Cannabis, cannabinoids and health outcomes in persons with HIV (PWH)

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Conflict of Interest Disclosure Statement

- The presenter has no conflicts to declare.

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Learning Objectives

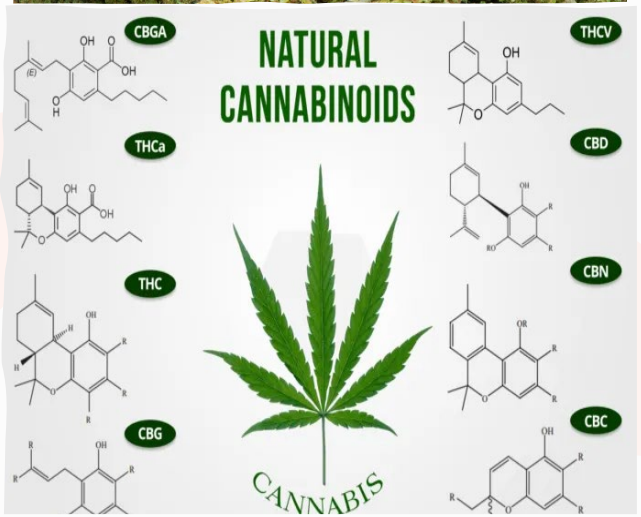
1. Describe the prevalence, & patterns of cannabis use in People with HIV (PWH)
2. Describe reasons for cannabis use in PWH
3. Describe the endocannabinoid system
4. Discuss the impact of cannabis, cannabinoids on health outcomes of PWH

Cannabis vs. Cannabinoids

Cannabis refers to the dried leaves and flowering tops of the *Cannabis sativa* or *Cannabis indica* plant.

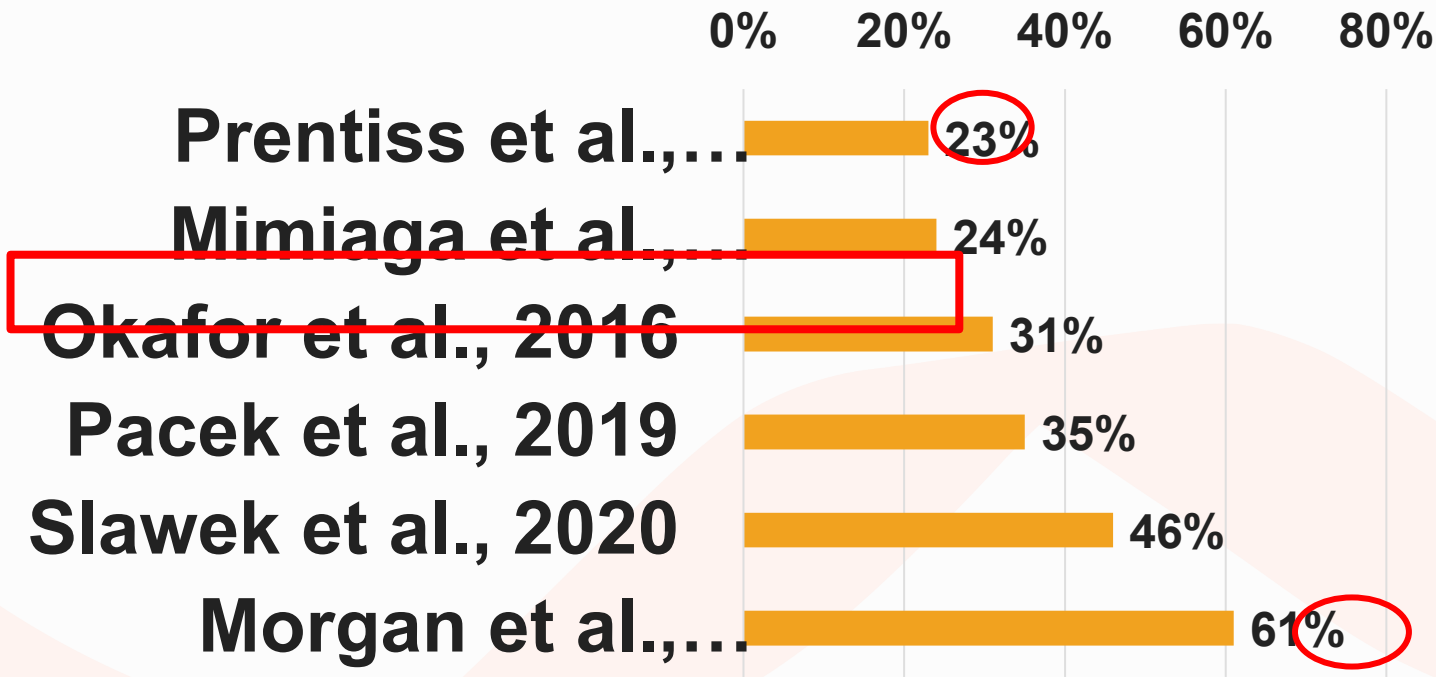
Cannabinoids refers to the active chemicals in the *cannabis plant,* that are responsible for its effects when consumed

- Delta-9 tetrahydrocannabinol (THC)
- Cannabidiol (CBD)



www.davidvanille.com
www.encore-labs.com

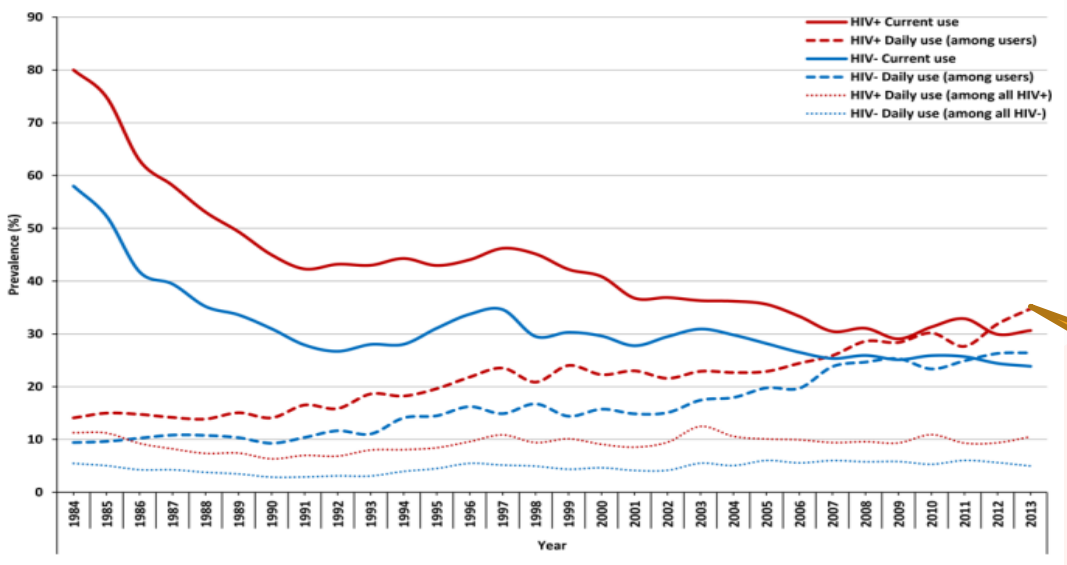
Prevalence of cannabis use in PWH



Okafor 2023. Unpublished

Trends in the prevalence of cannabis those who report use in PWH

Among men with HIV (MACS)

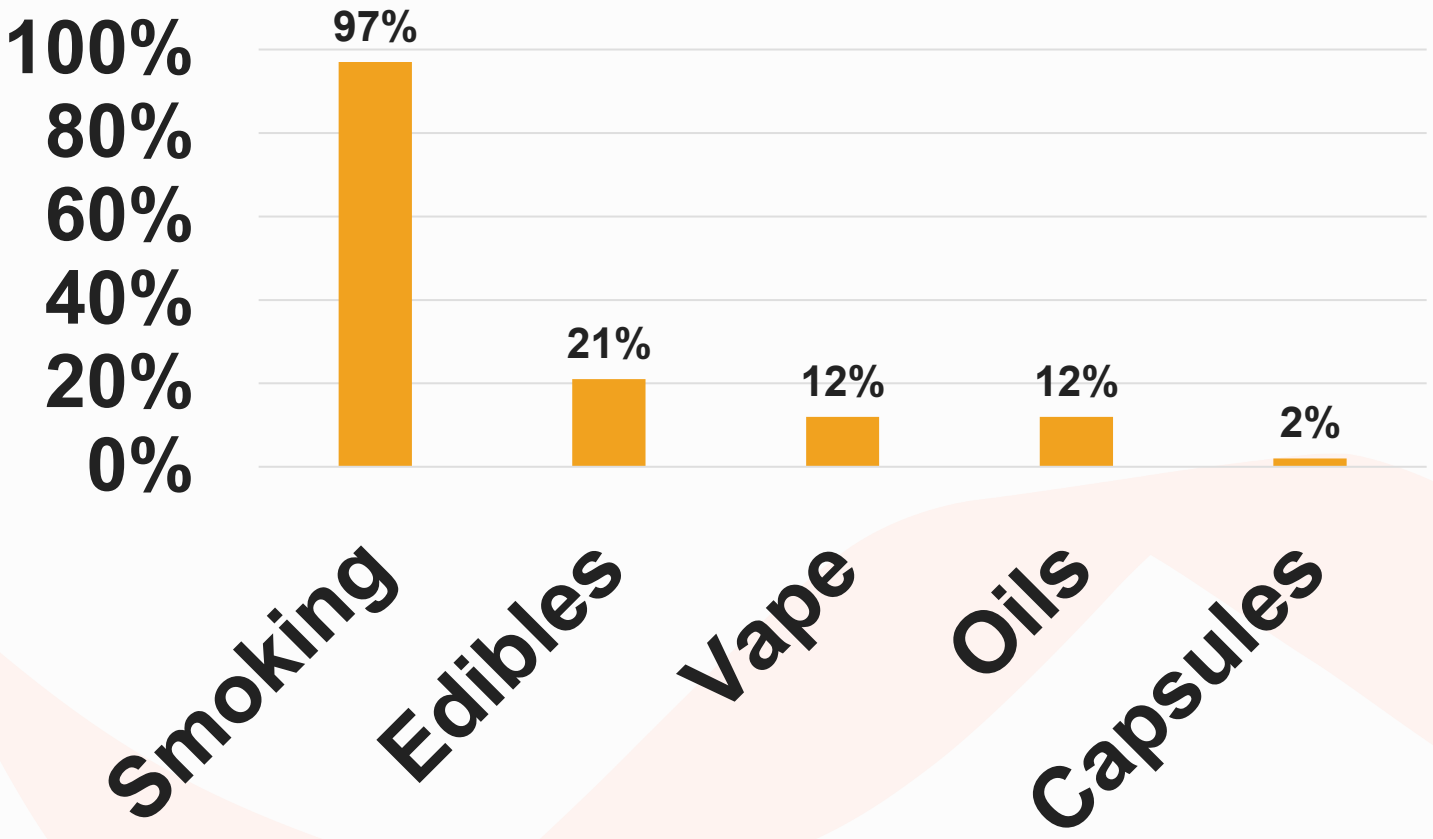


Prevalence of **daily** use (among users) = 35%

(Okafor et al., 2017)

MACS=Multicenter AIDS Cohort Study

Modes PWH use cannabis



Costiniuk et al., (2019)

Reasons PWH use cannabis (1)

Medical

- Physical pain relief
- Improve mood
- Anxiety
- Nausea
- Appetite stimulation
- Weight loss
- Sleep aid
- Side effects of ART meds

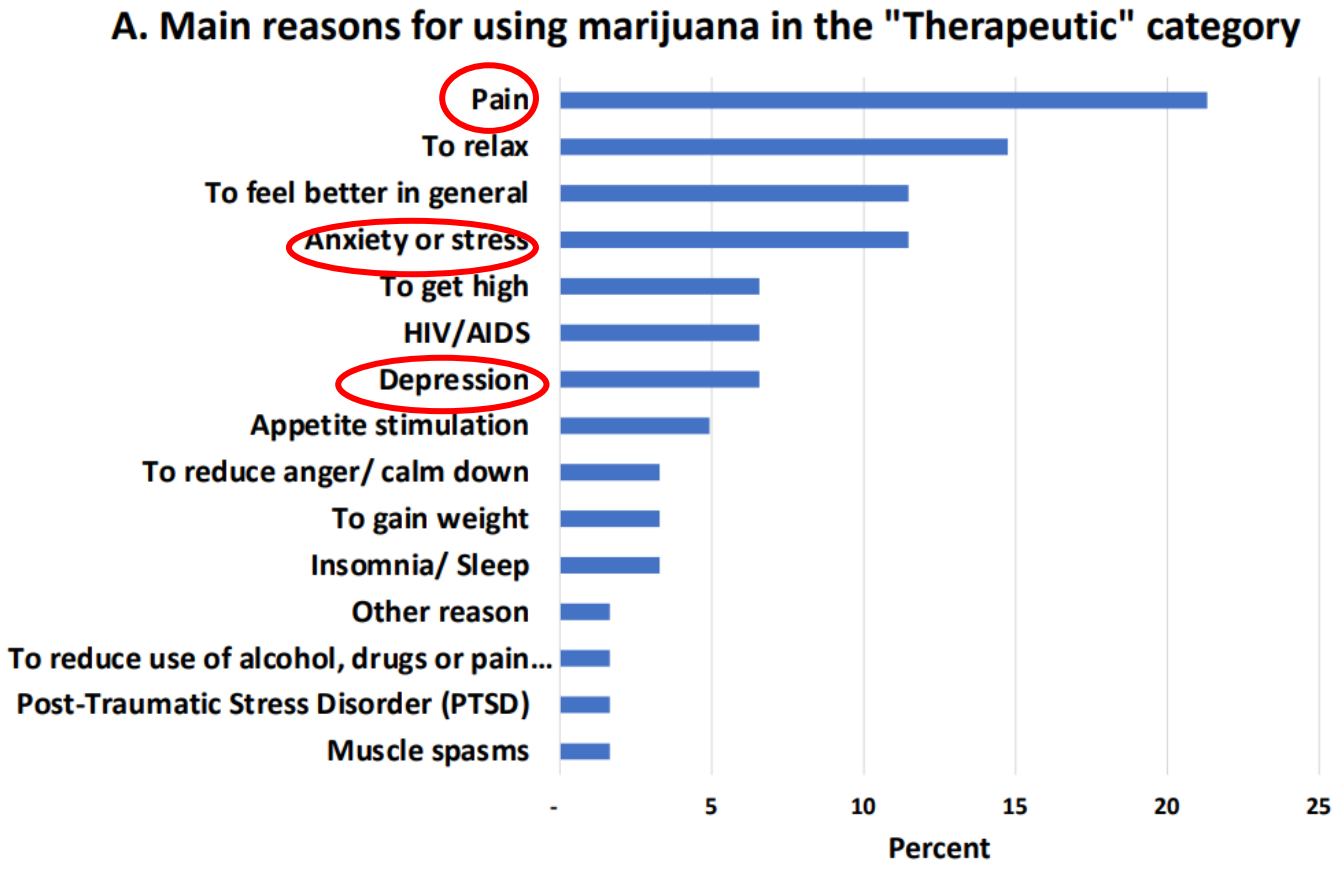
Non-medical

- To relax in a social setting

About 26% of women in with HIV who use cannabis report using exclusively for medical reasons

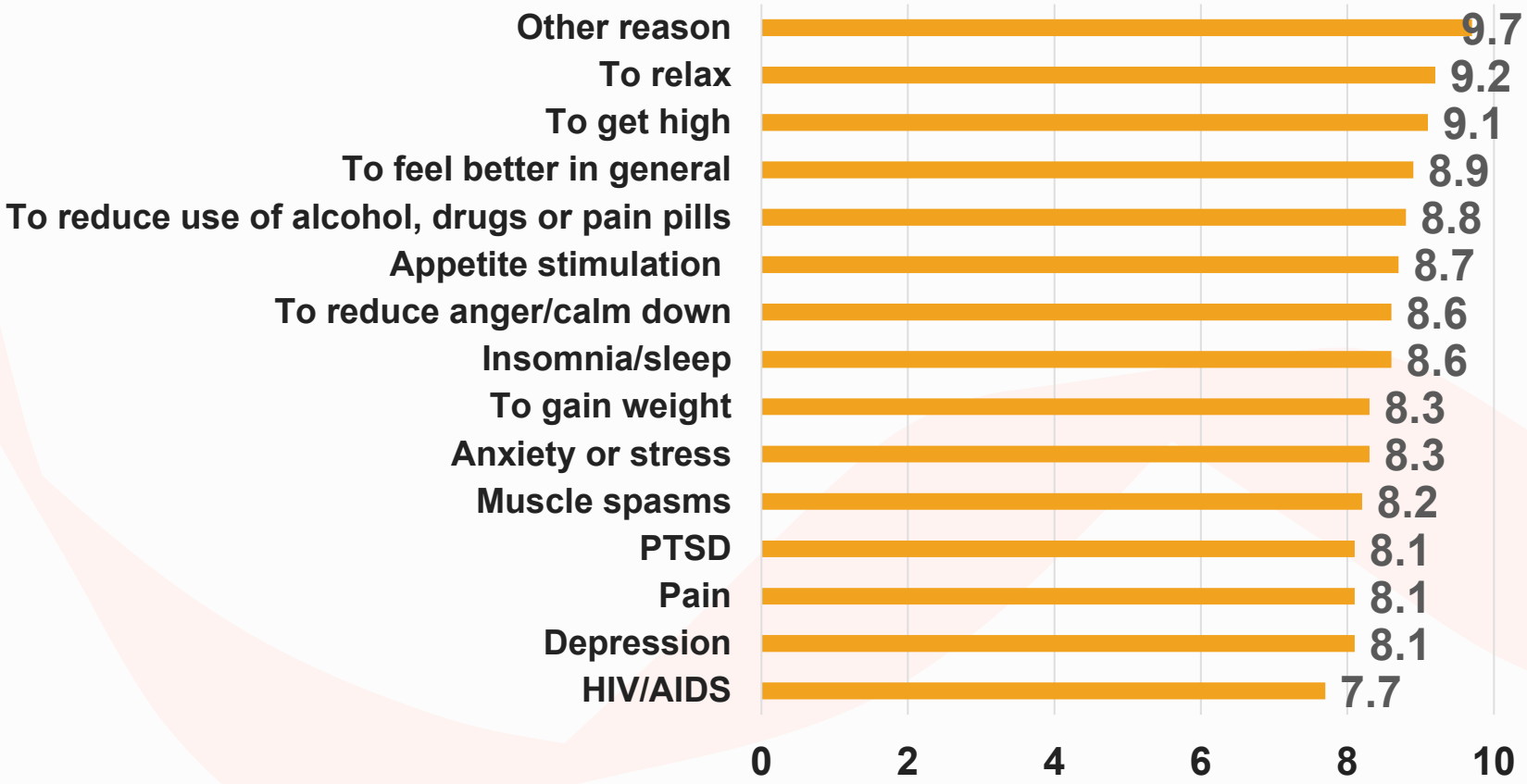
D'Souza., et al., 2012;
Woolridge., et al., 2005

Reasons PWH use cannabis (2)



Sajdeya et al., (2021)

Perceived effectiveness of cannabis use in PWH



Sajdeya et al., (2021)

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FDA Approved cannabinoid-based medications

- **Marinol/Syndros** (Dronabinol – a synthetic cannabinoid) – for the treatment of nausea/vomiting caused by anti-cancer medication. Loss of appetite in PWH

- **Cesamet** (Nabilone – synthetic cannabinoid) - for the treatment of nausea/vomiting caused by anti-cancer medication

- **Epidiolex** (CBD) – for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome, or tuberous sclerosis complex (TSC) in patients 1+ years of age.

The endocannabinoids system (ECS)

The Human Endocannabinoid System

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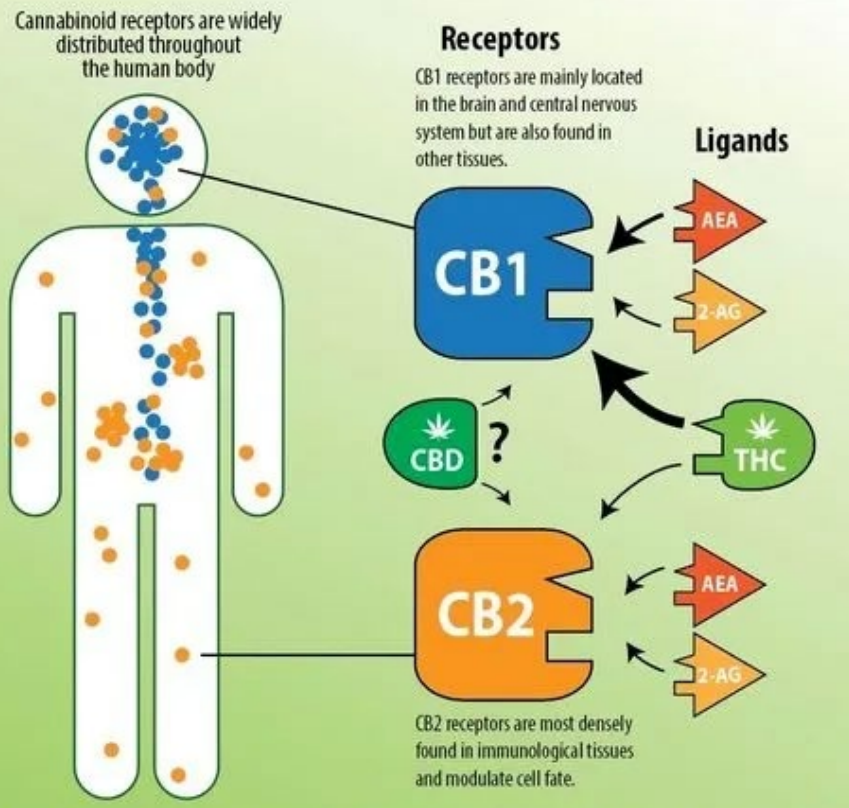
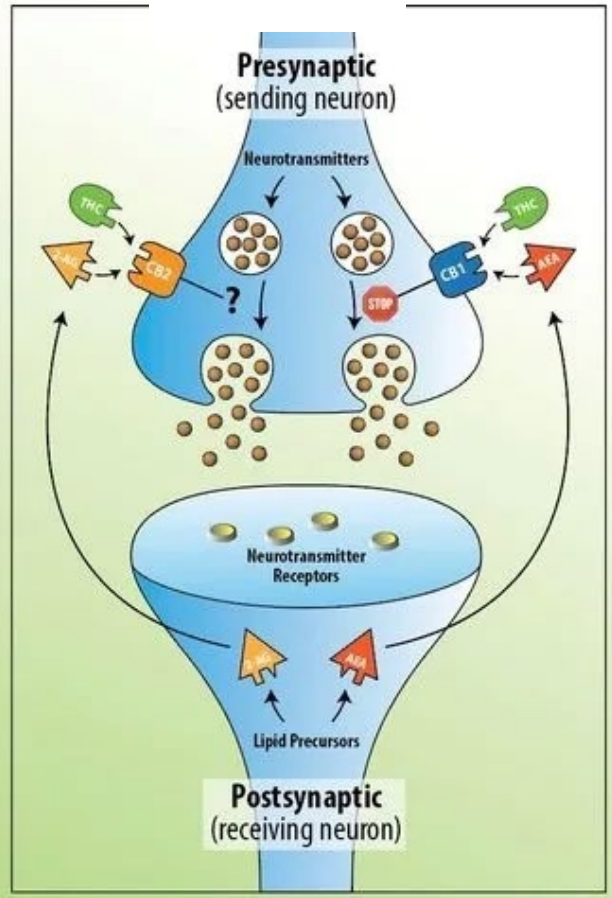
The endocannabinoid system (ECS) consists of cannabinoid receptors, endocannabinoids and their metabolic enzymes. Two major cannabinoid receptors, CB1 and CB2, and two main endocannabinoids, anandamide (AEA) and 2-arachidonoyl-glycerol (2-AG), have been identified. Human endocannabinoids and plant cannabinoids, such as THC and CBD, bind to cannabinoid receptors with great specificity, much like a lock and key. Activation of the cannabinoid receptors inhibits the release of neurotransmitters. The ECS plays a key role in homeostasis and regulates many physiological processes such as inflammation and pain perception, immunity, neuropathy and metabolism.





AEA binds to the CB1 receptor with greater affinity than CB2 whereas 2-AG binds both receptors with equal affinity. THC binds the CB1 receptor with greater affinity than the CB2 receptor and it has been suggested that binding effects of THC mimic AEA. CBD has low affinity for both receptors but interacts at low concentrations. It has been proposed that binding effects of CBD are mimetic to 2-AG.

physicianslab.com/cbd-and-the-endocannabinoid-system/

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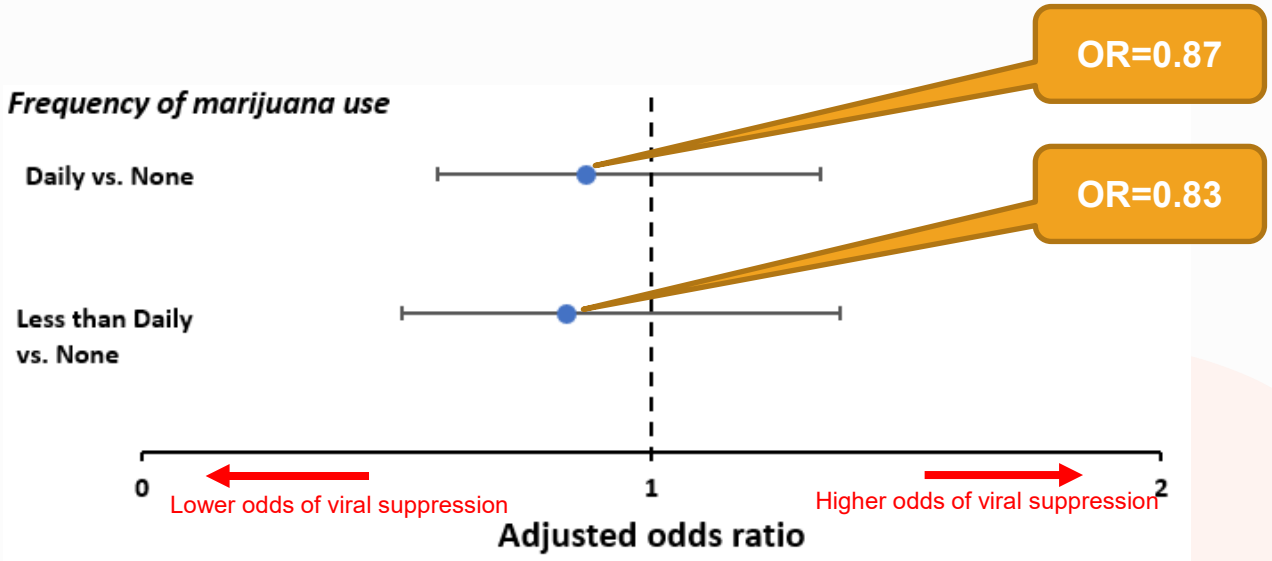
Impact of cannabis use on viral load suppression (< 200 copies/ml)



Cannabis use associated with **lower** odds of viral suppression, confidence intervals were imprecise (i.e., p=>0.05)

Okafor et al., 2016

Impact of cannabis use on viral load detectability

Table 2 Indicators of self-reported cannabis use and clinical outcomes, adjusted for age, sex, race, and other substance use

	Patients with at least one visit with cannabis use versus patients never reporting cannabis use	Patient visits with cannabis use in 7 days prior versus patient visits with no cannabis use in 7 days prior	Number of times cannabis used in the preceding 7 days (difference per time used)
Difference in predicted square root CD4 count (cells/mm^3) (95% CI)	0.580 (−0.334, 1.495)	−0.052 (−0.378, 0.482)	−0.027 (−0.084, 0.030)
Difference in predicted BMI (kg/m^2) (95% CI)	−0.767 (−1.697, 0.162)	−0.090 (−0.330, 0.150)	−0.019 (−0.051, 0.013)
Odds ratio for detectable HIV-1 RNA (< 50 copies/mL plasma) at a given clinical visit (95% CI)	2.02* (1.28, 3.17)	1.72* (1.10, 2.72)	1.08* (1.01, 1.16)

Cannabis use was associated with increased odds of viral detectability (p=>0.05)

Lee et al., 2020

Impact of cannabis use on viral load

Table 2. **Changes in Viral Load Level by Group**

Variable	Marijuana Group ($n = 20$)	Dronabinol Group ($n = 22$)	Placebo Group ($n = 20$)
Change between day 0 and day 21 (2 time points), *n (%)*			
Increase $>$ 0.5 $\log_{10}$ copies/mL	1 (5)	0 (0)	1 (5)
Increase $\geq$ 0.5 $\log_{10}$ copies/mL	4 (20)	2 (9)	5 (25)
Decrease $<$ 0.5 $\log_{10}$ copies/mL	2 (10)	7 (32)	3 (15)
Decrease $\geq$ 0.5 $\log_{10}$ copies/mL	3 (15)	2 (9)	0 (0)
No change	10 (50)	11 (50)	11 (55)
Unadjusted mean difference in viral load from placebo group (95% CI), *$\log_{10}$ copies/mL*	−0.19 (−0.48 to 0.01)*	−0.24 (−0.55 to −0.06)†	—
Adjusted mean difference in viral load from placebo group (95% CI)‡, *$\log_{10}$ copies/mL*	−0.06 (−0.26 to 0.13)§	−0.07 (−0.24 to 0.06)§	—
Average change in viral load at day 21 (repeated measures: 9 time points), *$\log_{10}$ copies/mL*			
Adjusted mean difference in viral load from placebo group (95% CI)‖	−0.07 (−0.30 to 0.13)§	−0.04 (−0.20 to 0.14)§	—

The estimated average difference in log10 viral load from baseline to day 21 between smoked marijuana vs. placebo was -0.07 (95% CI, -0.30 to 0.13; p>0.2)

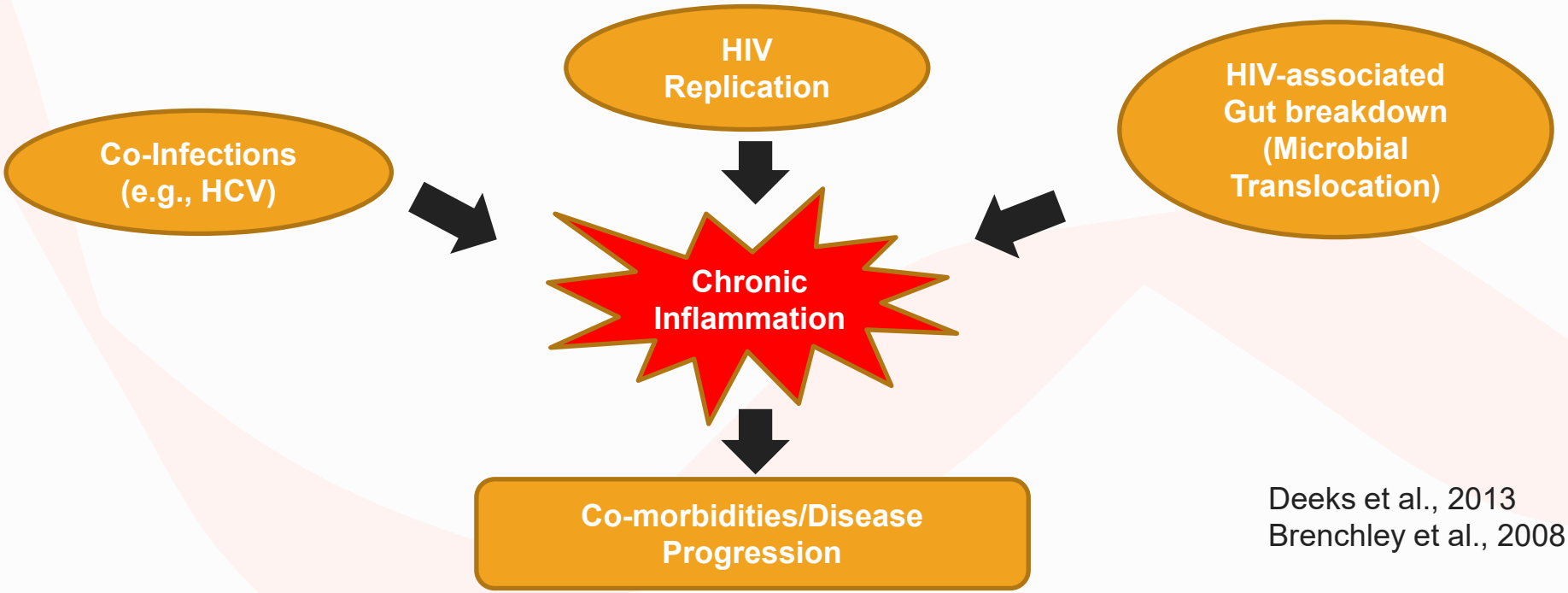
Abrams et al., 2003

Clinical implications

- Majority of the observational studies on the impact of cannabis use on viral load suppression in PWH although imprecise, indicate adverse effects
- Data from one Randomized Controlled Trial (RCT) shows benefit for viral load suppression, with unclear clinical implications

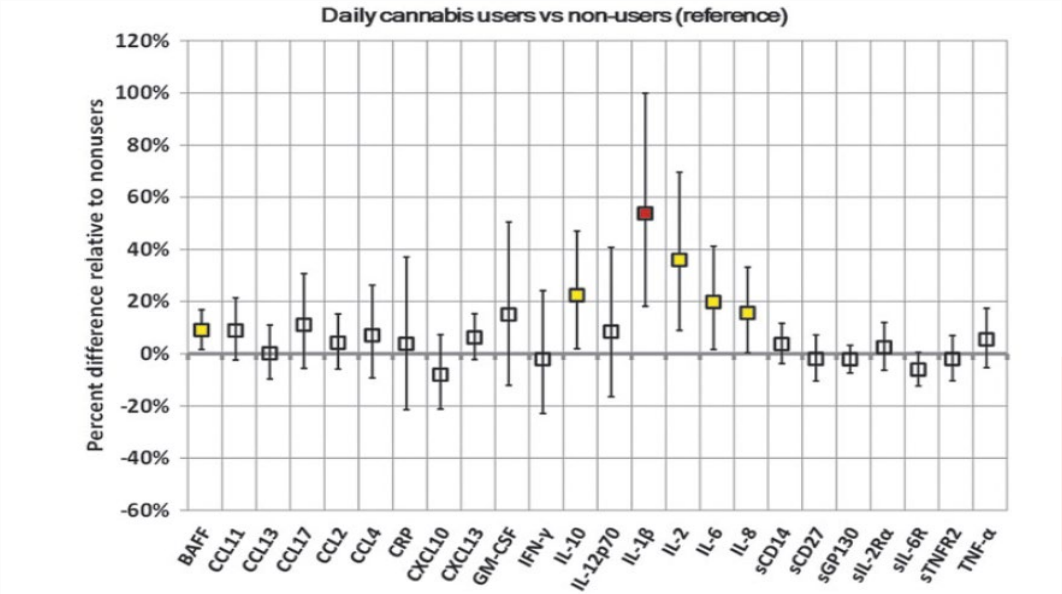
Impact of cannabis use on immune system activation and inflammation

Drivers of chronic inflammation in PWH



Deeks et al., 2013
Brenchley et al., 2008

Cannabis use and plasma biomarkers of inflammation in PWH



Daily cannabis use was significantly associated with higher plasma concentrations of IL-1β, IL-2, IL-6 and IL-8 and IL-10 ($p<0.05$)

Krask, Okafor, et al., 2020

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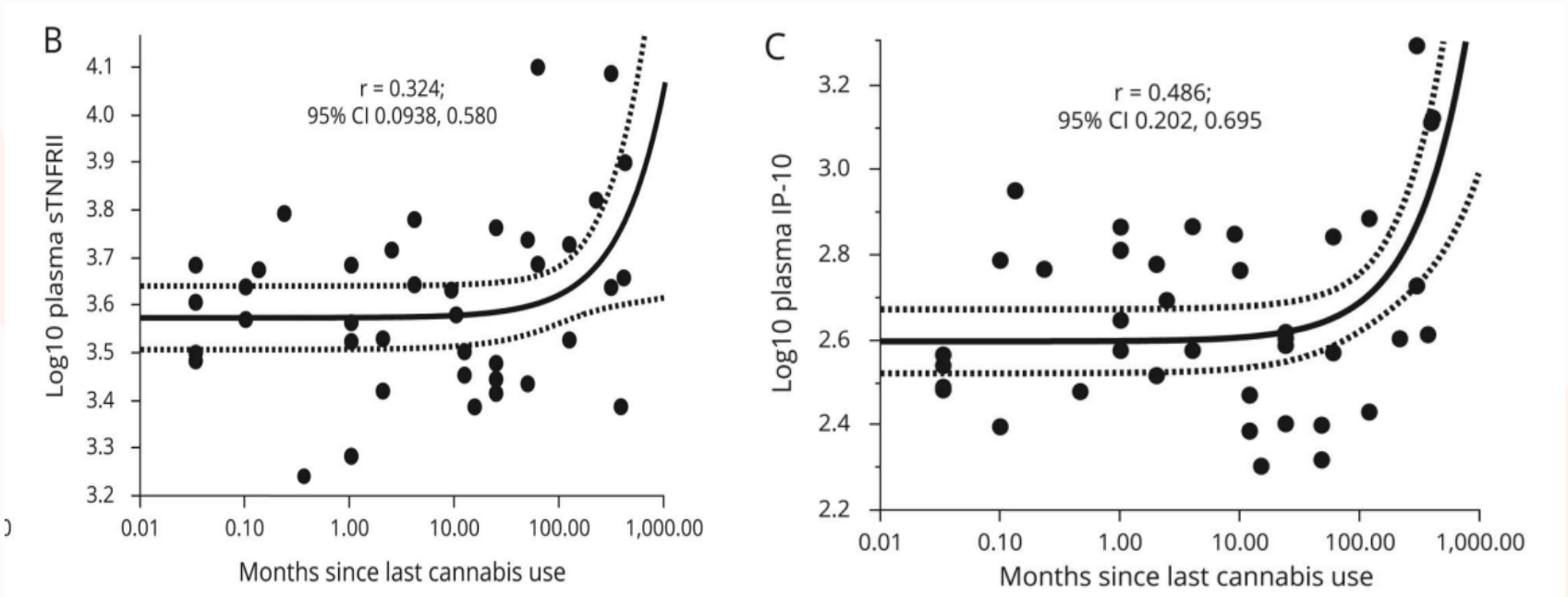
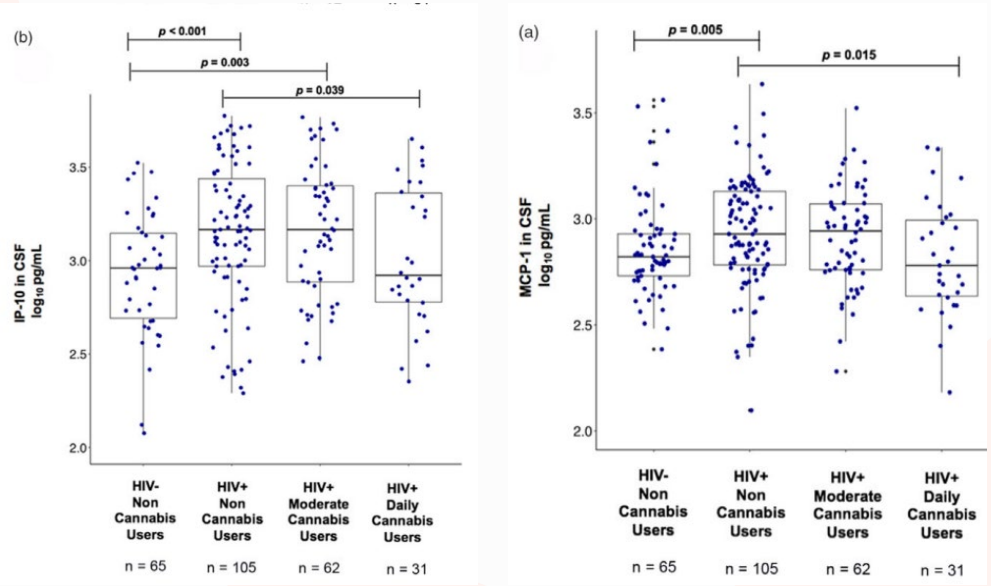
Cannabis use and plasma biomarkers of inflammation in PWH



More recent cannabis use associated with reduced IP-10 and sTNFRII in plasma

Ellis et al., 2020

Cannabis use and CSF biomarkers of inflammation in PWH



Daily marijuana use was associated with lower levels of pro-inflammatory chemokines MCP-1 and IP-10 in CSF

Plasma markers of inflammation showed no difference by cannabis use.

Watson et al., (2021)

Current Project

- To determine relationship between plasma quantitated delta-9 Tetrahydrocannabinol (THC) metabolites with:

(1) Biomarkers of inflammation

(2) HIV viral load

National Institute on Drug Abuse

K01DA047912

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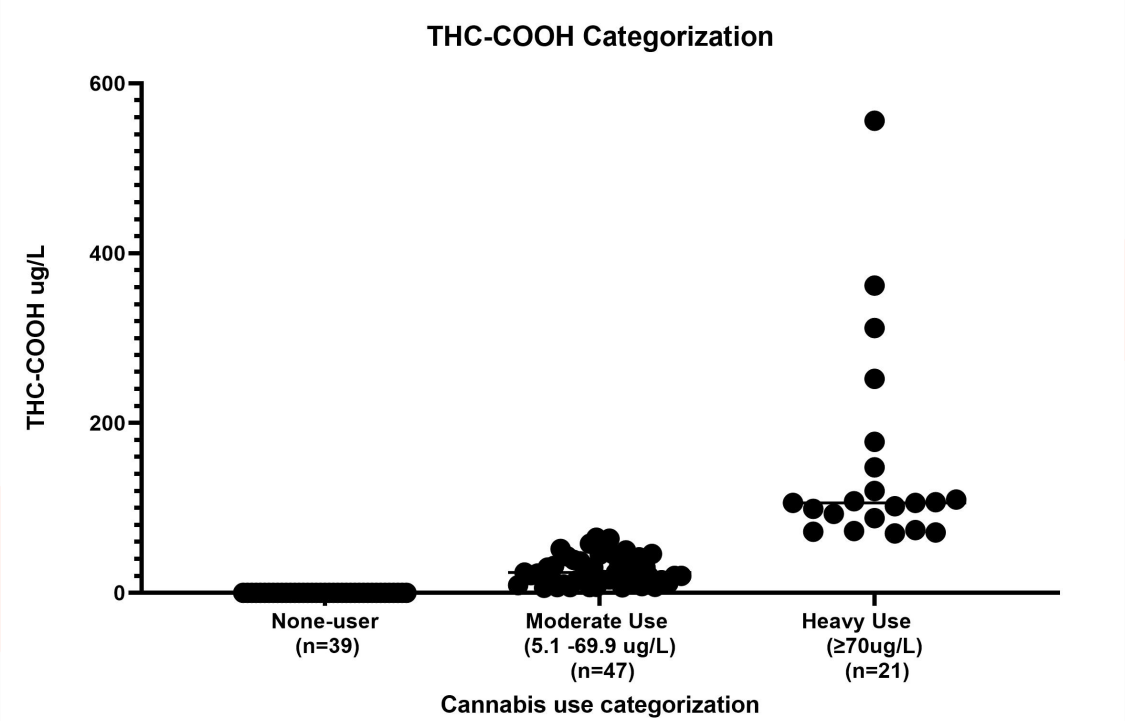
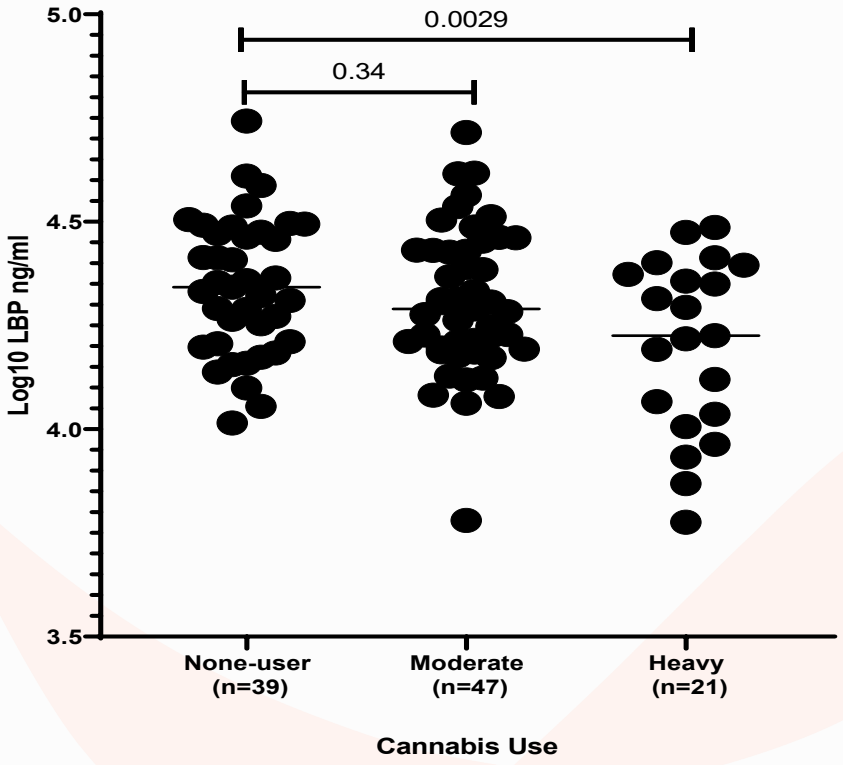
Cannabis metabolites (THCCOOH) Categorization



Heavy use=20%
Moderate use=44%
Non-use=36%

Heavy vs. non cannabis use associated with lower plasma LBP



All other biomarkers showed no difference by cannabis use.

Okafor et al. Unpublished

Clinical implications?

- Lipopolysaccharide Binding Protein (LBP) binds to and enhances host response to lipopolysaccharide (LPS)
- LPS is a component of the outer layer of gram-negative bacteria
- Our finding suggests that heavy cannabis use in this sample may be associated with reduced LBP (microbial translocation)
- Clinical implications remain unclear

Summary

- Cannabis use is common in PWH
- Medical use is common in PWH
- Additional clinical studies are needed to understand the beneficial/adverse effects of cannabis use on health of PWH

Seeking Black/African American or Latino Gay/Bisexual Men for a Research Study

What is the study about?

Black/African American and Latino Gay and Bisexual Men are needed for a study to understand the things that may make it easy or hard for you to use an injection or shot every other month that can prevent you from getting HIV

What will you do?

Complete a confidential online questionnaire that will take no more than 30 minutes. You may also be invited to participate in a focus group.

Compensation:

Compensation in the form of electronic Visa Gift Card will be provided for your time completing the survey

Are you eligible?

- HIV-negative
- Aged18-34
- Black /Latino

Scan the QR code to participate

For more information email:
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NIH National Institute on Drug Abuse

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SCAETC Social Media

Resources

- National Clinician Consultation Center http://nccc.ucsf.edu/
  - HIV Management
  - Perinatal HIV
  - HIV PrEP
  - HIV PEP line
  - HCV Management
  - Substance Use Management
- AETC National HIV Curriculum https://aidsetc.org/nhc
- AETC National Coordinating Resource Center https://targethiv.org/library/aetc-national-coordinating-resource-center-0
- Additional trainings scaetcecho@salud.unm.edu
- www.scaetc.org