

Special Considerations in People With HIV

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| Summary Recommendations |
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| <p>COVID-19 Vaccination</p> <ul style="list-style-type: none">• The COVID-19 Treatment Guidelines Panel (the Panel) recommends that people with HIV receive COVID-19 vaccines, regardless of their CD4 T lymphocyte (CD4) cell count or HIV viral load, because the potential benefits outweigh the potential risks (AIIb).• For people with untreated or advanced HIV, the Panel recommends following the most recent COVID-19 vaccination schedule from the Centers for Disease Control and Prevention (CDC) for people who are moderately or severely immunocompromised. The CDC defines advanced HIV as CD4 counts <200 cells/mm³, a history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV. <p>Diagnosis of SARS-CoV-2 Infection</p> <ul style="list-style-type: none">• The Panel defers to CDC recommendations for diagnostic molecular or antigen testing for SARS-CoV-2 infection in people with HIV who develop signs and symptoms that suggest acute COVID-19. <p>Managing COVID-19 in People With HIV</p> <ul style="list-style-type: none">• The recommendations for the triage, management, and treatment of COVID-19 in people with HIV are the same as those for the general population (AIII).• Nonhospitalized people with HIV and mild to moderate COVID-19 may be eligible to receive the therapies that are currently recommended for treatment (see Therapeutic Management of Nonhospitalized Adults With COVID-19). However, in situations where there are logistical constraints for administering these therapies, priority should be given to those with untreated or advanced HIV (AIII). See Prioritization of Anti-SARS-CoV-2 Therapies for the Treatment of COVID-19 in Nonhospitalized Patients When There Are Logistical Constraints for details.• People with HIV who are receiving a 5-day course of ritonavir-boosted nirmatrelvir (Paxlovid) to treat COVID-19 can continue using their antiretroviral therapy (ART) doses of ritonavir or cobicistat without alteration or interruption.• In patients with advanced HIV who have suspected or laboratory-confirmed SARS-CoV-2 infection, clinicians should consider HIV-associated opportunistic infections in the differential diagnosis of clinical symptoms and consider consulting an HIV specialist.• When starting treatment for COVID-19 in patients with HIV, clinicians should pay careful attention to potential drug-drug interactions and overlapping toxicities among COVID-19 treatments, antiretroviral (ARV) medications, antimicrobial therapies, and other medications (AIII). <p>Managing HIV in People With COVID-19</p> <ul style="list-style-type: none">• People with HIV who develop COVID-19, including those who require hospitalization, should continue their ART and their medications for the treatment or prevention of opportunistic infections whenever possible.• Clinicians treating COVID-19 in people with HIV should consult an HIV specialist before adjusting or switching a patient's ARV medications.• An ARV regimen should not be modified for the purpose of preventing or treating SARS-CoV-2 infection.• Clinicians should consult with an HIV specialist about the timing of ART in people who present with COVID-19 and untreated HIV. <p>Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See Guidelines Development for more information.</p> |

Introduction

Approximately 1.2 million people in the United States are living with HIV. Most of these individuals are in care, and many are receiving antiretroviral therapy (ART) and have well-controlled disease.¹ Similar to COVID-19, HIV disproportionately affects racial and ethnic minorities and people living in

low-income settings in the United States; these demographic groups also appear to have a higher risk of poor outcomes for COVID-19.² Many people with HIV have 1 or more comorbidities or conditions that may put them at higher risk of severe COVID-19.³

Clinical Outcomes of COVID-19

In some of the initial case series of people with COVID-19 in Europe and the United States, no significant differences were observed in the clinical outcomes of COVID-19 between people with HIV and people who did not have HIV.⁴⁻¹¹ Several subsequent studies have reported worse outcomes for patients with HIV and COVID-19, especially in patients with CD4 T lymphocyte (CD4) cell counts <200 cells/mm³.¹²⁻¹⁸ Many of these studies were done before the widespread use of COVID-19 vaccines; however, people with advanced HIV may have a suboptimal response to vaccines.^{19,20}

Prevention of COVID-19

The COVID-19 Treatment Guidelines Panel (the Panel) recommends that people with HIV receive COVID-19 vaccines, regardless of their CD4 count or HIV viral load, because the potential benefits outweigh the potential risks (**AIIb**). People with HIV were included in the clinical trials of the 2 mRNA vaccines (Pfizer and Moderna) and the glycoprotein vaccine (Novavax) that are currently available through Emergency Use Authorizations and/or approval from the Food and Drug Administration.²¹⁻²³ Typically, people with HIV who are receiving ART and who have achieved virologic suppression respond well to licensed vaccines. Data from studies that used COVID-19 vaccines in people with HIV confirm that people who are receiving ART and have normal CD4 counts have good immunologic responses to the vaccines.²⁴⁻²⁶ However, vaccine response rates are generally lower in people with lower CD4 counts (e.g., <200 cells/mm³).^{19,20,27}

For people with untreated or advanced HIV, the Panel recommends following the most recent [COVID-19 vaccination schedule](#) from the Centers for Disease Control and Prevention (CDC) for people who are moderately or severely immunocompromised. The CDC defines advanced HIV as CD4 counts <200 cells/mm³, a history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV. Patients who have poor adherence or who experience virologic failure while on ART may have a similar risk of severe COVID-19 as those with untreated HIV. For additional considerations regarding vaccination in people who are immunocompromised, see [Special Considerations in People Who Are Immunocompromised](#).

There is currently no clear evidence that antiretroviral (ARV) medications can prevent SARS-CoV-2 infection. Some studies suggested that tenofovir disoproxil fumarate/emtricitabine may play a role in preventing SARS-CoV-2 acquisition or hospitalization or death associated with COVID-19; however, the significance of these findings is unclear.²⁸⁻³⁰ These studies may not have adequately controlled for confounding variables such as age and comorbidities. In addition, most of these studies were conducted in unvaccinated patients.

Diagnostic and Laboratory Testing for COVID-19

Diagnosis of SARS-CoV-2 Infection in People With HIV

The Panel defers to CDC recommendations for diagnostic molecular or antigen testing for SARS-CoV-2 infection in people with HIV who develop signs and symptoms that suggest acute COVID-19. See [Testing for SARS-CoV-2 Infection](#) for more information. There is currently no evidence that the performance characteristics of nucleic acid amplification tests (NAATs) and antigen tests differ in people with or without HIV when diagnosing acute SARS-CoV-2 infection. Antibody tests should not be used to diagnose current SARS-CoV-2 infection. Currently, antibody tests are not recommended for assessing

SARS-CoV-2 immunity following COVID-19 vaccination or for assessing the need for vaccination in a person who is unvaccinated. However, if serologic testing is performed in a patient with HIV, the results should be interpreted with caution because cross-reactivity between antibodies to SARS-CoV-2 and HIV has been reported.³¹

Correlation of CD4 Count in People With HIV and COVID-19

The normal range for CD4 counts in healthy adults is about 500 to 1,600 cells/mm³. People with HIV who have a CD4 count of ≥ 500 cells/mm³ have similar cellular immune function to those without HIV. In people with HIV, a CD4 count < 200 cells/mm³ meets the definition for AIDS. For patients receiving ART, the hallmark of treatment success is a plasma HIV RNA measurement below the level of detection by a polymerase chain reaction assay. Lymphopenia is a common laboratory finding in patients with COVID-19. Therefore, in patients with HIV, clinicians should note that CD4 counts obtained during acute COVID-19 may not accurately reflect the patient's HIV disease stage.

There have been some reports of people with advanced HIV who have presented with COVID-19 and another coinfection, including *Pneumocystis jirovecii* pneumonia and other opportunistic infections.³²⁻³⁶ In patients with advanced HIV who have suspected or laboratory-confirmed SARS-CoV-2 infection, clinicians should consider HIV-associated opportunistic infections in the differential diagnosis of clinical symptoms and consider consulting an HIV specialist.

Clinical Presentation of COVID-19

It is currently unknown whether people with HIV have a higher incidence of SARS-CoV-2 infection or a higher rate of progression to symptomatic disease than the general population. Approximately 50% of people with HIV in the United States are aged > 50 years,³⁷ and many have comorbidities that are associated with more severe COVID-19. These comorbidities include hypertension, diabetes mellitus, cardiovascular disease, a history of smoking, chronic lung disease, chronic liver disease, and cancer.³⁸

There are a number of case reports and case series that describe the clinical presentation of COVID-19 in people with HIV.^{4-11,28,39} These studies indicate that the clinical presentation of COVID-19 is similar in people with and without HIV. Most of the published reports describe populations in which the majority of individuals with HIV are receiving ART and have achieved virologic suppression. Consequently, the current understanding of the impact of COVID-19 in people with advanced HIV and low CD4 counts or persistent HIV viremia is limited.

Managing COVID-19 in People With HIV

The recommendations for the triage, management, and treatment of COVID-19 in people with HIV are the same as those for the general population (**AIII**). Nonhospitalized people with HIV and mild to moderate COVID-19 may be eligible to receive the therapies that are currently recommended for treatment (see [Therapeutic Management of Nonhospitalized Adults With COVID-19](#)). However, in situations where there are logistical constraints for administering these therapies, priority should be given to those with untreated or advanced HIV (**AIII**).

When starting treatment for COVID-19 in patients with HIV, clinicians should pay careful attention to potential drug-drug interactions and overlapping toxicities among COVID-19 treatments, ARV medications, antimicrobial therapies, and other medications (**AIII**).

Among the antiviral drugs recommended for nonhospitalized patients with COVID-19, drug-drug interactions are a special concern with the use of ritonavir-boosted nirmatrelvir (Paxlovid). People with HIV who are receiving a 5-day course of ritonavir-boosted nirmatrelvir to treat COVID-19 can continue

using their ART doses of ritonavir or cobicistat without alteration or interruption. Before prescribing ritonavir-boosted nirmatrelvir to a patient who is not already on a ritonavir-based or cobicistat-based regimen, clinicians should carefully review the patient's concomitant medications, including over-the-counter medications, herbal supplements, and recreational drugs, to evaluate potential drug-drug interactions. Clinicians should use resources such as [Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir \(Paxlovid\) and Concomitant Medications](#), the Food and Drug Administration [prescribing information](#) for ritonavir-boosted nirmatrelvir, and the [Liverpool COVID-19 Drug Interactions website](#) for additional guidance on identifying and managing drug-drug interactions.

In hospitalized patients, the appropriate treatment strategy depends on disease severity (see [Therapeutic Management of Hospitalized Adults With COVID-19](#)). Dexamethasone, which is recommended for use in combination with baricitinib or tocilizumab for some patients with severe or critical COVID-19, is an immunosuppressive agent. The safety of using this drug in patients who are immunocompromised, including those with advanced HIV, has not been studied. Therefore, patients with advanced HIV who are receiving dexamethasone should be closely monitored for secondary infections.

Dexamethasone is a dose-dependent inducer of cytochrome P450 3A4 and could potentially lower the levels of certain coadministered ARV drugs. More than a single dose of dexamethasone **is not recommended** for patients receiving rilpivirine as part of their ARV regimen. Clinicians should consult an HIV specialist before administering dexamethasone to these patients. It is currently unknown whether administering ≤ 10 days of dexamethasone impacts the clinical efficacy of other ARV drugs. Patients with HIV who are receiving dexamethasone as treatment for COVID-19 should follow up with their HIV care providers to assess their virologic response.

Although some ARV drugs were studied early in the pandemic for the treatment of COVID-19, none of these agents have been shown to be effective.

Managing HIV in People With COVID-19

People with HIV who develop COVID-19, including those who require hospitalization, should continue their ART and their medications for the treatment or prevention of opportunistic infections whenever possible. If a patient with HIV needs to receive the next dose of the long-acting injectables cabotegravir/rilpivirine, ibalizumab, or lenacapavir while hospitalized for COVID-19, clinicians should make arrangements with the patient's hospital provider to continue administering the medication without interruption. ART interruption may lead to rebound viremia, and, in some cases, the emergence of drug resistance. If the appropriate ARV drugs are not on the hospital's formulary, administer medications from the patient's home supplies, if available.

Clinicians treating COVID-19 in people with HIV should consult an HIV specialist before adjusting or switching a patient's ARV medications. An ARV regimen should not be modified for the purpose of preventing or treating SARS-CoV-2 infection. Many drugs, including some ARV agents (e.g., lopinavir/ritonavir, boosted darunavir, tenofovir disoproxil fumarate/emtricitabine), were evaluated in clinical trials or have been prescribed off-label to treat or prevent SARS-CoV-2 infection. Lopinavir/ritonavir and darunavir/cobicistat have not been found to be effective for the treatment of COVID-19.^{40,41}

For patients receiving an investigational ARV medication as part of their ARV regimen, arrangements should be made with the investigational study team to continue the medication, if possible.

For critically ill patients who require tube feeding, some ARV medications are available in liquid formulations, and some ARV pills may be crushed. Clinicians should consult an HIV specialist and/or pharmacist to assess the best way to continue an effective ARV regimen for a patient with a feeding tube. Information may be available in the drug product label or from the [Toronto General Hospital](#).

For people who present with COVID-19 and have either a new diagnosis of HIV or a history of HIV but are not receiving ART, the optimal time to start or restart ART is currently unknown. For people with HIV who have not initiated ART or who have been off therapy for >2 weeks before presenting with COVID-19, an HIV specialist should be consulted about initiating or reinitiating ART as soon as clinically feasible. If ART is initiated, maintaining treatment and linking patients to HIV care upon hospital discharge is critical. If an HIV specialist is not available, clinical consultation is available by phone through the [National Clinician Consultation Center](#).

Considerations in Pregnant and Lactating People

Pregnant or recently pregnant individuals are at a higher risk of severe illness and death from COVID-19 than nonpregnant individuals (see [Special Considerations During Pregnancy and After Delivery](#)). Although the data on pregnancy and maternal outcomes in individuals who have COVID-19 and HIV are limited, a prospective meta-analysis demonstrated that pregnant individuals with COVID-19 and HIV had a 67% greater risk of being admitted to the intensive care unit and a 72% greater risk of needing critical care.⁴² An observational study from Botswana found that offspring who were exposed to both HIV and SARS-CoV-2 had a high prevalence of adverse birth outcomes.⁴³

Given the severity of COVID-19 in pregnant or recently pregnant individuals, COVID-19 vaccines should be offered to all pregnant and lactating individuals and to those who are planning to become pregnant, including those who are also living with HIV. Pregnant individuals with HIV who have COVID-19 should be triaged, managed, and treated the same way as pregnant individuals without HIV. Clinicians should consider any additional comorbidities when assessing the risk of severe COVID-19 in these patients. See [Pregnancy, Lactation, and COVID-19 Therapeutics](#) for information regarding the therapies recommended for the treatment of COVID-19.

Pregnant individuals with HIV who are hospitalized for COVID-19 should continue their ART and opportunistic infection treatment and prophylaxis. Clinicians should consult an HIV specialist if any changes to ARV regimens are needed.

Considerations in Children

In general, children appear less likely to become severely ill with COVID-19 than adults. In the few publications that have described cases of COVID-19 among children or adolescents with HIV, most cases were mild, and HIV did not appear to be an independent predictor of severe COVID-19.⁴⁴⁻⁴⁷ Children with HIV who are eligible should receive COVID-19 vaccines and booster doses regardless of their CD4 count or viral load. Children with HIV and COVID-19 or multisystem inflammatory syndrome in children (MIS-C) should receive the same treatment as children without HIV. See [Therapeutic Management of Hospitalized Children With COVID-19](#), [Therapeutic Management of Nonhospitalized Children With COVID-19](#), and [Therapeutic Management of Hospitalized Children With MIS-C, Plus a Discussion on MIS-A](#) for more information.

Parents of children with HIV and COVID-19 should be advised to continue their child's ART without interruption if the child is being managed at home. For children with HIV who are hospitalized for COVID-19, ART should be continued for the duration of hospitalization.

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