

## Identifying HIV care enrollees at-risk for cannabis use disorder

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### ABSTRACT

Increased scientific attention given to cannabis in the United States has particular relevance for its domestic HIV care population, given that evidence exists for both cannabis as a therapeutic agent and cannabis use disorder (CUD) as a barrier to antiretroviral medication adherence. It is critical to identify relative risk for CUD among demographic subgroups of HIV patients, as this will inform detection and intervention efforts. A Center For AIDS Research Network of Integrated Clinical Systems cohort ( $N = 10,652$ ) of HIV-positive adults linked to care at seven United State sites was examined for this purpose. Based on a patient-report instrument with validated diagnostic threshold for CUD, the prevalence of recent cannabis use and corresponding conditional probabilities for CUD were calculated for the aggregate sample and demographic subgroups. Generalized estimating equations then tested models directly examining patient demographic indices as predictors of CUD, while controlling for history and geography. Conditional probability of CUD among cannabis-using patients was 49%, with the highest conditional probabilities among demographic subgroups of young adults and those with non-specified sexual orientation (67–69%) and the lowest conditional probability among females and those 50+ years of age (42% apiece). Similarly, youthful age and male gender emerged as robust multivariate model predictors of CUD. In the context of increasingly lenient policies for use of cannabis as a therapeutic agent for chronic conditions like HIV/AIDS, current study findings offer needed direction in terms of specifying targeted patient groups in HIV care on whom resources for enhanced surveillance and intervention efforts will be most impactful.

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Increased scientific attention to cannabis encompasses its potential as a therapeutic agent for some health conditions and impetus to public health challenges. Both sides of this pendulum impact persons living with HIV/AIDS (PLWHA). Cannabis has benefits for managing weight loss, neuropathy, nausea, and pain (Abrams et al., 2007; Cohen, Heinz, Ilgen, & Bonn-Miller, 2016; de Jong, Prentiss, McFarland, Machezano, & Israelski, 2005; Lutge, Gray, & Siegfried, 2013), yet cannabis use disorder (CUD) is linked to poor antiretroviral medication adherence and virologic outcomes (Bonn-Miller, Oser, Bucossi, & Trafton, 2014). In the United States, a 23% cannabis use rate among PLWHA more than triples that of the general population (SAMHSA, 2011), though estimates do vary by demography (Hosek, Harper, & Domanico, 2005; Marshall et al., 2015). That some

PLWHA use cannabis to effectively manage aspects of their health (Fogarty et al., 2007; Furler, Einarson, Millson, Walmsley, & Bendayan, 2004) and others develop a dependence syndrome broadly characteristic of that seen for alcohol, tobacco, and illicit drugs (Budney & Hughes, 2006) underscores a need to identify HIV care enrollees at-risk for CUD.

Lack of diagnostic specificity and caveats common to single-site trials (i.e., selection bias, geographic isolation, historical artifact) have limited the evidence regarding the domestic prevalence of CUD in extant HIV care literature. However, recent work (Hartzler et al., 2016), based on a 10,000+ Center For AIDS Research Network of Integrated Clinical Systems (CNICS) cohort, more conclusively estimates CUD prevalence at 31%. The current study seeks to document lifetime prevalence rates of

cannabis use, conditional probabilities of CUD among cannabis users, and demographic predictors of CUD in this CNICS cohort. Given ongoing movement toward more lenient cannabis policies for specified medical conditions including HIV/AIDS, findings may identify HIV care enrollees for whom targeted surveillance and intervention efforts will be most impactful.

## Methods

This report utilized CNICS (2016), an open access platform initiated in 1995 for longitudinal observation of PLWHA linked to care. Available data derive from documentation of patient care visits, medication/laboratory information, and patient-reports collected via web-based survey. Continual integration of data from seven CNICS-affiliate sites enabled analyses of cannabis use rates as well as conditional probabilities and demographic predictors of CUD without sampling biases and surrogate endpoints inherent in clinical trials (Hughes, 2006).

## Data sources

This work is restricted to patient demography and 90-day retrospective reporting on the Alcohol, Smoking, and Substance Involvement Test [ASSIST (Humeniuk et al., 2008)]. Patient demography included age, gender, ethnicity, race, transgender status, and sexual orientation (the latter collected only among recent enrollees at three sites). Cannabis reporting specified: (1) an “involvement score” comprised endorsed dependence symptoms (e.g., inability to cut down; craving; consequent role failure; health, social, legal, or financial problems) whereby a validated diagnostic threshold identified cases of CUD (Humeniuk et al., 2008), and (2) prevalence of lifetime use whereby conditional probabilities of CUD were then calculated.

## Participants

The cohort ( $N=10,652$ ) completed a patient-report battery at a routine clinic visit between 01 January 2007 and 31 December 2014. The CNICS-affiliate sites were at Harvard University, Johns Hopkins University, University of Alabama-Birmingham, University of California-San Diego, University of California-San Francisco, University of North Carolina-Chapel Hill, and University of Washington. Patients deemed medically unstable, appearing intoxicated, evidencing significant cognitive impairment, or unable to speak English or Spanish did not complete the assessment.

## Analytic strategy

Initial review of distributional properties for patient demography prompted decisions to: (1) create age groups (i.e., 18–29, 30–39, 40–49, 50+ years), (2) transform race and ethnicity to a single “race/ethnicity” index (non-Hispanic White, non-Hispanic Black, Hispanic, and Other), and (3) retain transgender status and sexual orientation for descriptive analyses only, given low base rate (<1%) of affirmative response for the former and poor demographic representativeness for the latter. Prevalence of lifetime cannabis use and conditional probability of CUD among reported cannabis users were computed for the aggregate sample and by demographic indices.

Given the nested multisite design, a set of generalized estimating equations (GEEs) tested population-average models for a logistic outcome (CUD, no CUD) while accounting for the non-independence of observations among site enrollees (Hubbard et al., 2010). All models specified robust covariance structure, given the large aggregate sample size. Preliminary models revealed significant geographical variance in CUD rate among the CNICS sites, and historical variance in CUD rate among the four biennia (i.e., 2007–2008, 2009–2010, 2011–2012, 2013–2014) during which substance use disorder (SUD) assessment occurred. Thus, site and assessment biennia were included as covariates in a multivariate model. Likewise, preliminary models confirmed patient age group, gender, and race/ethnicity as bivariate CUD predictors, prompting their inclusion in the multivariate model.

## Results

### Sample demography

Age ranged from 18 to 84 years ( $M = 43.71$ ,  $SD = 10.62$ ), distributed as 12% 18–29-year-olds, 22% 30–39-year-olds, 36% 40–49-year-olds, and 30% 50+ year-olds. Gender was 83% male. Distribution of race/ethnicity was 49% Non-Hispanic White, 34% Non-Hispanic Black, 13% Hispanic, and 4% Other. Less than 1% affirmed transgender status. In the subsample ( $n = 1716$ ) self-reporting sexual orientation, 75% endorsed “Lesbian, Gay, or Homosexual”, 16% “Straight or Heterosexual”, 6% “Bisexual”, 2% “Something Else”, and 2% “Don’t Know”. Table 1 notes the corresponding subsample sizes.

### Prevalence of prior cannabis use and conditional probability of CUD

Table 1 also notes for the aggregate sample and each demographic index the prevalence of lifetime cannabis

**Table 1.** Sample demography and conditional probabilities of cannabis use disorder.

	Demographic subsample	Prior use of cannabis (%)	Conditional probability of CUD
Aggregate sample	10,652	6587 (62%)	49%
<i>Patient demography</i>			
Age group			
18–29 years	1254	810 (65%)	67%
30–39 years	2310	1465 (63%)	55%
40–49 years	3901	2448 (63%)	46%
50+ years	3187	1864 (59%)	42%
Gender			
Male	8882	5815 (66%)	50%
Female	1770	772 (44%)	42%
Race/ethnicity			
Non-Hispanic White			
Non-Hispanic White	5278	3844 (73%)	47%
Non-Hispanic Black			
Non-Hispanic Black	3632	1788 (49%)	52%
Hispanic			
Hispanic	1270	686 (54%)	54%
Other			
Other	472	269 (57%)	49%
Transgender			
Yes			
Yes	87	49 (56%)	47%
No			
No	10,565	6538 (62%)	49%
Sexual orientation ( <i>n</i> = 1716)			
Lesbian, Gay, or Homosexual			
Lesbian, Gay, or Homosexual	1280	1007 (79%)	48%
Straight or Heterosexual			
Straight or Heterosexual	278	175 (63%)	53%
Bisexual			
Bisexual	95	75 (79%)	56%
"Something Else"			
"Something Else"	34	29 (85%)	69%
"Don't Know"			
"Don't Know"	29	12 (41%)	67%

Sample consists of HIV+ persons enrolled in services and completing a patient-report assessment between 01 January 2007 and 31 December 2014; patient demography based on self-report; sexual orientation collected at three of the seven CNICS sites since 2012; "prior use of cannabis" based on patient-reporting on the ASSIST; cases of CUD identified via validated diagnostic threshold for ASSIST cannabis involvement scores.

use and corresponding conditional probability of CUD. A majority reported cannabis use, with conditional probability of CUD approaching 50%. Prior cannabis use was particularly prevalent among those endorsing "Lesbian, Gay, or Homosexual" and "Bisexual" orientations (79% apiece) as well as Non-Hispanic Whites (73%). Conditional probability of CUD was most concentrated among 18–29-year-olds (67%) and two non-specified

sexual orientation categories (i.e., "something else", "don't know") (67–69%).

### Multivariate prediction of CUDs

Overall model statistics revealed several effects. One was age group, Wald  $X^2(3) = 22.55$ ,  $p < .001$ , though with non-significant interactions with site and assessment biennia. Higher CUD rate was indicated among younger age groups relative to 50+ year-olds. Another effect was gender, Wald  $X^2(1) = 32.97$ ,  $p < .001$ , with gender  $\times$  site interaction, Wald  $X^2(1) = 6.42$ ,  $p < .05$ , and gender  $\times$  assessment biennia interaction, Wald  $X^2(1) = 4.40$ ,  $p < .05$ . The CUD rate was higher among males compared to females. Upon closer examination, the gender effect was substantive (>10% points) at three sites, modest (3–8% points) at three sites, and absent at the remaining site. Further, the gender effect was substantive (12–16% points) in 2007–2012 but more modest (8% points) in 2013–2014. There was also a race/ethnicity effect, Wald  $X^2(3) = 36.41$ ,  $p < .001$ , and race/ethnicity  $\times$  assessment biennia interaction, Wald  $X^2(3) = 13.27$ ,  $p < .01$ . Differences were modest between the "Other" referent group and Non-Hispanic Whites, Non-Hispanic Blacks, and Hispanics. Race/ethnicity variance was greatest in 2007–2008 (12–20% points), but attenuated in all subsequent biennia (4–8% points). Table 2 presents beta values with 95% confidence interval limits as well as corresponding standard errors, Wald  $X^2$  values, and odds-ratios with 95% confidence interval limits for the multivariate model.

### Discussion

In this multiregional CNICS cohort, 49% of lifetime cannabis users screened positive for CUD – a rate clearly exceeding the 12–36% range reported of past-year cannabis users in community sampling efforts (Gruca,

**Table 2.** Multivariate prediction of cannabis use disorder.

	Beta value	95% CI (lower, upper)	Standard error	Wald $X^2(1)$	Odds-ratio	95% CI (lower, upper)
Age group						
18–29 years	1.27	(.70, 1.83)	.29	19.44***	3.54	(2.02, 6.22)
30–39 years	.56	(.09, 1.02)	.24	5.38*	1.74	(1.09, 2.78)
40–49 years	.17	(–.25, .59)	.21	.62	1.18	(.78, 1.80)
50+ years (referent)	0				1.00	
Gender						
Male	1.54	(1.01, 2.06)	.27	32.97***	4.64	(2.75, 7.84)
Female (referent)	0				1.00	
Race/ethnicity						
Non-hispanic White						
Non-hispanic White	.63	(–.37, 1.63)	.51	1.53, ns	1.88	(.69, 5.11)
Non-hispanic Black						
Non-hispanic Black	–.48	(–1.49, .54)	.52	.85, ns	.62	(.22, 1.72)
Hispanic						
Hispanic	–.25	(–1.51, 1.01)	.64	.15, ns	.78	(.22, 2.76)
Other (referent)	0				1.00	

Notes: Based on aggregate sample of  $N = 10,652$  of HIV+ persons enrolled in services and completing a patient-report assessment between 01 January 2007 and 31 December 2014; patient demography based on self-report; cases of CUD identified via validated diagnostic threshold for ASSIST cannabis involvement scores; odds-ratios reflect likelihood of CUD relative to the indicated referent category; CNICS enrollment site and assessment biennia (i.e., 2007–2008, 2009–2010, 2011–2012, 2013–2014) included as covariates; \*\*\* $p < .001$ , \*\* $p < .01$ , \* $p < .05$ .

Agrawal, Krauss, Cavazos-Rehg, & Bierut, 2016; Hasin et al., 2016). Study findings include greater CUD prevalence among demographic subgroups of young adults and those with non-specified sexual orientation, with young adulthood and male gender emerging as multivariate model predictors of CUD. Findings concerning influences of patient age and gender on CUD prevalence also mirror those of community sampling efforts, whereas absence of clear race/ethnicity influences adds to an equivocal pattern of related results (Mimiaga et al., 2013; Wu et al., 2013). Based on sensitivity analyses, greater CUD prevalence among those with non-specified sexual orientation is consistent with morbidity findings in broader SUD literature (Lee et al., 2015; Mereish, Lee, Gamarel, Zaller, & Operario, 2015).

Study caveats bear mentioning. These include: (1) setting representativeness, given that these are all university-based sites, (2) selection bias, as data collection that excluded those appearing intoxicated, and (3) omission of demographic indicators (i.e., education, employment, income) that interact with substance abuse to influence HIV course and outcome (Oldenburg, Perez-Brumer, & Reisner, 2014). Influence of such caveats may be mitigated by the size and diversity of this CNICS cohort, secure procedures whereby patient-reports of cannabis-related behavior were gathered, and use of an established patient-report instrument with diagnostic threshold to identify cases of CUD for which there is strong, cross-cultural empirical validation.

## Conclusions

This study documents nearly half of cannabis-using HIV care enrollees as having CUD, identifies subgroups wherein CUD concentration is greater, and specifies CUD predictors among patient demographic indices. Study findings are timely, as balancing of the aforementioned pendulum that cannabis presents as both therapeutic agent and drug of abuse for PLWHA is continually challenged by progressive shifts in legislative policy (Pacula, Hunt, & Boustead, 2014). Such policies increase the need for CUD surveillance and intervention efforts in domestic HIV care settings. Given existing resource challenges faced by many HIV care settings, these findings may inform patient subgroups on whom surveillance and intervention efforts may focus.

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## Disclosure statement

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