



It has been suggested that PLWH are not very likely to develop a severe form of COVID-19 infection because some antiretroviral treatment (ART) regimens may have some activity against the coronavirus.<sup>10</sup> In this regard, ritonavir was investigated but did not prove effective against the SARS-Cov-2 in clinical studies.<sup>11</sup> Another antiretroviral drug suspected to have an anti-COVID-19 effect is tenofovir, given its structural similarity with remdesivir. Both drugs can tightly bind the RNA-dependent RNA polymerase (RdRp) of the SARS-Cov-2. Moreover, a recent trial with remdesivir showed that the drug significantly reduced recovery time and improved survival in hospitalized COVID-19 patients.<sup>12</sup> Therefore, tenofovir may also be active against the SARS-Cov-2 and could represent a promising tool in the fight against COVID-19.<sup>13</sup> Studies are underway to confirm its efficacy against the SARS-Cov-2.<sup>14</sup>

So far, little is known on the impact of COVID-19 on the medical follow-up and well-being of PLWH as the pandemic evolves. Besides causing a multiorgan disease, COVID-19 also poses a threat to the emotional and social well-being of PLWH and could interfere with routine HIV care by overburdening health facilities.<sup>1</sup> Anxiety and depressive disorders have previously been reported in PLWH,<sup>15–17</sup> and it is expected that the COVID-19 outbreak would exacerbate these symptoms because of widespread fear that is partly fueled by COVID-19 misinformation through the social media.<sup>18</sup> Also, little is currently known regarding the continuity of HIV care during the COVID-19 outbreak with the associated restrictions, particularly in resource-limited settings with underperforming health care systems. Confinement may lead to poor ART adherence as a result of disruptions in the supply chain and concerns about increased exposure to coronavirus in hospital settings, thereby discouraging PLWH from showing up for follow-up visits.<sup>19</sup> Recently, the South African National Laboratory Service reported a 10% drop in viral load testing in the public sector, suggesting indeed an interruption of HIV care.<sup>9</sup> In view of all these knowledge gaps, we conducted a survey to assess the possible consequences of the COVID-19 pandemic on the health and psychosocial well-being of PLWH, their access to health care services, and ART provision.

## METHODS

### Study Design

This was a cross-sectional study conducted among PLWH between April 9, 2020, and May 17, 2020. An online questionnaire was designed to assess the impact of the current COVID-19 pandemic on the life of PLWH. Respondents were invited to participate by filling the questionnaire through a web link that was disseminated through the networks of various associations that support PLWH, including the European AIDS Treatment Group, Sensoa (Flemish center of expertise for sexual health), and RNP+Brasil (National Network of PLWH in Brazil). The questionnaire consisted of 4 parts as follows: inquiring on sociodemographic data, HIV-related information, COVID-related data, and questions on personal health as well as screening tests for psychosocial

disorders (anxiety and depression). The screening tests used were the Population Health Questionnaire (PHQ-2) for depression<sup>20</sup> and the Generalized Anxiety Disorder (GAD-2) tool for anxiety.<sup>21</sup> The questionnaire was available in English, Dutch, French, Russian, and Portuguese; it was hosted on the secure website of the International Citizen Project COVID-19.<sup>22</sup> Only respondents who were at least 18 years old and who self-confirmed being PLWH were included. There were no exclusion criteria. An e-consent was required before submitting the responses. Participants were not promised nor given any form of compensation for their participation. A duplicate of the survey template can be found in the supplementary material of this article (see Appendix 6, Supplemental Digital Content, <http://links.lww.com/QAI/B524>). The study protocol was approved by the Ethics Committee of the University of Antwerp (Belgium), Ref: 20/14/179.

### Definitions

Generalized anxiety disorders were defined as having a GAD-2 score of at least 3. Similarly, all respondents who scored 3 or more on the PHQ-2 screening tool were considered as having major depressive disorders. Based on self-reported flu-like symptoms, the World Health Organization (WHO) clinical case definition for COVID-19 was applied on our data; any respondent who had experienced fever associated with at least one respiratory symptom (cough, shortness of breath, sore throat, and coryza) was considered as a suspected case of COVID-19.<sup>23</sup>

### Statistical Analyses

Continuous variables were reported as mean with SD (mean  $\pm$  SD) and compared across groups using nonparametric tests. Categorical variables were summarized into numbers with percentages; proportions were compared using the Yates-corrected  $\chi^2$  test. A multiple logistic regression analysis was performed to investigate factors associated with the development of flu-like illness since January 2020, when the COVID-19 started spreading to other countries and continents beyond the initial focus in China. Covariates for the final model were purposefully selected and included: sociodemographic variables (age, sex, and country classification as lower-income and middle-income countries [LMIC] vs high-income countries [HIC] based on the World Bank data<sup>24</sup>), COVID-19 prevention (observance of physical distancing and mask use), and other health-related information (CD4 count, flu vaccination received during the past 12 months, treatment with tenofovir-containing ART regimens, and adaptation of HIV care during the lockdown). The rationale for choosing these covariates is summarized in the supplementary material (see Appendix 5, Supplemental Digital Content, <http://links.lww.com/QAI/B524>). All statistical tests were two-sided;  $P < 0.05$  was considered statistically significant, and 95% CIs were computed. Statistical analyses were performed in R version 3.6.2.

## RESULTS

### Participant Characteristics

Data from 317 respondents were eligible for analysis. The mean age was 43.4 ± 11.7 years (range: 19–75); men were more represented in our study population (Table 1). Responses originated from 32 countries, half of which were classified as LMIC. Of note, most participants resided either in Belgium (n = 102, 32.2%) or Brazil (n = 89, 28.1%); 59 (18.6%) responses originated from Eastern European countries (Supplementary appendix 1). Anxiety and depressive disorders were found in 72 (22.7%) and 74 (23.3%) participants, respectively, (Table 1); 50 PLWH (15.8%) had both anxiety and depressive disorders.

Regarding HIV treatment, the most frequently used antiretroviral molecules among our participants were tenofovir in 193 (60.8%), lamivudine in 144 (45.4%), and dolutegravir in 131 (41.3%). Thirteen (4.2%) participants reported an interruption of ART during the COVID-19 lockdown period. Difficulties related to ART refill during the COVID-19 pandemic included ART stock out at the clinic/pharmacy in 6 (1.9%);

**TABLE 1.** Characteristics of Study Participants

Characteristics	Observed	N
Age, yr: mean (SD)	43.4 (11.7)	317
Sex: n (%)		317
Male	227 (71.6%)	
Female	87 (27.4%)	
Others	3 (0.9%)	
Highest education level: n (%)		317
Primary	10 (3.2%)	
Secondary	88 (27.8%)	
Undergraduate	102 (32.2%)	
Postgraduate	117 (36.9%)	
Religion: n (%)		317
Christian	148 (46.7%)	
Muslim	10 (3.2%)	
Others	35 (11.0%)	
None	124 (39.1%)	
Marital status: n (%)		312
Single	136 (43.6%)	
Stable relationship	28 (9.0%)	
Cohabitation	53 (17.0%)	
Married	58 (18.6%)	
Divorced	25 (8.0%)	
Widowed	12 (3.8%)	
Most recent CD4 count, cells/μL: mean (SD)	682 (325)	241
CD4 count < 250 cells/μL: n (%)	19 (7.9%)	241
Viral load undetectable during the last follow-up: n (%)	288 (94.4%)	305
Anxiety, GAD-2 score ≥3: n (%)	72 (22.7%)	317
Depression, PHQ-2 score ≥3: n (%)	74 (23.3%)	317
Vaccinated against flu in the past 12 mo: n (%)	183 (57.7%)	317
COVID-19 test results: n (%)		18
Positive	4 (22.2%)	
Negative	14 (77.8%)	

inability to go collect ART due to mobility restrictions in 21 (6.6%); and financial constraints in 2 (0.6%) participants. One hundred four (32.8%) participants reported some form of adaptation of HIV care during the COVID-19 lockdown period; adaptation strategies ranged from changing the amounts of ART refills to teleconsultation for HIV follow-up (Table 2).

One hundred thirty-eight (44.2%) respondents reported being less likely to interrupt ART during the lockdown period; meanwhile, 11 (3.5%) were more likely to interrupt their treatment, and another 163 (52.2%) were as likely to stop ART as before the COVID-19 lockdown. More than half of the respondents (200 PLWH [63.1%]) reported recreational substance use, including consumption of alcohol, tobacco, and marijuana (see Appendix 4, Supplemental Digital Content, <http://links.lww.com/QAI/B524>).

### COVID-19–Reported Symptoms and Preventive Behaviors in PLWH

Among the 140 (44.2%) PLWH who had experienced a cold since January 2020, the most frequent self-reported symptom was coryza (65.7%). Similar symptoms were reported by PLWH with a history of flu vaccination during the past 12 months and those who were not vaccinated (Table 3). Of note, all 4 PLWH who reported positive COVID-19 test results had at least one flu-like symptom. Applying the WHO clinical definition for COVID-19<sup>23</sup> on our entire study population (while assuming no previous contact with an infected individual), it was revealed that 54 (17.0%) of respondents were classified as suspected COVID-19 cases.

Regarding coronavirus-related behaviors, most of the participants reported adhering to the protective measures to reduce their risk of contracting or spreading COVID-19; 285 (89.9%) observed the 1–2 m physical distancing, 209 (65.9%) used face masks, 277 (87.4%) regularly washed their hands with water and soap during the day, 190 (89.9%) covered their mouth when coughing, and 200 (63.1%) avoided as much as possible to touch their face (eyes, nose, and mouth). Observance of COVID-19 preventive measures was not different among PLWH who reported anxiety/depressive disorders and those who did not. A few disparities were noted between the characteristics and preventive behaviors of

**TABLE 2.** Reported Adaptations for HIV Care During the COVID-19 Lockdown Period (n = 104)

Adaptation Strategy	Frequency	Percentage
Increased ART refill quantity	67	64.4%
Reduced ART refill quantity	1	1.0%
Changed location for ART refill	12	11.5%
Phone consultation	25	24.0%
Self-monitoring	10	9.6%
Change in ART regimen	5	4.8%
Obtain ART without seeing a doctor	5	4.8%
Obtain ART without laboratory workup	1	1.0%
ART prescription sent by email	3	2.9%
ART sent by post	3	2.9%
Follow-up by another doctor	1	1.0%

**TABLE 3.** Symptoms Reported by 140 PLWH Who Experienced a Cold Between January and May 2020

Self-Reported Symptom	Overall (N = 140)	Flu Vaccine: No (n = 71)	Flu Vaccine: Yes (n = 69)	P*
Fever	56 (40.0%)	30 (42.3%)	26 (37.7%)	0.704
Headaches	82 (58.6%)	41 (57.7%)	41 (59.4%)	0.977
Dry cough	52 (37.1%)	24 (33.8%)	28 (40.6%)	0.513
Productive cough	54 (38.6%)	30 (42.3%)	24 (34.8%)	0.463
Sore throat	84 (60.0%)	41 (57.7%)	43 (62.3%)	0.704
Coryza	92 (65.7%)	51 (71.8%)	41 (59.4%)	0.171
Loss of smell (anosmia)	17 (12.1%)	10 (14.1%)	7 (10.1%)	0.649
Loss of taste (ageusia)	18 (12.9%)	11 (15.5%)	7 (10.1%)	0.489
Shortness of breath	22 (15.7%)	11 (15.5%)	11 (15.9%)	1.000
Myalgia	53 (37.9%)	27 (38.0%)	26 (37.7%)	1.000
Fatigue	73 (52.1%)	42 (59.2%)	31 (44.9%)	0.130
Nausea	19 (13.6%)	11 (15.5%)	8 (11.6%)	0.670
Diarrhea	34 (24.3%)	15 (21.1%)	19 (27.5%)	0.492
Symptoms duration $\geq$ 2 weeks†	42/136 (30.9%)	25/69 (36.2%)	17/67 (25.4%)	0.236

\*Yates-corrected  $\chi^2$  test.  
†4 missing values.

respondents who resided in LMIC compared with those in high-income settings (Table 4).

We also compared our findings based on the continent of residence of the respondents as follows: Europe (n = 202), Latin America (n = 90), and Asia (n = 23); the 2 PLWH who

**TABLE 4.** Comparison of PLWH Residing in LMIC and HIC

	High Income (n = 145)	Low-Middle Income (n = 172)	P‡
Age, yr: mean (SD)	47.5 (12.5)	40 (9.8)	<0.0001
Most recent CD4 count: mean (SD)	676 (295)*	686 (344)†	0.855
Anxiety disorders: n (%)	25 (17.2%)	47 (27.3%)	0.045
Depression disorders: n (%)	27 (18.6%)	47 (27.3%)	0.091
Adaptation of HIV care: n (%)	35 (24.1%)	69 (40.1%)	0.004
ART interruption: n (%)	5 (3.6%)	8 (4.7%)	0.831
Recreational substance use: n (%)	103 (71.0%)	97 (56.4%)	0.010
Observe physical distancing: n (%)	137 (94.5%)	148 (86.0%)	0.022
Face mask use: n (%)	58 (40.0%)	151 (87.8%)	<0.0001
Reported flu symptoms: n (%)	63 (43.4%)	77 (44.8%)	0.903
Reported flu vaccination: n (%)	88 (60.7%)	95 (55.6%)	0.420

\*52 missing data.  
†24 missing data.  
‡Yates-corrected  $\chi^2$  test or Mann-Whitney U test as appropriate.

resided in Africa were excluded from this analysis. We observed that PLWH in Asia were younger and had the lowest flu vaccination rates, whereas physical distancing was most frequently observed by PLWH in Europe (see Appendix 2, Supplemental Digital Content, <http://links.lww.com/QAI/B524>). In addition, no significant differences were noted in the prevalence of anxiety ( $P = 0.833$ ) and depression ( $P = 0.650$ ) across the continents. Further comparisons within the European continent revealed that PLWH from Eastern European countries (n = 59) were less often vaccinated against flu and used face masks more frequently compared with those residing in Western Europe (n = 143) (see Appendix 3, Supplemental Digital Content, <http://links.lww.com/QAI/B524>). Similar proportions of PLWH in Eastern and Western Europe had depressive disorders ( $P = 0.171$ ); however, anxiety tended to be more frequent among Eastern Europe residents, albeit nonsignificantly (30.5% vs 17.5% in Western Europe;  $P = 0.062$ ) (see Appendix 3, Supplemental Digital Content, <http://links.lww.com/QAI/B524>).

### Factors Associated With the Development of Flu-like Illness During the COVID-19 Outbreak

A multiple logistic regression model was constructed to investigate relevant factors that may be associated with the development of flu-like symptoms among PLWH. We did not include the participants' CD4 count in the final model because that information was not available for many participants (76 missing values), and moreover, no association was observed between CD4 count and the development of flu-like symptoms when conducting bivariate analysis (odds ratio = 1.000; 95% CI: 0.999 to 1.001;  $P = 0.951$ ). We observed that previous vaccination against flu and reported adaptations to ensure continuity of HIV care during the COVID-19 outbreak significantly reduced the odds of PLWH developing flu-like symptoms during the COVID-19 outbreak. The use of tenofovir-containing ART regimen had no impact on the odds of developing flu-like symptoms among our participants.

### DISCUSSION

Our study provides more insights into the impact of the COVID-19 pandemic on the lives of PLWH around the world. The outbreak has undeniably had its toll on HIV care and has stimulated different adaptations of the health care systems to ensure that PLWH still receive proper follow-up and treatment. Only 18 (5.7%) PLWH had been tested for COVID-19, although the application of WHO diagnostic criteria revealed that the actual number of suspected COVID-19 cases requiring testing in our study population was 3 times higher. This indeed demonstrates that actions against COVID-19 still fall short in many countries, even when it concerns special populations like PLWH.

The GAD-2 and PHQ-2 screening tools revealed that almost one-quarter of PLWH had at least one psychosocial disorder. Considering the entire study population, generalized anxiety disorders were less frequently observed in our survey when compared with previous findings among PLWH before the onset of COVID-19<sup>15,16</sup>; however, the differences in

methodologies make it difficult to compare studies. The prevalence of major depressive disorders was much higher in our survey than that observed among PLWH in Kenya using similar methods in a COVID-free setting.<sup>17</sup> A meta-analysis has highlighted that the burden of depression among PLWH was highest in South America<sup>25</sup>; our data showed a similar tendency because the highest prevalence of depression was observed in the Latin American continent (26.7%), although this was not significantly different from the prevalence of depression in Europe and Asia. Furthermore, depression tended to be more frequent among PLWH residing in LMIC compared with HIC, but the difference was not significant. Meanwhile, anxiety was clearly more prevalent among LMIC participants (Table 4); the unequal burden of psychosocial problems in these 2 settings could be related to a higher perceived social judgment and stigma vis-à-vis PLWH in developing countries.<sup>26</sup> Although poverty and psychosocial stress have been associated with an increased risk for substance use,<sup>27,28</sup> our survey found that LMIC residents resorted to recreational substances less frequently than their counterparts in HIC. The reasons underpinning this observation are probably multifactorial, spanning from financial constraints for substance purchase, to the varied sociocultural acceptance of substance use in LMIC.

Besides the disparities in psychosocial well-being, we noted that PLWH in LMIC were younger and were less likely to observe physical distancing than PLWH residing in HIC. These findings reflect the demographic structure and crowded living conditions often encountered in low-income settings.<sup>29</sup> Although a younger population presents a lower risk for COVID-19 morbidity and mortality,<sup>30</sup> preventive measures are still crucial in these communities to limit coronavirus transmission to more vulnerable persons, such as those who are older or with comorbid conditions. Fortunately, the higher rates of mask use reported among PLWH in LMIC may help curb the spread of the disease in these settings where physical distancing is difficult.

Our multivariable model (Table 5) showed that PLWH who had been vaccinated against flu within the 12 months preceding the survey were less likely to experience flu-like symptoms even amidst of the COVID-19 pandemic. Yearly flu vaccination in PLWH is currently internationally recommended.<sup>31</sup> Flu vaccination will reduce the number of PLWH who develop flu-like symptoms and the anxiety generated by these symptoms in the context of a COVID-19 epidemic. It also will reduce the workload of the health care workers because it will decrease the number of suspected cases requiring clinical attention and confirmatory testing. Our findings equally suggest that once the flu-like illness has developed in PLWH, previous flu vaccination has no effects on the prevalence and duration of symptoms (Table 3). Whether the flu shot confers specific protection against COVID-19 is yet to be established.<sup>32</sup>

Our study describes the experiences of PLWH during the ongoing COVID-19 pandemic in a multicountry setting. Nonetheless, our results must be interpreted in light of a number of limitations. This was a cross-sectional survey of the situation during the ongoing pandemic, and it is therefore not possible to know to what extent COVID-19 was

**TABLE 5.** Predictive Factors for the Development of Flu-like Illness Among PLWH

Covariates	Crude OR (95% CI)	Adjusted OR (95% CI)	P
Age	0.997 (0.979 to 1.016)	1.000 (0.980 to 1.022)	0.935
Female sex	0.865 (0.522 to 1.423)	0.799 (0.466 to 1.360)	0.412
Residence in LMIC	1.055 (0.676 to 1.648)	1.054 (0.590 to 1.884)	0.859
Physical distancing observance	1.175 (0.563 to 2.521)	1.200 (0.554 to 2.667)	0.647
Face mask use	1.167 (0.731 to 1.872)	1.274 (0.730 to 2.237)	0.396
Flu vaccination in the past 12 mo	0.528 (0.335 to 0.830)	0.512 (0.320 to 0.818)	0.005
Tenofovir ART regimen	1.042 (0.662 to 1.644)	1.188 (0.732 to 1.939)	0.487
Adaptation HIV care during the lockdown period	0.555 (0.339 to 0.897)	0.513 (0.307 to 0.848)	0.010

AIC, Akaike information criterion; OR, odds ratio; Model AIC = 430.7.

responsible for the reported findings. In addition, the web-based nature of our survey introduces an important sampling bias because only individuals of a certain socioeconomic class with access to the Internet and willing to contribute to science will participate. Moreover, it is impossible to verify the veracity of the information provided by the respondents. We also acknowledge that our convenience-based sample size may be small. However, considering the exceptional circumstances imposed by the ongoing COVID-19 outbreak, we are confident our findings still provide useful insights into the realities faced by PLWH during this pandemic.

In conclusion, COVID-19 and associated restrictive measures have adversely impacted the well-being and follow-up of PLWH. It seems that LMIC residents are more affected than those residing in high-income settings. Furthermore, routine flu vaccinations and adaptations of health care systems to ensure continuity of HIV care during the pandemic may minimize the development of flu-like illness among PLWH, thereby reducing personal stress and preventing additional strain on the health care providers. Although more research is needed to confirm these findings, it is important that health systems devise innovative approaches for anti-retroviral provision and psychosocial support to PLWH during such outbreaks.<sup>19</sup>

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