HIV Update: An Epidemic Transformed

An evidence-based review of new developments in HIV treatment and prevention.

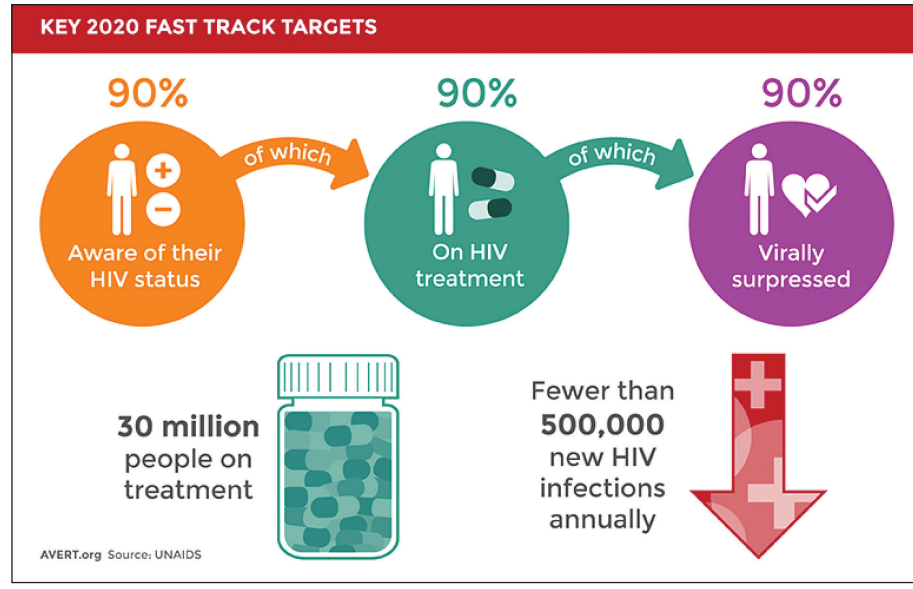
ABSTRACT: The field of HIV treatment and prevention has evolved rapidly over the past four decades. New therapies that are more potent and streamlined have transformed HIV into a chronic disease, while the use of such preventive strategies as preexposure prophylaxis and postexposure prophylaxis provide effective options for reducing the risk of HIV infection. These medical breakthroughs have enabled more people living with HIV (PLWH) to reach older adulthood. But they also mean that nurses are seeing more PLWH who have developed long-term complications of living with HIV or of exposure to antiretroviral therapy, as well as concurrent chronic conditions associated with advanced age. Nurses play a critical role in caring for PLWH and those at risk for HIV infection. This article discusses HIV epidemiology, describes the current state of HIV treatment and prevention, and highlights common comorbidities often seen in PLWH who are over age 50.

Keywords: HIV, older adults, PEP, postexposure prophylaxis, preexposure prophylaxis, PrEP, prevention, treatment

"I wasn't supposed to be here," said John Marchese to the nurse as he watched the last few drops of his chemotherapy drug infuse into the port implanted in his chest. (This case is a composite based on my experience.) The nurse caring for him smiled while preparing to disconnect his IV tubing and flush the port. Mr. Marchese, age 69, was finishing his last round of chemotherapy for stage II lung cancer. He, like many other patients the nurse had recently cared for, had several additional chronic conditions, including type 2 diabetes, hyperlipidemia, and coronary artery disease. What distinguished Mr. Marchese from the nurse's other patients was that he had been living with HIV for 32 years. But given the tremendous advances in the treatment and prevention of HIV over the past several decades, patients like Mr. Marchese are no longer a rarity.

Nearly 38 years after the Centers for Disease Control and Prevention (CDC) reported that five young, white, previously healthy gay men in Los Angeles had been diagnosed with pneumocystis pneumonia and other infections suggestive of immune dysfunction,[1] significant progress has been made in the management and prevention of what is now known as HIV infection. The availability of effective HIV antiretroviral therapy (ART) has transformed a disease that once meant an early death into a chronic illness. Today, a 20-year-old diagnosed with HIV infection is estimated to have a life expectancy of more than 70 years.[2] As new HIV treatments and novel preventive

interventions have been developed, the mean age of people living with HIV (PLWH) has risen, and nurses continue to play a vital role in all aspects of patient care. This article reviews current epidemiologic trends in HIV, summarizes the latest information on ART, highlights common comorbidities (particularly among older PLWH), and describes the latest options in HIV prophylaxis.



The 90–90–90 targets for HIV–AIDS treatment and prevention were set in 2014 by the Joint United Nations Programme on HIV/AIDS (UNAIDS), which aims to achieve all three by 2020. Image © Credit-Avert.org. Source: UNAIDS.

EPIDEMIOLOGIC TRENDS

CDC data from 2015 suggest that nearly 1.13 million people ages 13 and older living in the United States have diagnosed or undiagnosed HIV infection, the majority (56%) of whom are males who acquired HIV through sex with another male.[3] Females account for roughly 23% of all HIV cases, with 78% having acquired the virus through heterosexual sex. The racial and ethnic breakdown is as follows:

- black, 42%
- white, 30%
- Hispanic or Latino, 22%
- multiracial, 4%
- Asian, 1%
- other, less than 1%

U.S. mortality rates (reflecting deaths from any cause) among people with a diagnosis of HIV have gradually declined in recent years, from 5.2 per 100,000 in 2012 to 4.8 per 100,000 in 2016.[4] During this period, HIV-associated deaths declined from 7,216 in 2012 to 6,160 in 2016.[5,6]

An overall decline in U.S. incidence. The annual incidence of new HIV diagnoses in the United States dropped from 41,180 in 2012 to 38,281 in 2017, representing a decrease of 7%.[4] Although there were reductions during this period in all major risk groups, including men who have sex with men (MSM), people who inject drugs, and heterosexuals, diagnoses increased among the following ethnic groups: American Indians and Alaska Natives, Asians, and those of Hispanic or Latino origin.

U.S. incidence among MSM. In 2017, MSM remained the population most affected by HIV in the United States and its six dependent areas (Puerto Rico and the U.S. Virgin Islands, among others), accounting for 66% of all HIV diagnoses (25,748/38,739) and 82% of HIV diagnoses among males (25,748/31,239).[4] Between 2012 and 2016, the incidence of HIV among MSM varied by race and ethnicity, increasing 12% among Hispanics or Latinos, remaining stable among blacks, and decreasing 14% among whites.[7] It has been estimated that the lifetime risk of acquiring HIV for MSM in the following ethnic groups is[8]

- one in two among blacks.
- one in five among Hispanics or Latinos.
- one in 11 among whites.

U.S. incidence by age and sex. In 2016, adults ages 20 through 29 accounted for the largest percentage (about 37%) of new HIV infections in the United States and its six dependent areas, while people over age 50 accounted for about 17% of new infections that year, most of whom (41%) were age 54 or younger.[4] Nearly 19% of new HIV infections in 2017 occurred in female adults and adolescents, with more than half (59%) diagnosed in black women who acquired HIV through heterosexual contact.[4] The lifetime risk of acquiring HIV has been estimated to be one in 253 for females and one in 68 for males.[8]

Among transgender populations, data on HIV incidence and prevalence are limited, but a recent analysis found that between 2009 and 2014 more than 2,300 transgender women and men were newly diagnosed with HIV, with transgender women accounting for 84% of cases.[9]

THE HIV CARE CONTINUUM: A GLOBAL GOAL

The process of screening for and diagnosing HIV, initiating ART in people with newly diagnosed HIV, and reducing their viral loads to undetectable levels is often referred to as the "HIV care continuum."[10] In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) launched the following 90–90–90 targets, with the aim of achieving all three by the end of 2020[11]:

- 90% of PLWH will know their HIV status
- 90% of PLWH who know their status will be receiving treatment
- 90% of PLWH who are receiving treatment will achieve and maintain viral suppression, with some countries requiring viral loads to be undetectable for reporting purposes

The continuum provides a framework for assessing the care of PLWH. At the end of 2016, seven countries had achieved this ambitious goal: Botswana, Cambodia, Denmark, Iceland, Singapore, Sweden, and the United Kingdom.[11] Progress continues to be made worldwide, but in the United States only 86% of all PLWH are aware of their HIV status, 63% receive HIV treatment, and 49% have an undetectable viral load.[10]

Many factors can influence the success of meeting the targets along the continuum, including stigma, income, race, and mental health or substance use comorbidities.[12-14] Nurses can help patients meet targets in all phases of the continuum by

- normalizing and advocating for routine HIV testing.
- providing outreach and support to people who may be reluctant or unable to seek medical care.
- promoting adherence in patients receiving ART so they may keep their HIV viral load at an undetectable level.

Table 1. Approved HIV Antiretroviral Therapy for the Treatment of HIV-1 Infection[a]

Drug Class	Generic Name	Trade Name
Nucleoside/ nucleotide reverse transcriptase inhibitor (NRTI)	Abacavir	Ziagen
	Didanosine	Videx
	Emtricitabine	Emtriva
	Lamivudine	Epivir
	Stavudine	Zerit
	Tenofovir alafenamide	Vemlidy
	Tenofovir disoproxil fumarate	Viread
	Zidovudine	Retrovir
Integrase strand transfer inhibitor (INSTI)	Bictegravir	Available only as a component of Biktarvy
	Dolutegravir	Tivicay
	Elvitegravir	Vitekta
	Raltegravir	Isentress
Protease inhibitor	Atazanavir	Reyataz
	Darunavir	Prezista
	Fosamprenavir	Lexiva
	Indinavir	Crixivan
	Lopinavir	Available only as a component of Kaletra
	Nelfinavir	Viracept
	Ritonavir	Norvir
	Saquinavir	Invirase
	Tipranavir	Aptivus
Nonnucleoside reverse transcriptase inhibitor (NNRTI)	Delavirdine	Rescriptor
	Doravirine	Pifeltro
	Efavirenz	Sustiva
	Etravirine	Intelence
	Nevirapine	Viramune
	Rilpivirine	Edurant
Entry inhibitor	Enfuvirtide	Fuzeon
	Maraviroc	Selzentry
CD4-directed postattachment HIV-1 inhibitor	Ibalizumab	Trogarzo

[a]For a list of FDA-approved single-tablet regimens, see https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/536/coformulated-single-tablet-regimens.

NEW PARADIGMS AND OPTIONS IN ART

Since combination ART for HIV became widely available in the mid-1990s, treatment options and clinical guidelines that inform practice have continued to evolve. The U.S. Department of Health and Human Services (HHS) updates guidelines for HIV management every six to 12 months. Recent approvals of new drug classes and clinical trial data have transformed HIV care.

The benefits of ART have been well documented and include preserved immune function, improved quality of life, and reduced risk of HIV transmission.[15] However, the answer to the question of how soon after diagnosis should ART be initiated has varied throughout the years.

Earlier ART guidelines used CD4+ cell counts and HIV viral load as indicators for initiating treatment. ART was recommended only for those whose CD4+ cell count fell below 350 cells/mm^3. The rationale for delaying ART was to limit exposure to possible treatment-related adverse effects of early-generation therapy, such as the nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) azidothymidine, or AZT (now called zidovudine [Retrovir]); the protease inhibitors saquinavir (Invirase), ritonavir (Norvir), nelfinavir (Viracept), and indinavir (Crixivan); and the entry inhibitor enfuvirtide (Fuzeon). These

were used in older regimens requiring multiple tablets and multiple day dosing and were associated with such adverse effects as body fat redistribution (lipodystrophy), insulin resistance, anemia, kidney stones, gastrointestinal problems, lactic acidosis, and peripheral neuropathy. This "wait and watch" paradigm has been abandoned and ART is now recommended regardless of CD4+ cell count or viral load.[16]

The START (Strategic Timing of Antiretroviral Therapy) study was a major factor in revising the ART recommendations. START was a large, international trial in which a group of PLWH who had CD4+ cell counts of at least 500 cells/mm^3 were randomly assigned either to receive ART immediately or to follow what in 2011 was the standard of care for initiating ART—that is, to defer treatment until their CD4+ cell counts fell to 350 cells/mm^3 or they developed AIDS or another condition for which ART was then indicated.[17, 18] Those who started ART at higher CD4+ cell counts had a 54% lower mortality rate than those who deferred therapy. Data from the START trial and other similar studies led to the revision of the ART guidelines, and in 2018 the HHS published *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*, which specify no CD4+ cell count or viral load prerequisites for the receipt of ART, calling for all PLWH to receive it.[16]

Rapid start. More recently, the idea of initiating ART regardless of CD4+ cell count has been further modified. Referred to as "rapid start," this model recommends initiating ART on or as close as possible to the day of HIV diagnosis—and it has shortened the length of time it takes a person to achieve virologic suppression of HIV. At San Francisco's Rapid ART Program Initiative for HIV Diagnoses (RAPID), the protocol is to initiate ART in all PLWH within five days of HIV diagnosis unless the person is at risk for fatal immune reconstitution inflammatory syndrome.[19] Time from diagnosis to first undetectable viral load dropped from 134 days in 2013 to 61 days in 2016.[19] This 54% reduction suggests the benefit and success of rapid start as a means of engaging people in care, reducing HIV transmission in the community, and supporting the goals of the HIV care continuum. Although the recommendations regarding ART initiation have changed, the patient counseling, education, and support provided by nurses are still vitally important in promoting treatment adherence and engagement in care.

NEW DRUG CLASSES AND TREATMENT OPTIONS

Currently, there are six classes of antiretroviral drugs, and more than 20 different antiretroviral agents are approved by the U.S. Food and Drug Administration (FDA) for HIV treatment (see Table 1). Over the years, HIV therapy options have improved significantly. Today, many PLWH can be treated with a single-tablet regimen, rather than with a complex regimen involving multiple pills taken several times a day. Although single-tablet regimens may not be suitable for all PLWH, most people with newly diagnosed HIV may now choose among several such regimens.

Table 2. HHS Guidelines Preferred First-Line Antiretroviral Therapy for Most People Living with HIV[16]

Bictegravir–Tenofovir AF–Emtricitabine (Biktarvy)[a]
Dolutegravir (Tivicay) **with either** Tenofovir AF–Emtricitabine (Descovy)[b] **or** Tenofovir DF–Emtricitabine (Truvada)[c]
Dolutegravir–Abacavir–Lamivudine (Triumeq)[a]
Raltegravir (Isentress) **with either** Tenofovir AF–Emtricitabine (Descovy)[b] **or** Tenofovir DF–Emtricitabine (Truvada)[c]

AF = alafenamide; DF = disoproxil fumarate; HHS = Department of Health and Human Services.
[a] This is a single tablet regimen.
[b] Creatinine clearance must be > 30 mL/min.
[c] Creatinine clearance must be > 60 mL/min.

The HIV treatment paradigm has for the last two decades called for the use of at least three different drugs from two different drug classes. For most PLWH, the initial therapy has included two NRTIs plus a drug from another class, usually an integrase strand transfer inhibitor (INSTI). (See Table 2.[16]) Alternatively, a protease inhibitor or a nonnucleoside reverse transcriptase inhibitor (NNRTI) could be used as the third agent.[16] NRTIs and INSTIs work by inhibiting the production of reverse transcriptase and integrase, respectively, two key enzymes needed for the virus to reproduce. In recent years, however, potential long-term adverse effects associated with some NRTIs, such as renal and cardiovascular disease, as well as reduced bone mineral density, have raised concerns.[20-22] Subsequently, NRTI-sparing options have received more attention.

NRTI-sparing options. In 2017, a pill combining an INSTI with an NNRTI, dolutegravir–rilpivirine (Juluca), was the first NRTI-sparing, single-tablet regimen approved by the FDA as a replacement ART for PLWH whose viral loads were undetectable. In such patients, study data showed this combination to be as effective as the traditional three-drug ART regimens while minimizing NRTI toxicities and limiting drug–drug interactions.[23] The tablet is taken once daily with food and should not be used in conjunction with proton pump inhibitors, which can significantly lower rilpivirine plasma concentrations, thereby reducing virologic response.[24]

A new advisory regarding dolutegravir, which is available as a stand-alone agent (Tivicay) and is a component of Juluca, as well as of two other single-tablet regimens—dolutegravir–abacavir–lamivudine (Triumeq) and dolutegravir–lamivudine (Dovato)—

was issued in May 2018.[25] Higher rates of neural tube defects were noted in pregnant women receiving dolutegravir-containing regimens, and as a result women with HIV who were pregnant or thinking of becoming pregnant were advised to consider an alternative HIV regimen. New data, however, suggest that this risk is significantly lower than initially thought, prompting the World Health Organization to recommend dolutegravir as the preferred HIV treatment in all populations, including pregnant women.[26]

Pharmacokinetic boosters. Some ART regimens require a pharmacokinetic boosting agent, which reduces dosing frequency, often allowing for once-daily dosing.[16] The two boosting agents most often used are the cytochrome P-450 3A inhibitor cobicistat (Tybost) and the protease inhibitor ritonavir.[16] Pharmacokinetic boosters should be used with caution because they increase the likelihood of drug–drug interactions.[27] Although it is always important to review all patient prescriptions and over-the-counter medications, it is particularly so when counseling patients on an ART regimen that includes a boosting agent.

The CD4-directed postattachment HIV-1 inhibitor ibalizumab (Trogarzo) is effective against multidrug-resistant HIV,[28] which is estimated to affect fewer than 5% of people receiving ART.[29] Recently approved by the FDA, ibalizumab is used in combination with other antiretrovirals and is administered by IV infusion every two weeks.[28] The most common adverse effect is diarrhea, which affects about 20% of patients. Other adverse effects include dizziness and rash, which affect about 13% of patients, as well as nausea, fatigue, and pyrexia. Most adverse effects (87%) are mild to moderate in severity.[28]

The newest FDA-approved medication is Dovato, the single-tablet INSTI–NRTI regimen. It is currently indicated for PLWH who have no prior history of ART. Although the tablet's two components (dolutegravir and lamivudine) are not new, combining two drugs from different classes in a single tablet is part of the new paradigm, which moves away from the more common triple-drug regimen.[30, 31]

COMORBIDITIES AMONG OLDER PLWH

CDC data indicate that 47% of PLWH in the United States were age 50 or older in 2015.[32] In the coming decade, the percentage of PLWH over age 50 is expected to rise.[2] The aging of this population means health care providers are increasingly likely to see PLWH presenting with comorbidities that historically have not been associated with HIV, such as cardiovascular disease, chronic kidney disease, type 2 diabetes, cancer, and other noncommunicable diseases that become more common in advanced age. Some research suggests that, in addition to advanced age, excess morbidity among older PLWH may be due to long-term effects of inflammation and immune dysregulation brought on by HIV or to potential long-term effects of ART.[33]

Cardiovascular disease. Recent findings suggest that PLWH may be at greater risk for cardiovascular diseases, including myocardial infarction, atherosclerotic disease, dyslipidemia, and stroke, than people without HIV.[34, 35] Although the reasons for these differences are not clear, it has been suggested that the inflammatory effects of chronic HIV infection may accelerate atherosclerosis.[34, 35]

The NRTI abacavir (Ziagen) has been associated with higher rates of cardiovascular events compared with other NRTIs.[36] The current HHS treatment guidelines recommend limiting the use of abacavir in people who are at elevated risk for cardiovascular disease, such as those who are obese or have hypertension.[16] In PLWH who have heart disease or are at elevated risk for it, management is similar to that in people without HIV: reducing risk by using statins, eating a healthy diet, exercising, maintaining a healthy weight, and not smoking.[37]

Chronic kidney disease commonly affects PLWH, with the estimated prevalence exceeding 50% in some studies.[38] The development of chronic kidney disease in this population has been attributed to such factors as ART, hypertension, and type 2 diabetes.[39] Clinicians should monitor their patients' renal function closely and adjust the dosage of ART and other medications accordingly. For people with more advanced chronic kidney disease, organ transplants are becoming more widely available. PLWH undergoing kidney transplants have had similar outcomes to those of HIV-uninfected people undergoing kidney transplants.[40]

Type 2 diabetes rates have been found to be higher in PLWH than in people without HIV, with prevalence estimated as nearly 4% higher in PLWH, who may develop type 2 diabetes in the absence of obesity and at earlier ages than those without HIV.[41] Although use of ART has been associated with higher rates of type 2 diabetes in PLWH, characteristics such as obesity remain a risk factor. Detection and screening for type 2 diabetes are similar among PLWH and those without HIV, though some data suggest that measuring glycated hemoglobin may underestimate the prevalence of type 2 diabetes in PLWH, whereas the use of oral glucose tolerance testing may be more accurate in identifying type 2 diabetes in these patients.[42] There are no specific diabetes management guidelines for PLWH; treatment recommendations for oral or injectable glucose-lowering medications and therapeutic goals for glycemic control are the same for PLWH as for people without HIV.

Malignancies. A recent analysis of mortality rates among nearly 47,000 people living in North America who were receiving ART for HIV between 1995 and 2009 found that 9.8% of deaths in this cohort were attributable to cancer—2.6% to AIDS-defining

cancers (such as Kaposi sarcoma and non-Hodgkin lymphoma) and 7.1% to non–AIDS-defining cancers (such as lung and liver cancers), generating cancer-attributable mortality rates of 86 and 239 per 100,000 person-years, respectively.[43] Lung cancer, liver cancer, and non-Hodgkin lymphoma accounted for a large proportion of the cancer-associated deaths. The investigators concluded that, even as AIDS mortality rates and deaths due to AIDS-defining cancers decline among PLWH, deaths due to non–AIDS-defining cancers may rise.[43] Since smoking and infection with such oncogenic viruses as hepatitis C, hepatitis B, and human papillomavirus are more prevalent among PLWH, interventions to reduce the cancer burden may include promoting smoking cessation and vaccination for these viruses.[44]

Neurologic changes. *HIV-associated neurocognitive disorder* is a cluster of neurologic conditions, whose overall prevalence is estimated to range from 20% to 55%.[45] The various manifestations include asymptomatic neurocognitive impairment, mild neurocognitive disorder, and HIV-associated dementia. Since the introduction of combination ART, the most serious form, HIV-associated dementia, has become rare, but the milder forms remain common and symptoms can slowly progress from difficulty with concentration, memory, and executive function to psychomotor slowing and affective symptoms such as depression and irritability. Data suggest that PLWH who develop HIV-associated neurocognitive disorder have lower long-term survival rates. Although various nonantiretroviral agents, such as memantine (Namenda), have been used to treat HIV-associated neurocognitive disorder, none has shown clear clinical benefit.[45] Exercise has been shown to provide modest improvement in cognitive function among PLWH.[46] But ART remains the greatest protection against HIV-associated neurocognitive disorder and should be initiated in all PLWH who are not currently receiving it—not only to prevent neurocognitive decline, but to help PLWH achieve undetectable viral loads.

Peripheral neuropathy. Some PLWH who started receiving early-generation ART long ago may develop painful peripheral neuropathy. A recent analysis estimated its prevalence in PLWH to be approximately 31%, with risk factors including advanced age, higher CD4+ cell counts, and tobacco use.[47] Management of peripheral neuropathy involves limiting or stopping any medications that may worsen neuropathic symptoms and initiating the use of medications known to relieve neuropathic pain, such as gabapentin (Neurontin) or tricyclic antidepressants.

CARING FOR OLDER PLWH

Nursing considerations for the aging population of PLWH are focused on preventing and reducing the effects of noncommunicable comorbidities. Patient teaching should stress the importance of the following:

- tobacco cessation
- nutritional recommendations for reducing risk of heart disease
- age-related cancer screenings
- medication adherence
- receiving vaccines for oncogenic viral infections, such as hepatitis C, hepatitis B, and human papillomavirus

Reviewing medication lists for drug–drug interactions and assessing and monitoring patient pain levels can also improve the health and quality of life for older PLWH.

Table 3. Baseline Evaluation for PrEP[15]

Laboratory Testing	Education and Counseling
• HIV antigen–antibody • Creatinine • Hepatitis A, B, C serology • Urinalysis • Pregnancy • Gonorrhea and chlamydia (consider oral, urine, cervical, and rectal testing based on type of exposure) • Syphilis	• Truvada should be taken daily. • Truvada does not protect against other sexually transmitted infections; barrier methods should still be used. • Teach patients about signs and symptoms of acute HIV infection. • Reinforce importance of follow-up appointments every 90 days.

PrEP = preexposure prophylaxis.

HIV PREVENTION

Just as HIV treatment has evolved, so too has the field of HIV prevention. While traditional preventive measures such as the use of barriers to prevent sexual transmission and routine HIV testing are still important, new biomedical preventive options are now available. The use of preexposure prophylaxis (PrEP) and postexposure prophylaxis (PEP) have given patients and providers more opportunities to curb the spread of HIV infection.

PrEP. The availability of PrEP, which reduces the risk of acquiring HIV, has played a pivotal role in curbing the HIV epidemic. Currently, the only FDA-approved form of PrEP is the single-tablet regimen Truvada, containing the NRTIs tenofovir disoproxil fumarate and emtricitabine. Traditionally, these two NRTIs have been used to treat HIV in combination with other antiretrovirals. However, in July 2012, the FDA approved use of Truvada as part of a comprehensive prevention strategy for adults and adolescents who are not infected with HIV and weigh at least 35 kg (77 lbs).[15,48] Truvada is taken orally once daily, with or without food. Use of PrEP may benefit people who[15]

- have multiple sex partners.
- were recently diagnosed with a sexually transmitted infection.

PEP for Health Care Workers[55]

- Occupational transmission of HIV to health care workers is rare.
- The risk of HIV transmission after percutaneous exposure to HIV-infected blood has been estimated to be 0.3%.
- Use of safety devices (for example, gloves, goggles, needleless systems, safety caps, and retractable needle systems) can minimize the risk of needlestick injuries.
- Health care workers who are exposed to a needlestick should be evaluated as soon as possible after the incident.
- Treatment with ART should begin as quickly as possible after exposure, but no more than 72 hours after exposure.
- The duration of PEP is four weeks.
- Whenever possible, the HIV status of the source patient should be determined to guide the appropriate use of PEP.
- Health care workers should be counseled to take precautions (for example, use barrier methods during sexual contact, do not donate blood or tissue, avoid pregnancy and breastfeeding if possible) to prevent secondary transmission, especially during the first six to 12 weeks after exposure.
- For health care workers started on PEP, HIV testing should occur at baseline, six weeks, and four months after exposure if a combination HIV antigen–antibody test is used for monitoring.

ART = antiretroviral therapy; PEP = postexposure prophylaxis.

- report inconsistent condom use.
- were recently prescribed nonoccupational PEP.
- inject drugs or share drug-use paraphernalia.

Efficacy of Truvada in reducing HIV infection in at-risk populations has been shown to be about 99%, with the greatest benefit among people who demonstrated regular adherence to therapy.[49, 50] It is important for people taking PrEP to have their HIV status monitored regularly to ensure they remain uninfected. Patients must be HIV uninfected to be eligible for PrEP, and before starting PrEP, the patient's HIV-negative status must be confirmed. Any patients experiencing flu-like symptoms, which may be suggestive of acute HIV infection, should defer PrEP until their HIV status can be confirmed and other baseline laboratory testing performed.[15] (See Table 3.[15]) Since tenofovir disoproxil fumarate can affect renal function, patients with a creatinine clearance of less than 60 mL/min should not be prescribed Truvada.[15]

The components of Truvada are also active against hepatitis B, so PLWH who have chronic hepatitis B and discontinue PrEP need to be monitored closely because they may experience a hepatitis B flare-up. Although pregnancy is not a contraindication for Truvada, there are insufficient data on its use as an HIV prophylaxis during pregnancy. Providers are encouraged to report pregnant patients receiving Truvada to the antiretroviral pregnancy registry to monitor and document birth outcomes. U.S. Public Health Service guidelines recommend that patients who initiate Truvada for PrEP return every three months for screening and monitoring.[15]

Although PrEP has been available in the United States since 2012, uptake has been limited. One study estimates that of the 1.2 million people who would benefit from PrEP, only 5% are receiving it.[51] And though MSM and heterosexual adults who are black make up the largest group with PrEP indications, only a small percentage of this group uses PrEP.[52] Factors that limit more widespread PrEP use include the following[14, 53]:

- lack of awareness among both clinicians and patients that Truvada is available for prevention
- internalized stigma related to sexual practices, sexual identity, or race
- patients' fear of being perceived as sexually promiscuous
- providers' discomfort discussing patients' sexual history
- poverty, lack of insurance coverage, and inequities in Medicaid and health care access programs

Although most insurance companies cover Truvada for PrEP, copayments vary considerably, putting the cost of the medication, which can be as high as $2,000 per month, out of reach for many patients.[54] However, a number of states, patient advocate programs, and the manufacturer have established copay and medication assistance programs. The National Alliance of State and Territorial AIDS Directors has compiled an online information page detailing the assistance these programs offer and eligibility requirements (see www.nastad.org/prepcost-resources/prep-assistance-programs). A generic version of Truvada for PrEP will be available in September 2020. Patient advocates are cautiously optimistic that this may lower the cost for U.S. consumers.[54]

A new PrEP alternative—emtricitabine–tenofovir alafenamide (Descovy), which is currently approved only for HIV treatment—is expected to receive FDA approval this fall.

PEP. Nonoccupational PEP is prescribed as a means of reducing the risk of HIV infection in people who have been potentially exposed to HIV outside of a health care setting—for example, people who have an isolated high-risk exposure (such as an unplanned condomless sexual encounter) and who are not receiving PrEP. Nonoccupational PEP is similar to the PEP provided to health care workers who have been potentially exposed to HIV through a needlestick or a patient's bodily fluids (see *PEP for Health Care Workers*[55]).

PEP involves taking ART for 28 days following HIV exposure to help reduce or minimize the risk of infection. The most common regimen for PEP is Truvada with an INSTI, either raltegravir (Isentress) or dolutegravir. This intervention needs to be initiated as

soon as possible after the exposure, but no more than 72 hours afterward.[56] Unlike PrEP, the use of which is supported by several placebo-controlled trials, the evidence for PEP is based on animal models and observational studies. Nonetheless, these studies suggest a reduction in HIV transmission, and PEP is now considered the standard of care for post-HIV exposure.[56]

Baseline laboratory studies upon initiating PEP should include HIV antigen–antibody testing—but treatment with PEP should be started immediately, before the results of the baseline testing are available. Monitoring and follow-up HIV testing are usually conducted at four and 12 weeks after treatment is initiated.[56] During this time, patients should be counseled as follows:

- If engaging in sexual contact, continue to use barrier methods until your HIV status is confirmed at 12 weeks.
- Self-monitor for signs and symptoms of acute HIV infection, which include flu-like symptoms, and report any symptoms to your health care provider as soon as possible.

Nurses can educate and counsel patients who may be at risk for acquiring HIV on the availability of PrEP and PEP to reduce their risk. At the same time, nurses can reinforce the added benefits of using barrier methods during sexual encounters and the importance of obtaining regular screenings for sexually transmitted infections.

'Treatment as prevention' and U=U. Preventing the spread of HIV by helping PLWH maintain an undetectable viral load (defined as fewer than 200 copies/mL) is referred to as "treatment as prevention" or TasP.[57] An observational multicenter study including both heterosexual and MSM couples in which one partner is receiving ART for HIV and the other is HIV negative has shown that the risk of sexually transmitting the virus is negligible to nonexistent if the partner with HIV maintains an undetectable viral load for at least six months.[58] More recently, the National Institute of Allergy and Infectious Diseases also endorsed the "undetectable = untransmittable" campaign, or U=U.[59] This campaign reframes the benefits of ART as it destigmatizes the idea that living with HIV is socially marginalizing. Nurses working with PWLH or with people whose partner is living with HIV can reinforce this message and emphasize the benefits of ART. They can address the issue of sexual health as it relates to the fear of transmitting HIV to others and can advocate for PLWH to receive full access to treatment.

A GLIMPSE INTO THE FUTURE

The future of HIV treatment and prevention is promising. Topical microbicides intended for PrEP are currently under investigation, as well as long-acting injectable ART formulations and implants (similar to long-acting contraceptive implants) that can be used either to treat or to prevent HIV infection.[60] The discovery of a vaccine still eludes scientists, but research continues.

Another area of continuing exploration is the quest for an HIV cure. Until recently, only one patient had been believed to have been cured of HIV. Known as the "Berlin patient," he was cured in 2007 after receiving bone marrow transplants for his leukemia from a donor with a protein mutation called CCR5.[61] This past March, however, a team of infectious disease physicians from the University of Cambridge announced that a second apparent HIV cure had occurred under similar circumstances. A man identified as the "London patient" received a bone marrow transplant for his Hodgkin lymphoma, also from a donor with the CCR5 mutation, after which physicians discovered that the HIV virus had completely disappeared from his bloodstream.[62,63] The patient stopped taking ART 16 months later, and at 18-month follow-up he continued to be free of the virus.

Although researchers point out that bone marrow transplants, which can have fatal complications, are not suitable treatments for the majority of PLWH for whom ART poses far fewer risks, this second case provides hope that for PLWH who require a bone marrow transplant to treat a malignancy, it may be appropriate to search for a donor with the CCR5 mutation.[64]

THE ROLE OF NURSES

As HIV treatment and prevention continue to evolve, nurses are central to all aspects of HIV care, regardless of the clinical setting. It's imperative that nurses working in the acute care setting be able to anticipate and understand the physical and psychological needs of PLWH, who may be admitted for treatment of any number of noncommunicable diseases associated with advanced age, long-term ART, or long-term complications associated with HIV. Nurses working in the community or primary care setting have numerous opportunities to identify patients at risk for HIV infection, informing them of prevention strategies such as PrEP and PEP, and to promote ART adherence among PLWH, while teaching them about strategies to reduce risk factors for other chronic diseases, such as heart disease and diabetes. Working together, nurses and other health care providers can help end the epidemic. ▼

For 17 additional continuing nursing education activities on the topic of HIV, go to www.nursingcenter.com/ce.

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