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SHORT REPORT

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# HCV cure: an appropriate moment to reduce cannabis use in people living with HIV? (ANRS CO13 HEPAVIH data)

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## Abstract

**Background:** Thanks to direct-acting antivirals, hepatitis C virus (HCV) infection can be cured, with similar rates in HCV-infected and HIV–HCV co-infected patients. HCV cure is likely to foster behavioral changes in psychoactive substance use, which is highly prevalent in people living with HIV (PLWH). Cannabis is one substance that is very commonly used by PLWH, sometimes for therapeutic purposes. We aimed to identify correlates of cannabis use reduction following HCV cure in HIV–HCV co-infected cannabis users and to characterize persons who reduced their use.

**Methods:** We used data collected on HCV-cured cannabis users in a cross-sectional survey nested in the ANRS CO13 HEPAVIH cohort of HIV–HCV co-infected patients, to perform logistic regression, with post-HCV cure cannabis reduction as the outcome, and socio-behavioral characteristics as potential correlates. We also characterized the study sample by comparing post-cure substance use behaviors between those who reduced their cannabis use and those who did not.

**Results:** Among 140 HIV-infected cannabis users, 50 and 5 had reduced and increased their use, respectively, while 85 had not changed their use since HCV cure. Cannabis use reduction was significantly associated with tobacco use reduction, a decrease in fatigue level, paying more attention to one's dietary habits since HCV cure, and pre-HCV cure alcohol abstinence ( $p = 0.063$  for alcohol use reduction).

**Conclusions:** Among PLWH using cannabis, post-HCV cure cannabis reduction was associated with tobacco use reduction, improved well-being, and adoption of healthy behaviors. The management of addictive behaviors should therefore be encouraged during HCV treatment.

**Keywords:** Cannabis, Marijuana, HIV, Hepatitis C, Sustained virological response, HCV cure, Smoking, Behavioral changes

## Introduction

In Western countries, AIDS is no longer the principal cause of death in people living with HIV (PLWH)

[1–3]. Accordingly, HIV infection can be considered a chronic disease [4] associated with multiple comorbidities in aging people. In contrast, recent medical advances in hepatitis C virus (HCV) infection, specifically direct acting antivirals (DAA), provide a quick cure [5], and represent an important turning point in HIV–HCV co-infected people's lives. This clinical change impacts quality of life [6–10] and foster behavioral changes [10, 11].

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As psychoactive substance use is highly prevalent in HIV–HCV co-infected patients [12–15], we may expect HCV cure to impact substance use behavior. The benefits of cannabis and cannabinoid use for HIV infection management and less severe treatment side-effects, are widely recognized [16, 17], and PLWH frequently report their therapeutic use [18–22]. However, cannabis use may also promote pulmonary disease [23] and cognitive impairments in PLWH [24]. As cannabis use [14, 15, 21] and cannabis dependence [25] are frequent in HIV–HCV co-infected patients, it is important to explore changes in use after HCV cure. Using data from a cross-sectional survey embedded in the ANRS CO13 HEPAVIH cohort, we aimed to identify correlates of cannabis use reduction following HCV cure in HIV–HCV co-infected cannabis users, and to characterize persons who reduced their use.

## Material and methods

### Study design and data collection

ANRS CO13 HEPAVIH is an ongoing French national multicenter prospective cohort of HIV–HCV co-infected patients. Initiated in 2005, it investigates clinical and socio-behavioral issues surrounding HIV–HCV coinfection [26]. A total of 1859 patients followed in 29 hospital wards throughout metropolitan France were included in the cohort between October 2005 and March 2016, in three consecutive phases. Designed and implemented in accordance with the Declaration of Helsinki, the cohort and nested surveys were approved by the ethics committee of Cochin University Hospital in Paris. Patients provided written informed consent to participate.

A cross-sectional survey nested in the ANRS CO13 HEPAVIH cohort was conducted between February 2018 and May 2019 to document patient-reported outcomes, with a focus on perceived changes after HCV cure. All patients enrolled in the cohort and still followed-up in participating clinical centers at the time of the survey were offered to participate. A self-administered questionnaire (SAQ) collected data. The cohort is observational, therefore counselling and advice potentially received by participants depended solely on their physician.

The SAQ included questions related to sociodemographic characteristics, HCV transmission mode, recent substance use, cannabis dependence using the Cannabis Abuse Screening Test (CAST) [27], and reason for using cannabis (therapeutic motive or not). Other questions asked about changes since HCV cure in patients' use of psychoactive substances (tobacco, cannabis, alcohol, other substances), physical activity, attention paid to dietary habits, and body weight gain. For questions documenting changes in substance use after HCV cure,

respondents had to choose one answer among the following four: “No, nothing has changed”, “Yes, my use has decreased”, “Yes, my use has increased”, “Not concerned (no use)”.

### Study population

The population of the present study included HCV-cured cannabis users who participated in the cross-sectional survey and answered the SAQ item documenting perceived changes in cannabis use after cure. Patients who answered that they were not concerned by cannabis use were excluded from analyses.

### Statistical analysis

First, descriptive statistics were used to present the study population's main characteristics. Comparisons were performed between patients who reported a reduction in cannabis use after HCV cure and those who did not (Chi-square test for categorical variables, Wilcoxon rank-sum test for continuous variables). Logistic regression models were then run to identify correlates of decreased cannabis use following HCV cure (study outcome). Socio-demographic variables and behavioral changes since HCV cure were tested as potential correlates. Only variables with a liberal  $p$ -value  $< 0.20$  in the univariable analyses were considered eligible for the multivariable model. The final multivariable model was built using a backward stepwise procedure. The likelihood ratio test ( $p < 0.05$ ) was used to define the variables to maintain in the final model.

Second, characteristics of substance use after HCV cure were compared between patients who reduced their cannabis use and those who did not using Chi-square tests. All statistical analyses were performed using SAS software version 9.4 for Windows (SAS, Cary, NC, USA).

## Results

Among the 448 survey participants, of the 421 HCV cured, two had no data on post-HCV cure changes in cannabis use. A total of 279 out of 419 patients reported no cannabis use (“Not concerned” answer) and were excluded from the analysis. The study population therefore comprised 140 individuals. Among them, 50 (35.7%) reported to have reduced their cannabis use after HCV cure, five had increased it, and 85 reported no change. The study sample mainly comprised men (74.3%), and median age was 55.7 years (Table 1). Six participants declared they quit cannabis.

Post-HCV cure decrease in cannabis use was associated with tobacco use reduction, pre-HCV cure alcohol

**Table 1** Study sample characteristics and factors associated with post-HCV cure cannabis use reduction (logistic regression model, ANRS HEPAVIH cohort, n = 140)

Variable	Total n (%)	Cannabis use reducers n (%)	Cannabis use non- reducers n (%)	p-value <sup>1</sup>	Univariable analyses			Multivariable analysis			
					OR	95% CI	p-value	aOR	95% CI	p-value	
Gender				0.730							
Male	104 (74.3)	38 (76.0)	66 (73.3)		1.15	0.52–2.56	0.730				
Female	36 (25.7)	12 (24.0)	24 (26.7)		1						
Age (median, [IQR]) (years)	55.7 [53.0–58.5]	56.1 [53.2–58.6]	55.4 [52.9–58.5]	0.995	1.00	0.93–1.07	0.984				
HCV transmission mode				0.123							
Drug injection	91 (65.0)	38 (76.0)	53 (58.9)		1						
Sexual transmission	23 (16.4)	6 (12.0)	17 (18.9)		0.49	0.18–1.37	0.173				
Other	26 (18.6)	6 (12.0)	20 (22.2)		0.42	0.15–1.14	0.089				
Change in tobacco use <sup>2</sup>				<0.001							0.014
No use	9 (6.4)	4 (8.0)	5 (5.6)		4.58	1.06–19.78	0.041	3.84	0.67–22.09	0.131	
Reduction	57 (40.7)	35 (70.0)	22 (24.4)		9.11	3.96–20.96	<0.001	4.32	1.58–11.78	0.004	
No reduction	74 (52.9)	11 (22.0)	63 (70.0)		1			1			0.003
Change in alcohol use <sup>2</sup>				<0.001							<0.001
No use	39 (27.9)	22 (44.0)	17 (18.9)		9.54	3.61–25.24	<0.001	7.71	2.39–24.87	<0.001	
Reduction	34 (24.3)	20 (40.0)	14 (15.6)		10.54	3.85–28.81	<0.001	3.32	0.94–11.72	0.063	
No reduction	67 (47.9)	8 (16.0)	59 (65.6)		1			1			
Change in other substance use <sup>2</sup>				0.004							
No use	108 (77.1)	35 (70.0)	73 (81.1)		1.20	0.43–3.35	0.730				
Reduction	11 (7.9)	9 (18.0)	2 (2.2)		11.25	1.86–68.13	0.008				
No reduction	21 (15.0)	6 (12.0)	15 (16.7)		1						
Changes in physical activity <sup>2</sup>				0.238							
Stable	85 (60.7)	26 (52.0)	59 (65.6)		1						0.244
Increase	39 (27.9)	16 (32.0)	23 (25.6)		1.58	0.72–3.47	0.256				
Reduction	16 (11.4)	8 (16.0)	8 (8.9)		2.27	0.77–6.70	0.138				
Changes in fatigue level <sup>2</sup>				0.021							0.073
Stable	63 (45.0)	15 (30.0)	48 (53.3)		1			1			
Reduction	63 (45.0)	30 (60.0)	33 (36.7)		2.91	1.36–6.23	0.006	3.12	1.15–8.46	0.025	
Increase	14 (10.0)	5 (10.0)	9 (10.0)		1.78	0.52–6.13	0.362	2.95	0.61–14.15	0.177	
Changes in dietary habits <sup>2</sup>				<0.001							0.045
Stable	92 (65.7)	21 (42.0)	71 (78.9)		1			1			
Paying more attention	40 (28.6)	25 (50.0)	15 (16.7)		5.64	2.52–12.59	<0.001	3.33	1.22–9.14	0.019	
Paying less attention	8 (5.7)	4 (8.0)	4 (4.4)		3.38	0.78–14.69	0.104	3.01	0.48–18.79	0.237	
Change in body weight <sup>2</sup>				0.073							
No change or reduction	84 (60.0)	24 (48.0)	60 (66.7)		1						

**Table 1** (continued)

Variable	Total n (%)	Cannabis use reducers n (%)	Cannabis use non- reducers n (%)	p-value <sup>1</sup>	Univariable analyses		Multivariable analysis	
					OR	95% CI	aOR	95% CI
Increase < 5 kg	33 (23.6)	14 (28.0)	19 (21.1)		1.84	0.80–4.25		0.153
Increase ≥ 5 kg	23 (16.4)	12 (24.0)	11 (12.2)		2.73	1.06–7.02		0.038

aOR: adjusted odds ratio; HCV: hepatitis C virus; IC: confidence interval; IQR: interquartile range

<sup>1</sup> Chi-square (categorical variables) or Wilcoxon rank-sum test (continuous variables)

<sup>2</sup> Self-reported post HCV-cure changes

**Table 2** Characteristics related to psychoactive substance use according to post-HCV cure reduction in cannabis use (cross-sectional survey nested in the ANRS CO13 HEPAVIH cohort, n = 140)

Variable	Total	Reduction in cannabis use after HCV cure		
		Yes	No	p-value <sup>1</sup>
Reason for using cannabis (n = 126)				0.324
Therapeutic	51 (40.5)	16 (34.8)	35 (43.8)	
Recreational only	75 (59.5)	30 (65.2)	45 (56.3)	
Recent substance injection <sup>2</sup>				0.454
No	139 (99.3)	50 (100.0)	89 (98.9)	
Yes	1 (0.7)	0 (0.0)	1 (1.1)	
Cannabis dependence (n = 129) <sup>3</sup>				0.904
No risk	64 (49.6)	22 (48.9)	42 (50.0)	
Low risk	65 (50.4)	23 (51.1)	42 (50.0)	
High risk	0 (0.0)	0 (0.0)	0 (0.0)	
Opioid substitution therapy (n = 133)				0.462
No	107 (80.5)	37 (77.1)	70 (82.4)	
Current therapy	26 (19.6)	11 (22.9)	15 (17.7)	
Cannabis use frequency (n = 126)				<0.001
Never	6 (4.8)	6 (13.0)	0 (0.0)	
Sometimes	51 (40.5)	29 (63.0)	22 (27.5)	
Regularly or daily	69 (54.8)	11 (23.9)	58 (72.5)	
Other substance use <sup>4</sup>				0.041
No	127 (90.7)	42 (84.0)	85 (94.4)	
One or more	13 (9.3)	8 (16.0)	5 (5.6)	
AUDIT-C score	2.5 [0–5]	2 [0–4]	3 [0–5]	0.245
Alcohol use <sup>5</sup>				0.068
Not at risk	78 (55.7)	33 (66.0)	45 (50.0)	
At risk	62 (44.3)	17 (34.0)	45 (50.0)	
Tobacco use (n = 138)				0.001
No current use	19 (13.8)	11 (22.9)	8 (8.9)	
1 to 5 cig/d	32 (23.2)	17 (35.4)	15 (16.7)	
6 to 10 cig/d	41 (29.7)	12 (25.0)	29 (32.2)	
More than 10 cig/d	46 (33.3)	8 (16.7)	38 (42.2)	

AUDIT-C: Alcohol Use Disorders Identification Test Concise; cig/d: cigarette per day

<sup>1</sup> Chi-square (categorical variables) or Wilcoxon rank-sum test (continuous variables)

<sup>2</sup> In the previous 4 weeks

<sup>3</sup> Cannabis dependence assessed by Cannabis Abuse Screening Test [27]. A score < 3 defined 'no risk', a score ≥ 3 and < 7 defined 'low risk', and a score ≥ 7 defined 'high risk'

<sup>4</sup> Any use of other substances (cocaine, heroin, crack, ecstasy, street Subutex, amphetamines, LSD, cathinone) in the previous 4 weeks

<sup>5</sup> At-risk use was defined as an AUDIT-C score ≥ 4 for men and ≥ 3 for women [42]

use abstinence ( $p=0.063$  for alcohol use reduction), a decrease in fatigue level and paying more attention to one's dietary habits (Table 1).

After HCV cure, regular or daily cannabis use was reported by most patients (54.8%), recreational use being predominant (59.5% of patients). No patient was at high risk of cannabis dependence (Table 2).

Those who reduced their cannabis consumption were more likely to use the drug less frequently, to have recently used other psychoactive substances (excluding

alcohol and tobacco) and to smoke fewer tobacco cigarettes after HCV cure ( $p=0.068$  for alcohol use) (Table 2).

## Discussion

In this study, approximately one third of PLWH reduced their cannabis use after being cured of HCV. This reduction was associated with a reduction in tobacco use, pre-HCV cure alcohol abstinence, a decrease in fatigue level, and paying greater attention to one's diet.

These results confirm previous findings that HCV cure is accompanied by behavioral changes, including changes in substance use [10, 11]. However, data on these changes are scarce [28], particularly in the HCV cure era, and especially for cannabis use, which is highly prevalent and partly motivated by therapeutic goals in PLWH.

Concomitant reduction in tobacco use is important for PLWH who reduce their cannabis use, as they are highly exposed to tobacco-related harms, a major morbidity and mortality risk factor in this population [29–31]. Cannabis and tobacco use frequently co-occur [32], especially in Europe [33]. Moreover, both drugs seem to reinforce each other [34, 35]. Accordingly, cannabis use impairs the chances of tobacco cessation [36], including in HIV–HCV co-infected people [15]. This phenomenon has also been documented for polysubstance use generally speaking [37, 38].

Our results suggest that HCV cure is an appropriate moment to engage in addictive behavior management, especially using a holistic approach for all substances. Our findings also suggest that lifestyle modifications post-HCV cure may include dietary changes. This is in line with studies showing that HCV cure is associated with increased self-care [39, 40], ability and motivation to plan for the future, self-confidence, and empowerment [40, 41]. However, our results also suggest that a reduction in cannabis (and tobacco) use in the PLWH population does not translate into abstinence.

We did not find any association between a therapeutic motive for cannabis use and post-cure reduction. However, participants who reduced their use were more likely to have experienced a decrease in their level of fatigue. This result suggests that the level of therapeutic benefit which HCV cure brings may only lead to a marginal reduction. Having said that, we cannot exclude reverse causality whereby the decrease in fatigue is the consequence of reduced cannabis use.

One of the study's main limitations is that it is based on self-reports. We also had no data on physicians' attitude and counselling regarding substance use after HCV cure. Moreover, we were not able to take into account the time since HCV cure in our models, and therefore the persistence of the observed reductions in use. However, our results still provide clues about the potential of using HCV treatment as a teachable moment for addiction treatment in PLWH.

## Conclusion

Among cannabis users living with HIV, post-HCV cure cannabis reduction was associated with tobacco use reduction, and approached significance for alcohol use reduction. The management of addictive behaviors should be emphasized during HCV treatment, and

further research is needed to explore the psychosocial mechanisms at play in smoking behaviors among PLWH, especially regarding cannabis use.

## Abbreviations

CAST: Cannabis abuse screening test; DAA: Direct acting antivirals; HCV: Hepatitis C virus; PLWH: People living with HIV; SAQ: Self-administered questionnaire.

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#### Authors' contributions

TB designed the study, analyzed the data, wrote the original draft and reviewed it. PM, PM, DZ, HA, LE, PS, DSC and PC designed the study and reviewed the manuscript. CL analyzed the data. FM designed the study, reviewed the manuscript and supervised this work. All authors read and approved the final manuscript.

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#### Availability of data and materials

The datasets generated and analysed during the current study are not publicly available due to personal data but are available from the corresponding author on reasonable request.

#### Declarations

##### Ethics approval and consent to participate

Designed and implemented in accordance with the Declaration of Helsinki, the cohort was approved by the ethics committee of Cochin University Hospital in Paris. Patients provided written informed consent to participate.

##### Consent for publication

Not applicable.

##### Competing interests

The authors declare that they have no competing interests.

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