Crack cocaine use frequency is associated with HIV disease severity independent of antiretroviral therapy exposure

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Overview

In a prospective cohort study, we estimated the independent effect of time-updated crack cocaine use frequency on HIV disease severity, adjusting for antiretroviral therapy (ART) exposure and other relevant confounders

Background

- Among HIV-infected individuals, people who use drugs (PWUD) experience **increased HIV disease severity** and HIV-associated morbidity and mortality
- However, the independent effect of specific drugs, particularly **crack cocaine use**, on HIV disease severity is not well understood.
- Prior evidence suggests that plasma HIV viral load is elevated during periods of crack cocaine use **independent of ART exposure**.

Objective: We sought to evaluate the effect of crack cocaine use frequency on HIV disease severity among HIV-positive PWUD

Methods

Design: We analyzed data from the ACCESS study, an open **prospective cohort** of HIV-positive people who use unregulated drugs.

Participants: Eligible participants were age 18 or older, HIV seropositive, reported recent use of unregulated drugs, and resided in the Greater Vancouver Regional District.

Measures: HIV disease severity was measured using the Veterans Aging Cohort Study (VACS) Index, which is a validated prognostic index.

Main analyses: Multivariable generalized linear mixed-effects models were used to estimate the independent effect of time-updated crack cocaine use frequency on HIV disease severity, adjusting for ART exposure and relevant confounders.

Sensitivity analyses: E-values were calculated to assess the potential influence of unmeasured confounders.

Results

- Between 2005 and 2018, **806 individuals** were recruited and contributed 8,537 observations.
- At baseline, the frequencies of crack cocaine use in the previous 180 days were: **none (23%), less than weekly (19%), weekly (28%), and daily or greater (30%)**.
- In multivariable models adjusted for ART exposure and other confounders, **daily or greater frequency of crack cocaine use was significantly associated with higher VACS Index scores** (β = 0.9, 95% confidence interval: 0.2, 1.6) as compared to none.
- E-values indicated that some model covariates (below) were **more robust to unmeasured confounding**

Sensitivity Analyses

Table S1. E-values of GLME estimates of frequency of crack cocaine use and other factors on VACS Index score

Covariate	Modeled Category	Multivariable β (95% CI)	E-value for β	E-value for 95% CI
Crack use	None (intercept)	24.0 (22.3, 25.6)		
	< Weekly (vs. none)	-0.1 (-0.7, 0.5)	1.12	1.00
	Weekly (vs. none)	0.3 (-0.4, 0.9)	1.21	1.00
	≥ Daily (vs. none)	0.9 (0.2, 1.6)	**1.43**	1.15
Sex	Male (vs. non-male)	-1.9 (-3.5, -0.2)	**1.76**	1.18
Age	Per year	0.8 (0.7, 0.8)	1.40	1.38
Ethnicity	White (vs. non-white)	0.1 (-1.4, 1.7)	1.12	1.00
IDU[a]	Yes (vs. no)	-0.2 (-0.7, 0.3)	1.17	1.00
Unstable housing[a]	Yes (vs. no)	1.0 (0.3, 1.6)	**1.47**	1.23
ART exposure[a]	Per 100 days	-5.0 (-5.4, -4.6)	**2.87**	2.70
MMT[a]	Yes (vs. no)	0.6 (-0.1, 1.3)	1.34	1.00
Incarcerated[a]	Yes (vs. no)	0.2 (-0.8, 1.1)	1.15	1.00
Binge alcohol use[a]	Yes (vs. no)	-0.6 (-1.1, 0)	1.32	1.02
Time since ART initiation	Per week	0 (-0.01, 0.01)	1.01	1.00

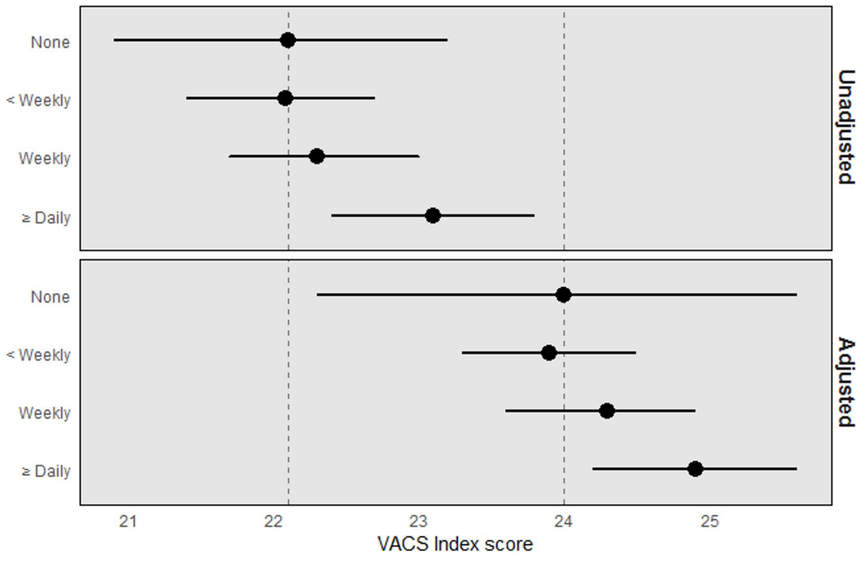
[a] Prior six months

Conclusions

- Daily or greater frequency of crack cocaine use was **significantly associated** with increased HIV disease severity independent of ART exposure and other sociodemographic, behavioral, social/structural, and clinical characteristics.
- The observed effect has important **implications** for **research and clinical care** of HIV-positive people who use crack cocaine.
- Future investigations should interrogate the potential **biological mechanisms** and **behavioral/socio-structural factors** that may **mediate** the relationship between crack cocaine use frequency and HIV disease severity.

Crack cocaine use frequency may influence HIV disease severity in a **dose-response manner**; additional confirmatory research is needed

Figure 1: VACS Index by frequency of crack cocaine use



All adjusted models are adjusted for age, sex at birth, ethnicity, injection drug use, unstable housing, engaging in methadone maintenance therapy, recent incarceration, binge alcohol use, weeks since ART initiation, and adherence to ART.

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