# When to Initiate ART

Medical Care Criteria Committee, June 2016

## TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART Initiation Upon Diagnosis</td>
<td>1</td>
</tr>
<tr>
<td>Benefits and Risks of Antiretroviral Therapy</td>
<td>5</td>
</tr>
<tr>
<td>Risk of Progression to AIDS-Defining Illness</td>
<td>8</td>
</tr>
<tr>
<td>Prognosis According to CD4 Cell Count and Viral Load in the Pre-HAART and HAART Eras</td>
<td>9</td>
</tr>
<tr>
<td>FDA Pregnancy Categories</td>
<td>10</td>
</tr>
<tr>
<td>Counseling and Education Before Initiating ART</td>
<td>11</td>
</tr>
<tr>
<td>Special Considerations</td>
<td>14</td>
</tr>
<tr>
<td>Initiating ART Following Acute Opportunistic Infections</td>
<td>16</td>
</tr>
<tr>
<td>All Recommendations</td>
<td>18</td>
</tr>
</tbody>
</table>
ART Initiation Upon Diagnosis

Medical Care Criteria Committee, June 2016

RECOMMENDATIONS

Recommending and Initiating ART

- Clinicians should recommend ART for all patients with a diagnosis of HIV infection. (A1)
  - To the extent permitted by law, the terms “clinical/symptomatic HIV illness or AIDS,” “AIDS or HIV-related illness,” and other similar terms shall mean laboratory-confirmed HIV diagnosis (source: NYSDOH June 23, 2016 Policy Statement Defining Program Eligibility by HIV Status).
- Clinicians should counsel patients with seronegative partners about the reduction of HIV transmission risk when 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 follows:
  - Discuss benefits and risks of ART with the patient (A3)
  - See the NYSDOH AI guideline When to Initiate ART > Counseling and Education Before Initiating ART
  - 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. The patient should make the final decision of whether and when to initiate ART. (A3)
- When the decision to initiate treatment is made, ART should be prescribed and monitored by, or in consultation with, clinicians who have experience in managing ART. (A2)

Notes:

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

Results from the START trial [INSIGHT START 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). Patients with chronic infection and higher CD4 counts are at low risk for short-term adverse outcomes, allowing time for proper assessment, education, and engagement of the patient in the decision to treat.
In START, a randomized trial initiating ART in treatment-naive 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 [INSIGHT START 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 350–500 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 [CASCADE Collaboration 2011; Cain et al. 2011; COHERE 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.

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 [Marin et al. 2009; SMART Study Group et al. 2006; Ho et al. 2010; Ho et al. 2012; Lichtenstein et al. 2010], neurocognitive dysfunction [Tozzi et al. 2007; Garvey et al. 2011; Winston et al. 2012; Ellis et al. 2011], decreased risk of severe bacterial infections [O’Connor et al. 2017], and some non-HIV-related malignancies [Silverberg et al. 2011; Bruyand et al. 2009; Guiget et al. 2009; 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 351–500 cells/mm³ range were able to achieve similar immunologic responses as younger men who initiated at lower CD4 counts [Li et al. 2011].

A NEW HIV DIAGNOSIS IS A CALL TO ACTION

- 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.

Studies have shown that, for pregnant women with HIV, the administration of ART during pregnancy and/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 2011; CDC 2010], 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.
KEY POINT

- 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.

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).

References


Benefits and Risks of Antiretroviral Therapy

Medical Care Criteria Committee, November 2017

☑️ 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 less than three active 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

Effective antiretroviral therapy (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. 2016; Lundgren et al. 2015]. Thus, ART should be recommended to all individuals with HIV infection (see the NYSDOH AI guideline When to Initiate ART).

With proper selection of an initial regimen (see the NYSDOH AI 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 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 risk of sexual transmission of HIV during virological suppression is negligible. ART should be recommended to all patients with HIV infection in order 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.

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**A NEW HIV DIAGNOSIS IS A CALL TO ACTION**

- 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.

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**Risks**

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 antiretrovirals 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/mm$^3$) 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 persons with lower CD4 counts. Patients at increased risk should be informed of the potential for a paradoxical clinical worsening after ART initiation.
References


**Risk of Progression to AIDS-Defining Illness**

Adapted from the DHHS Guidelines for the Use of Antiretroviral Agents in HIV-infected Adults and Adolescents (2006)

<table>
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<th><strong>CD4 ≤200 Plasma Viral Load (copies/mL)</strong> [a]</th>
<th>% AIDS (AIDS-Defining Complication) [b]</th>
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a. Data from the Multi-Center AIDS Cohort Study (MACS).
b. MACS numbers reflect plasma HIV RNA values obtained by version 2.0 bDNA testing. RT-PCR values are consistently 2- to 2.5-fold higher than bDNA values, as indicated. It should be noted that the current generation bDNA assay (3.0) gives similar HIV-1 RNA values as RT-PCR except at the lower end of the linear range (<1,500 copies/mL).
c. In this study, AIDS was defined according to the 1987 CDC definition and does not include asymptomatic individuals with CD4 T cell counts <200 mm$^3$.
d. Too few subjects were in the category to provide a reliable estimate of AIDS risk.
e. A recent evaluation of data from the MACS cohort of 231 individuals with CD4 T cell counts >200 and <350 cells/mm$^3$ demonstrated that of 40 (17%) individuals with plasma HIV RNA <10,000 copies/mL, none progressed to AIDS by 3 years (Alvaro Munoz, personal communication). Of 28 individuals (29%) with plasma viremia of 10,000-20,000 copies/mL, 4% and 11% progressed to AIDS at 2 and 3 years, respectively. Plasma HIV RNA was calculated as RT-PCR values from measured bDNA values.
Prognosis According to CD4 Cell Count and Viral Load in the Pre-HAART and HAART Eras

FDA Pregnancy Categories

**Category A:** Adequate and well-controlled studies of pregnant women fail to demonstrate a risk to the fetus during the first trimester of pregnancy (and there is no evidence of risk during later trimesters).

**Category B:** Animal reproduction studies fail to demonstrate a risk to the fetus and adequate and well-controlled studies of pregnant women have not been conducted.

**Category C:** Animal reproduction studies fail to demonstrate a risk to the fetus and adequate and well-controlled studies of pregnant women have not been conducted.

**Category D:** Positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experiences, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.

**Category X:** Studies in animals or reports of adverse reactions have indicated that the risk associated with the use of the drug for pregnant women clearly outweighs any possible benefit.
Counseling and Education Before Initiating ART
Medical Care Criteria Committee, June 2016

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 (A3) (see text)
  ▫ 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 at the start of care for all individuals with HIV, 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 [Salzburg Statement 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. 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.

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 [Cohen et al. 2011; Quinn et al. 2000; Castilla et al. 2005; Donnell et al. 2010] (The risk of viral transmission still exists even when the plasma viral load is undetectable; ART is not a substitute for primary HIV prevention measures, such as avoiding needle sharing, practicing safer sex [Politch et al. 2012].)
• Decreased risk of several severe bacterial infections [O’Connor et al. 2017]

Disadvantages of early ART in asymptomatic patients:
• Potential drug–related reduction in quality of life in otherwise asymptomatic individuals [Erikkson et al. 2005; Guaraldi et al. 2008; Burgoyne et al. 2008]
• Possibility of greater cumulative side effects from ART [Volberding and Deeks 2010]
• Possibility for earlier development of drug resistance and limitation in future [Barth and Aitken 2012]
  antiretroviral options if adherence and viral suppression are suboptimal
• Possibility for earlier onset of treatment fatigue
• Higher prescription drug costs for the individual
NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE CLINICAL GUIDELINES PROGRAM

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. 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).

References


Special Considerations
Medical Care Criteria Committee, May 2017

☑️ RECOMMENDATIONS

Circumstances When ART Initiation is Urgent
- 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)
  - See NYSDOH Linkage, Retention, and Treatment Adherence Initiative
- Although ART is recommended for all patients with HIV, the urgency of initiation is increased under the following circumstances:
  - AIDS-defining condition (A1)
    - See the NYSDOH AI guideline When to Initiate ART > Initiating ART Following Acute Opportunistic Infections
  - Pregnancy [a] (A1)
  - Symptomatic from HIV, including any of the following:
    - HIV-associated neurocognitive disorder (A2). HAND is currently used to encompass a hierarchy of progressive patterns of central nervous system involvement ranging from asymptomatic neurocognitive impairment (ANI), to minor neurocognitive disorder (MND), to the more severe HIV-associated dementia (HAD).
    - Severe thrombocytopenia (A2)
    - HIV-associated nephropathy (A2)
    - HIV-related malignancies (A2)
    - Chronic hepatitis B or C infection [b,c] (A2)
    - Age 50 or older (A2)

Preparing Patients to Start ART
- Except in cases when initiation of treatment is urgent, clinicians should educate and prepare patients before initiating ART in those with barriers to adherence, including active alcohol or drug use; lack of insurance, transportation, or housing; depression; mistrust of medical providers; or a poor social support system. (A3)
  - See the NYSDOH AI guideline When to Initiate ART > Initiating ART Following Acute Opportunistic Infections

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)

Notes:
- 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.
- 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
- In co-infected patients with HCV, attention should be paid to interactions between the planned ART and HCV therapy.
**Barriers to Adherence**

Patients who are at high risk for poor adherence may benefit if initiation of ART is temporarily deferred while further patient education efforts are undertaken. In these patients, the risk of viral resistance and eventual treatment failure may outweigh any clinical benefit from earlier treatment before strict adherence can be expected [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. In patients who are pregnant, or 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.

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. Except when initiation of treatment is clinically urgent, more than one visit before initiating ART is advisable to ensure adequate understanding of the importance of adherence and to address barriers or impediments to therapy. These may include but are not limited to active alcohol or drug use; lack of insurance, transportation, or housing; depression; mistrust of medical providers; or a poor social support system. These barriers should not necessarily preclude initiation of ART; some may not be completely modifiable before starting therapy and will require ongoing attention and use of supportive services throughout the course of 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.

**References**


Initiating ART Following Acute Opportunistic Infections

Medical Care Criteria Committee, June 2016

**RECOMMENDATIONS**

**Patients with Acute OIs**

- 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 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 tuberculosis (TB), clinicians should initiate ART in patients with HIV 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)

In a randomized study, patients who initiated ART at a median of 12 days from 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 [Blanc et al. 2011; Havlir et al. 2011; Abdool 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.

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; NIAID 2012; Torok et al. 2011; Boulware et al. 2014; Bisson et al. 2013]. 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
Medical Care Criteria Committee, June 2016

✅ ALL RECOMMENDATIONS

Recommending and Initiating ART
• Clinicians should recommend ART for all patients with a diagnosis of HIV infection. (A1)
  ▫ To the extent permitted by law, the terms “clinical/symptomatic HIV illness or AIDS,” “AIDS or HIV-related illness,” and other similar terms shall mean laboratory-confirmed HIV diagnosis (source: NYSDOH June 23, 2016 Policy Statement Defining Program Eligibility by HIV Status).
• Clinicians should counsel patients with seronegative partners about the reduction of HIV transmission risk when 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 follows:
  ▫ Discuss benefits and risks of ART with the patient (A3)
  ▫ See the NYSDOH AI guideline When to Initiate ART > Counseling and Education Before Initiating ART
  ▫ 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. The patient should make the final decision of whether and when to initiate ART. (A3)
• When the decision to initiate treatment is made, ART should be prescribed and monitored by, or in consultation with, clinicians who have experience in managing ART. (A2)

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

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 (A3) (see text)
  ▫ 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)

Circumstances When ART Initiation is Urgent
• 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)
  ▫ See NYSDOH Linkage, Retention, and Treatment Adherence Initiative
• Although ART is recommended for all patients with HIV, the urgency of initiation is increased under the following circumstances:
  ▫ AIDS-defining condition (A1)
  ▫ See the NYSDOH AI guideline When to Initiate ART > Initiating ART Following Acute Opportunistic Infections
  ▫ Pregnancy [a] (A1)

Continued next page
ALL RECOMMENDATIONS – CONTINUED

Circumstances When ART Initiation is Urgent, continued
- Symptomatic from HIV, including any of the following:
  - HIV–associated neurocognitive disorder (A2). HAND is currently used to encompass a hierarchy of progressive patterns of central nervous system involvement ranging from asymptomatic neurocognitive impairment (ANI), to minor neurocognitive disorder (MND), to the more severe HIV–associated dementia (HAD).
  - Severe thrombocytopenia (A2)
  - HIV–associated nephropathy (A2)
  - HIV–related malignancies (A2)
  - Chronic hepatitis B or C infection \[b,c\] (A2)
  - Age 50 or older (A2)

Preparing Patients to Start ART
- Except in cases when initiation of treatment is urgent, clinicians should educate and prepare patients before initiating ART in those with barriers to adherence, including active alcohol or drug use; lack of insurance, transportation, or housing; depression; mistrust of medical providers; or a poor social support system. (A3)
  - See the NYSDOH AI guideline When to Initiate ART > Initiating ART Following Acute Opportunistic Infections

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 OIs
- 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 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 tuberculosis (TB), clinicians should initiate ART in patients with HIV 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)

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