

# Highly Active Antiretroviral Therapy (HAART) in 2006

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*A continuing medical education activity sponsored by NAMCP*

## Summary

The human immunodeficiency virus (HIV) epidemic continues to be a significant public health issue around the world. Highly active antiretroviral therapy (HAART), the use of various medication combinations, has transformed HIV infection from a death sentence into a chronic manageable disease. To best manage patients, minimize costs, and prevent drug resistance, patients need assistance with adhering to their complicated therapeutic regimens.

## Key Points

- HIV infection remains a significant worldwide problem with 5 million new cases yearly.
- With HAART, the death rate from HIV has declined significantly.
- With HAART, HIV infection has become a chronic, manageable disease.
- Patient adherence to therapy is one of the key determinants in preventing drug-resistant HIV virus.
- Medical costs for patients with HIV infection increase when drug resistance occurs.
- Assisting patients with adherence to prevent resistance can be a significant role for managed care.

HUMAN IMMUNODEFICIENCY VIRUS was introduced into the human population when hunters became exposed to infected blood of the African Green chimpanzee.<sup>1</sup> The majority of virus found in the United States is type 1 group M and subtype B.<sup>2</sup> There is much more diversity in the virus in other countries.

Worldwide, 40 million people are estimated to have HIV and 5 million new cases occur each year (see Exhibits 1 and 2).<sup>3</sup> About 20 million people have died from the virus. The biggest epidemic is in Africa, but the fastest growth of cases is in Eastern Europe and the former Soviet Union.

The HIV epidemic in the U.S. started off as an epidemic in the homosexual community and it is now slowly shifting into a people-of-color epidemic. People of color are disproportionately representative in terms of people with HIV.<sup>2</sup> For example, one out of five black men between the ages of 40 and 49 in New York is HIV positive. Thirty four percent of new cases are in black women. Mortality is six times higher in black men than it is in white men, and that is partly because of access to care.<sup>4</sup> Overall, even though African

Americans make up only approximately 13 percent of the U.S. population, one half of the estimated new numbers of HIV/AIDS diagnoses in the U.S. in 2004 were for African Americans.<sup>2</sup> Another part of the epidemic is continued high-risk sexual behaviors among young homosexual men.<sup>2</sup>

One success story with HIV is the reduction in mother-to-child transmission in many countries. Pediatric HIV in the developed world is rapidly becoming a thing of the past. The vast majority of women with HIV can have uninfected babies as long as the mother is getting treatment.

Although progress has been made in preventing the spread of the virus, there needs to be more political recognition and willingness to assist in halting the continuing spread of HIV infections. The U.S. needs more public health infrastructure and better public education on this issue.

The long-term outlook on HIV infection changed in 1995 with the introduction of the protease inhibitor, the first highly active antiretroviral. Since the highly active antiretroviral therapy era began, HIV infection is no

Exhibit 1: Adults and Children Living with HIV/AIDS<sup>3</sup>

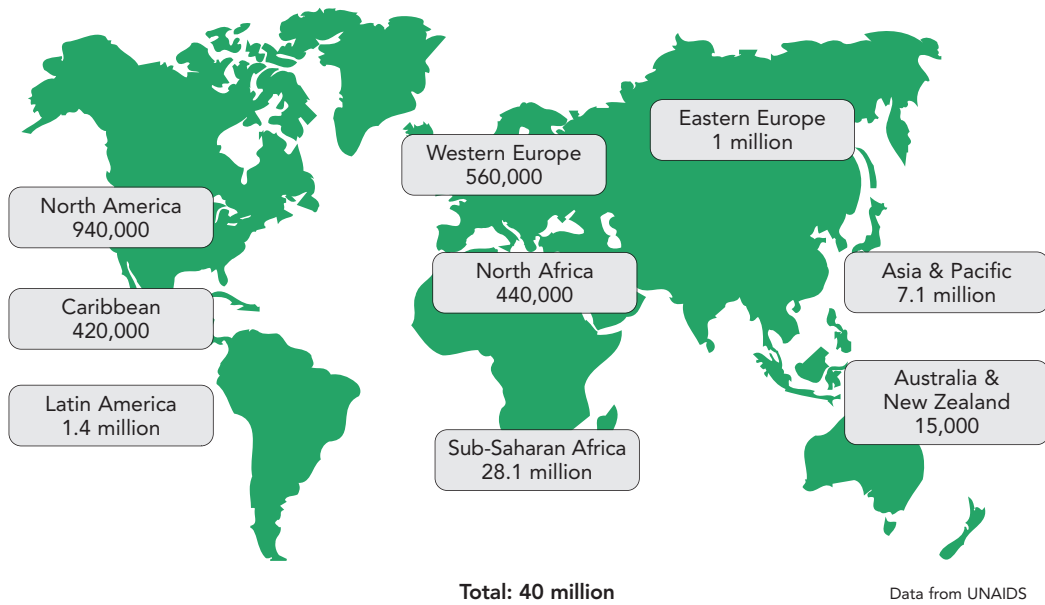
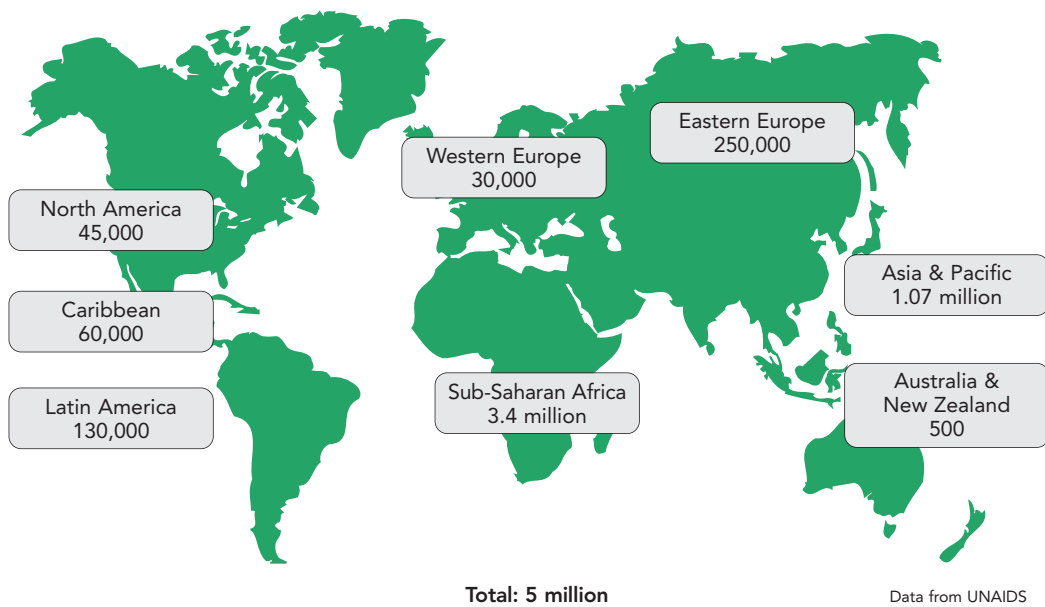


Exhibit 2: Annual New Infections of HIV in Adults and Children<sup>3</sup>

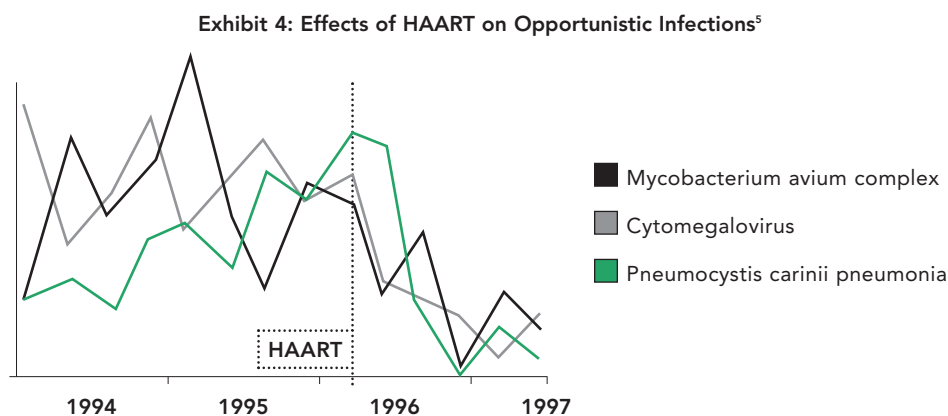
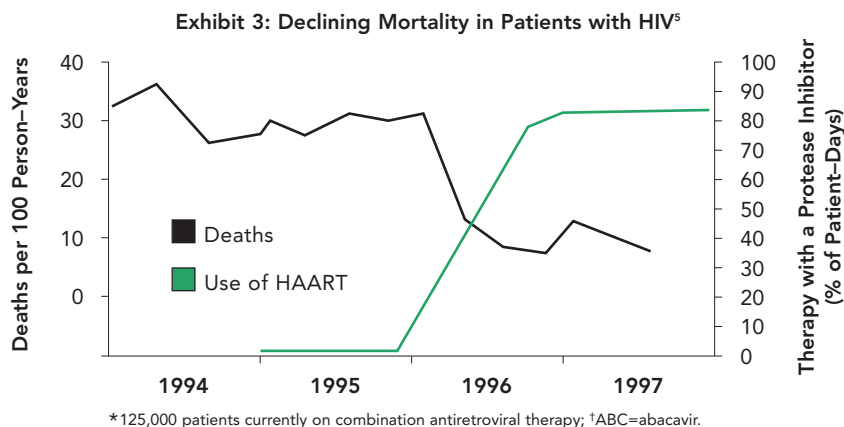


longer a death sentence. Use of these therapies has been associated with substantial declines in HIV-associated morbidity and mortality in recent years (see Exhibit 3).<sup>5</sup> HAART has significantly reduced the incidence of opportunistic infections including *Pneumocystis carinii* pneumonia (PCP), *Cytomegalovirus* (CMV), and *Mycobacterium avium* complex (MAC). See Exhibit 4.<sup>5</sup>

With the success of HAART in suppressing the HIV virus, hepatitis C virus infection is now of great

concern in the HIV-infected population. Because each infection has many of the same risk factors, hepatitis C and HIV commonly occur in combination. Hepatitis C is rapidly becoming the leading cause of death for people with HIV because these patients are now living long enough to sustain significant liver damage. Unfortunately the medications currently available to treat hepatitis C are not particularly effective.

Exhibit 5 details the current guidelines for when to



**Exhibit 5: Updated DHHS Guidelines—When to Start Treatment<sup>6</sup>**

Clinical Category	CD4+ Cell Count	Plasma HIV-1 RNA	General Guidelines
AIDS-defining illness or severe symptoms	Any Value	Any Value	Treat
Asymptomatic	<200	Any Value	Treat
Asymptomatic	200-350	Any Value	Treatment should be offered following full discussion of pros and cons of treatment
Asymptomatic	>350	100,000	Most clinicians recommend deferring therapy, but some clinicians will treat
Asymptomatic	>350	<100,000	Defer therapy

treat patients with HIV infection.<sup>6</sup> Guidelines for HIV are constantly changing because of new evidence. Recent evidence suggests that treatment should begin before the CD4 count falls below 350.

Exhibit 6 lists the currently available antiretroviral

medications. Many different combinations of these agents are used. Usually three different antiretrovirals are used. Which combination is chosen will depend on whether a patient is treatment naïve or if resistance is present. Other factors in selecting the combination

**Exhibit 6: Current Antiretroviral Medications**

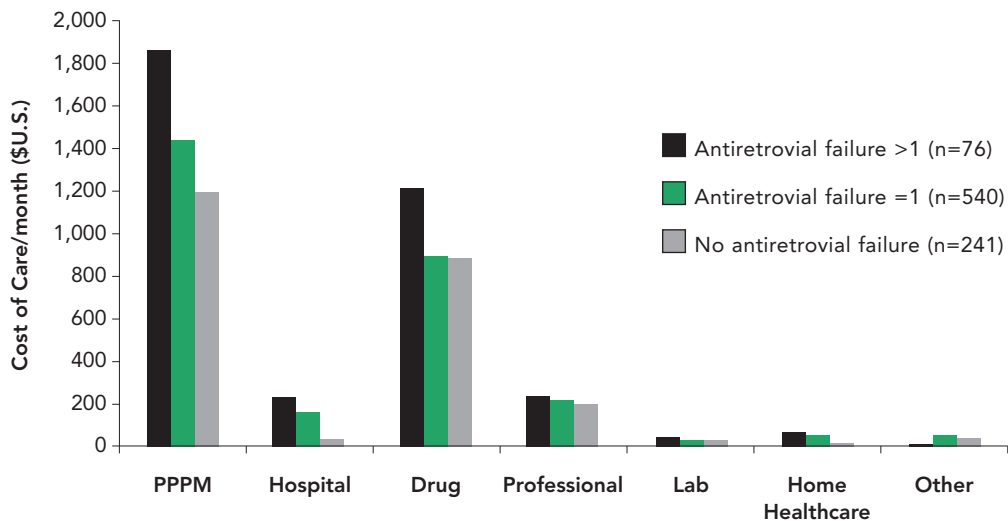
Nucleoside Reverse Transcriptase Inhibitor (NRTI)	
Abacavir	ABC
Didanosine	DDI
Emtricitabine	FTC
Lamivudine	3TC
Stavudine	D4T
Zidovudine	ZDV, AZT
Zalcitabine	DDC
Tenofovir	TDF

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)	
Delavirdine	DLV
Efavirenz	EFV
Nevirapine	NVP

Protease Inhibitors	
Amprenavir	APV
Atazanavir	ATV
Fosamprenavir	FPV
Indinavir	IDV
Lopinavir	LPV
Nelfinavir	NFV
Ritonavir	RTV
Saquinavir	SQV

Fusion Inhibitor	
Enfuvirtide	T-20

**Exhibit 7: Comparative Cost of Care for All Patients<sup>9</sup>**



include potential adverse effects, current treatment guidelines, and possible drug interactions. For example, the preferred regimen for treatment naïve patients includes a non-nucleoside reverse transcriptase inhibitor (NNRTI) plus two nucleoside reverse transcriptase inhibitors (NRTI).<sup>6</sup>

In recent years, HAART regimens have improved because of better medication efficacy and easier regimens. Previously, patients had to take large numbers of tablets or capsules multiple times daily.

More combination products as well as products that require fewer tablets and fewer daily doses have been introduced. Various trials have been conducted and are ongoing to determine the best treatment regimens and whether therapy can be safely stopped periodically based on viral suppression. So far, continuous treatment appears to be the best solution for most patients in order to continue viral suppression and prevent medication resistance.

Antiviral drug resistance can be one of the causes for

HIV therapy failure. Recent data suggest that the prevalence of drug resistance is about 14.5 percent.<sup>6</sup> Resistance testing is becoming more common. The most common use is to test newly infected patients to determine if they have a resistant virus, making it possible to better plan therapy. Testing also is done when a patient fails antiviral therapy. Viral phenotyping is done when a patient is multi-drug resistant. With viral phenotyping, the virus is tested against different antivirals.

Adherence to HAART therapy is a significant factor in reducing the development of drug-resistant virus and in reducing therapy failure. Patients who miss enough doses of HAART therapy rapidly develop drug-resistant virus. At less than 95 percent adherence, 50 percent of patients develop drug-resistant virus.<sup>7</sup> Resistance and antiretroviral therapy failure are not random or inevitable, but they are predictable outcomes with a number of controllable factors. The incidence of good adherence and full viral suppression depends on the expertise of the people taking care of the patients. Patient factors clearly associated with the risk of decreased adherence—such as active substance abuse, depression, and lack of social support—need to be addressed with patients before initiation of antiretroviral therapy.<sup>8</sup>

Exhibit 7 compares the treatment costs for patients who fail therapy and those who have success.<sup>9</sup> Patients who fail therapy have much higher costs because they are more likely to be sicker, be hospitalized, and require more expensive combinations of HAART. Good care in HIV to prevent medication failure means patients must be very adherent to their medication. Some strategies to enhance adherence to HAART are outlined in Exhibit 8.<sup>8</sup> Promoting adherence to therapy is a significant role for managed care in the cost-effective management of HIV-infected patients.

The future of treatment and control of HIV infection is exciting. Significant work is ongoing on vaccines, improved single-pill combination therapy, long-acting medications for once-weekly administration, and better treatments for hepatitis C. **JMCM**

#### Exhibit 8: Improving Adherence to HAART<sup>8</sup>

- Support and reinforcement
- Simplified dosing strategies
- Reminders, alarms, timers, and pill boxes
- Ongoing patient education
- Trust in healthcare provider

## References

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## Faculty

**Trevor Hawkins** is associate clinical professor at the University of New Mexico and medical director at Southwest CARE Center in Santa Fe, N.M.

## Disclosure

Dr. Hawkins receives research funding from Pfizer, Gilead, Tibotec, and GlaxoSmithKline. He also serves on the speakers' bureaus for Gilead, GlaxoSmithKline, Abbott, Bristol Myers-Squibb, and Boehringer-Ingelheim. Dr. Hawkins serves on advisory boards for Gilead and Cytodyn.

## Accreditation

The National Association of Managed Care Physicians (NAMCP) is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. NAMCP designates this activity for a maximum of 1 *AMA PRA Category I credits*<sup>™</sup>. Each physician should claim credit commensurate with the extent of their participation in the activity.

The American Association of Managed Care Nurses (AAMCN) has been approved as a provider of continuing education by the Virginia Nurses Association (VNA) for the period of Jan. 1, 2004, to Dec. 31, 2006. VNA is accredited as an approver of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation. Nurses who complete this activity will be awarded 1.2 contact hours.

This activity has been approved by the American Board of Managed Care Nursing for 1.2 contact hours toward CMCN recertification requirements.

This activity was held live at the NAMCP Spring Managed Care Forum. This activity is valid from Sept. 1-Dec. 31, 2006.

## POST TEST

### INSTRUCTIONS

Read the article, answer the post test questions, complete the evaluation form, and submit to Ann Patrick either by fax 804-747-5316 or mail: 4435 Waterfront Drive, Suite 101, Glen Allen, VA 23060.

1. HIV affects all genders, race, or sexual orientation the same.
  - a. True
  - b. False
  
2. Mother-to-child transmission is becoming a thing of the past.
  - a. True
  - b. False
  
3. HAART has made a significant impact on the incidence of opportunistic infections in HIV patients.
  - a. True
  - b. False
  
4. HIV patients are now at risk for death from Hepatitis C not HIV.
  - a. True
  - b. False
  
5. In addition to many other factors, the combination of antiretroviral therapy should be based on:
  - a. Whether the patient is treatment naive
  - b. The presence of resistance
  - c. Current treatment guidelines
  - d. Potential side effects and drug interactions
  - e. All of the above
  
6. The development of resistance and therapy failure is dependant on adherence.
  - a. True
  - b. False
  
7. Patients with active substance abuse, depression, and a lack of social support should be counseled about therapy adherence prior to the initiation of HAART.
  - a. True
  - b. False
  
8. Therapy failure requires more hospitalizations and more expensive combinations of HAART resulting in higher costs during the continuum.
  - a. True
  - b. False
  
9. Managed care's role in treating HIV should be promoting therapy adherence.
  - a. True
  - b. False

## HAART ANSWER SHEET

There is only one correct answer per question.  
Circle your answers clearly.

1. a b
2. a b
3. a b
4. a b
5. a b c d e

6. a b
7. a b
8. a b
9. a b

## ACTIVITY EVALUATION

**1. Please evaluate this activity based on the following scale:**

4 Excellent    3 Good    2 Fair    1 Poor

Activity met my expectations

4            3            2            1

Activity was free of bias

4            3            2            1

Activity content was understandable

4            3            2            1

Presenters were free of bias

4            3            2            1

Method of learning was beneficial

4            3            2            1

I will change my practice patterns by (please specify):

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My practice patterns will not change.

Name: \_\_\_\_\_

MD     DO     Other \_\_\_\_\_

Mailing Address: \_\_\_\_\_

City: \_\_\_\_\_

State: \_\_\_\_\_    ZIP: \_\_\_\_\_

Phone: \_\_\_\_\_

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Send my certificate by:

U.S Mail     E-mail

I heard about this activity from:

Colleague     Internet     e-News     Journal