Purpose and Development of This Guideline

Goals

This guideline on diagnosis and management of acute HIV infection was developed by the Medical Care Criteria Committee of New York State Department of Health AIDS Institute (NYSDOH AI) to guide clinicians in NYS who provide ambulatory, inpatient, and emergency medical care for adults ≥18 years old who present with signs or symptoms of acute HIV infection or report an exposure within the past 4 weeks.

This guideline provides evidence-based clinical recommendations for the diagnosis and treatment of acute HIV infection in adults, with the goals of ensuring that NYS clinicians are able to:

- Recognize the risks for and signs and symptoms of acute HIV, include HIV infection in the differential diagnosis, and consider HIV testing in any person who presents with signs and symptoms suggestive of influenza (“flu”), mononucleosis (“mono”), or other viral syndromes, including suspected COVID-19.
- Perform appropriate diagnostic and confirmatory testing when HIV infection is suspected and manage the treatment of acute HIV.
- Meet the NYS requirements for reporting and partner notification.
- Recommend or offer immediate initiation of antiretroviral therapy (ART) to improve the patient’s health and reduce the risk of HIV transmission; refer and confirm that patients can access optimal HIV care.
- Initiate or refer the patient for prevention services.

TERMINOLOGY

- **Acute HIV infection**: Describes the period immediately after infection with HIV when an individual is viremic and has detectable p24 antigen or has HIV RNA without diagnostic HIV antibodies. In the medical literature, “primary HIV infection” may describe this same period.
- **Recent infection**: Generally used to describe the 6-month period after infection occurs.
- **Early infection**: May refer to acute or recent infection, after which infection is defined as chronic.

Recognizing and diagnosing acute HIV infection is crucial to linking patients to care early and presents an important opportunity to reduce HIV transmission. Factors that may contribute to the increased risk for transmission during acute infection include:

- Hyperinfectivity associated with both markedly high viral load levels (often much greater than 10 million viral copies/mm$^3$) and increased infectiousness of the virus [Quinn, et al. 2000; Ma, et al. 2009].

For many reasons, detecting acute HIV infection is an essential link in the chain of prevention. Evidence demonstrates that patients with a recent diagnosis of HIV are more likely to reduce risk behaviors if they are given counseling at the time of testing [Steward, et al. 2009; Fonner, et al. 2012] and are linked to primary HIV care [Metsch, et al. 2008]. In addition, for those who elect to initiate ART, their risk of transmission is significantly diminished [Cohen, et al. 2011; Cohen, et al. 2016].

**KEY POINTS**

- HIV is highly transmissible during acute infection; rapid initiation of antiretroviral therapy (ART) reduces transmission, with significant public health benefits, and early viral suppression preserves immune function, with significant clinical benefits for the individual with HIV.
- Acute HIV often has nonspecific signs and symptoms and often goes unsuspected and undetected. This committee urges a high index of suspicion for acute infection and HIV testing for any individual who reports recent high-risk behavior or presents with signs or symptoms of influenza, mononucleosis, or other viral syndromes.
- When HIV infection is diagnosed, immediate linkage to care is essential; ART dramatically reduces HIV-related morbidity and mortality, and viral suppression prevents HIV transmission.
- The urgency of ART initiation is even greater if the newly diagnosed patient is pregnant, has acute HIV infection, is ≥50 years old, or has advanced disease. For these patients, every effort should be made to initiate ART immediately, ideally on the same day as diagnosis.
- All clinical care settings should be prepared, either on-site or with a confirmed referral, to support patients in initiating ART as rapidly as possible after diagnosis.
- When a diagnosis of acute HIV infection is made, clinicians should discuss the importance of notifying all recent contacts and refer patients to partner notification services, as mandated by New York State Law. The NYSDOH can provide assistance if necessary.
  - See [NYSDOH Provider Reporting & Partner Services](http://www.hivguidelines.org) for more information about required reporting.

**NEW YORK STATE LAW**

- **New York State Law** mandates that physicians must offer an HIV test to all patients aged 13 years and older (or younger with risk) if a previous test is not documented, even in the absence of symptoms consistent with acute HIV.
- Effective November 28, 2016, amendments to the New York State Public Health Law removed the requirement for written or oral informed consent prior to ordering an HIV-related test, including elimination of written consent for HIV testing in New York State correctional facilities and removing references to consent forms. The objective of the update is to eliminate barriers to HIV testing and make HIV testing comparable to the manner in which other important laboratory tests are conducted. HIV testing remains voluntary, and patients have the right to refuse an HIV test, but obtaining written or oral consent for testing is no longer required in any setting. At a minimum, patients must be advised orally that an HIV test is going to be performed.
  - See [HIV Testing, Reporting and Confidentiality in New York State 2017-18 Update: Fact Sheet and Frequently Asked Questions New York State Department of Health AIDS Institute](http://www.hivguidelines.org)
- **NYS Public Health Law Article 21** (Chapter 163 of the Laws of 1998) requires the reporting of individuals with HIV as well as AIDS to the NYSDOH. The law also requires that reports contain the names of sex or needle-sharing partners known to the medical provider or whom the infected individual wishes to have notified. The Medical Provider Report Form (PRF) (DOH-4189) must be completed within 14 days of diagnosis for individuals with the following diagnoses or with known sex or needle-sharing partners:
NEW YORK STATE LAW

- Initial/new HIV diagnosis: First report of HIV antibody positive test results.
- Previously diagnosed HIV infection (non-AIDS): Applies to a medical provider who is seeing the patient for the first time.
- Initial/new diagnosis of AIDS: Including <200 CD4 cells/µL or opportunistic infection (AIDS-defining illness).
- Previously diagnosed AIDS: Applies to a medical provider who is seeing the patient for the first time.
- Known sex or needle-sharing partners of individuals with diagnosed HIV infection.

See NYSDOH Provider Reporting & Partner Services

Guideline Development

This guideline was developed by the NYSDOH AI Clinical Guidelines Program, which is a collaborative effort between the NYSDOH AI Office of the Medical Director and the Johns Hopkins University School of Medicine, Division of Infectious Diseases.

Established in 1986, the goal of the Clinical Guidelines Program is to develop and disseminate evidence-based, state-of-the-art clinical practice guidelines to improve the quality of care provided to people who have HIV, HCV, or sexually transmitted infections; people with substance use issues; and members of the LGBTQ community. NYSDOH AI guidelines are developed by committees of clinical experts through a consensus-driven process.

The NYSDOH AI charged the Medical Care Criteria Committee (adult HIV and related guidelines) with developing evidence-based clinical recommendations for the diagnosis and management of acute HIV infection. The resulting recommendations are based on an extensive review of the medical literature and reflect a consensus among this panel of experts. Each recommendation is rated for strength and quality of the evidence (see below). If recommendations are based on expert opinion, the rationale for the opinion is included.

NYSDOH AI Clinical Guidelines Program Ratings Scheme, Updated June 26, 2019 [a]

Strength of Recommendation Ratings

<table>
<thead>
<tr>
<th>A</th>
<th>Strong recommendation</th>
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<tr>
<td>B</td>
<td>Moderate recommendation</td>
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<tr>
<td>C</td>
<td>Optional</td>
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Quality of Supporting Evidence Ratings

<table>
<thead>
<tr>
<th>1</th>
<th>Indicates that the evidence supporting a recommendation is derived from published results of at least one randomized trial with clinical outcomes or validated laboratory endpoints.</th>
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<tbody>
<tr>
<td>*</td>
<td>Indicates that the evidence supporting a recommendation is strong because it is based on a self-evident conclusion(s) or conclusive, published in vitro data, or because the recommendation articulates well-established, accepted practice that cannot be tested because ethics would preclude a clinical trial.</td>
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<tr>
<td>2</td>
<td>Indicates that the evidence supporting a recommendation is derived from published results of at least 1 well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.</td>
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<tr>
<td>2†</td>
<td>Indicates that the evidence supporting a recommendation has been extrapolated from published results of well-designed studies (including nonrandomized clinical trials) conducted in populations other than those specifically addressed by a recommendation. One example would be results of studies conducted predominantly in a subpopulation (e.g., one gender) that the committee determines to be generalizable to the population under consideration in the guideline. When this rating is assigned to a recommendation, the source(s) of the extrapolated evidence and the rationale for the extrapolation are provided in the guideline text.</td>
</tr>
<tr>
<td>3</td>
<td>Indicates that a recommendation is based on the expert opinion of the committee members. The rationale for the recommendation is provided in the guideline text.</td>
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With the June 2019 update, the ratings for quality of supporting evidence were expanded to add the * rating and the 2† rating.
Presentation and Diagnosis

**RECOMMENDATIONS**

### Presentation

- Clinicians should include acute HIV infection in the differential diagnosis for *anyone* (regardless of reported risk) who presents with signs or symptoms of influenza (“flu”), mononucleosis (“mono”), or other viral syndromes (A3), especially when the patient:
  - Presents with a rash. (A2)
  - Requests HIV testing. (A3)
  - Reports recent sexual or parenteral exposure to a person with or at risk of HIV infection. (A2)
  - Presents with a newly diagnosed sexually transmitted infection. (A2)
  - Presents with aseptic meningitis. (A2)
  - Is pregnant or breastfeeding. (A3)
  - Is currently taking antiretroviral medications for pre- or post-exposure prophylaxis (PrEP or PEP). (A3)

- Diagnostic HIV RNA testing should be considered for patients who present with compatible symptoms (see **Box 1: Acute Retroviral Syndrome**), particularly in the presence of a sexually transmitted infection [Patel, et al. 2006] or a recent sexual or parenteral exposure with a partner known to have HIV or with unknown HIV serostatus. (A2)

### When Acute HIV Infection Is Suspected

- Clinicians should always perform a plasma HIV RNA assay in conjunction with an antigen/antibody combination screening test. (A2)
- Clinicians should use a 4th-generation antigen/antibody combination assay (preferred) as the initial HIV screening test according to the CDC’s Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens.
  - If the screening test is reactive, clinicians should perform an HIV-1/HIV-2 antibody-differentiation immunoassay to confirm HIV infection. (A1)
  - **Note:** When rapid antibody screening is performed, even with a rapid 4th-generation test, a laboratory-based 4th-generation immunoassay is recommended for follow-up diagnostic HIV testing.

### Diagnosis

- Clinicians can presume the diagnosis of acute HIV when high levels (>10,000 copies/mL) of HIV RNA are detected in plasma with sensitive nucleic acid amplification testing (NAAT), and the result of the HIV screening or type-differentiation test is negative or indeterminate. (A2)
- When a low-level quantitative HIV RNA viral load result (<10,000 copies/mL) is obtained in the absence of serologic evidence of HIV infection, the clinician should repeat HIV RNA testing *and* perform a 4th-generation antigen/antibody combination assay to exclude a false-positive result. (A2)
  - **Note:** A serologic test result that does not meet the criteria for HIV infection is a nonreactive screening result (antibody or antibody/antigen combination) or a reactive screening result with a nonreactive or indeterminate antibody-differentiation confirmatory result.
- Clinicians should seek expert consultation when an ambiguous HIV result is obtained for an individual taking PrEP because the diagnosis of acute HIV can be particularly challenging in patients taking PrEP. (A3) See NYSDOH AI guideline *PrEP to Prevent HIV and Promote Sexual Health > Suspected Acute HIV.*

### ART Initiation

- If a diagnosis of acute infection is made based on HIV RNA testing, clinicians should recommend ART initiation without waiting for serologic confirmation. (A2) See *When to Initiate ART, With Protocol for Rapid Initiation.*
- When a pregnant individual is diagnosed with acute infection by HIV RNA testing, the clinician should not wait for the result of a confirmatory test to initiate ART; initiation of ART is strongly recommended for pregnant patients. (A2) See the NYSDOH AI guideline *HIV Testing During Pregnancy, at Delivery, and Postpartum*


**RECOMMENDATIONS**

**Partner Notification**

- Clinicians should offer assistance with partner notification and refer patients to other sources for partner notification assistance (NYSDOH Partner Services or NYC CNAP). (A2)

The time from HIV infection to detection of the virus depends on the test that is used. *Figure 1: Window of Detection for HIV, Based on Test Used* illustrates the window of detection of HIV infection according to antibody, antibody/antigen combination, and HIV RNA tests.

**Figure 1: Window of Detection for HIV, Based on Test Used [a]**

![Figure 1: Window of Detection for HIV, Based on Test Used](image)

*Note: Nucleic acid amplification testing (NAAT) is performed to detect HIV RNA. Enzyme immunoassay testing (EIA) is performed to detect HIV antibodies (second- and third-generation EIA) or HIV antibody/antigen (fourth-generation EIA).*

a. Reprinted from CDC > HIV Diagnostic Tests > Newer, Improved HIV Tests Allow for Earlier HIV Detection

**Presentation**

Patients acutely infected with HIV will often experience at least some symptoms of acute retroviral syndrome (ARS). Fever and influenza- or mononucleosis-like symptoms are common in acute HIV infection but are nonspecific. Rash, mucocutaneous ulcers, oropharyngeal candidiasis, and meningismus are more specific and should raise the index of suspicion (see below for a more extensive list of signs and symptoms). The mean time from exposure to onset of symptoms is generally 2 to 4 weeks, with a range of 5 to 29 days; however, some cases have presented with symptoms up
to 3 months after exposure [Apoola, et al. 2002]. Theoretically, this time course may be prolonged in patients who become infected while on PEP or PrEP.

### Box 1: Acute Retroviral Syndrome [a]

Signs and symptoms of ARS with the expected frequency among symptomatic patients are listed below [a]. The most specific symptoms in this study were oral ulcers and weight loss; the best predictors were fever and rash. The index of suspicion should be high when these symptoms are present.

- Fever (80%)
- Tired or fatigued (78%)
- Malaise (68%)
- Arthralgias (joint pain) (54%)
- Headache (54%)
- Loss of appetite (54%)
- Rash (51%)
- Night sweats (51%)
- Myalgias (pain in muscles) (49%)
- Nausea (49%)
- Diarrhea (46%)
- Fever and rash (46%)
- Pharyngitis (sore throat) (44%)
- Oral ulcers (mouth sores) (37%)
- Stiff neck (34%)
- Weight loss (>5 lb; 2.5 kg) (32%)
- Confusion (25%)
- Photophobia (24%)
- Vomiting (12%)
- Infected gums (10%)
- Sores on anus (5%)
- Sores on genitals (2%)


### Diagnosis

Acute HIV infection is often not recognized in the primary care setting because the symptom profile is similar to that of influenza, mononucleosis, and other common illnesses. Furthermore, patients often do not recognize that they may have recently been exposed to HIV. Therefore, the clinician should have a high index of suspicion for acute HIV infection in a patient who may have recently engaged in behavior involving sexual or parenteral exposure to another individual’s blood or body fluids and who is presenting with a febrile, influenza-, or mononucleosis-like illness. Identifying acute HIV infection during pregnancy is particularly important because effective intervention can prevent mother-to-child transmission [Patterson, et al. 2007].

High levels of HIV RNA detected in plasma through sensitive NAAT, combined with a negative or indeterminate HIV screening or type-differentiation test, support the presumptive diagnosis of acute HIV infection [Robb, et al. 2016; DHHS 2019].

When low-level viremia is reported by HIV RNA testing (<5,000 copies/mL) in the absence of serologic confirmation of HIV infection, HIV RNA testing should be repeated to exclude a false-positive result [Hecht, et al. 2002]. Repeat HIV RNA testing with a result that indicates the presence of low-level viremia may represent true HIV infection, warranting appropriate counseling regarding transmission risk and initiation of ART.

HIV RNA levels tend to be very high in acute infection; however, a low value may represent any point on the upward or downward slope of the viremia associated with acute infection or could simply represent chronic infection. HIV RNA can also be suppressed during acute infection in patients who are taking PrEP. Plasma HIV RNA levels during acute infection do not appear significantly different in patients who are and are not symptomatic [Patterson, et al. 2007]. Viremia occurs approximately 1 to 2 weeks before the detection of a specific immune response. Patients diagnosed with acute infection by HIV RNA testing should always receive follow-up diagnostic testing 3 weeks later to confirm infection (see the CDC [CDC 2013, 2014]. Figure 2: Diagnostic Testing for HIV Infection illustrates diagnostic testing for acute HIV infection.
KEY POINTS

- The diagnosis of acute HIV infection requires a high degree of clinical awareness. The nonspecific signs and symptoms of acute HIV infection are often not recognized or attributed to another viral illness.
- Diagnostic HIV RNA testing should be considered for all patients who present with compatible symptoms (see signs and symptoms of ARS, above), particularly in the context of a sexually transmitted infection [Patel, et al. 2006] or a recent sexual or parenteral exposure with a partner known to have HIV or a partner whose HIV serostatus is not known.
- Individual laboratories have internal protocols for reporting HIV tests with preliminary results. The terms used when preliminary results cannot be classified include indeterminate, inconclusive, nondiagnostic, and pending validation. Clinicians can contact the appropriate laboratory authority to determine the significance of nondefinitive results and the recommended supplemental testing, particularly when acute HIV infection is suspected. Clinicians are advised to become familiar with the internal test-reporting policies of their institutions.

FIGURE 2. Diagnostic Testing for Acute HIV Infection

Person presents with signs/symptoms of acute HIV infection or reports an exposure in the past 4 weeks.

Perform HIV RNA test [a] PLUS HIV antibody/antigen screening test

HIV RNA not detected AND antibody/antigen nonreactive

No laboratory evidence of HIV infection [d]

HIV RNA detected with <5000 copies/mL PLUS no serologic evidence of HIV infection [b]

Retest HIV RNA

HIV RNA not detected

HIV RNA detected

Serologic confirmation of HIV infection [c]

Confirmed HIV infection. Recommend ART

Presumptive diagnosis of acute HIV infection

Recommend ART in consultation with an experienced HIV care provider

3 weeks later, perform diagnostic testing according to the CDC HIV testing algorithm

Notes:
- viremia will be present several days before antibody detection
- The absence of serologic evidence of HIV infection is defined as nonreactive screening result (antibody or antibody/antigen combination) or a reactive screening result with a nonreactive or indeterminate antibody–detection confirmatory result.
- Serologic confirmation as defined by the CDC HIV testing algorithm. Western blot is no longer recommended as the confirmatory test because it may yield an indeterminate result during the early stages of seroconversion and may delay confirmation of diagnosis.
- No further testing is indicated

New York State Department of Health AIDS Institute: www.hivguidelines.org
Management, Including While on PEP or PrEP

RECOMMENDATIONS

Management

- Clinicians should recommend antiretroviral therapy (ART) to all patients diagnosed with acute HIV infection. (A1)
- Clinicians should inform patients about the increased risk of transmitting HIV during acute infection and for the 6 months following infection in patients who do not initiate ART. (A2)
- As part of the initial management of patients diagnosed with acute HIV infection, clinicians should:
  - Consult with a care provider experienced in the treatment of acute HIV infection. (A3)
  - Obtain HIV genotypic resistance testing for the protease (A2), reverse transcriptase (A2), and integrase (B2) genes at the time of diagnosis.
- Patients taking post-exposure prophylaxis (PEP): When acute HIV infection is diagnosed in an individual receiving PEP, ART should be continued pending consultation with an experienced HIV care provider. (A3)
- Patients taking pre-exposure prophylaxis (PrEP): Because the risk of drug-resistant mutations is higher in patients who acquire HIV while taking PrEP, clinicians should consult with an experienced HIV care provider and recommend a fully active ART regimen. (A3)
  - See the NYSDOH AI guideline PrEP to Prevent HIV and Promote Sexual Health > Managing a Positive HIV Test Result
  - Clinicians who do not have access to experienced HIV care providers should call the Clinical Education Initiative (CEI) Line at 1-866-637-2342.
- When a patient agrees with the clinician’s recommendation to initiate ART during acute HIV infection:
  - The clinicians should implement treatment to suppress the patient’s plasma HIV RNA to below detectable levels. (A1)
  - Clinicians should perform baseline laboratory testing listed in Box 2: Baseline Laboratory Testing Checklist for all patients initiating ART immediately; ART can be started while awaiting laboratory test results. (A3)

Patients are at greatest risk for transmitting HIV during periods of high viremia early in infection. Clinicians should counsel patients with acute HIV about the increased risk of transmission during the 6 months after infection. Partner notification [Golden, et al. 2004], counseling on safer sex, and screening for other sexually transmitted infections are all essential in the management of any new HIV diagnosis.

Consultation: When choosing an ART regimen for a patient with acute HIV infection, clinicians should consult a care provider experienced in treating acute HIV infection.

- Data are insufficient to support a specific ART regimen(s) for the treatment of acute HIV infection; instead, the choice of regimen should be made based on recommendations for selecting an initial ART regimen.
- The risks of transmitted resistance should be considered when prescribing ART while awaiting HIV resistance results.
- The risks of acquired mutations should be considered in those who acquire HIV while on PrEP.

Clinicians who do not have access to experienced HIV care providers should call the CEI Line at 1-866-637-2342.
All Recommendations

☑️ ALL RECOMMENDATIONS: DIAGNOSIS AND MANAGEMENT OF ACUTE HIV INFECTION

Presentation

- Clinicians should include acute HIV infection in the differential diagnosis for *anyone* (regardless of reported risk) who presents with signs or symptoms of influenza (“flu”), mononucleosis (“mona”), or other viral syndromes (A3), especially when the patient:
  - Presents with a rash. (A2)
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  - Presents with aseptic meningitis. (A2)
  - Is pregnant or breastfeeding. (A3)
  - Is currently taking antiretroviral medications for pre- or post-exposure prophylaxis (PrEP or PEP). (A3)
- Diagnostic HIV RNA testing should be considered for patients who present with compatible symptoms (see Box 1: *Acute Retroviral Syndrome*), particularly in the presence of a sexually transmitted infection [Patel, et al. 2006] or a recent sexual or parenteral exposure with a partner known to have HIV or with unknown HIV serostatus. (A2)

When Acute HIV Infection Is Suspected

- Clinicians should always perform a plasma HIV RNA assay in conjunction with an antigen/antibody combination screening test. (A2)
- Clinicians should use a 4th-generation antigen/antibody combination assay (preferred) as the initial HIV screening test according to the *CDC’s Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens*.
  - If the screening test is reactive, clinicians should perform an HIV-1/HIV-2 antibody-differentiation immunoassay to confirm HIV infection. (A1)
  - **Note:** When rapid antibody screening is performed, even with a rapid 4th-generation test, a laboratory-based 4th-generation immunoassay is recommended for follow-up diagnostic HIV testing.

Diagnosis

- Clinicians can presume the diagnosis of acute HIV when high levels (>10,000 copies/mL) of HIV RNA are detected in plasma with sensitive nucleic acid amplification testing (NAAT), and the result of the HIV screening or type-differentiation test is negative or indeterminate. (A2)
- When a low-level quantitative HIV RNA viral load result (<10,000 copies/mL) is obtained in the absence of serologic evidence of HIV infection, the clinician should repeat HIV RNA testing *and* perform a 4th-generation antigen/antibody combination assay to exclude a false-positive result. (A2)
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ART Initiation

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Partner Notification

- Clinicians should offer assistance with partner notification and refer patients to other sources for partner notification assistance (NYSDOH Partner Services or NYC CNAP). (A2)

Management

- Clinicians should recommend antiretroviral therapy (ART) to all patients diagnosed with acute HIV infection. (A1)
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  - The clinicians should implement treatment to suppress the patient’s plasma HIV RNA to below detectable levels. (A1)
- Clinicians should perform baseline laboratory testing listed in *Box 2: Baseline Laboratory Testing Checklist* for all patients initiating ART immediately; ART can be started while awaiting laboratory test results. (A3)

References


Buzon M, Siess K, Sone A. Treatment of early HIV infection reduces viral reservoir to levels found in elite controllers. Abstract 151. CROI; 2012 Mar 5-8; Seattle, WA.


Lafeuillade A, Hitinger G, Lambry V. Long-term control of HIV reservoir after a 2-year ART course at acute infection. Abstract 358. CROI; 2012 Mar 5-8; Seattle, WA.


Phanuphak N, Teeratakulpisarn N, Mungyu P. Time to undetectable HIV RNA in ano-genital compartment of acute HIV Thai male subjects treated with 5- and 3-drug HAART. Abstract S55. CROI; 2012 Mar 5-8; Seattle, WA.


How This Guideline Was Developed

This guideline was developed by the New York State (NYS) Department of Health (DOH) AIDS Institute (AI) Clinical Guidelines Program, which is a collaborative effort between the NYSDOH AI Office of the Medical Director and the Johns Hopkins University School of Medicine, Division of Infectious Diseases.

Established in 1986, the goal of the Clinical Guidelines Program is to develop and disseminate evidence-based, state-of-the-art clinical practice guidelines to improve the quality of care provided to people with HIV, hepatitis C virus, or sexually transmitted infections; people with substance use issues; and members of the LGBTQ community. NYSDOH AI guidelines are developed by committees of clinical experts through a consensus-driven process.

Medical Care Criteria Committee (MCCC) for adult HIV care guidelines: The NYSDOH AI charged the MCCC (adult HIV and related guidelines) with developing evidence-based recommendations for clinicians in NYS who provide care to individuals with HIV. The purpose of the Diagnosis and Management of Acute HIV Infection clinical practice guideline is to guide clinicians in NYS who provide ambulatory, inpatient, and emergency medical care for adults ≥18 years old who present with signs or symptoms of acute HIV infection.

Committee makeup: Members of the MCCC (see Box A1: MCCC Leaders and Members, below) were appointed by the NYSDOH AI to ensure representation of clinical practice in all major regions of the state, relevant medical disciplines and subspecialties, key NYS agencies, community stakeholders, and patient advocates. Individuals confirmed as MCCC members are required to disclose any potential conflicts of interest; disclosures are reviewed and approved by the NYSDOH AI Office of the Medical Director (see Funding and Disclosure of Potential Conflicts of Interest, below).

Committee role: Committee members actively participate in guideline development, including evidence review, drafting of recommendations and text, manuscript review, consensus approval of all recommendations, and rating of recommendations.

Committee leadership: Working with the lead author, the MCCC Writing Group reviewed and refined the manuscript, facilitated consensus approval of all recommendations, and addressed feedback from the Committee at large.

Johns Hopkins University (JHU) Editorial Role: The JHU editorial team coordinated, guided, and documented all Committee activities and edited the guideline material for clarity, flow, and style.

MCCC Writing Group (all Committee members and reviewers are listed in Box A1, below)
- Joseph P. McGowan, MD, FACP, FIDSA, Chair
- Steven Fine, MD, PhD, Co-Vice-Chair (effective January 2021)
- Rona Vail, MD, Co-Vice-Chair (effective January 2021)
- Samuel T. Merrick, MD, Chair Emeritus
- Charles J. Gonzalez, MD, AI Medical Director
- Asa Radix, MD, MPH, FACP, AAHIVS
- Christopher J. Hoffmann, MD, MPH, Director, JHU-NYSDOH Guidelines Program

AIDS Institute and JHU Editorial and Program Management Team
- Laura Duggan Russell, MPH, AI Guidelines Program Manager
- Mary Beth Hansen, MA, JHU Guidelines Project Director
- Johanna Gribble, MA, JHU Medical Editor
- Jen Ham, MPH, JHU Medical Editor
- Rachel Lastra, JHU Medical Editor
- Jesse Ciekot, JHU Program Coordinator
Box A1: MCCC Leaders and Members (when this guideline was developed)

Unless noted otherwise, Committee members had no disclosures of financial relationships with commercial entities

**Leadership**

- **Chair** (effective March 2018): Joseph P. McGowan, MD, FACP, FIDSA, North Shore University Hospital, Manhasset, NY
- **Co-Vice-Chair** (Vice-Chair effective March 2018; Co-Vice-Chair effective January 2021): Steven M. Fine, MD, PhD, University of Rochester Medical Center, Rochester, NY
- **Co-Vice-Chair** (effective January 2021): Rona M. Vail, MD, Callen-Lorde Community Health Center, New York, NY
- **Chair Emeritus** (effective March 2018): Samuel T. Merrick, MD, New York-Presbyterian-Weill Cornell, New York, NY
- **Medical Director**: Charles J. Gonzalez, MD, New York State Department of Health AIDS Institute, New York, NY (May 2018)
- **Clinical Advisor to the AIDS Institute** (effective June 2021): Lyn Stevens, MS, NP, ACRN, New York State Department of Health AIDS Institute, Albany, NY
- **Director, JHU-NYSDOH AI Guidelines Program**: Christopher J. Hoffmann, MD, MPH, Johns Hopkins University School of Medicine, Baltimore, MD

**Contributing Members**

- Jessica M. Atrio, MD, MSc, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY
- Oni J. Blackstock, MD, MHS, Health Justice, New York, NY
- James C. M. Brust, MD, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY
- Ethan A. Cowan, MD, MS, Icahn School of Medicine at Mount Sinai, New York, NY
- Elliot DeHaan, MD, New York-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY
- Mary E. Dyer, MD, Hudson River Healthcare, Monticello, NY
- John J. Faragon, PHARMD, BCPS, AAHIVP, Albany Medical Center, Albany, New York
- Shauna H. Gunaratne, MD, MPH, Columbia University Medical Center, New York, NY
- Bruce E. Hirsch, MD, FACP, FIDSA, AAHIVS, North Shore University Hospital, Manhasset, NY
- Christine A. Kerr, MD, Galileo Health
- Jeremy D. Kidd, MD, MPH, New York-Presbyterian Hospital, Columbia University, New York, NY
- Hector I. Ojeda-Martinez, MD, Nuvance Health/Health Quest Medical Practice, Poughkeepsie, NY
- Asa E. Radix, MD, MPH, FACP, AAHIVS, Callen-Lorde Community Health Center, New York, NY
- Sanjiv S. Shah, MD, MPH, AAHIVM, AAHIVS, NYC Health + Hospitals/Gotham Health, Gouverneur, New York, NY
- Noga Shalev, MD, Columbia University Medical Center, New York, NY
- Eugenia L. Siegler, MD, Weill Cornell Medical College, New York, NY
- Maria Teresa (Tess) Timoney, MS, RN, CNM, Bronx Prevention Center, ICAP at Columbia, Bronx, NY
- Benjamin W. Tsai, MD, MPH, Bureau of HIV/AIDS Prevention and Control, New York City Department of Health and Mental Hygiene, New York, NY
- Marguerite A. Urban, MD, University of Rochester School of Medicine and Dentistry, Rochester, NY
- Antonio E. Urbina, MD, The Mount Sinai Hospital, Comprehensive Health Program–Downtown, New York, NY
  - Scientific Advisor: Gilead, Viiv, Merck
- Geoffrey A. Weinberg, MD, University of Rochester School of Medicine and Dentistry, Rochester, NY

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All active MCCC members, invited consultants and coauthors, peer reviewers, and program staff are required to disclose financial relationships with commercial entities, including gifts that may be actual conflicts of interest or may be perceived as conflicts. These individuals must disclose financial relationships annually, for themselves, their partners/spouses, and their organization/institution. On their annual disclosures, MCCC members are asked to report for the previous 12 months and the upcoming 12 months.
All reported financial relationships with commercial entities are reviewed by the NYSDOH AI guidelines program to assess the potential for undue influence on guideline recommendations made by the Committee.

All guideline recommendations received consensus approval of the full MCCC, and the final review and approval of the recommendations were performed by the Committee Chair and the NYSDOH AI Medical Director and Deputy Medical Director, none of whom reported conflicts of interest.

**Evidence collection and review:** The NYSDOH AI guideline development process is based on a strategic search and analysis of the published evidence. Box A2 illustrates the evidence review and selection process.

**Box A2: Evidence Collection and Review Processes**

- **NYSDOH AI and MCCC defined the goal of the guideline:** To inform NYS clinicians about care for patients who present with signs or symptoms of acute HIV infection.
- **MCCC appointed a lead author who conducted a systematic literature search in PubMed using MeSH terms; all searches were limited to studies that**
  - 1) were published within the previous 5 years;
  - 2) involved only human subjects; and
  - 3) were published in English.
- **Lead authors reviewed studies identified through searches and excluded based on the following criteria:** Publication type, study design, participants, and clinical relevance to the guideline.
- **Author and editorial staff conducted additional searches using PubMed and online databases to identify:**
  - Studies published prior to the 5-year search limit.
  - Studies published during the guideline development process.
  - Recent conference abstracts.
  - Older studies known to provide strong evidence in support of specific recommendations or to undergird expert opinion.
- **Lead authors developed and the Writing Group and then all MCCC members reviewed and approved evidence-based guideline recommendations:**
  - Writing Group reviewed, deliberated, refined, and approved draft recommendations.
  - MCCC members reviewed, provided written comment on, deliberated, and reached consensus on recommendations.
  - Members of the Writing Group reviewed the cited evidence and assigned a 2-part rating to each recommendation to indicate the strength of the recommendation and the quality of the supporting evidence; consensus reached on ratings.
  - Additional evidence identified and cited during the rating process (see below).
- **Ongoing update process:**
  - JHU editorial staff will surveil published literature on an ongoing basis to identify new evidence that may prompt changes to existing recommendations or development of new recommendations.
  - JHU editorial staff will ensure that the MCCC reviews new studies at least 4 times per year, and more often if newly published studies, new drug approval, or drug-related warning indicate the need for an immediate change to the published guideline.
  - JHU editorial staff will track, summarize, and publish ongoing changes to the guideline.
  - MCCC will review and approve substantive changes to, additions to, or deletions of recommendations.
  - MCCC will initiate a full review of the guideline 4 years after the original publication date.
  - NYSDOH AI will publish a comprehensive update 5 years after the original publication date.

**Recommendation development and rating process:** When this guideline was originally developed, the standard development process was followed. Clinical recommendations were developed by consensus based on a synthesis of the current evidence collected through the systematic search described above. If no data were available, the recommendations are based on expert opinion, and this status is indicated in the rating and the text. Once consensus among the Writing Group members was reached, the guideline was reviewed by the full MCCC, and consensus was reached on all recommendations. Writing Group review discussions were recorded, and recordings were reviewed carefully to ensure that all decisions and changes were captured and integrated into the manuscript. Members of the Writing Group then individually reviewed the evidence for each recommendation and assigned a 2-part rating (see below). The individual ratings were compiled into a report distributed to all raters, and conference call discussions were held to deliberate ratings for which consensus was needed. Once all raters agreed on the interpretation of evidence and ratings for all recommendations, the guideline was sent to the NYSDOH AI for review and approval.
The current guideline reflects a review and update that was completed at the 3-year anniversary of publication. New literature was reviewed by a member of the MCCC and minor updates were made, which were then reviewed and approved by the Writing Group.

### AIDS Institute Clinical Guidelines Program: Recommendations Ratings (updated June 2019 [a])

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<thead>
<tr>
<th>Strength of Recommendation Ratings</th>
<th>A</th>
<th>Strong recommendation</th>
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a. With the June 2019 update, the ratings for quality of supporting evidence were expanded to add the * rating and the 2† rating.

**Guideline updates:** Members of the MCCC or an invited lead author who is not an MCCC member will monitor developments in an ongoing structured manner to maintain guideline currency. Once the guidelines are published on the program website, [www.hivguidelines.org](http://www.hivguidelines.org), and indexed in the National Library of Medicine, any updates will be made to the HTML document and all collateral materials as needed as new, peer-reviewed literature is published if evidence is made available that changes best practices.

Notification of newly published studies will be automated, and the Writing Group will review new data as available. Newly published data that provide support for existing recommendations will be cited in the text, and the studies will be added to the reference list(s).

If newly published data prompt a revision to recommendations or rationale, the lead author and the Writing Group will propose appropriate edits and determine whether the changes warrant review and approval by the entire MCCC. If MCCC review is required, JHU will distribute updates via email, and a conference call will be convened if required. Deletion of existing recommendations, addition of any new recommendations, or substantive changes to existing recommendations will prompt MCCC review and consensus.

The full guideline will be reviewed and updated on the third and the fifth anniversary of original publication and more often if an evidence-based change in recommendations is required.
When to Initiate Antiretroviral Therapy, With Protocol for Rapid Initiation

Lead authors Asa Radix, MD, MPH, and Noga Shalev, MD, with the Medical Care Criteria Committee, updated January 2020

Note: In January 2020, the MCCC published this updated guideline, which combines two guidelines published earlier: When to Initiate ART and Rapid ART Initiation. This updated and combined guideline replaces both.

Contents

Purpose of This Guideline ..................................................................................................................................................... 2
Benefits and Risks of Antiretroviral Therapy ..................................................................................................................... 3
  Benefits of ART ................................................................................................................................................................. 4
  Risks of ART ...................................................................................................................................................................... 5
  Risks of Untreated HIV ....................................................................................................................................................... 5
Rationale for Rapid ART Initiation ...................................................................................................................................... 6
  Reduced Treatment Delays and Loss to Follow-Up ............................................................................................................ 7
  Benefits for the Patient With HIV .................................................................................................................................. 7
  Rapid ART Initiation Is Safe ........................................................................................................................................... 8
Counseling and Education Before Initiating ART ........................................................................................................... 8
Protocol for Rapid ART Initiation ....................................................................................................................................... 9
  Figure 1: Protocol for Rapid ART Initiation .................................................................................................................... 10
  Reactive HIV Screening Test Result ............................................................................................................................... 10
  Counseling ......................................................................................................................................................................... 11
  Medical and Psychosocial Assessment .......................................................................................................................... 11
  Box 1: Medical History Checklist ................................................................................................................................ 12
  Baseline Laboratory and Resistance Testing .................................................................................................................. 12
  Box 2: Baseline Laboratory Testing Checklist ............................................................................................................... 12
General Principles in Choosing a Regimen for Rapid ART Initiation ................................................................................ 13
  Choosing a Regimen for Rapid ART Initiation ................................................................................................................ 13
  Preferred and Alternative Regimens for Rapid ART Initiation ......................................................................................... 14
    Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults ................................ 14
    Table 2: Preferred Regimens for Rapid ART Initiation in Pregnant Adults .................................................................. 15
  Rapid ART Initiation Follow-Up .................................................................................................................................... 16
  Paying for Rapid ART Initiation .................................................................................................................................. 16
Special Considerations ............................................................................................................................................................ 17
  Long-Term Nonprogressors and Elite Controllers ........................................................................................................ 18
  Barriers to Adherence ....................................................................................................................................................... 18
  Patients With Acute Opportunistic Infections ................................................................................................................ 18
All Recommendations ............................................................................................................................................................ 25
All Good Practices ................................................................................................................................................................. 27
Appendix: Use of Dolutegravir in Individuals of Childbearing Capacity ........................................................................... 28
When to Initiate Antiretroviral Therapy, With Protocol for Rapid Initiation

→ A NEW HIV DIAGNOSIS IS A CALL TO ACTION

- In support of the October 30, 2019, NYSDOH and NYC Health confirmation of rapid ART initiation as the standard of care for HIV treatment in New York, this committee supports rapid, and ideally, same-day initiation of ART in patients newly diagnosed with HIV.
- In support of the NYSDOH AIDS Institute’s January 2018 call to action for patients newly diagnosed with HIV, this committee stresses the following:
  - Immediate linkage to care is essential for any person diagnosed with HIV.
  - For the person with HIV, antiretroviral therapy (ART) dramatically reduces HIV-related morbidity and mortality.
  - Viral suppression helps to prevent HIV transmission to sex partners of people with HIV and prevents perinatal transmission of HIV.
- The urgency of ART initiation is even greater if the newly diagnosed patient is pregnant, has acute HIV infection, is ≥50 years of age, or has advanced disease. For these patients, every effort should be made to initiate ART immediately, and ideally, on the same day as diagnosis.
- All clinical care settings should be prepared, either on-site or with a confirmed referral, to support patients in initiating ART as rapidly as possible after diagnosis.
- For HIV therapy to be successful over time, the initiation of ART should involve both the selection of the most appropriate regimen and the acceptance of the regimen by the patient, bolstered by education and adherence counseling. All are critical in achieving the goal of durable and complete viral suppression.
  - See the NYSDOH AI guideline Selecting an Initial ART Regimen.

Purpose of This Guideline

This guideline was developed by the New York State Department of Health (NYSDOH) AIDS Institute (AI) for primary care providers and other practitioners to encourage initiation of antiretroviral therapy (ART) at the time of HIV diagnosis in ART-naive adults, and ideally, on the same day, or within 72 hours, an approach referred to as “rapid initiation of ART.” The NYSDOH AI January 2018 call to action emphasized the importance of starting ART at the time of HIV diagnosis and promotes scale-up of this approach to treating people newly diagnosed with HIV. The NYSDOH and NYC Health Dear Colleague Letter of October 30, 2019, confirms that initiation of ART on the same day that an individual has a reactive result on an HIV screening test, or is diagnosed with HIV, or on the first clinic visit is the recommended standard of care for HIV treatment in New York. To support the standard of ART initiation upon diagnosis, toward that end, this guideline:

- Provides guidance for choosing safe and efficacious ART regimens based on known patient characteristics, before results of recommended resistance testing or baseline laboratory testing are available.
- Identifies antiretroviral regimens to avoid for rapid ART initiation.
- Provides guidance for recognizing when rapid initiation is not appropriate.
- Encourages clinicians to seek the assistance of an experienced HIV care provider when managing patients with extensive comorbidities.
- Integrates current evidence-based clinical recommendations into the healthcare-related implementation strategies of the NYS Ending the Epidemic initiative, which seeks to end the AIDS epidemic in NYS by the end of 2020.
- Provides guidance on funding sources for sustainable access to ART.
**Guideline development:** This guideline was developed by the NYSDOH AI Clinical Guidelines Program, which is a collaborative effort between the NYSDOH AI Office of the Medical Director and the Johns Hopkins University School of Medicine, Division of Infectious Diseases.

Established in 1986, the goal of the Clinical Guidelines Program is to develop and disseminate evidence-based, state-of-the-art clinical practice guidelines to improve the quality of care provided to people who have HIV, hepatitis C virus, or sexually transmitted infections; people with substance use issues; and members of the LGBTQ community. NYSDOH AI guidelines are developed by committees of clinical experts through a consensus-driven process.

The NYSDOH AI charged the Medical Care Criteria Committee (adult HIV and related guidelines) with developing evidence-based clinical recommendations for rapid ART initiation. The resulting recommendations are based on an extensive review of the medical literature and reflect consensus among this panel of experts. Each recommendation is rated for strength and quality of the evidence (see below). If recommendations are based on expert opinion, the rationale for the opinion is included.

**NYSDOH AI Clinical Guidelines Program Ratings Scheme, Updated June 26, 2019 [a]**

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**Benefits and Risks of Antiretroviral Therapy**

**☑ RECOMMENDATION: Benefits and Risks of ART**

- Clinicians should recommend antiretroviral therapy to all patients with HIV infection. (A1)

Antiretroviral therapy (ART) refers to the use of pharmacologic agents that have specific inhibitory effects on HIV replication. The use of fewer than three agents is not recommended for initiating treatment. These agents belong to six distinct classes of drugs: the nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs, NtRTIs), the non-nucleoside reverse transcriptase inhibitors (NNRTIs), the protease inhibitors (Pis), the fusion inhibitors (FIs), the CCR5 co-
receptor antagonists, and the integrase strand transfer inhibitors (INSTIs). See all commercially available antiretroviral drugs that are FDA-approved for the treatment of HIV/AIDS.

Benefits of ART

ART has led to dramatic reductions in HIV-associated morbidity and mortality [CDC 2017]. In resource-rich settings, life expectancy of patients with HIV infection with access to early ART is approaching that of the general population [Siddiqi, et al. 2016]. A number of randomized clinical trials have demonstrated the benefits of ART in reducing HIV-related morbidity and mortality, irrespective of the degree of immune suppression at treatment initiation [Severe, et al. 2010; Lundgren, et al. 2015]. Thus, ART should be recommended to all individuals with HIV infection.

With proper selection of an initial regimen (see the NYSDOH guideline Selecting an Initial ART Regimen) and good patient adherence, durable virologic suppression (i.e., lifetime control of viral load) is achieved in virtually all patients with HIV infection. Virologic suppression almost invariably leads to immunological recovery, followed by reductions in the incidence of opportunistic infections and malignancies.

The measurable goals of treatment include:

- Viral suppression as measured by HIV-1 RNA level below the limits of detection.
- Immune reconstitution as measured by an increase in or maintenance of the CD4 cell count.
- Reduction in HIV-associated complications, including AIDS- and non–AIDS-related conditions.

ART also reduces morbidity and mortality from non–HIV-related causes. In a randomized study comparing continuous ART with CD4-guided treatment interruption, a mortality benefit was observed in subjects on continuous ART [El-Sadr, et al. 2006]. This benefit was attributed to a reduction in deaths from cardiovascular, renal, and hepatic causes. ART decreases the inflammatory milieu associated with ongoing HIV replication. It is postulated that ART-mediated reductions in proinflammatory cytokines lead to lower rates of clinical complications associated with the proinflammatory state [Hileman and Funderburg 2017].

Reducing HIV transmission: In addition to its direct health benefit to the individual with HIV infection, ART is a critical component of the overarching public health goal of eliminating HIV transmission. Antiretroviral treatment as prevention (TasP) is associated with greater reductions in HIV transmission than any preventative modality studied to date. In HPTN 052, a large randomized clinical trial of serodiscordant couples, early treatment of the infected partner was associated with a 96% reduction in HIV transmission compared with a delayed treatment approach [Cohen, et al. 2011]. In long-term follow-up of study participants, linked transmissions between partners were thought to occur only when the index partner was viremic [Cohen, et al. 2016]. In the observational PARTNERS study, no phylogenetically linked HIV transmission was observed in serodiscordant couples in which the index partner was virologically suppressed on ART [Rodger, et al. 2016]. The evidence thus suggests that the risk of sexual transmission of HIV during virological suppression is negligible. ART should be recommended to all patients with HIV infection to prevent transmission to sex partners and, by extrapolation, to needle-sharing partners. Despite its potent benefit in reducing HIV transmission, ART does not obviate the use of condoms or clean syringes. Those harm reduction measures, along with the use of PrEP for partners who do not have HIV infection, will help reduce the incidence of other STIs and viral hepatitis and should be integrated into patient counseling at ART initiation.

Reduced complications: Accumulating evidence suggests that patients who initiate ART earlier or spend less cumulative time with detectable plasma viremia are less likely to suffer certain complications, such as cardiovascular disease [El-Sadr, et al. 2006; Marin, et al. 2009; Ho, et al. 2010; Lichtenstein, et al. 2010; Ho, et al. 2012], neurocognitive dysfunction [Tozzi, et al. 2007; Ellis, et al. 2011; Garvey, et al. 2011; Winston, et al. 2012], decreased risk of severe bacterial infections [O’Connor, et al. 2017], and some non–HIV-related malignancies [Bruyand, et al. 2009; Guiguet, et al. 2009; Silverberg, et al. 2011; Sigel, et al. 2012]. Cohort data also demonstrate that although older patients are likely to achieve virologic suppression, they are less likely to achieve an immunologic response, as measured by an increase of CD4 count by 100 cells/mm³, and that patients >55 years old may be at higher clinical risk even after starting therapy [Sabin, et al. 2008]. The poor immunologic recovery seen in older patients is associated with higher morbidity and mortality, particularly cardiovascular events [van Lelyveld, et al. 2012]. In one study, men ≥50 years of age who initiated ART with CD4 counts in the 351 to 500 cells/mm³ range were able to achieve similar immunologic responses as younger men who initiated at lower CD4 counts [Li X, et al. 2011].

Reduced perinatal transmission of HIV: Studies have shown that for pregnant women with HIV, the administration of ART during pregnancy or intrapartum significantly reduces the risk of mother-to-child transmission (MTCT) of HIV [Connor, et al. 1994; Guay, et al. 1999]. In addition, a large study showed a 96% reduction in transmission between serodiscordant
heterosexual couples when the positive partner was receiving ART [Cohen, et al. 2011], adding to the body of evidence that lower viral load reduces transmission risk. ART is now part of the established strategy aimed at reducing HIV transmission and is an essential component of prevention interventions along with risk-reduction counseling, safer-sex practices, and avoidance of needle-sharing. Although the majority of patients both in New York and worldwide present later in the course of their HIV infection [Althoff, et al. 2010; CDC 2010, 2011], ongoing efforts to offer universal HIV testing to all patients over age 13 may begin to identify patients earlier in their disease who can benefit from immediate treatment.

Risks of ART

Despite the excellent tolerability of contemporary ART regimens, adverse reactions, side effects, long-term drug toxicities, and drug-drug interactions continue to pose some relative or limited risks. Patients must be counseled about the potential for ART-associated adverse events in the short and long term. These risks include tolerability issues, which may affect quality of life, as well as possible long-term toxicities—primarily a low relative risk of renal and cardiovascular disorders or decreased bone density of uncertain clinical significance [Friis-Moller, et al. 2010; Monteiro, et al. 2014; Hoy, et al. 2017]. Renal and bone density issues are largely eliminated with newer formulations of ARVs. Fatal drug reactions from ART are exceedingly rare.

Many ART combinations are now available in single-pill, fixed-dose combination formulations. Thus, the pill burden associated with early antiretroviral regimens has been largely eliminated. Nevertheless, lifelong adherence to medications may constitute a challenge to some, particularly when treatment with a single daily tablet is not feasible.

When compared with early antiretroviral combinations, contemporary ART regimens (see the NYSDOH AI guideline Selecting an Initial ART Regimen) are associated with higher rates of durable virologic suppression. Lack of virologic suppression in a patient on ART should prompt the clinician to evaluate patient adherence and provide intensive support for those reporting challenges in this domain. Failure to achieve and maintain virologic suppression may lead to the emergence of resistance-associated mutations (RAMs). A large cohort study has demonstrated that virologic failure with contemporary ART regimens is associated with the infrequent emergence of RAMs [Scherrer, et al. 2016]. Nevertheless, RAMs can emerge with current first-line therapies. Resistance to antiretroviral medications may compromise the potential for long-term virologic suppression, simple dosing schedules, and the tolerability of future treatment options.

ART initiation is associated with a risk of immune reconstitution inflammatory syndrome (IRIS). IRIS is a clinical syndrome characterized by new or worsening infectious and non-infectious complications observed after the initiation of ART (see the NYSDOH AI guideline Management of IRIS). The risk of IRIS increases when ART is begun at low CD4 cell counts (<100 cells/mm³) or with the presence of specific opportunistic infections. Although the risk of IRIS is not a contraindication to initiating ART, clinicians and patients should be aware that the risk of developing IRIS is increased among individuals with lower CD4 counts. Patients at increased risk should be informed of the potential for a paradoxical clinical worsening after ART initiation.

Risks of Untreated HIV

Results from the START trial [Lundgren, et al. 2015] and strong cohort data show that untreated HIV infection leads to increased morbidity and mortality from both HIV-related and non-HIV-related conditions, even at high CD4 counts.

Together with the dramatic reduction of transmission risk with effective treatment, these data support the initiation of ART regardless of CD4 count in all adequately prepared patients, including patients diagnosed with acute HIV infection (for more discussion see the NYSDOH AI guideline Diagnosis and Management of Acute HIV). Patients in care who are documented long-term nonprogressors or elite controllers are a group that may warrant special consideration (see the Special Considerations section of this guideline).

In START, a randomized trial initiating ART in treatment-naïve patients with CD4 counts >500 cells/mm³ versus waiting for a decrease to ≤350 cells/mm³ before initiation showed a 53% reduction in serious illness and death in the early ART group [Lundgren, et al. 2015]. Data from NA-ACCORD, a large observational cohort study, showed that both morbidity and mortality were improved by initiation of ART in patients with CD4 counts in the high or even normal range [Kitahata, et al. 2009]. A significantly decreased risk of death was observed in patients who initiated therapy at CD4 counts >500 cells/mm³ compared to those who deferred to <500 cells/mm³, as well as in the cohort who initiated ART in the 350 to 500 cells/mm³ range compared with those deferring to <350 cells/mm³ [Kitahata, et al. 2009]. Although other cohort studies demonstrated only a minimal survival advantage [Wright, et al. 2011] or no survival advantage among those starting ART at the highest CD4 counts, they did confirm the benefits of initiating ART at levels ≤500 cells/mm³ [Cain, et al.
2011; CASCADE Collaboration 2011; Young, et al. 2012]. Another showed an approximately 33% reduction in the risk of death from end-stage liver disease, non-AIDS infections, and non-AIDS-defining cancers with each 100 cells/mm³ increase in CD4 count [Marin, et al. 2009]. A randomized study of early versus deferred therapy in patients with CD4 counts in the 350-550 cells/mm³ range showed no mortality benefit [Cohen, et al. 2011]; however, this study has significant limitations, most notably a relatively brief follow-up period.

Rationale for Rapid ART Initiation

**RECOMMENDATIONS: Rationale for Rapid ART Initiation**

- Clinicians should recommend antiretroviral therapy (ART) for all patients with a diagnosis of HIV infection. (A1)
- Clinicians should offer rapid initiation of ART—preferably on the same day (A1) or within 72 hours—to all individuals who are candidates for rapid ART initiation (see text) and who have:
  - A confirmed HIV diagnosis (A1), or
  - A reactive HIV screening result pending results of a confirmatory HIV test (A2), or
  - Suspected acute HIV infection, i.e., HIV antibody negative and HIV RNA positive (A2).
- Clinicians should counsel patients with seronegative partners about the reduction of HIV transmission risk after effective ART is initiated and viral suppression is achieved, and should strongly recommend ART for patients with seronegative partners. (A1)
- Clinicians should evaluate and prepare patients for ART initiation as soon as possible; completion of the following should not delay initiation:
  - Discuss benefits and risks of ART with the patient. (A3)
  - Assess patient readiness. (A3)
  - Identify and ameliorate factors that might interfere with successful adherence to treatment, including inadequate access to medication, inadequate supportive services, psychosocial factors, active substance use, or mental health disorders. (A2)
- Clinicians should refer patients for supportive services as necessary to address modifiable barriers to adherence. An ongoing plan for coordination of care should be established. (A3)
- Clinicians should involve patients in the decision-making process regarding initiation of ART and which regimen is most likely to result in adherence. The patient should make the final decision of whether and when to initiate ART. (A3)
- If the patient understands the benefits of rapid initiation but declines ART, then initiation should be revisited as soon as possible.
- In patients with advanced HIV (or AIDS), ART should be initiated even if barriers to adherence are present. In these cases, referrals to specialized adherence programs should be made for intensified adherence support. (A2)
- After ART has been initiated, response to therapy should be monitored by, or in consultation with, a clinician with experience in managing ART. (A2)

The New York State Department of Health (NYSDOH) HIV Clinical Guidelines Program and the U.S. Department of Health and Human Services (DHHS) recommend initiation of ART for all patients with a confirmed HIV diagnosis regardless of their CD4 cell count or viral load, for the benefit of the individual with HIV (reduced morbidity and mortality) [Zolopa, et al. 2009; Lundgren, et al. 2015] and to reduce the risk of transmission to others [Cohen, et al. 2016]. Initiating ART during early HIV infection may improve immunologic recovery (CD4 T cell counts) and reduce the size of the HIV reservoir [Jain, et al. 2013]; there is also evidence that initiating ART at the time of diagnosis reduces treatment delays and improves retention in care and viral suppression at 12 months [Ford, et al. 2018].
Reduced Treatment Delays and Loss to Follow-Up

Standard practice protocols for ART initiation have produced preventable delays, and the required wait for confirmatory HIV diagnostic and baseline laboratory test results (including resistance testing) along with required medical visits can unnecessarily delay the start of treatment by as long as 4 weeks. Problems in accessing insurance or waiting for activation of public benefits may also cause delays. It is estimated that in 2016, only 75.9% of individuals diagnosed with HIV in the U.S. HIV care continuum were linked to care within 1 month [CDC 2018]. Individuals with HIV who are not linked to care are at risk of having sustained viral loads and ongoing HIV transmission.

Rapid initiation of ART may reduce delays and improve viral suppression rates in people with HIV. Rapid or same-day ART initiation, which is preferable, or initiation within 3 days of a newly positive HIV test is the strategy endorsed by the World Health Organization [WHO 2017] and is an essential component of the New York State Ending the Epidemic initiative. Mathematical modeling demonstrates that a test-and-treat strategy, with immediate initiation of ART and prevention approaches, could lead to elimination of new HIV infections [Granich, et al. 2009].

Benefits for the Patient With HIV

Several observational and clinical trials have demonstrated the individual-level benefits of rapid ART initiation [Ford, et al. 2018]. An early pilot of this approach in San Francisco, California, demonstrated that patients initiating ART within 1 or 2 days had a shorter time (median, 1.8 months) to viral suppression (HIV RNA ≤200 copies/mL) than those offered the standard of care (4.3 months) or than historical controls (7.2 months) [Pilcher, et al. 2017]. A longer-term follow-up of 225 patients at the same center found that, of patients who had access to rapid initiation, 95.8% had achieved viral suppression at least once and 92.1% had achieved it at the last recorded visit [Coffey, et al. 2019]. These individual-level benefits have been replicated in other U.S. and international studies that demonstrated improved viral suppression with shortened time to ART initiation [Rosen, et al. 2016a; Koenig, et al. 2017; Colasanti, et al. 2018]. After implementing rapid ART initiation at a hospital clinic in Atlanta, Georgia, time to viral suppression fell from 77 days, before the intervention, to 57 days [Lundgren, et al. 2015], and average time to ART initiation decreased from 21 to 7 days; both findings were statistically significant [Colasanti, et al. 2018].

Another demonstrated benefit is an improved rate of retention in care [Amanyire, et al. 2016; Rosen, et al. 2016a; Koenig, et al. 2017]. In the RapIT trial in South Africa, patients newly diagnosed with HIV were randomized to rapid ART initiation or standard of care [Rosen, et al. 2016b]. The participants in the rapid initiation arm had higher rates of ART initiation at 90 days (97% vs. 72%) and higher rates of retention in care and viral suppression (HIV RNA ≤400 copies/mL) at 10 months (relative risk, 1.26 [1.05–1.50]). The average cost per patient to achieve viral suppression was lower in the intervention arm, demonstrating that this strategy of care may also be cost-effective [Long, et al. 2017]. Studies conducted in China and South Africa support the cost-effectiveness of rapid ART initiation [Zulliger, et al. 2014; Wu, et al. 2015; Ford, et al. 2018]. Rapid ART initiation is efficacious, safe, and highly acceptable, with few patients declining the offer of immediate ART [Pilcher, et al. 2017; Coffey, et al. 2019].

Modeling evidence suggests the potential for rapid ART initiation to significantly reduce HIV transmission in the community, although this has been directly modeled only in the context of South Africa [Granich, et al. 2009]. In the United States, linkage to and retention in HIV care are significant gaps in the HIV care continuum, with an estimated 64% of individuals with HIV receiving any HIV care and 49% being retained in care during 2016 [CDC 2019]. Models have translated these gaps in care to their effect on HIV transmission in the United States, demonstrating that between 43% and 49% of new HIV transmissions are attributable to individuals who have been diagnosed with HIV but are not receiving ART and have not been retained in care [Skarbinski, et al. 2015; Li Z, et al. 2019]. Because it is designed to help close this care gap, rapid ART initiation greatly reduces new HIV infections, hastening the achievement of HIV incidence reduction goals in New York State.
Rapid ART Initiation Is Safe

In the San Francisco study discussed above [Pilcher, et al. 2017], 89.7% of patients used integrase strand transfer inhibitor (INSTI)-containing regimens and 12.8% used protease inhibitor–containing regimens. The predominant INSTI-based regimen was dolutegravir plus emtricitabine/tenofovir disoproxil fumarate. The clinic did not have any cases of major resistance mutations to the prescribed ART regimen, and no regimen switches were made because of resistance. Two patients had their regimens changed because of rash, and in 10 cases, the regimen was simplified to a single-tablet regimen.

Of 149 patients initiating ART through a program in New York City, only 1 required a regimen change because of subsequently detected resistance [Blank, et al. 2018].

Rapid ART initiation is safe. Most designated regimens for rapid ART initiation are the same regimens that are recommended as initial treatment in the existing NYSDOH, International Antiviral Society–USA, and DHHS guidelines. These regimens are well-tolerated and effective, and the likelihood of drug resistance is low based on the current prevalence of drug resistance [NYCDHMH 2018].

--- RESOURCES ---

- The CEI Line provides primary care providers in New York State the opportunity to consult with clinicians who have experience managing ART. The CEI Line can be reached at 1-866-637-2342 or 1-585-273-2793.
- The AIDS Institute maintains a voluntary NYSDOH AIDS Institute Provider Directory to assist with identification of experienced providers in New York State.
- Experienced care providers can also be identified through the American Academy of HIV Medicine (AAHIVM) and the HIV Medicine Association (HIVMA).

Counseling and Education before Initiating ART

☑️ RECOMMENDATIONS: Counseling and Patient Education

- Counseling and education should include the following:
  - Basic education about HIV, CD4 cells, viral load, and resistance. (A3)
  - Available treatment options and potential risks and benefits of therapy (see text). (A3)
  - The need for strict adherence to avoid the development of viral drug resistance. (A2)
  - Use of safer-sex practices and avoidance of needle-sharing activity, regardless of viral load, to prevent HIV transmission or superinfection. (A3)
  - Clinicians should involve the patient in the decision-making process regarding initiation of ART. (A3)

Discussion of ART should occur when a positive HIV test result is obtained, regardless of CD4 count. The clinician and patient should discuss the benefits of early ART (see below) and individual factors that may affect the decision to initiate, such as patient readiness or reluctance and adherence barriers. Clinicians should involve the patient in the decision-making process regarding initiation of ART [Salzberg Global Seminar 2011]. When clinicians and patients engage in shared decision-making, patients are more likely to choose to initiate ART and to achieve an undetectable viral load [Beach, et al. 2007]. Misconceptions about treatment initiation should be addressed, including the implication that starting ART represents advanced HIV illness or that taking ART may adversely affect therapeutic levels of gender-affirming hormones [Braun, et al. 2017]. Initiating ART before symptoms occur allows patients to stay healthier and live longer.

The risks and benefits of early ART to discuss with patients when making the decision of whether and when to initiate ART are outlined below. It should be emphasized that the START trial provided definitive evidence that the benefits of early initiation of ART outweigh the potential disadvantages.
Benefits of early ART in asymptomatic patients:
(early therapy = initiation at CD4 counts >500 cells/mm³)

- Delay or prevention of immune system compromise [Lewden, et al. 2007].
- Possible lower risk of antiretroviral resistance [Uy, et al. 2009].
- Decreased risk of sexual transmission of HIV [Quinn, et al. 2000; Castilla, et al. 2005; Donnell, et al. 2010; Cohen, et al. 2011]. HIV cannot be transmitted sexually when the plasma viral load is undetectable; ART is not a substitute for primary HIV prevention measures, such as avoidance of needle sharing [Politch, et al. 2012].
- Decreased risk of several severe bacterial infections [O’Connor, et al. 2017].
- Potential decrease in size of viral reservoir and preservation of gut-associated lymphoid tissue with initiation during acute HIV, i.e., within the first 6 weeks [Jain, et al. 2013; Novelli, et al. 2018].

Disadvantages of early ART in asymptomatic patients:

- Possibility of greater cumulative side effects from ART [Volberding and Deeks 2010].
- Possibility for earlier onset of treatment fatigue.

→ RESOURCES

- Patients who do not have health insurance may qualify for Medicaid or the NYSDOH HIV Uninsured Care Program, which provides access to free health care (HIV drugs, primary care, home care, and the ADAP Plus Insurance Continuation Program, or APIC) for residents who have HIV and are uninsured or underinsured. The program is open Monday-Friday, 8:00AM-5:00PM and can be reached: in state 1-800-542-2437; out-of-state 1-518-459-1641; TDD 1-518-459-0121. If eligible, patients may also consider treatment options through enrollment in clinical trials. A resource that may help with this process is the AIDS Clinical Trials Information Service (1-800-TRIALS-A).

Protocol for Rapid ART Initiation

☑️ RECOMMENDATIONS: Protocol for Rapid ART Initiation

- To determine whether a patient is a candidate for rapid antiretroviral therapy (ART) initiation, the clinician should confirm that the individual has any of the following (A1):
  - A reactive point-of-care HIV test result, or confirmed HIV diagnosis, or suspected acute HIV infection, or known HIV infection, and
  - No prior ART (i.e., treatment naive) or limited prior use of antiretroviral medications, and
  - No medical conditions or opportunistic infections that require deferral of rapid ART initiation, including suspected cryptococcal or tuberculous meningitis.
- Clinicians should perform baseline laboratory testing listed in Box 2: Baseline Laboratory Testing Checklist for all patients who are initiating ART immediately; ART can be started while awaiting laboratory test results. (A3)

→ SELECTED GOOD PRACTICE REMINDERS

- For patients with a reactive HIV antibody screening test that is pending confirmation, make sure the patient understands the benefits of rapid ART initiation and the following:
  1. Reactive screening test results are not formally diagnostic, because false-positive results are still possible;
→ SELECTED GOOD PRACTICE REMINDERS

2. A confirmatory (diagnostic) HIV test will be performed;
3. ART will be discontinued if the confirmatory test result is negative and continued if it is positive;
4. The benefit of starting ART early, after a presumptive positive screening test, outweighs the negligible risk of taking ART for a few days and then stopping it if confirmed HIV negative.

- Provide the result of the confirmatory HIV test as soon as it is available; discontinue ART if the result is negative and reinforce adherence and next steps if it is positive.
- If a patient declines rapid ART initiation, discuss options for deferred initiation of ART, link the patient with HIV primary care, and outline next steps.

Figure 1: Protocol for Rapid ART Initiation

Reactive HIV Screening Test Result

When the result of a patient’s initial HIV point-of-care screening test is reactive, established practice is to obtain a blood specimen for diagnostic HIV testing because of the possibility of false-positive screening results. This is particularly important for individuals who are not at high risk of acquiring HIV. However, supplemental testing results may not be available for several days, introducing the risk that a patient will not return. The goal of the rapid ART initiation protocol is to assess whether a person with a reactive HIV screening test result (or a confirmed HIV diagnosis) is also a candidate for same-day initiation of ART. If so, then the rapid ART initiation protocol is to provide counseling on HIV transmission and the benefits of ART, initiate ART that day or within 3 days, and link the person expeditiously to HIV primary care. Thus, the protocol recommends immediate initiation of ART while awaiting confirmatory HIV test results.

Patients who are candidates for rapid ART initiation:

- Have a new reactive point-of-care HIV test result or a new HIV diagnosis (confirmed through the Centers for Disease Control and Prevention HIV testing algorithm) or acute HIV infection (HIV antibody negative and HIV RNA positive) or known HIV, and
- Are treatment-naive, or
- Have a history of limited ART use (e.g., a person who stopped first-line therapy for reasons other than regimen failure), as long as concern for acquired drug resistance is low (requires a case-by-case determination).

Patients with a new reactive HIV test result can be retested using a second point-of-care test from a manufacturer different from that of the first test to further minimize the possibility of a false-positive result. It is not necessary to retest with a second point-of-care test before providing ART, but given the possibility of a false-positive screening result, a
laboratory-based confirmatory HIV test should always be performed to establish a diagnosis of HIV. If the confirmatory HIV test result is negative, ART can be discontinued.

→ KEY POINT

- Patients with a new reactive HIV test result can be retested using a second point-of-care test from a different manufacturer than that of the first test, if available, to further minimize the possibility of a false-positive result.
  - See the NYSDOH AI guideline *HIV Testing > Characteristics of FDA-Approved Rapid HIV Tests* for a list of available point-of-care HIV tests.

Counseling

A reactive HIV screening result should prompt a care provider to counsel the patient about the benefits and risks of ART and about HIV transmission risk, including the consensus that *Undetectable Equals Untransmittable (U=U)*. When patients are initiated on ART on the same day as their reactive HIV test result, the priorities for patient education and counseling include:

- Confirming the diagnosis of HIV.
- Managing disclosure, if indicated.
- Adhering to the ART regimen.
- Recognizing and responding to side effects.
- Following through with clinic visits.
- Assessing health literacy.
- Managing lifelong ART: Navigating acquisition of and paying for medications required for lifelong therapy, including pharmacy selection, insurance requirements and restrictions, co-pays, and prescription refills.
- Identifying and addressing psychosocial issues that may pose barriers to treatment.
- Referring for substance use and behavioral health counseling if indicated.
- Referring for housing assistance if indicated.
- Ensuring the patient knows how to reach the care team if needed, to address the adverse effects of medications or other concerns.

→ KEY POINT: HEALTH LITERACY

- According to the *National Network of Libraries of Medicine*, health literacy requires:
  - The ability to understand instructions on prescription drug bottles, appointment slips, medical education brochures, and doctor’s directions and consent forms.
  - The ability to negotiate complex healthcare systems.
  - Reading, listening, analytical, and decision-making skills, and the ability to apply these skills to health situations.
- Resources:
  - *AHRQ Short Assessment of Health Literacy—Spanish and English*
  - *AHRQ Rapid Estimate of Adult Literacy in Medicine—Short Form*
  - *AHRQ Short Assessment of Health Literacy for Spanish Adults*
  - *Health Literacy Tool Shed (funded by the U.S. National Libraries of Medicine)*

Medical and Psychosocial Assessment

Medical assessment of a patient with a new reactive HIV test result should include history or signs or symptoms of opportunistic infection(s). ART should be delayed and appropriate medical management initiated if tuberculous (TB) meningitis or cryptococcal meningitis are suspected (see below) [WHO 2017], if cytomegalovirus retinitis is suspected, or if the patient has any evidence of advanced HIV disease on clinical exam.
To identify the potential for pre-existing drug-resistant virus, the initial assessment should also include the patient’s history of pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) use and previous ART use for people who are re-engaging in care [Ford, et al. 2018]. See Box 1: Medical History Checklist, below.

**Box 1: Medical History Checklist**

When taking a medical history before rapid ART initiation, ask about:

- Date and result of last HIV test
- Serostatus of sex partners and their ART regimens if known
- Previous use of antiretroviral medications, including as PrEP or PEP, with dates of use
- Comorbidities, including a history of renal or liver disease, particularly hepatitis B infection
- Prescribed and over-the-counter medications
- Drug allergies
- Substance use
- Symptoms, to assess for active cryptococcal and TB meningitis
- Psychiatric history, particularly depressive or psychotic symptoms or any history of suicidality
- Possible pregnancy and childbearing plans in individuals of childbearing potential

**Deferral of ART initiation:** If the patient understands the benefits of rapid initiation but declines ART, then initiation should be revisited as soon as possible. In some circumstances, such as in the rare case of suspected cryptococcal or TB meningitis, rapid ART is not recommended (see the Patients With Acute Opportunistic Infections section of this guideline). Patients who present with signs and symptoms suggestive of pulmonary or intracranial and ophthalmologic infections should receive further assessment before initiating ART on the same day as a reactive HIV screening test result.

ART initiation should be delayed in any person presenting with signs or symptoms suggestive of meningitis, including headache, nausea or vomiting, light sensitivity, and changes in mental status. Treatment of TB meningitis was investigated in a clinical trial in Vietnam in which immediate initiation of ART was compared with ART initiated 2 months after TB treatment [Torok, et al. 2011]. There were significantly more grade 4 adverse effects in individuals who initiated ART immediately than in those who delayed. Among patients with cryptococcal meningitis, early initiation of ART has been associated with adverse outcomes, including death [Boulware, et al. 2014]; therefore, it is recommended that ART be deferred until after the induction phase of treatment for cryptococcal meningitis has been completed (see DHHS: Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV).

It is clear that co-treatment of HIV and pulmonary TB improves survival. In the SAPIT trial in South Africa, there was a 56% relative reduction in mortality when ART was initiated within 4 weeks of TB treatment initiation, compared with when it was started after TB treatment was completed (hazard ratio, 0.44; 95% confidence interval, 0.25–0.79; P=.003), although symptoms of immune reconstitution inflammatory syndrome (IRIS) were greater in patients who started ART earlier [Abdool Karim, et al. 2010]. However, it is not clear that ART initiation prior to initiation of pulmonary TB treatment is the best course of action. Care providers should weigh the benefits of rapid ART initiation against the potential drawbacks of pill burden, drug interactions, and the risk of IRIS.

**Baseline Laboratory and Resistance Testing**

All patients with a reactive HIV test result should undergo the baseline laboratory testing listed in Box 2, below. For discussion of baseline testing, see the NYSDOH AI guideline Selecting an Initial ART Regimen > ART-Initiation Laboratory Testing. It is not necessary to wait for these test results before initiating ART.

**Box 2: Baseline Laboratory Testing Checklist**

- HIV-1/2 antigen/antibody assay
- HIV quantitative viral load
- Baseline HIV genotypic resistance profile
- Baseline CD4 cell count
- Testing for hepatitis A, B, and C viruses
- Comprehensive metabolic panel (creatinine clearance, hepatic profile)

- See CDC > Sexually Transmitted Infections Treatment Guidelines, 2021 > Screening
- Urinalysis
- Pregnancy test for individuals of childbearing potential
General Principles in Choosing a Regimen for Rapid ART Initiation

**RECOMMENDATIONS: General Principles in Choosing a Regimen for Rapid ART Initiation**

- Clinicians should involve their patients when deciding which antiretroviral therapy (ART) regimen is most likely to result in adherence. (A3)
- Before initiating ART, clinicians should:
  - Assess the patient’s prior use of antiretroviral medications, including pre-exposure prophylaxis (PrEP), which may increase the risk for baseline resistance. (A2)
  - Assess for any comorbidities and chronic coadministered medications that may affect the choice of regimen for initial ART. (A2)
  - At the time of HIV diagnosis, obtain genotypic resistance testing for the protease (A2), reverse transcriptase (A2), and integrase (B2) genes.
  - Ask individuals of childbearing potential about the possibility of pregnancy, their reproductive plans, and their use of contraception. (A3)
- For ART-naive patients, clinicians should select an initial ART regimen that is preferred; see Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults. (A1)
- Clinicians should reinforce medication adherence regularly. (A3)
- Clinicians should obtain a viral load test 4 weeks after ART initiation to assess the response to therapy. (A3)
  - See the NYSDOH AI guideline Virologic and Immunologic Monitoring for more information.

**SELECTED GOOD PRACTICE REMINDERS**

- Follow up within 24 to 48 hours, by telephone or another preferred method, with a patient who has initiated ART to assess medication tolerance and adherence.
- If feasible, schedule an in-person visit for 7 days after ART initiation.

Choosing a Regimen for Rapid ART Initiation

The preferred medications for rapid ART initiation are based on the established regimens for individuals who are ART-naive and are restricted to those that can be safely initiated in the absence of readily available baseline laboratory testing results, such as viral load, CD4 count, and HLA-B*5701. The preferred regimens have a high barrier to resistance, are well tolerated, and limit the potential for drug-drug interactions. Initial regimens should be selected on the basis of patient preferences and clinical characteristics, and a preferred regimen should be used whenever possible (see Table 1, below).

One regimen (tenofovir alafenamide/emtricitabine/cobicistat/darunavir [TAF/FTC/COBI/DRV]) has been studied formally in the setting of rapid ART initiation, in a phase 3, open-label, single-arm, prospective, multicenter study without the benefit of resistance testing and produced high rates (96%) of viral suppression (HIV RNA <50 copies/mL) at 48 weeks [Huhn, et al. 2019].

When following a rapid ART initiation protocol, care providers should avoid regimens containing abacavir because results of HLA-B*5701 testing are not likely to be available. Similarly, rilpivirine should be avoided in any patient who has a viral load >100,000 copies/mL and in any patient whose viral load is unknown.

Efavirenz is associated with a higher risk of central nervous system side effects and of transmitted drug resistance mutations [Kagan, et al. 2019]; therefore, it is not recommended for rapid ART initiation.

Clinics that have implemented rapid ART initiation frequently design pre-approved regimens that consider local patterns of transmitted drug resistance and drug toxicity [Pilcher, et al. 2017].

There is a greater possibility that HIV drug resistance mutations may emerge and reduce the efficacy of an initial ART regimen in patients with a new reactive HIV screening test or a new HIV diagnosis who have taken tenofovir disoproxil
fumarate/emtricitabine (TDF/FTC) or tenofovir alafenamide fumarate/emtricitabine (TAF/FTC) as PrEP since their last negative HIV test. Results of a recent study in New York City demonstrated that individuals who had taken PrEP in the 3 months prior to a new HIV diagnosis were significantly more likely than those who never used PrEP (26% vs. 2%; \( P<.0001 \)) to have resistance mutations (M184I/V/IV/MV) to lamivudine/emtricitabine (3TC/FTC) [Misra, et al. 2019]. For such patients, the initial regimen should consist of an integrase strand transfer inhibitor plus a boosted protease inhibitor and 2 nucleoside reverse transcriptase inhibitors. An option for treatment in this scenario is provided in Table 1, below. The initial regimen may be simplified once results of baseline genotypic testing have been reviewed.

- See the NYSDOH AI guideline Selecting an Initial ART Regimen for more information.

### Preferred and Alternative Regimens for Rapid ART Initiation

**Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults**, below, includes initial preferred and alternative regimens for rapid ART initiation in nonpregnant adults. The regimens are listed alphabetically. For specific details on choosing a regimen, see the discussions in other sections of this guideline and the package inserts for the drugs listed below.

**Providing ART:** Some clinics provide patients with the first dose of ART and a 30-day prescription when a rapid ART initiation protocol is being followed [Pilcher, et al. 2017]. Others may provide a 7-day ART starter pack or a 30-day prescription.

| Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults |
|----------------------------------|---------------------------------|-------------------|
| **Regimen** | **Comments** | **Rating** |
| **Preferred Regimens** | | |
| Tenofovir alafenamide/ emtricitabine/bictegravir (TAF 25 mg/FTC/BIC; Biktarvy) | • Available as a single-tablet formulation, taken once daily.  
• TAF/FTC should not be used in patients with a creatinine clearance (CrCl) <30 mL/min; re-evaluate after baseline laboratory testing results are available.  
• Contains 25 mg of TAF, unboosted.  
• Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after BIC; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food. | A1 |
| Tenofovir alafenamide/ emtricitabine and dolutegravir* (TAF 25 mg/FTC and DTG; Descovy and Tivicay) | • TAF/FTC should not be used in patients with CrCl <30 mL/min; re-evaluate after baseline laboratory testing results are available.  
• Contains 25 mg of TAF, unboosted.  
• Two tablets once daily.  
• Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food. | A1 |
| Tenofovir alafenamide/ emtricitabine/darunavir/cobicistat (TAF 10 mg/FTC/DRV/COBI; Symtuza) | • Available as a single-tablet formulation, taken once daily.  
• Contains 10 mg TAF, boosted.  
• TAF/FTC should not be used in patients with CrCl <30 mL/min; re-evaluate after baseline laboratory testing results are available.  
• Pay attention to drug-drug interactions. | A2 |
| **Alternative Regimen** | | |
| Tenofovir alafenamide/ emtricitabine and raltegravir (TAF 25 mg/FTC and RAL HD; Descovy and Isentress HD) | • TAF/FTC should not be used in patients with CrCl <30 mL/min; re-evaluate after baseline laboratory testing results are available.  
• To date, no clinical trials have been conducted with TAF and RAL; data are based on bioequivalence pharmacokinetic studies. | B1 |
Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
<th>Rating</th>
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<tbody>
<tr>
<td>Dolutegravir* and darunavir/cobicistat/tenofovir alafenamide/emtricitabine (DTG/DRV/CObI/TAF/FTC 10 mg/FTC; Tivicay and Symtuza)</td>
<td>TAF/FTC should not be used in patients with CrCl &lt;30 mL/min; re-evaluate after baseline laboratory testing results are available.</td>
<td>A3</td>
</tr>
<tr>
<td></td>
<td>Documented DTG resistance after initiation in treatment-naive patients is rare.</td>
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<tr>
<td></td>
<td>Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food.</td>
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</tr>
<tr>
<td></td>
<td>Tenofovir disoproxil fumarate (TDF) may be substituted for TAF; TDF/FTC is available as a single tablet (brand name, Truvada).</td>
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<tr>
<td></td>
<td>Lamivudine (3TC) may be substituted for FTC.</td>
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<tr>
<td></td>
<td>3TC/TDF is also available as a single tablet.</td>
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<tr>
<td>Medications to Avoid</td>
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</tr>
<tr>
<td>Abacavir (ABC)</td>
<td>ABC should be avoided unless a patient is confirmed to be HLA-B*5701 negative.</td>
<td>A3</td>
</tr>
<tr>
<td>Rilpivirine (RPV)</td>
<td>RPV should be administered only in patients confirmed to have a CD4 cell count ≥200 cells/mm³ and a viral load &lt;100,000 copies/mL.</td>
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<tr>
<td>Efavirenz (EFV)</td>
<td>EFV is not as well tolerated as other antiretroviral medications, and nonnucleoside reverse transcriptase inhibitors have higher rates of resistance.</td>
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</tbody>
</table>

*See Appendix: Use of Dolutegravir in Individuals of Childbearing Capacity.

Reducing the risk of perinatal transmission of HIV requires timely identification of HIV infection in a pregnant individual and 3-drug ART initiated as soon as possible after diagnosis. Pregnancy is not a contraindication to rapid ART initiation. Adherence to an ART regimen during pregnancy should be encouraged, as should coordination among HIV and obstetric care providers (see the NYSDOH AI guideline Prevention of Mother-to-Child HIV Transmission).

Table 2, below, includes initial preferred regimens for rapid ART initiation in pregnant adults.

Table 2: Preferred Regimens for Rapid ART Initiation in Pregnant Adults

See also: DHHS: Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infections and Interventions to Reduce Perinatal HIV Transmission in the United States.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
<th>Rating</th>
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<tbody>
<tr>
<td>Tenofovir disoproxil fumarate/emtricitabine and dolutegravir* (TDF/FTC and DTG; Truvada and Tivicay)</td>
<td>Should not be initiated during the first trimester (&lt;14 weeks), gestational age measured by last menstrual period.</td>
<td>A1</td>
</tr>
<tr>
<td></td>
<td>TDF/FTC should not be used in patients with creatinine clearance (CrCl) &lt;50 mL/min; re-evaluate after baseline laboratory testing results are available.</td>
<td></td>
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<tr>
<td></td>
<td>Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food.</td>
<td></td>
</tr>
</tbody>
</table>
Table 2: Preferred Regimens for Rapid ART Initiation in Pregnant Adults

See also: DHHS: Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infections and Interventions to Reduce Perinatal HIV Transmission in the United States.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Comments</th>
<th>Rating</th>
</tr>
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</table>
| Tenofovir disoproxil fumarate/ emtricitabine and atazanavir and ritonavir (TDF/FTC and ATV and RTV; Truvada and Reyataz and Norvir) | - TDF/FTC should not be used in patients with CrCl <50 mL/min; re-evaluate after baseline laboratory testing results are available.  
- Carefully consider drug-drug interactions with RTV.  
- Scleral icterus from benign hyperbilirubinemia due to ATV may be a patient concern.  
- The recommended dose of ATV is 300 mg once daily in the first trimester; the dose increases to 400 mg once daily in the second and third trimesters when used with either TDF or a histamine-2 receptor antagonist.  
- This regimen can be initiated in the first trimester. | A2 |
| Tenofovir disoproxil fumarate/ emtricitabine and darunavir and ritonavir (TDF/FTC and DRV/RTV; Truvada and Prezista and Norvir) | - Twice-daily DRV/RTV dosing (DRV 600 mg plus RTV 100 mg with food) is recommended in pregnancy.  
- TDF/FTC should not be used in patients with CrCl <50 mL/min; re-evaluate after baseline laboratory testing results are available.  
- Twice-daily DRV/RTV dosing (DRV 600 mg plus RTV 100 mg with food) is recommended in pregnancy.  
- Regimen can be initiated in the first trimester. | A2 |
| Tenofovir disoproxil fumarate/ emtricitabine and raltegravir (TDF/FTC and RAL; Truvada and Isentress) | - RAL 400 mg twice daily is recommended in pregnancy, not once-daily RAL HD.  
- TDF/FTC should not be used in patients with CrCl <50 mL/min; re-evaluate after baseline laboratory testing results are available.  
- Administer as TDF/FTC once daily and RAL 400 mg twice daily.  
- The recommended dose of RAL is 400 mg twice daily without regard to food.  
- This regimen can be initiated in the first trimester. | A2 |

*See Appendix: Use of Dolutegravir in Individuals of Childbearing Capacity.

Rapid ART Initiation Follow-Up

Standard good practice is to follow up by telephone or in-person within 48 hours after a person initiates ART, to assess for adverse effects, answer questions, and encourage adherence. If feasible, based on clinic protocol and individual patient needs, an in-person follow-up visit with a medical care provider is encouraged within 7 days of ART initiation. If an in-person visit is not feasible, then follow-up by telephone is encouraged.

Once laboratory test results are available, ART should be discontinued if an HIV diagnosis is not confirmed. In this case, the patient may be assessed or referred for PrEP if there is ongoing risk of HIV exposure (see the NYSDOH AI guideline PrEP to Prevent HIV and Promote Sexual Health > Candidates for PrEP). If the HIV diagnosis is confirmed, the ART regimen may be adjusted if necessary (e.g., if there is significant renal disease). Further adjustments may be required if major resistance mutations are found that will compromise the effectiveness of the initial regimen. Arrangements should be made for a viral load test 4 weeks after ART initiation to assess adherence and troubleshoot any problems with maintaining treatment. See the NYSDOH AI guideline Virologic and Immunologic Monitoring for more information.

Paying for Rapid ART Initiation

Lack of insurance coverage for antiretroviral therapy (ART), a high co-pay, or large out-of-pocket costs may pose a significant barrier to rapid ART initiation for some patients. Addressing financial requirements for ART initiation and helping patients identify sources of payment assistance is an essential component of the rapid ART initiation protocol. Options for residents of New York State (NYS), regardless of immigration status, are described below.

For patients who are underinsured or uninsured: The NYS Department of Health Uninsured Care Programs (UCP) provide access to free medications, outpatient primary care, home care, and insurance premium payments for NYS residents who are uninsured or underinsured. Acknowledging the critical need for rapid access to ART, UCP has revised the enrollment process to facilitate same-day enrollment.
NYS residents who do have health insurance but need help with out-of-pocket costs (co-pays, deductibles, etc.) and meet eligibility criteria may be eligible for help from the UCP.

Information for contacting the new enrollment unit is listed below.

### → RESOURCE: NYSDOH UNINSURED CARE PROGRAMS

- **Hours of Operation:** Monday – Friday, 8:00 AM – 5:00 PM
- **Telephone:**
  - In state, toll free: 1-800-542-2437 or 1-844-682-4058
  - Out of state: 1-518-459-1641
  - TDD: 1-518-459-0121
- **Address:** Empire Station, P.O. Box 2052, Albany, NY 12220-0052

A care provider must be enrolled as an ADAP Plus provider on the day that services are provided to receive reimbursement. New York State Medicaid Program providers are eligible to enroll in the UCP. To become an enrolled provider, contact the UCP Provider Relations Department at 1-518-459-1641 or email damarys.feliciano@health.ny.gov. Eligible providers will be activated on the date the application is received.

**For patients with existing health insurance:** People who have insurance coverage may be eligible for medication and copay assistance to cover the cost of out-of-pocket expenses.

- For dolutegravir: [https://www.myviivcard.com/](https://www.myviivcard.com/).
- For emtricitabine, tenofovir disoproxil fumarate, and bictegravir: [https://www.gileadadvancingaccess.com/get-started-advancing-access](https://www.gileadadvancingaccess.com/get-started-advancing-access).
- For darunavir/cobicistat/emtricitabine/tenofovir alafenamide: [https://www.janssencarepath.com/patient/symtuza/cost-support](https://www.janssencarepath.com/patient/symtuza/cost-support).

### Special Considerations

**✓ RECOMMENDATIONS: Special Considerations**

#### Long-Term Nonprogressors and Elite Controllers

- Decisions to initiate ART in long-term nonprogressors (A2) and elite controllers (A3) should be individualized.
- Clinicians should consult with a provider experienced in the management of ART when considering whether to initiate ART in long-term nonprogressors and elite controllers. (A3)

#### Patients With Acute Opportunistic Infections

- Clinicians should recommend that patients beginning treatment for acute opportunistic infections (OIs) initiate ART within 2 weeks of OI diagnosis (see next recommendation for exceptions). (A1)
- Clinicians should not immediately initiate ART in patients with tuberculous (TB) meningitis or cryptococcal meningitis. (A1)
- Consultation with a clinician with experience in management of ART in the setting of acute OIs is recommended. (A3)
- For all other manifestations of TB, clinicians should initiate ART in patients with HIV as follows:
  - For patients with CD4 counts ≥50 cells/mm³: as soon as they are tolerating anti-TB therapy and no later than 8 to 12 weeks after initiating anti-TB therapy. (A1)
  - For patients with CD4 counts <50 cells/mm³: within 2 weeks of initiating anti-TB therapy. (A1)
RECOMMENDATIONS: Special Considerations

Notes:

a. For recommendations on initiating ART in pregnant women with HIV, refer to the DHHS Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States.

b. Initial ART regimens for patients with chronic hepatitis B must include NRTIs that are active against hepatitis B. See the NYSDOH AI guideline HBV-HIV Coinfection.

c. In co-infected patients with HCV, attention should be paid to interactions between the planned ART and HCV therapy.

Long-Term Nonprogressors and Elite Controllers

- **Long-term nonprogressors** demonstrate a lack of disease progression, marked by no symptoms and low viral loads in the absence of therapy during long-term follow-up. Most published studies of long-term nonprogressors include 7-10 years of follow-up [Casado, et al. 2010].

- **Elite controllers** suppress HIV to low but detectable levels (<50-75 copies/mL) for many years [Okulicz, et al. 2010].

The role of early ART initiation in long-term nonprogressors or elite controllers is unclear. At this time, there are not enough data to recommend for or against initiation of ART in long-term nonprogressors and elite controllers. Close monitoring of CD4 count and viral load level may be an acceptable approach. Declines in CD4 count should prompt consideration of initiation of ART. Elite controllers have demonstrated CD4 cell increases after initiation of ART [Okulicz, et al. 2010]. Another study found higher rates of hospitalizations in elite controllers compared to treatment suppressed patients, particularly for cardiovascular and psychiatric conditions [Crowell, et al. 2015]; however, there were important limitations in this analysis and it does not provide definitive evidence in favor of treating this rare population based on current information [Karris and Haubrich 2015]. The clinician and patient should discuss the current data on the risks and benefits of early ART as well as individual factors that may affect the decision to initiate, such as patient readiness and reluctance, adherence barriers, CD4 cell count and viral load, comorbidities, age, and partner serodiscordance. If treatment is delayed, clinicians should counsel patients about the risk of HIV transmission to partners.

Barriers to Adherence

Although the current first-line regimens used for ART are much easier to tolerate with fewer side effects than earlier combinations, they are not free of side effects (see the NYSDOH AI guideline Selecting an Initial ART Regimen > Available ART Regimens). Their use requires a lifelong commitment from the patient. Patients who prefer not to take medication, or who do not understand the significance of skipping doses, are at high risk for poor adherence and subsequent viral resistance. In patients with barriers to adherence, the risk of viral resistance and eventual treatment failure may outweigh any clinical benefit from earlier treatment [Politch, et al. 2012]. These patients should remain under particularly close observation for clinical and laboratory signs of disease progression [Wallis, et al. 2012]. ART should be initiated as soon as the patient seems prepared to adhere to a treatment regimen. When initiation of treatment is clinically urgent, such as for patients who are pregnant, have HIV-related malignancies, HIV-associated nephropathy, symptomatic HIV, older age, severe thrombocytopenia from HIV, chronic hepatitis, or advanced AIDS, it is appropriate to initiate ART even if some barriers to adherence are present. In these cases, referrals to specialized adherence programs should be made for intensified adherence support.

Barriers such as alcohol or drug use; lack of insurance, transportation, or housing; depression; mistrust of medical providers; or a poor social support system should not necessarily preclude rapid initiation of ART. The option of rapid initiation of ART should be offered to all individuals with HIV, except when medically contraindicated. Barriers to care can be addressed with appropriate counseling and support services. In some cases, patients will require ongoing attention and use of supportive services.

Patients With Acute Opportunistic Infections

In a randomized study, patients who initiated ART at a median of 12 days from the start of OI therapy had better outcomes, as measured by disease progression and death, without an increase in adverse events, compared to those who
initiated ART at a median of 45 days from presentation [Zolopa, et al. 2009]. Although this study excluded patients with active TB, three randomized controlled trials in patients newly diagnosed with HIV and pulmonary TB have demonstrated a significant mortality benefit when ART was initiated during the first 2 months of starting anti-TB therapy and a further benefit when those who were severely immunocompromised initiated therapy in the first 2 weeks [Abdool Karim, et al. 2011; Blanc, et al. 2011; Havlir, et al. 2011]. Although antiretroviral agents and anti-TB medications can have overlapping toxicities, ART should be initiated within the first 8 to 12 weeks of starting anti-TB therapy. Patients with CD4 counts <50 cells/mm³ should receive ART within the first 2 weeks of initiating anti-TB therapy.

Tuberculous meningitis and cryptococcal meningitis are exceptions; there are data showing that early initiation of ART increases adverse events and mortality in this setting [Lawn, et al. 2011; Torok, et al. 2011; NIAID 2012; Bisson, et al. 2013; Boulware, et al. 2014]. Close attention should be paid to possible drug-drug interactions between OI therapy and ART. In some cases, determining the optimal timing for initiating ART in patients with OIs can be complex and may require consultation with a clinician with experience in management of ART in this context.

After initiating ART, clinicians need to be alert to the possibility of immune reconstitution syndromes as CD4 cell counts are restored (see the NYSDOH AI guideline Management of IRIS).

References


All Recommendations

### All RECOMMENDATIONS: When to Initiate Antiretroviral Therapy, With Protocol for Rapid Initiation

#### Benefits and Risks of ART
- Clinicians should recommend antiretroviral therapy to all patients with HIV infection. (A1)

#### Rationale for Rapid ART Initiation
- Clinicians should recommend antiretroviral therapy (ART) for all patients with a diagnosis of HIV infection. (A1)
- Clinicians should offer rapid initiation of ART—preferably on the same day (A1) or within 72 hours—to all individuals who are candidates for rapid ART initiation (see text) and who have:
  - A confirmed HIV diagnosis (A1), or
  - A reactive HIV screening result pending results of a confirmatory HIV test (A2), or
  - Suspected acute HIV infection, i.e., HIV antibody negative and HIV RNA positive (A2).
- Clinicians should counsel patients with seronegative partners about the reduction of HIV transmission risk after effective ART is initiated and viral suppression is achieved, and should strongly recommend ART for patients with seronegative partners. (A1)
- Clinicians should evaluate and prepare patients for ART initiation as soon as possible; completion of the following should not delay initiation:
  - Discuss benefits and risks of ART with the patient. (A3)
  - Assess patient readiness. (A3)
  - Identify and ameliorate factors that might interfere with successful adherence to treatment, including inadequate access to medication, inadequate supportive services, psychosocial factors, active substance use, or mental health disorders. (A2)
- Clinicians should refer patients for supportive services as necessary to address modifiable barriers to adherence. An ongoing plan for coordination of care should be established. (A3)
- Clinicians should involve patients in the decision-making process regarding initiation of ART and which regimen is most likely to result in adherence. The patient should make the final decision of whether and when to initiate ART. (A3)
- If the patient understands the benefits of rapid initiation but declines ART, then initiation should be revisited as soon as possible.
- In patients with advanced HIV (or AIDS), ART should be initiated even if barriers to adherence are present. In these cases, referrals to specialized adherence programs should be made for intensified adherence support. (A2)
- After ART has been initiated, response to therapy should be monitored by, or in consultation with, a clinician with experience in managing ART. (A2)

#### Counseling and Patient Education
- Counseling and education should include the following:
  - Basic education about HIV, CD4 cells, viral load, and resistance. (A3)
  - Available treatment options and potential risks and benefits of therapy (see text). (A3)
  - The need for strict adherence to avoid the development of viral drug resistance. (A2)
  - Use of safer-sex practices and avoidance of needle-sharing activity, regardless of viral load, to prevent HIV transmission or superinfection. (A3)
- Clinicians should involve the patient in the decision-making process regarding initiation of ART. (A3)

#### Protocol for Rapid ART Initiation
- To determine whether a patient is a candidate for rapid antiretroviral therapy (ART) initiation, the clinician should confirm that the individual has any of the following (A1):
- A reactive point-of-care HIV test result, or confirmed HIV diagnosis, or suspected acute HIV infection, or known HIV infection, and
- No prior ART (i.e., treatment naive) or limited prior use of antiretroviral medications, and
- No medical conditions or opportunistic infections that require deferral of rapid ART initiation, including suspected cryptococcal or tuberculous meningitis.

- Clinicians should perform baseline laboratory testing listed in Box 2: Baseline Laboratory Testing Checklist for all patients who are initiating ART immediately; ART can be started while awaiting laboratory test results. (A3)

General Principles in Choosing a Regimen for Rapid ART Initiation

- Clinicians should involve their patients when deciding which antiretroviral therapy (ART) regimen is most likely to result in adherence. (A3)
- Before initiating ART, clinicians should:
  - Assess the patient’s prior use of antiretroviral medications, including pre-exposure prophylaxis (PrEP), which may increase the risk for baseline resistance. (A2)
  - Assess for any comorbidities and chronic coadministered medications that may affect the choice of regimen for initial ART. (A2)
  - At the time of HIV diagnosis, obtain genotypic resistance testing for the protease (A2), reverse transcriptase (A2), and integrase (B2) genes.
  - Ask individuals of childbearing potential about the possibility of pregnancy, their reproductive plans, and their use of contraception. (A3)

- For ART-naive patients, clinicians should select an initial ART regimen that is preferred; see Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults. (A1)

- Clinicians should reinforce medication adherence regularly. (A3)

- Clinicians should obtain a viral load test 4 weeks after ART initiation to assess the response to therapy. (A3)
  ○ See the NYSDOH AI guideline Virologic and Immunologic Monitoring for more information.

Long-Term Nonprogressors and Elite Controllers

- Decisions to initiate ART in long-term nonprogressors (A2) and elite controllers (A3) should be individualized.
- Clinicians should consult with a provider experienced in the management of ART when considering whether to initiate ART in long-term nonprogressors and elite controllers. (A3)

Patients With Acute Opportunistic Infections

- Clinicians should recommend that patients beginning treatment for acute opportunistic infections (OIs) initiate ART within 2 weeks of OI diagnosis (see next recommendation for exceptions). (A1)
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a. For recommendations on initiating ART in pregnant women with HIV, refer to the DHHS Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States.

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c. In co-infected patients with HCV, attention should be paid to interactions between the planned ART and HCV therapy.
All Good Practices

☑️ All GOOD PRACTICES: When to Initiate Antiretroviral Therapy, With Protocol for Rapid Initiation

Protocol for Rapid ART Initiation

- For patients with a reactive HIV antibody screening test that is pending confirmation, make sure the patient understands the benefits of rapid ART initiation and the following:
  5. Reactive screening test results are not formally diagnostic, because false-positive results are still possible;
  6. A confirmatory (diagnostic) HIV test will be performed;
  7. ART will be discontinued if the confirmatory test result is negative and continued if it is positive;
  8. The benefit of starting ART early, after a presumptive positive screening test, outweighs the negligible risk of taking ART for a few days and then stopping it if confirmed HIV negative.

- Provide the result of the confirmatory HIV test as soon as it is available; discontinue ART if the result is negative and reinforce adherence and next steps if it is positive.

- If a patient declines rapid ART initiation, discuss options for deferred initiation of ART, link the patient with HIV primary care, and outline next steps.

General Principles in Choosing a Regimen for Rapid ART Initiation

- Follow up within 24 to 48 hours, by telephone or another preferred method, with a patient who has initiated ART to assess medication tolerance and adherence.

- If feasible, schedule an in-person visit for 7 days after ART initiation.
Appendix: Use of Dolutegravir in Individuals of Childbearing Capacity

Lead author Geoffrey A. Weinberg, MD, with the Medical Care Criteria Committee, May 2021

Evidence from multiple studies indicates no difference in rates of total birth defects among infants exposed to antiretroviral (ARV) medications during the first trimester compared with infants exposed later in pregnancy. ARVs are generally considered safe and may be taken by pregnant patients with HIV without increasing the risk of infant birth defects. The MCCC is providing the following updated information for medical care providers concerning preliminary reports that previously had linked dolutegravir (DTG) to neural tube defects (NTDs) in infants exposed to dolutegravir during the periconception period [Zash, et al. 2018; Zash, et al. 2019; Reefhuis, et al. 2020].

Potentially increased NTDs and DTG: NTDs are birth defects, including meningomyelocele and spina bifida, thought to occur early after conception during development of the embryonic neural tube. The neural tube closes by approximately 8 weeks gestational age, which is 8 weeks after the last menstrual period or approximately 6 weeks post-conception. Ingestion of folic acid or folate by a pregnant individual significantly lowers the rate of NTDs; all individuals in the United States who are pregnant or trying to conceive and engaged in prenatal care are routinely administered 400 µg of folic acid daily. The background rate of NTDs in the general population in the United States and other countries that routinely fortify food with folate or folic acid is low: approximately 0.07% of all births (7/10,000 births) [Reefhuis, et al. 2020].

In 2018, an unplanned interim analysis of a large observational clinical trial conducted in Botswana, a country where food is not routinely fortified with folate or folic acid, was performed. The researchers found NTDs in 0.94% of 426 infants exposed at conception to maternal DTG-based antiretroviral therapy (ART) compared with 0.12% of 11,300 infants exposed to non–DTG-based ART. Importantly, however, as more data were collected, the rates of infant NTDs markedly declined [Zash, et al. 2018; Zash, et al. 2019; Antiretroviral Pregnancy Registry Steering Committee 2020; Zash 2020; DHHS 2021]. The latest available data, through April 2020, now show that the rate of infant NTDs with maternal DTG-based ART use at conception is not any greater than it is in infants exposed to non–DTG-based ART at conception: 0.19% [Antiretroviral Pregnancy Registry Steering Committee 2020; Zash 2020; DHHS 2021]. No increases have been found in the registry data or through pharmacovigilance database studies from Europe and the United States [Vannappagari and Thorne 2019; van De Ven, et al. 2020]. Nor have any differences been found in the rates of NTDs among infants in a randomized controlled open-label phase 3 trial of DTG-based versus EFV-based ART in pregnant individuals, though the median gestational age at enrollment in this trial was 22 weeks, and all enrollees were at 14 weeks or more gestational age at enrollment [Lockman, et al. 2021].

Benefits of DTG: There are many known benefits of DTG as a component of ART for all adults, pregnant or not, and many children. DTG is potent, rapidly reduces viral load, has a high barrier to HIV genetic resistance, and is generally well-tolerated. Moreover, folate deficiency is uncommon in countries such as the United States. Thus, both the U.S. Department of Health and Human Services and the World Health Organization consider DTG a preferred ARV drug for individuals with HIV in all trimesters of pregnancy, and those with HIV who are trying to conceive. If an alternative ART regimen that does not include DTG is the best choice, alternatives to DTG during pregnancy include raltegravir, ritonavir-boosted atazanavir, or ritonavir-boosted darunavir (see the NYSDOH AI guideline Selecting an Initial ART Regimen > Specific Factors to Consider and Discuss With Patients). No data currently exist to support the use of bictegravir during pregnancy or the period surrounding conception. Further, cobicistat-boosted regimens containing elvitegravir, darunavir, or atazanavir are not recommended due to reduced levels of the integrase inhibitors given with cobicistat during pregnancy.

References


Lockman S, Brummel SS, Ziemba L, et al. Efficacy and safety of dolutegravir with emtricitabine and tenofovir alafenamide fumarate or tenofovir disoproxil fumarate, and efavirenz, emtricitabine, and tenofovir disoproxil fumarate HIV antiretroviral therapy regimens started in pregnancy (IMPAACT 2010/VESTED): a multicentre, open-label, randomised,


