



MCOs' Guide to HIV/AIDS Drug Therapies



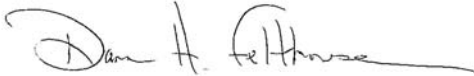
Dear Colleague:

We pleased to publish the *MCOs' Guide to HIV/AIDS Drug Therapies*. The screening, diagnosis and treatment of HIV infection demands the talents of physicians, pharmacists, nurses, case managers, social workers and many more credentialed health care professionals. The advent of highly effective antiretroviral drugs in the late 1990s has changed the face of HIV/AIDS from essentially a death sentence to a chronic condition that is able to be managed—successfully and for long periods of time—in ambulatory care settings.

This Guide was developed to help managed care organizations (MCOs) and their customers better understand effective approaches in the HIV/AIDS therapeutic area, including the role of highly active antiretroviral therapies (HAART). The Pharmacy Benefit Management Institute, LP (PBMI) gratefully acknowledges the support of Gilead Sciences, Inc. (Gilead) to research and produce this report. The PBMI team would like to thank the following organizations for their help with our research: Aetna Pharmacy Management, A-Med Specialty Pharmacy, BioScrip, Diplomat Specialty Pharmacy, Horizon Blue Cross Blue Shield, MemberHealth, Mirixa Corporation, Ramsell Public Health Rx, and Walgreens Specialty Pharmacy. We also would like to extend our appreciation to the members of the Guide Advisory Board (see list on page II) for their guidance on this project.

We hope you find this report to be helpful as you work to improve the quality of health care services for your members. It is our mission to support you in your work to keep your members and communities healthy and vital.

Cordially,



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About Pharmacy Benefit Management Institute

The Pharmacy Benefit Management Institute, LP (PBMI) provides research, continuing education, and Web resources to help health care benefit executives work with their pharmacy benefit managers to improve the design and management of drug benefit programs. You can learn more about PBMI at www.pbmi.com. For more information about this research, contact us at info@pbmi.com.

Editor's Note: Reference citations follow the style guidelines of the American Psychological Association. The report text follows Associated Press style guidelines to support the work of journalists and editors who may use this report as a reference tool.

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Purpose

The availability of highly active antiretroviral therapies (HAART) in the late 1990s changed the face of the AIDS crisis in developed countries. Research clearly documents the cost-effectiveness of this evidence-based approach to managing this otherwise fatal disease. Transmission of the HIV virus is preventable; yet diagnosed cases of HIV infection continue to grow. Gilead Sciences, Inc. provided financial support for this Guide. PBMI and Gilead identified the HIV/AIDS therapeutic area as an important case study to 1) illustrate the value of drug therapies to increase life expectancy and minimize morbidity, and 2) highlight the importance of developing ways to increase patient adherence to prescribed medications.

Market Research

PBMI conducted a secondary literature review on drug treatment protocols and benefit design for HIV/AIDS therapies. PBMI used the information gathered in this literature review to develop an in-depth qualitative interview guide for managed care organizations with HIV/AIDS populations and/or organizations involved in supporting HIV/AIDS patients. Telephone interviews were conducted with managed care organizations, pharmacy benefit managers, and specialty pharmacy organizations to develop this guide about HIV/AIDS drug therapy and the challenges in managing the spread of this highly infectious disease.

Here's what we learned from the 33 organizations we talked with about their work in the HIV/AIDS therapeutic area:

- Managed care plans, pharmacy benefit managers, and specialty pharmacies alike recognize that adherence to HAART is critical to successful management of HIV/AIDS.
- Each organization uses its best strategies and tools—patient consults conducted by nurses and/or pharmacists, telephone call center protocols, refill reminders, patient-specific reports for prescribers, pill boxes, patient-centered regimens, simplifying therapy as much as possible—for improving adherence when managing the care of people with HIV/AIDS.

- Clinicians working with HIV/AIDS populations benefit from ongoing continuing education about the disease state, recommended screening and treatment guidelines, drug therapies, and adherence strategies.
- The availability of HIV/AIDS lab values (CD4 cell counts, viral loads) combined with medication possession ratios allow for easy and cost-effective measurement of patient adherence. HIV/AIDS patient management programs may become effective case studies for improving patient adherence to therapies for other more common chronic diseases like diabetes, hypertension, and hyperlipidemia.

Gilead does not endorse nor support the strategies and approaches described in the Marketplace Examples.

Dedicated Advisory Board

PBMI identified a list of industry experts and payers to serve as members of an advisory board dedicated to this project. These experts helped to guide the development of interview questions and content creation for the *MCOs' Guide to HIV/AIDS Drug Therapies*.

Call to Action

HAART has advanced the treatment of HIV/AIDS and increased life expectancy. To continue this success, health care organizations—health plans, insurance companies, pharmacy benefit managers, specialty pharmacies—managing HIV/AIDS must:

- Support health care providers in their efforts to comply with the U.S. Centers for Disease Control and Prevention guidelines for screening, early diagnosis and treatment,
- Join forces to increase adherence to therapies to curb viral resistance to HAART, and
- Monitor medical care and drug treatment to optimize outcomes.

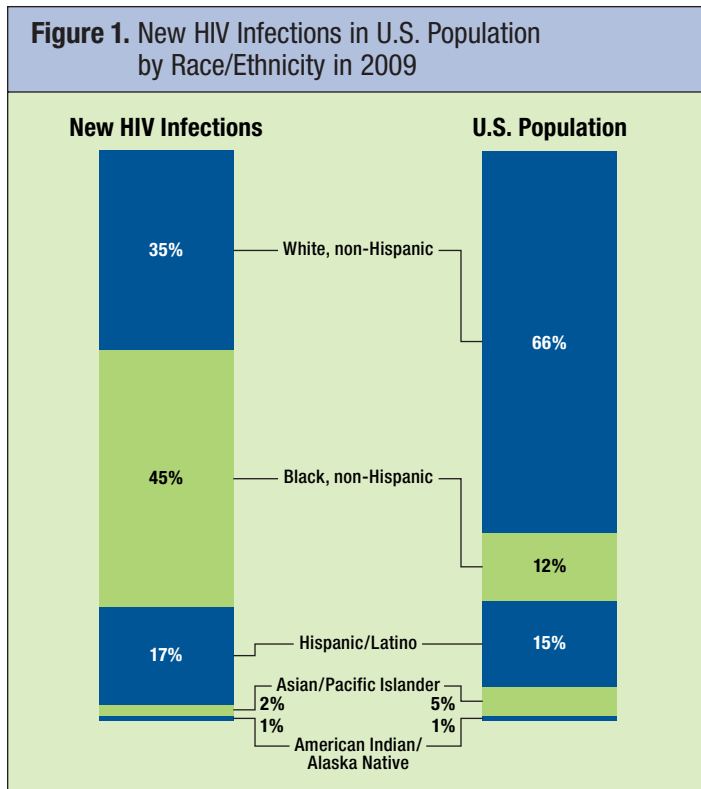
Overview of HIV/AIDS Disease: Life Expectancy and Prognosis

The advent of HAART in the late 1990s changed the face of HIV disease and AIDS from a fatal disease to a chronic condition that is able to be managed—successfully and for long periods of time—in ambulatory care settings. AIDS is caused by HIV infection which results in the death of CD4 lymphocytes.

Although treatment improvements have had significant impact on reducing HIV-related morbidity and mortality, HIV/AIDS remains a deadly transmissible disease. Consider these statistics about HIV/AIDS in the United States from the Henry J. Kaiser Family Foundation¹:

- Number of new HIV infections in 2006 = 56,300
- Number of people estimated to be living with HIV/AIDS = 1.1 million
- Number of people with AIDS = 468,000
- Number of AIDS deaths since epidemic began = 583,298
- Number of AIDS deaths in 2007 = 14,561
- Percent of people infected with HIV who don't know they're infected: 21% of the total believed to be infected.

The epidemic has a disproportionate impact on certain populations including racial and ethnic minorities as illustrated in Figure 1.



Source: The Henry J. Kaiser Family Foundation *HIV/AIDS Policy Fact Sheet on The HIV/AIDS Epidemic in the United States* (February 2009) Retrieved June 3, 2009 from <http://www.kff.org/hiv/aids/3029.cfm>.

Cases of AIDS have been reported in all 50 states and the District of Columbia. The AIDS case rate per 100,000 people quantifies the concentration of cases after accounting for differences in population size in multiple places as shown in Table 1.

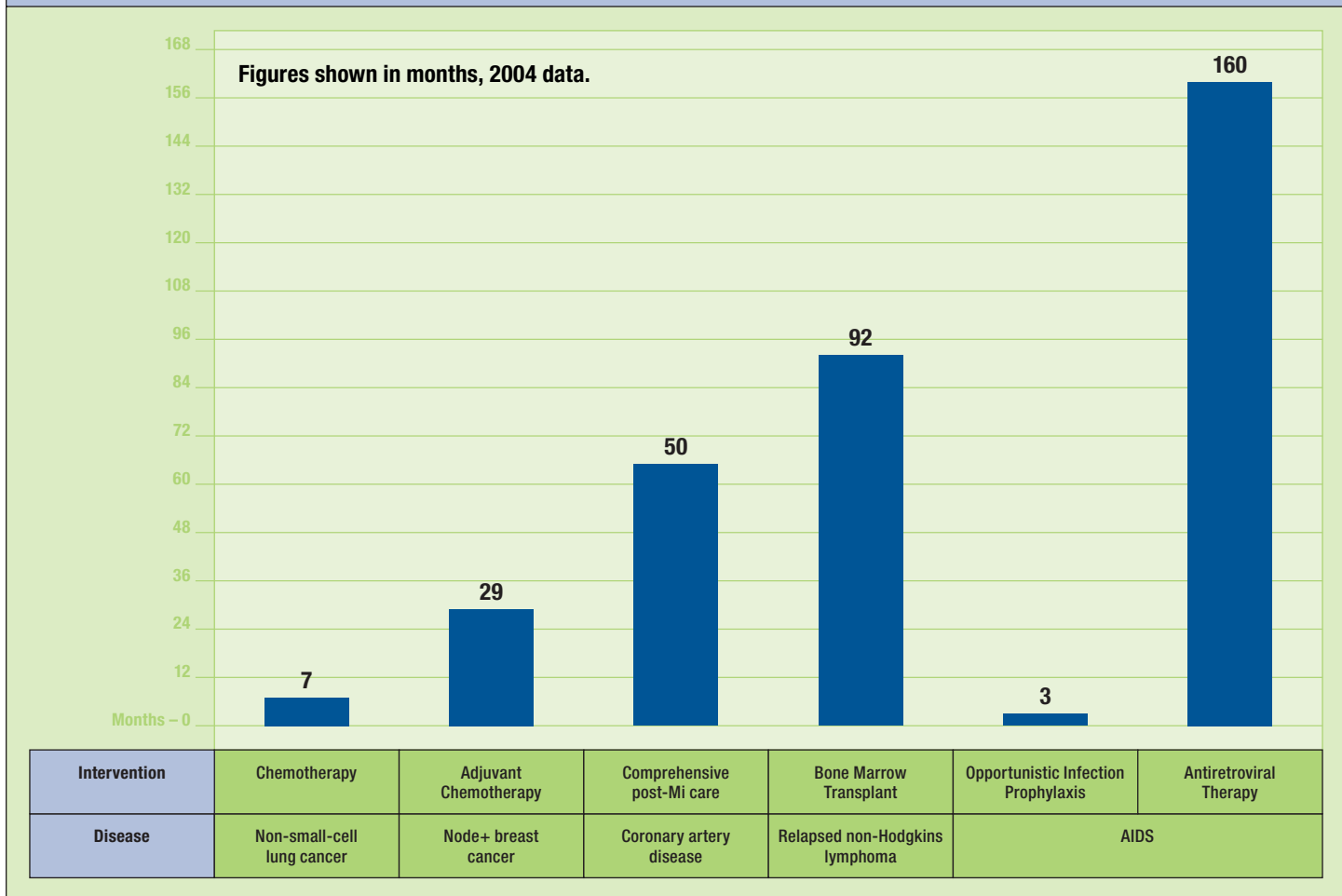
Table 1. Regions with High Concentrations of AIDS Cases

| Geographic Area | AIDS Cases Per 100,000 People |
|-------------------------------|-------------------------------|
| District of Columbia | 148.1 |
| U.S. Virgin Islands | 31.4 |
| New York | 24.9 |
| Maryland | 24.8 |
| Florida | 21.7 |
| Puerto Rico | 21.5 |
| Louisiana | 20.5 |
| Delaware | 19.8 |
| Georgia | 19.7 |
| South Carolina | 16.8 |
| Overall U.S. Case Rate | 12.5 |

Source: CDC. (2009). *HIV/AIDS Surveillance Report*, 19. Retrieved June 12, 2009 at <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2007report/table16.htm>.

The U. S. Centers for Disease Control (CDC) report that 1.1 million Americans were living with HIV in 2006, an increase of 11% from 2003.² As a result of better treatment, people with HIV are living longer than ever before. The improvements in life expectancy as a result of antiretroviral therapy and proactively managing opportunistic infections associated with HIV/AIDS are dramatic as shown in Figure 2.

Figure 2. Comparing Survival Gains From Treatment



Source: Walensky, R.P., Paltiel, A.D, Losina, E., Mercincavage, L.M., et al. (2006). The survival benefit of AIDS treatment in the United States. *Journal of Infectious Diseases*, 194,11-19.

The increase in the number of people with HIV means more people can spread the infection, yet new infection rates are relatively stable. These data suggest HIV testing and prevention efforts may be becoming increasingly effective.

Online Resources on HIV/AIDS in the United States

AIDS.gov
www.aidsinfo.nih.gov

The Henry J. Kaiser Family Foundation
www.kaisernetwork.org
<http://www.kff.org/hivaids/index.cfm>

National Center for Health Statistics
<http://www.cdc.gov/nchs/fastats/aids-hiv.htm>

U.S. Centers for Disease Control and Prevention
 Background information on HIV/AIDS
<http://www.cdc.gov/hiv/>

Importance of Highly Active Antiretroviral Therapy (HAART) Drug Classes

The U.S. Department of Health and Human Services (DHHS) issues treatment guidelines for management of people with HIV infection. There are separate guidelines for treatment of 1) adults and adolescents, 2) children, 3) pregnant women and prevention of mother-to-child transmission, and 4) for prevention of opportunistic infections. A national panel of physicians, researchers, clinical pharmacologists, and HIV treatment advocates write and update the guidelines. The guidelines address³:

- Baseline evaluation
- Laboratory testing for HIV RNA (viral load), CD4 cell count, drug resistance
- When to initiate therapy
- Choice of initial regimen
- When to change therapy
- Adherence
- Side effects and drug toxicity
- Treatment of acute HIV infection
- Special considerations for adolescents, pregnant women, injection drug users, and people coinfecting with HIV and hepatitis B, hepatitis C, or tuberculosis
- Prevention counseling for HIV-infected people

Each set of clinical guidelines is available online at www.aidsinfo.nih.gov and [http://aidsinfo.nih.gov](http://www.aidsinfo.nih.gov).

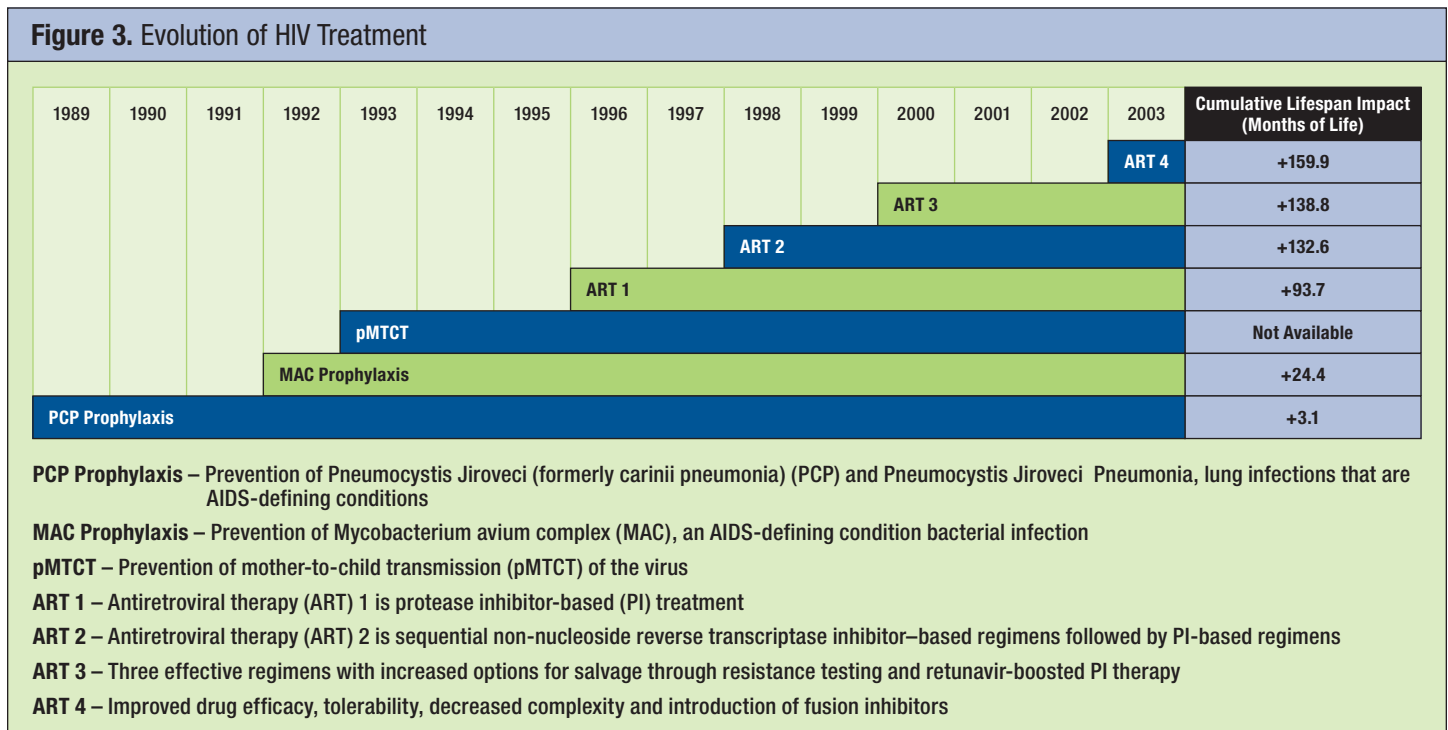
The MCOs' Guide to HIV/AIDS Drug Therapies focuses on the prescription drugs included in the DHHS guidelines and the important role of pharmacy care in effective treatment of HIV/AIDS.

Drugs used to control the replication of HIV are called antiretroviral medications. There are six classes of U.S. Food and Drug Administration-approved antiretrovirals. These drugs are described in Tables 2-7. When a combination of three or more medications from different classes is prescribed, the regimen is called highly active antiretroviral therapy or HAART.

The primary goals⁴ of antiretroviral therapy are to:

- Improve quality of life
- Reduce HIV-related morbidity and prolong survival
- Restore and/or preserve immunologic function
- Maximally and durably suppress viral load
- Prevent HIV transmission from mother to child, to sexual partners, and others

Medical and pharmacy care advancements together have contributed to the increasing lifespan of people with HIV as illustrated in Figure 3.



Source: Walensky, R.P., Paltiel, A.D., Losina, E., Mercincavage, L.M., et al. (2006). The survival benefit of AIDS treatment in the United States. *Journal of Infectious Diseases*, 194,11-19.

Tables 2-7 detail the six classes of drugs and combination therapies available to treat HIV.

| Table 2. Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) | | | |
|---|-----------------------------|-------------------|-----------------------------|
| Mechanism of Action | Chemical Entity Name | Brand Name | Drug Abbreviation(s) |
| NNRTIs bind to and inhibit HIV reverse transcriptase, a DNA polymerase enzyme HIV needs to make copies of itself. | delavirdine | Rescriptor® | DLV |
| | efavirenz | Sustiva® | EFV |
| | etravirine | Intelence® | ETR |
| | nevirapine | Viramune® | NVP |

| Table 3. Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs) | | | |
|--|---|-------------------|-----------------------------|
| Mechanism of Action | Chemical Entity Name | Brand Name | Drug Abbreviation(s) |
| NRTIs are faulty versions of nucleosides (building blocks) that HIV needs to replicate. When HIV uses an NRTI instead of a normal building block, virus reproduction is stalled. * Denotes generic for some dosage forms available. | abacavir | Ziagen® | ABC |
| | abacavir/lamivudine | Epzicom® | |
| | abacavir/lamivudine/zidovudine | Trizivir® | |
| | didanosine* | Videx®, Videx EC® | ddl |
| | emtricitabine | Emtriva® | FTC |
| | emtricitabine/tenofovir disoproxil fumarate | Truvada® | |
| | lamivudine | Epivir® | 3TC |
| | lamivudine/zidovudine | Combivir® | |
| | stavudine* | Zerit® | d4T |
| | tenofovir disoproxil fumarate | Viread® | TDF |
| zidovudine* | Retrovir® | AZT, ZDV | |

| Table 4. Protease Inhibitors (PIs) | | | |
|---|-----------------------------|-------------------|-----------------------------|
| Mechanism of Action | Chemical Entity Name | Brand Name | Drug Abbreviation(s) |
| Bind to and inhibit HIV protease, an enzyme HIV needs to make copies of itself. | atazanavir | Reyataz® | ATV |
| | darunavir | Prezista® | DRV |
| | fosamprenavir | Lexiva® | FPV |
| | indinavir | Crixivan® | IDV |
| | lopinavir/ritonavir | Kaletra® | LVP/r |
| | nelfinavir | Viracept® | NFV |
| | ritonavir | Norvir® | RTV |
| | saquinavir | Invirase® | SQV |
| | tipranavir | Aptivus® | TPV |

| Table 5. Entry Inhibitors | | | |
|----------------------------------|-----------------------------|-------------------|-----------------------------|
| Mechanism of Action | Chemical Entity Name | Brand Name | Drug Abbreviation(s) |
| Block HIV entry into cells. | enfuvirtide | Fuzeon® | ENF |
| | maraviroc | Selzentry® | MVC, T20 |

| Table 6. Integrase Strand Transfer Inhibitor | | | |
|---|-----------------------------|-------------------|-----------------------------|
| Mechanism of Action | Chemical Entity Name | Brand Name | Drug Abbreviation(s) |
| Binds to and inhibits integrase, a protein HIV uses to insert its viral genetic material into the material of an infected cell. | raltegravir | Isentress® | RAL |

| Table 7. Multiclass Fixed Dose Combination | | | |
|--|--|-------------------|-----------------------------|
| Mechanism of Action | Chemical Entity Name | Brand Name | Drug Abbreviation(s) |
| Contain 2 or more anti-HIV medications from 2 or more therapeutic classes. | efavirenz/emtricitabine/tenofovir disoproxil fumarate (DF) | Atripla® | |

Sources: Compiled from U.S. Food and Drug Administration. (2008) *Drugs Used in the Treatment of HIV Infection*. Retrieved May 28, 2009 at <http://www.fda.gov/oashi/aids/virals.html>. Approved generic formulations of antiretroviral drugs used in the treatment of HIV infection. Retrieved May 28, 2009 at <http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm118944.htm>.

Prescribing Guidelines

For patients new to antiretroviral treatment, DHHS guides recommend a HAART regimen of:

- One NNRTI (Table 2) taken with two NRTIs (Table 3), or
- One PI (Table 4) taken with two NRTIs.
- One integrase strand transfer inhibitor (Table 6) taken with two NRTIs.

The guidelines include dosing, pharmacokinetics and common adverse side effects. Detailed tables provide detailed information to support prescribers' selection of therapy for each patient.

The guidelines also address how to manage the treatment-experienced patient. The document discusses regimen simplification to address which patients are good candidates for reducing pill burden.

Importance of First Drug Regimen

Patient adherence is critical to treating HIV/AIDS. A person's first drug regimen is the best regimen for reducing viral loads and minimizing drug resistance. The risk of treatment failure increases markedly with minor lapses in patient adherence.⁵ Treatment failure, in turn, results in drug resistance, disease progression, and increased mortality.

In the developed world, treatment failure is defined by virologic failure. This occurs if HIV RNA can be detected in a patient's plasma despite the use of antiretroviral therapy. One study (n=81 patients) shows virologic failure in 22% of patients with > 95% adherence, 61% of those with 80-94.9% adherence, and 80% of those with < 80% adherence. Those with adherence ≥ 95% had fewer hospitalization days and no opportunistic infections or death.⁶ These data from 2000 are likely to be significantly better today.

There also is a relationship between adherence and immune response as demonstrated by an increase in CD4 cells in adherent patients.⁷ High adherence results in maximal therapeutic drug exposure, limiting viral replication and maintaining viral suppression, hence decreasing the chances of drug resistance development. Intermediate adherence permits low-level or intermittent viral replication and poses the highest risk for resistance.^{8,9}

MARKETPLACE EXAMPLE: Firms Combine Expertise to Develop Medication Therapy Management

Pharmacists will take the lead in improving communication among patients and prescribers in a new medication therapy management (MTM) program for HIV/AIDS.

Mirixa Corporation and Ramsell Pharmacy Solutions are working together to develop this MTM product to be piloted in 2009-2010. Mirixa, sponsored by the National Community Pharmacists Association (NCPA), has a contracted network of 46,000 pharmacies in the United States that offers in-store MTM, patient adherence programs and care management to their clients. Ramsell Public Health Rx is a pharmacy benefits manager (PBM) focused solely on serving the public health sector with a focus on HIV/AIDS.

“MTM will be a tool to assist with adherence needs, counseling and support,” said Colleen Higgs, PharmD, president of Ramsell Pharmacy Solutions, the clinical division of Ramsell Public Health Rx. “The benefit of MTM is enhancement of communication among patient, physician and pharmacist.”

The goals of this new MTM platform for HIV/AIDS are to:

- Improve quality of life for members
- Increase ability to avoid adverse drug events
- Anticipate side effects
- Preserve treatment options for the future because typically the first drug regimen is the best regimen

Mirixa began working with Ramsell in August 2008 to develop an intervention protocol for HIV/AIDS that addresses the areas where pharmacists will be engaged. The protocol or tool covers core areas of MTM with areas of specialization for HIV/AIDS. Medication possession ratios (MPRs) will be supplied to pharmacists to let patients know how they are doing. The MPRs tie back into the lab data which give patients a target to work toward to improve their health status.

“We view the pharmacist as a coach, a behavior change agent to help people with HIV/AIDS,” said Rebekah Jackowski, RPh, clinical pharmacist for Mirixa.

Both companies envision MTM as bridging the gap among pharmacist, physician and patient. A letter announcing the program to the physicians will be sent before a patient’s MTM visit. The letter will outline the benefits of MTM.

The MTM platform will provide viral load, CD4, information on resistance and MPRs for key medications to the pharmacist conducting the MTM patient activities. The MTM protocol also includes links to online treatment guidelines, expected side effects, and side effect management information. The pharmacist will add any information on herbals and over-the-counter medications the patient is taking to the patient profile.

Reporting and Metrics

The outputs from the MTM patient consultation will be 1) medication record to share with primary care provider, and 2) medication action plan. Pharmacists will use the SOAP format—the same format providers use for medical charts—to document the medication action plan. (SOAP is an acronym for the subjective, objective, assessment and plan structure used in problem-oriented records for organizing medical follow-up and monitoring.) The current target is four patient-pharmacist visits per year.

Ongoing outcomes measures will track 1) MPR for identified patients, 2) changes in viral load, and 3) CD4 count. The pilot studies also will include inferred rates of opportunistic pre- and post infections, medical visits, emergency room visits and hospitalizations.

MARKETPLACE EXAMPLE: Medication Possession Ratio Serves As Reliable Metric

The adage—you can't manage what you can't measure—is especially true in treating HIV/AIDS. A medication possession ratio or MPR (Figure 4) is a reliable metric for tracking how frequently people take their prescribed medications.

"MPR has been widely used and validated as a proxy for drug adherence," says Katherine Thweatt, senior manager of clinical quality, for Universal American Corp., formerly MemberHealth.

Figure 4. Calculating Adherence to Prescription Drug Therapy

$$\text{Medication Possession Ratio (MPR)} = \frac{\text{Sum of days' supply of drug}}{\text{Number of days between first fill and last refill plus days' supply of last refill}}$$

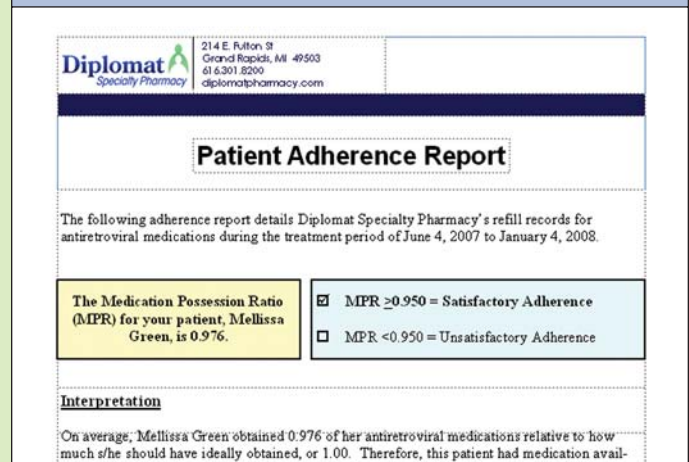
Using prescription drug claims data to calculate MPR is an increasingly reliable way to measure adherence to prescription drug regimens. MPR is expressed as a ratio < 1. A value of 1 means all refills have been processed. A value > 1 would imply early refilling behaviors. The industry truncates the value at 1, an indication of perfect compliance. An MPR ≥ 0.95 is the target for HAART adherence.

Source: Sikka, R., Xia, F., & Aubert, R.E. (2005). Estimating medication persistency using administrative claims data. *The American Journal of Managed Care*, 11, 449-457.

"Eighty percent of people with HIV/AIDS are taking care of themselves," says MikeLynn Salthouse, RN, vice president of business development for Diplomat Specialty Pharmacy. "It's the other 20% that we all need to focus on how best to help them adhere to their medication regimens," she said. Diplomat is the nation's largest privately owned specialty pharmacy with six specialty pharmacy locations.

Diplomat works one on one with patients through monthly medication follow-up calls and quarterly clinical reviews of medication regimens. Patient adherence reports with patient-specific medication possession ratios are developed and sent to prescribing physicians as shown in Figure 5.

Figure 5. Effective Reporting Includes Patient-specific Data



Source: Heidi Michels, PharmD, HIV Clinical Pharmacist, Diplomat Specialty Pharmacy. (January 2008) *HIV Navigator Program Presentation*.

Universal American, a Prescription Drug Plan (PDP) for the Medicare Part D drug benefit, serves 700,000 dual eligibles or low income beneficiaries which include about 5,000 people with HIV/AIDS. Universal American Corp.'s Part D benefit is offered exclusively through a community pharmacy network. The plan design allows for 90-day fills at the community pharmacy network, comprised of 65% to 70% independent pharmacies and 30% to 35% chain pharmacies. Thweatt and her colleague Alan Pendergrass, manager of analytics and outcomes, recently led a patient adherence intervention for HAART.

Adherence Intervention

The PDP sought to increase the number of HAART beneficiaries with a Medication Possession Ratio (MPR) > 95%. Members who had claims for antiretroviral drugs and an MPR < 95% were included in an intervention. Their physicians were the target audience for a letter-based initiative to increase HAART adherence. The group included 1,285 members, with an average age of 48. Some were eligible for both Medicaid and Medicare. At baseline, the average MPR was 73%.

Letters were sent to prescribing physicians with patient-specific MPR data, duration, and start and end date of therapy. In addition to providing quantifiable information about compliance, the letter referenced the consequences of nonadherence and the importance of a multidisciplinary approach to improve adherence. It encouraged physicians to use the data to discuss medication adherence with noncompliant patients.

Results

Universal American Corp.'s study showed an immediate increase in MPR among HIV patients whose physicians received MPR data and educational materials reinforcing a discussion about compliance. At 90, 180, and 265 days post-intervention, an aggregate analysis of adherence to antiretroviral therapy revealed a significant increase in baseline MPR by 10%, 7%, and 6% respectively. Post-intervention results at 90, 180, and 265 days indicated 46% (n=588), 32% (n=406), and 27% (n=350) of intervention patients achieved an MPR > 95%. The decrease in average MPR over time supports the value of frequently providing compliance measurement and educational interventions to physicians of HIV patients.

MARKETPLACE EXAMPLE: Managed Care Plans, Specialty Pharmacies Work to Improve Adherence

The side effect list is long: diarrhea, fatigue, flatulence/bloating, headache, nausea, peripheral neuropathy, skin rashes, and weight loss among many others. These side effects are difficult for people with a complex chronic disease to manage while trying to lead a “normal” life. Pharmacists who care for people with HIV/AIDS understand that improving adherence to HAART depends a lot on effective side effect management.

“Adherence strategies for HIV/AIDS includes directing patients to infectious disease specialists, looking at viral loads, prophylactic medications to prevent opportunistic infections, flu shots, and HIV antiviral medications,” says Phil Bonaparte, MD, vice president of clinical affairs and chief medical officer for Medicaid programs for Horizon Blue Cross Blue Shield, a managed care organization that provides care for 3.6 million lives. There are < 1,900 Medicaid members who are HIV positive. “If you do these little things, the quality of life is better and side effects are minimized.”

“Trust in the provider is critical in HIV/AIDS,” said George W. Kridner, PharmD, FASCP, vice president of clinical pharmacy operations for A-Med Specialty Pharmacy. A-Med Specialty Pharmacy, part of A-Med Health Care, is a medical and infusion supply company in Huntington Beach, Calif. As a result, A-Med developed a high touch compliance program specifically for HIV/AIDS to increase adherence to prescribed drug regimens.

Personalized Care

In-person, outbound telephone calls are initiated by A-Med customer service personnel and then passed to a pharmacist if the patient is having problems with medications. A detailed algorithm allows personnel to 1) counsel patients on drug-drug interactions including over-the-counter (OTC) medications, herbal supplements and street drugs, 2) document patient-reported CD4 counts and viral loads, 3) assess compliance by collecting data to calculate medication possession ratios, and 4) track demographics to ensure delivery information is current.

“We take time to ask patients about OTCs, herbal supplements, and street drugs because they are used frequently in the HIV/AIDS population,” Kridner said. “The HIV/AIDS community is close knit so they often recommend herbal remedies to one another. As pharmacists, we are accessible and can help educate patients about how to take the right medications.”

“Successful patient compliance requires individualized approaches for patients,” says Sara Deno, PharmD, manager of clinical services for BioScrip, the country’s largest publicly traded independent specialty pharmacy company. It is the current exclusive provider of HIV medication for United Health Group. BioScrip has community pharmacies in 27 cities to offer the choice of both retail and specialty pharmacy services to United’s members with HIV/AIDS. “We provide multiple distribution methods (including home delivery and community pharmacies), linkage to financial support programs, 24/7 access to clinicians for therapy support, care management programs, and private counseling rooms at community pharmacies,” Deno said.

“The industry as a whole is seeing specialty pharmacy, managed care organizations, and manufacturers trying different modalities for increasing compliance,” Deno said. Table 8 summarizes the many critical strategies for improving adherence to HAART.

“A patient is more than one disease,” said Glen Pietrandoni, manager of the HIV/AIDS Program for Walgreens Specialty Pharmacy, a national

specialty pharmacy provider. “There are other medications and issues as they age.” Walgreens reviews adherence every time a patient refills a prescription by accessing online, real-time patient-specific profiles. Walgreens is building a database to measure and report medication possession ratio to physician, payer and pharmacy.

Table 8. Strategies to Improve Adherence to Antiretroviral Therapy

| Strategy |
|---|
| Use a multidisciplinary team (nurses, social workers, pharmacists, medication managers) to provide an accessible, trustworthy health care team |
| Establish a trusting relationship with each person with HIV/AIDS |
| Establish person’s readiness to start drug therapy |
| Identify potential barriers before beginning drug therapy: <ul style="list-style-type: none"> Psychosocial issues Active substance abuse or at high risk for relapse Low literacy level Busy daily schedule and/or travel away from home Skepticism about HAART Lack of prescription drug coverage or resources to purchase prescription drugs |
| Provide tools to support person with HIV/AIDS: <ul style="list-style-type: none"> Referrals for mental health and/or substance abuse treatment Resources to obtain prescription drug coverage Pill boxes |
| Involve the person with HIV/AIDS in drug regimen selection by reviewing the following for each option: <ul style="list-style-type: none"> Potential side effects Dosing frequency Pill burden (number of pills per day) Drug storage requirements Food requirements Consequences of nonadherence |
| Assess adherence to drug therapy at every provider visit: <ul style="list-style-type: none"> Simple checklist to complete in waiting room Assessment by multiple members of health care team Ask open-ended questions about drug therapy such as, “<i>In the last three days, please tell me how you took your medications.</i>” |
| Identify the type of nonadherence: <ul style="list-style-type: none"> Failure to fill and refill the prescriptions Failure to take the right dose(s) at the right time(s) Nonadherence to food requirements |
| Identify the reasons for nonadherence: <ul style="list-style-type: none"> Adverse side effects from medications Complexity of regimen including pill burden, dosing frequency, etc. Difficulty swallowing large pills Forgetfulness Failure to understand dosing instructions Inadequate understanding of drug resistance and its relationship to adherence Pill fatigue |
| Assess and simplify drug regimen if/when possible |

Source: Panel on Antiretroviral Guides for Adults and Adolescents, Department of Health and Human Services. (December 1, 2009) *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents*, 113.

Online Resources on HAART Drug Therapies

AIDSinfo Drug Database

U.S. Department of Health and Human Services
[www.aidsinfo.nih.gov/DrugsNew/Default.aspx?MenuItem=Drugs
&Search=On](http://www.aidsinfo.nih.gov/DrugsNew/Default.aspx?MenuItem=Drugs&Search=On)

Antiretroviral Pregnancy Registry

<http://www.apregistry.com/>

Clinical Treatment Guidelines

www.aidsetc.org
[http://aidsinfo.nih.gov/Guidelines/Default.aspx?MenuItem=
Guidelines](http://aidsinfo.nih.gov/Guidelines/Default.aspx?MenuItem=Guidelines)

HIV InSite

University of California San Francisco Center for HIV Information
<http://hivinsite.ucsf.edu/InSite>

National Library of Medicine

Drug Information
<http://sis.nlm.nih.gov/hiv/drugs.html>

U.S. Centers for Disease Control and Prevention

HIV/AIDS Treatment Information
<http://www.cdc.gov/hiv/topics/treatment/index.htm#hivatis>

U.S. Department of Health and Human Services

The AIDS Infonet
www.aidsinfo.nih.gov

U.S. Food and Drug Administration

HIV/AIDS List Serve
<http://www.fda.gov/oashi/aids/listserve/archive.html>

Challenges Remain for Managed Care Organizations

Many challenges remain for the health care practitioners and managed care organizations providing care and treatment to those with HIV/AIDS. Identifying patients who need care for HIV is the first step in controlling the epidemic.

The U.S. Centers for Disease Control and Prevention (CDC) has published HIV screening recommendations that favor an opt-out strategy for screening in all health care settings, which means testing should be performed in all patients between the ages of 13 and 64, without the need for informed consent unless the patient declines or “opts out” of testing. These guidelines are posted at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm>. Several medical specialty organizations have endorsed the CDC recommendations (Table 9) and provide HIV/AIDS continuing education for their members and other health care professionals.

Many rapid HIV antibody tests became available in 2002 to augment blood tests that required several days or weeks to provide results. A newer HIV test is an enzyme immunoassay or rapid test that only requires a drop of blood or saliva and yields results within 10 minutes with high sensitivity and specificity rates.¹⁰ Although a positive test result requires confirmation with a Western blot test to detect HIV proteins in the blood, a negative test result is conclusive. These highly accurate tests that provide low cost test results make screening for HIV achievable in any health care setting.

Table 9. Organizations Supporting 2006 CDC HIV Screening Guidelines

| Medical Organization | Screening | | Consent and Pretesting | |
|---|-------------------------|--|--|---|
| | All Patients Ages 13-64 | All Patients Seeking or Initiating Treatment for TB, STDs, or Blood-related Diseases | Voluntary and Undertaken Only With Understanding That Testing is Planned | Provide Information and Allow Opt-Out Testing Unless Patient Declines |
| <i>Full Endorsement of Guidelines</i> | | | | |
| American Academy of Pediatrics | • | • | • | • |
| American College of Nurse-Midwives | • | • | • | • |
| American College of Physicians | • | • | • | • |
| American Medical Association | • | • | • | • |
| Emergency Nurses Association | • | • | • | • |
| HIV Medicine Association | • | • | • | • |
| <i>Partial Endorsement of Guidelines As Noted</i> | | | | |
| American Academy of Family Physicians | | • | • | • |
| American Academy of HIV Medicine | | | • | • |
| American College of Obstetricians and Gynecologists | • | | | • |
| Association of Nurses in AIDS Care | | | • | |
| National Association of Community Health Centers | • | | | |

Source: Bartlett, J.G., Branson, B.M., Fenton, K., et al. (2008) Opt-out testing for human immunodeficiency virus in the United States: progress and challenges. *The Journal of the American Medical Association*. 300, 945-951.

MARKETPLACE EXAMPLE: Veterans Administration Changes Paradigm on HIV Screening

VA Offers Resources for Patients, Providers

Patient Information: <http://www.hiv.va.gov/vahiv?page=pt-home>

Provider Information: <http://www.hiv.va.gov/vahiv?page=pr-home>

One of the nation's leading health care organizations, the U.S. Department of Veterans Affairs Veterans Health Administration (VHA), has moved from risk-based HIV screening to routine testing. The VHA provides health care benefits to 5.5 million veterans.

"Research shows that proper treatment can extend the life of people with HIV infection," said David Ross, MD, PhD, director of Clinical Public Health Programs for the Department of Veterans Affairs Public Health Strategic Health Care Group. "State-of-the-art treatment for HIV/AIDS can extend the life of a patient with HIV or AIDS by a dozen years or more which can be longer than treating patients for heart disease or lymphoma," he said. "This is why routine HIV screening is so important."

Beginning August 17, 2009¹, the VHA only requires patients to provide verbal informed consent for HIV testing. This eliminates the lengthy process of providing pre-test and post-test counseling and securing written consent. Providers give HIV infection and HIV testing educational materials to each patient when requesting consent for the HIV test. This policy is consistent with the U.S. Centers for Disease Control and Prevention guidelines.

Screening Raises Awareness

"People who don't get tested don't think they are at risk for HIV," said Ross. "When a person tests positive for HIV, we can begin treatment at any of the VHA's 150 health care facilities and 900 outpatient clinics. Although not low enough, our HIV/AIDS death rate is dropping as a result of early detection and treatment," reported Ross. "The incidence of HIV-related infections also is dropping."

Drug therapy is one component of comprehensive treatment of HIV/AIDS. The VHA national formulary includes all U.S. Food and Drug Administration-approved drugs to treat HIV/AIDS. Ross reports that newly approved HIV/AIDS drugs are added to the formulary rapidly after FDA approval.

"If HIV test results are negative, we take the opportunity to help keep our patients healthy," said Ross. "Our providers can refer patients to whatever services they may need to manage substance abuse or other behaviors that potentially put them at risk for contracting the HIV infection. The VA's goal is to test all veterans at least once for HIV."

Additional online resources for patients and consumers are listed below.

Patient Resources on Screening, Testing

English

Center for Disease Control National HIV and AIDS Testing Resources
<http://www.hivtest.org/>

Medline article on ELISA/Western blot tests for HIV
<http://www.nlm.nih.gov/medlineplus/ency/article/003538.htm>

Spanish

Center for Disease Control National HIV and AIDS Testing Resources
http://www.hivtest.org/index_sp.cfm

Medline article on ELISA/Western blot tests for HIV
<http://www.nlm.nih.gov/medlineplus/spanish/ency/article/003538.htm>

Global assessment of testing policies in transition
http://www.phac-aspc.gc.ca/aids-sida/publication/hivtest/pdf/hivtest_e.pdf

MARKETPLACE EXAMPLE: Plan Design, Formulary Support Access to Treatment Options

Medical oversight of HIV/AIDS is increasingly complex. Plan design tools such as closed formularies, step therapy, and other utilization management techniques may create unnecessary barriers to care.

“The long-term nature of HIV/AIDS makes preserving physician choice of treatment regimens very important,” says Ed Pezalla, MD, national medical director for Aetna Pharmacy Management. Aetna is a managed care company that provides pharmacy care to 11.2 million members and medical care to 19.1 million members.

“Aetna does not want to create any barriers to HIV/AIDS treatment,” says Pezalla. “It is up to the prescriber to identify the best drug therapy for their patients. The majority of Aetna HAART prescribers are practitioners that specialize in treatment of HIV/AIDS. The disease, similar to oncology, is too difficult to manage in a tightly controlled environment.”

Formulary Strategy

“About three years ago, Aetna had a majority of HIV/AIDS drugs on third tier with some utilization controls in place,” says Dawn Erdman, RPh, pharmacy clinical program manager for Aetna Pharmacy Management.

“Our new strategy is to preserve treatment options by placing most of our drugs on formulary status,” she says. “Drugs placed on specific tiers are based upon treatment guidelines from the National Institutes of Health, which are reviewed every year.” Now Aetna has most anti-retroviral agents on formulary as preferred drugs. Except for quantity limits, there are not a lot of controls on utilization.

Aetna Pharmacy Management has been dispensing HIV/AIDS at retail and mail but is now including specialty pharmacy as well in an effort to increase case management service for HIV/AIDS patients. Case management services are provided on both the medical and pharmacy side. Medical and pharmacy use the same system to share notes from disease management and other programs. There is a pharmacist consultation on the pharmacy side to counsel patients on side effects, how to take their medications, and other drug-drug interaction questions. Case management activities on the medical side focus on provider issues and depression.

Call to Action

HIV infection is preventable if our health care organizations work together to screen for the disease and treat it effectively when present. It is critical for all managed care organizations to:

- Support opt-out screening and early diagnosis in concert with CDC guidelines
- Collaborate to increase adherence by managing side effects effectively and proactively
- Adopt lessons learned from disease management and case management protocols from other chronic conditions to support prescribers, pharmacists, and patients involved in HIV/AIDS care
- Monitor medical care and drug treatment together in a comprehensive way to ensure people with HIV/AIDS get quality, ongoing health care services

Online Resources for MCOs

American Academy of HIV Medicine
Association Website for Clinicians
<http://aahivm.org/>

Educational Website
<http://www.thebody.com/content/art33168.html>

HIV ePharmacotherapy Network
University at Buffalo School of Pharmacy and
Pharmaceutical Sciences
<http://www.hiv.buffalo.edu/>

HIV Medical Association
<http://www.hivma.org/>

Infectious Diseases Society of America
Patient Resources for People Living With HIV/AIDS
<http://www.idsociety.org/Content.aspx?id=1840>

Johns Hopkins AIDS Service
Includes downloads for handheld devices
<http://www.hopkins-aids.edu/>

Tufts School of Medicine
Resources on role of good nutrition in living with HIV/AIDS
<http://www.tufts.edu/med/nutrition-infection/hiv/>

The terms below are defined to help readers. A comprehensive reference, *Glossary of HIV/AIDS-Related Terms* published by the U.S. Department of Health and Human Services, is online at www.aidsinfo.nih.gov.

Acquired immunodeficiency syndrome (AIDS) – A disease of the body’s immune system, caused by the human immunodeficiency virus (HIV), characterized by the death of CD4 cells. CD4 cells are an important part of the body’s immune system.

CD4 cell – CD4 cells also are known as helper T cells or CD4 lymphocytes. They are a type of infection-fighting white blood cell. The CD4 cell count is used to determine when to initiate antiretroviral therapy or opportunistic infection prophylaxis.

Entry/Fusion inhibitors – A type of antiretroviral drug that blocks HIV entry into cells.

Highly active antiretroviral therapies (HAART) – Six classes of prescription drugs used to aggressively suppress HIV replication and progression of HIV disease. The typical HAART regimen combines three or more anti-HIV drugs.

Human immunodeficiency virus (HIV) – The virus that causes acquired immunodeficiency syndrome (AIDS). Part of the retrovirus family, two types of HIV have been identified. HIV-1 is responsible for most infections in the world. HIV-2 is primarily found in West Africa.

Integrase inhibitors – A type of antiretroviral drug that disables integrase, a protein HIV uses to insert its viral genetic material into the DNA of an infected cell.

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) – A type of antiretroviral drug that binds to and disables reverse transcriptase, a protein HIV needs to replicate itself.

Nucleoside/Nucleotide reverse transcriptase inhibitors (NRTIs) – A type of antiretroviral drug that inhibits the reverse transcription process by mimicking the cellular material HIV needs to replicate. When HIV uses an NRTI instead of a normal building block, virus reproduction is stalled.

Prophylaxis – Treatment to prevent onset of a disease or set of symptoms.

Protease inhibitors (PIs) – A type of antiretroviral drug that disables protease, a protein HIV needs to replicate.

Treatment-experienced patients – Individuals that have taken antiretroviral therapy, usually with development of drug resistance.

Treatment-naïve patients – Term used to describe individuals who have not taken antiretroviral therapy.

Viral load (VL) – The amount of HIV RNA in plasma. VL is an important indicator of how well antiretroviral therapy is working.

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- ⁴ Coffey, S. (2008, November). Comprehensive Guideline Summary. AIDS Education and Training Centers National Resource Center, 8. Retrieved June 12, 2009 at http://aidsetc.org/ppt/p02-et/guidelines/nrc_adultcomppline_11-08.ppt#332,8,Goals of Therapy and Tools to Achieve Goals.
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