

# Regular Marijuana Use is Associated with Poor Viral Suppression in HIV-Infected Adolescents and Young Adults

Amelia B. Thompson<sup>1,2,3</sup> · Scott E. Gillespie<sup>4</sup> · Jasper Hood<sup>2,3</sup> ·  
LaTeshia Thomas-Seaton<sup>3,5</sup> · Sophia A. Hussen<sup>3,6</sup> · Andres F. Camacho-Gonzalez<sup>2,3</sup>

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**Abstract** There is a paucity of data regarding the impact of drug use on HIV suppression and care retention among adolescents and young adults (AYAs). We recruited a clinic-based sample of HIV infected AYAs to assess the prevalence of self-reported drug use. Clinical data, including retention and viral suppression, were abstracted from the electronic medical record. Logistic regression was used to evaluate marijuana and illicit drug use associations and to identify other risk factors. Of 200 participants (mean age 21, 2.4 years, 69% horizontally infected), 46% reported current drug use, with marijuana as the most commonly used drug. Any illicit drug use (aOR 1.99, 95% CI 1.06–3.73,  $p = 0.032$ ) and lower education (aOR 2.11, 95% CI 1.09–4.08,  $p = 0.046$ ) were associated with poor viral suppression in multivariable analyses. Considering marijuana use only, an association with poor viral suppression was more pronounced (aOR 2.10, 95% CI 1.12–3.94,  $p = 0.021$ ). Drug use did not have a significant association with retention in care,

but AYAs who were retained in HIV care were less likely to have poorly suppressed HIV (aOR 0.22, 95% CI 0.10–0.49,  $p < 0.001$ ). High prevalence of marijuana use among HIV infected AYAs, and its association with poorly suppressed HIV, demonstrates the need for intervention strategies to decrease its consumption.

**Resumen** Existe una carencia de información sobre el impacto del consumo de drogas ilícitas en la obtención de una carga viral no detectable y en la retención en cuidado médico de adolescentes y adultos jóvenes (AAJ) con VIH. Este estudio reclutó AAJ VIH positivos para evaluar la prevalencia del uso de drogas ilícitas. Igualmente se analizó la asociación entre su consumo, u otros posibles factores de riesgo, con la presencia de una carga viral detectable y la falta de retención en cuidado médico. Datos clínicos incluyendo carga viral y retención en cuidado médico fueron abstraídos de la historia clínica. De 200 participantes (edad promedio  $21 \pm 2.4$  años, 69% infectados de manera horizontal), 46% reportaron uso actual de drogas ilícitas, siendo marihuana la droga más comúnmente utilizada. El resultado del análisis multivariable asoció el uso de cualquier droga ilícita (aOR = 1.99, 95% CI: 1.06-3.73,  $p = 0.032$ ), y el tener un bajo nivel educativo (aOR = 2.11, 95% IC: 1.09-4.08,  $p = 0.046$ ) con la presencia de una carga viral detectable. Al considerar únicamente el consumo de marihuana, la asociación con un control viral inadecuado fue más pronunciada (aOR = 2.10, 95% CI: 1.12-3.94,  $p = 0.021$ ). El uso de drogas ilícitas no mostró una asociación significativa con la retención en cuidado médico, pero los AAJ que se mantuvieron en cuidado médico presentaron una menor probabilidad de tener control inapropiado del VIH (aOR = 0.22, 95% CI: 0.10-0.49,  $p < 0.001$ ). La alta prevalencia del uso de marihuana entre AAJ VIH positivos, y su asociación con un control viral inadecuado, demuestran la necesidad de de-

✉ Amelia B. Thompson  
amelia.thompson@duke.edu

<sup>1</sup> Division of Pediatric Infectious Diseases, Department of Pediatrics, Duke University School of Medicine, 2 Genome Court, DUMC Box 103020, Durham, NC 27710, USA

<sup>2</sup> Division of Pediatric Infectious Diseases, Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA

<sup>3</sup> Ponce Family and Youth Clinic, Grady Infectious Diseases Program, Grady Health Systems, Atlanta, GA, USA

<sup>4</sup> Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA

<sup>5</sup> Children's Healthcare of Atlanta, Atlanta, GA, USA

<sup>6</sup> Hubert Department of Global Health, Emory University Rollins School of Public Health, Atlanta, GA, USA

sarrollar estrategias de intervención enfocadas a disminuir su consumo.

**Keywords** HIV · Adolescents · Retention · Drug use · Marijuana

## Introduction

Of the estimated 1.24 million persons living with HIV/AIDS in the United States at the end of 2013, roughly 84% of those diagnosed with HIV had been linked to care within 3 months of diagnosis [1]. However, only 55% achieved viral suppression, defined as a viral load (VL) < 200 copies/mL, at the most recent VL test [1]. In adolescents and young adults (AYAs) ages 13–24 years, 80% of those with an HIV diagnosis were linked to care within 3 months of diagnosis, but only 44% achieved viral suppression by year-end [1]. Some postulate that age-related discrepancies begin early in the care continuum due to low rates of voluntary HIV testing in the AYA population [2]. However, additional barriers to linkage to and retention in care such as stigma, housing instability, transportation difficulties, unemployment, mental health problems and substance abuse may account for the difficulties in achieving higher rates of viral suppression once an HIV diagnosis has been established [2–5]. Community-based interventions have been designed to reduce some of those barriers, with moderate success [3]. However, the challenges facing this population are multi-factorial, and given the increasing HIV transmission rates in AYAs, it is clear that many of those factors have yet to be fully elucidated and addressed [6].

Non-injection drug use (NIDU) is prevalent in the AYA community. The 2015 Youth Risk Behavior Surveillance Summary (YRBSS) reported a high prevalence of marijuana use in Black (50%) and Hispanic (46%) male students [7]. A large, multi-site cohort showed weekly or more frequent marijuana use in 28% of HIV infected AYAs with higher odds of substance abuse in young men who have sex with men (MSM) [8]. Of note, black MSM AYAs currently represent the demographic group with the highest risk of HIV acquisition in the United States with a 133% increase in HIV diagnoses from 2002 to 2011 [6]. Over the past few years, adult recreational marijuana use has become more socially acceptable and is swiftly gaining status for legal use within the United States and internationally [9, 10]. Recent studies have shown a decreased perception of harm due to marijuana use, with concurrent increase in the frequency of use in AYAs following its legalization for adult recreational use [11, 12]. Concerns have also been raised about increasingly available alternative methods of marijuana use, such as vaporizers and edibles, which may be perceived as less harmful by AYAs [13–15]. To our knowledge,

very few studies have attempted to elucidate the effect of NIDU on aspects of the continuum of care in HIV positive AYAs. Some have shown that AYA regular marijuana users demonstrate decreased knowledge of their HIV status and adherence to antiretroviral therapy (ART), but no significant relationship with the other metrics in the HIV continuum of care has been established [16–18]. Studies in adults have had conflicting results, with some showing lower ART adherence and increased missed clinic visits in marijuana-dependent HIV-infected persons, while others have not [19–26].

The purpose of this study is to assess the prevalence of illicit drug use in an HIV-infected AYA population and to determine the association of drug use with viral suppression and retention in HIV specific care. In addition, we hope to elucidate the AYAs own perception of the effects of drug use on their HIV management. We hypothesize that HIV infected AYAs will have a high prevalence of NIDU, and that its use is negatively associated with HIV viral suppression and retention in HIV specific health care services.

## Methods

### Participants

This single-center, cross-sectional study was conducted at the Ponce de Leon Family and Youth Clinic (PFYC) in Atlanta, GA. We enrolled AYAs between 13 and 24 years of age with HIV-1 infection, as documented in the medical record, who had been established in care at least 6 months prior to enrollment from October 2013 to February 2016. They were consented for participation immediately before or after their clinic visits after determining that they would have sufficient time to complete the survey. In order to be consented for the study, they had to have previous knowledge and understanding of their HIV diagnosis. Informed consent/assent was obtained from all individual participants included in the study and/or their guardians. Individuals were excluded if they could not understand spoken and written English or were unwilling to participate in the study. Ethical approval for this study was obtained from the Emory University institutional review board and Grady Memorial Hospital research oversight committee.

### Data Collection

All participants self-administered a one-time, paper survey. Demographic variables collected included age, race, education level and sexual orientation. Drug use patterns, including perceived impact on medical care, were assessed using the Adolescent Alcohol and Drug Involvement Scale (AADIS) to determine if participants would warrant a full substance abuse assessment [27]. For the purposes of this

study, drug users were defined as having used marijuana, cocaine, heroin, methamphetamines, inhalants, hallucinogens, ecstasy or any other illicit drug once or more in the 6 months prior to enrollment in the study. Alcohol users were defined similarly. We also collected data on other relevant covariates including psychiatric disease diagnosed by the clinic psychologist and defined using the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria, housing stability which was defined as secure and routine access to reasonable quality housing [28], presence of a social support system which was defined as at least one friend or family member who is aware of the HIV diagnosis and provides mental and emotional support, HIV transmission mode and source of drugs or alcohol. CD4 + T cell counts and HIV RNA VL at the time of enrollment and over the 6 months prior to enrollment were abstracted from medical records.

### Outcome Variables

The primary outcomes of interest were viral suppression and retention in care. HIV suppression was defined as maintaining a mean VL < 200 copies/ml over the 6-month period prior to completion of the survey to account for potential viral blips. Retention in HIV medical care was based on scheduled clinic visits with medical providers who have prescribing privileges. Walk-in visits, subspecialty visits or supportive service visits were not included. Additionally, visits that were canceled in advance by the patient or provider were not included. Retention in care was defined as attending 90% or more of scheduled clinic visits in the 6 months prior to completion of the survey [29].

### Statistical Analysis

Descriptive statistics and visual plots were used to evaluate distributions of clinical outcome variables among drug use versus no drug use participants. Statistical comparisons between usage groups were made using two-sample t-tests and Chi square tests of independence, or their non-parametric equivalents (Kolmogorov–Smirnov tests and Fisher's exact tests). Univariate and multivariate logistic regression was conducted to examine the associations between drug use and the outcomes of concern, viral suppression and retention in care, while controlling for potential confounding variables such as education levels, transportation, housing stability, sources of drug acquisition and psychiatric disorders. Similar analyses were performed for alcohol use. Multivariable analysis was guided by univariable results, and final model selections were based upon the strongest predictors. Model fits were assessed via receiver operating characteristic curve (ROC) and Akaike Information Criterion (AIC) statistics. Statistical significance was assessed at the 0.05 significance

level, and all statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

## Results

### Prevalence of Drug Use

A total of 244 persons met eligibility criteria; and 200 (82%) of these consented for study participation. Among the 200 participants, the mean age was 21 years (standard deviation (SD) 2.4 years),  $p < 0.001$ , 74% were male, 93% identified as Black or African American and 31% had perinatally acquired HIV. Sixty two percent of the participants identified as homosexual or bisexual, 59% had received some high school education, and an additional 41% were enrolled in or had completed college, graduate school or a trade school (Table 1). According to the AADIS scores, 113 (56.5%) of our cohort warranted a full substance abuse assessment. Using our study definition, forty-six percent of participants reported current illicit drug use, with marijuana (45.5%) being the most commonly used, followed by powder cocaine (3.5%). Sixty-four percent reported alcohol use. Six percent reported using two or more illicit drugs. There was no report of phencyclidine (PCP) or heroin use in this group (Fig. 1). Of the drug users, there was a significant predominance of males (84.8%), and the majority were homosexual or bisexual (80.4%). Additionally, the drug user group was predominantly comprised of participants who had acquired HIV horizontally (82.6%) (Table 1). There was no statistically significant difference in demographic characteristics at enrollment such as education level, transportation type, housing stability and the presence of social support, or in disease characteristics such as VL, CD4 count and the presence of a mental disorder between drug users and non-drug-users (Table 1).

### Viral Suppression

Univariate analysis demonstrated that participants who reported illicit drug use were more likely to have poor HIV suppression (OR 2.03, 95% CI 1.15–3.58,  $p = 0.014$ ). However, alcohol use was not significantly associated with viral suppression (OR 1.05, 95% CI 0.59–1.87,  $p = 0.864$ ). Demographic factors such as sexual orientation and age were not significantly associated with poor viral suppression. The source of alcohol or drugs was also not significantly associated with poorly suppressed HIV. Lower educational attainment was marginally associated with poorly suppressed HIV (High School or Less vs. College or More: OR 1.71, 95% CI 0.94–3.12,  $p = 0.08$ ) (Table 2). Type of transportation, unstable housing and social support were not associated with poorly suppressed HIV. In

**Table 1** HIV-infected adolescents and young adults in Atlanta, GA. Baseline demographic and HIV disease characteristics stratified by drug use status

Characteristic	Patient drug use status				Test statistic	p value <sup>a</sup>
	Drug users (N = 92)		Non-drug users (N = 108)			
	Mean, Median, or n	SD, IQR, or %	Mean, Median, or n	SD, IQR, or %		
Male sex	78	(84.8%)	69	(63.9%)	$\chi^2(1) = 11.1$	< 0.001
Age of participant	21.6	(1.7)	20.5	(2.7)	$t(184) = -3.3$	0.001
Black race (N = 199)	83	(91.2%)	102	(94.4%)	$\chi^2(1) = 0.79$	0.374
Sexual orientation						
Heterosexual	18	(19.6%)	59	(54.6%)	$\chi^2(2) = 28.1$	< 0.001
Gay/Lesbian/Questioning	64	(69.6%)	37	(34.3%)		
Bisexual	10	(10.9%)	12	(11.1%)		
Education (N = 196)						
High school or less	52	(57.8%)	63	(59.4%)	TP = 0.01	0.265
Other	36	(40%)	36	(34%)		
College or more	2	(2.2%)	7	(6.6%)		
Any mental disorder	53	(57.6%)	55	(50.9%)	$\chi^2(1) = 0.89$	0.345
Transportation (N = 34)						
Private	2	(14.3%)	5	(25%)	TP = 0.26	0.672
Public	12	(85.7%)	15	(75%)		
Stable housing (N = 199)	76	(82.6%)	97	(90.7%)	$\chi^2(1) = 2.8$	0.093
Social support, current	77	(83.7%)	94	(87%)	$\chi^2(1) = 0.45$	0.504
Horizontally HIV-infected	76	(82.6%)	62	(57.4%)	$\chi^2(1) = 14.8$	< 0.001
CD4 count (cells/mm <sup>3</sup> )						
At enrollment	425	(256.5–578)	437.5	(312.5–595.5)	S = 8,908.5	0.410
Mean over previous 6 months	414.5	(260–558.5)	442.5	(298.5–588)	S = 8,739.5	0.216
HIV-1 RNA VL (copies/mL)						
At enrollment	40	(40–126)	40	(40–50.5)	D = 0.15	0.191
Mean over previous 6 months	827	(40–18,861)	40	(40–3,818.5)	D = 0.22	0.021

RNA ribonucleic acid, SD standard deviation, IQR interquartile range

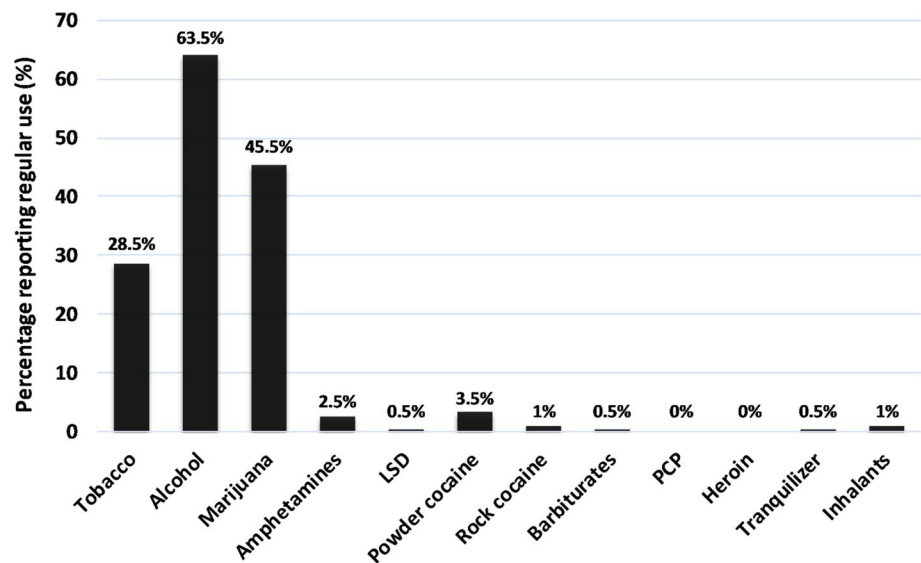
<sup>a</sup>P Value by  $\chi^2$  test for categorical measures and two-sample t-tests or non-parametric equivalents (Wilcoxon rank-sum or Kolmogorov–Smirnov) for continuous measures, test statistics:  $\chi^2(DF)$  Chi square,  $t(DF)$  t-test, TP Fisher's exact test table probability, S Wilcoxon rank-sum test, D Kolmogorov–Smirnov test difference

multivariate analysis, illicit drug use was significantly associated with poor HIV suppression (aOR 1.99, 95% CI 1.06–3.73,  $p = 0.032$ ), as was lower educational attainment (aOR 2.11, 95% CI 1.09–4.08,  $p = 0.046$ ). Race and retention in care were also significant factors (aOR 4.57, 95% CI 1.11–18.84,  $p = 0.036$  and aOR 0.22, 95% CI 0.10–0.49,  $p < 0.001$ , respectively), and any mental disorder had a marginal significance (aOR 1.80, 95% CI 0.96–3.37,  $p = 0.069$ ). Interactions terms between drug use, any mental disorder and viral suppression were further considered and found to be insignificant. Utilizing these same covariates, secondary multivariate analyses found marijuana use alone was significantly associated with a lack of viral suppression (aOR 2.10, 95% CI 1.12–3.94,  $p = 0.021$ ) (Table 2).

## Retention in Care

Of all enrolled participants, 22% of drug users and 27% of non-drug users met the definition of retention in care. As stated, AYAs who were retained in HIV care were more likely to be virally suppressed (aOR 0.22, 95% CI 0.10–0.49,  $p < 0.001$ ) (Table 2), but interestingly, drug use was not significantly associated with retention in HIV care (OR 1.32, 95% CI 0.69–2.54,  $p = 0.403$ ). Similarly, alcohol use was not associated with retention in care (OR 0.80, 95% CI 0.40–1.58,  $p = 0.520$ ) (Table 3). Furthermore, using two or more drugs or marijuana only was not significantly associated with retention in care. Participants who did not have stable housing were more likely to have poor retention in care (OR 2.78, 95% CI 0.80–9.69,  $p = 0.109$ ). Those who

**Fig. 1** HIV-infected adolescents and young adults in Atlanta, GA. Drug use frequency stratified by type. *LSD* lysergic acid diethylamide, *PCP* phencyclidine



had a support system were less likely to have poor retention in care (OR 0.45, 95% CI 0.15–1.36,  $p = 0.156$ ), though neither measure reached statistical significance (Table 3).

### Self-Evaluation

Participants were asked to report any perceived effects of drugs and alcohol use on their HIV care. Fourteen percent reported missing their HIV medications due to alcohol or drug use at least once per week. Ten percent reported missing HIV specific appointments due to alcohol or drug use at least once in the last 6 months. When asked about sexual intercourse, 33% reported having sex under the influence of drugs or alcohol at least once in the last month. Seven (3.5%) participants reported that they always had sex while intoxicated. Participants reported that they started to drink or use drugs because they liked the feeling they got while intoxicated (33%), were bored (29%), or were stressed or tense (29%).

Initiation of drug and alcohol use began for most participants after age fifteen (56%), but a small percentage (2%) reported using drugs or alcohol before age ten. Participants who began using drugs and alcohol before age 15 years were more likely to have poor viral suppression and were less likely to be retained in care than those who began at or after age 15 years (OR 1.79, 95% CI 0.86–3.74,  $p = 0.119$  and OR 0.61, 95% CI 0.24–1.52,  $p = 0.287$  respectively), but neither of these measures were statistically significant. Nearly half of participants (49%) started using drugs and alcohol due to curiosity, while 13% reported that they tried those substances initially to escape their problems. The majority (54%) of participants purchased drugs or alcohol themselves, 22% obtained them from friends and 5% obtained drugs or alcohol from parents or relatives. Twelve percent of

participants use drugs or alcohol with their parents or adult relatives, but most, 60%, used drugs or alcohol with friends or relatives their own age.

Most participants (62%) denied any long-term effects of drugs or alcohol on their lives, but a few reported that drug or alcohol use caused them to lose friends (5%), resulted in punishment at home (7%), facilitated a fight or property destruction (3%) or resulted in an accident, injury or arrest (5%). A large proportion (49%) thought that their drug and alcohol use was normal for their age, although 26 (13%) reported that they had been advised to cut down on or get professional help to manage their alcohol or drug use. Univariate analyses modeling short and long-term effects of drug and alcohol use did not reveal any significant associations with viral suppression or retention in care. However, those who had previously overdosed on drugs or alcohol were more likely to have poor viral suppression (OR 4.42, 95% CI 0.89–21.82,  $p = 0.068$ ).

### Discussion

This study is one of only a few to elucidate the prevalence of illicit drug use and the associations with aspects of the continuum of care in a cohort of horizontally and perinatally HIV infected AYA who are enrolled in care. Our findings suggest that frequent marijuana use and lower educational attainment is associated with poor HIV viral suppression, but they are not associated with retention in HIV specific care. Furthermore, isolated alcohol use is not significantly associated with viral suppression or retention in care. Comorbid psychological disorders, housing stability and ease of access to transportation did not have a significant impact on these outcomes in our patient population. Early initiation of

**Table 2** HIV-infected adolescents and young adults in Atlanta, GA. Unadjusted and adjusted logistic regression models for poorly suppressed HIV

Characteristic	Unadjusted		Adjusted <sup>a</sup> —illicit drugs		Adjusted <sup>a</sup> —marijuana	
	OR (95% CI)	p value	aOR (95% CI)	p value	aOR (95% CI)	p value
Age (years)	1.05 (0.93–1.18)	0.410				
Horizontal transmission	1.40 (0.76–2.56)	0.281				
Race/ethnicity						
African American/Black	3.33 (0.90–12.31)	0.072	4.57 (1.11–18.84)	0.036*	4.63 (1.12–19.15)	0.034*
Other	Reference		Reference		Reference	
Sexual orientation						
Heterosexual	1.41 (0.54–3.68)	0.719				
Gay/Lesbian/Questioning	1.16 (0.46–2.96)					
Bisexual	Reference					
Education						
High School or Less	1.71 (0.94–3.12)	0.080	2.11 (1.09–4.08)	0.046*	2.10 (1.08–4.05)	0.048*
Other	0.45 (0.09–2.32)		0.60 (0.11–3.47)		0.60 (0.11–3.48)	
College or more	Reference		Reference		Reference	
Any illicit drug use (excluding tobacco or alcohol)	2.03 (1.15–3.58)	0.014*	1.99 (1.06–3.73)	0.032*		
Marijuana only	2.12 (1.20–3.73)	0.010*			2.10 (1.12–3.94)	0.021*
Alcohol only	1.05 (0.59–1.87)	0.864				
Obtained alcohol or drugs from:						
Parents	0.78 (0.21–2.86)	0.710				
Siblings	0.89 (0.19–4.07)	0.877				
Home	0.79 (0.13–4.81)	0.795				
Friends	0.92 (0.47–1.82)	0.819				
Self	1.52 (0.86–2.66)	0.149				
> 90% visit attendance	0.25 (0.12–0.53)	<0.001*	0.22 (0.10–0.49)	<0.001*	0.22 (0.10–0.48)	<0.001*
Any mental disorder	1.54 (0.88–2.71)	0.131	1.80 (0.96–3.37)	0.069	1.81 (0.96–3.40)	0.066
Transportation						
Private	1.25 (0.20–7.75)	0.811				
Public	Reference					
Unstable housing, current	1.46 (0.64–3.33)	0.375				
Social support, current	1.75 (0.77–3.98)	0.182				

Unsuppressed HIV is defined as mean VL copies > 200 within the 6 months prior to study enrollment

Multivariable ROCs each = 0.74; OR odds ratio, aOR adjusted odds ratio

<sup>a</sup>Adjusted model includes all covariates with univariate *P* values < 0.1

drug and alcohol use may be a risk factor for poor viral suppression and poor retention in care, however, our study did not demonstrate this with statistical significance. The high rates of substance use, particularly marijuana, in this cohort suggests the need for implementation of routine screening measures for substance abuse in these health care settings.

Our results differed slightly from those identified in the Adolescent Trials Network cohort. In their multi-center cohort, they also demonstrated a high prevalence of drug use in AYAs ages 12 to 26 years [8]. However, their rates of regular marijuana use were significantly lower than our cohort of primarily black AYA MSM (27.5% vs. 45.5%). Even after adjusting to ensure congruent definitions of

regular marijuana use (weekly or more), our rates remained higher at 36.1%. Notably, our cohorts differed in some basic demographic characteristics: 51% of their cohort was 21 years or older, while the same age range comprised 65% of our cohort. Our cohort was primarily black or African American (92.5%) compared with their 64%. Finally, the composition of gay/lesbian/questioning or bisexual (61.5%) participants was higher in our study, as compared with their 51.4% [8]. These differences may explain why an association between viral suppression and marijuana use was not detected in their study. The uConnect cohort in Chicago of young black MSM ages 16 to 29 years displayed more demographic similarities to our study participants. Indeed,

**Table 3** HIV-infected adolescents and young adults in Atlanta, GA. Unadjusted regression models for poor retention in care

Characteristic	Unadjusted	
	OR (95% CI)	<i>p</i> value
Age (years)	1.00 (0.87–1.15)	0.999
Transmission		
Horizontal	1.11 (0.56–2.21)	0.773
Race/ethnicity		
African American/Black	1.84 (0.58–5.77)	0.299
Other	Reference	
Sexual orientation		
Heterosexual	0.84 (0.27–2.57)	0.924
Gay/Lesbian/Questioning	0.94 (0.32–2.83)	
Bisexual	Reference	
Education		
High school or less	0.65 (0.32–1.34)	0.212
Other	0.30 (0.07–1.27)	
College or more	Reference	
Any illicit drug use (excluding tobacco or alcohol)	1.32 (0.69–2.54)	0.403
Two or more drugs	3.40 (0.43–27.26)	0.249
Marijuana only	1.29 (0.67–2.47)	0.449
Alcohol only	0.80 (0.40–1.58)	0.520
Obtained alcohol or drugs from		
Parents	0.75 (0.19–3.02)	0.686
Siblings	NA	
Home	0.48 (0.08–2.96)	0.429
Friends	1.30 (0.58–2.95)	0.526
Self	1.29 (0.68–2.46)	0.439
Any mental disorder	0.94 (0.49–1.80)	0.859
Unstable housing, current	2.78 (0.80–9.69)	0.109
Social support, current	0.45 (0.15–1.36)	0.156

Poor retention in care is defined as < 90% attendance at scheduled clinic visits within the 6 months prior to study enrollment

OR odds ratio, aOR adjusted odds ratio

their rates of marijuana use were more consistent with our group, with intermittent use (any use up to multiple times per week) at 41.1% and heavy use (at least once per day) at 32% [17]. They, however, limited their analysis to measuring the association of intermittent versus heavy marijuana use on the various aspects of the care continuum, without comparing marijuana users to non-users. As a result, our study is the only one to our knowledge that provides such an analysis in a cohort that reflects the current HIV epidemic in AYAs in the United States. The association that we have identified between illicit drug use, particularly marijuana, and poorly suppressed HIV suggests that this may be an important barrier to bridging the gaps in the care continuum for AYAs. In the setting of increased frequency of marijuana use and decreased perception of harm in AYAs, it is imperative that

screening for marijuana and other drug use should routinely be implemented in clinics where HIV-infected AYAs receive their care [8, 11, 12, 30].

Notably, our cohort of AYAs used marijuana more than twice as much as they used tobacco. Other drugs, such as methamphetamines and cocaine, were used much less frequently. This is in contrast to other cohorts where daily tobacco use was more frequent than marijuana use and weekly or intermittent use of marijuana and tobacco were comparable [8]. Longitudinal studies have shown an association between early-onset regular marijuana use and neurocognitive decline as well as poor short-term and working memory [31]. These neurocognitive effects of marijuana use, therefore, may contribute to the forgetfulness that some adolescents cite as their primary reason for non-adherence to treatment for their chronic medical conditions [32, 33]. On the community level, social and structural factors may interact with illicit drug use to negatively affect viral suppression and care retention. Exposure to violence, a factor that we did not evaluate in this study, has been associated with increased marijuana use and decreased adherence to antiretroviral medications in a cohort of HIV positive young adult, black MSM [34]. Settings that exhibit a high threat of community violence demonstrate the real and perceived challenges to HIV positive persons in maintaining their adherence to HIV specific medications and retention in care [35].

There are a variety of negative implications of regular marijuana use in HIV positive AYAs. Researchers have shown that AYAs using marijuana showed impaired inhibitory processes compared with adults who used the same drug [36]. Given that adult black MSMs have demonstrated frequent marijuana use (> 60%), particularly as a sex-drug (in > 20%) with associated condomless sex, AYAs are at high risk of unprotected intercourse while under the influence [34, 37]. Additionally, black AYA MSMs with heavy marijuana use are more likely to be unaware of their HIV status than those who never used marijuana [17]. Interestingly, one-third of our participants reported recently having sexual intercourse under the influence of drugs or alcohol. These findings suggest an increased risk of HIV transmission within these high risk vulnerable populations would be associated with regular marijuana use. Self-perceived effects of drug and alcohol use, however, were not significantly associated with viral suppression or retention in care.

Substance abuse interventions targeting the AYA population must address attitudes toward the drug and perception of their health consequences. The United States Food and Drug Administration (FDA) *The Real Cost* campaign on tobacco use has successfully increased adolescents' perceptions of the serious health consequences of cigarette smoking and decreased the rates of smoking initiation in this population [38, 39]. There are challenges to replicating such a campaign for marijuana use since the known harmful effects of

marijuana use may be less provocative. Therefore, interventions to reduce marijuana use will likely remain on a clinic- or neighborhood-level scale.

The role of education is less clear. Our study demonstrated an association between lower educational attainment and poor viral suppression, but not retention in care. Low health literacy has been associated with lower educational attainment, but is also seen in highly educated populations [40]. Studies have shown that adults with lower health literacy are more likely to have detectable viral loads and poorer medication adherence than their peers who exhibit higher levels of health literacy [41, 42]. This discrepancy has been particularly visible in African Americans living in the southern United States [43]. Studies have not replicated these findings in adolescents. Health literacy, measured by the Test of Functional Health Literacy in Adults (TOFHLA), did not predict self-reported medication adherence in a convenience sample of HIV-infected adolescents. However, those with lower literacy skills, defined as below-grade-level reading according to the Rapid Estimate of Adult Literacy in Medicine-teen (REALM-teen), had lower medication adherence [44]. In a larger, multi-site cohort of HIV-infected adolescents, health literacy was not significantly associated with viral load or medication adherence when adjusting for educational level or age [45]. Further studies to evaluate the associations between education, health literacy and the HIV care continuum in the HIV-infected AYA population are warranted.

This study's findings must be interpreted in the context of several limitations. Prior to approaching a potential participant, their health care provider was asked if there would be sufficient time to administer the survey. In approximately fifteen cases, the subject could not be approached during that particular clinic visit due to the potential negative impact on clinic flow, but remained eligible for study consent in the future. Additionally, in our survey, we used standard terminology for the most frequently used illicit drugs, as well as more common vernacular. However, the drug names were not exhaustive and few participants utilized the "other" option that would allow them to indicate drug use that was not listed on the survey. The data were also self-reported and as such were subject to recall and social desirability biases despite reassurance that each questionnaire was confidential and without identifiers. Finally, the sample was taken from AYAs who attended an HIV specific clinic and so would not be generalizable to the broader population of HIV positive AYAs, who either have not yet been diagnosed or who have been diagnosed but opt out of HIV specific care.

Despite these limitations, our study does enhance current knowledge about this population and the correlates of drug use and the HIV care continuum. Given the lack of association in our study between social support, stable housing and psychological disorders with the outcomes of

concern, further research is required to determine additional factors that might contribute to the effects of marijuana use on poor viral suppression. Previous studies have posited an interplay between cannabinoids and the immune response to HIV and other infections but results have varied [46]. Such an interaction might establish biological factors, in addition to behavioral associations, that might explain the results we have found in our study.

## Conclusions

In summary, HIV-infected AYAs demonstrated substantial rates of marijuana use, and this was associated with an increased risk of poorly suppressed HIV. Given the increasing acceptability of marijuana for medical and recreational use, this population is at substantial risk and clinicians should provide routine screening for drug abuse in their HIV clinics and provide resources for intervention where appropriate.

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## Compliance with Ethical Standards

**Conflicts of interest** Andres F. Camacho-Gonzalez has received research support from Gilead Sciences (Notice of Award: 380-37362) and Janssen Pharmaceuticals (Notice of Award: 39688).

**Ethical Approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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