Test and Treat

Pre-Exposure Prophylaxis

Prevention with Positives

HIGH-IMPACT PREVENTION

The history of fighting HIV in the United States now spans more than 3 decades, and the number of tools that have proven effective at preventing infection is greater than at any time in the past: a safe blood supply; access to condoms; substance abuse screening and treatment; treatment of other sexually transmitted infections; and, in recent years, the introduction of "treatment as prevention."

This and other interventions have helped reduce annual new HIV infections from an estimated high of 130,000 at the height of the AIDS epidemic in the mid-1990s[1] to 50,000 in 2009.[2] Despite the sharp decline in new HIV infections, however, more people are living with HIV than ever before, thanks in part to more potent, better tolerated, and less complex antiretroviral therapy (ART).

As the number of people living with HIV/AIDS (PLWHA) in the United States—now estimated at nearly 1.2 million—continues to rise, the potential for HIV transmission has increased exponentially. To combat this problem, the National HIV/AIDS Strategy mounted a call to action for more intensive and innovative prevention efforts targeting the populations hardest hit by HIV and those at greatest risk of infection, including men who have sex with men (MSM), African-Americans, Hispanics/Latinos, injection drug users, and transgender women.[2,5]

"In addition to efforts aimed at HIV-positive individuals to reduce the risk of HIV transmission to uninfected partners, it has become increasingly clear that we should direct high-impact prevention strategies to those most at risk [for HIV infection]," says Tracy Matthews, director of

DID YOU KNOW?

- HIV prevention saves lives and health care costs.
- HIV testing is covered under the Affordable Care Act.
- The Affordable Care Act also expands coverage for HIV/AIDS treatment.
- From 1991 to 2006, HIV prevention efforts have averted more than 360,000 HIV infections[3] and saved approximately $129.9 billion.[4]

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DIRECTOR'S NOTES

We stand at a turning point in this epidemic, one where we can say with confidence that we can make dramatic reductions in new HIV infections. Although the challenges have not dissipated, we have many prevention, outreach, and treatment strategies in our toolbox, as well as an increased emphasis on shared learning across agencies, States, and communities. If we are to be truly effective in our efforts, we must use every tool at our disposal—and we must use them more efficiently than ever before.

This is what high-impact prevention is all about. It's acknowledging that HIV requires a multifaceted response, as varied as it is persistent. It is an approach that HRSA and the Ryan White HIV/AIDS Program are pursuing with vigor. We are increasing testing and linkages to care efforts. We are targeting areas and populations that are hardest hit by the epidemic. We know that if we can keep people in care and treatment, transmissibility is lowered dramatically, which in turn prevents new infections.

By using every tool we have, from pre-exposure prophylaxis to Test-and-Treat to prevention with positives, we pave an ever-brighter future for people with HIV and help ensure that those at risk for the disease, never receive a positive diagnosis. The next chapter in HIV care is a bright one, so let's pick up our tools and get going.

Laura W. Cheever
Associate Administrator for HIV/AIDS, HRSA

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U.S. Department of Health and Human Services
Health Resources and Services Administration, HIV/AIDS Bureau
5600 Fishers Lane, Room 7–05
Rockville, MD 20857
Telephone: 301.443.1993

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Photographs
Cover: A patient uses a pill box to manage her medications and stay adherent.

Copies are available to be downloaded at www.hab.hrsa.gov.

the Clinical Unit in the Office of the Associate Administrator of the HIV/AIDS Bureau at the Health Resources and Services Administration (HRSA).

Evidence demonstrates that ART can not only hamper the virus's progression in HIV-infected people but also can prevent infections from taking hold among healthy people who are exposed to the virus. The result is that a cornerstone of the Nation's HIV prevention efforts now relies on the same drugs to both treat and prevent HIV/AIDS. This issue of *HRSA CAREAction* focuses on prevention efforts—particularly Test and Treat and Pre-Exposure Prophylaxis (PrEP)—that are taking hold in HRSA-supported communities nationwide.

TEST AND TREAT

Test and Treat is an HIV prevention strategy that aggressively tests people for HIV and, for those found to be HIV positive, provides linkage to care so that they can begin immediate, lifelong ART treatment.

"As more individuals go onto antiretroviral therapy and their viral load is suppressed, the total amount of virus in the community falls, and this reduces the overall danger [of HIV transmission]," explains Bernard Branson, senior advisor for laboratory diagnostics in the Division of HIV/AIDS Prevention at the Centers for Disease Control and Prevention (CDC). "Test and Treat is seen as a method capable [of curbing] the epidemic," says Branson. In the past, "ART typically has been given far too late after the initial infection, [allowing] time for the infected person to pass the virus on to others."

Patients on ART are far less infectious because the drugs sharply suppress the amount of HIV in the body. A recent multi-study review of HIV-discordant heterosexual couples estimated an HIV transmission rate ranging from 0.0 to 0.14 per 100 person years when the HIV-positive partner has an undetectable viral load.[6]

Though a focus on HIV testing is hardly new—the CDC has recommended routine screening for HIV for everyone aged 13–64 as part of regular medical care since 2006—it received a boost in 2012 when the U.S. Preventive Services Task Force, a government-backed group of doctors and scientists, called for routine HIV screening for all Americans aged 15–65.[7] New guidelines from the task force have been released and will expand

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reimbursement for HIV testing, removing one of the barriers to widespread testing. (Under the Affordable Care Act, insurers are required to cover preventive services that are recommended by the task force.)

Additionally, 2012 Federal recommendations stated that all adults and adolescents testing positive for HIV should immediately begin ART treatment, regardless of CD4 count.[8] Previously, many providers waited to initiate ART until evidence showed that the patient's immune system was severely compromised.

The new recommendation, developed by the U.S. Department of Health and Human Service (HHS) Panel on Antiretroviral Guidelines for Adults and Adolescents, a working group of the Office of AIDS Research Advisory Council, was based, in part, on mounting evidence over the past decade of the benefit of ART as a means of prevention. Using treatment as prevention gained greater traction in 2011 when data from a landmark clinical trial known as HIV Prevention Trials Network (HPTN) 052 found that the use of ART in primarily heterosexual HIV-infected individuals could reduce HIV transmissibility by 96 percent. The results were the first from a major randomized clinical trial to indicate that treating an HIV-infected person could reduce the risk of sexual transmission of HIV to an uninfected partner.[9]

HPTN 052, which began enrolling participants in 2005, was conducted at 18 sites in 8 countries on 3 continents. It recruited 1,736 serodiscordant couples, most of whom were heterosexual; 38 male/male couples (3 percent) participated. To be eligible to enroll in the study, the HIV-positive partner had to have a CD4 count between 350 and 550 cells/mm^3 at baseline. Couples were randomly assigned to one of two groups. In the first group, infected partners began receiving antiretroviral drugs right away. In the second group, infected partners waited to start treatment until either their CD4 counts dropped below 250 cells/mm^3 or they developed an AIDS-related illness. All study participants were counseled on how to protect against HIV transmission and were given free condoms and other prevention services.[9] It is important to note, however, that HPTN 052 enrolled stable couples known to be in stable, serodiscordant relationships which may limit the generalizability of the findings.

In the group that waited to start treatment, 27 infections occurred in which the virus was genetically linked to the infected partner. All of these infections occurred while the infected partner was not yet taking antiretroviral drugs. In the group that started treatment right away, only one genetically linked infection occurred. In addition to reducing HIV transmission, beginning treatment right away appeared to be better for patients' health. For example, only 3 cases of tuberculosis (TB) occurred in infected partners who began ART immediately, compared with 17 among those in the group that waited to start treatment—an 82 percent reduction in TB cases.[9]

"One of the justifications for Test and Treat is that the earlier someone gets treated after HIV infection, the healthier he or she will be in the long run," says Branson. "The other argument for Test and Treat is that patients whose HIV is suppressed by medication—to levels undetectable in the blood—are far less likely to pass the virus on to others."

The CDC estimates that approximately 1 in 5 PLWHA are unaware of their infection[1]—a precarious position that not only increases their risk for disease progression and failing health but allows them unknowingly to infect others with the virus. Data suggest that more than 50 percent of new HIV infections are transmitted by the 21 percent of people who are infected with HIV but do not know it.[10]

"Getting people tested so they know their status is a critical first step because once they know their status, they are far less likely to engage in risky activities for transmitting the virus," Branson explains. "The next steps are linking them to care to receive treatment, and then making sure they stay in care."

Unfortunately, a host of barriers exist at each step of the "treatment cascade" that challenge the effectiveness of Test and Treat and that must be addressed before this approach can reach its full potential. (For more information about the treatment cascade, see http://blog.aids.gov/2013/01/new-video-illustrates-hiv-treatment.html). If any component of Test and Treat is incomplete or underused, the entire strategy is likely to be less effective. Common challenges to Test and Treat include the following:

- **Getting tested.** People most at risk for HIV—minority or young MSM and people without access to health care, for example—are often the hardest to

reach for testing. Another problem is identifying people who are newly infected—often soon after having tested negative—and considered hyperinfective. "These people must be retested—[if] possible every couple [of] months," said Branson.

- **Delayed linkage to care.** Thirty-one percent of newly diagnosed persons delay the start of HIV medical care for 6 months or longer.[11] This delay can mean the difference between years of healthy living or poorer health and an earlier death. It also creates a larger window of opportunity for HIV transmission.

  In addition, both a growing body of data and strong anecdotal evidence point to a gap in understanding and practice among doctors concerning when to start HIV-infected patients on ART. A recent study found that only 1 in 7 clinicians immediately began treatment of patients who tested positive.[12]
- **Retention in care.** Retention in HIV care is required for patients to fully realize the benefits of treatment.[13] Early missed visits are common and have been associated in the short term with delayed initiation of ART and in the long term with poor clinical outcomes.[14] To address this issue, HRSA launched the in+care Campaign to help PLWHA remain in or return to care. Learn more about it at www.incarecampaign.org.
- **Adherence.** A recent study found that when HIV-infected individuals start ART, adherence and viral load suppression is great. However, the greatest threat to Test and Treat strategies isn't nonadherence but individual, clinic, and other structural challenges that create larger gaps earlier in the treatment continuum causing many to be lost to care before ever initiating ART.[15] Failure to access ART and achieve and sustain viral load suppression poses an increased risk of HIV transmissibility.[16] To prevent drug resistance and transmission, barriers preventing HIV-infected people from ART must be removed and, once initiated, PLWHA must rigorously adhere to their pill-taking regimen (see sidebar, p. 8, *Adherence, Retention Key to Both Pre-Exposure Prophylaxis and Test and Treat*).
- **Attrition:** One-year attrition has been observed in upwards of 25 to 30 percent of patients following initial enrollment in outpatient HIV care, compromising the potential benefit of Test and Treat strategies.[17,18]

A CDC-led cross-agency study is underway to evaluate the effectiveness of Test and Treat strategies in Washington, DC and the Bronx, two locales with some of the Nation's highest rates of HIV infection. As part of this multi-year study, known as HPTN 065, researchers will also observe expanded testing and linkage activities in four non-intervention communities—Chicago, Houston, Miami, and Philadelphia—to help assess the influence of changing trends in HIV testing and care expansion in the United States.

HPTN 065 is a major protocol with five interlinked components.[19]

- **Expanded HIV testing.** The first component involves social mobilization activities to promote community-wide HIV testing, as well as activities to increase universal HIV screening of both patients seen in hospital emergency rooms and those admitted as hospital inpatients. The goal is to increase the proportion of people who are tested for HIV so that those who are infected will know their status and can be linked to appropriate HIV care. This aspect of the study supplements expanded testing efforts already under way in Washington, DC and the Bronx. To date, activities to expand hospital-based HIV testing are taking place in 16 participating hospitals in Washington, DC and the Bronx. Social mobilization aimed at encouraging MSM to be tested for HIV at least twice a year is taking place via various media outlets in both DC and the Bronx.
- **Linkage to care.** The second component evaluates whether financial incentives (in the form of gift cards) can increase the linkage of HIV-positive people from HIV testing sites to HIV clinics. Half of the 37 participating testing sites will distribute coupons that HIV-positive patients can redeem for gift cards after they have been linked to care in HIV clinics, and the other half are using their usual methods for linking patients to HIV clinics.
- **Viral suppression.** The third study component evaluates whether financial incentives (in the form of gift cards) can increase the number of HIV-positive patients who take their HIV medication in the manner required to achieve and maintain a suppressed viral load. Half of the 39 participating HIV clinics will award the financial incentives to patients who successfully achieve viral suppression, whereas the other half will use standard methods to support ART adherence.

- **Prevention for positives.** The fourth component evaluates a prevention intervention to reduce risk behaviors, such as unsafe sex or injection drug use. Participants at 12 sites will be randomized to receive a computerized prevention intervention or standard-of-care prevention.
- **Patient and provider surveys.** The fifth component of the study involves surveying both HIV-positive patients receiving medical care and HIV care providers to assess their knowledge and attitudes about the use of ART for the treatment and prevention of HIV and the use of financial incentives. A baseline provider survey was successfully completed by 165 ART-prescribing clinicians between September 2010 and May 2011. Baseline data showed that more than half of HIV providers surveyed in Washington, DC and the Bronx now recommend ART for anyone with a CD4 count below 500 cells/mm^3, and three-quarters say they would consider starting ART for any HIV-positive person in a serodiscordant relationship.[12]

Researchers hope that results from HPTN 065, expected in late 2013 and 2014, will yield important information that could guide the future development of large, randomized, community-level clinical trials of full implementation of the Test and Treat strategy in the United States.

HRSA and HIV Testing

HRSA's AIDS Education and Training Centers (AETC) offer technical assistance and training to expand HIV testing and counseling in medical care settings. AETC training sessions on Federal HIV testing guidelines have reached more than 50,000 providers. Thanks in part to these training sessions, hundreds of sites have implemented routine HIV testing. HRSA Bureau of Primary Health Care (BPHC) providers, who serve patients in some of the communities hardest hit by HIV/AIDS, are also working toward the goal of increased HIV testing; for more information, see www.bphc.hrsa.gov. BPHC has also expanded its commitment to serving people infected with HIV with recommendations to bolster testing and

SPNS: LEADING THE WAY IN LINKING TO HARD-TO-REACH POPULATIONS

HRSA's Special Projects of National Significance (SPNS) Program has several programs underway to both increase the testing of populations at greatest risk for HIV infection and to link people found to be HIV infected to treatment and care.

One initiative in particular, Enhancing Linkages to HIV Primary Care & Services in Jail Settings, has been especially successful in reaching people who had previously fallen out of care and often have both serious, unmanaged infectious diseases and mental illnesses. This initiative funded 10 demonstration sites for 5 years to design, implement, and evaluate innovative methods for linking people living with HIV/AIDS who were in jail or had recently been released from jail to primary care services within the community's continuum of HIV care. Strategies included flexible and suitable case management approaches that promoted durable linkages and follow-up as people moved between jail and the community.

Best practices and implementation guidance to replicate this work are currently being developed as part of the Integrating HIV Innovative Practices (IHIP) project. Recently, IHIP distilled lessons learned across population-specific initiatives into an Engaging Hard-to-Reach Populations training manual and associated curriculum that can be found at https://careacttarget.org/ihip. Other IHIP products include the Integrating Buprenorphine into HIV Primary Care Settings training manual, curriculum, and training webinars to meet the needs to opioid-dependent people, helping them reduce risky behaviors and stay medication adherent.

Several new SPNS projects target other high-risk and hard-to-reach populations—including the homeless, women of color, and transgender persons—to meet the changing needs of the HIV epidemic and of those most at risk of becoming infected with the virus and continue to improve and advance HIV prevention and care. For more information, see www.hab.hrsa.gov/abouthab/partfspns.html.

referral, linkage, and retention in care. For more information, see www.bphc.hrsa.gov/policiesregulations/policies/pal201013.html and www.bphc.hrsa.gov/policiesregulations/policies/pal20106.html.

In addition, HRSA has given priority to the Ryan White Early Identification of Individuals with HIV/AIDS (EIIHA) legislation, a comprehensive strategy to identify, counsel, test, inform, and refer both HIV-positive and undiagnosed people to appropriate services. The legislation:

- Calls for a comprehensive plan to estimate the number of HIV-infected people living in each State, as well as an estimate of the number who do not know their HIV status;
- Defines activities to be undertaken by each State to find people who do not know their HIV status and make them aware of it;
- Determine the manner in which States will provide undiagnosed people who are made aware of their HIV status with access to medical treatment for HIV/AIDS; and
- Calls for efforts to remove legal barriers to routine HIV testing, including State laws and regulations.

EIIHA has several implications for the AIDS Drug Assistance Program (ADAP), the largest component of the Ryan White HIV/AIDS Program. As the payer of last resort, ADAP provides treatment for those who would otherwise be unable to access these lifesaving medicines. Firstly, EIIHA may generate new clients and require the capacity to serve a greater number of people newly diagnosed with HIV/AIDS. Secondly, increased planning efforts will be needed to predict the proportion of those newly diagnosed people who are likely to be Ryan White eligible. Thirdly, it marks a shift toward considering ADAP as a prevention tool by focusing on getting people onto medication as early as possible to reduce transmission.

PRE-EXPOSURE PROPHYLAXIS

Like Test and Treat, pre-exposure prophylaxis (PrEP) is one of the most promising prevention strategies to emerge in recent years. Experts hope that PrEP, when combined with other prevention methods, will help to reverse the HIV/AIDS epidemic.

In July 2012, the U.S. Food and Drug Administration (FDA) approved the first PrEP drug, Truvada (tenofovir/emtricitabine), to reduce the risk of sexual transmission of HIV among healthy individuals who test negative for HIV but who are at high risk for HIV infection.[20] The CDC has issued guidance for clinicians using PrEP for MSM, heterosexually active adults and adolescents, and injection drug users (IDUs).[21] The CDC guidance encourage clinicians to:

- Target PrEP to persons at very high risk for HIV acquisition;
- Deliver PrEP as part of a comprehensive set of prevention services;
- Provide counseling regarding risk reduction and the importance of PrEP medication adherence;
- Ensure people prescribed PrEP are confirmed to be HIV negative prior to use; and
- Provide regular monitoring of HIV status, side effects, adherence, and risk behaviors.

Truvada is an oral, once-a-day pill that combines two drugs commonly used for HIV prophylaxis. It does not rid the body of HIV; rather, it prevents the virus from replicating in the body. Truvada has few side effects beyond gastrointestinal discomfort, though in rare cases people taking it have experienced liver and kidney toxicity and loss of bone density.

Given the rates of efficacy of Truvada in clinical trials, CDC officials have used words like "game changer" and "breakthrough" to describe the new findings but have cautioned that PrEP alone is not the solution to HIV/AIDS, nor should it be used as the first line of defense against the virus. This is because it has been proven effective only when used with condoms and other HIV prevention methods and within the context of a controlled clinical trial; it is not yet known how effective it will be in the real world, without the intensive support and monitoring available in a clinical trial setting.

The FDA's approval of Truvada was based on two large, randomized, double-blinded, placebo-controlled trials: one in HIV-negative men and transgender women who have sex with men and one in heterosexual serodiscordant couples. Results from these trials showed that when Truvada was used consistently, it reduced the risk of transmission of HIV infection by as much as 75 percent.[22] The trials consisted of:

- **iPrEX.** The Chemoprophylaxis for HIV Prevention in Men (iPrEx) trial evaluated Truvada in 2,499 men or transgender women who have sex with men. All trial participants tested negative for HIV at baseline but reported engaging in sexual practices that put them

> ***"What we're looking at here with PrEP is an entirely new and very exciting HIV prevention strategy."***

at high risk for infection, such as inconsistent or no condom use during sex with a partner of positive or unknown HIV status, a high number of sex partners, and exchange of sex for money or commodities. Half of the trial's participants were randomly allocated to receive Truvada and half a placebo. Both groups of participants also received HIV education and testing, as well as condoms. Results showed that Truvada reduced the risk of acquiring HIV infection by 42 percent compared with placebo. Efficacy was strongly correlated with drug adherence.[23,24]

- **Partners PrEP trial.** The Partners PrEP trial—the largest study to date to examine the effectiveness of PrEP—enrolled 4,758 serodiscordant heterosexual couples in Kenya and Uganda. The trial evaluated the efficacy and safety of tenofovir alone (Viread), Truvada, or placebo in preventing HIV infection in the uninfected partner. One-third of the uninfected partners were randomly allocated to receive tenofovir, one-third Truvada, and one-third a matching placebo daily. All participating couples received a comprehensive package of HIV prevention services, include intensive safe sex counseling, HIV testing, free condoms, testing and treatments for sexually transmitted infections, and monitoring and care for HIV infection. Results showed that, compared with placebo, tenofovir reduced the risk of becoming infected by 67 percent and Truvada reduced the risk of becoming infected by 75 percent. When analyses considered whether participants were adherent, PrEP was associated with an approximately 90 percent reduction in HIV infection risk.[25]

"What we're looking at here with PrEP is an entirely new and very exciting HIV prevention strategy," says Amy Lansky, deputy director for surveillance, epidemiology, and laboratory sciences at the CDC's Division of HIV/AIDS Prevention. "It blocks the virus from taking hold. It blocks people from getting infected." The CDC has released interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults.[26]

The only dosing strategy of PrEP with proven efficacy is daily use; however, clinical trials are underway to determine if the drug can be used less frequently and still work. Concerns have emerged about its use in nonresearch settings. Chief among these is adherence (see sidebar, p. 8, *Adherence, Retention Key to Both Pre-Exposure Prophylaxis and Test and Treat*). If a person taking Truvada is partially adherent and subsequently becomes infected with HIV, the risk that the virus will become resistant to the drug is higher than it would have been if he or she had not taken Truvada—the very drug that would likely have been used to treat the infection. For this reason, HIV-negative people who are taking Truvada must be retested for HIV every few months.

Some public health officials are also concerned about a phenomenon known as *risk compensation*—that is, if PrEP is made available, increasing numbers of people will choose not to use condoms or take other measures to prevent HIV infection. Although the jury is still out, researchers have not shown an increase in riskier behavior among people taking Truvada to prevent HIV infection.

"Simply put, it is important to remember that PrEP is not a magic bullet," says Lansky. "It must be obtained and used in close collaboration with health care providers to ensure [that patients receive] regular HIV testing, risk reduction and adherence counseling, and careful safety monitoring."

PREVENTION WITH POSITIVES

Taking responsibility for preventing HIV transmission is an important concern for most people with HIV, and HIV-infected people who are aware of their HIV infection tend to reduce behaviors that might transmit HIV to others.[27,28,29,30,31,32,33,34] A focus on preventing HIV transmission by those living with the virus has thus become a central tenet of the Nation's HIV prevention strategy.

Unfortunately, data continue to demonstrate gaps in practice. For example, as many as one-third to three-fourths of HIV medical providers do not ask their patients about sexual behavior or drug use, despite reports that HIV-infected patients want to discuss prevention efforts.[35] It is vital that providers remember that each patient visit presents an opportunity to discuss effective prevention interventions.

ADHERENCE, RETENTION KEY TO BOTH PRE-EXPOSURE PROPHYLAXIS AND TEST AND TREAT

It is well documented that adherence to antiretroviral therapy (ART) can keep HIV under control to the point that plasma HIV-1 RNA levels become undetectable. This finding has not only vastly reduced both morbidity and mortality from HIV/AIDS, but also has the potential to dramatically reduce HIV transmission.

Unfortunately, despite the clear benefits of ART therapy and the availability of fixed-dose drug regimens that have made it easier for people living with HIV/AIDS (PLWHA) to achieve viral suppression, a recent study suggests that fewer than 20 percent of patients achieve an undetectable viral load because of intentional or unintentional poor adherence to ART.[39]

Difficulty adhering to medical regimens is not unique to PLWHA and is a challenge for patients living with many chronic, lifelong illnesses.[40] Unfortunately, HIV is unforgiving of even episodic nonadherence; adherence rates of less than 95 percent may cause a viral rebound, leading to opportunistic infections and an increase in HIV/AIDS symptoms and a greater likelihood of infecting others with the virus.[8]

Many factors contribute to patient nonadherence to ART regimens, including pill burden, socioeconomic status, cultural differences, adverse medication effects, poor health literacy, depression, substance abuse, potential drug-drug interactions, and poor patient–provider relationships.[8,41] Perhaps the most challenging factor contributing to nonadherence, however, is retention in care. Recent estimates suggest that as few as 69 percent of people diagnosed with HIV are linked to care; of those, only about 59 percent are retained in care.[11]

Only with successful linkage to and retention in care can the benefits of ART be achieved, yet few validated strategies exist for improving this aspect of care. To address this challenge, the International Association of Physicians in AIDS Care convened a panel to develop evidence-based recommendations to optimize entry into and retention in care and ART adherence for people with HIV.[42] The guidelines can be accessed at http://annals.org/article.aspx?articleid=1170890.

As part of comprehensive care for patients with HIV infection, providers must address challenges to adherence and retention when working with patients to achieve adherence to a treatment regimen. Strategies used to improve adherence to ART or medications for chronic health conditions, as well as existing and emerging best practices for improving entry into and retention in care, can be used to support Test and Treat and PrEP. These strategies include:

- Facilitating accurate knowledge and understanding of medication benefits and requirements;
- Monitoring of adherence by providers;
- Building self-efficacy for adherence; and
- Providing social support and resources to address mental health issues, substance abuse, or severe economic or housing constraints.

HRSA's HIV/AIDS Bureau (HAB) is addressing these issues by supporting a robust spectrum of medical services that include HIV counseling and patient education on the importance of treatment adherence. In recent years, the HAB's shift toward supporting medical case management has assisted in increasing treatment access and HIV medication education.

For more information about adherence, see www.aidsinfonet.org/fact_sheets/view/405.

The CDC, HRSA, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America recommended in 2003 that providers of HIV clinical care promote several interventions to improve the health of, and prevent ongoing HIV transmission from, adults and adolescents infected with HIV in the United States.[36] These interventions include:

- Linkage to and retention in HIV medical care;
- Initiation of and adherence to treatment as a prevention strategy;

- Risk screening and risk-reduction interventions;
- Partner services;
- Sexually transmitted disease services;
- Reproductive health care for both women and men and prevention of mother-to-child transmission of HIV; and
- Other medical and social services that influence HIV transmission, such as substance use and mental illness services.

A cross-agency collaboration is now underway to update, expand, and consolidate these recommendations, with special attention directed to HIV care providers in health care settings; HIV prevention providers in community-based organizations; HIV and AIDS program staff in health departments; specialists in HIV and AIDS policies for public- and private-sector health systems and community-based programs; and specialists in HIV service coverage, funding, and reimbursement. The updated recommendations are expected by 2014.

Meanwhile, HRSA has described a number of interventions aimed at HIV prevention in PLWHA in its 2011 *Guide for HIV/AIDS Clinical Care*.[35] Effective provider-initiated actions include the following:

- Establish rapport and provide services in an understanding, nonjudgmental manner.
- Conduct a quick, detailed behavioral risk assessment.
- Assess the patient's readiness for change and approach any proposal to address a high-risk behavior in a step-wise manner.
- Customize messages.
- Recognize that patients may have competing priorities and pressures that may result in risky sexual and drug-use behaviors.

Multiple HRSA Special Projects of National Significance (SPNS) initiatives have specifically targeted prevention efforts in HIV-positive people. For example, the Prevention with HIV-Infected Persons Seen in Primary Care Settings Initiative was designed to address the need for interventions targeting HIV-positive people in clinical care, prevent transmission to uninfected individuals, and prevent re-infection among people who are already infected.[37] Sixteen grantees were tasked with identifying which HIV prevention interventions work best in different target populations, from MSM of color to rural drug users; how clinicians can best assess risk and promote behavior change, and what obstacles exist to conducting HIV prevention activities with HIV-infected people in a clinical setting and how can they be overcome. For more information on findings from the Prevention with HIV-Infected Persons Seen in Primary Care Settings Initiative, see http://hab.hrsa.gov/abouthab/special/primarycaresettings.html.

ONLINE RESOURCES

AETC National Resource Center: Supporting HIV Education for Health Care Professionals
www.aids-ed.org

AIDS Education Training Centers
www. hab.hrsa.gov/abouthab/partfeducation.html

Care is Prevention (from the Living History Project)
www.hab.hrsa.gov/livinghistory/timeline/2012.htm

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents
www.aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

High-Impact HIV Prevention: CDC's Approach to Reducing HIV Infections in the United States
www.cdc.gov/hiv/strategy/dhap/pdf/nhas_booklet.pdf

HIV/AIDS Care & Treatment in Health Centers
www.bphc.hrsa.gov/policiesregulations/policies/pal201106.html

HIV in the United States: Stages of Care
http://www.cdc.gov/nchhstp/newsroom/docs/2012/Stages-of-CareFactSheet-508.pdf

HIV Testing in Health-Care Settings
www.bphc.hrsa.gov/policiesregulations/policies/pal201013.html

How the Affordable Care Act Helps People Living with HIV/AIDS: 2011 and Beyond
www.healthcare.gov/news/factsheets/2011/11/hiv-aids11092011a.html

in+care Campaign
www.incarecampaign.org

Pre-Exposure Prophylaxis (PrEP)
www.cdc.gov/hiv/prep/

Special Projects of National Significance
www.hab.hrsa.gov/abouthab/partfspns.html

Target Center: Tools for the Ryan White Community
https://careacttarget.org/

Test and Treat: A New Paradigm for Slowing the Spread of HIV (HRSA CareAction, January 2012)
www.hab.hrsa.gov/newspublications/careactionnewsletter/hab_test_and_treat_january_careaction_pdf.pdf

KEEP YOUR EYE ON . . . MICROBICIDES

What will be the next promising preventive HIV intervention to emerge? Many say it will be microbicides.

Microbicides are antimicrobial products that are formulated for application to the surface of the vagina or rectum to prevent HIV transmission during sexual intercourse. Microbicides can take various forms, including gels, creams, tablets, and drug-impregnated vaginal rings. One study showed that a microbicide gel containing tenofovir demonstrated 39 percent efficacy at preventing HIV infection when applied vaginally within 12 hours before and within 12 hours after sex.[43] Among women who used it consistently, the gel reduced the risk of acquiring HIV infection by more than 50 percent.[38]

It is thought that microbicides, which are designed to be self-administered, may be more effective than condoms in preventing HIV infection because women would not have to negotiate their use, as they often must do with condoms.

> In many settings, women are unable to insist on the use of condoms or other [preventive] methods," says HRSA medical officer Rupali Doshi. "A female-controlled method to prevent HIV transmission is very desirable because it would make it possible for a woman to protect herself and her partner from HIV without his cooperation or knowledge."

Many trials studying various forms of microbicides are under way. One of the largest, known as Microbicide Trials Network (MTN) 020, expects to enroll almost 3,500 participants in 5 countries to determine whether the antiretroviral drug dapivirine can safely prevent HIV infection when it is continuously released into the vagina from a silicone ring that is replaced once a month. Results are expected in early 2015.

In November 2012, the U.S. Food and Drug Administration (FDA) issued draft guidance to assist those developing vaginal microbicides for the prevention of HIV infection. The guidance provides information about the types of both nonclinical studies and clinical trials that are needed to advance the development of vaginal microbicides and focuses on drug development issues unique to vaginal microbicides, including safety and Phase III trial considerations. The FDA guidance is available at www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm328834.htm.

For more information about microbicide research, see www.mtnstopshiv.org.

Another initiative, the OPTIONS Project, was a physician-delivered intervention for HIV-positive patients in clinical care that took advantage of the unique relationship between providers and HIV-infected people to define risk-reduction behaviors that are efficacious and feasible given providers' increasingly limited time and resources.[38] Originally launched with 15 grantees, the OPTIONS program has been replicated and evaluated across a variety of HIV clinical settings.

CONCLUSION

Although great progress has been made in the fight against HIV/AIDS in the United States, more people are in need of HIV testing, prevention, and treatment services today than at any point in U.S. history, and many communities bear a disproportionate burden of HIV disease.

Renewed, coordinated, and intensified strategies to address the HIV/AIDS epidemic are vital, and HRSA is prepared to lead the way. By using a combination of effective strategies targeted toward populations and communities hardest hit by the disease, health providers can maximize the impact of their work. Both PrEP and Test and Treat exemplify these efforts. Used together with Prevention with Positives strategies, existing behavior-based interventions such as the use of condoms and clean needles and emerging tools such as microbicides, which offer an entirely new way to protect against the disease (see sidebar above, *Keep Your Eye On . . . Microbicides*), health care providers are making progress at reducing new HIV infections, improving the health of PLWHA, and reducing HIV-related health disparities.

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