HIV and COVID-19: review of clinical course and outcomes

Lauren K. Barbera¹, Kevin F. Kamis², Sarah E. Rowan²,³,⁴, Amelia J. Davis⁴, Soraya Shehata¹, Jesse J. Carlson², Steven C. Johnson⁴ and Kristine M. Erlandson⁴

¹University of Colorado, School of Medicine, Aurora, CO, USA; ²Denver Public Health, Denver, CO, USA; ³Denver Health, Division of Infectious Diseases, Denver, CO, USA; ⁴University of Colorado, Department of Medicine, Division of Infectious Diseases, University of Colorado, Aurora, CO, USA

Background: Understanding the relationship between HIV and SARS-CoV-2 has important public health implications.

Objective: To summarize current research on COVID-19 among people with HIV (PWH) as published through 15 July 2021.

Methods: We conducted a search of PubMed, Scopus, preprint databases (medRxiv, bioRxiv), and the references of publications found using key terms relevant to COVID-19 (‘COVID-19’ OR ‘SARS-CoV-2’ OR ‘coronavirus’) AND to HIV (‘HIV’ OR ‘Human Immunodeficiency Virus’ OR ‘AIDS’ OR ‘Acquired Immunodeficiency Syndrome’). We summarized all articles that reported data or opinions on SARS-CoV-2 and HIV coinfection.

Conclusions: Although many initial case series and cohort studies found no increased risk for SARS-CoV-2 infection or severe COVID-19 outcomes among PWH, recent studies have signaled an increased risk for severe COVID-19 disease progression even in the setting of well-controlled HIV. Whether this is due to the increased prevalence of comorbidities in PWH and other social determinants of health is unknown. These conflicting findings highlight the continued need for COVID-19 related research among PWH that addresses COVID-19 disease course as well as exacerbation of existing comorbidities already disproportionately represented among PWH.

KEYWORDS: Human immunodeficiency virus, SARS-CoV-2, COVID-19, coinfection

Introduction

When COVID-19, the disease caused by the novel coronavirus SARS-CoV-2, began to surface in late 2019 and early 2020, healthcare officials and providers assumed that individuals with Human Immunodeficiency Virus (HIV) infection and other immunocompromising conditions would be at particularly high risk of both acquisition and severe disease.¹ Without effective antiretroviral therapy (ART), HIV leads to depletion of CD4 T-lymphocytes, resulting in a weakened adaptive immune response.² In the presence of effective ART, the cellular immune response recovers to variable degrees; however, individuals with HIV appear to remain at greater risk for many infections, including pneumococcal pneumonia, influenza, meningococcal disease, herpes virus infections, and tuberculosis.²⁻⁷

As COVID-19 precipitated widespread closures of businesses, schools, and community gatherings, healthcare agencies, and other critical operations scrambled to determine how to provide essential services to patients while protecting their employees. In an attempt to limit potential spread to patients and employees, many clinics converted to virtual or telephone-based visits.⁸ However, as businesses, schools, and healthcare facilities have gradually resumed in-person services, the ongoing risk for acquiring SARS-CoV-2 infection, or developing severe disease, remain somewhat elusive.

While increasing age, obesity, diabetes, and Black or Hispanic race/ethnicity have consistently been linked to acquisition and severe disease in U.S. populations, the role of other factors, such as HIV, in contributing to risk of COVID-19 acquisition and disease...
severity have been less certain.9–14 Furthermore, people with HIV (PWH) frequently have overlapping risk factors for COVID-19, often at rates higher than the general population. These risks include being male, Black or Hispanic, smoking, older age, and medical comorbidities.15–23 Lastly, despite effective ART, PWH have higher levels of inflammation, one of the key factors driving the development of severe respiratory disease, thromboembolic disease, and other poor outcomes with COVID-19.24,25 Parsing out the added risk of HIV with or without ART in the setting of these other epidemiologic and physiologic risks is therefore challenging.

Methods
To better understand what is currently known about the relationship between HIV and COVID-19 acquisition and disease severity, we conducted a search of PubMed, Scopus, preprint databases (medRxiv, bioRxiv), and the references of publications found using key terms relevant to COVID-19 ('COVID-19' OR 'SARS-CoV-2' OR 'coronavirus') AND to HIV ('HIV' OR 'Human Immunodeficiency Virus' OR 'AIDS' OR 'Acquired Immunodeficiency Syndrome') between 1 March 2020 and 15 July 2021. Of 2210 initial results we considered each study that reported data or opinions on COVID-19 among PWH, applying extra filters to access articles related to ‘symptoms’, ‘severity’, ‘hospitalization’, ‘mental health’, ‘access to care’ and ‘ART’. This resulted in the 212 articles presented in this review. We then summarized the risk for acquiring COVID-19, presenting symptoms of COVID-19, severity of COVID-19 illness, and impacts on mental health and access to care during the COVID-19 pandemic. We also report findings on the effects of antiretroviral therapy on COVID-19 risk and outcomes for PWH.

Discussion
Are people living with HIV more likely to contract SARS-CoV-2?
Many experts initially considered individuals living with HIV as a vulnerable group with regards to SARS-CoV-2 infection due to a greater burden of some comorbidities, higher systemic inflammation despite effective ART, and some degree of immune alteration even among those on effective ART with immune reconstitution.26–32 Whether this is true remains unclear. PWH account for approximately 0.7% of the general population of adults in the world, and roughly 0.5–1.5% of COVID-19 cases in various COVID-19 case series and cohort studies.28,33–36

One prospective cohort study of 5683 PWH observed a lower incidence of COVID-19 among PWH compared to the general population, suggesting a possible protective effect of HIV, ART, or less exposure through physical isolation and consistent use of personal protective equipment.37 However, this study was limited in that it did not control for ART use. Multiple other prospective cohort studies, limited by their study sizes, have found similar rates of SARS-CoV-2 among PWH and the general population.38–41 A study from San Francisco of 4252 PWH suggested that PWH were more susceptible to SARS-CoV-2 infection than those without HIV.42 Numerous other confounders, however, may have explained these differences: for example, 8% of PWH in San Francisco experience unstable housing as compared to the 1% of the San Francisco general population.42 As of 28 July 2020, the Centers for Disease Control and Prevention concluded that based on the limited data available, PWH on effective ART appear to have a similar risk for acquisition of SARS-CoV-2 as people who do not have HIV.43

It is important to note that multiple studies have attempted to distinguish the difference between test positivity and disease incidence. In a recent analysis of over 30,000 PWH in the USA, PWH were more likely to be tested for SARS-CoV-2 but did not have an increased percentage of COVID-19 positivity compared to individuals without HIV.44 However, the authors note that testing shortages and the potential for differential adherence to stay-at-home guidance by immunosuppression status could have influenced the outcome of the study. In contrast, researchers in Southern Italy found that PWH were more reluctant to obtain SARS-CoV-2 testing and thus were likely underdiagnosed with COVID-19, though this was an opinion piece and the conclusion was not backed by data.45

Do the presenting symptoms of COVID-19 differ among people with or without HIV?
In the general population, the most common presenting symptoms of COVID-19 include fever, cough, or shortness of breath (70%) and less commonly muscle aches (36%), headaches (34%), and loss of smell or taste (8%).9 A cohort of 286 PWH showed similar symptoms: cough (76.2%), fever (70.7%), and fatigue (66.0%).20 This study was especially strong as it took data from multiple states and countries. These results have been supported by numerous other studies.46–53 Besides one review, these studies are limited in their small sample size. Of note, other individual case studies have found that PWH may present with COVID-19
and opportunistic infections such as *Pneumocystis jirovecii* pneumonia and AIDS-related disseminated histoplasmosis, perhaps exacerbated by or contributing to presenting symptoms of COVID-19.  

**Are people living with HIV more likely to present with severe disease and/or be hospitalized for COVID-19?**

Similar to the general population, age and co-morbidities appear to be the strongest predictors of severe disease and mortality in PWH.  

Most PWH who develop symptomatic COVID-19 have at least one co-morbidity, most commonly hypertension, dyslipidemia, or type 2 diabetes mellitus.  

Per Dandach et al. (n = 286), 81% of PWH had at least one co-morbidity which impacted their COVID-19 clinical course.  

Data describing the likelihood of hospitalization due to COVID-19 among PWH is limited and mixed: rates of hospital admission among people living with HIV range from 0.8% to 1.8%. Notably, these rates derive from cohorts in numerous countries including Spain, China, and the United States, which may differ demographically with varying rates of comorbidities and clinical threshold for hospitalization. A retrospective, matched cohort study at a New York health system indicated PWH (n = 21) had a significantly higher rate of hospital admission but not intensive care unit admission, mechanical ventilation, or mortality, compared to people without HIV (n = 42). All PWH in this cohort were on ART, the majority had an undetectable viral load, and only six of 19 had a CD4 count < 200 cells/µL, thus limiting the ability to determine the effect of HIV severity of COVID-19 outcomes. A separate small analysis of 31 PWH hospitalized at a New York, NY hospital also found similar rates of hospitalization among those with or without HIV. In a much larger Veteran cohort of 107,636 patients with COVID-19, risk of hospital admission among PWH did not differ from those without HIV, although these results have not yet been published in a peer-reviewed paper.  

In a retrospective study in New York comparing 21 PWH with 42 matched-uninfected controls admitted with COVID-19, a similar burden of comorbidities and similar admission laboratory values were seen between PWH and uninfected controls. In addition, no statistically significant differences were seen between PWH and the uninfected controls when comparing consolidation, infiltrate, or opacity on chest imaging. Although the study was small, findings are strengthened by matching PWH and controls by admission date, age, body mass index, gender, tobacco history, and a history of chronic kidney disease, hypertension, asthma, chronic obstructive pulmonary disease, and heart failure. In summary, among PWH, risk factors for hospitalization and clinical presentation at the time of hospitalization appear to be influenced more by comorbidities or demographic risk factors seen in the general population (race/ethnicity, socio-economic status), and less by HIV-specific factors.

**Are people with HIV more likely to have severe outcomes?**

A number of studies on HIV and SARS-CoV-2 coinfection have addressed the question whether PWH have more severe outcomes than the general population (as defined by more ICU admissions, greater need for mechanical ventilation, and higher mortality rates). As summarized in Table 1, many large studies and smaller case reports have found greater likelihood of ICU admission and higher mortality rates among PWH than the general population. Indeed, of 3,460,932 patients in the public sector in South Africa, 16% were PWH and 22,308 (0.6%) were diagnosed with COVID-19. In this large study, HIV infection was associated with a doubling of COVID-19 mortality risk, independent of CD4 count or HIV viral load (though >90% were virologically suppressed). In a study of 17,282,905 adults (including 27,480 PWH) in the United Kingdom, a substantially higher risk of mortality was seen with COVID-19 in PWH than in the general population, although the actual number of deaths among PWH was only 25, thus limiting some of the conclusions. Furthermore, data were available on some comorbidities and demographics but not HIV-related characteristics (ART, CD4 count, or viral load). A landmark report by the World Health Organization (WHO) included 15,522 PWH and 168,649 adults without known HIV hospitalized with suspected or confirmed SARS-CoV-2 from 24 countries (96% from the WHO African Region). HIV was associated with an increased risk of severe or critical disease at admission compared to uninfected controls, after adjusting for age, sex, and underlying comorbidities. HIV was also independently associated with higher mortality risk. The majority of persons included were from South Africa, and no data were presented on ART, CD4 count, or virologic suppression. Two systematic reviews/meta-analyses also concluded that PWH had a higher risk of mortality, though only in studies of PWH from Africa and the United States. A smaller study of PWH in Brazil (n = 255) found that being Black/Mixed race and having lower education were associated with greater mortality in adjusted models, while age, sex, CD4 count, viral load, and
Table 1. Summary of 2020–2021 publications (through 15 July 2021) related to HIV and COVID-19.

| First author | Population | Location | Publication date | Journal | Description or findings |
|--------------|------------|----------|------------------|---------|------------------------|
| Zhu, F. | 1 PWH | China | 11-Mar-20 | J Med Virol | Described how PWH should be regarded as a vulnerable population in regard to COVID-19 |
| Chen, J. | 1 PWH | China | 14-Apr-20 | J Med Virol | Described a coinfected PWH with atypical CT imaging of the chest |
| Blanco, J.L. | 5 PWH | Spain | 15-Apr-20 | Lancet HIV | Described clinical course of patients (<50 years old) |
| Wang, M. | 1 PWH | China | 23-Apr-20 | Int J Infect Dis | COVID-19 and HIV (low CD4 count) led to a longer disease course |
| Aydin, O.A. | 4 PWH | Turkey | 29-Apr-20 | J Med Virol | Comorbidities are an important factor in mortality for coinfected PWH |
| Ridgway, J.P. | 8 PWH/1061 HIV negative controls | USA | 7-May-20 | AIDS Behav | PWH did not test positive for COVID-19 at a different rate than the general population |
| Härter, G. | 33 PWH | Germany | 11-May-20 | Infection | PWH did not have more severe morbidity or mortality than the general population |
| Gervasoni, C. | 47 PWH | Italy | 14-May-20 | Clin Infect Dis | PWH coinfected with COVID-19 had favorable outcomes as compared to the general population |
| Patel, R.H. | 1 PWH | USA | 22-May-20 | J Med Virol | Coinfected patient under treatment with ART had a less severe clinical presentation than the general hospitalized population |
| Iordanou, S. | 1 PWH | Republic of Cyprus | 25-May-20 | J Med Virol | Coinfected (PWH/COVID-19) patient had a prolonged need for mechanical ventilation and increased risk for thrombotic complications |
| Childs, K. | 18 PWH | United Kingdom | 27-May-20 | Clin Infect Dis | Black PWH were at higher risk of severe disease; ARTs did not appear to provide protection against COVID-19 severity |
| Vizcarra, P. | 51 PWH and COVID-19 positive/ 1288 PWH | Spain | 28-May-20 | Lancet HIV | Clinical presentation in PWH was similar to the general population, however, lower CD4 counts affected disease severity; PWH had a higher prevalence of comorbidities |
| Okoh, A.K. | 27 PWH | USA | 28-May-20 | J Acquir Immune Defic Syndr | Coinfected PWH presented similarly to the general population |
| Ridgway, J.P. | 5 PWH | USA | 29-May-20 | AIDS Patient Care STDs | A similar COVID-19 clinical course was seen in PWH as in the general population |
| Shalev, N. | 31 PWH | USA | 30-May-20 | Clin Infect Dis | HIV coinfected did not lead to increased rates of hospitalization; outcomes for PWH were similar to the general population |
| Suwanwongse, K. | 9 PWH | USA | 9-Jun-20 | J Med Virol | PWH did not have more favorable COVID-19 outcomes especially when their CD4 counts were low |
| Coleman, H. | 1 PWH | United Kingdom | 10-Jun-20 | AIDS | Pneumocystis jirovecii pneumonia and COVID-19 infection were observed in a PWH |
| Karmen-Tuohy, S. | 21 PWH/42 HIV negative controls | USA | 12-Jun-20 | J Acquir Immune Defic Syndr | PWH had a higher admission rate for COVID-19 but did not show significant differences in ICU admissions, mechanical ventilator use, or mortality |
| Benkovic, S. | 4 PWH | USA | 16-Jun-20 | J Med Virol | Clinical severity was not different in uncomplicated cases of |

(Continued)
| First author   | Population | Location | Publication date | Journal/Conference | Description or findings |
|---------------|------------|----------|------------------|--------------------|------------------------|
| Byrd, K.M.115 | 27 PWH     | USA      | 19-Jun-20        | J Int AIDS Soc     | COVID-19 and HIV coinfection as compared to the general population |
| Meyerowitz, E.A.75 | 47 PWH   | USA      | 25-Jun-20        | AIDS               | Coinfected PWH were on average 53.4 years old and a substantial proportion had comorbidities, were non-Hispanic Black, and lived or worked in a congregate setting |
| Del Amo, J.202 | 236 PWH and COVID-19 positive/77,590 PWH receiving ART | Spain | 26-Jun-20 | Ann Intern Med | The risk for COVID-19 hospitalization was 20.3 among patients receiving TAF/FTC, 10.5 among those receiving TDF/FTC, 23.4 among those receiving ABC/3TC, and 20.0 for those receiving other regimens |
| Sigel, K.74   | 88 PWH/405 HIV negative controls | USA | 28-Jun-20 | Clin Infect Dis | There was no difference in COVID-19 severity on admission by HIV status and PWH did not have more severe COVID-19 outcomes than the general population |
| Toombs, J.M.129 | 3 PWH   | United Kingdom | 29-Jun-20 | J Med Virol | PWH may be protected from severe COVID-19 if they are on ART |
| Ho, H.84      | 72 PWH     | USA      | 30-Jun-20        | J Infect Dis       | PWH were at higher risk for severe COVID-19 outcomes, especially those with increased markers of inflammation and immune dysfunction |
| Guo, W.76     | 14 PWH     | China    | 1-Jul-20         | J Int AIDS Soc     | HIV and COVID-19 coinfection led to a higher mortality rate and higher proportion of severe cases than the general population |
| Park, L.S.44  | 30,891 PWH/76,745 HIV negative controls | USA | 6-Jul-20 | AIDS 2020 Conference | PWH had higher COVID-19 testing rates but no evidence to support increased positivity or more severe outcomes |
| Ruan, L.102   | 4 PWH      | China    | 6-Jul-20         | J Med Virol        | PWH in the stage of AIDS had a more complicated clinical course than those not in AIDS |
| Gudipati, S.112 | 14 PWH  | USA      | 15-Jul-20        | J Acquir Immune Defic Syndr | PWH were not at a higher risk for severe COVID-19 outcomes |
| Mahmood, K.196 Cooper, T.J.140 | 1 PWH/70 PWH | USA | 15-Jul-20 | JACC Case Rep HIV Med | Coinfected PWH on a LVAD PWH with well-controlled disease are not at risk of poorer COVID-19 outcomes than the general population |
| Adachi, E.141 | 2 PWH      | Japan    | 15-Jul-20        | AIDS               | Transgender PWH have similar clinical course of COVID-19 as compared to the general population |
| Charre, C.39  | 77 PWH/27 PrEP users/19009 other patients | France | 17-Jul-20 | AIDS | The positivity rate appeared similar in HIV-infected patients, in PrEP users, and in other patients |
| Maggiolo, F.61 | 55 PWH and COVID-19 positive/69 PWH | Italy | 24-Jul-20 | J Med Virol | HIV coinfection did not protect from COVID-19 coinfection or from severe disease |
| Su, J.52      | 1 PWH      | China    | 1-Aug-20         | AIDS               | Described COVID-19 in a patient with AIDS; speculated that protease inhibitors might have a protective effect for COVID-19 |
| Stoeckle, K.116 | 30 PWH/90 HIV-negative controls | USA | 1-Aug-20 | Open Forum Infect Dis | |

(Continued)
| First author | Population | Location | Publication date | Journal | Description or findings |
|--------------|------------|----------|-----------------|---------|-------------------------|
| Sun, L.J.\textsuperscript{111} | 1 PWH | Singapore | 1-Aug-20 | J Acquir Immune Defic Syndr | A similar COVID-19 clinical course was seen in PWH as in negative controls. He recovered from a mild and uncomplicated clinical course of COVID-19 without treatment. |
| Calza, L.\textsuperscript{148} | 26 PWH | Italy | 3-Aug-20 | Infection | PWH had a similar COVID-19 clinical presentation to the general population. |
| Bhaskaran, K.\textsuperscript{19} | 27480 PWH/17.3 million adults | United Kingdom | 7-Aug-20 | Lancet | PWH had nearly three-fold higher risk of COVID-19 death than those without HIV after adjusting for age and sex. |
| Tian, C.\textsuperscript{108} | 1 PWH | China | 10-Aug-20 | Ann Palliat Med | Described favorable outcome in coinfected PWH. |
| Guo, W.\textsuperscript{138} | 11 PWH | China | 10-Aug-20 | Res Sq | PWH have comparable COVID-19 morbidity rates as the general population, |
| Marbaniang, I.\textsuperscript{158} | 167 PWH | India | 13-Aug-20 | Res Sq | 1/4 of PWH had anxiety during the COVID-19 pandemic. |
| Huang, J.\textsuperscript{34} | 35 PWH | China | 17-Aug-20 | Clin Infect Dis | PWH had similar COVID-19 mortality rates as those without HIV. |
| Parker, A.\textsuperscript{136} | 24 PWH/92 HIV negative controls | South Africa | 21-Aug-20 | S Afr Med J | Confined PWH had similar presentations and outcomes as those without HIV. |
| Boule, A.\textsuperscript{91} | 553,749 PWH | South Africa | 29-Aug-20 | Clin Infect Dis | HIV was independently associated with increased COVID-19 mortality. |
| Larzábal, F.J.\textsuperscript{7} | 1 PWH | Argentina | 31-Aug-20 | Medicina | Described a PWH hospitalized with Pneumocysti jirovecii and COVID-19 coinfection. |
| Molina-Iturritza, E.\textsuperscript{139} | 8 PWH | Spain | 1-Sep-20 | AIDS | The rate of COVID-19 in PWH is similar to the rate in the general population. |
| Sasset, L.\textsuperscript{70} | 2 PWH | Italy | 1-Sep-20 | AIDS | PWH had similar demographic and clinical characteristics to the general population. |
| Hu, Y.\textsuperscript{197} | 12 PWH | China | 1-Sep-20 | J Acquir Immune Defic Syndr | The value of ART for mitigation of COVID-19 infection is discussed. |
| Shekhar, R.\textsuperscript{110} | 5 PWH | USA | 1-Sep-20 | J Acquir Immune Defic Syndr | PWH may have a milder course of COVID-19 than the general population. |
| Madge, S.\textsuperscript{117} | 18 PWH | United Kingdom | 2-Sep-20 | Sex Transm Infect | PWH did not have prolonged hospital courses or worse outcomes compared to the general population. |
| Etienne, N.\textsuperscript{64} | 54 PWH and COVID-19 positive/4000 PWH | France | 3-Sep-20 | AIDS | PWH had worse COVID-19 outcomes when they were older age, male, had comorbidities, higher BMI, sub-Saharan Africa origins, had lower CD4 counts. |
| Inciarte, A.\textsuperscript{37} | 53 PWH and COVID-19 positive/5683 PWH | Spain | 3-Sep-20 | AIDS | Incidence rate of COVID-19 was lower in PWH compared to general population; clinical course of COVID-19 was not dependent on any HIV- or ART-related factor. |
| Winston, A.\textsuperscript{77} | 699 PWH/304 HIV negative controls | United Kingdom and Ireland | 3-Sep-20 | AIDS | PWH tended to have more comorbidities which was associated with poorer COVID-19 outcomes. |
| d’Ettore, G.\textsuperscript{31} | 1 PWH | Italy | 4-Sep-20 | Medicine | Coinfection of HIV and COVID-19 showed increased levels of IFNs/Il and T-cell activation as compared to healthy individuals with COVID-19. |
| Bertolini, M.\textsuperscript{64} | 1 PWH | Argentina | 9-Sep-20 | Int J STD AIDS | Described a male patient with AIDS-related disseminated
| First author                      | Population | Location | Publication date | Journal                       | Description or findings                                                                 |
|----------------------------------|------------|----------|-----------------|-------------------------------|------------------------------------------------------------------------------------------|
| Dandachi, D.                      | 286 PWH    | USA      | 9-Sep-20        | Clin Infect Dis               | Histoplasmosis associated with COVID-19; PWH were at higher risk for severe COVID-19 outcomes, especially those with comorbidities and lower CD cell counts |
| Akyala, A.                       | 4 PWH      | Nigeria  | 10-Sep-20       | Pan Afr Med J                 | PWH experienced a mild COVID-19 clinical course                                           |
| Nagarakanti, S.R.                | 23 PWH/23 HIV negative controls | USA | 19-Sep-20 | J Med Virol | Among PWH, there was not higher mortality, ICU admissions, or mechanical ventilation in PWH than in the general population |
| Chiappe Gonzalez, A.J.           | 1 PWH      | Peru     | 21-Sep-20       | Int J STD AIDS                | HIV/COVID-19 coinfection led to a fatal outcome                                           |
| Mondi, A.                        | 5 PWH      | Italy    | 25-Sep-20       | J Med Virol                   | PWH did not have more severe COVID-19 outcomes than the general population                |
| Isemia, V.                       | 30 PWH     | France   | 26-Sep-20       | Int J Infect Dis              | HIV was not a risk factor for COVID-19                                                   |
| Sun, S.                          | 703 PWH    | China    | Oct-20          | AIDS Behav                    | PWH reported high rates of anxiety, depression, and insomnia                             |
| Collins, L.F.                    | 20 PWH     | USA      | 1-Oct-20        | AIDS                          | PWH with more than 5 comorbidities, who are non-Hispanic Black, are male had more severe COVID-19 outcomes |
| Di Biagio, A.                    | 4 PWH      | Italy    | 1-Oct-20        | AIDS                          | Protease inhibitor-based regimens were not protective against contracting COVID-19 in PWH |
| Yamamoto, S.                     | 5 PWH      | Japan    | 2-Oct-20        | J Microbiol Immunol Infect    | PWH coinfected with COVID-19 have a similar clinical course as patients without HIV       |
| Kim, J.Y.                        | 1 PWH      | Korea    | 12-Oct-20       | Korean Med Sci                | PWH had a favorable clinical outcome with COVID-19                                        |
| Gamboa, E.                       | 1 PWH      | USA      | 17-Oct-20       | Cureus                        | Noted that CD4+ lymphocytes declined over the course of COVID-19 hospitalization in a PWH |
| Zhang, J.C.                      | 2 PWH      | China    | 19-Oct-20       | BMC Infect Dis                | Described the importance of accurate diagnosis for PWH with COVID-19 coinfection         |
| Geretti, A.M.                    | 115 PWH/47,424 HIV negative controls | United Kingdom | 23-Oct-20 | Clinical Infectious Diseases | Following additional adjustment for disease severity at presentation, mortality was higher in PWH |
| Yang, R.                         | 3 PWH/53 HIV negative controls | China | 27-Oct-20 | Expert Review of Respiratory Medicine | Low CD4 count was a risk factor for severe COVID-19 outcomes                               |
| Cabello, A.                      | 63 PWH     | Spain    | 27-Oct-20       | Int J Infect Dis              | Coinfected PWH do not have different outcomes based on severity of HIV or type of ARV treatment |
| Di Biagio, A.                    | 69 PWH     | Italy    | 1-Nov-20        | AIDS                          | Lower CD4 counts were associated with higher rates of COVID-19 hospital admission and more severe outcomes |
| Hadi, Y.B.                       | 404 PWH/49,763 HIV negative controls | USA | 1-Nov-20 | AIDS | Propensity-matched analysis showed no difference in outcomes for PWH compared to the non-HIV controls; higher mortality was related to comorbidities |
| Siewe Fodjo, J.N.                | 317 PWH    | Belgium, Brazil | 1-Nov-20 | J Acquir Immun Defic Syndr | 23.3% of PWH screened positive for depression and 22.7% screened positive for anxiety during the COVID-19 pandemic |
| Morani, Z.                       | 43 PWH     | Belize, USA | 2-Nov-20 | | (Continued) |
| First author | Population | Location | Publication date | Journal | Description or findings |
|--------------|------------|----------|-----------------|---------|-------------------------|
| Tesoriero, J.M. | 2988 PWH | USA | 6-Nov-20 | SN Compr Clin Med | Comorbidities and advanced age make PWH more prone to worse COVID-19 outcomes. PWH experienced poorer COVID-19 related outcomes than those without HIV. PWH who had higher levels of social support reported less depression during the COVID-19 pandemic. PWH had similar prevalence and type of COVID-19 symptoms as the general population. PWH were more susceptible to COVID-19 than those without HIV. |
| Jones, D.L. | 1554 PWH | Argentina, USA | 18-Nov-20 | MedRxiv | Two patients with normal CD4+ count had mild coinfections, a patient with low CD4+ count died. |
| D’Souza, G. | 2078 PWH/1333 HIV negative controls | USA | 19-Nov-20 | HIV Res Clin Pract | More PWH had adverse COVID-19 outcomes than the general population, perhaps due to comorbidities and other social determinants of health. |
| Sachdev, D. | 193 PWH and COVID-19 positive/4252 PWH | USA | 20-Nov-20 | J Acquir Immune Defic Syndr | PWH with advanced immunosuppression may not have an unfavorable COVID-19 disease outcome. |
| Turken, M. | 4 PWH | Turkey | 30-Nov-20 | Curr HIV Res | HIV serostatus was not associated with more severe disease. |
| Braunstein, S.L. | 2410 PWH | USA | 30-Nov-20 | Clin Infect Dis | PWH had increased symptoms of anxiety and depression during the COVID-19 pandemic. |
| Swaminathan, N. | 6 PWH | USA | 1-Dec-20 | J Med Virol | PWH had similar prevalence and type of COVID-19 symptoms as the general population. |
| Hardy, Y.O. | 3 PWH | Ghana | Dec-20 | Ghana Med J | PWH had increased symptoms of anxiety and depression during the COVID-19 pandemic. |
| Kowalska, J.D. | 34 PWH | Central and Eastern Europe | 13-Dec-20 | Int J Infect Dis | HIV patients with COVID-19 experienced a high degree of hospitalization and death. |
| Kuman Tuncel, O. | 307 PWH | Turkey | 17-Dec-20 | Turk J Med Sci | PWH had similar mortality when compared to other studies. |
| Hoffmann, C. | 175 PWH | Germany, Spain, Italy | 27-Dec-20 | HIV Med | PWH had similar mortality when compared to other studies. |
| Noe, S. | 500 PWH | Germany | 2-Jan-21 | Infection | There were no marked differences for PWH with and without SARS-CoV-2 co-infection. |
| Cooley, S.A. | 54 PWH/133 HIV negative controls | USA | 6-Jan-21 | J Neurovirol | PWH had increased symptoms of anxiety and depression during the COVID-19 pandemic. |
| Laracy, J. | 68 PWH/272 HIV negative controls | USA | 28-Jan-21 | Open Forum Infect Dis | PWH did not differ from HIV-uninfected controls by rate of mechanical ventilation or death. |
| Tesoriero, J.M. | 2988 PWH/2409 HIV negative controls | USA | 1-Feb-21 | JAMA Netw Open | PWH experienced poorer COVID-19 outcomes than the general population. |
| Patel, V.V. | 100 PWH/4513 HIV negative controls | USA | 1-Feb-21 | Acquir Immune Defic Syndr | PWH had increased risk of intubation but similarly frequent rates of AKI and in-hospital death as those without HIV. |
| Ceballos, M.E. | 36 PWH | Chile | 3-Feb-21 | Int J STD AIDS | No differences were found between PWH and the general population in the need for mechanical ventilation and death. |
| Nasreddine, R. | 101 PWH | Belgium | 9-Feb-21 | J Med Virol | HIV patients with COVID-19 experienced a high degree of hospitalization and death. |
| Delle Donne, V. | 98 PWH | Italy | 1-Mar-21 | Infez Med | Almost half of PWH experienced significant distress due to the COVID-19 pandemic. |
| First author | Population | Location | Publication date | Journal | Description or findings |
|--------------|------------|----------|-----------------|---------|-------------------------|
| Eybpoosh, S. | 90 PWH     | Iran     | 10-Mar-21       | Med J Islam Repub Iran | HIV infection was not a risk factor for increased COVID-19 severity and death |
| Sorbera, M.  | 211 PWH    | USA      | 16-Mar-21       | J Am Coll Clin Pharm | Telehealth for pharmacy services did not jeopardize patient outcomes |
| Weerasuria, M.| 153 PWH    | Australia| 17-Mar-21       | AIDS Res Hum Retroviruses | Telehealth was widely used; many PWH experienced negative mental health in the COVID-19 pandemic |
| Farinacci, D. | 1 PWH     | Italy    | 31-Mar-21       | AIDS Res Hum Retroviruses | HIV was not associated with adverse outcomes of COVID-19 |
| Durstenfeld, M.S. | 220 PWH | USA     | 7-Apr-21       | MedRxiv | HIV was not associated with adverse outcomes of COVID-19 |
| Mohindra, R.  | 1 PWH/1 HIV negative control | India | 7-Apr-21       | Virus disease | PWH had a similar clinical course to HIV negative persons |
| Liu, W.      | 1 PWH      | Taiwan   | 21-Apr-21       | J Formos Med Assoc | The clinical presentation of coinfected PWH were similar to other COVID-19 patients without HIV infection |
| Díaz, M.M.   | 156 PWH    | Peru     | 26-Apr-21       | MedRxiv | PWH reported increased anxiety and stress during the COVID-19 pandemic |
| Mang, S.     | 1 PWH      | Germany  | 26-Apr-21       | Clin Infect Dis | PWH coinfected with COVID-19 and Pneumocystis jirovecii |
| Siewe Fodjo, J.N. | 247 PWH | Brazil | 27-Apr-21       | Int J Environ Res Public Health | 27.1% of PWH screened positive for anxiety, 27.9% screened positive for depression during the COVID-19 pandemic |
| Spinelli, M.A. | 955 PWH/1062 HIV negative controls | USA | 29-Apr-21 | Lancet HIV | PWH had more cases of severe COVID-19 |
| Liang, M.    | 7718 PWH/196,043 HIV negative controls | China | 3-May-21 | Infect Dis Ther | Coinfected PWH were not associated with higher COVID-19 mortality |
| Merchant, E.A. | 1 PWH | USA | 7-May-21 | ID Cases | Coinfection PWH had PJP |
| Charifi, Y.  | 1 PWH      | Morocco  | 15-May-21       | Clin Case Rep | Coinfected PWH had pneumocystis with typical lesions |
| Massarvva, T. | 730 PWH     | Cyprus   | 17-May-21       | Epidemiol Health | Coinfected PWH had comparable clinical outcomes with the general population |
| Kumar, S.    | 167 PWH    | India    | 19-May-21       | New Microbes New Infect | Many PWH experience fear, anxiety and depression in the COVID-19 pandemic |
| Venturas, J. | 108 PWH/276 HIV negative controls | South Africa | 26-May-21 | J Infect | HIV is not a risk factor for severe COVID-19 disease or mortality |
| Ader, F.     | 583 patients | France | 26-May-21 | Clin Microbiol Infect | COVID-19 clearance and clinical status were not improved but lopinavir/ritonavir |
| Pujari, S.   | 86 PWH     | India    | 31-May-21       | AIDS Res Hum Retroviruses | Coinfected PWH had similar clinical outcomes as the general population; comorbidities are associated with more severe outcomes |
| Pujari, S.   | 94 PWH     | India    | 2-Jun-21        | Immun Inflamm Dis | Long-COVID is common among PWH with moderate-severe acute COVID-19 |
| Rocha, S.Q.  | 255 PWH    | Brazil   | 4-Jun-21        | AIDS Care | Skin color/race, and schooling remained significantly associated with higher COVID-19 mortality in PWH |
| Chanda, D.   | 122 PWH    | Zambia   | 4-Jun-21        | MMWR | Severe HIV is associated with increased risk of COVID-19 death |
| Di Castelnuovo, A. | 3,451 patients | Italy | 9-Jun-21 | Front med | DRV/c was associated with increased mortality |
| Wu, M.      | 68 PWH/980 HIV negative controls | China | 9-Jun-21 | Res Sq | Older age was considered a driving force for coinfection in PWH |

(Continued)
comorbidities were not. To the best of our knowledge, thus far only one study has investigated the risk of post-acute symptoms following COVID-19 and found that moderate to severe disease was associated with an increased risk of persistent symptoms in PWH.95

Dandachi et al. (n = 286) noted that patients with lower CD4 counts (<200 cells/mm³) may be at risk for more severe outcomes despite viral suppression and this was supported by other smaller studies.20,72,84,96–103 The results of Dandachi et al. are strong and generalizable as they pull data from 36 institutions across 21 states and three countries. However, the study did not collect data on social determinants of health or COVID-19 therapies, which may have differed and confounded the results. Greater comorbidity burden in PWH has also been associated with more severe COVID-19 outcomes.20,28,46,64,76,77,104

Other studies suggest that PWH have fewer COVID-19 complications, fewer admissions to the ICU, and lower mortality rates (as seen in Table 1).105–111 Larger cohorts from Spain, Italy, and the USA as well as many smaller studies have found no association or an unclear association between severity of outcomes such as ICU admission, need for mechanical ventilation, or mortality rates and HIV serostatus.34,38,44,61,74,80,99,112–147

In general, PWH appear to be at higher risk for severe COVID-19 outcomes even after considering demographic factors and comorbidities associated with severe disease. However, it is important to note that due to the quickly changing testing procedures and requirements for hospitalization throughout the pandemic, as well as the reliance on public health surveillance data and/or medical record review, the ability to truly distinguish severity of outcomes in PWH is difficult and often confounded.148 Regardless, preventive measures for PWH should be strongly encouraged (particularly vaccination) to limit disease severity.

How does COVID-19 impact the mental health of PWH?

The social distancing and quarantine strategies required to reduce the spread of SARS-CoV-2 have left many feeling isolated and lonely. This is especially impactful to PWH as they have increased worry about physical health (68%), mental health (66%), finances (50%), and accommodation (25%) during the COVID-19 pandemic.149 One study found that of 703 PWH, 61% of PWH reported depressive symptoms, 50% noted anxiety symptoms, and 39% experienced recent insomnia.150 Other smaller studies have also found increased rates of depression, anxiety, insomnia, and substance abuse in relation to the COVID-19 pandemic.151–162 Importantly, these rates are lower amongst people who report strong levels of social support in a large study from two countries.163

How does COVID-19 impact access to care for PWH?

The COVID-19 pandemic has restricted access to care for much of the population by restricting public transportation, suspending routine appointments, and adding financial hardships. PWH specifically are at high risk of treatment interruption due to reduced access to HIV clinics, reduction in primary care or specialty referrals, and difficulties refilling ART prescriptions.150,156,157,164–176 Telemedicine has proven to be
very effective in many countries as it provides flexibility in scheduling appointments, reduces the need for transportation, and provides privacy for patients not wanting to be seen attending an HIV clinic. However, telemedicine also presents barriers including technological challenges, client/provider experiences, digital literacy, low socio-economic status of client population, and reimbursement issues. Many countries have identified this imbalance in access to care both with HIV diagnosis and ongoing care and have provided at-home testing kits, distributed condoms with COVID-19 testing services, and mailed ART to ensure continuity of care.

How does ART influence acquisition of SARS-CoV-2 or severity of COVID-19?
In the USA, an estimated 61.5% of the 1.2 million persons living with HIV are virologically suppressed using ART. Consequently, most PWH who develop COVID-19 will be on suppressive ART. While maintaining suppressed viral load and a normal CD4 T-lymphocyte count likely decreases the risk of severe COVID-19, there is yet to be clear evidence that ART itself prevents the acquisition of SARS-CoV-2 infection or alters the rate of progression to severe disease. Three observational studies have suggested a potential protective role of tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) among PWH. The last of these adjusted for comorbidities, demographics, country of birth, and education level. As TDF/FTC tends to be avoided due to toxicity among older patients with more comorbid conditions, this finding may be due to confounders of younger age and fewer comorbidities, rather than a protective effect of the drug. Similarly, the HIV protease inhibitor lopinavir-ritonavir has in vitro activity against SARS-CoV-2 and some speculate that it may be protective against COVID-19. However, a randomized control trial of this medication in 199 HIV-negative persons with COVID-19 have failed to demonstrate a clinical benefit and other studies, including systemic reviews and meta-analyses, support the conclusion that ART does not serve a protective role against SARS-CoV-2 infection. A study of darunavir/cobicistat actually showed an increased mortality rate. However, this was an observational study that may have been affected by confounders.

General management of COVID-19 among PWH
The guidelines for management of care for PWH and COVID-19 does not differ from those without HIV, although the likelihood of severe disease and poor outcomes may be heightened. Thus, we suggest that the following principles of HIV management are important in persons who present with COVID-19:

- Public health precautions including hand hygiene, mask wearing, and physical distancing should be strictly adhered to.
- Compliance with routine vaccinations, including influenza, should be emphasized.
- COVID-19 vaccination should be given.
- Consideration could be given to telehealth visits in place of in-person visits to ensure continuity of care, particularly in areas of high COVID-19 rates and when there are no acute health concerns.
- For persons who are on HIV treatment, ART and opportunistic infection prophylaxis (if applicable) should be continued, if feasible based on the patient’s clinical condition.
- ART should not be adjusted in an attempt to treat COVID-19.
- With regards to COVID-19 treatment, there are no significant drug–drug interactions between remdesivir and ART. Dexamethasone is an inducer of hepatic metabolism of drugs and could decrease the levels of some co-administered ART. As the course of dexamethasone is typically limited to 10 days or less, it is unlikely that this interaction will be significant in most circumstances.
- If there is a need to adjust or change ART, consultation with an HIV specialist is recommended. For critically ill patients who require enteral feeding, some ART are available in liquid formulations and some pills may be crushed. Clinicians should consult an HIV specialist and/or pharmacist to assess the best way for a patient with a feeding tube to continue an effective regimen.
- Regarding prophylaxis for opportunistic infections, whether the lymphopenia associated with COVID-19 places PWH at higher risk for opportunistic infections is not currently known. As this lymphopenia is limited, the risk of acquiring infections is not expected to alter prophylactic therapy.
- As COVID-19 may occur more commonly in people with limited prior access or engagement to the healthcare system, the hospitalization is an opportunity to screen for HIV and other infections (hepatitis C, tuberculosis), as indicated. For persons who present with COVID-19 and a new diagnosis of HIV infection, the timing of starting ART is currently unknown. Currently, the Department of Health and Human Services guidelines recommend immediate initiation of ART in persons with newly diagnosed HIV infection. Immune reconstitution could help in the management of SARS-CoV-2 infection. In contrast, immune reconstitution could also exacerbate the inflammatory response and worsen respiratory failure or contribute to a hypercoagulable state in others. Other characteristics such as renal failure, thrombosis, or mechanical ventilation might suggest a delay in ART initiation to avoid further exacerbating inflammation. Consultation with an HIV specialist is advised.
Conclusion
Although initial case studies and small cohorts found similar rates of infection and severity in PWH, the growing literature in diverse settings throughout the course of the pandemic now suggests that PWH are at greater risk for severe disease, even with well-controlled HIV. As the pandemic continues, PWH should be counseled regarding the heightened risk from HIV, in addition to other demographic or comorbid factors. Precautions to limit unnecessary exposure and decrease risk for acquisition (i.e. handwashing, physical distancing, mask wearing) should be encouraged particularly during surges in infection rates. While the general care of PWH who also acquire SARS-CoV-2 infection does not differ from people without HIV, certain considerations regarding drug–drug interactions can be guided through consultation with an HIV specialist. Lastly, while separate from the direct complications of COVID-19, the isolation and loneliness experienced during this pandemic, potential interruptions of medication therapy, and reduced access to care may have an even more profound effect on those experiencing the stigma of HIV. Ensuring that PWH are able to stay connected to local resources and monitoring for the impact on mental health and well-being will have important long-term implications.

Disclosure statement
No potential conflict of interest was reported by the authors.

Funding
This work was supported in part by the National Institutes of Health, National Institute on Aging [R01AG054366-05S] and the GEMS-Health Professionals Program [R25HL103286]. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. KME has received grant funding from Gilead Sciences (paid to the University of Colorado Denver and the Associate Director of the Division of Infectious Diseases at the University of Colorado School of Medicine in Aurora, CO).

Notes on contributors

Lauren K. Barbera is an MD candidate at the University of Colorado School of Medicine in Aurora, CO.

Kevin F. Kamis, MPH, is a Researcher at Denver Public Health, a department within Denver Health and Hospital Authority, Denver, CO, USA.

Sarah E. Rowan, MD, is an Associate Professor in the Division of Infectious Diseases at the University of Colorado Denver and the Associate Director of HIV and Viral Hepatitis Prevention at Denver Public Health, a division of Denver Health and Hospital Authority.

Amelia J. Davis is a MD/MPH candidate at the University of Colorado School of Medicine and the Colorado School of Public Health in Aurora, CO.

Soraya Shehata is a MD/PhD candidate at the University of Colorado School of Medicine, currently completing her thesis work in the Molecular, Cellular, and Developmental Biology Department of CU Boulder.

Jesse J. Carlson is a Research Associate at Denver Public Health and an MPH candidate at the Colorado School of Public Health in Aurora, CO.

Steven C. Johnson, MD, is a Professor of Medicine and the Associate Division Head for Clinical Affairs in the Division of Infectious Diseases, Department of Medicine, at the University of Colorado School of Medicine in Aurora, Colorado.

Kristine M. Erlandson, MD, MS is an Associate Professor of Medicine and Epidemiology at the University of Colorado in Aurora, CO.

References
1 Fung M, Babik JM. COVID-19 in immuno-compromised hosts: what we know so far. Clin Infect Dis. 2021;72(2):340–350.
2 Maertens G, Bouille A, CD4 T-cell responses to combination antiretroviral therapy. Lancet. 2007;370(9585):366–368.
3 Marcus JL, Baxter R, Leyden WA, et al. Invasive pneumococcal disease among HIV-infected and HIV-uninfected adults in a large integrated healthcare system. AIDS Patient Care STDS. 2016;30(10):463–470.
4 Folaranmi TA, Kretz CB, Kamiya H, et al. Increased risk for meningococcal disease among men who have sex with men in the United States, 2012–2015. Clin Infect Dis. 2017;65(5):756–763.
5 Patel P, Bush T, Mayer KH, et al. Prevalence and risk factors associated with herpes simplex virus-2 infection in a contemporary cohort of HIV-infected persons in the United States. Sex Transm Dis. 2012;39(2):154–160.
6 Barrera-López P, Pérez-Riveros ED, Moreno-Montoya J, Ballesteros SM, Valencia SA, De la Hoz-Valle JA. Co-infection of other respiratory pathogens and HIV in COVID-19 patients: is there a pattern? J Med Virol. 2021;93(1):8–19.
7 Lázábal FJ, Vilela A, Brusca S, Saluzzi I, Ghergo GE, Angiono MA. Simultaneous diagnosis and favorable evolution of infection with Pneumocystis jirovecii, SARS-CoV-2 and advanced HIV. Medicina (B Aires). 2020;80(5):554–556.
8 Lau J, Knudsen J, Jackson H, et al. Staying connected in the COVID-19 pandemic: telehealth at the largest safety-net system in the United States. Health Aff (Millwood). 2020;39(8):1437–1442.
9 Stokes EK, Zambrano LD, Anderson KN, et al. Coronavirus disease 2019 case surveillance – United States. MMWR Morb Mortal Wkly Rep. 2020;69(24):759–765.
10 Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. Jama. 2020;323(20):2052–2059.
11 Price-Haywood EG, Burton J, Fort D, Seoane L. Hospitalization and mortality among black patients and white patients with Covid-19. N Engl J Med. 2020;382(26):2534–2543.
12 Lighter J, Phillips M, Hochman S, et al. Obesity in patients younger than 60 years is a risk factor for COVID-19 hospital admission. *BMC Infect Dis.* 2020;71(15):896–97.
13 Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020;395(10223):1054–1062.
14 Petrelli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ.* 2020;369:m1966.
15 CDC. HIV Surveillance Report: Supplemental Report. Estimated HIV incidence and prevalence in the United States, 2014–2018. Centers for Disease Control and Prevention. http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html. Published 2020. Accessed 1, 25.
16 Erlanson KM, Karris MY. HIV and aging: reconsidering the approach to management of comorbidities. *Infect Dis Clin North Am.* 2019;33(3):769–786.
17 Schouten J, Wit FW, Stolte IG, et al. Cross-sectional comparison of the prevalence of age-associated comorbidities and their risk factors between HIV-infected and uninfected individuals: the AGS/EZH cohort study. *Clin Infect Dis.* 2014;59(12):1787–1797.
18 Fields EL, Copeland R, Hopkins E. Same script, different approach to management of comorbidities. *Lancet.* 2020;7(7):554–556.
19 Bhaskaran K, Rentsch CT, MacKenna B, et al. HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform. *Lancet HIV.* 2021;8(1):e24–e32.
20 Dandachi D, Geiger G, Montgomery MW, et al. Characteristics, comorbidities, and outcomes in a multicenter registry of patients with HIV and coronavirus disease-19 [published ahead of print]. *Clin Infect Dis.* 2020. doi:10.1093/cid/ciaa1339.
21 Weiser JK, Tie Y, Beer L, Fanfair RN, Shouse RL. Racial/ethnic and income disparities in the prevalence of comorbidities that are associated with risk for severe COVID-19 among adults receiving HIV care, United States. *J Acquir Immune Defic Syndr.* 2020;86(3):297–304.
22 Patel RH, Acharya A, Chand HS, Mohan M, Byrareddy SN. Human immunodeficiency virus and severe acute respiratory syndrome coronavirus 2 co-infection: a systematic review of the literature and challenges. *AIDS Res Hum Retroviruses.* 2021;37(4):266–282.
23 Altuntas Aydin O, Kumbasar Karasmanoglu H, Kart Yasar K. HIV/SARS-CoV-2 coinfected patients in Istanbul, Turkey. *J Med Virol.* 2020;92(11):2288–2290.
24 Hattab S, Guiguet M, Carcelain G, et al. Soluble biomarkers of immune activation and inflammation in HIV infection: impact of 2 years of effective first-line combination antiretroviral therapy. *HIV Med.* 2015;16(9):553–562.
25 Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497–506.
26 Zhu F, Cao Y, Xu S, Zhou M. Co-infection of SARS-CoV-2 and HIV in a patient in Wuhan city, China. *J Med Virol.* 2020;92(6):529–530.
27 Suwanwongse K, Shabarek N. Clinical features and outcome of HIV/SARS-CoV-2 coinfected patients in The Bronx, New York City. *J Med Virol.* 2020;92(11):2387–2389.
28 Hadi YB, Naqvi SFZ, Kupec JT, Sarwari AR. Characteristics and outcomes of COVID-19 in patients with HIV: a multi-center research network study. *Aids.* 2020;34(13):F3–F8.
29 Ghosn E, T. Gabbidon K, Hanson P, Holyfield C. The impact of COVID-19 on HIV treatment and research: a call to action. *Int J Environ Res Public Health.* 2020;17(12):4548.
30 Laurence J. Why aren't people living with HIV at higher risk for developing severe coronavirus disease 2019 (COVID-19)? *AIDS Patient Care STDS.* 2020;34(6):247–248.
31 d’Estorre G, Recchia G, Ridolfi M, et al. Analysis of type I IFN response to cell activation in severe COVID-19/HIV-1 coinfection: a case report. *Medicine (Baltimore).* 2020;99(36):e21803.
32 Zhang JC, Yu XH, Ding XH, et al. New HIV diagnoses in patients with COVID-19: two case reports and a brief literature review. *BMC Infect Dis.* 2020;20(1):771.
33 Blanco JL, Ambrosioni J, Garcia F, et al. COVID-19 in patients with HIV: clinical case series. *Lancet HIV.* 2020;7(5):e314–e316.
34 Huang J, Xie N, Hu X, et al. Epidemiological, virological and serological features of COVID-19 cases in people living with HIV in Wuhan City: a population-based cohort study [published ahead of print]. *Clin Infect Dis.* 2020. https://doi.org/10.1093/cid/cia1186.
35 Shalev N, Scherer M, LaSota ED, et al. Clinical characteristics and outcomes in people living with HIV hospitalized for COVID-19. *Clin Infect Dis.* 2020;71(16):2294–2297.
36 WHO. Global Health Observatory (GHO) Data. who.int/gho/ hiv/en. Published 2020. Accessed October 3, 2020.
37 Inciarte A, Gonzalez-Cordon A, Rojas J, et al. Clinical characteristics, risk factors, and incidence of symptomatic coronavirus disease 2019 in a large cohort of adults living with HIV: a single-center, prospective observational study. *AIDS.* 2020;34(12):1775–1780.
38 Vizzarra P, Perez-Elias MJ, Quereda C, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. *Lancet.* 2020;7(1):627–634.
39 Charre C, Icard V, Pradat P, et al. COVID-19 attack rate in HIV-infected patients and in PrEP users. *AIDS.* 2020;34(12):1765–1770.
40 de Medeiros KS, Silva LAS d, Macedo LTA, et al. Potential impact of the COVID-19 in HIV-infected individuals: a systematic review. Impact of the COVID-19 in HIV-infected individuals. *Rev Assoc Med Bras.* 2021;67(Suppl 1):127–156.
41 Ridgway JP, Schmitt J, Friedman E, et al. HIV care continuum and COVID-19 outcomes among people living with HIV during the COVID-19 pandemic, Chicago, IL. *AIDS Behav.* 2020;24(10):2770–2772.
42 Sachdev D, Mara E, Hsu L, et al. COVID-19 susceptibility and outcomes among people living with HIV in San Francisco. *J Acquir Immune Defic Syndr.* 2021;86(1):19–21.
43 CDC. What to Know about HIV and COVID-19. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/hiv.html. Published 2020. Accessed October 1, 2020.
44 Park LS, Rentsch CT, Sigel K, et al. COVID-19 in the Largest US HIV Cohort. Paper presented at: AIDS 2020. 23rd International AIDS Conference 2020; Virtual.
45 Fusco FM, Sangiovanni V, Tiberio C, Papa N, Attipaldi L, Esposito V. Persons living with HIV may be reluctant to access to COVID-19 testing services: data from ‘D. Cotugno’ Hospital, Naples, Southern Italy. *AIDS.* 2020;34(14):2151–2152.
46 Collins LF, Moran CA, Oliver NT, et al. Clinical characteristics, comorbidities and outcomes among persons with HIV hospitalized with COVID-19 in Atlanta, Georgia. *AIDS.* 2020;34(12):1789–1794.
47 Härter G, Spinnner CD, Roider J, et al. COVID-19 in people living with human immunodeficiency virus: a case series of 33 patients. *Infection.* 2020;48(5):681–686.
48 Calza L, Bon I, Tedolini M, et al. COVID-19 in patients with HIV-1 infection: a single-centre experience in northern Italy. *Infection.* 2021;49(2):331–335.
49 Childs K, Post FA, Norcross C, et al. Hospitalized patients with COVID-19 and human immunodeficiency virus: a case series. *Clin Infect Dis.* 2020;71(8):2021–2022.
50 Ridgway JP, Farley B, Benoit JL, et al. A case series of five people living with HIV hospitalized with COVID-19 in Chicago, Illinois. *Aids Patient Care STDS.* 2020;34(8):331–335.
51 Gatechompol S, Avihingsanon A, Putcharoen O, Ruxrungtham K, Kuritzkes DR. COVID-19 and HIV infection co-pandemics and their impact: a review of the literature. *AIDS Res Ther.* 2021;18(1):28.
52 Su J, Shen X, Ni Q, et al. Infection of severe acute respiratory syndrome coronavirus 2 in a patient with AIDS. *AIDS.* 2020;34(10):1575–1576.
53 D’Souza G, Springer G, Gustafson D, et al. COVID-19 symptoms and SARS-CoV-2 infection among people living with HIV and COVID-19: review of clinical course and outcomes.
106 Patel RH, Pella PM. COVID-19 in a patient with HIV infection. Clin Infect Dis. 2020;71(12):e1021–e1029.
107 Liang M, Luo N, Chen M., et al. Prevalence and mortality due to COVID-19 in HIV-infected patients: a systematic review and meta-analysis. Infect Dis Ther. 2021;10(3):1267–1219.
108 Gervasoni C, Meraviglia P, Riva A, et al. Clinical features and outcomes of four HIV patients with COVID-19 in Wuhan, China. J Med Virol. 2021;93(1):133–136.
109 Brauneinstein SL, Lazar R, Wahnich A, Daskalakis DC, Blackstock OJ. COVID-19 infection among people with HIV in New York City: a population-level analysis of linked surveillance data. Clin Infect Dis. 2021;72(12):e1021–e1029.
110 Tuan C, Tang L, Wu J, et al. An HIV-infected patient with coronavirus disease 2019 has a favourable prognosis: a case report. Ann Palliat Med. 2021;10(5):5088–5112.
111 Qasim A, Mansour M, Kousa O, et al. A case of coronavirus disease 2019 in acquired immunodeficiency syndrome patient: a case report and review of the literature. Intractable Rare Dis Rep. 2020;9(4):256–259.
112 Shekhar R, Barton A, Sheikh AB, Upadhayay S, Salas NM. Coronavirus disease 2019 in patients with well-controlled human immunodeficiency virus on antiretroviral therapy. J Acquir Immune Defic Syndr. 2020;85(1):e1–e4.
113 Sun LJ, Wong SXL, Gollamudi S. A case of HIV and SARS-CoV-2 co-infection in Singapore. J Acquir Immune Defic Syndr. 2020;84(4):e23–e24.
114 Gudipati S, Brar I, Murray S, McKinnon JE, Yared N, Markowitz N. Descriptive analysis of patients living with HIV affected by COVID-19. J Acquir Immune Defic Syndr. 2020;85(2):123–126.
115 Benkovie S, Kim M, Sin E. Four cases: human immunodeficiency virus and novel coronavirus 2019 co-infection in patients from Long Island, New York. J Med Virol. 2020;92(11):2338–2340.
116 Nagarakanti SR, Okoh AK, Grinberg S, Bishburg E. Clinical outcomes of patients with COVID-19 and HIV coinfection. J Med Virol. 2021;93(3):1687–1693.
117 Byrd KM, Beckwith CG, Garland JM, et al. SARS-CoV-2 and HIV coinfection: clinical experience from Rhode Island, United States. J Int AIDS Soc. 2020;23(7):e25573.
118 Stoeckle K, Johnston CD, Janmat-Khalil DP, et al. COVID-19 in hospitalized adults with HIV. Open Forum Infect Dis. 2020;7(8):ofaa327.
119 Madge S, Barber TJ, Hunter A, Bhatani S, Lipman M, Burns F. Descriptive account of 18 adults with known HIV infection hospitalised with SARS-CoV-2 infection. Sex Transm Infect. 2021;97(5):392–393.
120 Kim JY, Kim JM, Peck KR. The first case of an HIV patient diagnosed with COVID-19 in Korea. J Korean Med Sci. 2020;35(9):e358.
121 Cajamare-Baron J, Guivarte-Navarro D, Uldrick TS, Ljungman P. COVID-19 patients with HIV coinfection in Wuhan, China. Expert Rev Respir Med. 2021;15(3):403–409.
122 Turbide J, Martineau A, Ko C, et al. Impact of COVID-19 in patients with concurrent co-infections: a systematic review and meta-analyses. J Med Virol. 2021;93(4):2385–2395.
123 Kowalska JD, Kase K, Vassilenko A, et al. The characteristics of HIV-positive patients with mild/asymptomatic and moderate/severe course of COVID-19 disease – a report from Central and Eastern Europe. Int J Infect Dis. 2021;104:293–296.
124 Gamboa E, Duran M, Gathe JC, Jr., Surani S, Varon J. COVID-19 coexisting with the human immunodeficiency virus: a case report. Cureus. 2020;12(10):e11066.
125 Elghnoodi S, Afshari M, Haghdoost A, AZ. Kazerooni P, Gouya MM, Tayeri K. Severity and mortality of COVID-19 infection in HIV-infected individuals: preliminary findings from Iran. Med J Islam Repub Iran. 2021;35:33.
126 Yang Y, Gui X, Zhang Y, Xiong Y, Gao S, Ke H. Clinical characteristics of COVID-19 patients with HIV coinfection in Wuhan, China. J Acquir Immune Defic Syndr. 2021;84(1):e1–e8.
127 Toombs JM, Van den Abbeele K, Democratis J, Merricks R, Mandal AKJ, Missouris CG. COVID-19 in three people living with HIV in the United Kingdom. J Med Virol. 2021;93(4):107–109.
128 Harden YO, Amenuke DA, Hutton-Mensah KA, Chadwick DR, Larsen-Reindorf R. Presentation and outcome of COVID-19 in HIV patients with high viral loads and opportunistic infections: a case series. Ghana Med J. 2020;54(4 Suppl):121–124.
129 Preu FA, van der Walt S, South Africa. S Afr Med J. 2020;110(10):982–987.
130 Motshwene MM, Tayeri K. Severity and mortality of COVID-19 infection among hospitalised adults in the U.S. [online]. medRxiv. 2021.
131 Lee KW, Yap SF, Ngeow YF, Lye MS. COVID-19 in people living with HIV. Int J Infect Dis. 2021;97(5):392–393.
132 Laracy J, Zucker J, Castor D, et al. HIV-1 infection does not change disease course or inflammatory pattern of SARS-CoV-2-infected patients presenting at a large urban medical center in New York City. Open Forum Infect Dis. 2021;8(2):ofab029.
133 Ceballos ME, Ross P, Lasso M, et al. Clinical characteristics and outcomes of people living with HIV hospitalized with COVID-19: a nationwide experience. Int J STD AIDS. 2021;32(5):435–443.
134 Patel VV, Felsen UR, Fisher M, et al. Clinical outcomes and inflammatory markers by HIV serostatus and viral suppression in a large cohort of patients hospitalized with COVID-19. J Acquir Immune Defic Syndr. 2021;86(2):224–230.
135 Noe S, Schabaz F, Heldwein S, et al. HIV and SARS-CoV-2 co-infection: cross-sectional findings from a German ‘hotspot’ of SARS-CoV-2. Infection. 2021;49(2):313–320.
136 Parker A, Koegelenberg C, Moodi MS, et al. High HIV prevalence in an early cohort of hospital admissions with COVID-19 in Cape Town, South Africa. S Afr Med J. 2020;110(10):982–987.
137 Cabello A, Zamaroo B, Nistal S, et al. COVID-19 in people living with HIV: a multicenter case-series study. Int J Infect Dis. 2021;102:310–315.
183 Sorbera M, Fischteti B, Khaimova R, Niewinski M, Wen K. Evaluation of virologic suppression rates during the COVID-19 pandemic with outpatient interdisciplinary HIV care [published ahead of print]. J Am Coll Clin Pharm. 2021. https://doi.org/10.1007/jacc.1422

184 Rivera A, Martinez P, Braunshtein S. Video-based HIV testing services among cisgender men who have sex with men as a component of an HIV behavioural surveillance study during the COVID-19 pandemic in New York City: implementation, feasibility and lessons learned [published ahead of print]. Sex Transm Infect. 2021. https://doi.org/10.1136/sextrans-2021-051110

185 Yelverton V, Qiao S, Weissman S, Olatosi B, Li X. Telehealth for HIV care services in South Carolina: utilization, barriers, and promotion strategies during the COVID-19 pandemic [published ahead of print]. AIDS Behav. 2021. https://doi.org/10.1007/s10461-021-03349-y

186 Winswood JJ, Fitzgerald L, Gardiner B, Hannon K, Howard C, Mutch A. Exploring the social impacts of the COVID-19 pandemic on people living with HIV (PLHIV): a scoping review [published ahead of print]. AIDS Behav. 2021. https://doi.org/10.1007/s10461-021-03300-1

187 Budak JZ, Scott JD, Dhanireddy S, Wood BR. The impact of COVID-19 on HIV care provided via telemedicine-past, present, and future. Curr HIV/AIDS Rep. 2021;18(2):98–104.

188 Htun Nyunt O, Wan NMA, Soan P, et al. How Myanmar is responding to the COVID-19 pandemic with outpatient interdisciplinary HIV care [published ahead of print]. J Int Assoc Provid AIDS Care. 2021;20:23259582211017742.

189 Jiang H, Xie Y, Xiong Y, et al. HIV self-testing partially filled the testing gap among men who have sex with men in China during the COVID-19 pandemic: results from an online survey. J Int AIDS Soc. 2021;24(5):e25737.

190 Nawej Tshikung O, Smit M, Marinosi A, et al. Caring for people living with HIV during the global coronavirus disease 2019 pandemic. AIDS. 2021;35(3):355–358.

191 Giuliani M, Donà MG, La Malfa A, et al. Ensuring retention in care for people living with HIV during the COVID-19 pandemic in Rome, Italy. Sex Transm Infect. 2021;97(4):317.

192 Wang H. HIV care during the coronavirus disease-2019 pandemic in Shenzhen, China. Curr Opin HIV AIDS. 2020;15(6):341–344.

193 Armbruster M, Fields EL, Campbell N, et al. Addressing health inequities exacerbated by COVID-19 among youth with HIV: expanding our toolkit. J Adolesc Health. 2020;67(2):290–295.

194 Harris NS, Johnson AS, Huang YA, et al. Vital signs: status of human immunodeficiency virus testing, viral suppression, and HIV pretreatment prophylaxis United States, 2013–2018. MMWR Morb Mortal Wkly Rep. 2019;68(48):1117–1123.

195 Posada-Vergara MP, Alzate-Ángel JC, Martínez-Buitrago E. COVID-19 and VIH. Colomb Med (Cali). 2020;51(2):e4327.

196 Mahmoud K, Rashed ER, Oliveros E, et al. Predisposition or protection?: COVID-19 in a patient on LVAD support with HIV/AIDS. JACC Case Rep. 2020;2(9):1337–1341.

197 Hu Y, Ma J, Huang H, Vermund SH. Coinfection with HIV and SARS-CoV-2 in Wuhan, China: a 12-person case series. J Acquir Immun Defic Syndr. 2020;85(1):1–5.

198 Akyalu AI, Iwu CJ. Novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) co-infection with HIV: clinical case series analysis in North Central Nigeria. Pan Afr Med J. 2020;37(47):47.

199 Chen J, Cheng X, Wang R, Zeng X. Computed tomography imaging of an HIV-infected patient with coronavirus disease 2019. J Med Virol. 2020;92(10):1774–1776.

200 Yamamoto S, Saito M, Nagai E, et al. Antibody response to SARS-CoV-2 in people living with HIV. J Microbiol Immunol Infect. 2021;54(1):144–146.

201 Mascaro S, Romanelli A, Carleo MA, Espósito V. Could HIV infection after the clinical course of SARS-CoV-2 infection? When less is better. J Med Virol. 2020;92(10):1777–1778.

202 Del Amo J, Polo R, Moreno S, et al. Incidence and severity of COVID-19 in HIV-positive persons receiving antiretroviral therapy: a cohort study. Ann Intern Med. 2020;173(7):536–541.

203 Berenguer J, Diez C, Martin-Vicente M, et al. Prevalence and factors associated with SARS-CoV-2 seropositivity in the Spanish HIV research network cohort [published ahead of print]. Clin Microbiol Infect. 2021. https://doi.org/10.1016/j.cmi.2021.06.023

204 Dall’occhio RN, Dessi A, De Vito A, Delogu G, Serra PA, Madeddu G. Early combination treatment with existing HIV antivirals: an effective treatment for COVID-19? Eur Rev Med Pharmacol Sci. 2021;25(5):2435–2448.

205 Cao B, Wang Y, Wen D, et al. A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. N Engl J Med. 2020;382(19):1787–1799.

206 Di Biagio A, Taramasso L, Dentone C, et al. Is a step-down antiretroviral therapy necessary to fight severe acute respiratory syndrome coronavirus 2 in HIV-infected patients? AIDS. 2020;34(12):1865–1867.

207 Alhuma'id S, Mutair AA, Alawi ZA, Almeed N, Zaidi ARZ, Tobaqy E. Mucositis and safety of lopinavir/ritonavir for treatment of COVID-19: a systematic review and meta-analysis. J Infect Dis. 2020;20(5):180.

208 Alavian G, Kolahdouzian K, Mortezaazadeh M, Torabi ZS. Antiretrovirals for prophylaxis against COVID-19: a comprehensive literature review. J Clin Pharmacol. 2021;61(5):581–590.

209 Hoffmann C, Casado JL, Härter G, et al. Immune deficiency is a risk factor for severe COVID-19 in people living with HIV. HIV Med. 2021;22(5):372–378.

210 Adler F, Peiffer-Smadja N, Poussy J, et al. An open-label randomized controlled trial of the effect of lopinavir/ritonavir, lopinavir/ritonavir plus IFN-β-1a and hydroxychloroquine in hospitalized patients with COVID-19 [published ahead of print]. Clin Microbiol Infect. 2021. https://doi.org/10.1016/j.cmi.2021.05.020

211 Amani B, Khanijahani A, Amiani B, Hashemi P. Lopinavir/ritonavir for COVID-19: a systematic review and meta-analysis. J Pharm Pharmacol. 2021;24:246–257.

212 Dorward J, Gbinigie O, Cai T, et al. The protease inhibitor lopinavir, boosted with ritonavir, as treatment for COVID-19: a rapid review. Antivir Ther. 2020;25(7):365–376.

213 Di Castelnuovo A, Costanzo S, Antinori A, et al. Lopinavir/ritonavir and darunavir/cobicistat in hospitalized COVID-19 patients: findings from the multicenter Italian CORIST study. Front Med (Lausanne). 2021;8(639970):639970.

214 Services USDoHaH. Interim Guidance for COVID-19 and Persons with HIV. https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0. Published 2020. Accessed August 25, 2020.

215 Services USDoHaH. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0. Published 2020. Accessed August 25, 2020.