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The Interplay between HIV and COVID-19: summary of the data and responses to date

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Abstract

Purpose of review: We examine the interplay between the HIV and COVID-19 epidemics, including the impact of HIV on COVID-19 susceptibility and severe disease, the effect of the COVID-19 epidemic on HIV prevention and treatment, and the influence of the HIV epidemic on responses to COVID-19.

Recent Findings: Evidence to date does not suggest that people living with HIV (PLWH) have a markedly higher susceptibility to SARS-CoV-2 infection, with disparities in the social determinants of health and comorbidities likely having a greater influence. The majority of literature has not supported a higher risk for severe disease among PLWH in Europe and the United States, although a large, population-based study in South Africa reported a higher rate of death due to COVID-19. Higher rates of comorbidities associated with COVID-19 disease severity among PLWH is an urgent concern. COVID-19 is leading to decreased access to HIV prevention services and HIV testing, and worsening HIV treatment access and virologic suppression, which could lead to worsening HIV epidemic control.

Conclusions: COVID-19 is threatening gains against the HIV epidemic, including the U.S. Ending the HIV Epidemic goals. The ongoing collision of these two global pandemics will continue to need both study and interventions to mitigate the effects of COVID-19 on HIV efforts worldwide.

Keywords

COVID-19; HIV; incidence; severe disease; clinical outcomes

Introduction

An unprecedented public health emergency is unfolding worldwide with the COVID-19 pandemic.[1] In response to multiple outbreaks from January-February 2020, a massive public health response was mounted globally, with cities, states and countries imposing school closures, prohibition of public gatherings, “shelter in place” ordinances, and closures of establishments that provide non-essential services. Medical care was also closed for “non-essential” functions. The COVID-19 epidemic led HIV clinics to cancel non-urgent visits;

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convert in-person visits to remote telephone visits for needed care; divert HIV and Infectious Diseases providers to inpatient, public health, occupational health, or logistical duties; and decrease routine laboratory testing and social services for people living with HIV (PLWH). In the space of weeks, the HIV care system globally changed from efforts to link and retain patients into care to instead limit in-person clinical visits for patients with chronic diseases. Although care is now opening up for patients with chronic illness worldwide, the impact of this paradigm shift for HIV testing, prevention and care worldwide will set back HIV epidemic control efforts for some time.

Beyond the effects of the COVID-19 pandemic on HIV outcomes, it is critical to examine whether HIV has an impact on COVID-19 susceptibility or severity of outcomes.[2, 3] Some of the risk factors for severe COVID-19[4–9] (older age,[10] CVD,[11] pulmonary disease[12, 13]) are more prevalent in PLWH than those without HIV, although HIV itself may not predispose to markedly more severe COVID-19 outcomes. Relatively large studies have now been published examining the impact of HIV on COVID-19 risk and outcomes, which now require synthesis.

No prior global pandemic of the scale of COVID-19 has overlapped temporally with the HIV pandemic, so periodic review of the interplay between the two infections is important for the field. In this review, we explore available evidence on the susceptibility of PLWH to SARS-CoV-2 infection and severe COVID-19 disease, the impact of COVID-19 and its public health response on control efforts for HIV, and similarities in responses to the two pandemics.

IMPACT OF HIV ON COVID-19

Impact of HIV on susceptibility to SARS-CoV-2 infection

Early data on the impact of HIV on susceptibility to COVID-19 infection was mostly limited to PLWH on antiretroviral therapy in the early stages of the COVID-19 epidemic when testing was primarily limited to those with symptoms (Figure 1). Two studies from Spain initially suggested a lower incidence of COVID-19 infection among PLWH compared to the general population. In a single center prospective cohort in Barcelona that included 5,683 PLWH (99%) on ART, 53 (0.9%, 95% confidence interval 0.7% - 1.3%) developed confirmed or suspected COVID-19 infection during the study period and the standardized incident rate ratio of confirmed infection was 38% (95% confidence interval 27%−52%) compared to the general population.[14] A prospective cohort study among HIV clinics in 60 hospitals that serve 77,590 PLWH in the Madrid region observed 236 diagnosed COVID-19 infections among PLWH. This study also estimated a lower age- and sex-standardized risk of confirmed COVID-19 infection among PLWH on ART than the general population (30 per 10,000 among PLWH vs 41.7 per 10,000 among the general population).[15] However, the estimated risk of infection was similar for PLWH when health care workers were excluded from the sample (30 per 10,000 among PLWH vs 33.0 per 10,000 among the general population).[15]

In contrast, a study in France which included 77 COVID-19 diagnoses among PLWH estimated similar attack rates of COVID-19 among PLWH and the general population; in

this study, HIV was not associated with COVID-19 infection in multivariable analysis.[16] A small population cohort in Wuhan, China observed similar standardized incidence rates of COVID-19 among 6,001 PLWH (0.38%, 95% confidence interval 0.24 – 0.53%) to the general population (0.45%, 95% confidence interval 0.45% - 0.46%).[17] In both studies 99% of PLWH were on ART during the study period. The Veterans Aging Cohort Study (VACS), which included 253 PLWH co-infected with COVID-19, found higher testing rates among PLWH than those without HIV, but similar test positivity rates, with 9.7% of PLWH vs 10.1% of HIV-uninfected veterans diagnosed with COVID-19 from February-April 2020.[18] Finally, in a population-based study in San Francisco, PLWH were more likely to test positive for COVID-19 during the first 6 months of community spread, with a 4.5% positivity rate among PLWH (193/4252) compared to 3.5% (9626/272,555) among people without HIV.[19] Among the PLWH co-infected with COVID-19 I this study, only 44% were virally suppressed at their most recent laboratory test.

The incidence of COVID-19 among PLWH may be more influenced by the differential impact of comorbidities and social determinants of health among PLWH that mediate risk of exposure to COVID-19 infection rather than HIV itself. Higher rates of chronic lung disease[12] and behaviors that impact lung function, such as cigarette smoking,[20] inhalational drug use,[21] and hazardous alcohol use[22, 23] among PLWH in the U.S. may also increase the risk of SARS-CoV-2 infection. PLWH experience higher rates of homelessness and unstable or crowded housing than the general population;[24, 25] and increased time in homeless shelters and congregate living settings may decrease their ability to socially distance or effectively quarantine.[26, 27] Among the 193 PLWH who tested positive for COVID-19 in San Francisco over the first 6 months of the pandemic, only 100 (55%) were housed. Conversely, PLWH who experienced the early days of the HIV pandemic may be more likely to shelter in place.

In conclusion, the studies to date do not support that PLWH are generally more susceptible to COVID-19 by virtue of HIV infection itself, although PLWH may be more likely to be tested for SARS-CoV-2, experience other risk factors (e.g. congregate living situations) that make social distancing difficult and increase the risk of exposure to the virus, and/or have increased rates of smoking or chronic lung disease which may increase the risk of infection once exposed.

Impact of HIV on severity of outcomes with COVID-19 disease

In general, PLWH seem to experience similar clinical outcomes with COVID-19 infection than those without HIV in series from the U.S. and Europe **(Figure)**.[14, 28–33, 17, 34, 35] The risk of severe COVID-19 outcomes was similar by HIV status in the VACS cohort, one of the largest cohorts of COVID-19/HIV co-infection (n=253) reported from the U.S. to date.[18] A multi-center registry-based cohort of 286 PLWH from 36 institutions in 21 U.S. states and 3 international sites (2 in Spain and 1 in Singapore) found clinical outcomes of similar severity to those reported among HIV-negative individuals in the U.S.[36] In this cohort, a CD4 count <200 was associated with decreased overall survival, while viral non-suppression was not.[36] PLWH who tested positive for COVID-19 in San Francisco (n=193) also did not experience an increased rate of severe illness relative to those without

HIV.[19] In a matched case-control study comparing 21 PLWH on ART to 42 HIV-uninfected patients hospitalized with COVID-19 in New York, PLWH had higher C-reactive protein (CRP) values and were more likely to have abnormal chest x-rays at admission.[37] Compared to the control group, a higher proportion of PLWH required ICU admission (29% vs 18%) and mechanical ventilation (24% vs 12%), however these differences were not statistically significant, and there were no differences in mortality (29% vs 24%, $p = 0.7$). [37] A small case series of 14 PLWH infected with COVID-19 in Wuhan observed a higher proportion of severe cases and higher mortality than the general population, however the median age and number of comorbidities was also higher among PLWH in that study compared to the general population of Wuhan.[38]

The largest study to address risk of death from COVID-19 among PLWH is a prospective cohort study in South Africa which includes 3,460,932 patients served by the public sector health care system in Western Cape Province, 3978 (16%) of whom are PLWH. In this province, 22,308 were diagnosed with COVID-19, from March 1 – June 9, 2020, of whom 625 died.[39] This cohort observed an increased hazard rate of COVID-19 death adjusted for age and sex among PLWH compared to the general population, with a standardized mortality ratio of 2.39 (95% confidence interval 1.96 – 2.86).[39] The median age of death from COVID-19 was also younger among PLWH compared to the general population in the Western Cape cohort and a greater proportion of COVID-19 deaths were in patients aged <50 years in those with vs without HIV (39% vs 13%). Several factors could explain the differences in the findings of the South African cohort compared to the European and American cohorts. For instance, only 55% of the South African cohort were on ART and virologically suppressed, and comorbidity burden also differed when compared with European and U.S. cohort, with high numbers of PLWH having uncontrolled diabetes and active tuberculosis.

In addition to the potential impact of HIV on COVID-19 susceptibility, PLWH globally may be more at risk for more severe disease from COVID-19 due to a disproportionate burden of known risk factors associated with severe COVID-19 disease.[40] Nearly half of the PLWH in the U.S. are older than 50 years.[10] PLWH have a higher rate of cardiovascular disease, [11] including hypertension,[41] and pulmonary disease[12, 13] than the general population, as well as high rates of smoking.[20, 42, 43] Published case series to date describe a high burden of comorbidities among PLWH who are co-infected with COVID-19 across different settings,[28, 33, 34, 38, 44, 45]. In the predominantly U.S. multi-center cohort of 286 PLWH, having 3 or more comorbidities was associated with both hospitalization and severe outcomes in adjusted analysis.[36]

The conclusion of all of these studies is that PLWH did not seem to be at increased risk of severe outcomes with COVID-19 in studies to date within the U.S. and Europe,[46] while HIV was associated with a higher mortality rate due to COVID-19 in a large cohort in South Africa. The larger population-based study in South Africa may better estimate the impact of HIV on severe COVID-19 disease, or differing comorbidity burdens and viral suppression between these settings could explain these differences. Comorbidities such as diabetes and cardiovascular disease that are prevalent among PLWH may compound potential risks of HIV itself, and controlling modifiable risk factors previously associated with COVID-19

disease severity among PLWH is therefore important for multiple reasons. Finally, longitudinal data from diverse settings across the world and across the spectrum of COVID-19 disease severity will eventually provide a more complete picture of the impact of HIV on COVID-19 disease over time.

The possible effect of antiretroviral therapy on COVID-19 disease susceptibility or outcomes

Speculation that PLWH may have reduced susceptibility to SARS-CoV-2 or severe COVID-19 outcomes has arisen from the fact that different antiretroviral therapy (ART) components have activity against enzymes involved in SARS-CoV-2 replication *in vitro*. Lopinavir has *in-vitro* activity against proteases from both SARS-CoV[47] and MERS-CoV[48] as well as some benefit in animal models of MERS-CoV.[49] Atazanavir also docks in the active site of SARS-CoV-2 major protease, blocks its activity *in vitro*, and inhibits SARS-CoV-2 replication in a cell line.[50] Early case series of HIV/COVID-19 infected patients described multiple instances of changing ART regimens to include protease inhibitors (PIs).[3, 30] However, two clinical trials have now examined the effect of lopinavir/ritonavir on the clinical course of COVID-19, including the pragmatic RECOVERY trial, and found no benefit in the PI in either shortening the disease course or decreasing mortality from COVID-19 [51, 52], and pharmacokinetic studies suggest that it will not achieve sufficient concentrations for efficacy against SARS-CoV-2 [53].

Tenofovir, a nucleotide analog which resembles remdesivir, has been shown to bind the SARS-CoV-2 polymerase *in vitro*.[54] In an analysis among PLWH and PrEP users from a single-center in France, tenofovir use (either in ART or PrEP) was not associated with the risk of COVID-19 infection or clinical course.[16] In contrast, tenofovir disoproxil fumarate (TDF)-based ART, but not tenofovir alafenamide (TAF), among a cohort of 77,590 PLWH across 60 clinics in Spain was associated with lower rates of both COVID-19 diagnosis and hospitalization.[15] This finding may actually reflect channeling bias, as patients who are healthier without comorbidities (such as renal insufficiency) may be more likely to be placed on a TDF-containing versus TAF-containing regimens. In the Western Cape Cohort, TDF was also associated with fewer COVID-19 related deaths, although PLWH not on TDF would be likely to be receiving second-line ART or have renal dysfunction in this setting. [39] A randomized controlled trial to ascertain whether TDF/emtricitabine protects healthcare workers from contracting SARS-CoV-2 in Spain is ongoing. Guidelines from the Department of Health and Human Services and the National Institutes of Health continue to recommend against changing ART for the purpose of preventing or treating COVID-19.[55, 56]

IMPACT OF COVID-19 ON HIV

Impact of COVID-19 on HIV epidemic control and the health of PLWH

The 1918 influenza pandemic influenced health outcomes for the public for decades afterwards due to disruptions in the medical system, interruptions in care for chronic illness, and the stress and turbulence of the time.[57–60] The recent Ebola outbreak in West Africa disrupted care for a number of chronic illnesses, including HIV via decreases in testing[61]

and ART access.[62, 10, 61, 63] Similarly, the impact of the shut-down of medical and social services for PLWH is likely to hamper HIV epidemic control. Indeed, the current crisis has the potential to significantly set back the progress made so far towards the UNAIDS 90–90-90 goals and the United States Ending the HIV Epidemic (EtHE) initiative.[64, 65]

Impact on HIV susceptibility, testing, prevention and treatment access—The COVID-19 epidemic has imperiled the health and well-being of PLWH, while disrupting the four key pillars of HIV epidemic control highlighted by the UNAIDS 90–90-90 and the United States Ending the HIV Epidemic initiatives: HIV Prevention, Diagnosis, Treatment, and Outbreak Control (Figure 2).[64] Beyond these four pillars, the COVID-19 pandemic is likely to have an impact on HIV susceptibility and risk, which may have decreased in the few months following the pandemic, but could increase due to adverse socioeconomic conditions resulting from the COVID-19 epidemic and widespread lockdowns.[66] For instance, in a survey of 20,238 LGBTQ individuals from 138 countries in April-May, 2020 presented at the *AIDS 2020* meeting in July, 57.8% reported having either lost their job, at high risk of losing their job, or being unsure about employment in the near future.[67] Moreover, 44% had experienced reductions in salary, 23% reported new food insecurity and 1% had exchanged sex for money or resources.

Disruption of health care systems due to COVID-19,[68] shelter-in-place orders,[61] and fear of infection at care sites[69] are also threatening access to HIV testing, prevention and treatment services. In the same study of >20,000 LGBTQ individuals across the world, over 50% reported uncertain or no access to PrEP during the pandemic.[67] A study of 3,520 PrEP users from a large PrEP provider in Boston reported a 72% decrease in PrEP initiations, an increase in refill lapses of 278%, and an 18% decrease in overall PrEP users.[70] In South Africa, a PrEP program for pregnant woman reported greater than two-fold higher odds of a missed visit, in spite of no reported change in sexual activity by patients.[71] Although one study in Australia showed that most people stopping PrEP reported a decrease in sexual behavior as the motivator, others reported concerns about contracting COVID-19 and difficulty making appointments as the reason for their PrEP discontinuation.[69] One strategy patients on PrEP have used due to lower sexual activity and/or decreased medication access during COVID-19 is to transition to 2–1-1/on-demand PrEP.[69, 72]

In other settings, COVID-19 has led to greater stigma, economic vulnerability, loss of housing, and continued or increased exposure to HIV for vulnerable populations,[73–75, 67] with greater stringency of lockdowns associated with less access to PrEP, condoms, and HIV testing.[76, 77] San Francisco has reported approximately a 40% decrease in HIV testing citywide, a 90% decrease in community-based HIV testing, and a 70% decrease in testing for sexually transmitted infections (STIs).[78] Alarmingly, a large sexual health clinic in Boston has reported an 85% decrease in overall HIV testing.[70] In many settings, contact tracers have been re-deployed to the COVID-19 epidemic,[79] which could potentially impact the ability of public health agencies to respond to HIV outbreaks.

In terms of the impact of the COVID-19 pandemic on HIV treatment, disruption in care services, lower access to antiretrovirals, and deepening of socioeconomic vulnerabilities -

including a loss of social support, increased food insecurity, and loss of stable housing - will all affect treatment access. In Wuhan, China, at the height of their COVID-19 epidemic, many health care facilities were converted into hospitals that only treated COVID-19 patients, leading to interruptions in non-COVID-19 care delivery, such as for HIV.[80] The city lockdown and cessation of public transportation also resulted in a lack of medication access for those with chronic diseases.[81, 82] Per a UNAIDS survey, one-third of PLWH in China on February 19, 2020, expressed concern that they would run out of ART in a few days, and half said they did not know where to procure their next ART refill.[81, 82] A large survey of over 10,000 men who have sex with men across 20 countries, which included over 1,000 PLWH, reported that approximately one-fifth of PLWH had not been able to access their provider, with only 14% reporting access to telemedicine, and nearly 50% had not been able to refill their HIV medicine remotely.[76, 77]

Even with access to telemedicine, the loss of the social services and in-person support available in HIV clinics for vulnerable patients will impact the health of PLWH. After shelter in place ordinances were mandated in San Francisco,[61] a large HIV clinic serving publicly-insured patients reported a 31% increase in the odds of unsuppressed viral loads, in spite of stable retention in care recorded via telemedicine, with homeless PLWH disproportionately impacted.[83] Although telemedicine may increase access to care services in the context of decreased access to in-person visits, it may not be sufficient to stem the deleterious effects of the pandemic.[75, 83] The digital divide,[84] decreased access to social services, and increasing socioeconomic and housing insecurity may disproportionately impact those with the greatest need, such as homeless PLWH, leading to worsening viral suppression, health outcomes, and potentially mortality.[75, 83, 85] Interruption of antiretroviral access, even if brief, could increase death up to 10% among PLWH in low and middle income countries according to a modelling study.[86] In another modeling study by UNAIDS, a six-month interruption in antiretroviral access across 50% of the population living with HIV could lead to nearly 300,000 excess deaths in sub-Saharan Africa next year.[87]

Impact on social determinants of health for PLWH—PLWH are particularly vulnerable to disruptions in health care due to increased rates of mental illness,[88] marginal housing,[89] food insecurity[90] substance use,[91] and other chronic diseases (e.g., DM, CVD) co-managed in the same clinic.[92] During the Ebola epidemic in West Africa, food insecurity, substance use, and poverty disproportionately impacted Ebola outcomes, but the impacts were magnified among PLWH.[93, 63, 62] PLWH who experience food insecurity often depend on clinic-run programs for social services, including access to food. PLWH with food insecurity already have higher rates of virologic failure and death,[94, 95] with food insecurity during and after the COVID-19 pandemic for PLWH expected to dramatically increase.[96]

Homeless PLWH also have substantially lower rates of HIV viral suppression and higher mortality than housed PLWH,[97, 85] and efforts to increase clinic-based ART access and support among homeless PLWH,[98] could be undermined by decreased funding and access to in-clinic services during and after the COVID-19 pandemic. Since the COVID-19 pandemic is associated with increased stress, anxiety, boredom, and social isolation, there is

concern that substance and alcohol consumption could increase as a coping mechanism.[99–105] Those with histories of alcohol and substance use disorders are at high risk of relapse under stressful situations.[106] The vast majority of PLWH in the U.S. have high rates of current or past substance use,[107] and therefore could experience relapse or increased substance use, threatening HIV care outcomes.[108, 109] Finally, PLWH, especially older PLWH, experience high rates of social isolation[91, 110, 111] – even prior to the COVID-19 pandemic – a situation that will worsen with physical distancing mandates.[105]

LESSONS FROM THE HIV PANDEMIC FOR THE COVID-19 PANDEMIC

Racial and Ethnic Disparities

Racial and ethnic disparities in COVID-19 incidence and outcomes have been described across multiple settings,[112–120] with racial and ethnic minority groups similarly disproportionately represented among HIV/COVID-19 co-infected patients. In France, PLWH with more severe COVID-19 disease were more likely to be from sub-Saharan Africa.[121] In London, HIV/COVID-19 coinfected patients were more likely to be Black than the general population of PLWH.[122] In Boston, in a case series of PLWH admitted to the hospital with COVID-19 infection, almost 80% were Black or Latinx compared with 40% of the catchment clinic population.[45] Multiple case series of PLWH hospitalized with COVID-19 in other metropolitan areas in the United States describe high proportions of Black patients: 85% of 20 PLWH hospitalized for COVID-19 across 3 hospitals in Atlanta were Black,[34] and 93% of patients in a case series of 27 PLWH hospitalized in New Jersey were Black, although the demographics of the source populations were not described.

Racial/ethnic disparities in COVID-19 disease appear to be influenced by the social determinants of health: crowded housing, employment in essential work, decreased healthcare access, greater comorbidity burden all likely contribute to greater disease burden among Black and Latinx PLWH.[112–119] Interventions will likely be needed to support the ability of people at-risk of COVID-19 to physically distance, such as food, housing, and economic assistance, or racial/ethnic disparities may worsen. Since the HIV epidemic has also had a disproportionate impact on racial and ethnic minorities, both in terms of HIV risk and poorer prevention and treatment outcomes, lessons from the HIV pandemic and support programs for PLWH should be translated for those at risk of COVID-19.

The HIV epidemic has informed scientific, regulatory, and public health responses to SARS-CoV-2

Regulatory and approval process—Finally, the lessons of the HIV epidemic have informed clinical responses to COVID-19 through their influence on disseminating paradigms for disease testing, contact tracing, clinical trial frameworks and the infrastructure for therapeutics and vaccine testing, and the influence at the FDA level on more rapid review and approval of potential testing platforms and treatments. Moreover, the lessons from the HIV field to COVID-19 extend to involving the community in testing and treatment campaigns, with community-based participatory research facilitating effective COVID-19 mitigation strategies.

Early in the pandemic, HIV protease inhibitors were tested out of hope that similarities between the coronavirus protease and the HIV protease could be leveraged, although trials to date have been disappointing.[123] Investments in HIV research over the last 4 decades have built capacity and infrastructure for immunology, vaccinology, and therapeutics research that has since been repurposed for the fight against COVID-19.[124] For instance worldwide recruitment processes, testing sites, and clinical trials networks such as the AIDS Clinical Trials Group (ACTG) are leading COVID-19 therapeutic trials; the HIV Vaccines Trial Network (HVTN) and the HIV Prevention Trials Network (HPTN) have contributed to the COVID-19 Prevention Trials Network, which is performing clinical trials for COVID-19 vaccines and monoclonal antibodies, characterizing immune responses to COVID-19 (HVTN 405/HPTN 1901), and has developed a COVID-19 specimen bank.[125]

The response to the HIV epidemic has helped facilitate a more rapid review and approval of COVID-19 drugs and has also facilitated a greater involvement of patients, clinicians, and advocates in the drug-development process. HIV advocacy organizations, such as Project Inform and The AIDS Coalition to Unleash Power (ACT-UP) advocated for faster reviews and approvals for severely debilitating or life-threatening diseases without effective treatments, most notably through the 1988 demonstration at the Federal Drug Administration (FDA) Parklawn headquarters.[126, 127] The FDA instituted rapid review and accelerated approval for life-threatening diseases with few available treatments in direct response to these efforts of HIV activists.[126–128] The parallel track, that was instituted in 1992, allowed people living with HIV who were not eligible for clinical trials to gain access to HIV medications while efficacy trials were still ongoing.[129, 130] To date, the availability of potential COVID-19 therapies such as remdesivir and convalescent plasma for those not eligible for clinical trials has been influenced by these changes in FDA policy.[130]

However, debates about the balance between demonstration of the efficacy and safety of treatments and the rights of patients to access potential treatments, highlighted prominently during the HIV epidemic, have already come to a head in response to review of potential COVID-19 therapies and vaccines under emergency use authorizations (EUA).[130] EUAs allow use of unapproved medical products to treat serious or life-threatening conditions in response to a declared public health emergency when alternatives do not exist.[131] U.S. HIV and Infectious Diseases specialists and professional societies have called for full licensure of a COVID-19 vaccine with independent scrutiny of vaccine data, rather than under an EUA, with the goal of combating public distrust and concerns about safety of a COVID-19 vaccine.[132]

Public health responses—The response to the HIV epidemic has also profoundly influenced public health strategies implemented to combat the COVID-19 epidemic. Contact tracing programs previously developed, at least in part, to battle the HIV epidemic have been expanded and repurposed to address the COVID-19 epidemic.[133–135] The need to provide testing within communities most at risk, at low-cost or no-cost with minimal barriers, was highlighted early in the HIV epidemic.[134] Efforts to combat stigma and avoid “quarantine shaming,” and the negative impacts of policies which stigmatize those with infectious diseases, are important lessons that public health experts are using to craft

COVID-19 policies derived from experience fighting the HIV epidemic.[133, 136] For instance, the “COVID-19 prevention toolbox,” modeled off of HIV prevention efforts, focuses on both the individual and socio-ecological factors that lead to disease risk and disease outcomes.[134, 133] COVID-19 prevention strategies influenced by this paradigm include: acknowledgement that physical distancing is not feasible for many vulnerable populations, the need for harm reduction interventions such as masking and expanded access to testing within communities most at risk, resources to combat food insecurity and lost income, and availability of quarantine hotels to combat the inability to social distance in a shelter, within crowded housing, or on the street.[137, 133, 138]

Conclusions

This review synthesizes the current level of evidence on how HIV influences COVID-19 susceptibility and outcomes and how the COVID-19 epidemic is disrupting HIV care. People living with HIV do not seem to have a markedly elevated risk for COVID-19 infection, although well-designed prospective cohorts are still needed. In sub-Saharan Africa, HIV may be a significant risk factor for severe outcomes with COVID-19, but ongoing study is needed. Conversely, the COVID-19 pandemic is threatening worldwide gains in UNAIDS 90:90:90 and U.S. Ending the HIV Epidemic targets by disrupting health systems, economies, and the health of people living with HIV. HIV has informed the public health response to COVID-19 and many lessons, including how to improve the disproportionate impact of infectious diseases among vulnerable populations, continue to be translated. The ongoing collision of these two global pandemics will continue to need study and interventions to mitigate the effects of COVID-19 on HIV efforts worldwide.

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Key points:

- Evidence to date does not suggest that people living with HIV have a markedly higher susceptibility to SARS-CoV-2 infection.
- The majority of literature has not supported a higher risk for severe disease among people living with HIV in Europe and the United States, although a large, population-based study in South Africa reported a higher rate of death due to COVID-19.
- COVID-19 is leading to decreased access to HIV prevention services and HIV testing, and worsening HIV treatment access and virologic suppression, which could lead to worsening HIV epidemic control.
- The experience of the HIV epidemic has influenced scientific, public health, and regulatory responses to COVID-19.

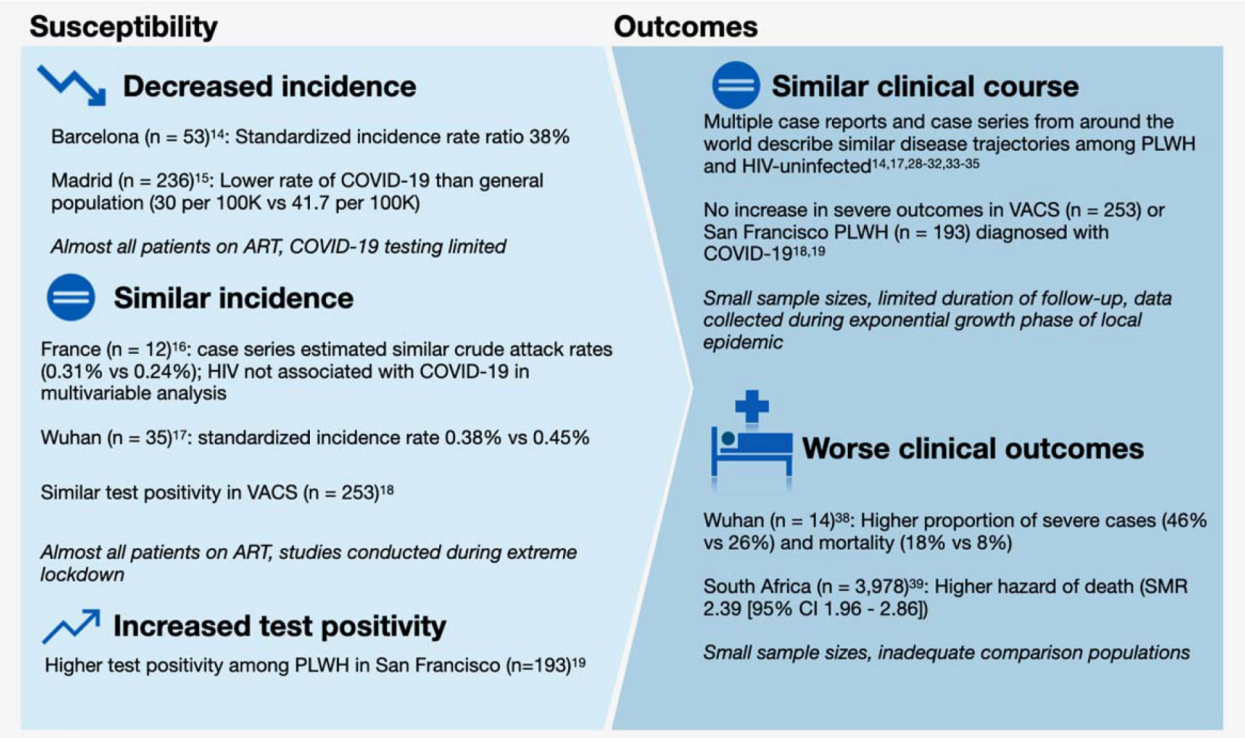

Figure 1:

Evidence to date of COVID-19 susceptibility and propensity to severe disease among people living with HIV compared to the general population

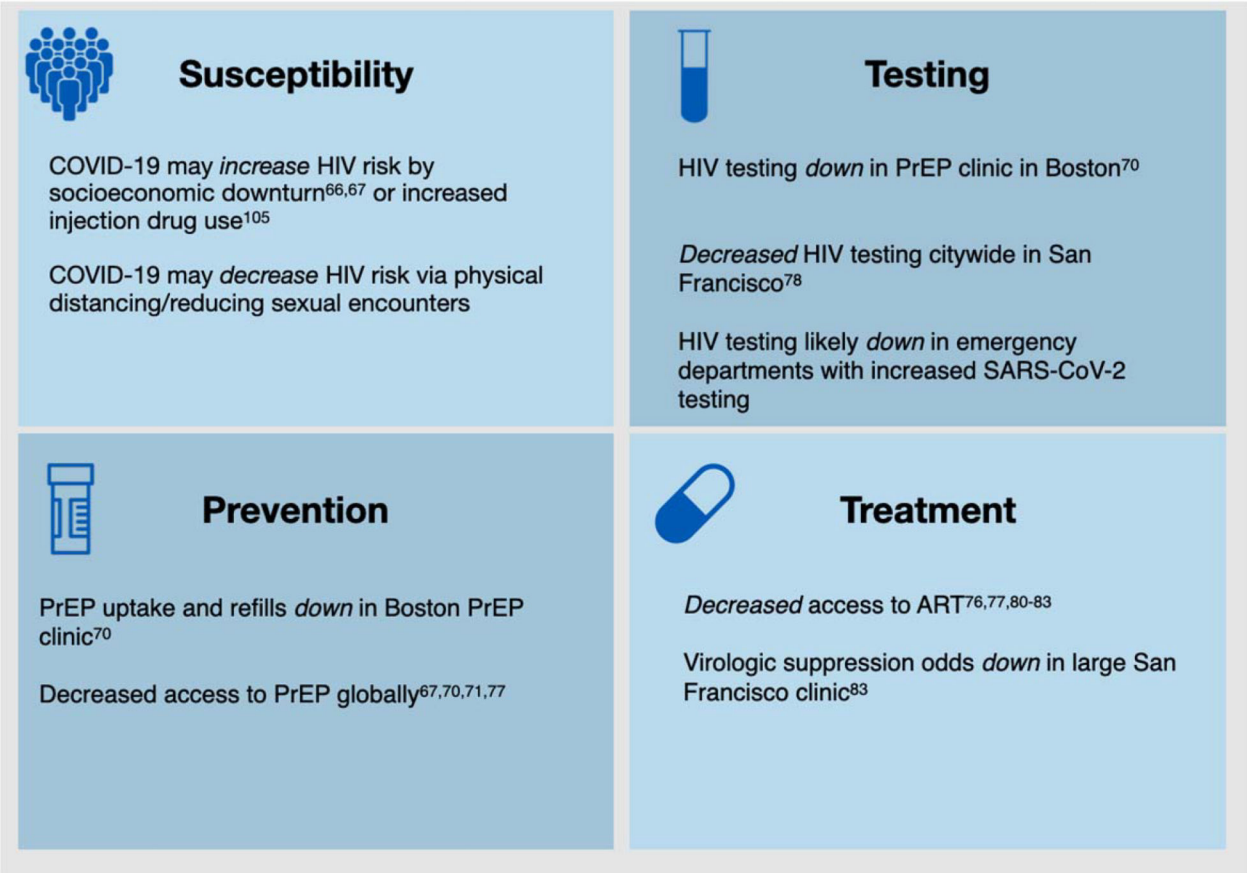

Figure 2:
Impact of COVID-19 on HIV susceptibility, testing, prevention, and treatment