likely associated with receiving alcohol-related care (Williams, Lapham, et al., 2017). However, no previous studies to our knowledge have sought to understand patient-level and facility-level predictors of the use of MAUD across HIV status, nor have they focused on individual medications. Identifying predictors may inform targeted approaches to expanding the use of MAUD, and may explain why facilities offer MAUD to remarkably different percentages of their patient population with AUD, ranging from 0% to 20.5% (Harris et al., 2010). Moreover, no prior studies have examined retention on AUD medications among PLWH or across a national sample of patients with and without HIV. The optimal duration of medication treatment of AUD is not known, but evidence suggests that treatment should continue for at least six months (Center for Substance Abuse Treatment, 2009; Substance Abuse and Mental Health Services Administration, 2015), a time frame that is also considered a quality indicator for the treatment of opioid use disorder (Williams, Nunes, et al., 2018). Retention on medications is therefore an important component of high-quality care and warrants study.

The objectives of our study were to 1) describe initiation of and retention on MAUD across HIV status and 2) identify patient- and facility-level predictors of both initiation and retention of MAUD across HIV status. Findings from this study are needed to inform health systems' strategies to implement and expand evidence-based care for PLWH who have AUD.

2. Material and methods

2.1. Study overview

We used data from fiscal years (FYs) 1998–2015 in the Veterans Aging Cohort Study (VACS) (Justice et al., 2006). Briefly, the VACS assembles national VA electronic medical record data from multiple sources, including the Corporate Data Warehouse and Pharmacy Benefits Management databases, to define a national population of HIV-infected veterans

under care and matched uninfected controls. The study was approved by the Human Investigations Committee at Yale University and the VA Connecticut Healthcare System. It was granted a waiver for informed consent and is HIPAA-compliant.

2.2. Study population and alcohol use disorder index episodes

VACS has 50,826 PLWH and 112,573 uninfected individuals, groupmatched by age, sex, and facility, with available clinical data. We identified those with an AUD index episode (hereafter termed “index episode”) using the following criteria: 1) an inpatient or outpatient encounter with a primary or secondary ICD-9 code diagnosis indicating alcohol dependence (303.x); and 2) no medication for AUD prescribed nor ICD-9 code indicating alcohol dependence documented in the prior five months. We limited our analyses to the first index episode for those with multiple episodes because these represent new opportunities to initiate MAUD; those with multiple episodes were censored as of the date of their second episode.

2.3. Initiation of and retention on medications

Initiation of MAUD was defined as a prescription fill for disulfiram, naltrexone (either oral or injectable formulations) or acamprosate within 30 days of the index episode (Thomas et al., 2011). Because previous studies examined longer time periods as opportunities for treatment (Harris et al., 2010; Harris et al., 2012; Williams, Lapham, et al., 2017), we also reported those who were prescribed medication within six months (i.e., 180 days) and one year (365 days) following the index episode.

Our definition of retention on MAUD used the proportion of days covered (PDC) metric (A. Lehmann et al., 2014), as has been used in previous analyses of the persistence of use of medications for AUD (Harris et al., 2012). Among those who had initiated MAUD, we defined retention as having been dispensed enough of a single medication to cover 80% of days throughout the six months after the index episode. Evidence from prior studies linked better outcomes with naltrexone when daily adherence exceeds this threshold (Baros, Latham, Moak, Voronin, & Anton, 2007; Pettinati, Volpicelli, Pierce, & O’Brien, 2000). Based on previous research (Harris et al., 2012), we anticipated low numbers of retention using this definition and so we also reported initiators who were prescribed over 30 days of the medication as another proxy for retention. These individuals received either filled an initial prescription that was longer than one month or a filled second prescription.

Although topiramate is not FDA-approved for AUD, we elected to query the initiation and retention of topiramate in sensitivity analyses because the strongest evidence for its use in AUD was published during our study period (Johnson et al., 2007) and for comparison with previous research (Williams, McGinnis, et al., 2018). Topiramate can be prescribed for conditions other than AUD; however, in a sample of 375,777 Veterans that examined predictors of topiramate prescription for AUD, multiple sensitivity analyses that controlled for other common indications for topiramate left the results virtually unchanged (Del Re, Gordon, Lembke, & Harris, 2013) so we did not control for other indications. We elected to not report the initiation and retention of gabapentin because it is not FDA-approved for AUD, the strongest evidence for its use in AUD was published near the end of our study

period (Mason et al., 2014), and it is far more commonly prescribed for uses other than AUD (Johansen, 2018; Wallach & Ross, 2018).

2.4. Patient- and facility-level predictors

Socio-demographic covariates included gender, race, ethnicity and age. Clinical covariates included a diagnosis of opioid use disorder (based on ICD-9 codes for opioid dependence), stimulant or amphetamine use (based on ICD-9 codes), current smoking (based on the electronic health record), severe mental illness (based on ICD-9 codes for schizophrenia, post-traumatic stress disorder, depression, and/or bipolar disorder), and hepatitis C virus status (based on laboratory data [positive antibody or viral load] or ICD-9 codes). In analyses restricted to PLWH only, we included receipt of antiretroviral therapy (ART) from Pharmacy Benefits Management data, mean CD4 cell count, and presence of an undetectable HIV-1 RNA viral load (defined as < 500 copies/mL) (both based on the chronologically closest laboratory data prior to the index episode). Given the variability of VA facility offerings for addiction treatment to patients in our sample, which include primary care, outpatient addiction, general psychiatry, and inpatient residential treatment, we also included facility-level variables plausibly related to medication receipt from the 2010 Drug and Alcohol Program Survey (DAPS) of programs' practices and available services. The 2010 DAPS was administered to 260 VHA facilities that provide addiction services and aggregated to the 129 VHA facilities defined by three-digit station codes. The DAPS is administered biannually by the VHA Program Evaluation and Resource Center and is usually completed by an on-site program manager. In 2010, the DAPS had a 100% response rate. Kappa statistics when comparing variables of interest across different years of DAPS administration suggested fair to moderate agreement (range 0.24–0.44); we chose the 2010 DAPS because of the availability of variables of interest.

Facility-level covariates included urbanicity based on rural-urban commuting codes (Hart, Larson, & Lishner, 2005), and facility complexity designated 1a (most complex), 1b, 1c, 2, or 3 (least complex). Level 1 facilities contain high volume, patient risk, teaching, and research capacity, and are divided into 1a (most complex), 1b, and 1c based on volume and intensive care services. Level 2 facilities contain lower patient complexity and some teaching and research, while level 3 facilities are smallest in terms of volume and contain little or no teaching/research (Veterans Health Administration, 2011). The complexity category refers to the entire facility and not specifically to addiction services. The DAPS variables in this study included those that may be indicators of access to care (availability of weekend or evening [defined as after 5pm] hours for outpatient addiction treatment) or openness to the use of medications in treatment (presence of 12-step programming on-site and the availability of opioid agonist treatment, including either buprenorphine or methadone for opioid use disorder on-site).

2.5. Statistical analyses

We characterized the population of patients with at least one index episode using descriptive statistics. Among those, we characterized those with and without medication initiation based on patient- sand facility-level characteristics stratified by HIV status. We also examined initiation and retention by specific medication. We used t-tests for continuous variables, or a

nonparametric counterpart for non-normally distributed continuous variables, and chi-square for categorical variables to compare characteristics by HIV status, considering $p < 0.05$ as statistically significant.

We used logistic regression in the overall sample to determine unadjusted and adjusted odds ratios for receipt of any medication associated with HIV status. Then, we performed analyses for PLWH and uninfected individuals separately, and in the models for PLWH we additionally assessed HIV-specific variables such as the receipt of ART, CD4 cell count, and presence of an undetectable HIV viral load. We performed sensitivity analyses to query the addition of topiramate as an AUD medication to the multivariable models. We also performed sensitivity analyses using broadened definitions of initiation: a prescription fill within 180 days and within 365 days from the AUD episode, as well as time-to-initiation analyses stratified by HIV status. Because disulfiram may be more effective in supervised settings (Skinner, Lahmek, Pham, & Aubin, 2014), the capacity for higher intensity care may be a predictor of disulfiram initiation and so we examined disulfiram utilization by facility complexity type, as a potential indicator of availability of supervised settings. We also performed post-hoc analyses clustering by site. We performed all descriptive statistics and models using STATA version 14.1 (StataCorp LLC, College Station, TX).

3. Results

3.1. Characteristics associated with medication initiation

We identified 35,027 individuals with at least one index AUD episode, of whom 10,603 were PLWH and 24,424 were uninfected controls (Supplemental Fig. 1). This sample is racially/ethnically diverse (33% white, 58% black, 7% Hispanic/Latino), almost all were male (98%), and the mean age was 51 years. Seventy-five percent were identified as currently smoking, 15% had an opioid use disorder diagnosis, and 34% were hepatitis C infected. Of patients with AUD, 67% received care in urban settings and 81% received care in a facility of level 1 complexity. Fifty percent of patients received care in facilities with weekend hours available at a substance use disorder treatment program, 91% in facilities with evening hours available, 72% in facilities where 12-step facilitation was available, and 59% in facilities where opioid agonist therapy was available for the treatment of opioid use disorder (Table 1). Absolute numbers of those initiating medications for AUD was relatively stable over time (Fig. 1).

3.2. Patterns of initiating and retaining AUD medications

Among patients with AUD, 359 (1.0%) initiated either disulfiram, naltrexone, or acamprosate within 30 days of the index episode. The prevalence of initiation among PLWH was 0.78% (n = 83) and the prevalence among uninfected individuals was 1.1% (n = 276, $p < 0.01$ for comparison). Naltrexone was the most common medication initiated (n = 218, 0.62%), and was less commonly initiated among PLWH (n = 48, 0.45%) than uninfected patients (n = 170, 0.70%; $p < 0.01$). Among the 359 total patients who initiated a medication for AUD, 49 (14% of initiators) were retained over six months. The proportion retained over six months did not differ between PLWH (n = 16, 19% of PLWH who initiated) and uninfected individuals (n = 33, 12% of uninfected individuals who initiated; Table 2).

Disulfiram initiation was more common in more complex facilities and was most commonly initiated in the most complex facility type (0.69%, $p < 0.01$ for the comparison across the five categories of complexity).

3.3. Predictors associated with the initiation and retention of medications for AUD

In the model that included both PLWH and those without HIV infection, HIV infection was associated with decreased odds of initiating any MAUD in both unadjusted (odds ratio 0.69, 95% confidence interval [CI] 0.54–0.88) and adjusted analyses (adjusted odds ratio [AOR] 0.66, 95% CI 0.51–0.85) (Table 3). In models stratified by HIV status, older age (for PLWH: AOR 0.78, 95% CI 0.61–0.99; for uninfected: AOR 0.70, 95% CI 0.61–0.80) and black race (for PLWH: AOR 0.63, 95% CI 0.39–1.00; for uninfected: AOR 0.63, 95% CI 0.48–0.83), were associated with decreased odds of initiation. Episode-year was associated with increased odds of initiation (for PLWH: AOR 1.06, 95% CI 1.00–1.12 and for uninfected: AOR 1.04, 95% CI 1.01–1.07). Decreasing facility complexity was associated with decreasing odds of initiation among PLWH and among uninfected persons. If opioid agonist treatment for opioid use disorder was offered on-site, there was a greater likelihood of MAUD initiation for PLWH (AOR 2.80, 95% CI 1.45–5.40). The presence of evening treatment hours was associated with a lower odds of MAUD initiation for PLWH (AOR 0.26, 95% CI 0.12–0.58). Among PLWH only, ART receipt, CD4 cell count > 200 cells/mL, and presence of an undetectable HIV-1 RNA were not associated with the initiation of MAUD.

Due to the small numbers of patients who were retained on medications, multivariable regression models could not be performed to identify patient- or facility-level predictors of retention.

3.4. Sensitivity analyses

Among all patients with AUD, 137 (0.39%) patients initiated topiramate within 30 days, including 25 PLWH (0.24% with an index episode) and 112 uninfected individuals (0.46%). With the additional consideration of topiramate as a MAUD, the model for initiation of medications for AUD did not change considerably; predictors retained their significance and directionality (data not shown). HIV status continued to be associated with decreased odds of medication initiation in the adjusted model that included topiramate as a classifying medication.

In models assessing initiation within 180 days and 365 days (instead of 30 days) of the index episode, results were similar. Both longer definitions for initiation captured more (and the same number of) initiators and produced a model with predictors of similar significance and directionality. HIV status was negatively associated with initiation in this adjusted model (AOR 0.70, 95% CI 0.57–0.86). When we examined time-to-initiation stratified by HIV status, PLWH trended towards initiating later than uninfected individuals, but this difference was not statistically significant (56 [SD 49] days versus 53 [SD 50] days; $p = 0.22$). Similarly, when we assessed retention as > 30 days of coverage for a medication over the 180 days following an index episode, more patients were retained, but neither HIV status

(AOR 1.83, 95% CI 0.84–4.01) nor other predictors were associated with retention. Post-hoc analyses clustering by site did not produce significantly different models.

4. Discussion

In this national study of over 35,000 patients in care, initiation of evidence-based MAUD was very low and PLWH were less likely than uninfected controls to initiate these medications in a timely manner. This is despite evidence that medications are effective for AUD and that AUD negatively impacts HIV-related care and outcomes. For both PLWH and uninfected controls, black race and older age were associated with a decreased likelihood of initiating MAUD, and decreasing facility complexity was associated with decreased likelihood of initiating. With each advancing calendar year, PLWH and uninfected controls were significantly more likely to initiate medications, but the rates remained low throughout the 12-year study period. The predictors of AUD medication initiation did not differ when considering a longer event-horizon to start of a medication, from within a month of AUD diagnosis to within a year. While disulfiram was more likely to be initiated in more complex facilities, it is not known whether disulfiram was prescribed in supervised or directly-observed settings. The very low number of patients retained on medications over six months did not allow for a valid estimate of predictors for retention in either PLWH or the uninfected.

Our findings add to the literature of the lack of substance use disorder treatment initiation for PLWH and for uninfected patients (Center for Substance Abuse Treatment, 2009; Fredericksen et al., 2015; G. B.D. Risk Factors Collaborators, 2016; Kraemer et al., 2019; Metsch et al., 2008; Williams, Lapham, et al., 2017; Wyse et al., 2019). Our overall sample had lower rates of initiation than other published studies likely because those studies allowed for longer periods of time between diagnosis and medication receipt, such as 180 days (Harris et al., 2012; Williams, Gupta, et al., 2017) or one year (Williams, Lapham, et al., 2017), and included data only from more recent time periods, when use of MAUD was higher. PLWH may be particularly unlikely to receive medications in a timely fashion because providers may be more likely to be unaware of their patients' alcohol use (Conigliaro et al., 2003). Among 1225 PLWH from 10 U.S. clinics, only half of those with unhealthy alcohol use reported discussing their drinking with their providers (Metsch et al., 2008). In a survey of 158 U.S. HIV care providers, few reported that they provided evidence-based alcohol-related care (Chander et al., 2016). Qualitative data among 80 HIV care researchers and 66 patients in eight U.S. clinical research sites demonstrated that patients may prioritize substance use disorder-related care lower than other domains of care, such as HIV stigma (Fredericksen et al., 2015). Finally, in a sample of 830,825 patients receiving care in VA facilities with positive screens for unhealthy alcohol use, HIV infection was associated with a 35% decreased odds of receiving medications for AUD after adjustment for other factors likely associated with receiving alcohol-related care (Williams, Lapham, et al., 2017). Our study on a large sample of PLWH with uninfected controls builds on these previously published findings by focusing on new AUD diagnoses as a treatment opportunity, examining both initiation and retention, and examining important patient- and facility-level targets that may inform strategies to expand evidence-based AUD treatment to PLWH and other vulnerable groups.

Factors associated with the use of MAUD in our study build upon those identified in previous studies in two key ways. First, our findings suggest that black PLWH may be particularly vulnerable to under-receipt of evidence-based treatment for AUD, building on similar previous findings regarding black patients (Williams, Gupta, et al., 2017). Following the Generations of Health Disparities Research framework (Kilbourne, Switzer, Hyman, Crowley-Matoka, & Fine, 2006) for a healthcare system, it is necessary first to understand the reasons for health disparities (e.g., factors that put may place black PLWH at higher risk for under-receipt of MAUD) as a foundation for intervention development and implementation. Therefore, future studies should assess the factors that sustain and contribute to identified disparities at multiple levels, from the individual to the macro or societal level (Alvidrez, Castille, Laude-Sharp, Rosario, & Tabor, 2019) and potential regional variation of those disparities (Cole, Wilson, & Trivedi, 2017). It is unclear what accounts for our findings regarding black PLWH, but prior literature suggests contributors could include patient-level factors such as patient preferences, trust in health systems, and health beliefs, as well as provider and systems-level factors such as interpersonal and structural racism and stigma, and regional variation in treatment resources and competencies. Further work is needed to explore these and other contributors in order to inform interventions to reduce racial disparities in the receipt of MAUD.

Second, the lower likelihood of initiation of MAUD that we identified associated with increasing age was interesting. It is unclear what accounts for this association, but it is possible that, as patients grow older, treatment of AUD may not rise to the top of the priority list due to higher prevalences of other chronic diseases and potential provider concern about adverse side effects or interaction with other medications. When we examined age as a categorical variable by decades, age was not significantly associated with initiating MAUD, suggesting that our findings were not driven by lower rates of initiation in geriatric populations, for whom limited evidence exists for the efficacy of MAUD (Lehmann & Fingerhood, 2018).

Third, previous studies found that providers and counselors who employ the 12-step model's treatment pedagogy (Wilcox, 1998) may have negative perceptions of the effectiveness and acceptability of MAUD (Abraham, Rieckmann, McNulty, Kovas, & Roman, 2011), and that organizations with on-site 12-step meetings are less likely to adopt AUD medication treatment plans (Oser & Roman, 2007, 2008). The presence of on-site 12-step programming was not a negative predictor of initiation of MAUD in our sample, however, suggesting that policymakers and administrators need not consider 12-step programming a barrier to MAUD expansion. Our finding that the availability of evening hours was associated with less likelihood of MAUD initiation may be related to a greater likelihood of exposure to other types of group therapy, but it is not known what services are offered during these evening hours. Finally, for the entire sample and for PLWH, availability of on-site of opioid agonist treatment was associated with greater odds of MAUD initiation. Efforts to expand evidence-based medications for opioid use disorder may thus extend to patients with AUD.

There is increasing evidence for the safety and efficacy of MAUD among PLWH and data to support their use through routine HIV treatment settings (Edelman, Moore, et al., 2018; Korthuis et al., 2017; Springer et al., 2017; Springer, Di Paola, Barbour, et al., 2018; Tetrault

et al., 2012; Walley et al., 2015), which makes our findings particularly concerning. While HIV providers report screening for alcohol use, knowledge about and confidence in prescribing MAUD is low (Chander et al., 2016). These data together suggest the need for active interventions to promote the use of these medications for this population. Academic detailing, an educational approach based on behavioral sciences that promotes rational prescribing among providers (Soumerai & Avorn, 1990) has shown promise in encouraging the evidence-based use of medications for other disorders (Trotter Davis, Bateman, & Avorn, 2017), and has been successfully implemented in the VHA and associated with improved receipt of AUD medications (Harris et al., 2016; U.S. Department of Veterans Affairs, 2017). Novel models of integrated care for HIV and AUD, either by specialty referral or care for AUD within HIV clinics (Edelman et al., 2016; Edelman et al., 2017) and community-based settings may provide insights on optimal strategies for improving AUD care for this population, and should be adaptable to the needs of less complex facilities. The low prevalence of retention on medications suggests that strategies that promote retention are needed, and these strategies may draw from those used to promote retention on ART such as through technology-based interventions or peer navigators (Mbuagbaw et al., 2018).

Our study has several limitations. First, the sample is limited to fiscal years 1998 through 2015 and so may not accurately reflect practice today. Specifically, several guidelines now include gabapentin and topiramate as first or second-line for the treatment of AUD (American Psychiatric Association, 2018; “VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders,” 2015). Our sensitivity analyses that included topiramate did not change our models however, suggesting some durability in predictors across medication types. Second, we relied upon ICD-9 codes for defining AUD episodes as well as covariate comorbidities, which may lead to under-reporting of conditions. Third, as our data were restricted to medications obtained from VHA pharmacies, we were unable to assess medications received from outside sources. However, the VHA offers generous pharmacy benefits (Smith & Joseph, 2003) and almost all PLWH patients receive their ART through the VHA (Justice et al., 2006). Fourth, since our analysis is limited to the first AUD index episode for patients who had multiple episodes, our results suggest an opportunity for future investigation on longitudinal patterns of initiation and retention, and reinitiation, of MAUD. Finally, our findings may not be generalizable to female patients or to patients receiving healthcare outside the VHA or to VA patients who do not meet the epidemiologic profile of HIV. However, the VHA is the largest provider of HIV care in the US and a leader in implementation of alcohol-related care (Williams et al., 2011), so our findings are directly relevant to a large and vulnerable patient population.

In summary, this national study in the largest U.S. health care system (a leader in health care quality) highlights important gaps in the care of AUD for PLWH. Rates of initiating and retention on evidence-based MAUD are low, and certain populations such as PLWH, black persons, and older individuals may require focused implementation strategies to expand the reach of AUD medications. Quality metrics and processes for audit and feedback regarding effectiveness of implementation strategies are needed to track and improve the quality of care for AUD (Pincus, Scholle, Spaeth-Rublee, Hepner, & Brown, 2016). Improved provider education about medications for AUD and more integration of AUD- and HIV-related care (Goldman, Spaeth-Rublee, & Pincus, 2015) have potential to improve the provision of

evidence-based alcohol treatment interventions among patients for whom AUD has particularly negative impacts on quality of care and clinical outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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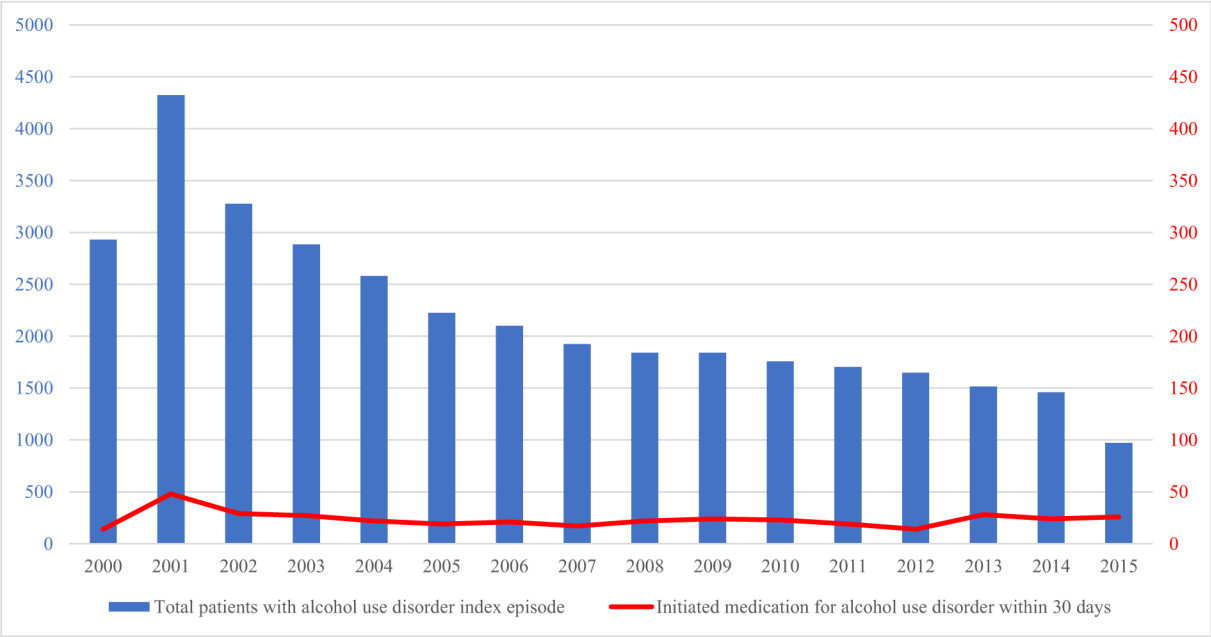

Fig. 1.

Alcohol use index episodes (blue bars) and initiation of any alcohol use disorder medication within 30 days from that index episode (red line) over time. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 1

Patient- and facility-level characteristics by initiation of any alcohol use disorder (AUD) medications within 30 days of the first index episode, among those with at least one index episode (n = 35,027).

	Total n = 35,027	PLWH n= 10,603		*p* value[a]	Uninfected n= 24,424		*p* value[a]
		Initiated n = 83	Did not initiate n = 10,520		Initiated n= 276	Did not initiate n = 24,148	
Sex, n (%)							
Male	34,419 (98)	80 (96)	10,243 (97)	0.58	271 (98)	23,825 (99)	0.50
Female	608 (2)	3 (4)	277 (3)		5 (2)	323 (1)	
Race/ethnicity[b], n (%)							
White	11,466 (33)	36 (43)	3217 (31)	0.07	112 (41)	8101 (34)	< 0.01
Black	20,325 (58)	41 (49)	6329 (60)		124 (45)	13,831 (57)	
Hispanic	2668 (7)	4 (5)	793 (7)		34 (12)	1837 (8)	
Other	568 (2)	2 (3)	181 (2)		6 (2)	379 (2)	
Age in years, mean (SD)	51 (8)	48 (9)	50 (8)	0.02	50 (8)	51 (8)	< 0.01
Hepatitis C, n (%)	11,928 (34)	34 (41)	5070 (48)	0.19	65 (24)	6759 (28)	0.10
Opioid use disorder, n (%)	5241 (15)	16 (19)	2096 (20)	0.88	39 (14)	3090 (13)	0.51
Stimulant use disorder, n (%)	1529 (4)	10 (12)	639 (6)	0.02	14 (5)	866 (4)	0.19
Current smoker, n (%)	26,109 (75)	60 (77)	7927 (80)	0.74	206 (79)	17,916 (78)	0.25
Comorbid mental illness n (%)[c]	12,066 (34)	26 (31)	3451 (33)	0.78	95 (34)	8494 (35)	0.79
Setting, n (%)							
Urban	23,539 (67)	60 (72)	6719 (64)	0.16	193 (70)	16,567 (69)	0.81
Rural	3472 (10)	2 (2)	696 (7)		28 (10)	2746 (11)	
(Missing)	8016 (3)	21 (25)	3105 (29)		55 (20)	4835 (20)	
Facility complexity, n (%)							
1a (most complex)	14,122 (40)	55 (66)	4437 (42)	< 0.01	132 (48)	9498 (39)	0.01
1b	8186 (23)	17 (20)	2655 (25)		58 (21)	5456 (23)	
1c	6308 (18)	8 (10)	1897 (18)		52 (19)	4351 (18)	
2	3561 (10)	2 (3)	859 (8)		23 (8)	2677 (11)	
3 (least complex)	2700 (8)	1 (1)	632 (6)		11 (4)	2056 (9)	
No designation	150 (1)	0 (0)	40 (1)		0 (0)	110 (1)	

	Total n = 35,027	PLWH n= 10,603		*p* value[a]	Uninfected n= 24,424		*p* value[a]
		Initiated n = 83	Did not initiate n = 10,520		Initiated n= 276	Did not initiate n = 24,148	
Weekend hours in addiction treatment clinic, n (%)	17,449 (50)	55 (66)	5257 (50)	< 0.01	137 (50)	12,000 (50)	0.99
Evening hours in addiction treatment clinic, n (%)	31,844 (91)	74 (89)	9615 (91)	0.47	251 (91)	21,904 (91)	0.89
Presence of on-site 12-step programming, n (%)	25,061 (72)	50 (60)	7528 (72)	0.02	201 (73)	17,282 (72)	0.64
Presence of on-site opioid agonist therapy for opioid use disorder, n (%)	20,808 (59)	68 (82)	6305 (60)	< 0.01	175 (63)	14,260 (59)	0.32
ART[d] receipt at episode, n (%)[e]	5950 (56)	45 (54)	5906 (56)	0.73			
CD4 count ≥ 200/mL, n (%)[e]	6053 (57)	53 (64)	6000 (57)				
CD4 count < 200/mL	1650 (16)	7 (8)	1643 (16)	0.18			
Missing	2900 (27)	23 (27)	2877 (27)				
HIV-1 VL < 500 c/mL, n (%)[e]	4280 (40)	39 (47)	4241 (40)	0.42			
HIV-1 VL ≥ 500 c/mL	3397 (32)	22 (27)	3375 (32)				
(Missing)	2926 (28)	22 (26)	2904 (28)				

Abbreviations: PLWH = person living with HIV; ART = antiretroviral therapy; VL = viral load.

[a]Chi-square test or t-test was used to compare differences across groups.

[b]Race and ethnicity data were collected separately, but all patients identifying as having Hispanic ethnicity are described here as “Hispanic” regardless of race. Those who did not identify as having Hispanic ethnicity are described here according to race.

[c]Comorbid mental illness included diagnoses in the prior year for schizophrenia, post-traumatic stress disorder, depression, or bipolar disorder.

[d]Combination antiretroviral therapy.

[e]Calculated for HIV-infected patients only, n = 10,603.

Table 2

Patterns of alcohol use disorder (AUD) medication prescriptions among patients initiating any medication within 30 days of the first index episode, with retention defined as being prescribed the classifying medication for at least 80% of the days over the 180 days following the index episode.

Characteristic	Total, n = 35,027	PLWH, n = 10,603	Not HIV-infected, n = 24,424	*p* value
Any AUD medication (not including topiramate)				
Initiation, n (%)	359 (1.0)	83 (0.78)	276 (1.1)	<0.01
Retention, n (%)	49 (0.14)	16 (0.15)	33 (0.14)	0.72
Any AUD pharmacotherapy (including topiramate)				
Initiation, n (%)	494 (1.4)	107 (1.0)	387 (1.6)	<0.01
Retention, n (%)	49 (0.14)	16 (0.15)	33 (0.14)	0.72
Naltrexone (PO)				
Initiation, n (%)	218 (0.62)	48 (0.45)	170 (0.70)	<0.01
Retention, n (%)	27 (0.10)	10 (0.10)	17 (0.10)	0.44
Disulfiram				
Initiation, n (%)	126 (0.36)	28 (0.26)	98 (0.40)	0.05
Retention, n (%)	22 (0.06)	6 (0.06)	16 (0.07)	0.76
Acamprosate				
Initiation, n (%)	22 (0.06)	7 (0.07)	15 (0.06)	0.88
Retention, n (%)	0 (0)	0 (0)	0 (0)	n/a
Topiramate				
Initiation, n (%)	137 (0.39)	25 (0.24)	112 (0.46)	<0.01
Retention, n (%)	0 (0)	0 (0)	0 (0)	n/a

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Table 3

Unadjusted and adjusted odds ratios for initiation of any alcohol use disorder (AUD) medication, stratified by HIV status.

Characteristic	All, unadjusted Odds ratios (95% CI) n = 35,027	All, adjusted Odds ratios (95% CI) n = 35,027	PLWH Odds ratios (95% CI) n = 10,603	Uninfected Odds ratios (95% CI) n = 24,424
HIV-infection	**0.69 (0.54–0.88)**	**0.66 (0.51–0.85)**	n/a	n/a
Male		0.80 (0.39–1.62)	0.70 (0.22–2.28)	0.84 (0.34–2.06)
Age (per 10-year increase)		**0.72 (0.64–0.81)**	**0.78 (0.61–0.99)**	**0.70 (0.61–0.80)**
Race/ethnicity[a]				
White		Ref	Ref	Ref
Black		**0.62 (0.49–0.78)**	**0.63 (0.39–1.00)**	**0.63 (0.48–0.83)**
Hispanic		1.02 (0.71–1.47)	0.50 (0.17–1.43)	1.20 (0.81–1.78)
Other		1.02 (0.50–2.11)	0.92 (0.22–3.91)	1.07 (0.47–2.46)
Hepatitis C		0.87 (0.68–1.12)	0.97 (0.60–1.58)	0.86 (0.64–1.16)
Opioid use disorder		1.13 (0.83–1.53)	1.07 (0.60–1.93)	1.16 (0.81–1.66)
Stimulant/amphetamine use		1.25 (0.81–1.93)	1.45 (0.72–2.95)	1.13 (0.65–1.99)
Current smoking		1.02 (0.80–1.30)	0.93 (0.57–1.53)	1.06 (0.80–1.40)
Comorbid mental illness[b]		0.91 (0.73–1.14)	0.85 (0.53–1.36)	0.93 (0.72–1.19)
Episode year (1-year increments)		**1.04 (1.02–1.07)**	**1.06 (1.00–1.12)**	**1.04 (1.01–1.07)**
Urban		1.03 (0.81–1.31)	1.19 (0.71–2.00)	0.99 (0.75–1.29)
Facility complexity				
1a (most complex)		Ref	Ref	Ref
1b		0.77 (0.58–1.03)	0.73 (0.40–1.33)	0.83 (0.60–1.15)
1c		0.76 (0.56–1.03)	**0.41 (0.18–0.92)**	0.89 (0.0.63–1.25)
2		**0.50 (0.32–0.78)**	**0.20 (0.05–0.87)**	**0.58 (0.36–0.93)**
3 (least complex)		0.41 (0.19–0.85)	0.14 (0.02–1.08)	**0.36 (0.19–0.69)**
Availability of weekend hours		1.01 (0.80–1.26)	1.32 (0.81–2.16)	0.92 (0.71–1.19)
Availability of evening hours		**0.60 (0.40–0.90)**	**0.26 (0.12–0.58)**	0.74 (0.47–1.17)
Presence of on-site 12-step programming		0.98 (0.77–1.25)	0.62 (0.38–1.02)	1.12 (0.84–1.49)
Presence of on-site opioid agonist treatment for opioid use disorder		**1.40 (1.08–1.82)**	**2.80 (1.45–5.40)**	1.18 (0.89–1.57)

Characteristic	All, unadjusted Odds ratios (95% CI) n = 35,027	All, adjusted Odds ratios (95% CI) n = 35,027	PLWH Odds ratios (95% CI) n = 10,603	Uninfected Odds ratios (95% CI) n = 24,424
cART receipt			0.76 (0.47–1.23)	
CD4 cell count ≥ 200			1.40 (0.81–2.41)	
Undetectable HIV-1 RNA viral load (< 500 copies/mL)			0.88 (0.57–1.36)	

Associations with $p < 0.05$ are shown in **bold**.

The adjusted model included all variables listed in the table.

[a]Race and ethnicity were collected as separate variables, but all patients identifying as having Hispanic ethnicity are described here as “Hispanic” regardless of race. Those who did not identify as having Hispanic ethnicity are described here according to race.

[b]Comorbid mental illness included diagnoses in the prior year for schizophrenia, post-traumatic stress disorder, depression, or bipolar disorder.