

# **Recommendation to Expand Antiretroviral Therapy to All Persons Living with HIV**

## **Frequently Asked Questions (FAQ) for Healthcare Providers**

### **December 1, 2011**

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The New York City Department of Health and Mental Hygiene (NYC DOHMH) now recommend that healthcare providers offer antiretroviral therapy (ART) to all people living with HIV regardless of their CD4 count. The recommendation is based on evidence that ART can improve the health of people living with HIV and that ART can prevent transmission of HIV from an HIV-infected person to an uninfected sexual partner.

We have prepared responses below to Frequently Asked Questions (FAQs) for providers about NYC DOHMH's new recommendation.

#### **FAQ for all providers**

##### **1. What is the evidence supporting treatment for individuals at any CD4 cell count?**

The evidence supports treatment for both individual and public health benefit.

###### Individual patient benefit:

Randomized controlled evidence supporting initiation of ART in patients with CD4 counts  $>500$  cells/mm<sup>3</sup> is not yet available. However, some (though not all) cohort studies have shown a benefit in patients with normal CD4 counts. The NA-ACCORD study, a “cohort of cohorts” incorporating data from 22 observational studies in the U.S. and Canada, showed that there was a mortality benefit for those who initiated ART at a CD4 count  $>500$  cells/mm<sup>3</sup> compared with those who initiated at CD4 counts below 500 cells/mm<sup>3</sup> [1]. Furthermore, in the recently published HIV Prevention Trials Network Study 052 (HPTN 052), there were lower rates of extrapulmonary tuberculosis in individuals who initiated ART earlier than in those who delayed treatment [2]. These studies, along with evidence that patients who initiate ART earlier are less likely to suffer a variety of HIV-related complications, including cardiovascular disease, certain cancers and deterioration of the immune system [3-5], support treatment of HIV-infected persons with ART, regardless of CD4 level. Two smaller cohort studies do not show benefit for those who initiate ART at CD4  $>500$  cells/mm<sup>3</sup> [6,7].

###### Public health benefit:

HPTN 052, a prospective clinical trial, found that treatment is highly efficacious (96%) in preventing sexual transmission of HIV, presumably by decreasing viral load to undetectable levels. In addition, numerous previous observational studies [8-10] and clinical trials in pregnant and postpartum women [11-13] support the public health benefit of treatment to prevent transmission. Studies in both heterosexual couples and pregnant women have shown that transmission occurs more frequently at high viral loads and less frequently at very low viral loads, demonstrating the relationship between viral load and transmission [14,15].

##### **2. Are there any patients for whom initiating ART is not recommended?**

Discussion of the benefits of ART should occur at the start of care for all HIV-infected patients, regardless of CD4 count, with the anticipation that ART will be initiated. Misconceptions about treatment initiation should be addressed, including any concerns that starting ART represents advanced HIV illness. Despite this, some patients may refuse ART. In addition, as with starting any new long-term medication, providers should assess patient readiness and carefully evaluate factors that might limit adherence. Those patients for whom a provider has considerable or proven concern about adherence and for whom arrangements cannot be made to facilitate or monitor initial adherence

should not be started on ART. *As with all aspects of routine medical care, the provider should involve the patient in this decision-making process.*

**3. Which providers should consider prescribing ART to their HIV-infected patients?**

Due to the complexity of HIV disease and its treatment (particularly the number of specific toxicities and drug-drug interactions), ART should be prescribed by providers with experience managing these medications. Appropriate training and continuous education are also critical to ensure optimal outcomes. A provider directory of experienced HIV providers in New York State is available at: [http://www.health.ny.gov/diseases/aids/resources/provider\\_directory/voluntary\\_hiv\\_providers.pdf](http://www.health.ny.gov/diseases/aids/resources/provider_directory/voluntary_hiv_providers.pdf)

**4. What should be discussed with patients prior to initiation of ART?**

As with all aspects of routine care, providers should involve the patient in the decision-making process regarding the initiation of ART. Providers should review the benefits and risks of treatment for each individual patient, including the most recent data on the benefits of early ART. The decision to initiate therapy continues to depend on many individual factors for each patient and currently requires a lifelong commitment by the patient.

The provider should assess the need for supportive services to assure the success of long-term ART, such as mental health and substance use treatment, and link patients to these services as appropriate. An ongoing plan for coordination of care among all service providers should be established and maintained.

**5. How does the New York recommendation differ from the current national HIV treatment guidelines?**

Two expert panels regularly update guidelines for HIV treatment in the United States: the Department of Health and Human Services (DHHS) Panel on Antiretroviral Guidelines for Adults and Adolescents[16] and the International AIDS Society-USA ART Panel[17]. The most recent versions were released in October 2011 and July 2010, respectively. Currently, the NYSDOH AIDS Institute's clinical guidelines for initiating ART are under revision to reflect this new recommendation and the results from HPTN 052 (visit [www.hivguidelines.org](http://www.hivguidelines.org)).

Currently, each expert panel recommends that HIV-infected persons with either CD4 <500 cells/mm<sup>3</sup> or a history of an AIDS-defining illness receive ART. Also, regardless of CD4 count, both panels agree that ART should be initiated in patients with pregnancy, HIV-associated nephropathy (HIVAN), or hepatitis B virus (HBV), when treatment of HBV is indicated.

For patients with CD4 >500 cells/mm<sup>3</sup>, the panels have different recommendations on whom to treat.

- **The DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents** was evenly divided on ART initiation for patients with CD4 >500 cells/mm<sup>3</sup>: 50% of members favored starting ART; 50% of members viewed ART as optional[16]. They consider the choice to be something for patient and provider to discuss, carefully weighing individual factors in the context of mutual understanding.
- **The International AIDS Society–USA Panel** recommended that ART be considered in asymptomatic individuals with CD4 >500 cells/mm<sup>3</sup> who meet at least one of the following criteria: HCV co-infection, symptomatic HIV disease, HIV-1 RNA >100,000 copies/mL, rapid

decline in CD4 cell count ( $>100/\mu\text{L}$  per year), active or high risk for cardiovascular disease, symptomatic primary HIV infection, and higher risk for secondary HIV transmission[17].

**6. Who will this change in recommendations affect?**

The majority of people living with HIV already have an indication to initiate ART, either because their CD4 count is  $<500$  cells/ $\text{mm}^3$  or because they meet other criteria described above. Among New York City residents newly diagnosed with HIV and reported to DOHMH for whom sufficient CD4 count data are available, approximately 70% have a first CD4 cell count  $<500$  cells/ $\text{mm}^3$ , meeting both the DHHS and IAS-USA ART thresholds for ART treatment. NYC DOHMH now recommends that all other people living with HIV be offered ART, regardless of CD4 count.

**7. What is the evidence base for treatment as prevention?**

HPTN 052 was the first randomized clinical trial to show that ART could prevent HIV transmission in serodiscordant couples. However, previous observational studies from Africa[9], Canada[8], and San Francisco[10] also support this finding. Since 1994, mother-to-child HIV transmission has been greatly reduced due to provision of ART for HIV-infected pregnant women before delivery and immediate provision of ART to exposed infants[11].

Although HPTN 052 studied predominantly heterosexual, serodiscordant couples, the remarkable 96% efficacy of the approach, evidence from related studies, and the biologic plausibility that early treatment reduces sexual transmission of HIV support the recommendation to offer ART to all people living with HIV, not just those in heterosexual relationships.

**8. What other relevant research is ongoing?**

A major new prospective clinical trial, known as the Strategic Timing of Antiretroviral Treatment (START) trial, is evaluating whether asymptomatic HIV-infected persons have less risk of developing AIDS or other serious illness if they begin taking ART earlier in their illness[18]. Conducted in 30 countries, the START trial will enroll 4,000 HIV-infected persons with  $\text{CD4} > 500$  cells/ $\text{mm}^3$  into two arms: immediate ART vs. delayed ART (when CD4 falls below 350 cells/ $\text{mm}^3$ ). START will study the potential individual health benefits and risks of each approach. It is anticipated that this study will be fully enrolled by December 2012; results may be available as early as March 2015.

**9. Who will pay for this expansion of ART?**

It is anticipated that this intervention will continue to be covered by each patient's insurance and, for uninsured or underinsured individuals, by the AIDS Drug Assistance Program (ADAP) for eligible patients. It is also expected that expanded ART will be a cost-effective intervention for people living with HIV/AIDS in New York[19]. Although this expansion will result in the increased cost of more people receiving ART, these medication costs should be offset by fewer hospitalizations and less HIV transmission.

**10. How will this recommendation affect antiretroviral resistance in New York State?**

Although there is concern about resistance, the incidence and prevalence of HIV drug resistance is stable or decreasing in countries, such as the United States and Canada, where optimal treatment is readily available, ART use is tailored to the results of resistance testing, and treatment is closely monitored with frequent viral load measurement [20]. Expanding ART in this context is not expected to substantively change this.

NYC DOHMH's HIV/AIDS surveillance program continuously monitors population-level HIV drug resistance patterns. From 2006 to 2009, primary HIV drug-resistance levels have remained around 10% with no disparities by transmission category, age, or race-ethnicity. The NYSDOH has seen similar levels of drug resistance statewide. Careful monitoring of resistance will continue.

**11. How will the impact of this recommendation be evaluated?**

NYSDOH and NYC DOHMH will work together to continuously collect and analyze data about New Yorkers with new or already established HIV infection. Evaluation of the new recommendation will include assessing trends in: (a) population-level viral load assessments (“community viral load”); (b) the proportion of persons with newly diagnosed HIV infection who have undetectable viral loads within 6-12 months after diagnosis; (c) primary HIV drug resistance; and (d) the incidence of new HIV diagnoses.

**12. Should different ART regimens be prescribed for those with CD4 counts >500 cells/mm<sup>3</sup>?**

No. Practitioners should select from among the same regimens used to treat anyone with HIV. The following links provide more detailed information about specific regimens to consider.

DHHS

<http://www.aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf>

IAS-USA

<http://jama.ama-assn.org/cgi/reprint/304/3/321.pdf>

HIV/AIDS Drug Information (NIH)

<http://www.aidsinfo.nih.gov/drugsNew/Default.aspx?MenuItem=Drugs>

HIV/AIDS Clinical Trials Information (NIH)

<http://aidsinfo.nih.gov/ClinicalTrials/Default.aspx?MenuItem=ClinicalTrials>

CDC

<http://www.cdc.gov/hiv/topics/treatment/resources.htm>

NYS Department of Health HIV Clinical Guidelines

<http://www.hivguidelines.org/>

**13. What about pregnant patients?**

The NYC DOHMH and NYSDOH continue to recommend initiation of ART for all HIV-infected pregnant women to optimize maternal health, decrease the risk of HIV transmission to the fetus, and prevent transmission to sexual partners. Prenatal care providers should collaborate with experienced HIV care providers to determine the optimal ART regimen. The benefits of continuing ART beyond the duration of the pregnancy should also be discussed.

**14. What about an HIV-infected person with high CD4 count and no symptoms who is in a stable relationship with a partner who is also infected with HIV?**

HIV-infected persons with CD4 counts >500 cells/mm<sup>3</sup> and no clinical symptoms who are in a relationship with an HIV-infected partner should be offered ART to reduce their risk of developing HIV-related complications. ART will also reduce the risk of transmission to any new partners.

**15. Does this change the recommendations about the use of PrEP?**

No. Based on the strength of current evidence, serodiscordant couples should not, at this time, rely on PrEP to prevent HIV transmission. Rather, serodiscordant couples should use barrier precautions (e.g., condoms), and the HIV-infected partner should receive ART, regardless of CD4 count or clinical symptoms.

A recent randomized clinical trial, the Chemoprophylaxis for HIV Prevention in Men study (iPrEx), showed that daily, oral tenofovir/emtricitabine (“Truvada”) was safe and effective in preventing HIV infection among uninfected but exposed men who have sex with men (MSM)[21]. Immediately after the release of the iPrEX study results, which showed modest efficacy (44%) in protecting against infection, CDC [provided detailed interim guidance](#) about pre-exposure prophylaxis (PrEP)[22], recommending that PrEP be considered only for MSM (the population enrolled in the original iPrEX clinical trial) and only after the exclusion of acute HIV infection and the adoption of other non-pharmacologic risk reduction measures.

Preliminary results of subsequent studies in African heterosexual couples (TDF-2 and Partners PrEP), released in July 2011, support the use of PrEP in men and women[23,24]. Recently, another trial, the FEM-PrEP Study, was stopped early by the Data Safety and Monitoring Board (DSMB) because it was judged highly unlikely that the study would demonstrate PrEP effectiveness in enrolled women[25]. To date, none of these subsequent PrEP studies have been published in peer-reviewed journals, and CDC has not yet made recommendations based on them.

**Note to providers regarding partner notification:** NYS Public Health Law Article 21 (Chapter 163 of the Laws of 1998) requires that medical providers talk with HIV-infected patients about their options for informing sexual and needle-sharing partners who they may have been exposed to HIV. The NYSDOH and NYC DOHMH can assist in notifying partners. NYC providers can call Contact Notification Assistance Program (CNAP) at: (212) 693-1419 or 311 or can fill out a Provider Report Form available on the NYC DOHMH’s website: [http://www.nyc.gov/html/doh/html/dires/hcpreporting\\_how.shtml](http://www.nyc.gov/html/doh/html/dires/hcpreporting_how.shtml).

For areas outside of NYC, each NYS county has a Partner Services staff dedicated to providing health care providers with technical assistance and partner notification services. Contact information for Partner Services can be found at: [http://www.health.ny.gov/diseases/communicable/std/partner\\_services/info\\_for\\_providers.htm](http://www.health.ny.gov/diseases/communicable/std/partner_services/info_for_providers.htm)

More information on Public Health Laws and Regulations can be found at <http://www.health.ny.gov/diseases/aids/regulations/>

## REFERENCES

1. Kitahata MM, Gange SJ, Abraham AG, Merriman B, Saag MS, et al. (2009) Effect of early versus deferred antiretroviral therapy for HIV on survival. *N Engl J Med* 360: 1815-1826.
2. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseini MC, et al. (2011) Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 365: 493-505.
3. Calmy A, Gayet-Ageron A, Montecucco F, Nguyen A, Mach F, et al. (2009) HIV increases markers of cardiovascular risk: results from a randomized, treatment interruption trial. *AIDS* 23: 929-939.
4. Kuller LH, Tracy R, Belloso W, De Wit S, Drummond F, et al. (2008) Inflammatory and coagulation biomarkers and mortality in patients with HIV infection. *PLoS Med* 5: e203.
5. Fisher SD, Miller TL, Lipshultz SE (2006) Impact of HIV and highly active antiretroviral therapy on leukocyte adhesion molecules, arterial inflammation, dyslipidemia, and atherosclerosis. *Atherosclerosis* 185: 1-11.
6. Sterne JA, May M, Costagliola D, de Wolf F, Phillips AN, et al. (2009) Timing of initiation of antiretroviral therapy in AIDS-free HIV-1-infected patients: a collaborative analysis of 18 HIV cohort studies. *Lancet* 373: 1352-1363.
7. Writing Committee for the CASCADE Collaboration (2011) Timing of HAART initiation and clinical outcomes in human immunodeficiency virus type 1 seroconverters. *Arch Intern Med* 171: 1560-1569.

8. Montaner JS, Lima VD, Barrios R, Yip B, Wood E, et al. (2010) Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. *Lancet* 376: 532-539.
9. Donnell D, Baeten JM, Kiarie J, Thomas KK, Stevens W, et al. (2010) Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet* 375: 2092-2098.
10. Das M, Chu PL, Santos GM, Scheer S, Vittinghoff E, et al. (2010) Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. *PLoS One* 5: e11068.
11. Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, et al. (1994) Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med* 331: 1173-1180.
12. Taha TE, Kumwenda J, Cole SR, Hoover DR, Kafulafula G, et al. (2009) Postnatal HIV-1 transmission after cessation of infant extended antiretroviral prophylaxis and effect of maternal highly active antiretroviral therapy. *J Infect Dis* 200: 1490-1497.
13. Cooper ER, Charurat M, Mofenson L, Hanson IC, Pitt J, et al. (2002) Combination antiretroviral strategies for the treatment of pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. *J Acquir Immune Defic Syndr* 29: 484-494.
14. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, et al. (2000) Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med* 342: 921-929.
15. Mofenson LM, Lambert JS, Stiehlm ER, Bethel J, Meyer WA, 3rd, et al. (1999) Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. Pediatric AIDS Clinical Trials Group Study 185 Team. *N Engl J Med* 341: 385-393.
16. Panel on Antiretroviral Guidelines for Adults and Adolescents (2011) Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. pp. 1-167.
17. Thompson MA, Aberg JA, Cahn P, Montaner JS, Rizzardini G, et al. (2010) Antiretroviral treatment of adult HIV infection: 2010 recommendations of the International AIDS Society-USA panel. *JAMA* 304: 321-333.
18. National Institutes of Health ClinicalTrials.gov website (2011) Strategic Timing of Antiretroviral Treatment (START).
19. Long EF, Brandeau ML, Owens DK (2010) The cost-effectiveness and population outcomes of expanded HIV screening and antiretroviral treatment in the United States. *Ann Intern Med* 153: 778-789.
20. Gill VS, Lima VD, Zhang W, Wynhoven B, Yip B, et al. (2010) Improved virological outcomes in British Columbia concomitant with decreasing incidence of HIV type 1 drug resistance detection. *Clin Infect Dis* 50: 98-105.
21. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, et al. (2010) Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 363: 2587-2599.
22. Centers for Disease Control and Prevention (CDC) (2011) Interim guidance: preexposure prophylaxis for the prevention of HIV infection in men who have sex with men. *MMWR Morb Mortal Wkly Rep* 60: 65-68.
23. Thigpen MC, Kebaabetswe PM, Smith DK, Segolodi TM, Soud FA, et al. (2011) Daily oral antiretroviral use for the prevention of HIV infection in heterosexually active young adults in Botswana: results from the TDF2 study [Abstract WELBC01]. IAS. Rome, Italy.
24. Baeten JM, Celum C, The Partners PrEP Study Team (2011) Antiretroviral Pre-Exposure Prophylaxis for HIV-1 Prevention among Heterosexual African Men and Women: The Partners PrEP Study [Abstract MOAX0106]. . IAS. Rome, Italy.
25. Family Health International (2011) FHI Statement on the FEM-PrEP HIV Prevention Study: FHI to Initiate Orderly Closure of FEM-PrEP.