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ORIGINAL PAPER

Comorbidity Burden and Health Care Utilization by Substance use Disorder Patterns among People with HIV in Florida

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Abstract

Substance use disorder (SUD), a common comorbidity among people with HIV (PWH), adversely affects HIV clinical outcomes and HIV-related comorbidities. However, less is known about the incidence of different chronic conditions, changes in overall comorbidity burden, and health care utilization by SUD status and patterns among PWH in Florida, an area disproportionately affected by the HIV epidemic. We used electronic health records (EHR) from a large southeastern US consortium, the OneFlorida + clinical research data network. We identified a cohort of PWH with 3 + years of EHRs after the first visit with HIV diagnosis. International Classification of Diseases (ICD) codes were used to identify SUD and comorbidity conditions listed in the Charlson comorbidity index (CCI). A total of 42,271 PWH were included (mean age 44.5, 52% Black, 45% female). The prevalence SUD among PWH was 45.1%. Having a SUD diagnosis among PWH was associated with a higher incidence for most of the conditions listed on the CCI and faster increase in CCI score overtime (rate ratio = 1.45, 95%CI 1.42, 1.49). SUD in PWH was associated with a higher mean number of any care visits (21.7 vs. 14.8) and more frequent emergency department (ED, 3.5 vs. 2.0) and inpatient (8.5 vs. 24.5) visits compared to those without SUD. SUD among PWH was associated with a higher comorbidity burden and more frequent ED and inpatient visits than PWH without a diagnosis of SUD. The high SUD prevalence and comorbidity burden call for improved SUD screening, treatment, and integrated care among PWH.

Keywords HIV · Substance use disorder · Comorbidity · Healthcare utilization · Electronic health records

Introduction

Substance use and substance use disorders (SUD) are common among persons with HIV (PWH) [1–3]. It has been estimated that 45–70% of PWH smoke tobacco, substantively higher than the proportion (~16%) among the general population [3, 4]. An analysis of data from the Center for AIDS Research Network of Integrated Clinical Systems (CNICS), a multi-site electronic health record (EHR)-based clinical cohort of PWH in the United States (US), revealed that almost half of PWH have been diagnosed with at least one substance use disorder [5]. Cannabis, alcohol, and stimulant use are the top three most common substance use disorders, and previous studies have shown that approximately 20% of PWH have polysubstance use disorder (i.e., having more than one SUD) [5]. Substance use has been associated with a wide range of comorbidities [6–9] and increased risk of hospitalization and Emergency Department (ED) visits [10].

Advances in HIV antiretroviral therapy (ART) have transformed HIV infection into a manageable chronic condition and helped achieve longer life expectancies for PWH [11]. With increased life expectancy, an increased prevalence of aging-related comorbidities has been observed among PWH [12, 13]. Yang et al. used electronic health record (EHR) data to compare the comorbidity burden before and after HIV diagnosis [14]. Among

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all included predictors, tobacco use had the strongest association with increased comorbidity; alcohol, cocaine, and cannabis use were also top predictors. Aging, HIV, SUD, multimorbidity, and higher treatment burden could have synergistic interactions with one another making individuals more susceptible to adverse clinical outcomes [15–17].

Care visit frequencies have been associated with overall comorbidity burdens and could supplement the comorbidity index to represent patterns in healthcare resource utilization [18, 19]. Frequent hospitalization and ED visits have been associated with complex health needs, high treatment burdens, and high healthcare costs [20–22]. Past studies have compared comorbidity risk, emergency department visit, and hospitalization frequency by substance use or use disorder status in both clinical [23, 24] and community settings [25, 26]. However, there are a lack of studies conducting these comparisons in PWH, especially for individuals with multimorbidity, defined as ≥ 2 concurrent chronic conditions [27] and for PWH living in Florida, an epicenter of the HIV epidemic in the US. Examining the comorbidity burden and healthcare utilization patterns using real-world clinical data can provide actionable insights to developing and implementing high-impact care delivery and management strategies that bridge the substance use treatment gaps for PWH in Florida, and ultimately accelerate progress along the HIV care continuum in a region disproportionately affected by the HIV epidemic.

Additionally, people with SUD are heterogeneous with different SUD types and combinations [25, 28, 29]. The use of different psychoactive substances is associated with varied mechanisms of action, levels of social marginalization or stigma, legal consequences, and risk of polysubstance use [28–31] which may, directly and indirectly, impact the comorbidity risk and healthcare utilization. A latent class analysis of a community sample in Florida has identified three main substance use patterns: tobacco use only, alcohol, marijuana, or tobacco use, and any use of stimulants, opioids, and other illicit substances [25]. Other research among PWH provides supporting evidence for this SUD pattern classification [3, 32, 33]. However, less is known regarding the comorbidity and care visit variations across people with different SUD patterns.

To address the public health needs and literature gap listed above, the presented work (1) estimates the prevalence of diagnosed SUD, polySUDs, and SUD patterns among PWH in Florida using statewide, integrated EHR and claims data, and (2) employees a longitudinal study design to test our hypothesis that having a SUD diagnosis is associated with an overall higher comorbidity burden, more inpatient visits, and more ED visits than in PWH without a SUD diagnosis. Additionally, we assess differences in the progression of chronic comorbidity accumulation and healthcare utilization characteristics by SUD patterns.

Methods

Data Source

We used EHR and administrative claims data from the OneFlorida + Clinical Data Research Network (OneFL) which includes EHR data from ten health systems across Florida linked to statewide claims from Medicaid and Medicare. OneFL comprises longitudinal health data from 17.2 million unique patients who received care in Florida between January 2012 to March 2021 [34]. It has been estimated that OneFL partners serve 40–50% of Florida's population, and the sociodemographic characteristics of the OneFL sample resemble the total Florida population [34]. The study was approved by the University of Florida Institutional Review Board (IRB202002581).

Identification of the HIV Cohort

Within OneFL, we previously developed and validated a computable phenotype algorithm to identify PWH [35]. The algorithm screens patient's medical records and identifies PWH if they had at least one HIV diagnostic code plus at least one of the following: (1) had at least one positive HIV laboratory test, including HIV RNA and antigen/antibody test, (2) had been prescribed ART, or (3) had three or more visits with corresponding HIV diagnostic codes. The algorithm achieved 98.9% sensitivity and 97.6% specificity. It has been estimated that 114,541 PWH in Florida in 2020 and 84% of them linked to care [36]. Our algorithm identified 71,363 PWH from OneFL (updated to early 2021), corresponding to ~70% of the number of PWH linked to care in Florida.

Study Design

A retrospective longitudinal cohort study design was used (Fig. 1). The index date was defined as the first HIV-related encounter: the first visit with an HIV diagnosis code, first positive HIV laboratory test, or first HIV ART prescription, whichever occurred first. The main exposure of interest was having a SUD diagnosis and the outcomes of interest were comorbidities summarized by the Charlson comorbidity index (CCI) and healthcare utilization (number of care visits per year). Health records

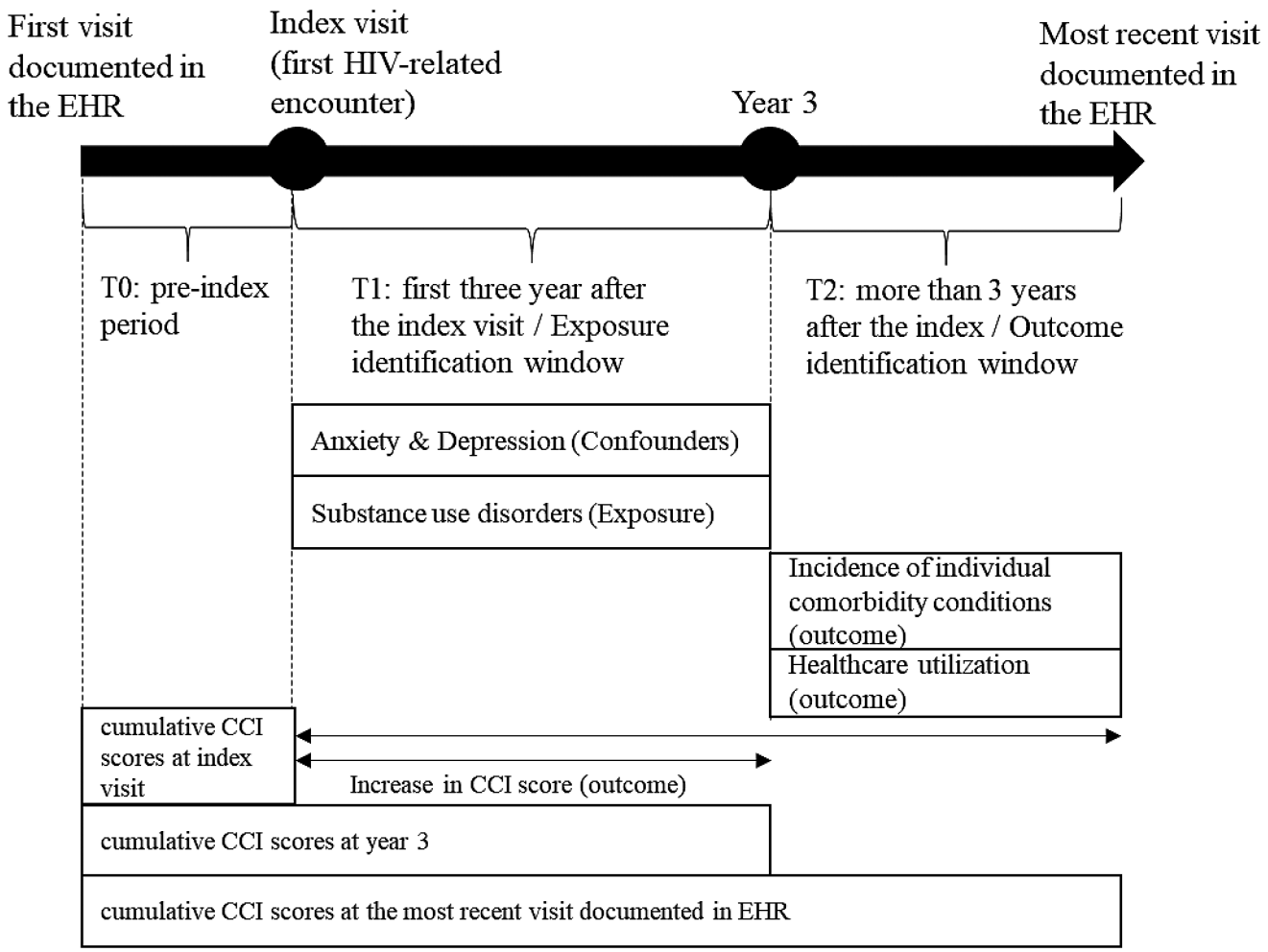

Fig. 1 Flowchart of sample timeline and variables assessment period

documented during the first three-year post-index date (T1 period) were used to identify exposure and confounding factors. Health records documented more than three years after the index visit and up to the most recent visit documented in the EHR (T2 period) were used to identify the outcomes. The three-year cutoff was selected after examining the distribution length of medical records available post-index data and to ensure a long enough window to capture SUD diagnosis.

The study sample was a subset of individuals who had at least three years of post-index date health records among the identified cohort of PWH. Therefore, all patients included had 1 + visit during the T1 and T2 periods, respectively. The length of T1 period is three years for all patients; the length of T2 period ranged from one to six years. T0 was defined as the period between the first clinical encounter in the EHR and the index visit. Patients whose first visit was an HIV-related encounter did not have a T0 period.

Measurements

Substance use Disorder

SUD diagnoses were identified using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) [37] and ICD-10-CM [38]. The ICD codes were selected based on computable phenotypes used in past research [39] and specified as tobacco use disorder (ICD-9 305.1; ICD-10 F17), alcohol use disorder (305.0, 303, 305.9; F10, 291), cannabis use disorder (305.2, 304.3; F12), cocaine use disorder (305.6, 304.2; F14), amphetamine and other stimulant use disorder (305.7, 304.4; F15), opioid use disorder (305.5, 304.0, 304.7; F11), sedative use disorder (305.4, 305.8, 304.1; F13), and hallucinogen use disorder (305.3, 304.5; F16), following the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [40]. The prevalence of each individual SUD was measured by having at least one of the above-mentioned ICDs recorded [24, 41,

42] during the first three-year post index visit (T1 period), regardless of any pre-index date diagnosis (T0 period).

Comorbidity Assessment

The Charlson comorbidity index (CCI) is the most widely used comorbidity index [43, 44]. It contains 16 chronic conditions, and each condition is assigned a weight according to its potential influence on mortality [43]. In our analyses. each individual condition included in the CCI was identified using the coding algorithm proposed by Deyo et al. for ICD-9-CM [45] and Quan et al. for ICD-10-CM [46]. To capture the post-exposure incidence of each individual comorbidity condition, the outcome was defined as having (1) a diagnosis code that occurred at least once in the medical record during the T2 period, and (2) no prior diagnosis during the T0 and T1 periods (Fig. 1).

Additionally, a comorbidity score was calculated using the original CCI weights [47], excluding HIV/AIDS since our sample are PWH. Cumulative CCI scores were calculated at the index visit, three years after the index visit, and at the most recent visit documented in the EHR. The cumulative score was calculated based on conditions that had at least one diagnosis code recorded ever before. For example, when calculating cumulative CCI scores at year 3, all EHR documented before the index visit (T0) and within the first three years after the index visit (T1 period) were examined and a condition was coded as present if a diagnosis occurred at least once during that time frame. These cumulative CCI scores supplemented the incidence of each individual comorbidity to better represent the prevalence of comorbidity and multimorbidity burdens. Having a cumulative CCI score between 1 and 2 indicates a mild comorbidity, 3–4 indicates moderate comorbidity, and ≥ 5 indicates severe comorbidity [47].

Health Care Utilization

The number of any care visits, including inpatient, outpatient, and ED visits, was estimated for each calendar year during the T2 period. Multiple care visits on the same day were counted only once. The average number of care visits, ED visits, and inpatient visits per year was calculated for each participant.

Covariates

Patient demographics, including age, sex, race and ethnicity were measured at enrollment. Age at index visit was calculated. Anxiety and depression were also included in the analysis as covariates since they are both common among people with SUD [48] and associated with higher comorbidity burden [49].

Analysis

We performed descriptive statistics to characterize the study sample, examine the prevalence of SUD among PWH within the first three years post index visit, and compare the incidence for each comorbidity condition, cumulative CCI score, and health care utilization by any SUD status. Based on cumulative CCI scores at different time points, increases in the score from the index visit to three years after the index visit and most recent visit were calculated. First, SUD was dichotomized into with or without SUD. Second, based on the most common polysubstance use disorder patterns observed, SUD pattern was classified into three mutually exclusive groups: (1) tobacco use disorder only, (2) any alcohol and/or cannabis use disorder with no other SUD except tobacco use disorder (alcohol/cannabis/tobacco use disorder only), and (3) any stimulant, opioid, sedative or hallucinogen use disorder with or without other SUD. Finally, comparisons were made across the three SUD patterns in the increase of cumulative CCI score over time and health care utilization indicators among people with any SUD.

Multivariable regression analysis was used with age, sex, race, ethnicity, anxiety, and depression controlled. Logistic regression was used for each comorbidity incidence; odds ratios (ORs) and corresponding 95% confidence interval (CI) were reported. Negative binomial regression was used for changes in CCI score over time and health care utilization (number of any care, ED, or inpatient visits per year); rate ratio (exp(β)) and corresponding 95% CI were reported. All analyses were conducted in SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Sample Characteristics and Substance use Disorder Prevalence

A total of 42,271 people with a confirmed HIV diagnosis and at least 3 years of post-index visit EHRs were identified from OneFL. The mean (SD) age at the index visit was 44.5 (12.9) years; 45.1% were female, 52.0% Black African American, and 15.8% Hispanic (Table 1). The top three most common comorbidity incidences were chronic pulmonary disease (12%), mild liver disease (11%), and renal disease (10%).

As shown in Tables 2 and 44.5% of PWH had at least one SUD. The most common substance-specific use disorders

Table 1 Sample demographic and bivariable comparison of demographic, comorbidity, and healthcare utilization, $n = 42,271$

	Total Mean (SD)/ Number (%)
	42,271
Mean age	44.5 (12.9)
Sex: female	19,063 (45.1%)
Race: Black or African American	21,978 (52.0%)
Race: White	12,866 (30.4%)
Race: Other	7,427 (17.6%)
Ethnicity: Hispanic	6,669 (15.8%)
Comorbidities (incidence)	
Myocardial infarction	2,239 (5.3%)
Congestive heart failure	3,323 (7.9%)
Peripheral vascular disease	3,512 (8.3%)
Cerebrovascular disease	3,268 (7.7%)
Dementia	1,191 (2.8%)
Chronic pulmonary disease	5,014 (11.9%)
Rheumatic disease	728 (1.7%)
Peptic ulcer	1,174 (2.8%)
Mild liver disease	4,603 (10.9%)
Diabetes without chronic complication	3,862 (9.1%)
Diabetes with chronic complication	3,007 (7.1%)
Hemiplegia or paraplegia	1,054 (2.5%)
Renal disease	4,355 (10.3%)
Malignant tumors	2,677 (6.3%)
Moderate or severe liver disease	707 (1.7%)
Metastatic tumor	840 (2.0%)
CCI score, mean (SD)	
Cumulative CCI score at index visit	0.3 (1.1)
Cumulative CCI score at year 3	2.1 (2.6)
Cumulative CCI score at most recent visit documented	3.5 (5.8)
Healthcare utilization, mean (SD)	
# of any care visits per year	9.3 (16.8)
# of ED visits per year	1.0 (0.9)
# of inpatient visit per year	2.4 (5.5)

Table 2 Prevalence of substance use-specific disorder during the first three years post index date among people with HIV, $n = 42,271$

Total	n	%
Any substance use disorder	18,789	44.5
Tobacco use disorder	15,942	37.7
Alcohol use disorder	6,296	14.9
Cannabis use disorder	3,973	9.4
Cocaine use disorder	4,393	10.4
Opioid use disorder	2,344	5.5
Sedative use disorder	598	1.4
Other stimulant use disorder	716	1.7
Hallucinogen use disorder	75	0.2
Number of substance use disorders*		
1	10,336	55.0
2	4,259	22.7
3	2,293	12.2
4+	1,901	10.1

* Among people who had any substance use disorder $n = 18,789$

were tobacco use disorder (37.7%), followed by alcohol (14.9%), cocaine (10.4%), and cannabis (9.4%) use disorders. Almost half (45%) of people with any SUD had two or more substance-specific use disorders. Supplement Fig. 1 describes SUD patterns. Among people with any SUD, 43.7% had tobacco use disorder only, 23.6% had alcohol or cannabis, or tobacco use disorder only, 32.7% had any stimulant, opioid, sedative, or hallucinogen use disorder. Within the "alcohol, cannabis or tobacco use disorder only" pattern, the most common SUD combination was alcohol and tobacco use disorder. Within the "any stimulant, opioid, sedative, or hallucinogen use disorder" pattern, the vast majority had 1 + SUDs, and mostly with cocaine or opioid use disorder.

Comparison between People with and Without any SUD

Having a SUD diagnosis among PWH was consistently associated with higher comorbidity for all conditions included in CCI (Table 3). After controlling for covariates (age, sex, race, ethnicity, depression, and anxiety) in regression models the largest comorbidity incidence differences between people with and without SUD among PWH were observed for moderate/severe liver disease (OR = 2.05, 95%CI 1.74, 2.41) and myocardial infarction (OR = 1.78, 95%CI 1.63, 1.96); whereas diabetes (OR = 1.07, 95%CI 0.99, 1.16 for diabetes with complication; OR = 1.11, 95%CI 1.03,1.19 for diabetes without complication) had the smallest/non-statistically significant comorbidity incidence differences.

Changes in cumulative CCI scores from index visit to three-year after and the most recent visit available were estimated and compared by SUD status (Table 3). The mean cumulative CCI scores at the index visit were 0.3 (Standard deviation/SD: 0.9) and 0.4 (SD: 1.3) for people with and without SUD, respectively. The mean score increased to 1.7 (SD: 2.3) and 2.6 (SD: 2.9) three-years post index visit and to 2.9 (SD: 3.2) and 4.2 (SD: 3.8) at the most recent visit for people with and without SUD, respectively.

In multivariable regression, compared to people without SUD, people with SUD were associated with a 45% increase in cumulative CCI score from the index visit to three-year after index visits (RR = 1.45, 95%CI 1.42, 1.49) and a 39% increase from the index visit to most recent visit (RR = 1.39, 95%CI 1.36, 1.42).

Relative to PWH but no SUD, people with SUD had a higher mean number of any care visits (7.8 vs. 11.0), ED visits (0.7 vs. 1.4), and inpatient visits (1.5 vs. 3.3) per year (Table 3). In multivariable regression, having a SUD diagnosis had the strongest association with more frequent inpatient visits (RR = 1.86, 95%CI 1.80, 1.93) across the three healthcare utilization indicators (Table 3).

Table 3 Association of having any substance use disorder diagnosis with comorbidity and healthcare utilization among people with HIV.

	PWH with no SUD	PWH with SUD	Any SUD vs. No SUD
	Mean (SD)/ Number (%)	Mean (SD)/ Number (%)	OR/RR (95% CI) [a]
	n = 23,482	*n* = 18,789	
Comorbidities listed in CCI (incidence)			
Myocardial infarction	934 (4.0%)	1,305 (7.0%)	1.78 (1.63, 1.96)
Congestive heart failure	1,528 (6.5%)	1,795 (9.6%)	1.54 (1.43, 1.66)
Peripheral vascular disease	1,615 (6.9%)	1,897 (10.1%)	1.55 (1.44, 1.67)
Cerebrovascular disease	1,552 (6.6%)	1,716 (9.1%)	1.46 (1.35, 1.57)
Dementia	543 (2.3%)	648 (3.5%)	1.62 (1.43, 1.84)
Chronic pulmonary disease	2,729 (11.6%)	2,285 (12.2%)	1.12 (1.05, 1.19)
Rheumatic disease	347 (1.5%)	381 (2.0%)	1.24 (1.06, 1.45)
Peptic ulcer	503 (2.1%)	671 (3.6%)	1.62 (1.43, 1.84)
Mild liver disease	2,139 (9.1%)	2,464 (13.1%)	1.50 (1.40, 1.60)
Diabetes without chronic complication	2,060 (8.8%)	1,802 (9.6%)	1.11 (1.03, 1.19)
Diabetes with chronic complication	1,632 (7.0%)	1,375 (7.3%)	1.07 (0.99, 1.16)
Hemiplegia or paraplegia	478 (2.0%)	576 (3.1%)	1.45 (1.27, 1.65)
Renal disease	2,277 (9.7%)	2,078 (11.1%)	1.17 (1.09, 1.25)
Malignant tumors	1,296 (5.5%)	1,381 (7.4%)	1.45 (1.33, 1.58)
Moderate or severe liver disease	264 (1.1%)	443 (2.4%)	2.05 (1.74, 2.41)
Metastatic tumor	392 (1.7%)	448 (2.4%)	1.60 (1.38, 1.84)
CCI score, mean (SD)			
Cumulative CCI score at index visit	0.3 (0.9)	0.4 (1.3)	--
Cumulative CCI score at year 3	1.7 (2.3)	2.6 (2.9)	--
Cumulative CCI score at most recent visit documented	2.9 (3.2)	4.2 (3.8)	--
Increase in CCI score from index visit to year3	1.4 (2.0)	2.2 (2.5)	1.45 (1.42, 1.49)
Increase in CCI score from index visit to the most recent visit documented	2.6 (3.0)	3.8 (3.6)	1.39 (1.36, 1.42)
Healthcare utilization, mean (SD)			
# of any care visits per year	7.8 (15.9)	11.0 (17.7)	1.23 (1.20, 1.26)
# of ED visits per year	0.7 (1.0)	1.4 (2.7)	1.73 (1.67, 1.78)
# of inpatient visits per year	1.5 (3.0)	3.3 (6.9)	1.86 1.80, 1.93)

a. Age, sex, race, ethnicity, depression, and anxiety were potential confounders adjusted for in all models

b. SD = standard deviation, SUD = substance use disorder, CCI = Charlson comorbidity index, ED = emergency department

Comparison Across Different SUD Patterns

Among PWH and across the SUD patterns, having any stimulant, opioid, sedative, or hallucinogen disorder was associated with the greatest increase in comorbidity burden over time, followed by people with alcohol, cannabis, or tobacco use disorder only. This same pattern was also observed for the three healthcare utilization indicators (Table 4).

Discussion

This study describes the prevalence of diagnosed SUD among patients with HIV in Florida and compares comorbidity burden and health care utilization across substance use patterns. The prevalence of overall and specific (alcohol, cocaine, and opioid) SUD in our sample was comparable to the prevalence observed among HIV care enrollees from the CNICS, a multistate EHR network-based HIV cohort in the US [5]. However, compared to their study, we found a lower prevalence of marijuana use disorder and other stimulant use disorders. The CNICS [5] used self-reported data from AUDIT-C [50] and ASSIST [51] to measure substance use disorder, while our analysis used ICD diagnostic codes from EHRs. This discrepancy in the SUD measurements may contribute to the differences in identified SUD prevalence. Geographic heterogeneity in SUD prevalence may also play a role, as wide variations in SUDs across study sites have been observed in Hartzler et al.'s [51] analyses. The CNICS sample used in their study did not include PWH in Florida (the University of Miami site for CNICS was added in 2021). The top four prevalent SUDs (namely tobacco, alcohol, marijuana, and cocaine) found in our sample were supported by other studies among PWH in Florida with substance use measures [2, 52].

PWH with SUD had higher care visits than PWH without SUD. Most of those visits were mainly inpatient or ED visits, which may indicate that higher healthcare utilization for

Table 4 Comparison across the different SUD patterns on their association with changes in cumulative comorbidity score and healthcare utilization among people with HIV and any SUD diagnosis (reference = people with tobacco use disorder only)

	alc/mj/tbc vs. tbc	sti/opi/sed/hall vs. tbc
	RR (95% CI) [a]	RR (95% CI) [a]
CCI score		
Increase in CCI score from index visit to year3	1.12 (1.08, 1.17)	1.29 (1.24, 1.34)
Increase in CCI score from index visit to the most recent visit documented	1.08 (1.04, 1.11)	1.21 (1.17, 1.25)
Healthcare utilization, mean (SD)		
# of any care visits per year	1.05 (1.01, 1.10)	1.20 (1.15, 1.25)
# of ED visits per year	1.15 (1.09, 1.21)	1.74 (1.66, 1.82)
# of inpatient visits per year	1.24 (1.16, 1.31)	1.93 (1.83, 2.04)

a. Age, sex, race, ethnicity, depression, and anxiety were potential confounders adjusted for in all models

b. SUD = substance use disorder, tbc = tobacco use disorder only, alc/can/tbc = alcohol, cannabis, or tobacco use disorder, sti/opi/sed/hall = stimulant, opioid, sedative, or hallucinogen use disorder, CCI = Charlson comorbidity index, ED = emergency department

people with SUD does not necessarily portend better health outcomes, and might reflect complex health needs with fragmented care, high treatment burdens, and high healthcare costs. This care utilization pattern indicates that the patient's healthcare needs are being addressed during acute episodes or emergencies rather than through proactive, coordinated, and continuous outpatient care. Our analysis indicates people with any stimulant/opioid/sedative/hallucinogen use disorder showed the highest risk for comorbidity and inpatient and ED visits across all SUD patterns. This finding is supported by past research that co-occurring stimulant and opioid use disorders contribute to adverse health outcomes, including higher morbidity and mortality [58, 59].

The incidence for each individual comorbidity listed in CCI and changes in cumulative CCI score suggests that having SUD is associated with an increased disease burden among PWH. Several mechanisms may explain this elevated disease burden. Firstly, there might be a direct causal link between SUD and increased comorbidity burden among PWH. Previous studies showed the causal role of alcohol use on liver disease [53, 54], cocaine use increases myocardial oxygen demand and accelerates atherosclerosis and therefore increases the risk for heart disease [55–57]. Our analyses found moderate/severe liver disease and myocardial infarction as major disease burdens among PWH with SUD compared to those without SUD. Moreover, HIV is an independent risk factor for increased morbidity, and PWH are at higher risk for comorbidities compared to the general population [60, 61]. PWH have approximately a 2-fold increased risk for cardiovascular disease, a 1.5-fold increased risk for malignancy, and are more likely to die from non-HIV/AIDS-related chronic medical conditions [62–64]. Substance use could have a drug-drug interaction effect with ART, leading to an increased risk for comorbidities. For example, alcohol has been found to interact with certain ART regimens and increase liver disease risk [65].

Our findings suggest PWH with SUD experience faster development in multimorbidity over time. The ending the HIV epidemic efforts are being undermined by the high burden of substance use and its associated morbidity; thus, additional efforts must be made towards addressing substance use and the gaps in substance use care (i.e., screening, education, and treatment) among PWH. Previous studies have shown persistent gaps in substance use care and services for PWH [66, 67], and our findings support a call to action to reduce these gaps and increase access to substance use services. Moreover, as findings from our study revealed that PWH and SUD have higher rates of healthcare visits, integrating substance use screening and treatment into these existing visits may be a missed opportunity [68]. This may include the use of evidence-based on-demand pharmacological interventions, such as medication-assisted treatment [69, 70], and targeted behavioral therapies [71], in both ED and outpatient settings to effectively reach and provide comprehensive care for PWH.

This study has some limitations. The use of having at least three years of EHR as an inclusion criterion allows a clear temporal relationship between exposure and outcome clear, however, it may also lead to selection bias and slight overestimation of comorbidity and healthcare utilization. Our sample represents PWH who were continuously enrolled in care and PWH who only engaged in care briefly may not be well represented in our sample. Additionally, a large proportion of PWH was identified from claims data and does not have laboratory results. Therefore, we are unable to include viral load and CD4 count in our analyses, which have been found in past studies to be associated with SUD and comorbidity burdens [72]. Furthermore, SUD was identified using ICD codes; these codes cannot accurately differentiate the severity and duration of SUDs which might also influence the comorbidity burden and healthcare utilization. Moreover, in our multivariable regression model, we controlled demographic and psychiatric conditions as confounders. However, there might still be residual confounders in the identified associations. Caution should be made when interpreting the OR/RR as causal effects. Additionally, social determinants of health, such as socio-economic status and occupational security, as well as societal factors like insurance coverage, could also impact health care utilization pattern among PWH. Future research studies could consider using conceptual frameworks

and Directed Acyclic Graphs (DAGs) to further examine the causal relationship behind the observed associations and identify actionable factors to reduce the healthcare burden. Future studies could also examine whether providing SUD treatment could reduce the risk of other comorbidities among PWH and whether specific treatments work better than others. Lastly, it is important to better understand how having these comorbidities complicate patient care management and how patients prioritize treatments for these different health conditions. This could better inform interventions to improve patient-centered care for PWH.

Conclusion

Our analyses revealed a high prevalence of SUDs among PWH, of which 44.5% of the cohort had at least one SUD. Nearly half of PWH with SUD exhibited two or more SUDs, with tobacco, alcohol, and cocaine being the most common substances involved. Our results support our hypothesis, as we found that PWH with SUDs experienced a higher burden of chronic comorbidities, a faster accumulation of comorbid conditions, and more frequent inpatient and ED visits. Additionally, we found that more healthcare utilization does not necessarily result in better healthcare outcome. Our results indicate people with any stimulant or opioid use disorder had the highest healthcare utilization, but also the fastest comorbidity accumulation. The higher healthcare utilization observed among those with any SUD mainly consists of more frequent ED and inpatient visits. This calls for prioritizing integrated and patient-centered care models that comprehensively address the complex healthcare needs of PWH and SUD, promoting timely screening, coordinated support, and improved treatment outcomes.

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