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# HIV, psychological resilience, and substance misuse during the COVID-19 pandemic: A multi-cohort study

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## ABSTRACT

*Objective:* The COVID-19 pandemic has dramatically impacted mental health, increasing rates of substance misuse. Resilience is a positive adaptation to stress that may act as a buffer against adverse mental health outcomes. Based on prior knowledge, we hypothesized that PLWH would display higher resilience than HIV-uninfected peers, and that high resilience would be associated with lower risk of substance misuse.
*Methods:* This analysis of the Collaborating Consortium of Cohorts Producing NIDA Opportunities (C3PNO) included data from six USA cohorts that administered a COVID-19-related survey with a 3-month follow-up during May 2020 and March 2021. All data was self-reported. The Brief Resilience Scale and General Anxiety Disorder-7 were utilized. Primary analyses consisted of multivariate generalized linear mixed models with random intercepts using binary logistic regression.
*Results:* A total of 1430 participants completed both surveys, of whom 670 (46.9%) were PLWH. PLWH had lower odds of anxiety (OR=0.67, 95% CI: 0.51–0.89) and higher odds of high resilience (OR=1.21, 95% CI: 1.02–1.44) than HIV-uninfected participants, adjusted for covariates. The presence of anxiety was associated with higher risk of misuse of all substances. High resilience was associated with lower risk of anxiety and misuse of substances, adjusted for covariates.
*Conclusions:* Psychological resilience was associated with lower risk of anxiety and substance misuse, potentially serving as a buffer against poor mental and behavioral health during the COVID-19 pandemic. Further research is needed to identify pathways of resilience in the context of substance misuse and comprehensive resilience-focused interventions.

## 1. Introduction

Since early March of 2020, the COVID-19 pandemic and the mitigation strategies put in place have had dramatic impacts on mental health and wellbeing around the world (Nochaiwong et al., 2021; Xiong et al., 2020). The public health response to COVID-19, such as social

isolation and quarantines, resulted in several unintended consequences that increased the risk of anxiety and depression, as well as substance misuse and overdoses (Czeisler, 2020; Daly et al., 2021; Ettman et al., 2020; Nguyen and Buxton, 2021; Twenge and Joiner, 2020). The rise in substance misuse is particularly alarming, given that prior to the pandemic, in 2019, 60% of the United States (U.S.) population aged 12 and older (or 165.4 million people) used substances, including tobacco, alcohol, and illicit drugs, and an estimated 20 million had a substance use disorder (SUD) (SAMSHA, 2019). In addition to SUDs, one in five (or 51.5 million) U.S. adults had a mental illness, which often co-occurs with SUDs (SAMSHA, 2019). The prevalence of mental health symptoms continued to increase throughout the pandemic while disruptions in health care services resulted in unmet mental health care needs for many (Organización Mundial de la Salud, 2020; Radfar et al., 2021; Vahratian, 2021). At the same time, many individuals may have been reluctant to seek treatment for SUDs due to stay-at-home orders and worries about contracting COVID-19 (Henretty et al., 2021; Mark et al., 2021).

The increased rate of substance misuse raises several concerns regarding its impact on people who use drugs (PWUD) and overwhelmed health care systems. A rapid and drastic rise in drug overdoses and overdose-related deaths led to an emergency health advisory by the Centers for Disease Control and Prevention (Centers for Disease Control and Prevention, 2020a; Friedman et al., 2021; Friedman and Akre, 2021; Wilson et al., 2020). Moreover, people with SUDs have been at increased risk of COVID-19 infection and poorer health outcomes (Wang et al., 2021). In turn, COVID-19 may increase the risk of overdose in PWUD (Volkow, 2020).

Furthermore, the pandemic exacerbated long-standing social and health disparities among underserved and vulnerable populations. Not surprisingly, pre-existing disparities in mental health conditions and substance misuse have only widened during the pandemic (Czeisler, 2020; McKnight-Eily, 2021). Among those who may be disproportionately affected by the pandemic are people living with HIV (PLWH), a socially vulnerable population overrepresented in U.S. minorities (Centers for Disease Control and Prevention, 2020b; Dailey et al., 2019). Indeed, COVID-19 infections correlate with social vulnerability (Dasgupta et al., 2020; Karaye and Horney, 2020) and with county-level HIV prevalence (Luan et al., 2021). The available evidence indicates that PLWH may have a heightened risk of poor COVID-19 outcomes, in part due to social determinants of health and multimorbidity (Mirzaei et al., 2020; Ssentongo et al., 2021). Historically, PLWH have been disproportionately affected by mental health problems, including substance misuse and dependence, compared to the general population and HIV-uninfected peers (Chhatre et al., 2021; Hartzler et al., 2016; Remien et al., 2019; Rubin and Maki, 2019; Shiau et al., 2017). On one hand, psychiatric illnesses can contribute to HIV infections (Hobkirk et al., 2015; Remien et al., 2019). On the other hand, psychiatric disorders can develop or worsen in PLWH due to neurologic manifestations of HIV (Hong and Banks, 2015; Rubin and Maki, 2019), antiretroviral therapy (ART)-related toxicity (Reeves et al., 2021; Treisman and Soudry, 2016), and psychosocial stressors, such as HIV-related stigma and loss of social capital (Halkitis et al., 2017; Remien et al., 2019; Rueda et al., 2016). That said, PLWH may benefit from psychological resilience developed through the process of adapting to and overcoming the adversities brought on by living with HIV (de Santis et al., 2013; Dulin et al., 2019; Halkitis et al., 2017).

Resilience, in general terms, is the process of coping with stress or trauma (Smith et al., 2013; Windle, 2011). In other words, it is a positive adaptation to adverse events, and may act as a buffer against adverse mental health outcomes. In PLWH, high resilience has been associated with lower depression and anxiety (McGowan et al., 2017; Thurston et al., 2018), improved health behaviors leading to higher ART adherence and viral suppression (Brewer et al., 2020; Dulin et al., 2019; Fletcher et al., 2020), safer sexual practices (McNair et al., 2017), and higher health-related quality of life (Fang et al., 2015). In the Miami

Adult Studies on HIV (MASH) cohort, PLWH exhibited higher resilience than their HIV-uninfected peers during the early months of the pandemic (Diaz-Martinez et al., 2021). Additionally, higher resilience in part accounted for lower anxiety and stress in PLWH. Based on these findings and the theory of HIV resilience (de Santis et al., 2013), we hypothesized that higher resilience in PLWH would predict lower risk of substance misuse. The study of resilience in the context of HIV infection and substance misuse may offer unique insights regarding public health emergencies related to infectious diseases, such as the COVID-19 pandemic. In this study, we conducted a multi-cohort investigation on the relationships between psychological resilience, anxiety, and substance misuse in people living with and without HIV.

## 2. Material and methods

### 2.1. Study design

We conducted a multi-cohort analysis of the National Institute of Drug Abuse (NIDA)-funded Collaborating Consortium of Cohorts Producing NIDA Opportunities (C3PNO). The consortium consists of nine cohorts across the USA and Canada: AIDS Care Cohort to Evaluate Access to Survival Services (ACCESS), AIDS Linked to the Intravenous Experience (ALIVE), Heart Study, Healthy Young Men (HYM), Johns Hopkins HIV Clinical Cohort (JHHCC), Miami Adult Studies on HIV [MASH], mSTUDY, RADAR, Vancouver Drug Users Study (V-DUS). These cohorts comprise a diverse population of people who use drugs (PWUD), PLWH, and HIV-uninfected participants, many of whom are at-risk of HIV infection. An in-depth description of the C3PNO cohorts was provided by Gorbach et al. (2021). The present study consists of an analysis of data from a COVID-19-related survey, which was administered to a convenience sample of 200 or more participants from each cohort. The surveys took approximately 20 min to complete and were administered through web-based platforms or interviewer-assisted via telephone. The C3PNO COVID-19 Cross-Cohort Survey is available at https://www.c3pno.org/.

For the purposes of this analysis, we included data from six USA cohorts (shown in Table 1), since only these cohorts administered the survey with a 3-month follow-up. The 1st wave was administered during May-December 2020 and the 2nd wave between October 2020 and March 2021. All participants were 21 years of age and older. The protocols for this research were approved by the Institutional Review Boards at each cohort's institution.

### 2.2. Assessments

In this study, we examined psychological resilience and anxiety in relation to substance use patterns during the pandemic among people living with and without HIV from the C3PNO cohorts. All data were self-reported, including demographics, housing status, employment status, and HIV status.

#### 2.2.1. Resilience

Psychological resilience was determined with the Brief Resilience Scale (BRS), which assesses resilience as "the ability to bounce back and recover from stress"(Smith et al., 2008). Scores range from 0 to 6; scores equal or above the sample median (3.5) were classified as high resilience.

#### 2.2.2. Anxiety

Symptoms of anxiety were assessed with the General Anxiety Disorder-7 (GAD-7) (Spitzer et al., 2006). The total score ranges from 0 to 21; scores of 10 or more may indicate the presence of anxiety.

#### 2.2.3. Substance use

The Alcohol Use Disorder Identification Test-Consumption (AUDIT-C) questionnaire was used to assess hazardous drinking (scores of $\geq 4$ for

**Table 1**
Main social and clinical characteristics of the participants.

|  | Total N (%) Median (IQR) | HIV- N (%) Median (IQR) | HIV+ N (%) Median (IQR) | P |
|---|---|---|---|---|
| **N** | **1430** | **760 (53.1)** | **670 (46.9)** | |
| **Months between surveys** | 4, 3–5 | 4, 3–5 | 4, 3–5 | |
| **Age**, years | 46, 27–57 | 30, 25–55 | 52, 38–59 | **< 0.001**[a] |
| **Sex**, male | 1100 (77.0) | 613 (80.9) | 487 (72.7) | **< 0.001**[b] |
| **Race/ethnicity** | | | | |
| Black, non-Hispanic | 826 (57.8) | 358 (47.1) | 468 (69.9) | **< 0.001**[c] |
| White, non-Hispanic | 160 (11.2) | 106 (14.0) | 54 (8.1) | |
| Hispanic | 363 (25.4) | 237 (31.2) | 126 (18.8) | |
| Other | 81 (5.6) | 59 (7.7) | 22 (3.3) | |
| **Unemployed** | 654 (45.7) | 347 (45.7) | 307 (45.8) | 0.951[b] |
| **Homeless** | 95 (6.6) | 60 (7.9) | 35 (5.2) | **0.044**[b] |
| **Mental health care**[d] | 1053 (74.3) | 538 (71.4) | 515 (77.6) | **0.009**[b] |
| **Treated for SUD**[e] | 165 (11.7) | 75 (10.1) | 90 (13.6) | **0.037**[b] |
| **C3PNO cohort** | | | | |
| ALIVE | 256 (17.9) | 176 (23.2) | 80 (11.9) | |
| HYM | 249 (17.4) | 194 (25.5) | 55 (8.2) | |
| JHHCC | 200 (14.0) | 0 | 200 (29.9) | |
| MASH | 311 (21.7) | 131 (17.2) | 180 (26.9) | |
| mSTUDY | 231 (16.2) | 104 (13.7) | 127 (19.0) | |
| RADAR | 183 (12.8) | 155 (20.4) | 28 (4.2) | |

Abbreviations: IQR, interquartile range; SUD, substance use disorder
Bolded values denote statistical significance, P < 0.05
[a] Mann-Whitney *U* test
[b] Chi-square test
[c] Likelihood-ratio Chi-square test
[d] Receiving mental health care prior to pandemic; n = 13 missing data
[e] Treated for SUD prior to pandemic; n = 24 missing data

men and ≥3 for women) (Bush et al., 1998). Participants were also asked how frequently they used cigarettes, cannabis, methamphetamines, cocaine, heroin and/or fentanyl, and prescription opioids in the past month; responses were dichotomized as "yes" (used once or more in the past month) or "no" (no use in the past month).

*2.2.4. Statistical analysis*

Descriptive statistics are reported as percentages for categorical data, as means ± standard deviations (SD) for continuous variables with a normal distribution, and as medians with 25th and 75th percentiles (interquartile range, IQR) for data with a non-normal distribution. The normality of the data's distributions was first determined using the Kolmogorov-Smirnov test, and the equality of variances was confirmed using Levene's test. Between-group differences were tested with Chi-square test, T test, or Mann-Whitney *U* test as adequate.

Primary analyses consisted of multivariate generalized linear mixed models with separate random intercepts using binary logistic regression. The random intercepts used were C3PNO cohort (each cohort was classified as a cluster), survey wave, and month of survey. This model generates a flexible marginal correlation among the repeated binary outcomes, including a declining association with increasing time separation, while retaining the property that the marginal probabilities follow a logistic regression model. The fixed effects include HIV status, age, sex, race/ethnicity, employment, homelessness, mental health care prior to pandemic, and treatment for SUD prior to pandemic. Due to substantial losses to follow-up, we performed an additional cross-sectional analysis using data from all participants during the 1st wave of the survey. Logistic regression parameters were summarized as odds ratios (OR) or relative risk (RR) with 95% confidence intervals (CI) and P-value.

## 3. Results

### 3.1. Cohort characteristics

A total of 2156 participants completed the 1st survey and 1430 (66.3%) completed the 2nd survey. The loss to follow-up ranged from 6.3% to 55.9% across cohorts. Consequently, this longitudinal analysis included data from 1430 participants who completed both surveys, of whom 670 (46.9%) were PLWH. A comparison of characteristics between the participants included in the analyses and those who were lost to follow-up can be found in Supplementary Table 1. Participants who were lost to follow-up were more likely to be HIV-uninfected and homeless, and to use cannabis and heroin/fentanyl than those who completed the 2nd survey wave.

The characteristics of the sample can be found in Table 1. The median time between surveys was 4 (3–5) months. The participants were 46 (27–57) years of age, 77% were male, 58% were Black non-Hispanic, and 25% were Hispanic. Nearly half of all participants were unemployed (45.7%) and 6.6% were homeless. Additionally, 74.3% and 11.7% were receiving mental health care and treatment for SUDs, respectively, prior to the pandemic; these were significantly more frequent among HIV+ than HIV- participants. PLWH were also significantly older of age with a larger proportion of non-Hispanic Blacks, but were less likely to be male, unemployed, and homeless than HIV- participants.

### 3.2. Anxiety and resilience

GAD-7 scores decreased between the 1st and 2nd waves (4 [0–9] to 3 [0–7], P < 0.001), but BRS scores remained stable (3.5, 3.0–4.0 at both waves, P = 0.458). There were significant differences on GAD-7 and BRS scores between cohorts during both waves (all P < 0.05); data not shown.

Resilience and anxiety were inversely correlated (Rho=−0.401, P < 0.001) and high resilience was associated with lower risk of anxiety (aRR=0.26, 95% CI: 0.20–0.34, P < 0.001). Overall, fewer PLWH reported anxiety symptoms compared to HIV-uninfected participants (17.8% vs. 26.5%, respectively; P < 0.001), but resilience did not differ (55.1% vs. 52.9%, respectively; P = 0.222).

Table 2 displays multivariable regression models for anxiety and high resilience. Significant predictors of anxiety included unemployment, receiving mental care and treatment for SUD prior to the pandemic, and homelessness. Compared to non-Hispanic Whites, non-Hispanic Blacks had lower odds of anxiety and a trend for lower odds of anxiety among Hispanics was observed. Age was associated with high resilience. Conversely, receiving mental health care prior to the pandemic, unemployment, and homelessness were associated with low resilience. PLWH, compared to HIV-uninfected participants, showed lower odds of anxiety (aOR=0.67, 95% CI: 0.51–0.89; P = 0.006) and higher odds of high resilience (aOR=1.21, 95% CI: 1.02–1.44; P = 0.029). Compared to the mSTUDY cohort, which had the lowest prevalence of high resilience (43.9%), the HYM and RADAR cohorts had lower odds of anxiety and higher odds of high resilience.

Due to the age discrepancy between PLWH and HIV-uninfected participants, we performed a sensitivity analysis among participants who were 29 years of age and older. The median age between PLWH (54, 45–60) and HIV-uninfected (54, 42–61) participants no longer differed (P = 0.820). PLWH had 1.30 (95% CI: 1.29, 1.31; P = 0 <0.001) times the odds of high resilience compared to HIV-uninfected participants, adjusted for covariates.

### 3.3. Substance use

During Wave 1, a total of 42.5% of participants reported hazardous drinking, 40.7% smoked cigarettes, 39.8% used cannabis, 8.9% used cocaine, 6.2% used methamphetamines, 3.0% used heroin/fentanyl, and 2.7% misused prescription opioids (Table 3, Fig. 1). Between Waves 1

**Table 2**
Predictors of anxiety and high resilience in C3PNO.

| | | Anxiety aOR (95% CI)[1] | P | High resilience aOR (95% CI)[a] | P |
|---|---|---|---|---|---|
| **Age (per 5 years)** | | 0.91 (0.82–1.01) | 0.083 | 1.06 (1.01–1.12) | **0.033** |
| **HIV status** | | | | | |
| | Negative | Reference | | Reference | |
| | Positive | 0.67 (0.51–0.89) | **0.006** | 1.21 (1.02–1.44) | **0.029** |
| **Working** | | | | | |
| | Yes | Reference | | Reference | |
| | No | 1.40 (1.13–1.75) | **0.002** | 0.81 (0.69–0.96) | **0.014** |
| **Mental health care** | | | | | |
| | No | Reference | | Reference | |
| | Yes | 1.57 (1.07–2.29) | **0.020** | 0.45 (0.39–0.56) | **< 0.001** |
| **Treated for SUD** | | | | | |
| | No | Reference | | Reference | |
| | Yes | 1.40 (1.07–1.81) | **0.013** | 0.80 (0.56–1.12) | 0.201 |
| **Homelessness** | | | | | |
| | No | Reference | | Reference | |
| | Yes | 1.84 (1.39–2.41) | **< 0.001** | 0.74 (0.56–0.97) | **0.033** |
| **Sex** | | | | | |
| | Male | Reference | | Reference | |
| | Female | 0.76 (0.57–1.02) | 0.073 | 0.88 (0.72–1.09) | 0.254 |
| **Race/ethnicity** | | | | | |
| White non-Hispanic | | Reference | | Reference | |
| Black non-Hispanic | | 0.47 (0.34–0.64) | **< 0.001** | 1.59 (0.90–1.48) | 0.249 |
| | Hispanic | 0.75 (0.54–1.03) | 0.080 | 0.88 (0.67–1.16) | 0.379 |
| | Other | 0.71 (0.42–1.21) | 0.213 | 1.03 (0.69–1.52) | 0.875 |
| **Cohort** | | | | | |
| | mSTUDY | Reference | | Reference | |
| | HYM | 0.62 (0.49–0.80) | **< 0.001** | 1.32 (1.05–1.67) | **0.018** |
| | JHHCC | 0.95 (0.48–1.88) | 0.898 | 0.82 (0.59–1.13) | 0.231 |
| | MASH | 1.05 (0.61–1.80) | 0.839 | 0.92 (0.67–1.27) | 0.637 |
| | ALIVE | 0.62 (0.32–1.20) | 0.157 | 1.26 (0.87–1.82) | 0.213 |
| | RADAR | 0.65 (0.48–0.89) | **0.007** | 1.37 (1.11–1.69) | **0.003** |

Abbreviations: aOR, adjusted odds ratio
Bolded values denote statistical significance, P < 0.05
[a] Odds ratios are adjusted for all of the variables shown.

and 2, there was a significant decline in hazardous drinking (42.5% to 39.7%, P = 0.027), but the use of all other substances remained stable. Fewer PLWH reported hazardous drinking and use of cannabis than HIV-uninfected participants; this effect was seen during both waves (Table 3). On the other hand, methamphetamine use was more common among PLWH during both waves (Table 3). Differences in hazardous drinking, cannabis use, and methamphetamine use between PLWH and HIV-uninfected participants were consistent between waves, but other than a slight decline in hazardous drinking, overall rates of substance misuse held steady during the two study waves.

Table 4 displays the results of multivariate generalized linear mixed models assessing the relationships of HIV, anxiety, and high resilience with substance misuse, adjusting for age, sex, race/ethnicity, housing, employment, HIV status, mental health care, and treatment for SUDs. To avoid multicollinearity due to the high correlation between resilience and anxiety, the two were kept separate from each other in multivariable regressions. The presence of anxiety was associated with higher risk of misuse of all substances. Conversely, high resilience was associated

**Table 3**
Substance misuse patterns by survey wave and HIV status.

| N | Total 1430 | HIV- 760 | HIV+ 670 | P[a] |
|---|---|---|---|---|
| **Hazardous drinking** | | | | |
| Wave 1 | 42.5% | 49.5% | 34.6% | **< 0.001** |
| Wave 2 | 39.7% | 45.3% | 33.3% | **< 0.001** |
| P[b] | **0.027** | **0.018** | 0.518 | |
| **Cannabis** | | | | |
| Wave 1 | 39.8% | 43.8% | 35.3% | **0.001** |
| Wave 2 | 38.3% | 41.8% | 34.3% | **0.004** |
| P[b] | 0.121 | 0.219 | 0.396 | |
| **Cigarette smoking** | | | | |
| Wave 1 | 40.7% | 39.5% | 42.1% | 0.313 |
| Wave 2 | 39.3% | 37.5% | 41.3% | 0.138 |
| P[b] | 0.197 | 0.218 | 0.653 | |
| **Cocaine** | | | | |
| Wave 1 | 8.9% | 8.5% | 9.5% | 0.512 |
| Wave 2 | 9.3% | 9.2% | 9.4% | 0.900 |
| P[b] | 0.721 | 0.614 | 0.999 | |
| **Heroin/fentanyl** | | | | |
| Wave 1 | 3.0% | 3.7% | 2.2% | 0.110 |
| Wave 2 | 2.9% | 3.7% | 2.1% | 0.075 |
| P[b] | 0.999 | 0.999 | 0.999 | |
| **Methamphetamines** | | | | |
| Wave 1 | 6.2% | 4.9% | 7.6% | **0.031** |
| Wave 2 | 6.4% | 4.2% | 9.0% | **< 0.001** |
| P[b] | 0.671 | 0.405 | 0.124 | |
| **Rx opioids** | | | | |
| Wave 1 | 2.7% | 2.4% | 3.0% | 0.468 |
| Wave 2 | 2.7% | 2.4% | 3.1% | 0.254 |
| P[b] | 0.999 | 0.999 | 0.999 | |

Bolded values denote statistical significance, P < 0.05
[a] Chi-square test
[b] McNemar's test

with lower risk of misuse of all substances with the exception of cannabis, although a trend was observed (P = 0.07).

### 3.4. Sensitivity analysis

Due to significant differences in HIV status and use of substances between participants who completed both study surveys and those who were lost to follow-up, we performed additional sensitivity analyses using data from the 1st survey on all 2156 participants. The results are similar to what was found in the longitudinal analyses of the 1430 participants who completed both surveys; see Supplementary Table 2. PLWH, compared to HIV-uninfected participants, had higher odds of high resilience (aOR=1.20, 95% CI: 1.01–1.42; P = 0.030) and lower odds of anxiety (aOR=0.62, 95% CI: 0.49–0.77; P < 0.001). High resilience was significantly associated with or showed a trend toward lower risk of hazardous drinking (aRR=0.84, 95% CI: 0.71–1.00; P = 0.057) and use of cannabis (aRR=0.83, 95% CI: 0.65–1.08; P = 0.049), methamphetamines (aRR=0.59, 95% CI: 0.43–0.79; P = 0.001), and heroin/fentanyl (aRR=0.60, 95% CI: 0.40–0.90; P = 0.014). Resilience was also inversely associated with cigarette smoking (aRR=0.95, 95% CI: 0.80–1.13; P = 0.595), use of cocaine (aRR=0.83, 95% CI: 0.65–1.08; P = 0.175) and misuse of prescription opioids (aRR=0.44, 95% CI: 0.15–1.22; P = 0.116), although none were statistically significant.

## 4. Discussion

We conducted a multi-cohort study of the Collaborating Consortium of Cohorts Producing NIDA Opportunities (C3PNO) to assess psychological resilience, anxiety, and substance misuse in people living with and without HIV during the COVID-19 pandemic. Resilience in this study refers to an individual's "ability to bounce back or recover from stress" (Smith et al., 2008). In this analysis of the combined C3PNO cohorts, data collected during the COVD-19 pandemic indicated that
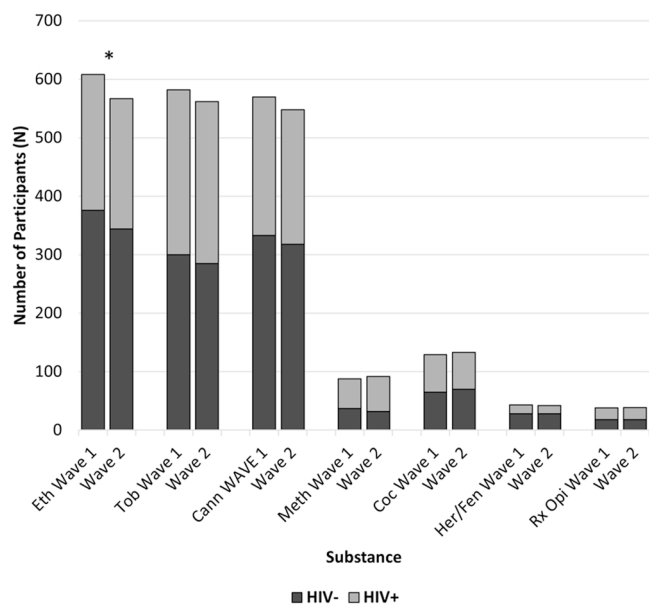
**Fig. 1.** Substance use patterns in the C3PNO multi-cohort during the COVID-19 pandemic Fig. 1 displays substance use patterns in the C3PNO multi-cohort during the two waves of surveys: wave 1 occurred between May-Dec 2020 and wave 2 occurred between Oct 2020-Mar 2021. The proportion of users of each substance is compared between study waves and by HIV status (dark shade for HIV-negative and light shade for HIV-positive). Significant differences were noted only for hazardous drinking, which showed a slight decline from 42.5–39.7% between the 1st and 2nd waves (P = 0.027), and was significantly less frequent among HIV-positive participants during both waves (P < 0.05). Abbreviations: Cann, cannabis; Coc, cocaine; Eth, ethanol (hazardous drinking); Her/Fen, heroin/fentanyl; Meth, methamphetamines; Rx Opi, prescription opioids; Tob, tobacco (cigarette smoking). *McNemar's test for Wave 1 vs. Wave 2; P < 0.05.

PLWH had higher odds for high resilience than HIV-uninfected participants after controlling for important factors such as sociodemographic characteristics and cohorts within C3PNO. In turn, high resilience was associated with lower risk of anxiety and substance misuse during the same period of time. These findings suggest that strategies to identify and strengthen resilience resources may help mitigate mental health problems and substance misuse in vulnerable populations. Further, learning from HIV resilience and the public health response to HIV may provide valuable insights for individual- and community-level resilience that could help increase preparedness for public health crises, such as the COVID-19 pandemic, potentially reducing the burden on the mental health and wellbeing of marginalized populations.

Among those disproportionately affected by the pandemic are PWUD, who are often highly vulnerable, underserved, and understudied (SAMSHA, 2019). Distress directly related to COVID-19, as well as the unintended social and economic consequences of lockdowns contributed to increased patterns of substance misuse, along with alcohol- and drug-related overdoses (Centers for Disease Control and Prevention, 2020a; Czeisler, 2020; Mougharbel et al., 2021; Nguyen and Buxton, 2021). This was foreseen by many, as stress has long been linked to substance abuse and risk of relapse (Yang et al., 2020). Alarmingly, a prevailing concern is that the pandemic will have long-lasting impacts on mental and behavioral health. For example, people who initiated misuse of substances during lockdowns may develop an SUD that may persist long after pandemic recovery. Disruptions to health systems may also make it more difficult for people with psychiatric disorders to seek and obtain adequate care and treatment. Moreover, bidirectional associations between COVID-19 and psychiatric conditions have been noted (Taquet et al., 2021).

The data presented in this study was collected between May 2020 and March 2021, and is likely not representative of usual patterns of substance misuse among C3PNO participants. Changes to the drug supply, such as decreased availability and quality along with increased costs have been reported by PWUD (Ali et al., 2021; Tamargo et al., 2021). For instance, cocaine use in the MASH cohort (a C3PNO cohort) declined by more than half during the early months of the pandemic (Tamargo et al., 2021). Therefore, some substances may have been less frequently used during the study period. Also, changes in the availability of some drugs may lead some individuals to shift towards more easily accessible substances, such as alcohol and prescription drugs. As such, changes in substance misuse may be due to changes in drug supply rather than personal choices. On the other hand, the United Nation's World Drug Report 2021 found that, despite initial disruptions, the global drug trade was largely unaffected throughout 2020 (United Nations Office On Drugs and Crime, 2021). This may explain why patterns of reported substance misuse among the C3PNO participants who completed both surveys remained stable throughout the study period, besides a slight decline in hazardous drinking among HIV-uninfected participants. Nevertheless, losses to follow-up must be taken into consideration, as participants who were lost to follow-up were more likely to smoke cigarettes (44.1% vs. 40.7%, P = 0.009), use cannabis (46.8% vs. 39.8%, P = 0.033) and heroin/fentanyl (6.1% vs. 3.0%, P < 0.001) than those who completed both surveys. Given the rise in incidence of substance-related overdoses during the pandemic, it is possible that some of the attrition in this study may be related to overdoses. Continued monitoring of substance use patterns in the C3PNO cohorts and other at-risk groups is warranted.

Many have pointed to the history of HIV as a model for the public health response to COVID-19. While there are several important distinctions between the HIV epidemic and the current COVID-19 pandemic, this study illustrates that lessons from HIV may extend to resilience and its impact on mental and behavioral health. Resilience has been conceptualized most commonly as the process of overcoming adversity, but it has also been used in reference to a trait (i.e. being resilient) and the outcome of such process (i.e. becoming resilient). What is common in all conceptualizations of resilience is that adversity is an antecedent and usually consists of traumatic events, disease processes, and daily stressors (Chmitorz et al., 2018; Rudzinski et al., 2017).

**Table 4**
HIV, resilience, and anxiety as predictors of substance misuse.

|  | Hazardous drinking | Smoking | Cannabis | Cocaine | Methamphetamine | Heroin/fentanyl | Prescription opioids |
|---|---|---|---|---|---|---|---|
| **HIV**, aRR (95% CI)[1] | 0.75 (0.62–0.90) | 0.95 (0.79–1.15) | 1.02 (0.80–1.30) | 1.07 (0.82–1.38) | 2.21 (1.61–3.04) | 0.72 (0.61–0.85) | 1.23 (0.74–2.03) |
| **P** | **0.002** | 0.620 | 0.884 | 0.636 | **< 0.001** | **< 0.001** | 0.430 |
| **Anxiety**, aRR (95% CI)[a] | 1.22 (1.02–1.48) | 1.40 (1.14–1.73) | 1.21 (1.02–1.45) | 1.85 (1.37–2.50) | 1.84 (1.32–2.56) | 2.17 (1.44–3.26) | 3.68 (1.95–6.96) |
| **P** | **0.030** | **0.001** | **0.034** | **< 0.001** | **< 0.001** | **< 0.001** | **< 0.001** |
| **Resilience**, aRR (95% CI)[a] | 0.84 (0.72–0.99) | 0.85 (0.72–0.99) | 0.87 (0.76–1.01) | 0.72 (0.55–0.94) | 0.64 (0.53–0.77) | 0.74 (0.59–0.94) | 0.57 (0.33–0.97) |
| **P** | **0.046** | **0.048** | 0.071 | **0.017** | **< 0.001** | **0.014** | **0.037** |

Abbreviations: aRR, adjusted relative risk
Bolded values denote statistical significance, P < 0.05
[a] Relative risk adjusted for C3PNO cohort, study wave, survey month, HIV status, age, sex, race/ethnicity, employment, homelessness, mental health care prior to pandemic, and treatment for SUD prior to pandemic.

With the advent of highly effective ART, HIV infection has become a manageable, chronic illness rather than a deadly disease. PLWH develop resilience as they learn to manage the infection, which includes engaging with health care providers and adhering to treatment. de Santis et al. (2013) described the process of resilience in HIV as one that entails (1) intrinsic and extrinsic motivation, (2) management of the disease, and (3) mastering of the disease. On the other hand, the circumstances that led to acquiring HIV, the unique trauma of an HIV diagnosis, along with the wide array of adversities brought on by it, may make it more difficult for PLWH to build resilience when compared to other conditions (de Santis et al., 2013; Nightingale et al., 2010).

Our findings show that PLWH had higher resilience and were less likely to report anxiety and substance misuse during the pandemic as compared to HIV-uninfected peers. Methamphetamine use was more frequent among PLWH than HIV-uninfected participants, and the use of other substances was either similar or lower among PLWH. However, resilience consistently showed a protective effect against substance misuse, including methamphetamine use. Notably, the higher resilience among PLWH seen in this study may be in part susceptible to survivorship bias, as those who build resilience by engaging in treatment and managing the disease are more likely to survive and participate in research studies. Nevertheless, since high resilience demonstrated a protective effect against anxiety and substance misuse, higher resilience may partly explain the lower risk of these among PLWH. Similarly, a study of PLWH in Argentina showed that resilience mitigated the impact of economic disruptions on mental health during the COVID-19 pandemic (Ballivian et al., 2020). Others have also shown that higher levels of resilience are associated with less perceived stress and higher life satisfaction in PWUD, two critical factors involved in SUDs (Yang et al., 2020). These results support the notion that psychological resilience serves as a buffer against poor mental health that may directly and indirectly protect from substance misuse.

Similar to PLWH, PWUD may develop resilience as they overcome SUDs, yet the circumstances surrounding substance misuse (e.g., stigmatization, loss of social capital) may also pose a barrier for resilience. As such, the relationship between resilience and substance misuse can be reciprocal and bidirectional. However, in the substance use literature, resilience is most commonly conceptualized as an outcome determined based on the presence or absence of substance use (Rudzinski et al., 2017). An excessive focus on resilience as an outcome fails to recognize the impact of resilience on substance use, as well as its malleability over time depending on circumstances. Further research is needed to understand the complex pathways between resilience and substance misuse. For instance, the effect of resilience on substance misuse may be in part mediated by anxiety, with higher resilience acting as a safeguard against anxiety, thereby reducing the risk of substance misuse. The potential complexity of these pathways is exemplified in a study by Yang et al. (2020), which found that positive affect, self-esteem, and social support partially mediated the effects of resilience on perceived stress and life satisfaction among PWUD. On the other hand, resilience may directly reduce the risk of substance misuse by enhancing cognitive control and mindfulness over urges to use and to avoid impulsive and social behaviors conducive to substance use (Alim et al., 2012).

Efforts to foster resilience within marginalized communities may help reduce the burden of mental health problems and increase preparedness for future public health threats. An advantage of studying resilience in the context of substance misuse is its strength-based approach. Rather than emphasizing the vulnerabilities of PWUD, resilience focuses on facilitators of well-being (e.g., coping skills) and other protective factors (e.g., social connectedness) that can help PWUD overcome their adversities. Particularly in marginalized populations, understanding social and cultural contexts may reveal hidden sources of resilience (Rudzinski et al., 2017). Nevertheless, resilience in the context of substance use has received relatively little attention (Rudzinski et al., 2017) and research on resilience-focused interventions is greatly limited (Chmitorz et al., 2018). Interventions must consider the multifactorial nature of resilience. In the context of substance use, an array of internal resilience resources are cited, including self-esteem, self-efficacy, personal skills, intellectual ability, religiosity/spirituality, and personality traits (Rudzinski et al., 2017). External resilience resources are often considered at the family, school, and community levels, while environmental and structural factors are often overlooked (Rudzinski et al., 2017). Efforts to enhance community resilience, which is fundamental for preparedness and recovery from public health crises, must address social and health inequities. Indeed, a key aspect of community resilience is health promotion, as the level of physical and psychological health of a population impacts their needs and ability to recover after crisis events (Chandra et al., 2018). Public health advocates and policymakers may foster community resilience by addressing social determinants of health and other sources of social, economic, and health disparities. These strategies will require the integration and involvement of governmental and non-governmental agencies.

Several strengths and limitations of the study must be considered. The data presented was self-reported, collected from convenience samples across C3PNO cohorts via in-person and telephone-administered surveys. As such, it is possible that the use of substances was under-reported. We also were unable to assess clinical data, such as HIV viral loads and CD4 cell counts among PLWH. On the other hand, the BRS and GAD-7 are highly validated and reliable instruments. In a review of resilience measures, Windle et al. (2011) identified the BRS as one of three scales with the highest psychometric properties for resilience. The generalizability of resilience among PLWH may be limited by survivorship bias. Nevertheless, resilience among PLWH was protective against adverse mental and behavioral health outcomes. There were also considerable losses to follow-up; however, a sensitivity analysis using cross-sectional data from all participants during the 1st survey wave also supported our hypotheses: PLWH had higher odds of high resilience than HIV-uninfected peers, and high resilience was associated with lower risk of substance misuse. The study is strengthened by the use of six C3PNO cohorts across the USA, consisting of marginalized and minority groups with a diverse population of PWUD, many living with or at-risk of HIV.

### 4.1. Conclusion

In this multi-cohort study, psychological resilience was associated with lower risk of anxiety and substance misuse, potentially serving as a buffer against poor mental and behavioral health during the COVID-19 pandemic. PLWH demonstrate higher resilience than HIV-uninfected peers, which may in part explain their lower risk of anxiety and substance misuse during the COVID-19 pandemic. Understanding resilience in PLWH may provide valuable insights on resilience resources in marginalized populations. Identifying and developing strategies to strengthen resilience resources in PWUD and groups at-risk for substance misuse may help mitigate the impact of the pandemic on mental health. Further research is needed to identify pathways of resilience in the context of substance misuse, comprehensive resilience-focused interventions, and to continue to monitor substance use patterns among vulnerable populations through the COVID-19 pandemic recovery.

**Author disclosures**

## Contributors

PMG and SS are the principal investigators for the Collaborating Consortium of Cohorts Producing NIDA Opportunities (C3PNO). MKB, JAT, and JDM wrote the initial version of the manuscript. IDE performed all statistical analyses. CSM, JHK and RNM provided scientific advice. CSM, GDK, SHM, RM, MDK, SJS, BM, RNM, JHK, SS, MJ and PMG critically revised the manuscript. All authors contributed to and have approved the final manuscript.

## Conflicts of interest

No conflicts of interest declared by any of the authors.

## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.drugalcdep.2021.109230.

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