



# Exposure to COVID-19 Pandemic-Related Stressors and Their Association With Distress, Psychological Growth and Drug Use in People With HIV in Nouvelle Aquitaine, France (ANRS CO3 AQUIVIH-NA Cohort-QuAliV-QuAliCOV Study)

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## Abstract

We investigated people living with HIV (PLWH)'s exposure to COVID-19 pandemic stressors and their association with distress, psychological growth, and substance use. PLWH in the ANRS CO3 AQUIVIH-NA cohort's QuAliV study (Nouvelle Aquitaine, France) completed an adapted CAIR Lab Pandemic Impact Questionnaire (C-PIQ) and reported substance use between 9/2021 to 3/2022. We described cumulative stressor exposure (score 0–16) and explored variation by PLWH characteristics (demographic, HIV-related, risk factors, psychosocial). Associations with distress (score 0–23), psychological growth (score 0–20), and substance use were assessed using regression models. Participants reported exposure to a median of 2 (IQR: 1–4) stressors. Stressor exposure was higher in working-age (<60) and psychosocially vulnerable PLWH. Exposure to an additional stressor correlated with a 0.7-point increase in distress scores (95% C.I. 0.5–1.0,  $p<0.001$ ), a 0.04-point increase (95% C.I. 0.01–0.07,  $p=0.002$ ) in psychological growth scores in working-age PLWH. In older PLWH, additional stressor correlated with a 0.8-point (95% C.I. 0.4–1.2,  $p<0.001$ ) increase in distress and a 0.1-point increase (95% C.I. 0.06–0.2,  $p=0.001$ ) in growth scores. Each additional stressor was associated with 1.2 (95% C.I. 1.0–1.4,  $p=0.02$ ) higher adjusted odds of cannabis use in working-age PLWH, and 1.2 (95% C.I. 1.0–1.4,  $p=0.004$ ) higher adjusted odds of drug use. Exposure to stressors was linked to increased distress, cannabis and drug use but also growth. Providers should not only be aware of risk (of severe COVID-19) but also be mindful of the social and psychological challenges PLWH face as these may affect their retention in care, especially during challenging times.

**Keywords** HIV · COVID-19 · Distress · Psychological growth · Cannabis · Drugs

## Introduction

In March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic, prompting public health responses to contain the spread of the SARS-COV-2 virus and prevent healthcare systems from being overwhelmed [1]. Measures such as closing borders, mandating social distancing, imposing lockdowns, and halting non-essential activities were crucial for containing the virus' spread but they were also distressing for populations [2]. By May 2020, the WHO had already acknowledged the pandemic's impact

on mental health and urged countries to consider it as part of their response [3, 4].

The pandemic, including measures taken to mitigate its spread, was a period marked by fear and uncertainty, during which people were socially distanced from their communities: those who share their interests, goals and values. Their mental health, defined as their ability to cope with the stresses of life, fulfil their potential, and contribute to their communities, was affected by these unprecedented circumstances [5]. While early studies worldwide revealed that the period exacerbated feelings of loneliness, anxiety, and depression [6–8], positive outcomes were also noted [9–11]. It was posited that in response to pandemic-related adversity or trauma some individuals would demonstrate resilience,

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adapting to the circumstances, while others might even experience psychological growth – developing a positive or renewed outlook on life [12, 13]. Finally, individuals may cope by smoking, drinking and using drugs [4, 14–17]. Or, on the contrary, restrictions may have hampered access to certain drugs and/or opportunities to use them, resulting in decreased use [18].

While the pandemic was ubiquitous, certain populations experienced the period more acutely than others. People living with HIV (PLWH), a heterogeneous group, may have been uniquely affected. First, they depend on medical/hospital-based care, which may have been disrupted by the pandemic [19–21], and second, they may be at greater risk of psychological distress and substance use due to fear of the disease for themselves and/or their loved ones [20, 22, 23] as well as their risk of developing severe COVID-19 [24], underlying psychosocial vulnerability [25] and history of substance use [26, 27]. That said, PLWH who have spent decades coping with the physical, psychological, and social challenges associated with their condition may be particularly resilient in the face of the pandemic [28–30].

We aimed to investigate how PLWH in Nouvelle Aquitaine, France – one of the vastest regions geographically—experienced the pandemic and whether exposure to pandemic-related adversity, hereafter referred to as “stressors”, was associated with greater pandemic-related distress, psychological growth, and substance use. We describe exposure to pandemic-related stressors overall and according to PLWH’s characteristics, exploring whether cumulative pandemic-related stressor exposure varied by individuals’ demographic or disease-related characteristics, their risk of severe COVID-19 and/or psychosocial vulnerability. We then assess the correlation between pandemic-related stressor exposure and pandemic-related distress, psychological growth and its association with smoking, problem drinking, cannabis and drug use.

## Methods

### Study Design

We conducted a cross-sectional survey (QuAliCOV) from September 2021 to March 2022 within the ANRS CO3 AQUIVIH-NA cohort to evaluate how PLWH experienced and were affected by the pandemic period. The ANRS CO3 AQUIVIH-NA cohort is a prospective, hospital-based cohort of adults ( $\geq 18$  years old) with an HIV-1 diagnosis in outpatient care at 15 internal/infectious disease departments in Nouvelle Aquitaine, France. Clinical Research Associates (CRAs) abstract clinical and epidemiological data from medical records and enter them in an electronic Case Report Form (eCRF) [31]. Laboratory data are transferred directly from

information systems or entered by CRAs. In addition to routinely-collected clinical, epidemiological and laboratory data, patient-reported outcomes including quality of life have been collected since 2018 via the QuAliV study, a repeated cross-sectional study conducted within the ANRS CO3 AQUIVIH-NA cohort [32, 33]. Cohort participants in participating centers are invited to complete a standardized questionnaire comprised of a battery of validated questionnaires following their regular outpatient consultation via a dedicated patient interface. Those without a secure Internet or personal e-mail are provided with an identical paper questionnaire and prepaid envelope. The cross-sectional QuAliCOV survey was launched in conjunction with the second wave of the QuAliV survey in a sub-sample of those who had completed the first wave of the QuAliV survey prior to the COVID-19 pandemic.

### Setting

The QuAliV study was ongoing at the beginning of the pandemic in six centers located in Bordeaux, Bayonne, Périgueux, and Agen. Participant recruitment varied based on their previous engagement with the QuAliV study (electronic versus analog questionnaire). Those who had completed an electronic baseline assessment received an email invitation to complete the QuAliCOV and QuAliV 2 surveys. Non-respondents were contacted by a CRA for assistance or offered a paper questionnaire at their next outpatient consultation. Those who had completed an analog assessment were contacted by phone and offered a paper questionnaire by mail or at their next outpatient consultation. Participants returned completed questionnaires by mail or in person. A CRA entered the responses into the eCRF.

### Participants

We considered the target population, those for whom the findings of the study are intended to apply or be generalized, to be all individuals actively followed (at least one consultation or hospitalization recorded) in participating centers between January 1, 2018 and December 31, 2022. Cohort/QuAliV study participants who had completed a baseline assessment before the first pandemic-associated lockdown (April 1, 2020) were considered eligible for the QuAliCOV survey if they were still alive and in care in participating centers. We considered those who voluntarily completed the QuAliCOV survey between September 1, 2021, and March 15, 2022 to be eligible for this analysis.

## Measures

### Outcomes

We adapted and translated the Complementary and Integrative Research (CAIR) Lab Pandemic Impact Questionnaire (C-PIQ) [34, 35], a 28-item measure assessing both COVID-19 exposure and COVID-19-related distress and psychological growth, presented in Annex 1. The C-PIQ combines the Coronavirus Stressor Survey [36], a 10-item measure of COVID-19-related stressors and the respondent's perceived impact of the pandemic, the CoRonavIruS Health Impact Survey (CRISIS), a questionnaire covering key domains relevant to mental distress and resilience during the pandemic [37], and the Posttraumatic Growth Inventory, a 21-item measure capturing the degree of the positive changes experienced in the aftermath of a traumatic event [38].

*COVID-19-related distress* was assessed via 6 items covering (i) consuming media about COVID-19, (ii) worrying about health, (iii) stressfulness of changes in social contacts, (iv) stressfulness of changes in one's life, (v) worsening of emotional/mental health and (vi) sleep disorders since the beginning of the pandemic. Items were rated on a five-point scales, except for the sleep-related item, which was rated on a four-point scale. Summed items yielded a total score ranging from 0 (best) to 23 (worst). *COVID-19-related psychological growth* was evaluated via 5 items comprising (i) strengthened relationships with others, (ii) new possibilities, (iii) awareness of personal strengths, (iv) spiritual change, and (v) increased appreciation of life. Items were rated on a five-point scales. Summed items resulted in a score ranging from 0 (worst) to 20 (best). Smoking, alcohol, cannabis, and drug use (poppers, cocaine, amphetamines/ecstasy/MDMA/methamphetamines, opiates, synthetic cathinone, GHB/GBL or synthetic cannabinoids) were self-reported via the QuAliv study using the Alcohol Use Disorders Identification Test (AUDIT-C), and Cannabis Abuse Screening Test (CAST) [32, 39, 40]. Other drug use in the past 12 months was collected via a single question on use of "other drugs to feel better or get high".

### Exposure

Stressors like "becoming ill with COVID-19", "being hospitalized due to COVID-19 infection", "job puts one at increased risk of exposure to COVID-19" or "difficulty getting food, medication, medical help or other necessities due to COVID-19 pandemic" (Annex I) were assessed separately depending on whether they were experienced by the respondent directly or by a loved one. Responses were dichotomously coded (yes/no). Each stressor, whether experienced by the respondent or their loved one was

attributed 1 with the exception of "death of a loved one due to COVID-19" which was attributed 2, resulting in a score ranging from 0 (exposed to no stressors) to 16 (exposed to all stressors).

### Other Variables

Demographic and epidemiological variables included age, sex (male or female), birthplace (France or elsewhere), mode of HIV acquisition (men who have sex with men [MSM], heterosexual contact, IV drug use or other). Disease-related variables included duration of HIV infection (< 5, 5–10, 10–15, 15+ years), Centers for Disease Control and Prevention (CDC) clinical categories for HIV and history of Hepatitis Virus C and B (HCV/HBV) co-infection, viral load (copies/mL) and CD4 count ( $\text{mm}^3$ ) (recorded in the 2 year prior to the QuAlivCOV assessment). Individual risk factors for severe COVID-19 were defined as the diagnosis/occurrence of at least one of the following: hypertension, cardiovascular disease, diabetes (since the beginning of follow-up), immunodepression (CD4 cell count < 200  $\text{mm}^3$ ) or obesity (Body Mass Index  $\geq 30$  in the two years before study period). Hypertension was defined as a systolic blood pressure  $\geq 140$  mm/Hg or diastolic blood pressure  $\geq 90$  mm/Hg for two consecutive visits (SBP  $\geq 130$  mm/Hg or DBP  $\geq 80$  mm/Hg in diabetics) or at least one antihypertensive treatment. Cardiovascular disease was defined as the diagnosis/occurrence of a myocardial infarction or a central nervous system vasculitis. Diabetes was defined as the diagnosis/occurrence of diabetes or at least 2 consecutive blood glucose measurements  $\geq 7$  mmol/L or at least one treatment with hypoglycemics or insulin.

Participants' underlying psychosocial vulnerability included hardship, prior depressive disorder and perceived HIV-related stigma. Hardship was determined based on responses to the Evaluation de la précarité et des inégalités de santé dans les Centres d'examen de santé or EPICES questionnaire, a multidimensional 11-item measure of individual social and economic hardship [41]. Baseline (prior to the pandemic (2018–2020)) depressive disorder was defined as a PHQ-9 score of  $\geq 10$ . The PHQ-9 is a validated 9-item self-report questionnaire that assesses the severity of depressive symptoms over the previous two weeks, with scores ranging from 0 to 27 [42]. A score of  $\geq 10$  indicates moderate to severe depressive symptoms. Perceived HIV-stigma was evaluated with the question: "To what extent are you bothered by people blaming you for your HIV status?". If participants responded "not at all", "a little"/"a moderate amount", or "very much"/"an extreme amount", we assumed that they experienced "none", "moderate" or "severe" HIV-stigma respectively.

## Study Size

We considered 374 participants who completed a QuAliCOV questionnaire.

## Statistical Analyses

We conducted analyses in STATA 16©. We explored missingness and performed Multivariate Imputation by Chained Equations [43] to address missing values of stressors score (proportions of missingness by item are presented in Annex 2), assuming that data were Missing-At-Random. We created 10 imputed datasets using logistic and linear regression models including age, sex and mode of HIV acquisition as independent variables. All subsequent analyses were performed on imputed datasets.

We compared participants' demographic/ epidemiological characteristics to those of participants actively followed up within the same centers of the ANRS CO3 Aquitaine-AQUIVIH-NA Cohort. Since participation in the survey was voluntary, we examined whether participants' demographic and epidemiological characteristics were similar to those who were eligible as well as PLWH followed in the same centers (target population). Frequencies and proportions were calculated for categorical variables and medians with the 1st and 3rd quartiles for continuous variables. We described the proportion of stressors experienced according to individual characteristics. We calculated median pandemic-related stressor exposure as well as pandemic-related distress and psychological growth scores. We created a dichotomous variable for smoking classifying individuals as either non-smoking/non-daily smoking or as nicotine dependent smokers. We created a dichotomous variable for alcohol use, classifying participants as either non-drinkers/no misuse (AUDIT-C Score < 3 for women and < 4 for men) or problem drinkers/alcohol use disorder (AUDIT-C Score  $\geq$  3 for women and  $\geq$  4 for men). Cannabis and other drugs use in the past 12 months was dichotomized as non-user versus user. Similarly, we described the number and frequency of smoking, drinking and drug use overall and by individual characteristics. We explored whether exposure to stressors and outcomes varied according to individual characteristics, using the Kruskal–Wallis equality-of-populations rank test for continuous and the Chi-square test for categorical variables. We then assessed the correlation between stressor exposure and pandemic-related distress, adjusting for pre-pandemic depressive disorder and HIV-related stigma, using linear regression. We assessed the correlation between stressors and psychological growth using zero-inflated Poisson regression to account for the negative binomial distribution of the outcome. Both analyses were stratified by age ( $\geq$  60 versus < 60). Finally, we examined the association between stressors and smoking, alcohol misuse,

cannabis, and drug use using bivariable and multivariable logistic regression. We assessed the association between stressors and cannabis use in younger and older PLWH, adjusting for prior depressive disorder and HIV-related stigma, and investigated the association between stressors and other drug use, adjusting for age.

## Results

### Participant Characteristics

Of the 1,116 eligible PLWH, we considered 374 who had completed the QuAliCOV survey between September 1, 2021 and March 15, 2022 for this analysis (Fig. 1). Compared to those in regular follow-up in participating centers (target population), they were older, more likely to be in care at a university/teaching (versus regional hospital) and born in France (versus abroad). Their clinical characteristics were otherwise similar (Annex 3). Seventy-six percent were men, aged 58 years old (yo) on average, and had been living with HIV for a median of 24 years. Nearly all were on ART and 95.7% were undetectable (HIV RNA < 50 copies/mL). Most had at least one risk factor for severe COVID-19 (78.1%), half were experiencing hardship (50.2%), a quarter reported pre-pandemic depressive disorder (25.8%), and 23.4% reported moderate/severe HIV-related stigma.

### Exposure to COVID-19-related Stressors

We describe COVID-19-related stressors exposure and median stressor-score by participants' characteristics in Fig. 2. Overall, the most commonly reported stressor was a loved-one having COVID-19 (51.3%) followed by having a job which put one at risk of COVID-19 exposure (28.9%). The least common (0.8%) was being hospitalized for COVID-19. Participants were exposed to a median of 2 stressors [IQR: 1–4], with younger individuals, those with no risk factors for severe COVID-19, pre-pandemic depressive disorder and HIV-related stigma reporting significantly higher cumulative exposure compared to their counterparts ( $\chi^2 = 10.86$   $p < 0.001$ ,  $\chi^2 = 5.28$   $p = 0.03$ ,  $\chi^2 = 6.14$   $p = 0.01$  and  $\chi^2 = 6.28$   $p = 0.04$  respectively).

### Pandemic-related Distress and Personal Growth and Substance Use

Pandemic-related distress and psychological growth scores and drug use are presented according to participant characteristics in Table 1 and Table 2 respectively. Participants reported a median distress score of 9 [6–13] and a median growth score of 3 [0–8]. One third of participants reported a growth score of zero, meaning no change

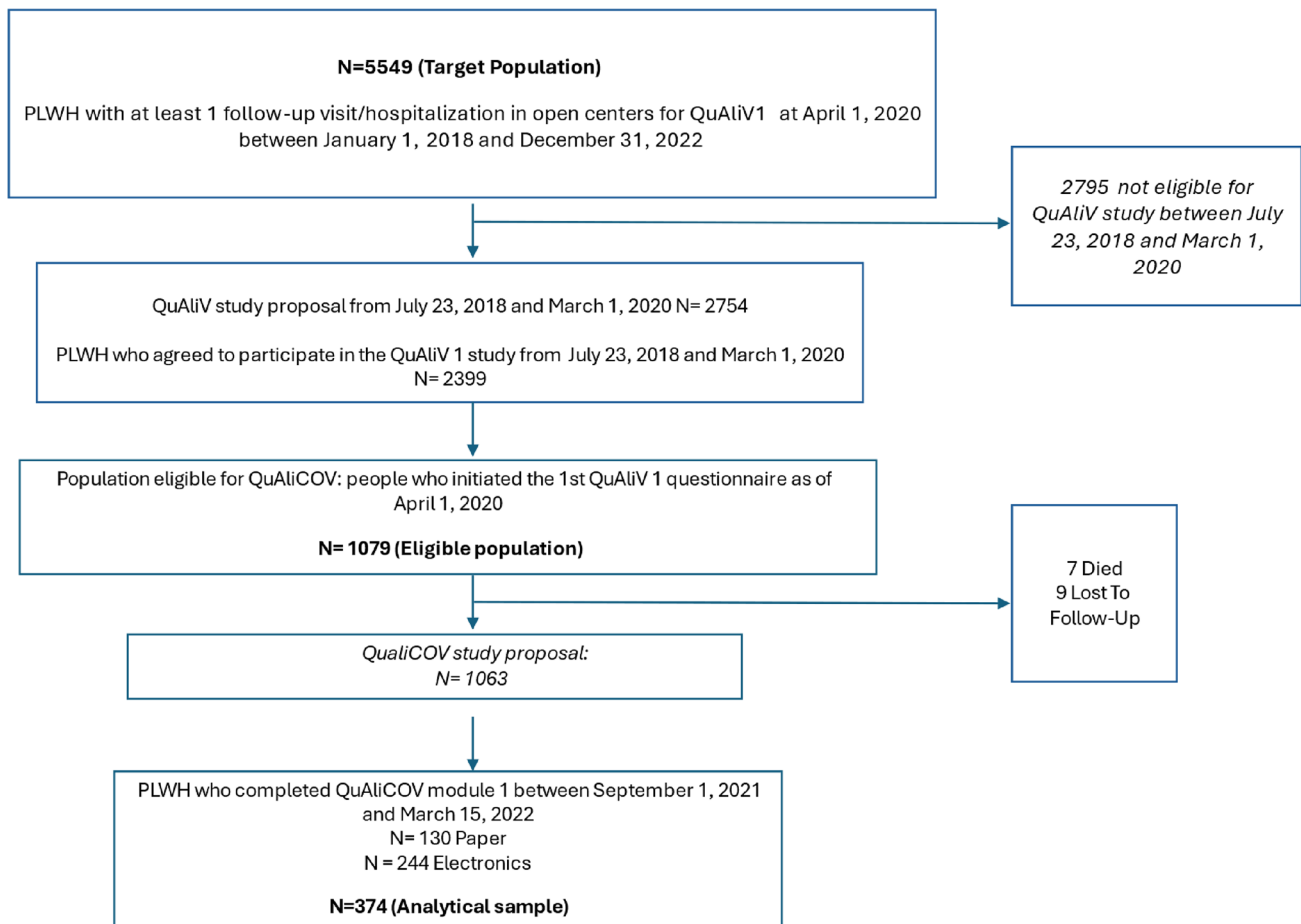


Fig. 1 Flowchart

occurred in their psychological growth. Individuals who were depressed or perceived HIV-related stigma before the pandemic had significantly higher distress scores compared to their counterparts (12 [9–16] of median distress score among participants with depressive syndrome versus 8 [5–12] among participants with no baseline depressive syndrome,  $\chi^2 = 32.10$   $p < 0.001$ ; 12 [8–16] median distress score among participant reporting severe HIV-related stigma, 11 [7–15] among participants reporting moderate, versus 9 [6–12] among participants reporting none,  $\chi^2 = 16.49$   $p < 0.001$ ), while PLWH who were not experiencing hardship had higher growth scores compared to those who were (4 [1–9] versus 2 [0–5] respectively,  $\chi^2 = 6.34$   $p = 0.01$ ). Overall, among the 374 participants, 28.3% reported smoking, 60.4% problem drinking/dependency, 19.0% cannabis and 12.8% other drugs use (Table 2). Smoking and other drug use were more frequent in younger PLWH and smoking, problem drinking/dependency, and cannabis use were more frequent in psycho-socially vulnerable PLWH.

### Association of Stressors and Distress, Growth, and Substance Use

For each additional stressor reported, participants experienced a 0.8-point increase in distress score (95%CI: 0.6–1.0,  $p < 0.001$ ). This effect remained consistent across age groups after adjustment for psychosocial vulnerability. For each additional stressor reported, participants experienced a 0.1-point increase in psychological growth score (95%CI: 0.04–0.08,  $p < 0.001$ ). This effect was consistent in both younger and older PLWH. While we found no association between cumulative stressor exposure and either smoking or problem drinking/dependency, for each additional stressor reported, the odds of cannabis and drug use increased by 20%. After stratifying by age and adjusting for psychosocial vulnerability, the crude association of stressor exposure and cannabis use was no longer present in older PLWH but remained significant in younger PLWH (adjusted Odds Ratio (aOR) 0.9 95%CI: 0.6–1.0,  $p = 0.39$  and aOR 1.2

			Happened to me							Happened to someone close to me							Covid-related stressors score			
			N (%)	Became ill with Covid-19 symptoms	Hospitalized for Covid-19	Professional risk of Covid-19 exposure	Lost job or income	Struggled with responsibilities at home	Issues accessing necessities (foods, medicines...)	Strained relationships with family, friends	Became ill with Covid-19	Hospitalized for Covid-19	Died of complications of the Covid	Professional risk of Covid-19 exposure	Lost job or income	Struggled with responsibilities at home	Struggled accessing necessities (foods, medicines...)	Strained relationships with family, friends	Median Stressor Score [IQR]	P-value <sup>1</sup>
Overall			374	16.4	0.8	20.1	8.3	5.2	13.7	21.8	51.3	16.0	6.9	28.9	14.1	11.7	8.6	19.9	2 [1-4]	
Sex	Male	285 (76.2)	17.1	1.1	20.1	8.6	4.6	12.6	21.0	53.8	17.5	6.9	29.9	13.8	13.2	9.0	19.7	2 [1-4]	0.31	
	Female	89 (23.8)	13.9	0.0	20.0	7.1	7.1	17.5	24.4	42.3	11.1	7.0	25.3	15.2	6.5	6.9	20.6	2 [0-3]		
Age (years)	<60	200 (53.5)	19.6	1.5	29.9	13.7	7.1	17.2	25.0	55.3	19.4	8.2	30.7	20.2	15.0	11.5	23.4	2 [1-5]	<0.001	
	≥60	174 (46.5)	12.7	0.0	8.5	1.8	3.0	9.6	18.0	46.6	12.1	5.4	26.8	6.9	7.7	5.1	15.7	1 [0-3]		
Acquisition mode	MSM	192 (51.3)	19.0	1.1	25.8	9.6	4.2	9.7	25.3	54.5	17.9	7.3	29.4	15.2	15.4	7.7	23.1	2 [1-4]	0.25	
	Heterosexual	117 (31.3)	10.3	0.0	16.2	6.3	4.4	14.7	17.1	49.5	14.6	5.3	29.6	9.9	6.1	9.3	15.6	2 [0-3]		
	IV drug use	41 (11.0)	17.5	0.0	7.9	7.5	7.5	25.0	23.1	32.5	12.5	10.5	23.7	17.5	12.5	12.8	21.6	1 [0-4]		
	Other	24 (6.4)	21.7	1.0	13.0	8.3	12.5	21.7	13.0	65.2	13.0	4.8	30.4	17.4	4.6	4.8	9.1	2 [1-3]		
Duration of HIV infection (years)	<5	123 (3.5)	38.5	7.7	23.1	15.4	0.0	7.7	30.8	69.2	38.5	0.0	23.1	25.0	16.7	0.0	33.3	3 [1-6]	0.12	
	5-10	44 (11.8)	28.6	4.8	38.1	13.6	9.3	9.5	25.0	67.5	27.5	10.8	31.6	13.2	21.1	5.4	29.0	3 [1-6]		
	10-15	42 (11.2)	12.5	0.0	29.0	15.4	15.4	26.3	27.5	40.5	9.8	5.1	21.6	20.0	21.1	10.8	15.8	2 [1-4]		
	15+	275 (73.5)	14.0	0.0	15.9	6.0	3.3	12.8	19.9	49.6	14.1	7.0	29.8	12.8	8.6	9.1	18.5	2 [0-3]		
AIDS	No	226 (60.8)	18.8	0.9	22.1	11.8	5.9	12.9	19.5	53.1	17.3	6.0	28.3	15.9	13.1	7.4	19.3	2 [1-4]	0.63	
	Yes	146 (39.3)	12.9	0.7	17.3	2.9	4.2	15.1	25.0	48.6	14.3	8.5	30.2	11.6	9.6	10.5	20.9	2 [0-4]		
Severe Covid-19 risk factor <sup>2</sup>	No	82 (21.9)	20.0	2.5	37.5	12.5	4.9	15.0	23.5	65.3	16.9	8.2	32.9	25.0	14.5	5.4	16.0	2 [1-5]	0.03	
	Yes	292 (78.1)	15.4	0.4	15.1	7.1	5.3	13.3	21.3	47.5	15.8	6.6	27.7	11.0	10.9	9.4	21.0	2 [0-3]		
Hardship <sup>3</sup>	No	144 (49.8)	13.4	0.7	20.7	4.3	2.8	8.6	20.4	59.4	16.1	7.3	31.4	12.8	10.8	7.9	16.7	2 [1-3]	0.79	
	Yes	145 (50.2)	19.3	1.4	20.7	12.9	8.6	20.2	20.9	45.4	16.5	5.9	28.6	13.9	13.3	8.1	22.4	2 [0-4]		
Depressive disorder <sup>4</sup>	No	256 (74.2)	15.0	0.8	19.7	7.3	3.2	7.8	17.3	52.1	16.7	7.2	28.7	13.8	11.4	5.1	15.0	2 [1-3]	0.01	
	Yes	89 (25.8)	19.8	1.1	25.6	11.5	12.5	32.2	36.1	50.0	15.3	8.5	28.4	14.6	13.8	18.2	35.1	3 [1-6]		
HIV Stigma	None	233 (76.6)	15.4	1.3	18.2	7.1	2.5	9.4	16.5	49.4	16.0	6.5	28.2	12.6	10.5	7.1	14.8	2 [1-3]	0.04	
	Moderate	37 (12.2)	19.7	0.0	24.6	14.1	9.1	20.3	30.8	56.9	16.9	13.8	26.7	21.7	17.5	13.8	28.1	3 [1-6]		
	Severe	34 (11.2)	17.0	0.0	21.7	4.2	12.2	22.9	35.4	55.6	17.0	2.1	33.3	8.5	8.5	8.9	34.0	2 [1-5]		

<sup>1</sup> Kruskal Wallis test<sup>2</sup> Defined as diabetes, hypertension, cardiovascular disease, CD4 count <200mm<sup>3</sup> or BMI ≥30<sup>3</sup> Hardship : EPICES, an individual and quantitative scale based on 11 questions regarding material and social problems (Deprived = Score ≥30)<sup>4</sup> Baseline PHQ-9 ≥10**Fig. 2** Description of COVID-19-related stressors exposure and median stressor score by individual characteristics (N = 374)

95%CI: 1.1–1.5,  $p=0.009$  respectively), whereas the association between stressor exposure and other drugs use was consistent after adjusting for age (aOR = 1.2 95%CI: 1.0–1.3,  $p=0.03$ ) (Table 3).

## Discussion

In this study, we provided evidence of PLWH's exposure to common pandemic-related stressors and their association with distress, psychological growth and cannabis and other

drugs use. Although, on average, exposure to pandemic-related stressors was relatively low, it was nevertheless associated with negative outcomes. There was also evidence that some PLWH experienced pandemic-related psychological growth. While the effect was relatively small, it was also positively correlated with exposure to stressors.

Unlike most studies which were conducted during the first months of the pandemic, our findings reflect the first three waves of the pandemic, offering a comprehensive view of its effects on an older, largely virologically-suppressed population of PLWH engaged in outpatient hospital-based care.

**Table 1** Median COVID-19-related distress and psychological growth, by individual characteristics

Characteristics	N (%)	Distress score <sup>a</sup> Median [Interquar- tile Range IQR]	p-value <sup>b</sup>	Growth score <sup>a</sup> Median [Interquar- tile Range IQR]	p-value <sup>b</sup>
<b>All participants</b>	<b>374</b>	<b>9 [IQR 6–13]</b>		<b>3 [IQR 0–8]</b>	
<b>Demographic-epidemiologic characteristics</b>					
Sex			0.48		0.10
Male	285 (76.2)	9 [6–13]		3 [0–7]	
Female	89 (23.8)	10 [6–13]		4 [0–9]	
Age (years)			0.52		0.61
< 60	200 (53.5)	9 [6–13]		3 [0–8]	
≥ 60	174 (46.5)	9 [6–12]		3 [0–7]	
HIV acquisition mode			0.19		0.37
MSM—Bi	192 (51.3)	9 [7–14]		3 [0–8]	
Heterosexual	117 (31.3)	9 [5–12]		3 [1–8]	
IV Drug use	41 (11.0)	10 [7–12]		1 [0–5]	
Other	24 (6.4)	8 [5–13]		2 [0–7]	
<b>HIV-related characteristics</b>					
Duration of HIV infection (years)			0.39		0.32
< 5	13 (3.5)	10 [8–17]		4 [2–8]	
5–10	44 (11.8)	9 [7–14]		3 [2–9]	
10–15	42 (11.2)	10 [7–14]		3 [1–9]	
15 +	275 (73.5)	9 [6–13]		3 [0–7]	
Last viral load < 50 copies	357 (95.7)	9 [6–13]	0.15	3 [0–8]	0.74
Last CD4 count < 200 mm <sup>3</sup>	1 (0.3)	-	-	-	-
AIDS	146 (39.3)	9 [7–13]	0.74	3 [0–8]	0.32
Past HCV infection	76 (20.8)	9 [5–12]	0.43	1 [0–6]	0.08
Past HBV infection	27 (7.5)	11 [7–15]	0.17	3 [1–5]	0.74
<b>Comorbidities</b>					
Diabetes	62 (16.6)	9 [5–13]	0.88	2 [0–5]	0.25
Hypertension	279 (74.6)	9 [6–13]	0.45	3 [0–6]	0.21
Cardiovascular disease	56 (15.0)	8 [5–13]	0.41	1 [0–6]	0.13
Body Mass Index ≥ 30	45 (12.5)	10 [7–14]	0.69	4 [1–9]	0.29
<b>Underlying risk and vulnerabilities</b>					
Risk factor for severe COVID-19 <sup>c</sup>			0.61		0.37
No	82 (21.9)	9 [6–12]		4 [1–8]	
Yes	292 (78.1)	9 [6–13]		3 [0–7]	
Hardship <sup>d</sup>			0.22		0.01
No	144 (49.8)	10 [7–13]		4 [1–9]	
Yes	145 (50.2)	9 [5–13]		2 [0–5]	
Depressive syndrome <sup>e</sup>			< 0.001		0.37
No	256 (74.2)	8 [5–12]		3 [0–8]	
Yes	89 (25.8)	12 [9–16]		3 [0–6]	
HIV Stigma			< 0.001		0.61
None	233 (76.6)	9 [6–12]		3 [0–8]	
Moderate	37 (12.2)	11 [7–15]		2 [0–6]	
Severe	34 (11.2)	12 [8–16]		3 [0–6]	

Bold value indicate values for all participants

<sup>a</sup>COVID-19-related distress score range from 0 (better) to 23 (worse)/Growth score range from 0 (worse) to 20 (better)

<sup>b</sup>Kruskal Wallis X<sup>2</sup> statistical test

<sup>c</sup>Individual risk factors were identified if the patient was presented with any of the following comorbidities: diabetes, hypertension, cardiovascular disease, CD4 count < 200 mm<sup>3</sup> or BMI ≥ 30

<sup>d</sup>Hardship: EPICES, an individual and quantitative scale based on 11 questions regarding material and social problems (Hardship = Score ≥ 30)

<sup>e</sup>Baseline PHQ-9 ≥ 10

**Table 2** Description of tobacco, alcohol, cannabis and other drug use, by individual characteristics

Characteristics	N (%)	Tobacco <sup>a</sup> n (%)	p-value <sup>b</sup>	Alcohol <sup>a</sup> n (%)	p-value <sup>b</sup>	Cannabis <sup>a</sup> n (%)	p-value <sup>b</sup>	Other drugs <sup>a</sup> n (%)	p-value <sup>b</sup>
All	<b>374</b>	<b>83 (28.3)</b>		<b>226 (60.4)</b>		<b>54 (19.0)</b>		<b>35 (12.8)</b>	
<b>Demographic-epidemiologic characteristics</b>									
Sex			0.16		0.07		0.70		0.003
Male	285 (76.2)	67 (30.5)		165 (57.9)		40 (18.5)		34 (16.1)	
Female	89 (23.8)	16 (21.9)		61 (68.5)		14 (20.6)		1 (1.6)	
Age (years)			0.002		0.19		0.34		0.02
< 60	200 (53.5)	56 (36.1)		127 (63.5)		33 (21.0)		26 (17.2)	
≥ 60	174 (46.5)	27 (19.6)		99 (56.9)		21 (16.5)		9 (7.4)	
HIV acquisition mode			0.004		0.82		< 0.001		0.001
MSM—Bi	192 (51.3)	48 (31.2)		116 (60.4)		24 (16.3)		29 (20.1)	
Heterosexual	117 (31.3)	16 (17.8)		70 (59.8)		8 (9.2)		1 (1.3)	
IV Drug use	41 (11.0)	14 (51.9)		27 (65.9)		19 (63.3)		3 (10.0)	
Other	24 (6.4)	5 (22.7)		13 (54.2)		3 (15.0)		2 (9.5)	
<b>HIV-related characteristics</b>									
Duration of HIV infection (years)			0.45		0.12		0.78		0.004
< 5	13 (3.5)	5 (45.5)		5 (38.5)		3 (25.0)		3 (25.0)	
5–10	44 (11.8)	11 (29.7)		32 (72.7)		7 (20.0)		10 (30.3)	
10–15	42 (11.2)	6 (20.0)		27 (64.3)		4 (12.9)		4 (13.8)	
15+	275 (73.5)	61 (28.4)		162 (58.9)		40 (19.4)		18 (9.1)	
Last viral load < 50 copies	357 (95.7)	80 (28.7)	0.56	218 (61.1)	0.17	52 (19.1)	0.94	32 (12.2)	0.14
Last CD4 count < 200mm <sup>3</sup>	1 (0.3)	—	—	—	—	—	—	—	—
AIDS	146 (39.3)	27 (24.6)	0.30	83 (56.9)	0.29	23 (21.5)	0.42	10 (9.5)	0.19
Past HCV infection	76 (20.8)	25 (46.3)	0.001	48 (63.2)	0.51	26 (44.8)	< 0.001	10 (17.2)	0.24
Past HBV infection	27 (7.5)	4 (17.4)	0.24	14 (51.9)	0.36	4 (20.0)	0.96	4 (20.0)	0.29
<b>Comorbidities</b>									
Diabetes	62 (16.6)	7 (14.9)	0.03	40 (64.5)	0.52	6 (14.3)	0.40	2 (5.0)	0.11
Hypertension	279 (74.6)	52 (24.9)	0.04	166 (59.5)	0.53	32 (15.8)	0.03	23 (12.0)	0.56
Cardiovascular disease	56 (15.0)	11 (26.3)	0.74	30 (53.6)	0.26	5 (13.2)	0.32	4 (10.8)	0.69
Body Mass Index ≥ 30	45 (12.5)	9 (23.1)	0.46	23 (51.1)	0.17	3 (8.1)	0.06	2 (5.9)	0.21
<b>Underlying risk and vulnerabilities</b>									
Risk factor for severe COVID-19 <sup>c</sup>			0.24		0.26		0.17		0.37
No	82 (21.9)	24 (33.8)		54 (65.9)		17 (24.6)		11 (15.9)	
Yes	292 (78.1)	59 (26.6)		172 (58.9)		37 (17.2)		24 (11.8)	
Hardship <sup>d</sup>			0.03		0.02		< 0.001		0.21
No	144 (49.8)	31 (22.6)		72 (50.0)		13 (9.5)		15 (11.0)	
Yes	145 (50.2)	45 (34.6)		93 (64.1)		36 (28.6)		19 (16.4)	
Depressive syndrome <sup>e</sup>			0.02		0.009		0.04		0.42
No	256 (74.2)	51 (24.9)		141 (55.1)		32 (16.2)		25 (13.2)	
Yes	89 (25.8)	27 (39.7)		63 (70.8)		19 (27.9)		6 (9.4)	
HIV stigma			0.01		0.92		< 0.001		0.82
None	233 (76.6)	46 (23.6)		146 (59.8)		25 (13.2)		22 (12.1)	
Moderate	37 (12.2)	20 (41.7)		39 (58.2)		16 (34.4)		6 (13.3)	
Severe	34 (11.2)	16 (40.0)		31 (62.0)		13 (33.3)		6 (15.8)	

Bold value indicate values for all participants

<sup>a</sup>Proportions of participants consuming

<sup>b</sup>Chi-square  $\chi^2$  statistical test

<sup>c</sup>Individual risk factors were identified if the patient was presented with any of the following comorbidities: diabetes, hypertension, cardiovascular disease, CD4 count < 200mm<sup>3</sup> or BMI ≥ 30

<sup>d</sup>Hardship: EPICES, an individual and quantitative scale based on 11 questions regarding material and social problems (Hardship = Score ≥ 30)

**Table 2** (continued)<sup>c</sup>Baseline PHQ-9  $\geq 10$ 

While this is a valuable perspective, it may also be a limitation. Participants completed the questionnaire retrospectively, with the benefit of hindsight, which may introduce recall bias. Although, the PLWHs included reflect in many respects (clinical characteristics) those in care, the study's design may have favored a more engaged and advantaged subset of individuals. Foreign-born PLWH, who have fewer risk factors for severe COVID-19, were under-represented. They may have also have experienced more pandemic-related stressors owing to their living (density of residential areas, household density) and working conditions (essential jobs, non-remote work jobs, use of public transport), characteristics which are thought to have been implicated in observed excess mortality due to COVID-19 in migrants in France [44].

Observed differences in stressor exposure were attributed to demographic and psychosocial characteristics. Specifically, working-age PLWH experienced more pandemic-related stressors on average. These differences appear to be driven by working conditions, household responsibilities, and financial insecurity, in line with research in the general population, underscoring the disproportionate impact of pandemic-related stressors on younger individuals [45, 46]. Moreover, psychosocially vulnerable individuals also reported greater exposure to pandemic-related stressors. We hypothesize that this may be because individuals grappling with depression and/or experiencing perceived-HIV stigma also report significantly poorer family and social ties and lower socioeconomic status, which are in turn significant sources of pandemic-related stress [47]. Alternatively, they may be more sensitive to external stressors [48, 49]. While recommendations issued by the Haute Autorité de Santé in the early days of the pandemic encouraged healthcare providers to remain in contact with all PLWH and especially the most vulnerable ones, including those with a history of mental illness, calling upon community-based organizations etc. as needed, it is unclear to what extent this recommendation was prioritized.

Pandemic-related distress refers to the emotional and psychological impact experienced as a result of the COVID-19 pandemic. It is distinct from depressive disorder in that it is a natural response to external circumstances rather than a persistent mood disorder. Cumulative exposure to pandemic-related stressors was correlated with greater distress as well as cannabis and drug use. This is consistent with research by Louis et al. demonstrating that the accumulation of pandemic-related stressors was associated with higher levels of distress [50]. Furthermore, fitting with Hong et al.'s scoping review on the impact of the COVID-19 pandemic on mental health

outcomes, associated factors, and coping strategies, stressor exposure was found to be associated with negative effects on psychological well-being, although the extent of this impact varied depending on individuals' ability to cope via social networks, exercises, meditation, art, spirituality, and interactions with family and friends [51]. The authors identified factors associated with poor mental health outcomes at the structural (financial insecurity, unemployment, economic hardship), interpersonal (lack of social support, social isolation, relationship changes), and individual level (being older and female). While we show that those who report hardship (beyond economic) are also more likely to smoke, drink heavily and use cannabis, we did not find hardship to be associated with either stressor exposure or greater distress. These findings may be due to the way in which the pandemic period may have affected participants' responses to certain items of the EPICES questionnaire, used to measure hardship. The items pertaining to engaging in hobbies, sports, etc. and contact with family members in the previous 12 months, which are typically indicative of hardship, may actually reflect restricted access to numerous establishments (e.g., cinemas, gyms, restaurants, museums, nightclub, casinos etc.) during the pandemic. Furthermore, we did not find that being female or older correlated with poorer outcomes. This difference may reflect the specificities of those in long-term care in our region. Additionally, Hong et al. found that previous mental health issues, poor antiretroviral adherence, fewer years since HIV diagnosis, and perceived risk of COVID-19 perception were linked to poorer outcomes. While we did not find time since HIV infection or risk of severe COVID-19 (such as a CD4 cell count of  $< 200$  mm<sup>3</sup> and comorbidities) to be associated with greater distress, this difference may be due to a difference in timing between our study and those conducted earlier in the pandemic. It is quite likely that, like those in the general population, PLWH's perception of risk evolved as more evidence emerged regarding risk factors as well as the availability and use of various strategies to mitigate individual risk (e.g., wearing masks).

PLWH in our setting and elsewhere face numerous challenges related to living with HIV and are subject to social determinants of health. In 2020, Shiau et al. proposed that a syndemic framework be adopted to conceptualize how the pandemic might impact PLWH, considering that they may be at greater risk of severe COVID-19 because of morbidity and socially-produced burdens [52]. As hypothesized by Shiau et al., we found evidence to suggest that those who were already psychosocially vulnerable (prior depressive disorder, stigma) were more affected by stressors and experienced greater distress than counterparts. There was nevertheless little evidence that the relationship between

**Table 3** Association between cumulative exposure to stressors and distress, growth, tobacco, alcohol, cannabis and other drug use, overall and stratified

Characteristics	Distress score	p-value <sup>a</sup>	Growth score	p-value <sup>b</sup>	Tobacco	p-value <sup>c</sup>	Alcohol	p-value <sup>c</sup>	Cannabis	p-value <sup>c</sup>	Other drugs	p-value <sup>c</sup>
<b>Univariable</b>												
N	312		281		265		329		262		260	
Stressor score	0.8 (0.6–1.0)	<0.001	0.1 (0.03–0.08)	<0.001	1.0 (0.9–1.1)	0.90	1.0 (0.9–1.1)	0.86	1.2 (1.1–1.3)	0.006	1.2 (1.1–1.4)	0.004
<b>Multivariable*</b>												
N	158		146						136		260	
Age < 60												
Stressor score	0.7 (0.5–1.0)	<0.001	0.04 (0.01–0.07)	0.002					1.2 (1.0–1.4)	0.02	1.2 (1.0–1.4)	0.004
N	128		115						106			
Age 60 +												
Stressor score	0.8 (0.4–1.2)	<0.001	0.1 (0.06–0.2)	0.001					1.0 (0.7–1.4)	0.06		

\*Multivariable regression for distress, growth and cannabis adjusted for pre-pandemic depressive syndrome and HIV-related stigma. Multivariable regression for other drug adjusted for age

<sup>a</sup>Linear regression t-test

<sup>b</sup>Zero-inflated Poisson regression z-test

<sup>c</sup>Logistic regression z-test

stressor exposure and distress was confounded by PLWH's underlying vulnerability. Moreover, we found exposure to stressors to be associated with a 20% increase in cannabis and other drugs use, in line with research suggesting that pandemic-induced stress and anxiety was associated with an increase in cannabis and other drug use among PLWH [17]. While these associations were statistically significant, their clinical significance warrants further exploration. While a number of efforts were made to ensure the continuity of care for those living with HIV via telemedicine and automatically renewed and/or extended ART prescriptions, wrap-around services, in spite of their importance, were often limited. Efforts should be made to ensure that those who may experience distress and/or who use drugs remain engaged in care as both are associated with poor adherence and virological outcomes [53]. Furthermore, greater consideration should be given to remote counselling, which may respond to the needs of some but not all of those who experienced pandemic-related distress and/or coped with increase cannabis and drug use.

Furthermore, we found exposure to stressors to be associated with increased psychological growth, reflecting a positive outlook in response to pandemic-related adversity. Psychological growth, while present, was modest and only present in some PLWH, namely those who did not report experiencing hardship. It appears that access to resources, both material and social, may have buffered PLWH, like those in the general population. Those who did not report experiencing hardship not only had better material resources (e.g. living in a couple, owning their home) but also social ones, namely having people they could count on in times of need and regular contact with their extended family members. Indeed, there is evidence that strong social connections reinforce feelings of belonging and have been associated with better mental health outcomes including psychological growth [54]. These support systems may have allowed them to grow in response to the trials of the pandemic [51, 55]. Furthermore, some PLWH may have been resilient, adapting to pandemic-related adversity. Research indicates that resilience enables people to maintain a sense of purpose and optimism, which can foster psychological growth under prolonged stress [56]. Finally, positive reappraisal — the cognitive reframing of difficult situations to find meaning or value in the experience — has also been shown to support growth by helping individuals see adversity as an opportunity for personal development [57]. Many PLWH may have already engaged in positive reappraisal to manage the emotional and psychological challenges of being diagnosed and living with HIV; therefore, they may have been in a position to positively reappraise the unprecedented circumstances imposed by the pandemic. These findings should incite healthcare providers to see social resources (family, social connections, peer-support groups) as well as material ones as a lever for ensuring that

PLWH are supported and remain engaged in care during challenging times.

## Conclusion

Working-age and psychosocially vulnerable PLWH experienced more pandemic-related stressors compared to their counterparts. Exposure to stressors was linked to increased distress, psychological growth, cannabis and drug use. Independent of stressor exposure, those lacking material and social resources or who were psychologically vulnerable experienced greater distress, were more likely to smoke, drink and use drugs, while the opposite was true for psychological growth. Healthcare providers should not only be aware of risk (of severe COVID-19) but also mindful of the social and psychological challenges PLWH face as these can significantly impact their ability to remain actively engaged in healthcare, especially during challenging times.

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**Author Contributions** JBF, DB and FB conceived the study. JBF led the analysis of the data and produced manuscript outputs with analysis contributions by DB, MH and FB. JBF and DB drafted and finalized the manuscript. MH, DN, SF, EL, PD, NR, CC, TP, PR, MAV, CK and OL were involved in the collection and harmonization of data. JBF, MH, DN, SF, EL, PD, NR, CC, TP, PR, MAV, CK, OL, LW, PB and DB reviewed the manuscript, provided critical inputs and approved the final manuscript.

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**Data Availability** The data that support the findings of this study are available on reasonable request from the corresponding author.

## Declarations

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**Ethical Approval** The ANRS CO3 AQUIVIH-NA Cohort received approval from the Comité de Protection des Personnes (CPP) du Sud-Ouest et d'Outre-Mer III (25 May 2016).

**Patient consent statement**: Informed consent was obtained from all individuals included in the cohort.

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