Rapid ART Initiation

Updates, Authorship, and Related Resources

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Intended users	Clinicians in New York State who provide medical care to adults who are diagnosed with HIV infection
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Contents

→ A NEW HIV DIAGNOSIS IS A CALL TO ACTION

- In support of the October 30, 2019, New York State Department of Health (NYSDOH) and New York City (NYC) Health confirmation of rapid antiretroviral therapy (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 (AI) January 2018 call to action for patients newly diagnosed with HIV, this committee stresses the following:
  - Immediate linkage to care is essential for any individual diagnosed with HIV.
  - ART dramatically reduces HIV-related morbidity and mortality in individuals with HIV.
  - Viral suppression helps 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 old, 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 NYSDOH AI for primary care providers and other practitioners to encourage initiation of ART at the time of HIV diagnosis in ART-naive adults, and ideally, on the same day or within 72 hours, in an approach referred to as rapid ART initiation. The NYSDOH AI January 2018 call to action emphasizes 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, is diagnosed with HIV, or at the first clinic visit is the recommended standard of care for HIV treatment in New York State. To support the standard of ART initiation upon diagnosis, 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 ART 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 New York State Ending the Epidemic initiative.
- Provides guidance on funding sources for sustainable access to ART.

Note on "experienced" HIV care providers: The NYSDOH AI Clinical Guidelines Program defines an "experienced HIV care provider" as a practitioner who has been accorded HIV Specialist status by the American Academy of HIV Medicine. Nurse practitioners (NPs) and licensed midwives who provide clinical care to individuals with HIV in collaboration with a physician may be considered experienced HIV care providers if all other practice agreements are met; NPs with more than 3,600 hours of qualifying experience do not require collaboration with a physician (8 NYCRR 79-5:1; 10 NYCRR 85.36; 8 NYCRR 139-6900). Physician assistants who provide clinical care to individuals with HIV under the supervision of an HIV Specialist physician may also be considered experienced HIV care providers (10 NYCRR 94.2).

Benefits and Risks of ART

☑ RECOMMENDATION

Benefits and Risks of ART

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

ART is the use of pharmacologic agents that have specific inhibitory effects on HIV replication. These agents belong to distinct classes of drugs with different mechanisms of action. See all commercially available antiretroviral (ARV) medications that are approved by the U.S. Food and Drug Administration for the treatment of HIV/AIDS.

Benefits of ART

ART has led to dramatic reductions in HIV-associated morbidity and mortality [CDC(a) 2022]. In resource-rich settings, life expectancy of patients with HIV infection with access to early ART is approaching that of the general population [Xia, et al. 2022; 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 [Lundgren, et al. 2015; Severe, et al. 2010]. Thus, ART should be recommended to all individuals with HIV infection.

With proper selection of 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. Virologic suppression almost invariably leads to immunologic recovery, followed by reductions in the incidence of opportunistic infections and malignancies.

The measurable goals of treatment include:

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

ART also reduces morbidity and mortality from causes not related to HIV. In a randomized study comparing continuous ART with CD4-guided treatment interruption, a mortality benefit was observed in participants 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].

Reduced HIV transmission: ART for people with HIV 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, avoidance of needle-sharing, and HIV pre- and post-exposure prophylaxis (PrEP and PEP). Antiretroviral treatment as prevention is associated with greater reductions in HIV transmission than any preventative modality studied to date. In HPTN 052, a large randomized clinical trial of HIV-serodifferent couples, early treatment of the partner with HIV 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 found to occur only when the index partner was viremic [Cohen, et al. 2016]. In observational studies, including the Opposites Attract, PARTNER, and PARTNER2 studies, no phylogenetically linked HIV transmission was observed in serodifferent couples in which the index partner was virologically suppressed on ART [Rodger, et al. 2019; Bavinton, et al. 2018; Rodger, et al. 2016]. The evidence thus suggests that the risk of sexual transmission of HIV during virologic 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 HIV PrEP for partners who do not have HIV infection, will help reduce the incidence of other sexually transmitted infections and viral hepatitis and should be integrated into patient counseling at ART initiation.

Reduced perinatal HIV transmission: Studies have shown that the administration of ART during pregnancy or intrapartum significantly reduces the risk of perinatal HIV transmission [Cohen, et al. 2011; Guay, et al. 1999; Connor, et al. 1994], adding to the body of evidence that lower viral load reduces transmission risk.

Reduced complications: Accumulating evidence suggests that early initiation of ART or reduced cumulative time with detectable plasma viremia is associated with reductions in the likelihood of certain complications, such as cardiovascular disease, neurocognitive dysfunction, severe bacterial infections, and some non-HIV-related malignancies, and delayed initiation of ART is associated with long-term disparities in clinical outcomes [Lundgren, et al. 2023; O'Connor, et al. 2017; Ho, et al. 2012; Sigel, et al. 2012; Winston, et al. 2012; Ellis, et al. 2011; Garvey, et al. 2011; Silverberg, et al. 2011; Ho, et al. 2010; Lichtenstein, et al. 2010; Bruyand, et al. 2009; Guiguet, et al. 2009; Marin, et al. 2009; Tozzi, et al. 2007; El-Sadr, et al. 2006]. Cohort data also demonstrate that although older patients are more likely than younger patients to achieve virologic suppression, they are less likely to achieve an immunologic response, as measured by an increase of CD4 count by 100 cells/mm^3, and that patients ≥55 years old may be at higher clinical risk even after starting ART [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 old with CD4 counts of 351 to 500 cells/mm^3 who initiated ART were able to achieve similar immunologic responses as younger men who initiated at lower CD4 cell counts [Li, et al. 2011].

Risks of ART

Despite the excellent tolerability of contemporary ART regimens, adverse effects, long-term drug toxicities, and drug-drug interactions continue to pose some relative or limited risk, which necessitates patient counseling 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, and possible long-term toxicities—primarily a low relative risk of renal and cardiovascular disorders or decreased bone density of uncertain clinical significance [Hoy, et al. 2017; Monteiro, et al. 2014; Friis-Moller, et al. 2010]. Excess weight gain has been observed in patients receiving regimens containing integrase strand transfer inhibitors (e.g., dolutegravir and bictegravir) and/or tenofovir alafenamide but the clinical significance is unknown, and investigation is needed [Palella, et al. 2023; Verburgh, et al. 2022; Bourgi(a), et al. 2020; Bourgi(b), et al. 2020]. Renal and bone density issues are largely eliminated with newer formulations of ARV medications. Fatal drug reactions from ART are exceedingly rare.

Many ARV combinations are now available in single-pill, fixed-dose combination formulations. Thus, the pill burden associated with early ART 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.

Compared with early ARV combinations, current preferred ART regimens 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 to 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 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 ARV 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. The risk of IRIS increases when ART is begun at low CD4 cell counts (<100 cells/mm^3) or with the presence of specific opportunistic infections [Manabe, et al. 2007]. 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 low CD4 cell 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 cell counts. Together with the dramatic reduction in HIV transmission risk with effective treatment, these data support initiating ART regardless of CD4 cell count, including in patients diagnosed with acute HIV infection. Patients in care who are documented *long-term nonprogressors* or *elite controllers* are a group that may warrant special consideration (see guideline section Special Considerations).

In START, a randomized clinical trial that compared initiating ART in treatment-naive patients with CD4 counts >500 cells/mm^3 versus waiting for a decrease to ≤350 cells/mm^3 before initiation, there was 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 cell 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/mm^3 compared with those who deferred therapy until CD4 count was <500 cells/mm^3, as well as in the cohort who initiated ART in the 350 to 500 cells/mm^3 range compared with those who deferred until CD4 count was <350 cells/mm^3 [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 cell counts, they did confirm the benefits of initiating ART at CD4 counts ≤500 cells/mm^3 [Young, et al. 2012; Cain, et al. 2011; CASCADE Collaboration 2011]. Another study 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/mm^3 increase in CD4 count [Marin, et al. 2009]. A randomized study of early versus deferred therapy in patients with CD4 counts of 350 to 550 cells/mm^3 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*
  - Acute HIV infection, i.e., are HIV antibody negative and HIV RNA positive (A2)
- Clinicians should counsel patients with HIV-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 HIV-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, the clinician should revisit the topic of initiation as soon as possible. (A*)
- Clinicians should initiate ART in patients with advanced HIV (or AIDS) 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, the clinician should monitor the patient's response to therapy or consult with an experienced HIV care provider. (A2)

The NYSDOH AI 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) [Lundgren, et al. 2015; Zolopa, et al. 2009] 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 [Massanella, et al. 2021; Jain, et al. 2013]; evidence also shows 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].

→ KEY POINTS

- Rapid ART initiation, the standard of care in New York State, is efficacious, safe, and highly acceptable, with few patients declining the offer of immediate ART.
- Patients with active substance use, untreated mental health conditions, immigration issues, or unstable housing deserve the highest standard of HIV care, including the option of rapid ART initiation. Potential barriers to medication adherence and care continuity can be addressed with appropriate counseling and linkage to support services.

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 2020, 82.4% of individuals diagnosed with HIV in the United States were linked to HIV medical care within 1 month of diagnosis [CDC(b) 2022]. Although not optimal, this reflects an increase since from 75.9% in 2016 [CDC(b) 2022], before the first reports of rapid ART initiation. Individuals with HIV who are not linked to care are at risk of having sustained viral loads and ongoing HIV transmission.

Rapid ART initiation 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 2021] 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

Shorter time to viral suppression: 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 [Mateo-Urdiales, et al. 2019; Mohammed, et al. 2019; Colasanti, et al. 2018; Koenig, et al. 2017; Rosen(b), et al. 2016]. 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]. After rollout of a city-wide rapid ART initiation program for people diagnosed with HIV in San Francisco, median time from first care visit to ART initiation decreased from 28 days to 1 day (by 96%) and median time from diagnosis to viral suppression decreased from 145 days to 76 days (by 46%) from 2013 to 2017 [Bacon, et al. 2021].

Increased retention in care: Rapid ART initiation leads to improved retention in care [Koenig, et al. 2017; Amanyire, et al. 2016; Rosen(b), et al. 2016]. In the RapIT trial in South Africa, patients newly diagnosed with HIV were randomized to rapid ART initiation or standard of care [Rosen(a), et al. 2016]. 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, the United States, and South Africa support the cost-effectiveness of rapid ART initiation [Benson, et al. 2020; Ford, et al. 2018; Wu, et al. 2015; Zulliger, et al. 2014]. Rapid ART initiation is efficacious, safe, and highly acceptable, with few patients declining the offer of immediate ART [Coffey, et al. 2019; Pilcher, et al. 2017].

Reduced HIV transmission: Modeling evidence suggests that rapid ART initiation may 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 74.1% of individuals with HIV receiving any HIV care and 50.6% being retained in care during 2020 [CDC(b) 2022]. 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 [Li, et al. 2019; Skarbinski, et al. 2015]. 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

Preexisting resistance to currently recommended regimens for rapid initiation is rare. In the San Francisco study discussed previously [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. Obtaining and following up on baseline laboratory testing is important, because some medical conditions, such as renal insufficiency, may require a change to a patient's ART regimen.

Of 149 patients initiating ART through a program in New York City, only 1 required a regimen change because of subsequently detected resistance [Pathela, et al. 2021].

Rapid ART initiation is safe. Most designated regimens for rapid ART initiation are the same regimens that are recommended for 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 2021].

◊ RESOURCES

To identify or consult with an experienced HIV care provider in New York State, see the following:

- NYSDOH AI Provider Directory
- Clinical Education Initiative (CEI) Line: 1-866-637-2342
- American Academy of HIV Medicine
- HIV Medicine Association

Counseling and Education Before Initiating ART

☑ RECOMMENDATIONS

Counseling and Education Before Initiating ART

- Clinicians should counsel and educate patients regarding the following:
  - Basic information about HIV, CD4 cell count, viral load, and resistance (A3)
  - Available treatment options and potential risks and benefits of therapy (see text) (A3)
  - Optimal adherence requirements to avoid development of viral drug resistance (A2)
  - Use of safer-sex practices during the first 6 months after ART is started or until the patient's viral load is suppressed, to prevent HIV transmission or superinfection (A3)
- Clinicians should involve the patient in the decision-making process regarding initiation of antiretroviral therapy (ART). (A3)

Discussion of ART should occur when a positive HIV test result is obtained, regardless of CD4 cell 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/mm^3)

- Reduction in HIV-related and non-HIV-related morbidity and mortality [Lundgren, et al. 2015; Ho, et al. 2012; Lewden, et al. 2012; Silverberg, et al. 2011; Ray, et al. 2010; Kitahata, et al. 2009; Marin, et al. 2009; Sterne, et al. 2009; Phillips, et al. 2007]
- 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 [Cohen, et al. 2011; Donnell, et al. 2010; Castilla, et al. 2005; Quinn, et al. 2000]. HIV is not transmitted *sexually* when the plasma viral load is undetectable; however, because there are insufficient data to support a reduced risk of transmission through shared needles, 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 [Novelli, et al. 2018; Jain, et al. 2013]

Disadvantages of early ART in asymptomatic patients:

- Possibility of greater cumulative adverse effects from ART [Volberding and Deeks 2010]
- Possibility of earlier development of drug resistance and limitation in future [Barth, et al. 2012] antiretroviral options if adherence and viral suppression are suboptimal [Barth, et al. 2012]
- Possibility of earlier onset of treatment fatigue

Protocol for Rapid ART Initiation

☑ RECOMMENDATIONS

Protocol for Rapid ART Initiation

- To determine whether a patient is a candidate for rapid ART initiation, the clinician should confirm that the individual has (A1):
  - A new reactive point-of-care HIV test result, a confirmed HIV diagnosis, suspected acute HIV infection, or known HIV infection, *and*
  - No prior ART (i.e., treatment naive, excluding PrEP and PEP) or limited prior use of antiretroviral medications, *and*
  - No medical conditions or specific opportunistic infections that require deferral of ART initiation, including suspected cryptococcal or TB meningitis and CMV retinitis
- 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)

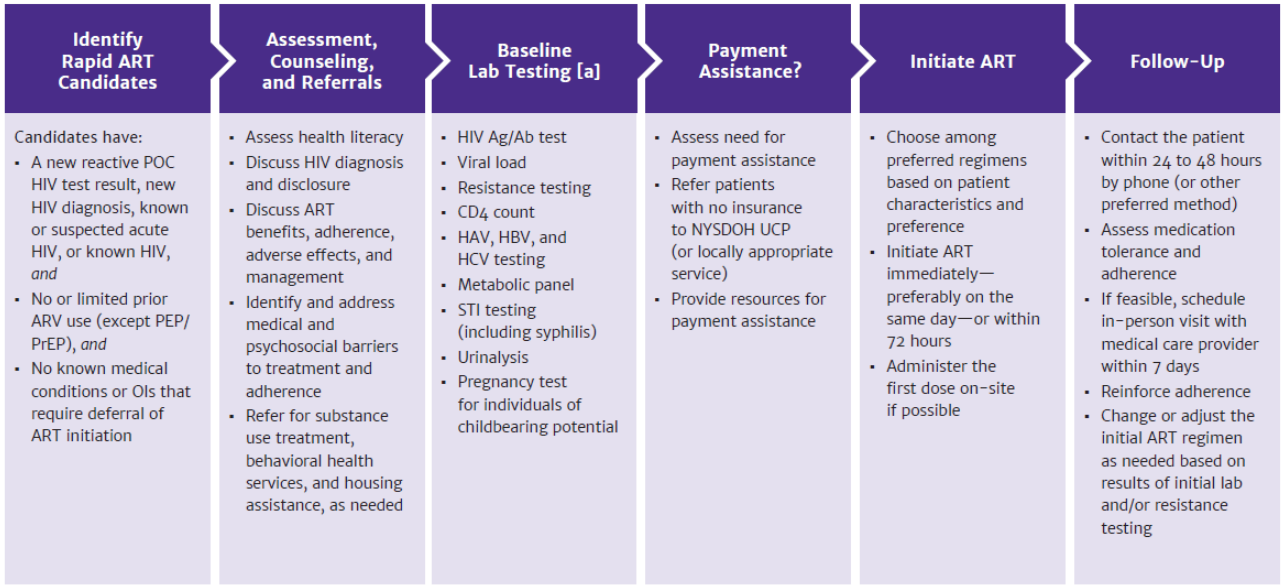
Abbreviations: ART, antiretroviral therapy; CMV, cytomegalovirus; PEP, post-exposure prophylaxis; PrEP, pre-exposure prophylaxis; TB, tuberculous.

→ SELECTED GOOD PRACTICE REMINDERS

Protocol for Rapid ART Initiation

- Ensure that patients with a reactive HIV antibody screening test that is pending confirmation understand the benefits of rapid ART initiation, as well as the following:
  - Reactive screening test results are not formally diagnostic, because false-positive results are still possible.
  - A confirmatory (diagnostic) HIV test will be performed.
  - ART will be discontinued if the confirmatory test result is negative and continued if it is positive.
  - 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 deferral of ART initiation, link the patient with HIV primary care, and outline next steps.

Figure 1: Protocol for Rapid ART Initiation



Abbreviations: Ag/Ab, antigen/antibody; ART, antiretroviral therapy; ARV, antiretroviral medication; HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; NYSDOH UCP, New York State Department of Health Uninsured Care Programs; OI, opportunistic infection; PEP, post-exposure prophylaxis; POC, point-of-care; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection.

Note:

a. ART can be started while awaiting laboratory test results.

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 patient 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 patient 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, a new HIV diagnosis (confirmed using the standard HIV laboratory testing algorithm), suspected acute HIV infection (HIV antibody negative and HIV RNA positive), or known HIV, *and*
- Are treatment naive or have limited prior use of antiretroviral medications (e.g., a patient who stopped first-line therapy for reasons other than regimen failure), excluding PEP or PrEP, as long as concern for acquired drug resistance is low (requires a case-by-case determination), *and*
- Have no medical conditions or opportunistic infections that require deferral of ART initiation, including suspected cryptococcal or TB meningitis or CMV retinitis

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 verify the result. See the NYSDOH AI guideline HIV Testing > Appendix: HIV Immunoassays Available in New York State 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 initiate 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
- Ensuring the patient knows how to reach the care team to address any potential adverse effects of medications or other concerns
- Following through with clinic visits
- Assessing health literacy (see resources below)
- Navigating acquisition of and paying for medications required for lifelong therapy, including pharmacy selection, insurance requirements and restrictions, copays, 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

◊ RESOURCES: HEALTH LITERACY

- National Library of Medicine:
  - An Introduction to Health Literacy
  - Health Literacy Tool Shed
- Agency for Healthcare Research and Quality:
  - Short Assessment of Health Literacy—Spanish and English
  - Rapid Estimate of Adult Literacy in Medicine—Short Form
  - Short Assessment of Health Literacy for Spanish Adults

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 TB meningitis or cryptococcal meningitis are suspected (see below) [WHO 2021], if cytomegalovirus retinitis is suspected, or if the patient has any evidence of advanced HIV disease on clinical exam.

To identify the potential for preexisting drug-resistant virus, the initial assessment (see Box 1, below) should also include the patient's history of PrEP and PEP use and previous ART use for people who are re-engaging in care [Ford, et al. 2018].

Box 1: Medical History Checklist

When taking a medical history before rapid antiretroviral therapy (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 pre- or post-exposure prophylaxis, with dates of use
- Comorbidities, including a history of renal or liver disease, particularly hepatitis B virus infection
- Prescribed and over-the-counter medications
- Drug allergies
- Substance use
- Any signs or symptoms of active cryptococcal or tuberculous meningitis, or visual changes associated with cytomegalovirus retinitis (see discussion of clinical manifestations in DHHS: Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV > Cryptococcosis, Mycobacterium tuberculosis Infection and Disease, and Cytomegalovirus Disease)
- 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 guideline section Special Considerations > Patients With Acute Opportunistic Infections). Patients who present with symptoms suggestive of CMV retinitis should be referred to an ophthalmologist for assessment and treatment. 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).

Cotreatment of HIV and pulmonary TB: It is clear that cotreatment 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 unclear whether 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-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 immunoassay
- HIV quantitative viral load test
- Baseline HIV genotypic resistance profile
- Baseline CD4 cell count
- Testing for hepatitis A, B, and C viruses
- Comprehensive metabolic panel (creatinine clearance, hepatic profile)
- Pregnancy test for individuals of childbearing potential
- Urinalysis
- Syphilis, gonorrhea, and chlamydia screening as per CDC: Sexually Transmitted Infections Treatment Guidelines, 2021 > Screening Recommendations

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 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 as 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)

Abbreviations: ART, antiretroviral therapy; PrEP, pre-exposure prophylaxis.

→ SELECTED GOOD PRACTICE REMINDERS

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.

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 and CD4 cell count. 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 alternative regimen (tenofovir alafenamide/emtricitabine/darunavir/cobicistat [TAF/FTC/DRV/COBI]) has been studied formally for 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 level <50 copies/mL) at 48 weeks [Huhn, et al. 2020].

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. Abacavir (ABC)-containing regimens are not recommended for initial ART, including rapid initiation, because of the association between ABC use and increased cardiovascular disease risk in people with HIV [Fichtenbaum 2024]. Similarly, rilpivirine should be avoided in any patient who has an HIV RNA level (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 adverse effects and of transmitted drug resistance mutations [Kagan, et al. 2019]; therefore, it is not recommended for rapid ART initiation.

The 2-drug ART regimen of dolutegravir/lamivudine (DTG/3TC) should not be used for rapid ART because a baseline HIV genotypic resistance profile and hepatitis B virus status are required before prescription of this regimen. In the STAT study, 131 participants newly diagnosed with HIV initiated ART with DTG/3TC within 14 days of their diagnosis and before availability of baseline laboratory testing results. The ART regimen was modified in 8 participants (6.1%), 5 of whom had HBV infection and 1 who had the M184V mutation at baseline. Although the majority of participants (98%) were virally suppressed at 24 weeks, this was a single-arm study, viral load test results were not available for 20 participants (15%) at 24 weeks, and participants with a baseline viral load ≥500,000 copies/mL were less likely to achieve viral suppression at 24 weeks than those with a baseline viral load <500,000 copies/mL [Rolle, et al. 2021].

Clinics that have implemented rapid ART initiation frequently design preapproved 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 result. In a study in New York City, individuals who had taken oral PrEP in the 3 months before 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 (INSTI) with a high barrier to resistance (e.g., DTG or bictegravir [BIC] or boosted DRV) and 2 nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs). 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.

For individuals who acquire HIV while receiving or after recently discontinuing long-acting injectable cabotegravir (CAB LA) as PrEP, there is a potential risk of selection of CAB and other INSTI resistance. In the HPTN 083 trial, 5 of 16 participants (31%) who acquired HIV in the CAB LA arm were found to have INSTI resistance mutations [Marzinke, et al. 2021]. The HPTN 077 study found detectable plasma CAB concentrations in 13% of men and 42% of women 76 weeks after they had discontinued CAB LA as PrEP, and it was estimated that in some cases the concentration of CAB could persist as long as 2.9 years in men and 4.3 years in women [Landovitz, et al. 2020]. Therefore, even remote use of CAB should be identified before considering rapid ART initiation, to determine the appropriate initial ART regimen, taking into account potential INSTI resistance. For such patients, the initial regimen should consist of a non-INSTI-based regimen (e.g., a boosted protease inhibitor and 2 NRTIs) while awaiting resistance test results.

Preferred and Alternative Regimens for Rapid ART Initiation

Table 1, 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 for Patients Not on PrEP		
Tenofovir alafenamide/emtricitabine/ bictegravir (TAF 25 mg/FTC/BIC; Biktarvy)	• TAF/FTC/BIC is available as a single-tablet formulation, taken once daily. • TAF/FTC should not be used in patients with CrCl <30 mL/min; re-evaluate after baseline laboratory testing results are available. • This regimen 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. • This regimen contains 25 mg of TAF, unboosted. • Administer as 2 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. • Documented DTG resistance after initiation in treatment-naive patients is rare.	A1
Tenofovir alafenamide/emtricitabine/ darunavir/cobicistat (TAF 10 mg/FTC/DRV/COBI; Symtuza)	• TAF/FTC/DRV/COBI is available as a single-tablet formulation, taken once daily. • This regimen 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
Regimen for Patients Who Have Taken TDF/FTC as PrEP Since Their Last Negative HIV Test [a]		
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. • Documented DTG resistance after initiation in treatment-naive patients is rare. • 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. • TDF may be substituted for TAF; TDF/FTC is available as a single tablet (brand name Truvada). • 3TC may be substituted for FTC; 3TC/TDF is available as a single tablet (brand name Cimduo).	A1
Tenofovir alafenamide/emtricitabine/ bictegravir (TAF 25 mg/FTC/BIC; Biktarvy)	• TAF/FTC/BIC is available as a single-tablet formulation, taken once daily. • TAF/FTC should not be used in patients with CrCl <30 mL/min; re-evaluate after baseline laboratory testing results are available. • This regimen 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

Table 1: Preferred and Alternative Regimens for Rapid ART Initiation in Nonpregnant Adults		
Regimen	**Comments**	**Rating**
Tenofovir alafenamide/emtricitabine/ darunavir/cobicistat (TAF 10 mg/FTC/DRV/COBI; Symtuza)	• TAF/FTC/DRV/COBI is available as a single-tablet formulation, taken once daily. • This regimen 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.	B2
Regimen for Patients Who Have Taken CAB LA as PrEP Within the Previous 14 Months		
Tenofovir alafenamide/emtricitabine/ darunavir/cobicistat (TAF 10 mg/FTC/DRV/COBI; Symtuza)	• TAF/FTC/DRV/COBI is available as a single-tablet formulation, taken once daily. • This regimen 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
Medications to Avoid		
• Abacavir (ABC) • Rilpivirine (RPV) • Efavirenz (EFV) • Dolutegravir/lamivudine (DTG/3TC)	• ABC should be avoided unless a patient is confirmed to be HLA-B*5701 negative. ABC-containing regimens are not recommended for initial therapy because of the association between ABC use and increased CVD risk in people with HIV. • RPV should be administered only in patients with a confirmed CD4 count ≥200 cells/mm^3 and an HIV RNA level <100,000 copies/mL. • EFV is not as well tolerated as other ARVs, and NNRTIs have higher rates of resistance than other classes. • DTG/3TC requires baseline resistance testing and is not recommended when HBV status is unknown.	A3
Abbreviations: 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; ARV, antiretroviral medication; BIC, bictegravir; CAB LA, long-acting injectable cabotegravir; COBI, cobicistat; CrCl, creatinine clearance; CVD, cardiovascular disease; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; FTC, emtricitabine; HBV, hepatitis B virus; NNRTI, non-nucleoside reverse transcriptase inhibitor; PrEP, pre-exposure prophylaxis; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate. **Note:** a. The initial ART regimen may be simplified based on results of genotypic resistance testing.		

Rapid ART Initiation During Pregnancy

Reducing the risk of perinatal HIV transmission 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 DHHS: Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States).

Rapid ART Initiation Follow-Up

Standard good practice is to follow up by telephone or in person within 48 hours after a patient 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. 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.

Paying for Rapid ART Initiation

Lack of insurance coverage for ART, a high copay, 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, regardless of immigration status, are described below.

For patients who are underinsured or uninsured: The NYSDOH Uninsured Care Programs (UCP) provide access to free medications, outpatient primary care, home care, and insurance premium payments for New York State 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.

New York State residents who do have health insurance but need help with out-of-pocket costs (copays, deductibles, etc.) and meet eligibility criteria may be eligible for help from the UCP.

Information for contacting the enrollment unit is listed below.

◊ RESOURCE: NYSDOH UNINSURED CARE PROGRAMS

- Uninsured Care Programs Online Portal
- 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
- Address: Empire Station, P.O. Box 2052, Albany, NY 12220-0052

A care provider must be enrolled as an AIDS Drug Assistance Program 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: ViiVConnect Savings Card
- For emtricitabine, tenofovir disoproxil fumarate, and bictegravir: Gilead Advancing Access Program
- For darunavir/cobicistat/emtricitabine/tenofovir alafenamide: Janssen CarePath

Accessing medications through clinical trials: If eligible, patients may also consider treatment options through enrollment in clinical trials (for more information, see NIAID: Clinical Trials).

Special Considerations

☑ RECOMMENDATIONS

Long-Term Nonprogressors and Elite Controllers

- Clinicians should individualize decisions to initiate ART in long-term nonprogressors (A2) and elite controllers (A3).
- Clinicians should consult with an experienced HIV care provider 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 OIs initiate ART within 2 weeks of OI diagnosis (see next recommendation for exceptions). (A1)
- Clinicians should not immediately initiate ART in patients with TB meningitis or cryptococcal meningitis (A1) or cytomegalovirus retinitis. (A3)

☑ RECOMMENDATIONS

- Clinicians should consult with a care provider experienced in managing ART in patients with acute OIs. (A3)
- For patients with all other manifestations of TB, clinicians should initiate ART as follows:
  - For patients with CD4 counts ≥50 cells/mm^3: 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/mm^3: within 2 weeks of initiating anti-TB therapy (A1)

Abbreviations: ART, antiretroviral therapy; TB, tuberculous.

Notes:

a. For recommendations on initiating ART in pregnant women with HIV, refer to DHHS: Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.
b. Initial ART regimens for patients with chronic HBV infection must include nucleoside/nucleotide reverse transcriptase inhibitors that are active against HBV.
c. In patients with HIV/HCV coinfection, attention should be paid to interactions between planned ART and HCV therapy.

Barriers to Adherence

Although the current first-line regimens used for ART are much easier to tolerate with fewer adverse effects than earlier combinations, they are not free of adverse effects. 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 ART initiation 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 effects, than those who initiated ART at a median of 45 days from presentation [Zolopa, et al. 2009]. Although this study excluded patients with active TB, 3 randomized controlled trials in patients newly diagnosed with HIV and pulmonary TB 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/mm^3 should receive ART within the first 2 weeks of initiating anti-TB therapy.

TB meningitis and cryptococcal meningitis are exceptions; data show that early initiation of ART increases adverse effects and mortality in this context [Boulware, et al. 2014; Bisson, et al. 2013; NIAID 2012; Lawn, et al. 2011; Torok, et al. 2011]. 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 who has experience managing ART in this context.

After initiating ART, clinicians need to be alert to the possibility of immune reconstitution inflammatory syndromes as CD4 cell counts are restored.

All Recommendations

☑ ALL RECOMMENDATIONS

Benefits and Risks of ART

- Clinicians should recommend antiretroviral therapy (ART) 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*
  - Acute HIV infection, i.e., are HIV antibody negative and HIV RNA positive (A2)
- Clinicians should counsel patients with HIV-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 HIV-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, the clinician should revisit the topic of initiation as soon as possible. (A*)
- Clinicians should initiate ART in patients with advanced HIV (or AIDS) 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, the clinician should monitor the patient's response to therapy or consult with an experienced HIV care provider. (A2)

Counseling and Education Before Initiating ART

- Clinicians should counsel and educate patients regarding the following:
  - Basic information about HIV, CD4 cell count, viral load, and resistance (A3)
  - Available treatment options and potential risks and benefits of therapy (see text) (A3)
  - Optimal adherence requirements to avoid development of viral drug resistance (A2)
  - Use of safer-sex practices during the first 6 months after ART is started or until the patient's viral load is suppressed, to prevent HIV transmission or superinfection (A3)
- Clinicians should involve the patient in the decision-making process regarding initiation of antiretroviral therapy (ART). (A3)

Protocol for Rapid ART Initiation

- To determine whether a patient is a candidate for rapid ART initiation, the clinician should confirm that the individual has (A1):
  - A new reactive point-of-care HIV test result, a confirmed HIV diagnosis, suspected acute HIV infection, or known HIV infection, *and*
  - No prior ART (i.e., treatment naive, excluding PrEP and PEP) or limited prior use of antiretroviral medications, *and*

☑ ALL RECOMMENDATIONS

  - No medical conditions or specific opportunistic infections that require deferral of ART initiation, including suspected cryptococcal or TB meningitis and CMV retinitis
- 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 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 as 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)

Long-Term Nonprogressors and Elite Controllers

- Clinicians should individualize decisions to initiate ART in long-term nonprogressors (A2) and elite controllers (A3).
- Clinicians should consult with an experienced HIV care provider 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 OIs initiate ART within 2 weeks of OI diagnosis (see next recommendation for exceptions). (A1)
- Clinicians should not immediately initiate ART in patients with TB meningitis or cryptococcal meningitis (A1) or cytomegalovirus retinitis. (A3)
- Clinicians should consult with a care provider experienced in managing ART in patients with acute OIs. (A3)
- For patients with all other manifestations of TB, clinicians should initiate ART as follows:
  - For patients with CD4 counts ≥50 cells/mm^3: 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/mm^3: within 2 weeks of initiating anti-TB therapy (A1)

Abbreviations: ART, antiretroviral therapy; CMV, cytomegalovirus; HBV, hepatitis B virus; HCV, hepatitis C virus; OI, opportunistic infection; PEP, post-exposure prophylaxis; PrEP, pre-exposure prophylaxis; TB, tuberculous.

Notes:

a. For recommendations on initiating ART in pregnant women with HIV, refer to DHHS: Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.
b. Initial ART regimens for patients with chronic HBV infection must include nucleoside/nucleotide reverse transcriptase inhibitors that are active against HBV.
c. In patients with HIV/HCV coinfection, attention should be paid to interactions between planned ART and HCV therapy.

All Good Practices

→ ALL GOOD PRACTICE REMINDERS (Rec Head)

Protocol for Rapid ART Initiation

- Ensure that patients with a reactive HIV antibody screening test that is pending confirmation understand the benefits of rapid ART initiation, as well as the following:
  - Reactive screening test results are not formally diagnostic, because false-positive results are still possible.
  - A confirmatory (diagnostic) HIV test will be performed.
  - ART will be discontinued if the confirmatory test result is negative and continued if it is positive.
  - 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 deferral of ART initiation, 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.

Abbreviation: ART, antiretroviral therapy.

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Supplement: Guideline Development and Recommendation Ratings

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Developer	New York State Department of Health AIDS Institute (NYSDOH AI) Clinical Guidelines Program
Funding source	NYSDOH AI
Program manager	Clinical Guidelines Program, Johns Hopkins University School of Medicine, Division of Infectious Diseases. See Program Leadership and Staff.
Mission	To produce and disseminate evidence-based, state-of-the-art clinical practice guidelines that establish uniform standards of care for practitioners who provide prevention or treatment of HIV, viral hepatitis, other sexually transmitted infections, and substance use disorders for adults throughout New York State in the wide array of settings in which those services are delivered.
Expert committees	The NYSDOH AI Medical Director invites and appoints committees of clinical and public health experts from throughout New York State to ensure that the guidelines are practical, immediately applicable, and meet the needs of care providers and stakeholders in all major regions of New York State, all relevant clinical practice settings, key New York State agencies, and community service organizations.
Committee structure	• Leadership: AI-appointed chair, vice chair(s), chair emeritus, clinical specialist(s), JHU Guidelines Program Director, AI Medical Director, AI Clinical Consultant, AVAC community advisor • Contributing members • Guideline writing groups: Lead author, coauthors if applicable, and all committee leaders
Disclosure and management of conflicts of interest	• Annual disclosure of financial relationships with commercial entities for the 12 months prior and upcoming is required of all individuals who work with the guidelines program, and includes disclosure for partners or spouses and primary professional affiliation. • The NYSDOH AI assesses all reported financial relationships to determine the potential for undue influence on guideline recommendations and, when indicated, denies participation in the program or formulates a plan to manage potential conflicts. Disclosures are listed for each committee member.
Evidence collection and review	• Literature search and review strategy is defined by the guideline lead author based on the defined scope of a new guideline or update. • A comprehensive literature search and review is conducted for a new guideline or an extensive update using PubMed, other pertinent databases of peer-reviewed literature, and relevant conference abstracts to establish the evidence base for guideline recommendations. • A targeted search and review to identify recently published evidence is conducted for guidelines published within the previous 3 years. • Title, abstract, and article reviews are performed by the lead author. The JHU editorial team collates evidence and creates and maintains an evidence table for each guideline.

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Recommendation development	• The lead author drafts recommendations to address the defined scope of the guideline based on available published data. • Writing group members review the draft recommendations and evidence and deliberate to revise, refine, and reach consensus on all recommendations. • When published data are not available, support for a recommendation may be based on the committee's expert opinion. • The writing group assigns a 2-part rating to each recommendation to indicate the strength of the recommendation and quality of the supporting evidence. The group reviews the evidence, deliberates, and may revise recommendations when required to reach consensus.
Review and approval process	• Following writing group approval, draft guidelines are reviewed by all contributors, program liaisons, and a volunteer reviewer from the AI Community Advisory Committee. • Recommendations must be approved by two-thirds of the full committee. If necessary to achieve consensus, the full committee is invited to deliberate, review the evidence, and revise recommendations. • Final approval by the committee chair and the NYSDOH AI Medical Director is required for publication.
External reviews	• External review of each guideline is invited at the developer's discretion. • External reviewers recognized for their experience and expertise review guidelines for accuracy, balance, clarity, and practicality and provide feedback.
Update process	• JHU editorial staff ensure that each guideline is reviewed and determined to be current upon the 3-year anniversary of publication; guidelines that provide clinical recommendations in rapidly changing areas of practice may be reviewed annually. Published literature is surveilled to identify new evidence that may prompt changes to existing recommendations or development of new recommendations. • If changes in the standard of care, newly published studies, new drug approval, new drug-related warning, or a public health emergency indicate the need for immediate change to published guidelines, committee leadership will make recommendations and immediate updates and will invite full committee review as indicated.

Table S2: Recommendation Ratings and Definitions		
Strength	**Quality of Evidence**	
A: Strong B. Moderate C: Optional	1	Based on published results of at least 1 randomized clinical trial with clinical outcomes or validated laboratory endpoints.
	*	Based on either a self-evident conclusion; conclusive, published, in vitro data; or well-established practice that cannot be tested because ethics would preclude a clinical trial.
	2	Based on published results of at least 1 well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.
	2†	Extrapolated from published results of well-designed studies (including nonrandomized clinical trials) conducted in populations other than those specifically addressed by a recommendation. The source(s) of the extrapolated evidence and the rationale for the extrapolation are provided in the guideline text. 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.
	3	Based on committee expert opinion, with rationale provided in the guideline text.