Title

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Journal

AIDS, 37(10)

ISSN

0269-9370

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Publication Date

2023-08-01

DOI

10.1097/qad.0000000000003625

Peer reviewed

HHS Public Access

Author manuscript

AIDS. Author manuscript; available in PMC 2024 August 01.

Published in final edited form as:

AIDS. 2023 August 01; 37(10): 1555–1564. doi:10.1097/QAD.0000000000003625.

Association of marijuana, tobacco and alcohol use with estimated glomerular filtration rate in women living with HIV and women without HIV

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Conflicts of interest

There are no conflicts of interest.

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Abstract

Objective: Marijuana, tobacco and alcohol use are prevalent among people with HIV and may adversely affect kidney function in this population. We determined the association of use of these substances with estimated glomerular filtration rate (eGFR) among women with HIV (WWH) and women without HIV.

Design: We undertook a repeated measures study of 1043 WWH and 469 women without HIV within the United States Women's Interagency HIV Study, a multicenter, prospective cohort of HIV-seropositive and HIV-seronegative women.

Methods: We quantified substance exposures using semi-annual questionnaires. Using pooled eGFR data from 2009 to 2019, we used linear regression models with multivariable generalized estimating equations to ascertain associations between current and cumulative substance use exposures with eGFR, adjusting for sociodemographics, chronic kidney disease risk factors and HIV-related factors.

Results: Marijuana use of 1–14 days/month versus 0 days/month was associated with 3.34 ml/min per 1.73 m^2 [95% confidence interval (CI) −6.63, −0.06] lower eGFR and marijuana use of >0.02–1.6 marijuana-years versus 0–0.2 marijuana-years was associated with 3.61 ml/min per 1.73 m^2 (95% CI −5.97, −1.24) lower eGFR. Tobacco use was not independently associated with eGFR. Alcohol use of seven or more drinks/week versus no drinks/week was associated with 5.41 ml/min per 1.73 m^2 (95% CI 2.34, 8.48) higher eGFR and alcohol use of >0.7–4.27 drink-years and >4.27 drink-years versus 0–0.7 drink-years were associated with 2.85 ml/min per 1.73 m^2 (95% CI 0.55, 5.15) and 2.26 ml/min per 1.73 m^2 (95% CI 0.33, 4.20) higher eGFR, respectively.

Conclusion: Among a large cohort of WWH and women without HIV, marijuana use was associated with a lower eGFR while alcohol use was associated with a higher eGFR.

Keywords

alcohol; estimated glomerular filtration rate; HIV; kidney; marijuana; tobacco; women

Introduction

Kidney disease strongly contributes to excess morbidity and mortality among people with HIV (PWH) [1]. Compared to the general population, PWH are at increased risk for chronic kidney disease (CKD). Studies have reported a two- to three-fold higher prevalence of CKD among PWH compared to match persons without HIV in the United States [2]. Contributing factors to CKD among PWH include direct and indirect effects of HIV, antiretroviral therapy (ART) nephrotoxicity and comorbidities including diabetes and hypertension [3]. Though several studies have implicated behavioral risk factors such as substance use in the development of CKD in the general population, whether these potentially modifiable risk factors negatively impact kidney function among PWH is unknown.

Data from previous studies have indicated a higher prevalence of marijuana, tobacco and alcohol use among PWH compared to persons without HIV [4,5]. In the general population,

substance use is associated with early onset of age-related diseases including CKD [6]. PWH develop comorbidities 10–20 years earlier compared to persons without HIV, and substance use may contribute to accelerated aging in this population [7,8]. Proposed mechanisms by which substance use promotes aging include increased oxidative stress, production of reactive oxygen species and chronic excess inflammation leading to cellular damage [9]. Substance abuse is also associated with poor sleep quality, poor nutrition and insufficient exercise which contribute to aging [10].

Though findings from studies conducted in the general population have indicated protective effects of moderate alcohol consumption and harmful effects of tobacco use on kidney function, their effects on kidney function in PWH have not been investigated [10–14]. In recent years, tobacco use has declined in the United States, but marijuana use has steadily increased, particularly among young adults [15]. The kidneys express cannabinoid receptors that may have beneficial or harmful effects when activated [16]. Limited data suggest that marijuana does not have negative effects on kidney function in the general population; however, PWH were not included in these studies [17,18]. Many recreational manufacturers now produce high potency marijuana that contains increased concentrations of tetrahydrocannabinol (THC), posing greater potential for addiction and more significant health risks [19].

Women account for 25% of adults with HIV in the United States and >50% of adults with HIV worldwide [20,21] yet are underrepresented in HIV and substance use research [22,23]. Recent data indicate greater than two-fold higher prevalence of tobacco and marijuana use among WWH compared to women without HIV [24]. We therefore investigated the association between self-reported marijuana, tobacco and alcohol use and estimated glomerular filtration rate (eGFR) in WWH and women without HIV in a repeated measures cross-sectional study. We explored acute and chronic effects of these substances on kidney function by evaluating associations between current and cumulative use and eGFR.

Methods

Study setting and population

The Women's Interagency HIV Study (WIHS) was a prospective, multicenter cohort study of WWH and women at historical risk for HIV in the United States [25]. Eligibility criteria and follow-up procedures for WIHS have been previously described [26,27]. Briefly, HIV-seropositive and HIV-seronegative women with similar demographic and behavioral characteristics were enrolled at six sites in Brooklyn, New York; the Bronx/Manhattan, New York; Washington, DC; Chicago, Illinois; San Francisco, California; and, Los Angeles, California. Data were collected using structured interviews and standardized physical and laboratory assessments, with study visits occurring every six months. WIHS data collection instruments are available at https://statepi.jhsph.edu/wihs/wordpress/. The institutional review boards at each study site approved the WIHS study protocol, and all participants provided written informed consent.

The present analyses included participants from 1994—1995 and 2001—2002 enrollment waves. The Los Angeles site closed in 2010 and was excluded from this analysis due to

inability to obtain sufficient eGFR data (n = 800). The *index date* was defined as the first study visit between October 2009 and September 2010 when serum creatinine and eGFR data were available and included WWH and women without HIV who were active in the study from April 2000 to September 2019 (Figure S1, Supplemental Digital Content, http://links.lww.com/QAD/C907). Participants with end-stage kidney disease or an eGFR <15 ml/min per 1.73 m^2 at the index visit (n = 63), those missing serum creatinine measurement at the index visit (n = 98), and those who HIV seroconverted during follow up (n = 26) were excluded, resulting in a sample size of 1512 participants.

Exposure variables

Marijuana, tobacco and alcohol use were self-reported at each semi-annual study visit. We used repeated measures of use of these substances between April 2000 to September 2019 to compute cumulative use (calculated from the preceding 10 years prior to each current visit, repeated at every visit). Current use was assessed from the index visit (October 2009–September 2010) until September 2019. Marijuana use was assessed with the question: 'Since your last study visit, have you used marijuana or hash?' Participants responding with a 'yes' were then asked 'On average, how often have you used marijuana or hash since your last study visit?' with the following response options: 'less than once a month', 'at least once a month, but less than once a week', 'once a week', '2–3 times a week', '4–6 times a week', 'once a day', and 'more than once a day'. Current marijuana use was categorized as: 0, 1–14, and more than 14 days per month. Data on marijuana use prior to enrollment were not collected. We calculated 10-year cumulative marijuana use based on the number of days used per month. This was converted to marijuana-years categorized by tertiles as 0–0.02, >0.02–1.6, >1.6 (1 marijuana-year equals 365 days of marijuana use) [18].

Current, former, or no tobacco use and quantity of use was ascertained according to the questions, 'Have you smoked more than 100 cigarettes in your lifetime?' and 'Do you currently smoke cigarettes?' and if you do smoke, 'How many cigarettes do you smoke on average each day?'. Lifetime pack-years was categorized as 0, 1–10 and more than 10 pack-years at enrollment and each follow up study visit. Participants were asked if they drank one or more alcoholic drinks per week and amount of alcohol use during the previous six months. Current alcohol use was categorized as none (0), mild-moderate (1–7) or heavy (>7 drinks per week). Data on alcohol use prior to enrollment in WIHS were not collected. We calculated 10-year cumulative alcohol use and reported use in drink-years (1 drink-year equals 365 drinks), categorized by tertiles as 0–0.7, >0.7–4.27, >4.27.

Outcome variable

Serum creatinine was measured at each visit using local laboratories for each study site. We used the 2009 CKD Epidemiology Consortium (CKD-EPI) equation without the race coefficient to calculate the eGFR from serum creatinine [28] and calculated pooled eGFR estimates using each available measure from the index date to September 2019. The creatinine assay was not standardized across WIHS sites until 2020. To account for variations in creatinine measurement due to site specific differences in creatinine assays, we incorporated site, visit and site × visit interaction terms into our models.

Covariates

Demographics, CKD risk factors, and HIV-related characteristics were assessed at each visit. Covariates at each person-visit were selected based upon known association with CKD or if statistically significant in unadjusted analyses. These included age, self-identified race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Other), educational attainment (less than high school, high school or higher), WIHS study site, enrollment cohort, diabetes mellitus (defined by fasting glucose ≥ 126 mg/dl, self-reported diabetes, self-reported diabetes medication use, or glycated hemoglobin ≥ 6.5%), hypertension (defined as systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mmHg, or self-reported history of hypertension and/or antihypertensive medication use). HIV covariates included $CD4^+$ T-cell count (<200, 200–349, 350–499, ≥500 cells/mm^3), plasma HIV RNA viral load (undetectable versus detectable) and cumulative tenofovir disoproxil fumarate (TDF) exposure. Plasma HIV RNA was classified as undetectable by a threshold ranging from 20 to 48 copies/ml. ART use was assessed via self-report and was binarized at each visit [29]. Dolutegravir (DTG) reduces tubular secretion of creatinine, leading to a reduction in creatinine clearance of 10–15 ml/min [30,31]. No WWH were on DGTat the index date but by 2016, the prevalence of DTG use among WWH increased to 36%. To account for differences in eGFR attributed to DTG use, we created a three-level HIV/DTG variable denoted as HIV-negative, HIV-positive/not using DTG at study visit and HIV-positive/using DTG at study visit. Rilpivirine and cobicistat also reduce tubular secretion of creatinine but their prevalence was much lower compared to DTG and therefore they were not included in our models.

Statistical analysis

We compared the characteristics of women by HIV serostatus at the index date using chi-square tests for categorical variables and Wilcoxon rank-sum tests for continuous variables. Linear regression models using generalized estimating equations (GEE) with an independence working correlation were conducted to estimate associations separately between each substance exposure (marijuana, tobacco, and alcohol) and eGFR. [32,33] Models were employed using two approaches: (1) fitting the most recent exposure and (2) fitting the 10-year cumulative exposure for marijuana and alcohol use and lifetime use for tobacco. When calculating 10-year cumulative substance use exposures, we allowed up to six visits to be missing and imputed the values for the missing visits as the mean of the nonmissing visits. To account for participants with fewer study visits, we performed sensitivity analyses using inverse probability weighting (IPW). Confounders were selected *a priori* based on prior literature and variables with a statistically significant association with eGFR in bivariate analyses. We adjusted for age, race/ethnicity, enrollment wave, study site, study visit, WIHS study site x visit interaction, education level, diabetes, hypertension, HIV serostatus and DTG use. WWH and women without HIV were analyzed together since interaction testing between HIV serostatus and each substance exposure were not statistically significant. We also performed analyses restricted to WWH which included $CD4^+$ T cell count, HIV RNA viral load, and cumulative TDF use. Significance was defined as $P \leq 0.05$. Analyses were performed using SAS version 9.4, SAS Institute Inc. Cary, North Carolina, USA.

Results

Baseline participant characteristics

The final analysis included 1512 participants; 1043 WWH with 14 481 study visits and 469 women without HIV with 6660 study visits. Table 1 shows the characteristics at the index visit. WWH were significantly older [46 years (IQR 41–52) versus 42 years (IQR 35–50), $P < 0.0001$], more likely to have health insurance (95% versus 84%, $P < 0.0001$), have lower body mass index [BMI: 28.3 kg/m^2 (IQR 23.9–33.8) versus 30.7 kg/m^2 (IQR 26.0–36.9), $P < 0.0001$] and have lower eGFR (99.8 ml/min per 1.73 m^2 (IQR 80.9–114.0) versus 102.7 ml/min per 1.73 m^2 (IQR 88.4–116.2), $P = 0.003$) compared to women without HIV. No significant differences in income, education level, diabetes or hypertension prevalence were observed. Among WWH, 86% had a CD4$^+$ cell count ≥200 cells/μl, 54% had an undetectable HIV viral load, and 60% were receiving TDF.

At the index visit, the prevalence of current marijuana use was significantly lower among WWH compared to women without HIV (14 versus 22%, $P < 0.0001$), and 10-year cumulative marijuana use was significantly lower in WWH compared to women without HIV ($P < 0.0001$). The prevalence of current tobacco use was lower among WWH compared to women without HIV (40 versus 46%, $P = 0.06$). More WWH reported no alcohol use in the past six months (61 versus 50%, $P < 0.001$) than women without HIV, and 10-year cumulative alcohol use was also lower in WWH compared to women without HIV ($P < 0.0001$). At the index date, we observed a high prevalence of use of multiple substances. Among participants, 26.1% reported current marijuana, tobacco and alcohol use, 18.1% reported current alcohol and tobacco use, 8.3% reported current marijuana and tobacco use and 3.1% reported current marijuana and alcohol use (Fig. 1).

Association of cumulative marijuana, tobacco and alcohol use with eGFR

Between 2009 and 2019, participants with cumulative marijuana use of >1.6 marijuana-years had a 2.31 ml/min per 1.73 m^2 lower eGFR (95% CI −4.87, 0.24, $P = 0.08$) compared to those with cumulative use of 0–0.02 marijuana-years (Table 2). Participants with cumulative marijuana use of >0.02 – 1.6 marijuana-years had a 3.61 ml/min per 1.73 m^2 lower eGFR (95% CI −5.97, −1.24, $P = 0.002$) compared to those with 0–0.02 marijuana-years. There was no statistically significant difference in eGFR among participants with 1 – 10 pack-years or more than 10 pack-years of lifetime tobacco use compared to never users. Participants with cumulative alcohol use of >0.07 – 4.27 drink-years had a 2.26 ml/min per 1.73 m^2 (95% CI 0.33, 4.20, $P = 0.02$) higher eGFR compared to those with cumulative use of 0–0.7 drink-years. Those with cumulative alcohol use of >4.27 drink-years also had a 2.85 ml/min per 1.73 m^2 (95% CI 0.55, 5.15, $P = 0.02$) higher eGFR compared to those with cumulative use of 0–0.7 drink-years. Associations of cumulative marijuana, tobacco and alcohol use with eGFR were similar in analyses restricted to WWH and in our sensitivity analysis (Table S1, Supplemental Digital Content, http://links.lww.com/QAD/C907).

Association of current marijuana, tobacco and alcohol use with estimated glomerular filtration rate

WIHS participants with marijuana use of 1–14 days per month had a 3.34 ml/min per 1.73 m^2 (95% CI −6.63, −0.06, $P = 0.05$) lower eGFR compared to those with use of 0 days per month (Table 3). Those reporting more than 14 days of marijuana use per month had 2.72 ml/min per 1.73 m^2 (95% CI −6.10, 0.65, $P = 0.11$) lower eGFR compared to those with 0 use per month but this was not statistically significant. We did not observe a statistically significant difference in eGFR between former and current tobacco users compared to never users. Participants with heavy alcohol use of more than 7 drinks per week had a 5.41 ml/min per 1.73 m^2 (95% CI 2.34, 8.48, $P = 0.0006$) higher eGFR compared to 0 drinks per week. Those with moderate alcohol use of 1–7 drinks per week had a 2.01 ml/min per 1.73 m^2 (95% CI −0.09, 4.10, $P = 0.06$) higher eGFR compared to 0 drinks per week. Associations for current marijuana, tobacco and alcohol use with eGFR were similar in analyses restricted to WWH and in our sensitivity analysis (Table S2, Supplemental Digital Content, http://links.lww.com/QAD/C907).

Discussion

In this well characterized, prospectively followed, and geographically diverse cohort of WWH and women without HIV in the United States, we observed differential associations between marijuana, tobacco and alcohol use with eGFR. Although current and cumulative marijuana use were both independently associated with lower eGFR, this association did not reach statistical significance in the highest category of use. Neither current nor lifetime tobacco use were independently associated with eGFR. Greater current and cumulative alcohol use were independently associated with higher eGFR. To our knowledge, this is the first study to characterize the association of current and cumulative use of these substances with kidney function among a large cohort of WWH and women without HIV. Although prior studies have reported a higher prevalence of substance use among PWH compared to persons without HIV, we found that women without HIV had a higher prevalence of marijuana and alcohol use and a trend toward higher tobacco use compared to WWH. A national sample evaluating patterns of substance use reported 1.7-fold higher lifetime marijuana use and 3-fold higher current marijuana use among PWH compared to persons without HIV [34]. Women without HIV in WIHS are recruited based on socio-behavioral characteristics associated with risk for HIV, which may explain why we did not observe a higher prevalence of substance use among WWH [26]. Baseline differences in health insurance status may also explain the higher prevalence of substance use among women without HIV compared to WWH. Lack of health insurance represents a barrier to treatment for substance use and prior studies have indicated that uninsured persons have a higher prevalence of substance use and dependence [35,36].

Our finding that marijuana use was associated with lower eGFR is contradictory to studies in non-HIV populations which have not identified an association of marijuana use with adverse kidney outcomes. A cohort of 647 middle-aged, hypertensive men followed from 1977 to 1999 reported two-fold higher risk of mild kidney function decline associated with marijuana use but this was not statistically significant [37]. The Coronary Artery Risk

Development in Young Adults Study evaluated cumulative marijuana use from 1985 to 2010 among 3765 adults 18–30 years of age and did not observe a longitudinal association of marijuana use with eGFR or albuminuria [18]. However, marijuana use was ascertained every 5 years in this study compared to semi-annual assessment in WIHS. Current and cumulative marijuana use were not associated with CKD progression in 3939 participants with eGFR 20–70 ml/min per 1.73 m^2 followed from 2003 to 2008 in the Chronic Renal Insufficiency Cohort Study [38]. Though we observed an association between current and cumulative marijuana use with lower eGFR among WWH and women without HIV, this association was only observed with moderate use, not the highest category of marijuana use, so we cannot rule out a type 1 error and residual confounding. However, the trend toward lower eGFR in those with highest use suggests that marijuana adversely affects kidney function.

One potential explanation for our findings that we considered is increasing marijuana potency over time. From 1995 to 2014, the Drug Enforcement Association analyzed more than 36 000 samples of marijuana and found that over 20 years there was a three-fold increase in the potency of marijuana and more than five-fold increase in the THC/CBD ratio [19]. Changes in marijuana potency were most pronounced after 2010, a time period after prior studies that investigated the association between marijuana use and kidney function. Although our study identified a negative association between marijuana use and eGFR between 2009 and 2019, a time period inclusive of use of higher potency THC, we did not observe a dose dependent effect, making it less likely that recent increases in THC concentrations explain our findings. Marijuana use has been associated with epigenetic changes linked to accelerated aging and may contribute to premature onset of age-related comorbidities [39]. Our data suggest that marijuana use is negatively associated with kidney function in WWH and women without HIV. This finding warrants further investigation, including potential pathophysiologic mechanisms, reproducibility in other populations and determining if there is an association with CKD and longitudinal changes in eGFR over time.

In the general population, tobacco use has been independently associated with lower eGFR, albuminuria and incident CKD [10,11,40,41]. A previous study of >400 hospitalized PWH demonstrated that smoking was independently associated with CKD and a dose–response relationship between packs smoked per day and CKD [41]. However, in our study, we did not observe an independent association between current or lifetime tobacco use and lower eGFR in adjusted models. After adjusting for age, the association between tobacco use and lower eGFR was completely attenuated, suggesting that age explains any potential differences.

We observed an incremental, graded association between current alcohol use and eGFR with an independent association between heavy alcohol use and higher eGFR and a trend toward higher eGFR with mild-moderate alcohol use. Multiple population-based cohort studies have demonstrated that alcohol consumption is inversely associated with incident CKD and end-stage kidney disease (ESKD) [12,13,40,42]. An analysis of more than 65 000 Chinese men showed that alcohol use of less than 21 drinks/week and more than 21 drinks/week compared to no use were both associated with a lower risk of ESKD [42]. Another analysis

of more than 9000 middle aged Japanese men demonstrated alcohol intake of 4–7 drinks/week was associated with a lower risk of incident CKD [12]. Though alcohol consumption appears to have protective effects on the kidney, this has been questioned since people that abstain from alcohol may do so due to worse health, a hypothesis that we were unable to evaluate fully in this study. Potential protective effects of alcohol use on the kidney may be mediated by increases in high-density lipoprotein and decreases in platelet aggregation, resulting in lower risk of atherosclerosis and a reduction in cardiovascular disease [43–46].

Our study has several strengths. WIHS uses standardized questionnaires across sites, which minimizes misclassification bias. Semi-annual updated substance exposures were captured, which allowed us to determine the association of time-updated and cumulative substance use with eGFR. Substance use was also quantified which allowed us to determine if there was a dose dependent relationship with GFR. However, our study also has several important limitations. First, substance use was self-reported and obtained via structured interviews which could have resulted in social desirability bias. Third, we were unable to consider changes in potency of marijuana used over time, which may have had differential effects on the kidney. However, the association of current marijuana use with eGFR was evaluated between 2009 and 2019, a contemporary time frame in which THC content has been reported to be significantly higher. Fourth, data on lifetime marijuana and alcohol use were not collected. Though there were missing data for 10-year cumulative exposures, our findings were qualitatively consistent in a sensitivity analysis using IPW which accounts for potential bias of informative drop out by overweighting the available visits to compensate for the missing visits in individuals who died or who were lost to follow up. Finally, it is possible that substance use was associated with subclinical kidney injury that would have been better detected by albuminuria or other urinary biomarkers which were not available in most of the WIHS cohort during our study period. Future studies are needed to determine the association of marijuana use with other biomarkers of kidney function, including cystatin C and urinary biomarkers of glomerular and tubular kidney injury such as urine albumin-creatinine ratio and kidney-injury molecule 1, respectively.

Conclusion

Among a large diverse cohort of WWH and women without HIV in the United States, alcohol use was associated with a higher eGFR and marijuana use was associated with a lower eGFR. Future studies should investigate the association between marijuana use and adverse kidney outcomes in PWH. Despite the lack of a negative association between eGFR and tobacco or alcohol use, given their association with adverse health outcomes, routine clinical care should include substance use screening and counseling that addresses potential health risks associated with substance use.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

Study design and conceptualization: M.F., D.H., Q.S., A. S., M.R.

Data analysis: D.H., Q.S.

Data interpretation: M.F., D.H., Q.S., A.S., M.R.

Written draft: M.F., M.R.

Review and editing: All authors.

Supervised: M.R.

Data in this manuscript were collected by the Women's Interagency HIV Study (WIHS), now the MACS/WIHS Combined Cohort Study (MWCCS).

The contents of this publication are solely the responsibility of the authors and do not represent the official views of the National Institutes of Health (NIH). MWCCS (Principal Investigators): Atlanta CRS (Ighovwerha Ofotokun, Anandi Sheth, and Gina Wingood), U01-HL146241; Baltimore CRS (Todd Brown and Joseph Margolick), U01-HL146201; Bronx CRS (Kathryn Anastos, David Hanna, and Anjali Sharma), U01-HL146204; Brooklyn CRS (Deborah Gustafson and Tracey Wilson), U01-HL146202; Data Analysis and Coordination Center (Gypsyamber D'Souza, Stephen Gange and Elizabeth Topper), U01-HL146193; Chicago-Cook County CRS (Mardge Cohen and Audrey French), U01-HL146245; Chicago-Northwestern CRS (Steven Wolinsky), U01-HL146240; Northern California CRS (Bradley Aouizerat, Jennifer Price, and Phyllis Tien), U01-HL146242; Los Angeles CRS (Roger Detels and Matthew Mimiaga), U01-HL146333; Metropolitan Washington CRS (Seble Kassaye and Daniel Merenstein), U01-HL146205; Miami CRS (Maria Alcaide, Margaret Fischl, and Deborah Jones), U01-HL146203; Pittsburgh CRS (Jeremy Martinson and Charles Rinaldo), U01-HL146208; UAB-MS CRS (Mirjam-Colette Kempf, Jodie Dionne-Odom, and Deborah Konkle-Parker), U01-HL146192; UNC CRS (Adaora Adimora and Michelle Floris-Moore), U01-HL146194. The MWCCS is funded primarily by the National Heart, Lung, and Blood Institute (NHLBI), with additional co-funding from the *Eunice Kennedy Shriver* National Institute Of Child Health & Human Development (NICHD), National Institute On Aging (NIA), National Institute Of Dental & Craniofacial Research (NIDCR), National Institute Of Allergy And Infectious Diseases (NIAID), National Institute Of Neurological Disorders and Stroke (NINDS), National Institute Of Mental Health (NIMH), National Institute On Drug Abuse (NIDA), National Institute Of Nursing Research (NINR), National Cancer Institute (NCI), National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Deafness and Other Communication Disorders (NIDCD), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute on Minority Health and Health Disparities (NIMHD), and in coordination and alignment with the research priorities of the National Institutes of Health, Office of AIDS Research (OAR). MWCCS data collection is also supported by UL1-TR000004 (UCSF CTSA), UL1-TR003098 (JHU ICTR), UL1-TR001881 (UCLA CTSI), P30-AI-050409 (Atlanta CFAR), P30-AI-073961 (Miami CFAR), P30-AI-050410 (UNC CFAR), P30-AI-027767 (UAB CFAR), P30-MH-116867 (Miami CHARM), UL1-TR001409 (DC CTSA), KL2-TR001432 (DC CTSA), and TL1-TR001431 (DC CTSA).

The authors gratefully acknowledge the contributions of the study participants and dedication of the staff at the MWCCS sites.

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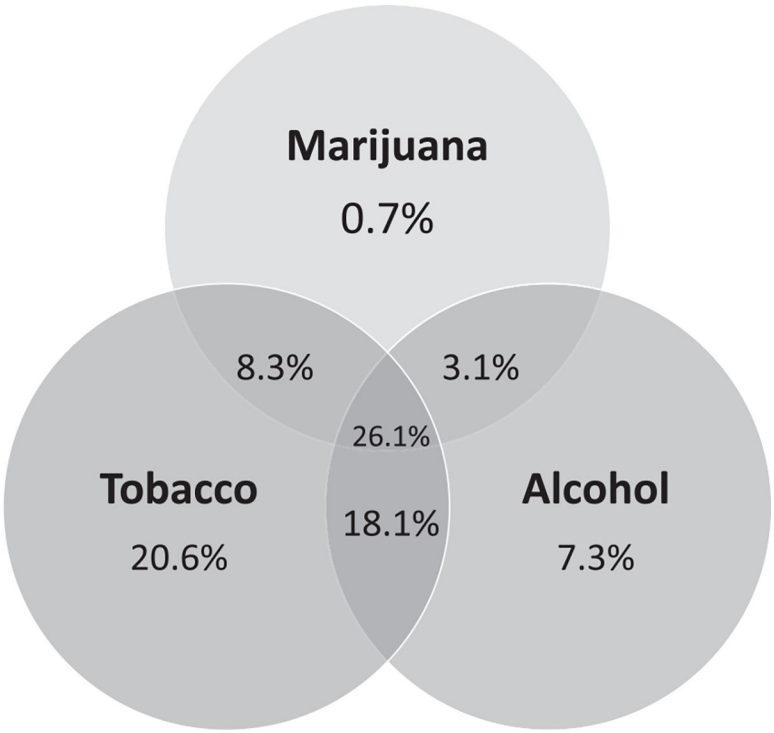

Fig. 1. Baseline prevalence of marijuana, tobacco and alcohol use among 1512 women living with and without HIV.

Table 1.

Characteristics of women living with HIV and women without HIV in 2009–2010.

	Women living with HIV *N* = 1043	Women without HIV *N* = 469	*P*-value
Age, median (IQR), years	46 (41 –52)	42 (35–50)	<0.0001
Race, *n* (%)			
Non-Hispanic white	129 (12%)	45 (10%)	0.09
Non-Hispanic black	654 (63%)	302 (64%)	
Hispanic	222 (21%)	98 (21%)	
Other	37 (4%)	24 (5%)	
Missing	1 (0%)	0 (0%)	
Income, *n* (%)			
<12 000/year	454 (43%)	192 (41%)	0.3
≥12 000/year	542 (52%)	258 (55%)	
Missing	47 (5%)	19 (4%)	
Education, *n* (%)			
<High school	347 (33%)	154 (33%)	0.87
≥High school	694 (67%)	314 (67%)	
Missing	2 (0%)	1 (0%)	
WIHS study center, *n* (%)			
Bronx/Manhattan	229 (22%)	133 (28%)	
Brooklyn	278 (27%)	115 (25%)	0.04
Washington DC	184 (18%)	76 (16%)	
San Francisco	185 (18%)	88 (19%)	
Chicago	167 (16%)	57 (12%)	
WIHS enrollment cohort, *n* (%)			
Original cohort (1994/1995)	630 (60%)	231 (49%)	<0.0001
New recruits (2001/2002)	413 (40%)	238 (51%)	
Hypertension	409 (39%)	178 (38%)	0.64
Diabetes mellitus	162 (16%)	75 (16%)	0.82
eGFR, median (IQR), ml/min per 1.73 m^2	99.8 (80.9–114.0)	102.7 (88.4–116.2)	0.003
BMI, median (IQR), kg/m^2	28.3 (23.9–33.8)	30.7 (26.0–36.9)	<0.0001

	Women living with HIV $N = 1043$	Women without HIV $N = 469$	P-value
Tobacco use, *n* (%)			
Never	283 (27%)	114 (24%)	
Former	342 (33%)	137 (29%)	0.06
Current	416 (40%)	218 (46%)	
Missing	2 (0%)	0 (0%)	
Lifetime tobacco use (pack-years), *n* (%)			
0	291 (28%)	116 (25%)	0.19
1–10	348 (33%)	183 (39%)	
>10	355 (34%)	148 (32%)	
Missing	49 (5%)	22 (5%)	
Alcohol use, *n* (%)			
Abstainer	636 (61%)	235 (50%)	
1–7 drinks/week	310 (30%)	159 (34%)	<0.0001
>7 drinks/week	96 (9%)	74 (16%)	
Missing	1 (0%)	1 (0%)	
10-year cumulative alcohol use (drink-year), *n* (%)			
0–0.7 drink-years	527 (51%)	160 (34%)	<0.0001
>0.7–4.27 drink-years	269 (26%)	128 (27%)	
>4.27 drink-years	206 (20%)	153 (33%)	
Missing	41 (4%)	28 (6%)	
Marijuana use			
0 days/month	889 (85%)	367 (78%)	
1–14 days/month	34 (3%)	19 (4%)	0.0004
>14 days/month	107 (10%)	82 (18%)	
Missing	13 (0%)	1 (0%)	
10-year cumulative marijuana use (marijuana-years), *n* (%)			
0–0.02	684 (66%)	250 (53%)	<0.0001
>0.02–1.6	180 (17%)	100 (21%)	
>1.6	138 (13%)	91 (19%)	
Missing	41 (4%)	28 (6%)	
$CD4^+$ cell count, (cells/μl), *n* (%)			

	Women living with HIV $N = 1043$	Women without HIV $N = 469$	*P*-value
<200	144 (14%)	-	-
200–349	161 (15%)	-	-
350–499	207 (20%)	-	-
>500	531 (51%)	-	-
HIV viral load, *n* (%)		-	-
Undetectable	560 (54%)	-	-
Detectable	483 (46%)	-	-
Antiretroviral therapy, *n* (%)		-	-
Tenofovir disoproxil fumarate, *n* (%)	621 (60%)	-	-
Dolutegravir, *n* (%)	0 (0%)		

Table 2.

Association of cumulative marijuana, tobacco and alcohol use with eGFR of women with HIV and women without HIV from 2009 to 2019.

	Model 1, parameter estimate (95% CI)	*P*-value	Model 2, parameter estimate (95% CI)	*P*-value
Marijuana *				
0–0.02 marijuana-years	–		–	–
>0.02–1.6 marijuana-years	−0.56 (−3.87, 2.48)	0.87	−3.61 (−5.97, −1.24)	0.002
>1.6 marijuana-years	3.90 (0.84, 6.95)	0.01	−2.31 (−4.87, 0.24)	0.08
Tobacco **				
0 pack-years	–		–	
1–10 pack-years	−2.18 (−5.17, 0.81)	0.15	1.15 (−1.30, 3.60)	0.36
>10 pack-years	−9.96 (−12.90, −7.02)	<0.0001	−0.98 (−3.61, 1.64)	*P* = 0.46
Alcohol ***				
0–0.7 drink-years	-		-	
>0.7–4.27 drink-years	5.07 (2.70, 7.44)	<0.0001	2.26 (0.33, 4.20)	0.02
>4.27 drink-years	5.64 (3.02, 8.26)	<0.0001	2.85 (0.55, 5.15)	0.02

Model 1 adjusted for WIHS site, study visit WIHS site x visit interaction. Model 2 adjusted for Model 1 þ age, race, education level, diabetes, hypertension, HIV, dolutegravir use.

*Adjusted for tobacco and alcohol use.

**Adjusted for marijuana and alcohol use.

***Adjusted for marijuana and tobacco use.

Table 3.

Association of current marijuana, tobacco and alcohol use with eGFR of all WIHS participants from 2009 to 2019.

	Model 1, parameter estimate (95% CI)	*P*-value	Model 2, parameter estimate (95% CI)	*P*-value
Marijuana *				
0 days/month	–		–	
1 –14 days/month	−1.41 (−5.48, 2.66)	0.50	−3.34 (−6.63, −0.06)	0.05
>14 days/month	2.14 (−2.14, 6.41)	0.33	−2.72 (−6.10, 0.65)	0.11
Tobacco **				
Never	–		–	
Former	−4.57 (−7.66, −1.47)	0.004	1.28 (−1.28, 3.84)	0.33
Current	−5.25 (−8.13, −2.36)	0.0004	−1.23 (−3.60, 1.14)	0.31
Alcohol ***				
0 drinks/week	-		-	
1–7 drinks/week	4.47 (1.95, 6.99)	0.0005	2.01 (−0.09, 4.10)	0.06
>7 drinks/week	6.99 (3.29, 10.69)	0.0002	5.41 (2.34, 8.48)	0.0006

Model 1 adjusted for WIHS site, study visit WIHS site × visit interaction. Model 2 adjusted for Model 1 + age, race, education level, diabetes, hypertension, HIV, dolutegravir use.

*Adjusted for tobacco and alcohol use.

**Adjusted for marijuana and alcohol use.

***Adjusted for marijuana and tobacco use.

AIDS. Author manuscript; available in PMC 2024 August 01.