Cannabis Use and Self-Reported Bothersome Symptoms in People with HIV

Cannabis
2025

researchmj.org
10.26828/cannabis/2025/000269
Volume 8, Issue 1

Aleksandra Wrona[1,2], Amy C. Justice[1,2], Janet P. Tate[1,2], Christopher T. Rentsch[1,2,3], Kirsha S. Gordon[1,2], Farah Kidwai-Khan[1,2], Michael J. Silverberg[4], Derek D. Satre[4,5], Vincent C. Marconi[6,7,8], Suzanne M. Ingle[9], Jonathan A. C. Sterne[9], Matthias Cavassini[10,11], Kendall Bryant[12], Kathleen A. McGinnis[1,2]

[1]VA Connecticut Healthcare Systems
[2]Department of Internal Medicine, Yale University School of Medicine
[3]London School of Hygiene and Tropical Medicine
[4]Division of Research, Kaiser Permanente Northern California
[5]Department of Psychiatry and Behavioral Sciences, University of California, San Francisco
[6]Atlanta VA Healthcare System
[7]Emory University School of Medicine
[8]Rollins School of Public Health, Emory University
[9]Population Health Sciences, Bristol Medical School, University of Bristol
[10]Lausanne University Hospital and University of Lausanne, Switzerland
[11]Swiss HIV Cohort Study
[12]National Institute on Alcohol Abuse and Alcoholism

ABSTRACT

Objective: While cannabis use is common among people with HIV (PWH), there have been few studies examining the association of use with health outcomes among PWH. We aimed to evaluate the association between cannabis use and bothersome physical and mental health symptoms using both self-report and a direct biomarker for cannabis use. **Method:** The Medications, Alcohol and Substance use in HIV Study (MASH) is a cross-cohort study focused on polypharmacy and substance use among PWH. Participants were enrolled from October 2018 to May 2022 in the Swiss HIV Cohort Study (SHCS), Kaiser Permanente Northern California (KPNC) HIV Cohort, and 7 sites (Atlanta, GA; Bronx, NY; Washington, DC; Houston, TX; Los Angeles, CA; New York, NY; and Nashville, TN) in the Veterans Aging Cohort Study - HIV (VACS-HIV). Participants submitted self-reported information on the presence/absence of symptoms in the prior 4 weeks, along with bothersome level, using the HIV Symptom Index, which is comprised of 20 symptoms commonly reported in PWH, including fatigue, diarrhea, fever, anxiety, and weight loss, among others. Concurrent self-reported substance use information was also collected, and participants provided nail clippings to be tested for cannabis use. We used logistic regression models, adjusted for age, sex, race/ethnicity, and cohort, to examine associations of self-report and biomarker-identified cannabis use with self-reported bothersome symptoms. **Results:** The analytic sample included 1,226 PWH who were predominantly male (85%), non-white (64%), with an average age of 57 years; 20% tested positive for cannabis use, and 23% reported recent cannabis use. Agreement between self-report and biomarker cannabis use was substantial (agreement 89%, kappa = 0.67). Put together, 27% either reported cannabis use or tested positive. Of the 20 symptoms included in the HIV Symptom Index, 19 were more prevalent at a bothersome level among those with cannabis use compared to those without. In adjusted models, the patterns of association remained for both self-reported and biomarker-confirmed cannabis use, and they

were particularly substantial for memory, depression, anxiety, and nausea. **Conclusions:** Cannabis use was common among PWH and was associated with a number of bothersome symptoms. While cannabis use may be used to treat loss of appetite, nausea/vomiting, and weight loss, the associations of cannabis use with depression, anxiety, and memory loss are concerning and deserve investigation.

Key words: = cannabis; biomarker; bothersome symptoms; HIV; agreement

Cannabis legalization has become increasingly common across the United States, leading to greater access and use among the general population, including people with HIV (PWH; Hasin et al., 2022). However, the health impacts of cannabis use, particularly among those with underlying conditions such as HIV, are not well understood given its complex mechanisms of action (Volkow et al., 2014). Cannabis use has been associated with several physical and psychological symptoms. Physical symptoms commonly associated with smoking cannabis use include respiratory complaints, such as coughing, wheezing, and phlegm (National Academies of Sciences et al., 2017; Tetrault et al., 2007), along with increased rates of pneumonia and other respiratory infections (Volkow et al., 2014). The effects of cannabis use on blood pressure are unclear, and associations remain inconsistent (Alshaarawy & Elbaz, 2016; Goyal, Awad, et al., 2017; Vallée, 2023). Cannabis use has also been associated with cognitive changes, including mild to moderate impairments in memory and attention (Bourque & Potvin, 2021; Gabrys, Robert & Porath, 2019). Additionally, cannabis use has been linked to depression and anxiety; however, the direction of the association is not well understood (Feingold & Weinstein, 2021; Gorfinkel et al., 2020; Stoner, ,2017; Volkow et al., 2017).

HIV/AIDS is a qualifying condition in all states with medical cannabis programs. Findings have been mixed as to whether cannabis use is associated with antiretroviral therapy (ART) use and adherence, which is crucial for HIV management (Costiniuk et al., 2019; Montgomery et al., 2019; Vidot et al., 2017; Zhang et al., 2018). While cannabis use has been shown to provide relief from various HIV-related symptoms, including pain, anxiety, and poor appetite (Andreae et al., 2015; Ellis et al., 2009; Goyal, Singla, et al., 2017; Mack & Joy, 2000; Woolridge et al., 2005), it has also been associated with other features that negatively impact quality of life for PWH, such as cognitive impairment (Cristiani et al., 2004), breathing problems (Lorenz et al., 2019), and impairments in host defense (Roth et al., 2002; Turcotte et al., 2016; Wenger & Crothers, 2019), although more studies are needed in these areas. PWH are frequently screened for self-reported bothersome symptoms in clinical and research settings in order to evaluate patient well-being and quality of life. These screenings are often conducted in the context of their HIV diagnosis and not for particular substance use; a prior study found that bothersome symptoms were more common among people who use alcohol among both people with and without HIV (Bahji et al., 2023). Potential bothersome symptoms include common physical (fatigue, aches/pains, nausea) and mental health (depression, anxiety) symptoms experienced by PWH. Given that medical outcomes such as viral load and CD4 count are commonly addressed in medical settings, screening for symptoms most commonly associated with HIV diagnosis helps capture outcomes that are more relevant to the patient experience. Symptoms identified as increasingly bothersome were more highly associated with outcomes and clinical severity than just "any level of symptom" (Justice, Holmes, et al., 2001). Moreover, since HIV symptoms may decrease patient quality of life and interfere with antiretroviral medication adherence, effective symptom management can greatly improve overall patient well-being.

Among the general U.S. population, non-medical past-year cannabis use grew from 10% to 13% among adults from 2002 to 2014 (Azofeifa, 2016; Carliner et al., 2017). Use is greater among young adults: according to the NIH Monitoring the Future study, a nationally representative

Corresponding Author: Kathleen McGinnis, DrPH, MS, VA Connecticut Healthcare System, 11ACSL-G, 950 Campbell Avenue. West Haven, Connecticut 06516. Phone: (810) 387-3211 ext. 13541. Email: kathleen.mcginnis3@va.gov.

sample of over 32,000 students across the United States who self-reported their substance use from February to June 2021, 43% reported past-year use compared to 17% in 2011 (National Institute on Drug Abuse, 2022). However, studies have found that cannabis use has been increasing across other age groups as well, including among older adults (Han & Palamar, 2020). According to one 2022 NIH study, past-year cannabis use was reported by 44% of adults ages 19 to 30, and by 28% of adults ages 35 to 50, representing the highest recorded cannabis endorsement over a 10-year period (National Institute on Drug Abuse, 2023; Patrick et al., 2023).

Cannabis use is overall lower in Europe compared to the United States, but prevalence of use has nevertheless increased by over 25% since 2010 (Manthey et al., 2021; *ESPAD Group, 2020*). According to the European Monitoring Centre for Drugs and Drug Addiction, past-year cannabis use among European adults aged 15 to 64 was 8% overall (European Monitoring Centre for Drugs and Drug Addiction, 2023). Compared to the NIH Monitoring the Future study, the 2019 European School Survey Project on Alcohol and Other Drugs study showed that lifetime use among 15- and 16-year olds, while less than the US, was still over 25% in countries such as the Czech Republic, Italy, and Latvia (*ESPAD Group, 2020).*

Cannabis use among U.S. military veterans has increased over the past decade following the trends of the general population. Nearly 12% of veterans used cannabis in the past 6 months in a 2021 study, compared to 9% in 2014 (Davis et al., 2018; M. L. Hill et al., 2021). Cannabis is often used to treat symptoms of post-traumatic stress disorder (PTSD), such as sleep problems and anxiety, as well as chronic pain associated with military service. Reports on the benefits of cannabis use on PTSD are largely anecdotal (Hill et al., n.d.); however, high-quality randomized controlled trials comparing cannabis use to a placebo group among individuals suffering from PTSD have been sparse (Rehman et al., 2021). In one study of 150 participants in 2020, those using THC-dominant cannabis reported a greater reduction in PTSD symptom severity over the course of a year compared to the control group who did not use cannabis (Bonn-Miller et al., 2022).

Given the increasing use of cannabis (Cash et al., 2020), that HIV is a qualifying condition for medical cannabis use, and the association of cannabis use with both cognitive and physical changes, there is a need to better understand the relationship between cannabis use and bothersome symptoms among PWH. With the success of ART on HIV suppression, PWH are living longer with a better quality of life. PWH are now entering middle and later age, and the study of this population and the modifying effects HIV has on a host of other age-related health issues has only begun to be explored. The Veterans Aging Cohort Study (VACS) is one of the largest cohorts of PWH in the world. We sought to evaluate the association between cannabis use and bothersome symptoms among aging PWH in VACS along with two non-veteran cohorts in Northern California (Kaiser Permanente) and in Switzerland (the Swiss HIV Cohort Study).

While self-reported data on substance use is frequently employed in research, it can result in underreporting due to social desirability bias. Comparing factors associated with cannabis use based on self-report to a validated biomarker can strengthen such findings. In this paper, we aimed to 1) evaluate the association between cannabis use and bothersome symptoms using both self-report and a direct biomarker for cannabis use and 2) examine whether patterns of associations between cannabis use and bothersome symptoms differed when using self-reported vs. biomarker-confirmed cannabis use.

METHODS

Study Design

The Medications, Alcohol, and Substance use in HIV (MASH) study is a multi-site cross-sectional study focused on polypharmacy and substance use in PWH. PWH on antiretrovirals (ARVs) were enrolled from October 2018 to May 2022 from the Kaiser Permanente Northern California (KPNC) HIV Cohort (Silverberg et al., 2020), Swiss HIV Cohort Study (SHCS; Scherrer et al., 2022), and 7 sites (Atlanta, GA; Bronx, NY; Washington, DC; Houston, TX; Los Angeles, CA; New York, NY; and Nashville, TN) of the VACS-HIV (Justice et al., 2006). Participants completed in-depth confidential surveys, including questions on substance use and the HIV Symptom Index (Justice, Holmes, et al., 2001), provided salivary samples, nail clippings, and blood spots for

substance use assessment, all at the time of study enrollment.

The study was approved by the Internal Review Boards (IRB) for the Department of Veterans Affairs (VA), Yale University, KPNC, and the Swiss HIV Cohort Study. Due to VA regulations and our ethics agreements, the analytic data sets used for this study are not permitted to leave the VA firewall without a Data Use Agreement. This limitation is consistent with other studies based on VA data.

Measures

Cannabis use. Cannabis use was measured in two ways: a self-report questionnaire and a validated biomarker. Self-reported questionnaires were given to all participants in the study across the three cohorts. In the Swiss cohort, questionnaires were translated into French and then back-translated in order to maintain and validate original meaning. Participant cannabis use was captured by selecting an answer to the following: "For each of the following drugs, please fill in the option that best indicates how often in the past 12 months you used each drug." A multiple choice selection included "have never tried," "no use in last year," "less than once a month," "1-3 times per month," "1-3 times per week," 4-6 times a week," and "every day." Positive self-reported cannabis use was defined as using marijuana 1-3 times per month or more frequently, because this cutoff had the best agreement with biomarker-confirmed cannabis use.

Biomarker-confirmed cannabis use was ascertained using nail samples. Cannabinoid presence in nail samples can be detected up to 6 months after cannabis use and thus is more appropriate for identifying chronic rather than occasional use (Cobo-Golpe et al., 2021; Shu et al., 2015). Specimens were sent to the United States Drug Testing Laboratories, Inc. (USDTL) and were initially tested using a 5 pg/mg immunoassay cutoff point to test for the drug metabolite Carboxy THC. Preliminary immunoassay testing may yield false negative and positive results due to structurally similar compounds found by testing surfactants (Antunes et al., 2023). For tests presumed positive by immunoassay, a second portion of the nail specimen was prepared for confirmation. Using mass spectrometry, quantitative values were generated and the applicable 0.02 pg/mg cutoffs were applied in order to determine whether the specimen was positive or negative for cannabinoids. Mass spectrometry is the gold standard for confirmatory analyses due to its high degree of specificity and ability to quantify substance amounts (Loos et al., 2016). Using a combination of both the immunoassay and mass spectrometry techniques, USDTL is able to capture reliable and accurate measurements of various substances within biologic specimens.

HIV Symptom Index. The HIV Symptom Index developed by Justice et al. in 2001 (Justice, Holmes, et al., 2001) is a commonly used self-report instrument to assess the presence and severity of bothersome symptoms within the past 4 weeks. It has demonstrated good reliability and validity and has been employed in various clinical and research settings to measure the effectiveness of interventions, monitor symptom burden, and improve patient care (Wang et al., 2022; Zuñiga et al., 2020). The symptoms within the index are not unique to HIV and were derived from previous quality-of-life indices used by clinicians to evaluate overall patient well-being (Anderson & Testa, 1994; Stephens et al., 1997a; Wilson & Cleary, 1995). The HIV Symptom Index is comprised of 20 items regarding common symptoms experienced by PWH, including fatigue, diarrhea, fever, anxiety, and weight loss, among others (Figure 1). Participants in the MASH study were asked to provide one of the following five responses for each symptom: "I do not have this symptom," "I have this symptom," along with one of the following: "it doesn't bother me," "it bothers me a little," "it bothers me," or "it bothers me a lot." For this study, we created a variable for each symptom representing having the symptom and being at least "a little" bothered, similar to previously established thresholds (Bahji et al., 2023; Justice, Chang, et al., 2001).

Demographic and other substance use variables. Age, sex, race and/or ethnicity, education, other substance use (listed below), and HIV mode of acquisition (e.g. men who have sex with men, injection drug use) variables were collected on the patient self-report survey. Additionally, variables for recent use of other substances were based on biomarkers: cotinine from saliva (>20 ng/mL) for smoking/tobacco use, phosphatidyl ethanol (PEth) from bloodspots (>20 ng/mL) for at least moderate alcohol use, and

metabolites of cocaine, amphetamine, and opioid use from fingernail clipping

Table 1. *Demographic Characteristics of MASH (n = 1,226)*

		Cannabis Use Self-Report or Biomarker	
	Combined	Yes	No
Variable	*N* = 1,226	*N* = 337	*N* = 889
Mean Age in Years (SD)	56.8 (12.0)	56.3 (12.2)	57.0 (11.9)
Male, N (%)	1,039 (85%)	305 (91%)	734 (83%)
Race/Ethnicity, N (%)			
Black	553 (45%)	158 (47%)	395 (44%)
White	447 (36%)	124 (37%)	323 (36%)
Hispanic	176 (14%)	47 (14%)	129 (15%)
Other/Unknown	50 (4%)	8 (2%)	42 (5%)
Education, N (%)			
<High School	141 (12%)	35 (10%)	106 (12%)
High School Graduate	338 (28%)	91 (27%)	247 (28%)
Some College	377 (31%)	107 (32%)	270 (31%)
College Graduate	370 (30%)	104 (31%)	266 (30%)
HIV Risk Group, N (%)			
MSM*	672 (55%)	206 (61%)	466 (52%)
IDU**	133 (11%)	50 (15%)	83 (9%)
MSW/WSM***	402 (33%)	78 (23%)	324 (37%)
Other/Unknown	19 (2%)	3 (1%)	16 (2%)
Cannabis Use, N (%)			
Neither Self-report or Biomarker	889 (73%)		
Self-report Only	90 (7%)		
Biomarker Only	49 (4%)		
Both Self-report and Biomarker	198 (16%)		
Other Substance Use (Biomarker), N (%)			
Tobacco	427 (35%)	175 (52%)	252 (28%)
Alcohol	375 (31%)	119 (35%)	256 (29%)
Cocaine	164 (13%)	61 (18%)	103 (12%)
Amphetamines	79 (6%)	29 (9%)	50 (6%)
Opioids	50 (4%)	24 (7%)	26 (3%)
Cohort, N (%)			
1	442 (36%)	85 (25%)	357 (40%)
2	267 (22%)	103 (31%)	164 (18%)
3	517 0(42%)	149 (44%)	368 (41%)

Note. *Men who have sex with men, **Injection drug use, ***Men who have sex with women / women who have sex with men

Analysis

Demographic characteristics, cannabis measures, and biomarker measures for other substances were summarized. Agreement between self-report and biomarker-confirmed cannabis use was evaluated using cross tabulation and kappa statistics. We also evaluated the association between biomarker-confirmed cannabis use and other substance use with chi-square statistics. For each symptom, the proportion with a reported bothersome symptom was calculated by cannabis use and evaluated graphically for both self-report and biomarker-confirmed cannabis use. We used logistic regression models, adjusted for age, sex, race and/or ethnicity, and cohort to examine adjusted associations of bothersome symptoms with self-report (at least monthly) and biomarker-identified cannabis use. For this sample of 1,226 with 337 who use cannabis, power of 80 and alpha

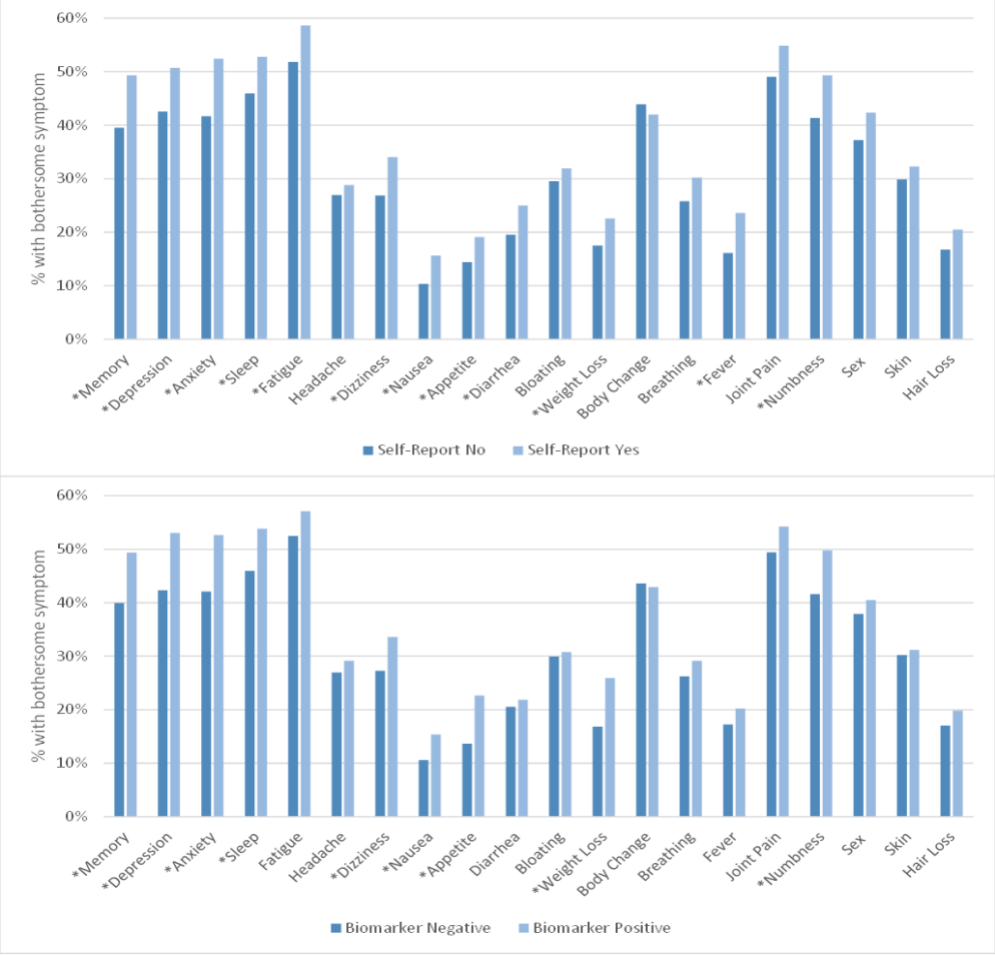
= 0.05, we are sufficiently powered to detect absolute differences ranging from 6% to 9% for bothersome symptoms that range in prevalence from 10% to 50%. As a sensitivity analysis, we also ran the logistic regression models using self-reported cannabis use at least weekly in place of at least monthly.

RESULTS

Demographic Charateristics

We identified 1,226 participants across the three cohorts who had survey and biomarker data available. Participants were mostly male (85%), Black (45%), with a mean age of 57 years (Table 1). Over 30% used alcohol (31% had PEth >20 ng/mL) and tobacco (35% had cotinine >20 ng/mL). Other substance use was less common; based on biomarkers, 13% had recent use of cocaine, 6% amphetamines, and 4% opioids (Table 1).

Figure 1. *Bothersome Symptoms by Recent Cannabis Use (n = 1,226)*



**Note*. Statistically significant at $p < .05$

Cannabis Self-Report vs. Biomarker

Cannabis use was common based on both self-reported at least monthly use (288 participants, 23%) and biomarker (247 participants, 20%) measures. Combined, 337 (27%) either endorsed cannabis use or had a positive biomarker test. Of those who reported cannabis use in the past month, 198 (69%) had a positive cannabis biomarker. Of those with a positive cannabis biomarker, 80% also self-reported cannabis use at least monthly. The kappa statistic (0.67) indicated substantial agreement. In comparing agreement of the biomarker-confirmed measure with multiple self-reported frequency cut points (at least weekly, at least monthly, at least yearly, ever), agreement was best, based on kappa statistics, with at least monthly use (Appendix Table 1).

Cannabis and Other Substance Use

Other substance use was more common among those with a positive cannabis biomarker test compared to those without, particularly tobacco (136, 56% vs. 291, 30%), cocaine (51, 21% vs. 113, 12%), amphetamines (23, 9% vs. 56, 6%), and opioids (21, 9% vs. 29, 3%) The same was true to a lesser extent for alcohol (83, 34% vs. 292, 30%) and fentanyl (3, 1.2% vs. 6, 0.6%) comparing those with and without a positive cannabis biomarker test.

Bothersome Symptoms by Cannabis Use

Bothersome symptoms were common; over 40% reported being at least a little bothered by symptoms related to mental health (memory, depression, anxiety) and physical health (sleep, fatigue, body changes, joint pain, and numbness). For both measures of cannabis use, those with cannabis use were more likely to report bothersome symptoms than those without (for 19 of the 20 symptoms), and the patterns of associations between cannabis use and bothersome symptoms were similar for both (Figure 1). Only the way a person perceives their body to look bothersome symptom was less likely among those with cannabis use compared to those without. Additionally, 9 of the 20 symptoms were found to be statistically significantly more likely among those with cannabis use compared to those without ($p < 0.05$) for both the self-reported and biomarker measures. These included all the mental health symptoms (memory, depression, anxiety), symptoms related to gastro-intestinal issues (nausea, appetite, diarrhea) and other physical health issues (weight loss, numbness in the hands/feet).

Based on the odds ratios and 95% confidence intervals generated from logistic regression models adjusted for age, gender, race/ethnicity, and cohort, those with cannabis use were more likely to have symptoms than those without for the majority of the 20 symptoms. The most substantial associations were related to anxiety (self-report: 1.45 [1.10, 1.90]; biomarker: 1.51 [1.13, 2.01]), nausea (self-report: 1.58 [1.06, 2.34]; biomarker: 1.50 [1.00, 2.26]), depression (self-report: 1.23 [0.94, 1.62]; biomarker: 1.44 [1.08, 1.91], and memory loss (self-report: 1.42 [1.08, 1.87]; biomarker: 1.41 [1.05, 1.87]; Table 2). Patterns were similar when using the at least weekly (instead of at least monthly) self-reported cannabis use variable in sensitivity analyses, although the association became stronger between cannabis use and four bothersome symptoms: appetite, body image, breathing, pain, and hair loss.

Overall, patterns were similar between the models using self-reported and biomarker-confirmed cannabis use, but there were some marked differences. For example, in certain instances, biomarker-confirmed cannabis use was more strongly associated with bothersome symptoms, as in the case of appetite (biomarker: 1.71 [1.19, 2.45]; self-report: 1.35 [0.94, 1.94]) and weight loss (biomarker: 1.55 [1.11, 2.17]; self-report: 1.22 [0.87, 1.71]). Conversely, self-reported cannabis use was substantially associated with fever, chills, or sweats (1.71 [1.22, 2.39]) whereas the biomarker was much less pronounced (1.26 [0.88, 1.80]; Table 2).

Table 2. *Association of Cannabis Use with HIV Symptoms from Adjusted Logistic Regression Models*

	Adjusted Odds Ratio (95% CI)*	
Symptoms	**Self-Report**	**Biomarker**
Trouble remembering	1.42 (1.08, 1.87)	1.41 (1.05, 1.87)
Felt sad, down, or depressed	1.23 (0.94, 1.62)	1.44 (1.08, 1.91)
Felt nervous or anxious	1.45 (1.10, 1.90)	1.51 (1.13, 2.01)
Difficulty falling or staying asleep	1.23 (0.93, 1.62)	1.28 (0.96, 1.71)

Fatigue or loss of energy	1.31 (0.99, 1.72)	1.22 (0.91, 1.62)
Feeling dizzy or light headed	1.28 (0.95, 1.71)	1.26 (0.93, 1.71)
Nausea or vomiting	1.58 (1.06, 2.34)	1.50 (1.00, 2.26)
Loss of appetite or change in the taste of food	1.35 (0.94, 1.94)	1.71 (1.19, 2.45)
Diarrhea or loose bowel movements	1.22 (0.88, 1.68)	1.00 (0.71, 1.42)
Problems with weight loss or wasting	1.22 (0.87, 1.71)	1.55 (1.11, 2.17)
Fever, chills, or sweats	1.71 (1.22, 2.39)	1.26 (0.88, 1.80)
Pain, numbness, or tingling in the hands or feet	1.34 (1.02, 1.77)	1.33 (1.00, 1.78)
Headache	1.11 (0.82, 1.51)	1.14 (0.83, 1.57)
Bloating, pain, or gas in your stomach	1.05 (0.79, 1.41)	0.99 (0.73, 1.35)
Changes in body looks (fat deposits/weight gain)	0.77 (0.58, 1.02)	0.89 (0.67, 1.19)
Cough or trouble catching breath	1.26 (0.94, 1.71)	1.16 (0.84, 1.59)
Muscle aches or joint pain	1.23 (0.93, 1.61)	1.17 (0.88, 1.56)
Problems with having sex (lack of interest/satisfaction)	1.04 (0.79, 1.38)	0.97 (0.73, 1.31)
Skin problems, such as rash, dryness, or itching	0.99 (0.74, 1.32)	0.96 (0.70, 1.30)
Hair loss/changes in the way your hair looks	1.16 (0.82, 1.65)	1.11 (0.77, 1.60)

*Models adjusted for age, gender, race and ethnicity, and cohort

DISCUSSION

In this large sample of PWH drawn from three health system-based cohorts, recent cannabis use was reported or detected in over 20% of study participants. Bothersome symptoms were very common, with eight of the twenty symptoms being reported in at least 40% of participants. Cannabis use was associated with an increased likelihood for most of the 20 bothersome symptoms in the HIV Symptom Index. While the associations of self-reported and biomarker-confirmed cannabis use with symptoms were not identical, the overall patterns were similar.

Agreement between self-reported and biomarker-confirmed cannabis use was good. Because both measures can identify some degree of use that the other measure might not, we cannot necessarily conclude that one measure is better than the other. The biomarker can detect chronic use up to six months prior but may not identify use that is only occasional, whereas occasional use can be identified if it is self-reported. Similarly, chronic use that was more than thirty days ago and within the past six months could be identified with the biomarker, but the survey items were not asked in a way to capture use in the past six months. Because of these issues, in some situations in which maximum identification is desired, it might be useful to combine the self-reported and biomarker-confirmed measures.

The cohorts used in this study tended to be comprised of older individuals (average age of 57

years) and were overwhelmingly male (85% overall). Additionally, a large portion of the study was made up of veterans from the VACS. However, strengths of this study include that it is racially/ethnically and geographically diverse, and both non-veterans and veterans were included. Further, the frequency of cannabis use is similar between our study to trends found outside of this population (*ESPAD Group*, 2020; National Institute on Drug Abuse, 2023; Manthey et al., 2021; Patrick et al., 2023). While there may be limited generalizability to other settings, Kaiser Permanente and the VA represent two of the largest HIV providers in the United States, and individuals enrolled in the Swiss HIV Cohort Study are generalizable to other PWH in Europe.

Analyses were cross-sectional, and we were not able to evaluate causality between cannabis use and bothersome symptoms. In some cases, cannabis was likely being used to self-medicate for symptoms that already existed. In other cases, cannabis use could have been causing or exacerbating bothersome symptoms. For example, we found that those who used cannabis were more likely to have gastrointestinal-related symptoms, and this may be due to the use of cannabis to treat loss of appetite, nausea/vomiting, and weight loss (Goyal, Singla, et al., 2017). Consistent with prior research (Feingold & Weinstein, 2021; Gorfinkel et al., 2020; Stoner, 2017; Volkow et al., 2017), we found cannabis use to be associated with depression, anxiety, and memory loss; this is concerning and deserves further investigation because while cannabis may be used to treat these symptoms, we are unable to evaluate the direction of causality in this study. We found that those who use cannabis are more likely to drink alcohol and smoke cigarettes, which may also have an effect on reporting of bothersome symptoms. Future research should explore whether polysubstance use plays a role in the association between cannabis use and bothersome symptoms. Additionally, future studies should consider reasons for smoking/consuming cannabis and whether they perceive their cannabis/substance use as the cause for bothersome symptoms.

Conclusion

Cannabis use was common among PWH and was associated with many bothersome symptoms for both self-reported and biomarker-confirmed cannabis use measures. While cannabis may be used to treat a variety of symptoms including loss of appetite, nausea/vomiting, weight loss, anxiety, and depression, the associations of cannabis use with deleterious mental health outcomes are concerning and deserve investigation to better establish temporal relationships. Although self-reported and biomarker-based cannabis measures capture slightly different aspects of cannabis use, there was high agreement between the two measures and their associations with bothersome symptoms were similar; therefore, we consider both to be valid measures of use.

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Funding and Acknowledgements: This work was supported by the National Institute on Alcohol Abuse and Alcoholism grants: U10-AA013566, U01-AA026224, U01-AA020790, U24-AA020794, U01-AA026209, and U01 AA026230. VM has received funding support from Emory Center for AIDS Research (P30AI050409) for work related to this manuscript. VM has received investigator-initiated research grants (to the institution) and consultation fees from Eli Lilly, Bayer, Gilead Sciences, Merck, and ViiV. MC's institution received research grants and expert opinion fees from Gilead and MSD. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Veterans Affairs or the National Institutes of Health.

Citation: Wrona, A., Justice, A. C., Tate, J. P., Rentsch, C. T., Gordon, K. S., Kidwai-Khan, F., Silverberg, M. J., Satre, D. D., Marconi, V. C., Ingle, S. M., Sterne, J. A. C., Cavassini, M., Bryant, K., & McGinnis, K. A. (2025). Cannabis use and self-reported bothersome symptoms in people with HIV. *Cannabis*, *8*(1), 177-190. https://doi.org/10.26828/cannabis/2025/000269

Issue Date: February 1, 2025


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