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Influence of comorbid drug use disorder on receipt of evidence-based treatment for alcohol use disorder among VA patients with alcohol use disorder and Hepatitis C and/or HIV

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ABSTRACT

Background: Alcohol use is risky for patients with hepatitis C virus (HCV) and/or human immunodeficiency virus (HIV) infection, but alcohol use disorder (AUD) treatment is underutilized in these populations. Comorbid drug use disorders (DUD) are common, but their influence on AUD treatment receipt is understudied. We evaluated the association between DUD and AUD treatment receipt in two national samples of patients with AUD, those with HIV and those with HCV, in the U.S. Veterans Health Administration.

Methods: Samples included patients with AUD and HCV and/or HIV among positive alcohol screens (AUDIT-C ≥ 5) documented 10/01/09-5/30/13 in the national electronic health record. Poisson regression models estimated incidence rate ratios for receiving specialty treatment (stop codes) and pharmacotherapy (filled prescription for naltrexone, disulfiram, acamprosate, or topiramate) within 365 days of positive alcohol screening for patients with DUD versus those without. Models were clustered on patient and adjusted for potential confounders.

Results: Among 22,039 patients with HCV/AUD, 45.2% (N = 9,964) had DUD, which was associated with receiving specialty treatment [adjusted incidence rate ratio: 1.89 (95% confidence interval 1.82–1.96)] and pharmacotherapy [aIRR: 1.50 (1.37–1.65)]. Among 1,834 patients with HIV/AUD, 56.9% (N = 1,043) had DUD, which was associated with receiving specialty treatment [aIRR: 1.94 (1.68–2.24)], but not pharmacotherapy.

Conclusions: Rates of AUD treatment receipt among patients with AUD and HCV and/or HIV were low overall, but likelihood of treatment receipt was generally higher among those with comorbid DUD. Future research should investigate mechanisms underlying these associations, such as enhanced readiness for treatment or differential provider prescribing or referral practices.

1. Introduction

Unhealthy alcohol use and alcohol use disorders are highly prevalent among people with hepatitis C virus (HCV) and among people with human immunodeficiency virus (HIV) (Armstrong et al., 2006; CDC, 2016; Galvan et al., 2002; Taylor et al., 2016; Tsui et al., 2016; Williams et al., 2016b), and alcohol use has unique harmful effects for persons with each of these infectious diseases. Alcohol and HCV have synergistic impacts on health. Among people with HCV, those who drink heavily are at increased risk for HCV-related liver diseases and mortality compared with those who do not (Donato et al., 2002; Fuster et al., 2014; Hutchinson et al., 2005; Safdar and Schiff, 2004; Szabo et al., 2006, 2010; Younossi et al., 2013), and among people with alcohol use disorder, those with HCV experience more healthcare utilization and mortality compared to those without HCV (Fuster et al., 2015; Tsui et al., 2006). Unhealthy alcohol use may also result in decreased receipt of antiviral treatment for HCV (Lin et al., 2017) and accelerated HCV viral replication (McCartney and Beard, 2010). Among those with HIV, alcohol use negatively influences HIV care engagement and adherence and multiple HIV-related outcomes, including mortality risk (Edelman et al., 2018; Vagenas et al., 2015; Williams et al., 2016a, 2018). Further, research suggests that people with HIV may be more

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susceptible to alcohol-related harm compared to those without HIV using alcohol at similar levels (Justice et al., 2016; McGinnis et al., 2016). Thus, people with HCV and/or HIV are particularly important target populations for the reduction of unhealthy alcohol use.

Alcohol use disorder (AUD) is the most severe form of unhealthy alcohol use (Saitz, 2005). There are effective behavioral and pharmacological treatments for AUD (Anton et al., 2006; Dawson et al., 2006; Jonas et al., 2014; Lingford-Hughes et al., 2012; NIAAA, 2007; Pettinati et al., 2005; Weisner et al., 2003), and specialty addictions treatment and/or prescription of pharmacotherapy are recommended for treatment of AUD (Department of Veterans Affairs, 2015; Jonas et al., 2014; National Institute for Health and Care Excellence, 2015; NIAAA, 2007). Pharmacological options include three FDA-approved medications (acamprosate, disulfiram, and oral or injectable naltrexone) (Jonas et al., 2014; NIAAA, 2007), and a fourth, topiramate, was found to have strong evidence for treatment of AUD in a meta-analysis (Jonas et al., 2014). Despite strong evidence for these treatments, they are underused among patients with AUD (Cohen et al., 2007; Harris et al., 2012; Rubinsky et al., 2015), and multiple barriers to treatment receipt and implementation have been documented (Alanis-Hirsch et al., 2016; Finlay et al., 2017; Hagedorn et al., 2016; Harris et al., 2013; Knudsen and Roman, 2014; Ober et al., 2017; Oliva et al., 2011; Williams et al., 2017a). People with infectious diseases (HCV and HIV) may be even less likely to receive evidence-based treatment for AUD compared to people without these conditions (Owens et al., 2018; Williams et al., 2017d).

Drug use is also prevalent among people with HCV and people with HIV (Alter, 2007; Armstrong et al., 2006; Bing et al., 2001; CDC, 2016), and comorbid drug use disorder (DUD) is common among people with AUD (Grant et al., 2015; Grant and Pickering, 1996; Grant et al., 2016; Stinson et al., 2005). Previous analyses of nationally-representative samples of U.S. residents have found that co-occurring DUD increases the likelihood of alcohol treatment utilization among people with AUD in the general population (Cohen et al., 2007; Dawson et al., 2012; Grant and Pickering, 1996; Ilgen et al., 2011; Stinson et al., 2005). In contrast, one previous study among patients from the national Veterans Health Administration (VA) found that DUD was not a significant predictor of receipt of specialty treatment for any substance use disorder (drugs or alcohol) among people with elevated levels of alcohol consumption (Glass et al., 2010). Specific to populations with infectious diseases, one analysis of data from the Women's Interagency HIV Study found that among women living with HIV who reported hazardous drinking, illicit drug use was associated with increased alcohol treatment utilization (Hu et al., 2016). Relatedly, another study among people with HIV found that while alcohol dependence was negatively associated with substance use treatment, drug dependence was positively associated with treatment (Orwat et al., 2011). To our knowledge, no studies have examined the association between comorbid DUD and receipt of AUD treatment among people with HCV specifically.

Further examination of the impact of comorbid DUD on receipt of treatment for AUD among people with HCV and HIV is warranted, particularly in a real-world care setting. The Veterans Health Administration (VA) is the largest provider of HCV and HIV care in the U.S. (Backus et al., 2015; Department of Veterans Affairs, 2017). Understanding the impact of comorbid DUD diagnosis on AUD treatment receipt among patient populations with HCV and HIV who have AUD and receive care in VA may have important implications for provider practice, as these populations have a high prevalence of comorbid DUD and are particularly susceptible to the harms of alcohol use. Thus, the present study aimed to evaluate the association between comorbid DUD and receipt of evidence-based AUD treatments among patients with HCV and patients with HIV. Results may inform future efforts to increase the provision of evidence-based care for AUD in these patient populations, both within and outside the VA healthcare system.

2. Methods

2.1. Setting, data source, and samples

The present study was conducted in the national VA health care system, comprised over 1,200 health care facilities serving over 9 million patients across the U.S. (Department of Veterans Affairs, 2018), and reflects a secondary analysis of data collected for a large study that assessed receipt of alcohol-related care across HIV status among VA patients with unhealthy alcohol use as determined by annual alcohol screening (Williams et al., 2017d). For the parent study, secondary data were extracted from the VA Corporate Data Warehouse (CDW), which is housed within VA's Informatics and Computing Infrastructure (VINCI), a national repository of clinical, pharmacy, administrative, enrollment, financial and utilization data for VA patients. Data were extracted for all patients with an outpatient appointment between 10/1/09 and 5/30/13 who had at least one documented positive alcohol screen during the study period. A positive alcohol screen was defined as an Alcohol Use Disorders Identification Test Consumption (AUDIT-C) score ≥ 5, consistent with the national performance measure for brief intervention used across the VA system (Lapham et al., 2012; Williams et al., 2017c). To examine outcomes, each screen was followed up to one year until 5/30/14. Multiple positive screens from the same patient could be included in the dataset during the study period if screens were at least nine months apart, consistent with VA's requirements for annual alcohol screening and the past-year timeframe of the screening instrument. Study procedures, including a waiver of HIPAA authorization and a waiver of written consent, were approved by the Institutional Review Board at VA Puget Sound Health Care System.

Two samples of patients were included in the present secondary analysis: 1) patients with HCV and AUD, and 2) patients with HIV and AUD. These samples were identified based on diagnostic codes from the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) in the 0–365 days prior to a positive screen and are not mutually exclusive (i.e., persons with either HIV or HCV may also have been diagnosed with the other condition). AUD was defined as having a documented diagnosis for alcohol abuse or dependence, excluding in remission (303.9–303.92, 305.0–305.02). HCV was defined as having one of the following diagnoses: chronic hepatitis C with (070.44) or without (070.54) hepatic coma, acute hepatitis C with (070.41) or without (070.51) hepatic coma, unspecified viral hepatitis C with (070.71) or without (070.70) hepatic coma, or hepatitis C carrier (V02.62). HIV was defined as having two outpatient or one inpatient diagnostic code(s) for AIDS (042) and/or HIV infection (V08), consistent with prior research (Fultz et al., 2006).

2.2. Measures

2.2.1. Primary independent variable

Comorbid DUD diagnosis was based on ICD-9-CM diagnostic codes in the 0–365 days prior to a positive AUDIT-C screen. Patients with abuse or dependence diagnoses for stimulants (including amphetamines and cocaine; 304.2–304.22, 305.6–305.62, 304.4–304.42, 305.7–305.72), opioids (304.0–304.02, 304.7–304.72, 305.5–305.52), cannabis (304.3–304.32, 305.2–305.22), hallucinogens (304.5–304.52, 305.3–305.32), or sedatives (304.1–304.12, 305.4–305.42) were classified as having comorbid DUD (excluding diagnoses for patients in remission).

2.2.2. Outcomes

The two outcomes of interest were receipt of any specialty AUD treatment and receipt of any AUD pharmacotherapy within 365 days following a positive AUDIT-C screen. Receipt of specialty AUD treatment was measured based on visit codes for inpatient or outpatient addiction treatment with an accompanying AUD diagnosis at the time of the visit code (Williams et al., 2014a). This definition includes

Table 1
Characteristics of VA outpatients with HCV and AUD: Overall and across comorbid drug use disorder status.

	DUD (N = 9,964)		No DUD (N = 12,075)		Chi-Square value	p-value	Total (N = 22,039)	
	N	(%)	N	(%)			N	(%)
Female	208	(2.1)	207	(1.7)	4.12	0.042	415	(1.9)
Age					215.79	< 0.001		
18-29	95	(1.0)	32	(0.3)			127	(0.6)
30-44	376	(3.8)	239	(2.0)			615	(2.8)
45-64	9,144	(91.8)	10,992	(91.0)			20,136	(91.4)
65+	349	(3.5)	812	(6.7)			1,161	(5.3)
Race/ethnicity					953.66	< 0.001		
American Indian/Alaska Native	145	(1.5)	174	(1.5)			319	(1.5)
Asian American/Pacific Islander	99	(1.0)	137	(1.2)			236	(1.1)
Black/African American	4,465	(45.5)	2,984	(25.7)			7,449	(34.8)
Hispanic/Latino	661	(6.7)	858	(7.4)			1,519	(7.1)
White	4,435	(45.2)	7,465	(64.3)			11,900	(55.6)
Marital status					381.07	< 0.001		
Divorced/Separated	4,459	(45.0)	5,583	(46.5)			10,042	(45.8)
Married	1,473	(14.9)	2,816	(23.5)			4,289	(19.6)
Never married/Single	3,588	(36.2)	3,158	(26.3)			6,746	(30.8)
Widowed	397	(4.0)	454	(3.8)			851	(3.9)
Opioid use disorder	3,308	(33.2)	0	(0.0)	4.7e+3	< 0.001	3,308	(15.0)
Stimulant use disorder	7,090	(71.2)	0	(0.0)	1.3e+4	< 0.001	7,090	(32.2)
Other drug use disorder[a]	4,968	(49.9)	0	(0.0)	7.8e+3	< 0.001	4,968	(22.5)
VA eligibility status					12.04	0.002		
Full VA coverage	1,730	(17.4)	1,897	(15.7)			3,627	(16.5)
Service connection < 50%	1,791	(18.0)	2,146	(17.8)			3,937	(17.9)
Non-service connected	6,443	(64.7)	8,032	(66.5)			14,475	(65.7)
Fiscal year of first AUDIT-C					3.36	0.339		
2010	4,347	(43.6)	5,128	(42.5)			9,475	(43.0)
2011	2,731	(27.4)	3,343	(27.7)			6,074	(27.6)
2012	1,970	(19.8)	2,450	(20.3)			4,420	(20.1)
2013	916	(9.2)	1,154	(9.6)			2,070	(9.4)
Major depression	2,387	(24.0)	1,237	(10.2)	747.05	< 0.001	3,624	(16.4)
Anxiety disorder	2,085	(20.9)	1,464	(12.1)	313.00	< 0.001	3,549	(16.1)
Post-Traumatic Stress Disorder (PTSD)	2,851	(28.6)	2,057	(17.0)	422.74	< 0.001	4,908	(22.3)
Other mood disorder	5,974	(60.0)	4,128	(34.2)	1.5e+3	< 0.001	10,102	(45.8)
Serious mental illness	2,747	(27.6)	1,186	(9.8)	1.2e+3	< 0.001	3,933	(17.9)

[a] Includes cannabis, hallucinogen, and/or sedative.

outpatient codes for individual, home visit and group substance use disorder treatment, and inpatient codes for residential rehabilitation, compensated work therapy, high intensity treatment, psychiatric and domiciliary care (a complete list of VA stop codes and bed sections included in this definition can be found in Williams et al., 2017d). Receipt of AUD pharmacotherapy was measured as at least one filled prescription for acamprosate, disulfiram, topiramate, or oral or injectable naltrexone, based on the date the medication was dispensed for inpatients and the date the medication was filled for outpatients (Harris et al., 2010).

2.2.3. Covariates

Covariates included demographic characteristics and mental health conditions, based on their associations with both drug use disorders and receipt of alcohol-related care (Bensley et al., 2017; Chen et al., 2018; Cohen et al., 2007; Dawson et al., 2012; Grant et al., 2016; Ilgen et al., 2011; Stinson et al., 2005; Williams et al., 2017b, 2012; Williams et al., 2017c). Demographic characteristics included sex (male/female), age group (18–29, 30–44, 45–64, 65+) categorized consistent with previous studies (Williams et al., 2017d, b), race/ethnicity (Asian American/Pacific Islander, Black, Hispanic/Latino, Native American, White), marital status (divorced/separated, married, never married/single, widowed) and eligibility for VA co-payment status (full VA coverage, service connection < 50%, no coverage) included as a proxy for socioeconomic status (Williams et al., 2012; Young et al., 2003). Mental health conditions were measured based on ICD-9-CM diagnostic codes in the 0–365 days prior to a positive AUDIT-C screen, and included major depression, anxiety disorder, post-traumatic stress disorder, other mood disorder, and serious mental illness (schizophrenia, bipolar disorder, psychosis). Additionally, fiscal year of positive AUDIT-C screen (2010, 2011, 2012, 2013) was included as a covariate to adjust for an increase in rates of alcohol-related care provided in VA nationally over time (Lapham et al., 2012).

2.3. Analyses

Patient characteristics collected at the time of first positive AUDIT-C screen were described at the patient level among patients in each sample: those with HCV and AUD and those with HIV and AUD. Chi-square tests of independence were used to assess differences across comorbid DUD status in each sample.

Consistent with previous studies (Owens et al., 2018; Williams et al., 2017d), modified Poisson regression models (Zou, 2004) were used to estimate relative rate and 95% confidence intervals of the two outcomes across comorbid DUD status, with positive AUDIT-C screens as the unit of analysis. Poisson regression was chosen to estimate relative rates (rather than odds ratios estimated through logistic regression) because outcomes were expected to be common (Greenland, 1995; Zou, 2004). Analyses were clustered at the patient level and standard errors were calculated using the robust sandwich estimator to account for correlation between AUDIT-C screens of the same patient, as well as for misspecification of the variance structure in the Poisson model (Greenland, 1995; Liang and Zeger, 1986; Zou, 2004). To examine the magnitude of effects, marginal predictions were calculated to describe predicted prevalence and 95% confidence intervals of the two outcomes in each group. Models were first fit unadjusted to identify the existing

Table 2
Characteristics of VA outpatients with HIV and AUD: Overall and across comorbid drug use disorder status.

	DUD (N = 1,043)		No DUD (N = 791)		Chi-Square value	p-value	Total (N = 1,834)	
	N	(%)	N	(%)			N	(%)
Female	25	(2.4)	13	(1.6)	1.26	0.262	38	(2.1)
Age					45.46	< 0.001		
18-29	14	(1.3)	16	(2.0)			30	(1.6)
30-44	129	(12.4)	106	(13.4)			235	(12.8)
45-64	876	(84.0)	597	(75.5)			1,473	(80.3)
65+	24	(2.3)	72	(9.1)			96	(5.2)
Race/ethnicity					142.80	< 0.001		
American Indian/Alaska Native	12	(1.2)	8	(1.0)			20	(1.1)
Asian American/Pacific Islander	7	(0.7)	6	(0.8)			13	(0.7)
Black/African American	770	(74.4)	373	(48.4)			1,143	(63.3)
Hispanic/Latino	73	(7.1)	71	(9.2)			144	(8.0)
White	173	(16.7)	312	(40.5)			485	(26.9)
Marital status					6.75	0.080		
Divorced/Separated	333	(32.2)	289	(37.1)			622	(34.3)
Married	109	(10.6)	90	(11.5)			199	(11.0)
Never married/Single	553	(53.5)	370	(47.4)			923	(50.9)
Widowed	38	(3.7)	31	(4.0)			69	(3.8)
Opioid use disorder	259	(24.8)	0	(0.0)	228.72	< 0.001	259	(14.1)
Stimulant use disorder	896	(85.9)	0	(0.0)	1.3e+3	< 0.001	896	(48.9)
Other drug use disorder[a]	446	(42.8)	0	(0.0)	446.93	< 0.001	446	(24.3)
VA eligibility status					2.90	0.235		
Full VA coverage	197	(18.9)	133	(16.8)			330	(18.0)
Service connection < 50%	185	(17.7)	162	(20.5)			347	(18.9)
Non-service connected	661	(63.4)	496	(62.7)			1,157	(63.1)
Fiscal year of first AUDIT-C					1.38	0.711		
2010	400	(38.4)	283	(35.8)			683	(37.2)
2011	289	(27.7)	233	(29.5)			522	(28.5)
2012	239	(22.9)	185	(23.4)			424	(23.1)
2013	115	(11.0)	90	(11.4)			205	(11.2)
Major depression	285	(27.3)	115	(14.5)	43.13	< 0.001	400	(21.8)
Anxiety disorder	183	(17.6)	110	(13.9)	4.44	0.035	293	(16.0)
Post-Traumatic Stress Disorder (PTSD)	233	(22.3)	109	(13.8)	21.72	< 0.001	342	(18.7)
Other mood disorder	653	(62.6)	307	(38.8)	102.12	< 0.001	960	(52.3)
Serious mental illness	324	(31.1)	94	(11.9)	94.05	< 0.001	418	(22.8)

[a] Includes cannabis, hallucinogen, and/or sedative.

association and prevalence in the samples, then subsequently adjusted for factors that may confound associations, including demographic characteristics, fiscal year of AUDIT-C screen and mental health diagnoses. Secondary analyses examined the association between specific DUDs (opioid, stimulant, and other) and all outcomes, and examined outcomes among patients diagnosed with both HIV and HCV. Analyses were conducted using Stata 15 software (StataCorp, 2017).

3. Results

3.1. Sample descriptions

Between 10/1/09 and 5/30/13, 830,825 patients (10.3% of patients with outpatient appointments eligible for AUDIT-C screening) screened positive for unhealthy alcohol use (AUDIT-C ≥ 5) with 1,172,606 total positive screens identified. Of these patients, 22,039 patients (2.7%; 30,765 screens) had diagnosed HCV and AUD, and 1,834 patients (0.2%; 2,401 screens) had diagnosed HIV and AUD. Among patients with HCV and AUD (N = 22,039), 9,964 (45.2%) had a comorbid DUD, and among patients with HIV and AUD (N = 1,834), 1043 (56.9%) had a comorbid DUD. Characteristics of patients in both samples are presented in Table 1 (HCV) and 2 (HIV) overall and across comorbid DUD status. For patients with HCV and AUD, most characteristics differed significantly across comorbid DUD status (p-values < 0.05). Those with comorbid DUD were more likely to be female, younger, Black/African American, never married/single, to have full VA coverage or service connection < 50%, and to be diagnosed with major depression, other mood disorder, PTSD, anxiety disorder, or serious mental illness (Table 1). For patients with HIV and AUD, some characteristics differed significantly across comorbid DUD status (p-values < 0.05). Specifically, those with comorbid DUD were more likely to be age 45–64 and Black/African American, and to be diagnosed with major depression, other mood disorder, PTSD, anxiety disorder, and serious mental illness (Table 2).

3.2. Association between comorbid DUD and receipt of AUD treatment

Among patients with HCV and AUD, 8,160 (37.0%) had documented AUD specialty addictions treatment and 1,693 (7.7%) had documented AUD pharmacotherapy within 365 days of positive AUDIT-C screen. Among patients with HIV and AUD, 741 (40.4%) had documented AUD specialty addictions treatment and 108 (5.9%) had documented AUD pharmacotherapy within 365 days of positive AUDIT-C screen.

Results of observation-level regression models for both samples are presented in Table 3. Among those with AUD and HCV, comorbid DUD was associated with increased likelihood of receiving both specialty addictions treatment and AUD pharmacotherapy in both unadjusted and adjusted analyses (Table 3). After adjustment, the predicted prevalence of receiving specialty addictions treatment was 52.8% (51.9–53.7) for those with DUD and 22.4% (21.8–23.1) for those without DUD (p < 0.001), and the predicted prevalence of receiving AUD pharmacotherapy was 11.3% (10.8–11.9) and 5.6% (5.2–6.0) for those with and without DUD, respectively (p < 0.001; Table 3). Although both associations were significant, the absolute difference in predicted prevalence for pharmacotherapy (difference of 5.7%) was

Table 3
Receipt of AUD treatment among VA patients with and without comorbid drug use disorder among those with HCV/HIV and AUD.

	DUD		No DUD		IRR[a]	95% CI	p-value[b]
	%	95% CI	%	95% CI			
Patients with HCV and AUD (N = 22,039)							
Receipt of any AUD specialty addictions treatment within 365 days following positive screen (AUDIT-C ≥ 5)							
Unadjusted	52.7	(51.8–53.6)	22.1	(21.4–22.7)	2.39	(2.31–2.47)	< 0.001
Adjusted[c]	52.8	(51.9–53.7)	22.4	(21.8–23.1)	1.89	(1.82–1.96)	< 0.001
Receipt of any AUD pharmacotherapy within 365 days following positive screen (AUDIT-C ≥ 5)[d]							
Unadjusted	11.2	(10.7–11.8)	5.5	(5.1–5.8)	2.05	(1.89–2.23)	< 0.001
Adjusted[c]	11.3	(10.8–11.9)	5.6	(5.2–6.0)	1.50	(1.37–1.65)	< 0.001
Patients with HIV and AUD (N = 1,834)							
Receipt of any AUD specialty addictions treatment within 365 days following positive screen (AUDIT-C ≥ 5)							
Unadjusted	52.9	(50.1–55.8)	22.5	(19.7–25.2)	2.35	(2.06–2.69)	< 0.001
Adjusted[c]	52.7	(50.0–55.5)	22.7	(20.0–25.4)	1.94	(1.68–2.24)	< 0.001
Receipt of any AUD pharmacotherapy within 365 days following positive screen (AUDIT-C ≥ 5)[d]							
Unadjusted	7.1	(5.6–8.6)	5.2	(3.7–6.6)	1.37	(0.97–1.93)	0.071
Adjusted[c]	7.2	(5.7–8.8)	5.1	(3.7–6.5)	1.21	(0.81–1.81)	0.345

[a] Incident Rate Ratio.
[b] p-value from test to evaluate if IRR is equal to one.
[c] Adjusted for gender, age, race/ethnicity, marital status, VA eligibility status, fiscal year in which positive AUDIT-C screen occurred, and mental health conditions.
[d] Includes acamprosate, disulfiram, topiramate, oral or injectable naltrexone.

smaller than for specialty treatment (difference of 30.4%).

Among patients with AUD and HIV, comorbid DUD was associated with increased likelihood of receiving AUD specialty treatment in both unadjusted and adjusted models, but was not significantly associated with receiving pharmacotherapy (Table 3). After adjustment, the predicted prevalence of receiving specialty addictions care was 52.7% (49.9–55.5) for those with DUD and 22.7% (20.0–25.4) for those without DUD ($p < 0.001$), and the predicted prevalence of receiving AUD pharmacotherapy was 7.2% (5.7–8.8) and 5.1% (3.7–6.5) for those with and without DUD, respectively ($p = 0.345$; Table 3).

Secondary analyses examining the association between specific DUDs (opioid, stimulant, and other) and all outcomes are presented in Supplementary Tables 1a-1c. Results were similar to the primary analyses among all subgroups, except that among patients with HIV, opioid use disorder was significantly associated with increased receipt of pharmacotherapy (Supplementary Table 1a). Results of secondary analyses among patients diagnosed with both HIV and HCV mirrored results among patients with only HIV (data not presented).

4. Discussion

This analysis of two large, non-mutually exclusive national samples of VA patients with AUD—those with HCV, and those with HIV—found that rates of AUD specialty addictions treatment and pharmacotherapy were low overall, particularly for pharmacotherapy (7.7% for HCV and 5.9% for HIV). However, having a comorbid DUD was associated with increased likelihood of receiving specialty addictions treatment for both groups and of receiving pharmacotherapy for those with HCV.

Findings from the present national study of VA patients with AUD and HCV and/or HIV are consistent with those of epidemiologic surveys of the general population (Cohen et al., 2007; Dawson et al., 2012; Grant and Pickering, 1996; Ilgen et al., 2011; Stinson et al., 2005), and studies of people with HIV (Hu et al., 2016; Orwat et al., 2011). Additionally, findings are similar to a previous VA study, which found that posttraumatic stress disorder was associated with increased receipt of AUD specialty addictions treatment and AUD pharmacotherapy (Chen et al., 2018), suggesting that other comorbidities may also increase receipt of treatment for AUD. However, one previous study of VA patients found that among patients with severe unhealthy alcohol use identified by alcohol screening, DUD was not a significant predictor of receiving specialty treatment for any substance use disorder, including drugs or alcohol (Glass et al., 2010). It is possible that differences between the previous study and the present study are related to differing samples and outcomes. In the present study, potentially eligible patients first screened positive for unhealthy alcohol use and then were included in analyses if they also had an AUD diagnosis, and the outcome was specialty treatment for AUD; in the Glass et al. study (2010), patients were included if they screened positive for unhealthy alcohol use, and the outcome was specialty treatment for any alcohol and/or drug use disorder. Differences may also relate to increased attention to provision of alcohol-related care in VA since the time of the previous study (Department of Veterans Affairs, 2015; Lapham et al., 2012). Finally, differences may relate to the specific focus in the present study on patients with infectious diseases in addition to AUD. Given the compounding influences of both AUD and DUD on both HCV and HIV, determinants of AUD treatment may differ in this sample from those in the general population of VA patients with severe unhealthy alcohol use and comorbid DUD.

The reasons underlying the association between comorbid DUD and receipt of treatment for AUD in these samples are unknown, but may be due to both provider and patient-level factors. For instance, providers who offer substance use treatment may have increased contact with persons with comorbid DUD, thus offering increased opportunities for treatment referral or provision. Studies have found that other mental health comorbidities (Chen et al., 2018; Glass et al., 2010) and greater alcohol use severity (Arndt et al., 2002; Burman et al., 2004; Kaner et al., 2001; Richmond et al., 1996; Volk et al., 1996) are associated with increased likelihood of receiving substance use disorder treatment and brief alcohol counseling. It is possible that multiple diagnoses and/or greater severity of problems may increase perceptions of risk, which could increase patient readiness to seek treatment and/or provider advice to seek treatment. Providers may also be less likely to prescribe pharmacotherapy or refer patients to AUD treatment if they do not have comorbid DUD, if they view AUD as less harmful than DUD. Alternatively, or in addition, patients with AUD and HCV and/or HIV who have comorbid DUD may be more likely to take up AUD treatment once it is prescribed or referred given multiple compounding health risks. This national study was conducted using secondary EHR data and thus

was unable to examine the respective roles of provider practices and patient uptake of treatment. However, future research is needed to assess the relative contributions of these two factors and how they are impacted by comorbid DUD diagnosis among patients with HCV and/or HIV, which may inform strategies to increase receipt of AUD treatment among these patients with and without comorbid DUD.

Overall, rates of AUD treatment were low across all groups, but especially among persons without comorbid DUD. These findings are concerning given the substantial health risks AUD poses to people with HIV and/or HCV, and given that sizeable proportions in each of these groups had diagnosed AUD only, without comorbid DUD (54.8% among HCV and 43.1% among HIV). Future work is needed to increase linkage to treatment, and especially to increase use of pharmacological treatments, among patients with infectious diseases who have diagnosed AUD but no comorbid DUD. It should be noted that some medications to treat AUD are metabolized through the liver (e.g., disulfiram, naltrexone), and therefore may raise concerns among providers who treat patients with HCV and other liver conditions. However, studies have demonstrated that these drugs are safe for persons with HCV and/or risk of hepatotoxicity with regular monitoring of liver function (Mitchell et al., 2012; Saxon et al., 1998; Tetrault et al., 2012).

There are several limitations to this study. Extracting EHR data enabled a large secondary analysis, but also introduced several limitations related to internal validity. First, although the AUD specialty addictions treatment outcome was defined as having an AUD diagnosis accompanying the visit code, there may have been some misclassification such that this measure captured treatment for other substance use disorders. Similarly, the AUD pharmacotherapy outcome may both over- and under-estimate medication treatment for AUD. Specifically, our measure included medications that are prescribed for indications other than AUD (naltrexone and topiramate) but did not differentiate between indications, and therefore may have resulted in overestimation of rates of AUD pharmacotherapy. On the other hand, we did not measure other medications that are increasingly being prescribed to treat AUD, such as gabapentin, and thus may have underestimated medication treatment. Unmeasured confounders that were not captured with EHR data may have resulted in residual confounding. Additionally, we are unable to interpret the association between DUD and receipt of AUD treatment as being evidence of causality in this analysis.

There are also limits to external validity. While VA is an ideal setting in which to conduct this study due to its ability to capture alcohol use and alcohol-related care in EHR data and large populations of patients receiving care for HCV and HIV, it may differ from other healthcare systems in several ways. As the VA is an integrated healthcare system that has implemented routine alcohol screening and in which addictions treatment is recommended in clinical guidelines (Department of Veterans Affairs, 2015), rates of treatment observed here may be higher than in other healthcare systems. Also, the VA patient population is largely male and older than other patient populations. Finally, because we identified patients with AUD among those with positive alcohol screening, results may not be generalizable to patients with AUD who do not receive alcohol screening and screen positive for unhealthy alcohol use.

Despite these limitations, this study demonstrated that among VA patients with AUD and HCV and those with AUD and HIV, rates of AUD specialty addictions treatment and pharmacotherapy were low overall, but significantly increased with presence of a comorbid DUD diagnosis (with the exception of pharmacotherapy among patients with HIV, which was non-significant). Findings suggest that having a comorbid DUD does not pose a barrier to receiving AUD treatment, but instead generally increases the likelihood of receiving treatment for AUD in these populations. Future research is needed to assess how comorbid DUD impacts provider practices and patient uptake of treatment, which may inform strategies to increase receipt of AUD treatment among the larger population of patients who do not have comorbid DUD.

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The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

Contributors

Ms. Frost led data analysis, interpretation, and manuscript writing. Dr. Williams led the creation of the secondary dataset and provided mentorship for data analysis, interpretation and revision of the manuscript. Ms. Matson and Dr. Tsui contributed to interpretation of findings and revision of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

The authors declare no conflicts of interest.

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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.2018.10.008.

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