

# HIV Specialist

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Challenges of  
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Saving Lives,  
Saving Dollars

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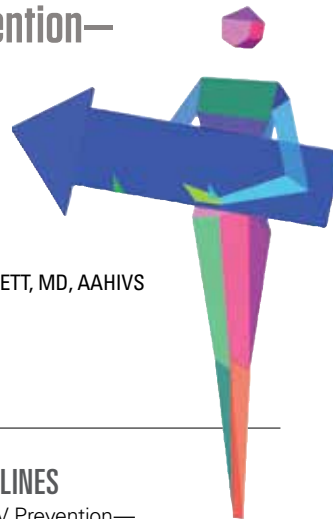
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BY JAMES M. FRIEDMAN, MHA  
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# The Best Strategy of All

**O**N JULY 30, 2015, the White House Office of National AIDS Policy released the update of the 2010 National HIV/AIDS Strategy. The updated National Strategy suggests targeting specific populations with aggressive outreach efforts including women, MSM, minorities and youth. AAHIVM always has kept each of these populations top of mind as we have crafted our educational offerings and programmatic activities. In fact, you'll recall that our July 2015 issue of *HIV Specialist* focused on Women and HIV. In the same vein, we turn our attention for this issue to the challenges in managing HIV in youth and young adults.

We all know that adolescents think they are immortal; they don't listen to anyone, and they certainly don't follow directions. These are not great habits to facilitate prevention and treatment of HIV. Plus, this is a generation that does not remember the horrific entry of HIV and AIDS into our society. The historic knowledge that has driven many into safer practices is simply not there.

Guest Editor Dr. Donna Futterman, Professor of Clinical Pediatrics and the Director of the Adolescent AIDS Program at the Einstein College of Medicine and the Children's Hospital at Montefiore, explores the challenges in working with this population along with a panoply of experts on adolescent HIV:

- Dr. Elizabeth Secord, Yana Gristan and Dr. Jill Meade discuss special issues of perinatally infected youth;
- Mary Tanney and Nellie Lazar write about adherence;
- Dr. Alisha Liggett writes about prevention of HIV in adolescents; and
- Laura Jadwin-Cakmak, Dr. Asa Radix, Dr. Gary Harper and Elliot Popoff speak to special issues that relate to transgender youth.

It is a great lineup for articles that will help practitioners meet the goals of the updated National HIV/AIDS Strategy.

While AAHIVM was pleased to see the specific at-risk populations identified in the National

Strategy, we were disappointed that one important contingent was omitted—older adults. Within the next few years, over half of the people living with HIV in the United States will be over 50 years of age, as well as one in six who are newly diagnosed.



James M. Friedman

We hope you will continue to visit our HIV-AGE.org website, which includes treatment strategies, journal articles, links and case studies for clinicians managing older patients with HIV.

Recently, the AAHIVM Board of Directors met in Chicago for one of two annual Board meetings. The Board approved our Policy Platform (available on our website), and voted to endorse the American Society of Health System Pharmacists' Guidelines on Pharmacist Involvement in HIV Care, which were

written by three AAHIVM pharmacists.

As we discussed all of the progress we have made this past year and presented the upcoming programmatic activities for 2016, I felt pride knowing that we are representing an outstanding membership of HIV care practitioners who are committed to helping ALL populations battle this disease. While it is wonderful to have a multi-year, overarching National HIV/AIDS Strategy, we recognize that your daily strategy is to help each and every HIV patient that walks through your door live a long and full life. And that really is the best strategy of all.

**I felt pride knowing that we are representing an outstanding membership of HIV care practitioners who are committed to helping ALL populations battle this disease.**

**HIV**

*James M. Friedman*



# In the NEWS

## HUD Offers Housing Funds for HIV+ Domestic Violence Victims

To help prevent victims of domestic violence living with HIV/AIDS from falling into homelessness, the U.S. Department of Housing and Urban Development (HUD) is making more than \$9 million available to state, local governments and non-profits. The funds are provided through the VAWA/HOPWA Project Demonstration—a collaborative effort between HUD's Office

of HIV/AIDS Housing (OHH) and the Department of Justice's Office of Violence Against Women (OVW). More than half of women living with HIV/AIDS in the U.S. do not have access to stable housing and are at higher risk of experiencing domestic violence.

Through this demonstration program, HUD will provide funding for transitional and other temporary rental housing assistance and supportive services to low-income persons living with HIV/AIDS who are victims of sexual assault, domestic violence, dating violence, or stalking. Grantees must partner with local domestic violence and sexual assault service providers for client outreach and engagement and for comprehensive supportive services.

The demonstration follows a recommendation by the

Federal Interagency Working Group on the Intersection of HIV/AIDS, Violence against Women and Girls, and Gender-Related Health Disparities to more effectively address HIV and intimate partner violence (IPV) among homeless and marginally housed women and girls. While the Working Group focuses on women and girls, the housing assistance and supportive services provided through the demonstration will be open to all eligible clients regardless of sex, gender identity, sexual orientation, familial status, marital status, race, color, religion, national origin, disability, or age.

The HOPWA program is the only Federal program dedicated to addressing the housing needs of persons living with HIV/AIDS and their families. Grantees partner with nonprofit organizations and housing agencies to provide housing and support to program beneficiaries.



## French Study Says Socioeconomic Status Linked to Viral Load

A new study by researchers from two Paris-area university hospitals contends that a poor socioeconomic score doubles the likelihood that HIV-positive adults would have a detectable viral load.

While half of the study participants came from Sub-Saharan Africa, the study, which used the Evaluation of Deprivation and Inequalities in Health Examination Centers (EPICES) score, found no link between country of origin and detectable viral load. EPICES is a standard scale used by French researchers to consider numerous socioeconomic factors that contribute to individual deprivation.

The study involved HIV-positive patients at outpatient clinics of two hospitals in Clamart and Bobigny between May 2013 and October 2014. All had taken ART for at least six months. They completed a survey that included questions on social benefit, health insurance, family structure, income, financial difficulties, leisure activities and social support.

## New WHO Guidelines Call for Broader Treatment Worldwide

The World Health Organization (WHO) issued new guidelines Sept. 30 stating that HIV patients should receive antiretroviral therapy of three drugs immediately upon diagnosis, and that pre-exposure prophylaxis (PrEP) should be offered to those at "substantial risk" of infection.

The recommendations would increase the number of people eligible for ARV treatment from 28 million under the previous standard to 37 million. Sub-Saharan Africa, which accounts for more than 70 percent of people living with HIV would be affected the most, as WHO estimates that nearly one in every 20 adults are infected with HIV.

Currently, only 15 million HIV-infected individuals receive ARVs. Studies have shown that early treatment is essential and that the drugs protect uninfected people regardless of how the virus is transmitted.

The guidelines are available here: [http://apps.who.int/iris/bitstream/10665/186275/1/9789241509565\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/186275/1/9789241509565_eng.pdf?ua=1)

## Researchers Discover Mechanism of Proteins to Block HIV

UNIVERSITY OF MISSOURI RESEARCHERS have discovered how specialized proteins can inhibit the HIV virus, opening the door for progress in the fight against HIV and for the production of advanced therapeutics to combat the disease.

Human cells express Interferon Induced Transmembranes (IFITM) proteins that possess antiviral characteristics and have been shown to inhibit such viruses including influenza A, West Nile, Dengue fever and Ebola.

In his study, Shan-Lu Liu, an associate professor in the University of Missouri (MU) Department of Molecular Microbiology and Immunology in the School of Medicine and an investigator in the Bond Life Sciences Center at MU, targeted IFITM proteins and their antiviral function.

"We've known that HIV-1, the most common HIV strain, can be transmitted from cell to cell or through a cell-free transmission in which the virus floats freely," said Liu. "Our research discovered that IFITM proteins can help inhibit the viral cell-to-cell infection, which is the most efficient way that HIV spreads."

Jingyou Yu, a doctoral student in MU's pathobiology graduate program, conducted experiments to show that IFITM proteins, particularly IFITM2 and IFITM3, block HIV cell-to-cell transmission. Yu then partnered with Minghua Li, also a graduate student in pathobiology, and discovered that IFITM proteins specifically interact with the HIV-1 envelope glycoprotein and inhibit its maturation that is required for viral infectivity and transmission.

Additionally, Liu worked with research labs in Canada and New York, to reproduce and verify his findings.

"By understanding and visualizing how some IFITM proteins can inhibit and block transmission, we are getting closer to finding better therapeutic approaches in the fight against HIV," said Liu.

The study, "IFITM Proteins Restrict HIV-1 Infection by Antagonizing the Envelope Glycoprotein," recently was published in *Cell Reports*. The work was supported by the National Institutes of Health.

## Videos Reveal in Real Time How HIV Spreads

How retroviruses like HIV spread in their hosts had been unknown—until a Yale team devised a way to observe this process in a living organism. The steps the virus takes to reach and spread in the lymph nodes of a mouse were captured on videos and described in the Oct. 2 issue of the journal *Science*.

The team led by Walther Mothes, associate professor of microbial pathogenesis and co-senior author Priti Kumar, assistant professor of medicine and microbial pathogenesis, used fluorescent imaging technology to capture the action as the viral particles bind to macrophages via a sticky protein located at the capsule of the lymph node (in blue). Movie: <http://bit.ly/1JuEcdO>

The captured viral particles open to a rare type of B-cell, seen in red in the accompanying film clip. The virus particles then attach themselves to the tail of these B-cells and are dragged into the interior of the lymph node. In one to two days, these B-cells establish stable connections with tissue, enabling full transmission of the virus. Movie: <http://bit.ly/1NZIUeR>

The insights provided by the videos identify a potential way to prevent HIV from infecting surrounding tissue—blocking the action of the sticky protein the virus uses to bind to macrophages so the virus' transmission could be halted, Mothes suggested.

The research was funded by the National Institutes of Health, The Leopoldina German National Academy of Sciences, and the China Scholarships Council.

Link to *Science* paper: <http://www.sciencemag.org/lookup/doi/10.1126/science.aab2749>

## A PROTEIN THAT NATURALLY FIGHTS HIV

Researchers have discovered that a protein, ERMAn1, works as a natural defense against HIV infection by stopping the virus from replicating.

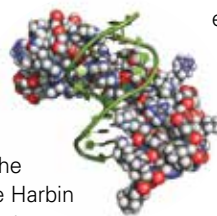
"In earlier studies, we knew that we could interfere with the spread of HIV-1, but we couldn't identify the mechanism that was stopping the process," said Yong-Hui Zheng, associate professor of microbiology and molecular genetics at Michigan State University and coauthor of the study in the *Journal of Biological Chemistry*.

"We now know that ERMAn1 is an essential key, and that it has the potential as a

antiretroviral treatment."

The next steps will be to test to determine if HIV resistance can be promoted by increasing ERMAn1 levels, said Zheng, who worked on the study with scientists from the Harbin Veterinary Research Institute, the Chinese Academy of Agricultural Sciences, and the University of Georgia.

Most viruses have viral envelopes, or protective skins, that comprise similar building blocks of the host the pathogens are trying to infect. On the surface of the



envelope, there are viral glycoproteins, known as Env spikes, which lead viruses to binding sites that allow infections to spread at the molecular level.

Zheng's lab was the first to show that HIV-1 envelope glycoprotein biosynthesis can be specifically inhibited by ERMAn1, which is a host enzyme to add sugars to proteins. By identifying ERMAn1 as the target that slows the spread of HIV-1, the team believes it has revealed a target in which future natural therapies can be developed.

The National Institutes of Health helped fund the project.

## Moving the Fight Forward

JIM SCOTT, PHARM.D., MED., FCCP, FASHP, AAHIVP  
Western University of Health Sciences, College of Pharmacy  
Pomona, CA

**J**IM SCOTT did his undergraduate degree, Masters in Education and Doctor of Pharmacy at the University of Florida in Gainesville. He did a Geriatrics Pharmacotherapy Residency at the Gainesville VAMC and an Infectious Diseases Fellowship at the University of Illinois at Chicago.

Scott recalls working with people with HIV first during his student days and continuously over the 20 years that have followed.

“For the first two and a half years after my training, I worked at a hospital in Buffalo, NY, doing mostly inpatient geriatric ID clinical service. I also worked part-time at various community hospitals throughout my training and my early years at my current position,” says Scott.

While his current position with Western University of Health Sciences College of Pharmacy consists mostly of academic administration, Scott draws from his history of practice as a clinical pharmacist at a large urban HIV clinic in Hollywood, CA.

“We had about 2,000 patients,” he recalls. “We had about five medical providers and a multidisciplinary staff of 30 to 40. While practicing, the patients were mostly MSM with a scattering of others, (FSM, MSF, FSF/M, Transgender). Probably 50% were Latino/a, 30% Caucasian, 15% Black and the remaining were Asian, Middle Eastern, multiracial, etc. The average age was about 35, but there were patients ranging in ages from 18 to 65.”

When he was in school in the early 1990's, Scott realized the breadth of HIV, through classes as well as friends. He also saw there were few options for treatment and realized that this was a devastating disease that a great deal of help would be needed to fight. Thus, he pursued postgraduate training programs that focused on HIV and just kept moving forward.

When he was preparing to be the first HIV clinical pharmacist at a clinic, Scott asked

experienced HIV clinical pharmacists, ‘if you could start all over again, how would you do it?’ This approach worked quite well for him.

“In my current role, I am involved in fighting HIV in a lot of ways I never dreamed of when I was in school,” Scott says. “I am working with professional societies like the American Academy of HIV Medicine (AAHIVM) and the International Association of Providers of AIDS Care (IAPAC) to give support and guidance to the frontline health care practitioners, as well as educating pharmacists and other health care providers who have minor, yet still important, roles in fighting HIV, and educating and motivating future pharmacists to be a part of the fight against HIV.”

### Addressing Barriers

Scott acknowledges that, in HIV care adherence to treatment regimens is always a battle that is a different with each patient. His approach has always been to identify what their barriers to adherence are and then work with them on those barriers.

Says Scott, “I have always believed that educating patients is the key, but it is important to educate them at their own level. Give them as much information as they want, but no more than they can digest. Once they have that information, they can make better decisions for themselves. This information may be about side effects but it also may be about pharmacokinetics. Most patients know nothing at all about how the drug moves around the body, about how long it stays in different parts. Giving them a better idea of this can

help many of them better understand the importance of adherence.”

Looking to the future, Scott would like to be involved in the leading edge of HIV treatment; whether continuing in an educating role or in his newest capacity, having recently received a formal invitation from the Food and Drug Administration (FDA) to be a consultant for the FDA Antimicrobial Drugs Advisory Committee (AMDAC). Scott predicts fairly optimistically that within the next 10 years treatment will be simplified to a monthly, maybe quarterly, long-acting injection.

Outside of his professional life, Scott is a part of a local community band with mostly LGBT members. After his freshmen year in college, he put his trombone down for 20 years and missed it almost every day. “Picking it up again was almost like being reborn,” muses Scott, “And it allowed me to continue working with the LGBT community in a different manner.”

Scott is the current Chair of AAHIVM's Pharmacists Committee and Chair of AAHIVM's Pharmacists Credentialing Subcommittee, playing a key role in AAHIVM's ability to certify pharmacists as HIV Pharmacists™.

Asked why he is a Member of AAHIVM, Scott says, “Although I was active with AAHIVM for a few years prior to becoming a Member, I didn't formally join until it was clear that AAHIVM was serious about being inclusive of other provider types. Treating a disease that is complicated medically and socioeconomically takes a team approach, and I feel AAHIVM is committed to fostering the health care team in fighting HIV.”

**HIV**







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## CHOOSE FROM 1 OF 2 TOPICS

### Case-based Discussions with National HIV Experts on:

#### TOPIC 1: Building Durable Treatment Regimens for the Long Term

Upon successful completion of this educational activity, participants should be better able to:

- Identify factors that have been shown to improve durability of response to first-line treatment regimens in HIV.
- Compare the ability of different antiretroviral agents to maintain long-term viral suppression under real-world conditions, including suboptimal patient adherence.
- Compare and contrast pharmacokinetic profiles of various agents recommended by the US Department of Health and Human Services for initial therapy to understand the impact of drug levels on suboptimal efficacy.

**OR**

#### TOPIC 2: Maximizing Outcomes and Reducing Resistance with a Realistic View of Adherence Challenges

Upon successful completion of this educational activity, participants should be better able to:

- Review the convenience, tolerability, and toxicity of antiretroviral therapy for HIV to improve patient adherence to treatment.
- Select therapeutic regimens that improve patient adherence to treatment and that are less likely to induce viral resistance.
- Compare the ability of different antiretroviral agents to maintain long-term viral suppression under real-world conditions, including suboptimal patient adherence.

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## ADOLESCENTS and HIV

# The Crisis and the Cure

BY DONNA FUTTERMAN, MD

**Y**OUTH REPRESENT THE FASTEST GROWING POPULATION OF NEW HIV INFECTIONS IN THE U.S. AND THROUGHOUT THE WORLD. Why? Every five years a new generation of young people makes its way through society. Practically speaking, the youth in high school sex education classes today were not there in 2010, and they will not be there in 2020.

Marketers know that to influence youth, messages, music and even products must be continually updated to appeal successfully to the particular needs, desires and aspirations of today's generation. For decades, this approach has worked for brands like Coke, Nike and Apple, so why not take a similar approach when it comes to "selling" youth ideas about HIV prevention and care with messages, media and messengers to which they can relate?

Despite alarming rates of new HIV infections, we live in the first era when antiretrovirals—used as treatment and prevention—could eradicate HIV altogether. It may not be a cure in the traditional sense, but we have the tools to end HIV. Our challenge is to make full use of these tools to achieve this long elusive goal.

Why do young people—in the U.S., particularly young black men who have sex with men, and in the rest of the world, young women—remain so vulnerable? Unfortunately, there are myriad reasons why youth are particularly at risk for HIV infection, including sexism and deep homophobia in multiple institutions, long-standing racial disparities, poverty, substance use, mental health challenges, histories of neglect, and sexual and physical abuse. Societal discomfort with youth sexuality, and consequently an avoidance of creating accurate and compelling safe sex messages, compound the lack of accurate information presented to adolescents.

In addition, the changes of adolescence, including physical maturation and brain development, also leave youth vulnerable. For example, the immature cervix, covered by only a single layer of columnar cells makes young girls more vulnerable to sexually transmitted infections than post-adolescent young women who have developed multilayer squamous epithelial cells on their cervixes. Furthermore, adolescents' brains are still in an active stage of maturation, including the frontal lobe, which is responsible for executive functions and judgment.

Ironically, the very successes we have achieved in treating HIV have diminished for many youth the fear of becoming infected, and thus they have helped to create a complacency around prevention. Finally, contributing to the resurgence of HIV among youth has been the failure of our medical community to step up and fully engage this chronic illness with the passion and public health leadership that is applied to more acute infections, such as Ebola or seasonal influenza.

With our understanding of the HIV epidemiology and where youth fall short on the HIV care and prevention continuum, we can analyze where and how to apply effective treatment, support and prevention interventions.

This will strengthen each step of the care cascade and ultimately eliminate new infections among youth. While this strategy overlaps many elements of the National HIV/AIDS Strategy, adolescents have unique needs that must be addressed if this approach is to succeed.

Statistics confirm what was easily predicted—infection rates rising fastest among youth—especially young black MSM. In 2009, persons 15-29 accounted for 39% of all new HIV infections in the U.S., almost double their percentage of the population (21%). In 2010, black youth (12% of the U.S. youth population) accounted for an estimated 57% (7,000) of all new HIV infections among youth in the United States, followed by Hispanic/Latino (20%, 2,390) and white (20%, 2,380) youth (CDC Youth Fact Sheet 2015). The rate of new infections among young black males aged 13 to 24 is 11 times as high as that of young white males and four times as high as young Hispanic males. Any way you interpret these numbers, it reflects an unnecessary and avoidable disaster.

According to multiple studies, at least 50% of MSM have sex with women at some point. We should not be surprised that infection rates among young women have started to rise again. Indeed, young women represent 23% of youth HIV cases compared to 20% among adult women. Even the once under control epidemic among Indiana injection drug users exploded recently with a new group of substance users moving from prescription opioid use to injection use. This shift resulted in 181 newly infected people, with several youth among the infected.

Most of the metrics for tracking HIV infection and prevention are based on the Continuum of Care model with a more recent addition of the prevention cascade (Gardener; Daskalakis, NYC DOH) The care continuum for HIV+ starts with testing, proceeds to linkage and retention in care, prescription of anti-retrovirals (ART) and finally the achievement of an undetectable viral load.

Strikingly, but not surprisingly, youth lag behind adults on key steps of the cascade. Youth are much less likely to have been tested for HIV than adults. An estimated 50% of HIV+ adolescents don't know their status compared to 14% of adults. Youth lag at the end of the care continuum as well. Only 7% of HIV-infected youth have reached an undetectable viral load, much lower than the 25-50% of adults who are virally suppressed. (Eighth IAS Conference on HIV Pathogenesis, Treatment, and Prevention, 2015)

For the youth who were virally suppressed, a key factor in their success was a prompt referral to youth-friendly services. Improvements in prompt



linkage to, and retention in, care and ultimately significant improvements in suppression of viral load must be addressed through research and implementation of programs that work. We must also employ social media, gaming apps and new ways to engage youth outside of brick and mortar venues/settings.

The prevention continuum emphasizes that those testing HIV negative should be assessed for risk. They should be in the appropriate prevention interventions, including ongoing testing that includes sexual partners, encouragement of condom use and pre-exposure prophylaxis (PrEP). Scaling up services for youth remains a key challenge with the following representing some of the unique issues for adolescents.

Clearly, we must expand HIV testing in youth-serving settings such as schools and youth clinics as well as venues frequented by at-risk youth to reduce testing disparities. Those most at-risk need to be engaged in ongoing testing—our experiences in the Bronx demonstrated that HIV+ youth had an average of five prior negative tests. The success of routine testing of pregnant women and the consequent near elimination of perinatal HIV in the U.S. must serve as a guidepost to action.

In addition to treatment as prevention, primary prevention must be reconceptualized and updated to reach today's youth. Research must be deployed to understand what prevention messages and media will resonate. Policy issues such as the lack of FDA licensing of PrEP for minor adolescents must be addressed in the context of the acknowledged right of youth to confidentially access contraception, STI and mental health treatment without parental permission. This current policy impasse means that a vulnerable population of those at risk for HIV do not currently have access to drug assistance programs or federally funded payment for PrEP.

In this issue, we present articles that address key challenges of HIV among youth: unique approaches to improving ART adherence, supporting and caring for transgender youth, the epidemiology and care issues of perinatally infected youth and, finally, the context and tools for HIV prevention in this population.

Although adolescents are currently lagging in all key outcomes of the care and prevention continuum, we have the tools to end this re-surgency epidemic. As President Obama has said, we know what to do. The question is will we do it? Engaging the passion of youth, along with mobilizing multiple sectors of society, will enable us to proudly create a generation without the fear and reality of infection with HIV/AIDS in their lives.

**HIV**



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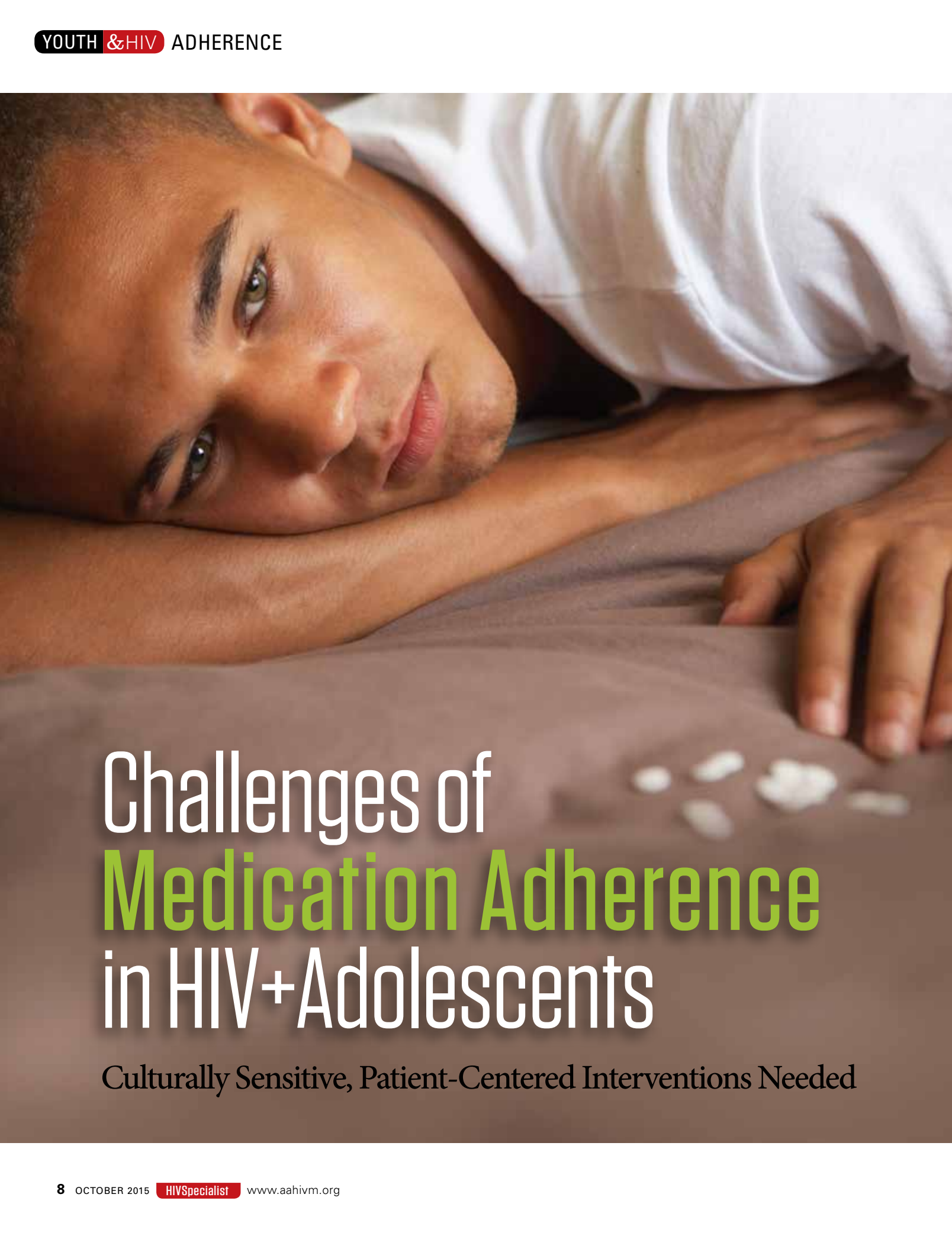
## Youth & the HIV Care Continuum

According to a new study by Massachusetts General Hospital and Fenway Health, just **40%** of HIV-infected adolescents and young adults (13-29 years) are aware of their HIV status, and of those diagnosed, only **62%** are connected to care within their first year of diagnosis.



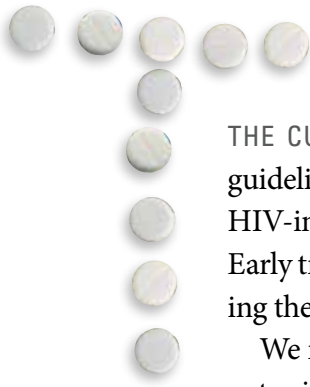
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Zanoni Brian C. and Mayer Kenneth H. AIDS Patient Care and STDs. March 2014, 28(3): 128-135.



# Challenges of Medication Adherence in HIV+Adolescents

Culturally Sensitive, Patient-Centered Interventions Needed



THE CURRENT Department of Health and Human Services treatment guidelines recommend starting antiretroviral therapy (ART) for all HIV-infected individuals as soon as possible, regardless of CD4 count. Early treatment is associated with improved outcomes, including reducing the risk of disease progression and prevention of viral transmission.

We now have evidence that the benefits of long-term medication far outweigh the possible and theoretical risks. There are four FDA-approved single tablet regimens to simplify taking daily medication. Why then, is it so hard to know when our HIV-infected adolescents are ready to start medication? What do they need to be successful?

The negative consequences of HIV are most prevalent with adolescents when cognitive, social and psychological difficulties challenge the backbone of HIV management, which is lifelong daily adherence to ART to reach viral suppression and improved health outcomes. Adolescents with other chronic illness find similar challenges to medication adherence as they often struggle to take daily medication in their effort to fit in with their peers. Missing medications may be a form of risk taking, like not using condoms or not wearing a seat belt.<sup>5</sup>

With guidelines supporting routine HIV testing among adolescents and improved testing mechanisms, there is opportunity to diagnose or “catch” recently infected patients or with acute or early HIV Infection (AHI). There is strong supporting treatment for persons with early HIV infection to maintain immune function, limit inflammation, and improve long term health outcomes.

Although a patient may be asymptomatic, often most adolescents already have moderate immune dysfunction by the time treatment begins due to missed testing and diagnostic opportunities when an adolescent presents with symptoms of AHI. As we advocate for routine HIV screening in all persons aged 13–64, we will find more adolescents who have been recently infected with HIV.

### Balancing Act

The trend toward earlier treatment is difficult for adolescent HIV providers, as we have long been advocates of waiting until our patients are ready to start therapy. As the number of youth living with HIV (YLH) continues to grow, we are faced both with the question of when to start, and how to get them ready to start as soon as possible. A recent study found that although a majority of providers believe adolescents need to follow the DHHS guidelines and start earlier, patient barriers such as lifestyle, nondisclosure to family, mental health and trauma, unstable housing and drug use hinder the medication initiation process. These barriers are reasons why providers don’t start adolescents on ART, in spite of their knowledge that it is beneficial.<sup>4</sup>

It is extremely difficult to predict medication success in behaviorally infected HIV positive adolescents, despite expertise in adolescent development and experience with prescribing lifelong therapy to adolescents with other chronic conditions. According to Tanney et al, a provider’s prediction of a patient’s adherence is only correct about 50% of the time<sup>12</sup> and research on factors predictive of optimal adherence for perinatally infected adolescents remains inconsistent. Tools such as Center for Adherence and Support Evaluation (CASE) have been



validated and can be used once a patient starts medication, but are not helpful to assess readiness.

The Adolescent Network (ATN), supported by National Institutes of Health-funded research, is in the process of developing HIV Treatment Readiness Measure (HTRM) for use by providers via an Audio Computer-Assisted Self-Interview (ACASI). The tool considers disclosure, psychosocial issues, connection to care, HIV medication beliefs, and alcohol and drug use. Preliminary data show promising findings and good test-retest reliability with the expectation that it can be used in a busy clinical setting to help the care team assess readiness and tailor interventions for patients.<sup>4</sup>

It is important to assess readiness because when patients are not prepared to start medication, the result can be treatment failure and resistance with fewer medications available for lifelong therapy. Lack of understanding of the need for lifelong ART puts adolescents at risk for suboptimal adherence. Those who are not ready to start medication despite their provider's recommendations often are in denial, feel hopeless, and have worsening anxiety and depression. Adjustment to an HIV diagnosis confounded with depression and other mental health disorders can take a long

time for some patients—and can interfere with the preferred timeline for beginning ART and attaining viral suppression.

It is a balancing act for a team to determine if waiting may be more potentially beneficial than immediately starting and risking drug resistance.

Youth living with HIV benefit from a trustworthy, non-judgmental adolescent-friendly HIV provider and clinical site. For those who don't want to disclose their HIV status to friends and family, it is crucial to maintain confidentiality as mandated by state laws. Having social support has been linked to better YLH adherence. However, it is difficult to help the patient build social support and encourage family members to support a patient's medication adherence if he or she is not ready to disclose their HIV status.

## Stigma and Stress Factors

A newly infected adolescent often faces dual stigma from being HIV positive, as well as coming out as gay. In some cases, HIV diagnosis for some heterosexual adolescents might be from a same sex encounter that they want to keep secret or of which they are ashamed. But, disclosure of HIV status to current and future partners is important. These individuals must take medication daily to stay well and reduce the risk of HIV transmission. They also need to protect themselves from acquiring other STDs.

Many psychological and psychosocial stressors can interfere with an adolescent's readiness and ability to adhere to a medication regimen. YLH, especially those who are older, have a high rate of risk factors, including substance abuse. HIV infected patients identify emotional factors as great barriers to treatment than the economic and social barriers that providers overestimate.<sup>14</sup>

Alcohol and drug abuse among YLH is common.<sup>3</sup> Poor medication adherence has been associated with alcohol use in this population and thus interventions targeted at reduced substance abuse can have a positive effect on adherence.<sup>10</sup> These include specialized interventions for YLH who are MSM, the population with the highest rate of alcohol abuse.<sup>11</sup> Motivational interviewing combined with cognitive behavioral therapy (CBT) has shown promise in decreasing substance use and illicit drug abuse among YLH.<sup>3</sup> Furthermore, individualized CBT and contingency management to decrease alcohol use also has a positive effect on medication adherence in an open pilot trial.<sup>3</sup> Currently, access to these services is difficult for YLH not in care at a research site, therefore more clinic-based and community interventions are needed.

Youth living with HIV have a high risk for depression and substance abuse,<sup>10</sup> making screening critical in conjunction with the medication readiness process. Access to mental health and substance abuse treatment services for YLH can be extremely difficult due to stigma and insurance issues. Promising clinic interventions for depression, therefore, have great potential to improve access to mental health services. Research suggests that a brief clinic-based motivational interviewing (MI) intervention

### Issues to consider in customizing an ART regimen for Youth living with HIV (YLH)

Issues	Plan
Preferences and Cognitive Ability	Single tablet regimens are preferred for convenience, decreased pill burden and side effects.
Size of pill, storage and refills	Teaching youth how to swallow pills, where they will keep pills, and how and where they will get refills.
Side Effects	Some youth may wish to be more independent & others may need daily or weekly contact to problem solve.
Communication with youth	Individualize communication plan as some youth require frequent check-ins by text, phone, email, or in person.
Communication among treatment team	Weekly team meetings to discuss medication adherence and challenges of youth engaged in care serve as reminder to contact youth who are not virally suppressed & need more assistance.
Technology	Setting alarm on watch or phone and/or medication app can help youth remember to take their ART.
Food	ART that requires food for absorption should be avoided if youth does not have daily access to food or has an erratic eating schedule.
Mental Health	Medications that include Efavirine with neuropsychological side effects as well as increased suicide risk should be avoided.
ART Medication Resistance, Interactions and Storage	Medications with most barrier to resistance (PI & DTG) for youth with daily adherence issues; interactions with birth control pills, Asthma meds, and Psych meds; how to store medications for access and avoiding disclosure of status if unknown to family and roommates.



improved depression. Those who attended at least two sessions improved readiness to change risk behaviors, which included adherence and drug use.<sup>12</sup>

Other hopeful research studies conducted among adults living with HIV could be tailored and studied among the adolescent population, specifically those based in motivational interviewing and CBT to improve adherence. Brown, et al, 2014 conducted a pilot study with CBT and individualized MM and showed improved medication adherence and reduced depressive symptoms in all subjects.<sup>1</sup>

## HIV Providers Can Help

HIV health care providers can buffer the negative effects of stigma on medication adherence. In one study, the impact of HIV stigma and its influence on medication adherence among HIV infected adolescent young women was low when health care satisfaction is high.<sup>7</sup> Stigma also must be addressed in the families and communities where patients live.<sup>12</sup>

The decision to start medication should be patient-centered and based on multi-disciplinary collaboration, taking into account an adolescent's ability to start and adhere to medication. Preparing an adolescent to take medication is a critical and resource-worthy endeavor that can contribute to lifetime adherence.

Admittedly, the medication readiness process can be both rewarding and challenging. Youth living with HIV have developmental tasks of gaining independence and formation of their self-concept, which includes living with HIV. Support from a social worker, access to mental health services and frequent follow-up visits at the clinic are crucial to establishing a therapeutic relationship and keeping the adolescent connected to care.

There is a large body of research that has looked at improving medication adherence in adolescents living with HIV. The most promising interventions are multi-factorial and customized for the patient, targeting the challenge of taking medications and taking steps to improve depression, reduce substance use and decrease other risk factors.

In a recent study, brief individualized motivational sessions impacted medication adherence at six months. An initial feasibility study of a computerized motivational intervention for adolescent living with HIV has also been promising, but needs to be duplicated in a larger study.<sup>14</sup>

Adhering to medication is crucial component of living a healthy life with HIV. YLH are at higher risk for negative outcomes because of higher rates of depression, substance abuse and other risk factors. All of these factors contribute to a youth's ability and drive to adhere to medication. YLH need culturally sensitive, tailored multi-factorial interventions to increase motivation and self-efficacy.

**HIV**

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CARE AND SUPPORT

# Transgender Adolescents

BY LAURA JADWIN-CAKMAK, MPH; ASA RADIX, MD, MPH, AAHIVS; ELLIOT POPOFF, MPH, and GARY W. HARPER, PhD, MPH

*Transgender is an umbrella term that refers to people whose gender identity does not align with their sex assigned at birth (See Table 1). This includes individuals on the trans feminine spectrum (i.e., those assigned a male sex at birth who identify as women, female, or transgender women) and individuals on the trans masculine spectrum (i.e., those assigned a female sex at birth who identify as men, male, or transgender men). This also includes individuals who identify outside of the gender binary—the classification of sex and gender into dichotomous categories of male and female, such as those who identify as gender nonconforming, genderqueer, genderfluid, or another gender.*

**T**RANSGENDER YOUTH TODAY are becoming aware of their transgender identity at earlier ages, necessitating those caring for adolescents to be prepared to meet their needs.

There is no single trajectory for transgender youth—for some youth a transgender identity emerges in early childhood, while for others a transgender identity first emerges with the onset of puberty or later in adolescence.<sup>1,2,3</sup> The onset of typical physical changes associated with puberty can be especially distressing for transgender youth and can trigger a cascade of psychosocial challenges during adolescence.<sup>4,5</sup>

As youth realize and assert a transgender identity at earlier ages, they may also transition in social, legal, and medical ways at younger ages than in previous years. It is increasingly common for adolescents to socially transition—i.e., to adopt a gender expression, name, and/or pronouns consistent with their gender identity—before entering high school.<sup>6</sup>

Legal transition may consist of legally changing one's name and gender marker on one's birth certificate, driver's license, and other forms of identification. Since state laws to legally change one's name and gender marker vary, such legal changes are not equally accessible to all transgender adolescents.

Making these legal changes has implications for an individual's employment status (e.g., it is generally much easier to get a job with a gender marker on an ID that matches one's gender expression), but may also have implications for medical insurance coverage (e.g., insurance companies may deny coverage of a Pap smear to a male individual).

Options to medically transition are currently available to transgender adolescents. Pubertal suppression for peri-pubertal adolescents (starting at Tanner stage 2–3) and hormone therapy for pubertal adolescents (starting around age 16) are now recognized as the standard of care for those experiencing strong, persistent *gender dysphoria*.<sup>5,7</sup>

Medical transition options also include gender-affirming surgeries, including breast augmentation or chest reconstruction, tracheal shave, genital surgeries, orchiectomy, hysterectomy/vaginectomy, and oophorectomy. Most surgeries are not performed until age 18, although individuals assigned a female sex at birth may be considered for chest reconstruction beginning at age 16.<sup>1,8</sup>

**Table 1. Definitions**

Gender identity	A person's deeply felt, inherent sense of being a girl, woman or female; a boy, man or male; a blend of male or female; or an alternative gender.
Sex assigned at birth	The sex (male or female) that was labeled at birth and listed on an individual's birth certificate; this is almost always based solely on external genital appearance.
Gender binary	The system of classification of sex and gender into dichotomous categories of male/masculine and female/feminine. The gender binary is socially constructed, and there are many cultures that have historically accepted and affirmed non-binary gender identities, such as the calabai and calalai of Indonesia, two-spirit Native Americans, and the hijra of India. In the U.S. today, common non-binary gender identities include genderqueer, gender nonconforming, and genderfluid.
Transition	The process of changing one's gender expression to align with one's gender identity.
Gender expression	The ways in which people communicate their gender identity to others through socially defined mannerisms, clothes, hairstyle, voice, and other forms of presentation.
Gender dysphoria	Psychological distress experienced due to an incongruence between one's body and gender identity.
Gender affirming procedures	Medical interventions used in order to align one's body with one's gender identity. Gender affirming procedures can include: the use of hormones to suppress puberty, masculinizing or feminizing hormone therapy, gender affirming surgery, including top or bottom facial surgeries
Cisgender	Cisgender refers to individuals whose gender identity aligns with their assigned sex at birth.





Medical intervention in adolescence has proven efficacious in improving the well-being of adolescents with gender dysphoria both during and well after treatment.<sup>9,10,11</sup> However, most transgender adolescents do not have access to these medical treatments—or may resort to accessing these treatments on the street through unregulated and untrained individuals—because of a lack of family support, limited access to knowledgeable providers, and/or a lack of insurance coverage.

Finally, it is important to note that not all transgender individuals experience a complete cross gender (i.e., male-to-female or female-to-male) identity, and individuals will vary in terms of the specific ways they desire to transition, as well as the resources available to them.

## HIV Prevalence

It has become increasingly apparent, despite gaps in HIV surveillance data, that transgender adolescents and young adults are disproportionately affected by HIV.

In 2010, youth comprised 17% of the U.S. population, but accounted for an approximately 26% of all new HIV infections in the United States<sup>12</sup>. Data on transgender individuals have not routinely been collected in the U.S. HIV surveillance system; however, available studies estimate that 27.7% of transgender women in the U.S. are living with HIV<sup>13</sup>, with African American and Latina transgender women being most at risk.<sup>13,14,15</sup> Few data are available on transgender men; however, estimated HIV prevalence is between 0–3%.<sup>13</sup>

Among transgender youth, several studies have similarly demonstrated high rates of HIV infection, with rates of 4.8–22% among transgender young women 16–19 and 2.4% among transgender young men.<sup>17</sup> Incidence data from states that routinely collect data on transgender persons show that new diagnoses among transgender women mainly occur in youth and young adults, especially those who are African American and Latina.

In New York City, from 2007 to 2013, 67% of the 212 new diagnoses of HIV infection among transgender people occurred in youth and young adults, with 12% among 13–19 year-olds.<sup>20</sup> Data from San Francisco show a similar trend with almost one in five new infections among transgender persons being found among those ages 18–24.<sup>21</sup>

Similar to adult populations, higher rates of HIV have been found among racial and ethnic minority transgender youth<sup>16,19</sup> and among those who engage in sex work.<sup>18</sup> Transgender youth are particularly susceptible to sex work due to family rejection, housing instability, employment discrimination and lack of access to gender affirming health services.<sup>16,22</sup> Additional HIV risk factors include high rates of substance use and condomless anal receptive sex.<sup>16,18,19,23,24</sup>

## Challenges Faced

To provide optimal HIV care to transgender adolescents, it is important to understand the various challenges faced by this population. Compared to the general adolescent population,

transgender adolescents are at increased risk for psychological distress and substance use, including depressive symptoms, increased rates of substance use and abuse, self-harm, and suicidal ideation and attempts.<sup>5,16,25–32</sup>

The increased risk of these negative outcomes are not a function of gender identity, but rather stem from the stresses due to prejudice, discrimination, rejection, harassment, and violence.<sup>33–36</sup> Bullying and violence from peers is common<sup>37,38</sup> and those who typically guide adolescents' development—parents and family members, teachers and school administrators, and religious leaders—may fail to provide support to transgender adolescents, sometimes even perpetrating discrimination or violence against them.<sup>39–41</sup>

Transgender adolescents also are more likely to experience homelessness and to drop out of school than their *cisgender* counterparts.<sup>43,44</sup> A lack of instrumental support from families and employment discrimination means that poverty and housing stability are prominent concerns in their lives, making participation in transactional sex and other areas of the underground economy the only options available to many.<sup>16,43,44</sup> Among transgender adults, transactional sex has been linked to other risk behaviors, including condomless anal receptive sex and the use of substances to cope with sex work.<sup>45</sup>

Finally, many transgender individuals of all ages lack access to health care, are unable to find providers knowledgeable of transgender health, and/or experience discrimination and stigma in the clinic setting.<sup>16,46</sup>

This may lead transgender adolescents to drop out of care and use street hormones and other methods, such as silicone injections, to transition without being monitored by a clinician. Taking hormones without supervision can result in undesired and potentially dangerous results. A lack of access to sterile needles and syringes to inject hormones can lead to needle sharing, a major risk factor for HIV and Hepatitis transmission among transgender populations.<sup>47</sup>

Silicone injections using adulterated, industrial-grade silicone—referred to as “pumping”—are used by some transgender adolescents and adults as a cosmetic filler, most often in the chest, buttocks, hips, and face.<sup>16,48</sup> In addition to risks from sharing needles during “pumping parties,” adverse effects include inflammatory reactions, edema, migrating globules, granuloma, pneumonitis, and death due to pulmonary embolism.<sup>48,49</sup> It is important for clinicians to be aware of and screen for these potentially dangerous practices among transgender adolescents.

Both transgender adolescents living with HIV and their providers may be concerned about the safety of hormone usage in the context of antiretroviral therapy. Estrogens, protease inhibitors and non-nucleoside reverse transcriptase inhibitors are primarily metabolized through the cytochrome P450 pathway. Although a potential exists for drug-drug interactions, studies evaluating ethinyl estradiol and antiretroviral therapy indicate that with the exception of fosamprenavir, where co-administration may result in decreased amprenavir levels, estrogen therapy

can be safely administered to persons receiving antiretroviral therapy. The other antiretroviral classes (integrase inhibitors, reverse transcriptase inhibitors, CCR5 receptor antagonists) are not affected by estrogen therapy. There are no significant interactions between spironolactone or testosterone therapy with antiretroviral therapy. The provision of culturally sensitive, affirming healthcare that meets the needs of transgender adolescents, including access to cross-sex hormone therapy when desired and indicated, is likely to promote their retention in care.

## Resilience Exhibited

There is a paucity of research focused on transgender adolescents, and most of the literature available on this population focuses on the challenges and risks faced by young transgender people.

However, it is also important to highlight the resilience exhibited by transgender adolescents. As a strengths-based framework for understanding why some people remain protected and healthy despite exposure to risks, resilience is characterized as a dynamic process whereby a person can positively adapt within contexts of significant adversity and avoid negative outcomes typically associated with risk exposure.<sup>50–53</sup>

Supportive families, acceptance from peers, friendships with other transgender individuals, and participation in Gay-Straight Alliances (GSAs; student-led, school-based clubs that aim to provide a safe place for LGBT students) all have been linked to positive outcomes for transgender adolescents.<sup>55–58</sup>

Because families of origin may be unsupportive, many transgender adolescents form families of choice, often participating in House and Ball communities, a subculture consisting primarily of young African American and Latino gay and bisexual men and transgender women. There they find support and acceptance, mitigating some of the negative effects of stigma and life stress.<sup>59–61</sup>

It has been recommended that primary and secondary HIV prevention efforts would be more efficacious if they incorporated a greater focus on a population's naturally occurring sources of resilience. More research on sources of transgender youth's resilience is needed so clinicians and others designing programs and interventions for transgender youth are able to capitalize on and enhance these sources of strength.

## Providing High-Quality, Effective Services

There are many things that clinicians serving adolescents with HIV can do to improve the quality of care provided to transgender youth.

The first is to ensure that transgender adolescents are treated with respect in every clinic interaction, from their first call to make an appointment, to the waiting room, to interactions with clinicians, to interactions with pharmacists. Transgender adolescents encounter prejudice and discrimination throughout many areas of their lives; countering these experiences by affirming youth's gender identity is vital to establishing a good health care experience.

**Table 2. Supporting transgender adolescents in healthcare settings**

**Clinicians and staff can improve the care provided to transgender adolescents by engaging the following supportive behaviors:**

Ask about and ensure all staff members consistently use patients' preferred name and gender pronouns, including in the waiting room

■ Feminine gender pronouns are she/her/hers, masculine gender pronouns are he/him/his, and non-binary gender pronouns include they/them/their, ze/hir/hir, zie/zir/zir, or avoiding pronouns and just using the person's name

Apologize if you make a mistake related to a patient's name or gender pronouns

Alter intake forms so that they use inclusive language and ask about patients' preferred name, the gender pronouns they use, and their gender identity

Ask each patient what words they use for their body parts and use those words to describe the patient's body

Make a gender neutral restroom available for patients

Increase your knowledge of transgender people's health issues

Be aware of and provide transgender patients with resources and referrals that are affirming of their gender identity and gender expression

Be knowledgeable about working with health insurance companies in order to meet the needs of transgender adolescents

**Additionally, clinicians and staff can improve the care provided to transgender adolescents by avoiding the following stigmatizing and unsupportive behaviors:**

Avoid making negative comments or gossiping about patients' gender identity or gender expression

Avoid asking inappropriate questions related to patients' gender identity or gender expression (e.g., asking about a patient's genitals when they are being seen for a cough)

Do not refuse care or offer limited services to a patient because of their gender identity or gender expression

Do not view patients' gender identity or gender expression as a mental illness

Do not make assumptions about patients' sexual orientation or sexual behaviors

Do not make assumptions about patients' desire to medically transition

To provide such care, clinicians and staff must understand the importance of social and cultural influences on transgender adolescents' health beliefs and behaviors and how these factors affect an individual's experiences.

We suggest this can be best achieved by moving away from a framework of cultural competence, which falsely implies that a person can achieve the outcome of competence in another person's culture, and toward a framework of cultural humility. This is a process whereby people continuously engage in self-reflection and self-critique as lifelong learners and reflective practitioners, and requires humility in how providers develop and maintain mutually respectful partnerships with both patients and communities, addressing the power imbalance that exists in the dynamics of the patient-provider relationship.<sup>62</sup>

Clinicians and staff can improve the care provided to transgender adolescents by increasing their knowledge of the medical and psychosocial issues faced by transgender youth and



engaging in cultural humility training focused on working with transgender adolescents. Specific ways to affirm transgender adolescents in health care settings are provided in *Table 2*. These practices were generated by a diverse group of transgender young adults serving as youth advisors for a research project focused on transgender and gender nonconforming youth's engagement in the HIV continuum of care.<sup>63</sup>

Finally, clinicians can improve the care provided to transgender adolescents by taking the time to understand what is most important to these patients. Clinicians should understand that HIV may not be transgender adolescents' most pressing need. Thus, inquiring about other areas of youth's lives, such as family relationships, housing and food stability, and providing needed resources will increase transgender adolescents' ability to stay engaged in care.

Clinicians should inquire about and tap into youths' sources of resilience. Given that many transgender adolescents have a strong desire for hormones, clinicians should strive to combine the provision of hormones and HIV care into the same visit when desired by the patient. If it is not possible to provide hormones during the HIV care visit, the clinician should attempt to ensure that patients who desire hormones are referred to a competent provider. Finding such providers may be challenging, and hormonal treatments may not be covered third-party payers. Reaching out to professional organizations such as WPATH, the World Professional Association for Transgender Health, as well as local organizations serving transgender populations may be of assistance in connecting transgender patients to needed resources.

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## Conclusion

Transgender adolescents are a vulnerable group who frequently experience prejudice and discrimination in the very settings responsible for fostering their growth and development: home, school, community, and healthcare settings. The high risk and prevalence of HIV among young transgender women, coupled with the difficulties in accessing high-quality, gender affirming HIV care, make this a high priority population for HIV specialists.

The limited research available with adult transgender men suggests that transgender young MSM may also be at high risk for HIV and therefore a high priority population as well. By gaining knowledge about the medical and social issues affecting transgender adolescents' health and well-being, and by providing care within a framework of cultural humility,

clinicians can better meet the needs of transgender adolescent patients, lessen the health disparities seen within this population, and promote retention in care for transgender adolescents living with HIV.

**HIV**

**Table 3. Resources for More Information on Transgender Health**

Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) Transgender Youth Resources: <a href="https://www.atnonline.org/public/TransYouthRes.asp">https://www.atnonline.org/public/TransYouthRes.asp</a>
The Fenway Institute: The National LGBT Health Education Center: <a href="http://www.lgbthealtheducation.org/">http://www.lgbthealtheducation.org/</a>
UCSF Center of Excellence for Transgender Health: <a href="http://transhealth.ucsf.edu/">http://transhealth.ucsf.edu/</a>
Children's Hospital Los Angeles Strengthening Youth Prevention Paradigms (SYPP Center): <a href="http://www.chla.org/webinars">http://www.chla.org/webinars</a>
World Professional Association for Transgender Health (WPATH): <a href="http://www.wpath.org">http://www.wpath.org</a>

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# Youth with Perinatal HIV

BY ELIZABETH SECORD, MD, YANA GRISTAN, AND JILL MEADE, PhD

**T**HE CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) reported the first four cases of perinatal HIV in 1980.<sup>1</sup> The number of cases rapidly increased in the US to peak at 1,650 in 1991.<sup>2</sup> The incidence of perinatal transmission dramatically declined with the introduction of prophylactic antiretroviral options for pregnant women, and dropped further with the initiative to ensure that all pregnant women were tested for HIV.<sup>3</sup>

These efforts resulted in a 95% decrease in perinatal infections in the U.S. since the mid-1990s.<sup>2</sup> Simultaneously, the introduction of adequate treatment regimens for HIV led to diminished mortality. The CDC estimates prevalence of perinatal HIV in the US at over 10,000 persons.<sup>4</sup> Some perinatal HIV patients are in their 30s, and many more are in their teens and 20s. Non-adherence to anti-retroviral medication secondary to intolerances, side effects and social stigma are the major challenges in caring for these youth.

SHUTTERSTOCK/ PIOTR MARCINKSI



## CASE I

*Ellie is a 19 year-old, African American (AA) woman with perinatally acquired HIV. Her mother died from AIDS when Ellie was two, her father died in prison from AIDS several years ago, and so, Ellie was raised by her aunt.*

*Ellie has been through several adherence programs for HIV, including multi-systemic therapy with her family, motivational interviewing (MI) focused on her, and a round of directly observed therapy with professionals with an MI background. All of these programs were successful for approximately a six to 12 month period with rebound to uncontrolled HIV viral load (VL). Her VL was 54,000 copies/ml and her absolute CD4+ T cell count 180 cells/mm.*

*Ellie stopped birth control at age 18 due to weight gain, and became pregnant within two months. The father of her baby was reported to be HIV+, also receiving care from the perinatal clinic. Anti-retroviral medication was re-prescribed and the need for adherence during pregnancy was discussed. The clinic advocate accompanied Ellie to her first two obstetrical prenatal appointments.*

*Unfortunately, however, Ellie did not stay adherent to her medication during the pregnancy and when Jake was born, Ellie's VL was 76,000. Ellie received intravenous zidovudine during labor and delivery, and reported giving zidovudine to Jake, as prescribed. His first HIV DNA at two weeks of life was positive, as was his HIV RNA (1,272,345 copies/ml). Antiretroviral therapy was started for Jake.*

The incidence of perinatal HIV dropped precipitously after the use of zidovudine during pregnancy was established as effective in decreasing transmission from mother to child in a multi-center trial of the Pediatric Aids Clinical Trial Network.<sup>3</sup> Zidovudine rapidly became the standard of care for pregnant women with HIV. Soon after, multi-drug therapy with zidovudine became the standard of care for HIV+ pregnant women.

The CDC recommendation for HIV testing for all pregnant women was significant in the attempt to assure that all women with HIV were identified and started on treatment. Recent advances for women with well controlled HIV viremia include: no need for intravenous zidovudine during labor and delivery, and a shortened period of infant zidovudine to four weeks.

If the mother's VL has not been controlled during pregnancy, a second drug, nevirapine, is added to the infant's regimen in three doses over the first several days of life, to optimize prophylaxis. The success with infant prophylaxis for HIV spurred other HIV prophylactic efforts such as occupational exposure prophylaxis, non-occupational post-exposure prophylaxis (nPEP) and pre-exposure prophylaxis (PrEP).

Unfortunately, we have seen an increase in the last 10 years in perinatal HIV cases in the U.S. because the incidence of high risk behaviors in teens has increased to a point where



a significant number of young women test HIV negative in the first trimester of pregnancy and become infected prior to delivery. A reluctance to request a second HIV test is a consistent barrier to identifying these women. Michigan has had seven infants born to young mothers (18-24 years old) with negative first trimester HIV tests who were infected during pregnancy (2006-2014)<sup>7</sup>. Three of the women would have been easily identified by risk factors, but four would not. The current recommendation in many states is retesting all pregnant women in the 3rd trimester, which is particularly important for youth. There also have been several reports of HIV infected infants born to perinatally infected youth.

*Jake's VL remained elevated. Social work, and eventually protective services, became involved. An aunt stepped in to help, as Ellie was becoming too ill. Ellie continued to struggle with her own medication adherence, and again, accepted in-home motivational interviewing for herself and to help her with Jake.*

*Ellie's new boyfriend moved in to help. She told us that she did not want him to know she was born with HIV, because, "I do not want him to think badly of my family", and so told the new boyfriend that she was infected as a teenager.*

*Ellie was unable to stay on medication, despite multiple interventions, and eventually died from progressive multifocal leukoencephalopathy. Jake is now in the care of his aunt and his VL has remained undetectable for three years. However, he continues to have developmental delay.*

## CASE II

*Steve, an AA college sophomore, with perinatally acquired HIV. Early in life, he lived with his mother, who struggled with drug addiction and was not able to consistently administer his HIV medication. She died of AIDS when Steve was six years-old and his paternal grandmother took over his care. When he first came to our clinic, Steve was reportedly on zidovudine, lamivudine, and ritonavir and his CD4+ T cell count was below 200 cells/mm. He was prescribed prescribed pneumocystis prophylaxis. He vomited consistently with his ritonavir and was amprenavir liquid instead. His first resistance assay revealed lamivudine and ritonavir resistance and likely resistance to amprenavir (virtual phenotyping). He was prescribed didanosine to replace the lamivudine, but no substitution was immediately available for the agenerase. Steve was maintained for a period of time on a suboptimal regimen until newer drugs were available, and then he was prescribed lopinavir/ritonavir with caution, because of his history of vomiting with ritonavir*



at full dose. He could not swallow pills yet, so his grandmother squeezed the gel caps and gave the mixture with chocolate syrup.

Meanwhile, Steve developed resistance to zidovudine and was prescribed abacavir. At this time, his resistance assay revealed current or historic resistance to: zidovudine, lamivudine, stavudine, nevirapine, delavirdine, efavirenz, indinavir, ritonavir, nelfinavir, saquinavir, and amprenavir.

At the age of 11, he learned to swallow pills and was successfully switched from liquids. His VL remained between undetectable and 1000 copies for a year, then his genotype revealed resistance to didanosine. He was prescribed tenofovir, but three months later, his grandmother began to complain that he was “sleeping all the time”, and thought it was from the new medication. He reported having “no friends”, and his grandmother reported: “We don’t have friends outside the house, we only need each other.”

When evaluation for depression was discussed, Steve’s grandmother refused any work-up or treatment for Steve’s depression. Anxiety, depression and sleep hygiene were discussed with the family, and Steve saw a psychologist in clinic, but refused therapy. Steve’s VL began to increase and at one point, he was hospitalized for taking three doses of his medication at one time after confrontation with his grandmother about missing medication. In-home adherence intervention was refused and throughout the first two years of high school, his VL remained between undetectable and 1000 copies. When he was 17, his VL began to climb and reached 52,000. Resistance to abacavir was identified and he was prescribed a double protease inhibitor regimen containing: lopinavir/ritonavir, darunavir with ritonavir boosting, and etravirine. He developed resistance to tenofovir, which was discontinued. He responded with a reduced VL after an in-home adherence program was accepted, but the regimen, which required twice a day medication doses, was difficult, and his grandmother was developing health problems, which interfered with her ability to assist.

The home-based program for adherence was modified to work directly with Steve and his VL dropped to undetectable. The family continued to refuse treatment for his depression, and initially refused any modification of his medication regimen to decrease the pill burden. When Steve started college, his VL began to increase. He reported extreme fatigue, and laboratory investigation revealed elevated muscle enzymes. His etravirine was held, and he requested a simpler once a day regimen. So, Steve was prescribed, with warning, once daily darunavir (which should be twice daily dosing for drug experienced patients), dolutegravir, and ritonavir. Further work-up of his elevated CPK was negative with an eventual diagnosis of benign idiopathic CPKemia syndrome, not related to his medication.

Steve declined to restart the etravirine, but after a six month period of undetectable VL, he began to have persistent elevation of his viremia. By first semester of his second year of college, he had a VL of 82,000 and, with review of his resistance, he accepted to change to a twice daily regimen of his darunavir and ritonavir, and agreed to add tenofovir/emtricitabine combination tablet, as was recommended by the Stanford Genotype Resistance Interpretation Algorithm.

Steve also reluctantly accepted an in-home/dormitory adherence intervention, which revealed many bottles of HIV medication without labels and multiple unused pills from various regimens. Further inquiry revealed that

Steve did not want his new girlfriend to become aware of his HIV status, and so was hiding the pills, which led to confusion and poor adherence.

It is relatively common for teens and young adults to become non-adherent with medical regimens. This developmentally normal struggle of being different from peers is amplified in youth with perinatal HIV and may lead to drug resistance. Years of incomplete adherence lead to acquired resistance that makes treatment choices very challenging.

Many interventions for improved adherence have been utilized in perinatal youth. Directly observed therapy is labor intensive, but may be useful in identifying technical problems. Multi-systemic therapy is an intensive family centered and community based treatment, which starts with identifying strengths and weakness in the family plan for medication delivery and then identifying and working toward those goals.<sup>6</sup>

MI is utilized widely to improve medical adherence and focuses on facilitating and engaging intrinsic motivation within the client in order to change behavior. It is a goal-oriented, client-centered counseling style for eliciting behavior change by helping clients to explore and resolve ambivalence.<sup>7</sup> All of the brief focused interventions described help short-term, but often, multiple therapies and multiple applications are necessary to ensure medication success. Illness stigma, poor self-care skills, mental health problems, and difficulties with transition to adult care compound the challenges faced by these youth.<sup>8,9,10</sup>

Direct partner notification was encouraged while anonymous notification was offered. Although all HIV+ youth are advised that disclosing to their partners prior to sexual activity is the goal to avoid secondary infection, many of our perinatal youth struggle with discussing their status. Steve agreed to disclose to his girlfriend and bring her in for HIV testing and to give us an opportunity to offer her PrEP. Depression screening and psychotherapy was finally accepted.

### CASE III

Samantha is a 23 year-old African American woman with perinatal HIV. She was born to a mother with a heroin addiction and was adopted, near birth, by a nurse who is not related to the biological family. Samantha

has been prescribed antiretrovirals since infancy, but had multiple side effects and toxicity issues. She had nausea and diarrhea with ritonavir, and tolerated neither regimens with ritonavir for therapy, nor low-dose ritonavir for boosting. Anti-emetics were tried, with some success, at various times in her life, but the associated sedation was prohibitive.

At the age of 17, Samantha had an episode of peri-orbital cellulitis complicated by an abscess, which required surgical drainage. That year she had three severe sinus infections, each requiring hospitalization for intravenous antibiotics. She developed severe diarrhea from clostridium

difficile after the second episode.

HIV medication adherence strategies were discussed at length with the family, and because of disease progression a new regimen without ritonavir was started. She then suffered an episode of pancreatitis from didanosine, was hospitalized for a month and had significant problems maintaining adequate weight.



**We have seen an increase in the last 10 years in perinatal HIV cases in the U.S. because the incidence of behavioral HIV in teens has increased to a point where a significant number of young women test HIV negative in the first trimester of pregnancy and become infected prior to delivery. A reluctance to request a second HIV test is a consistent barrier to identifying these women.**

*So, Samantha decided to discontinue all HIV medication. Although her T cell count was still above the prophylaxis level, her function assessed by mitogen stimulation was low. Throughout her high school years, she suffered from depression, which was never optimally treated due to multiple side effects of antidepressants.*

*At the age of 20, with her CD4+ T cell count below 50, she agreed to take prophylaxis for opportunistic infections, but had severe vomiting and diarrhea with trimethoprim and later had a drop in her neutrophil count on the dapsone, given as an alternative therapy. Other prophylaxis and HIV therapies were discussed, but she continued to refuse all medication.*

*"I know it upsets you and my family that I do not want treatment for my HIV, but I am so sick with everything that I try," she explained.. "I just want the rest of my time to be tolerable." She agrees to consider new therapies as offered, and remains in treatment with a psychiatrist*

*and a psychologist. She continues to come to our clinic for check-ups, but remains off all medications.*

Young adults with perinatally-acquired HIV, like adults with behavioral HIV, have often been exposed to many new antiretrovirals that ultimately result in toxicities or side effects which lead to discontinuation of all ART.

Some youth have minimal problems, but others, like Samantha, have a multitude of issues related to medication adherence.

*For Samantha, the repeated bad experience with taking medication led to aversions that have been generalized to all medications. She also appears to be predisposed to multiple drug toxicities.*

*A regimen of antidepressants and anti-emetic medication was employed, combined with supportive psychotherapy, to enable Samantha to successfully take anti-retroviral medication and antimicrobial therapy for an episode of pneumonia. Unfortunately, the success was short-lived. Within a month, she was off all medication again.*

More than half of our perinatal youth struggle with depression and are non-adherent with medication.

## Summary

Adherence to anti-retroviral therapy in youth remains a consistent barrier in the treatment of perinatally acquired HIV. Psychosocial issues, poor family support systems, depression and fear, resistance to medication, and drug side effects all contribute to non-adherence.

As new antiretroviral drugs become available, perinatally infected patients continue to become exposed to medications with unpredictable side effects. Hopefully improved tolerability of newer anti-retroviral medication with minimized toxicity will continue to serve as an important contribution in increasing adherence.

The use of family intervention services, motivational interviewing, directly observed therapy, and psychological therapy has helped to lower viremia and improve life skills in youth with HIV. Many perinatally infected youth require multiple and repeated interventions and long-term support to succeed.

**HIV**

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# HIV Prevention

## Saving Lives, Saving Dollars

BY ALISHA LIGGETT, MD, AAHIVS



**Treatment as prevention and virologic suppression rely first on early diagnosis, retaining patients in care, and ensuring adherence to the prescribed regimens.**

**W**HEN AIDS ARRIVED onto the national scene in the early 1980s, the diagnosis was tantamount to a death sentence. Shrouded in stigma, and likened to the modern day plague, little was known about this mysterious illness that caused eventual mortality. As one of the most politicized and feared illnesses, AIDS changed how individuals navigated sexual relationships in the modern world.

Fast-forward thirty years—the landscape of HIV care is over a generation in evolution. There are an estimated 62,000 youth living with HIV, and 32,000 of them are not aware of their status. Individuals ages 13 to 24 accounted for 26% (12,200) of new infections in 2010.<sup>1</sup> Despite reductions in HIV incidence in other age cohorts, youth are the fastest growing cohort of new HIV diagnosis.

In recent years, powerful prevention tools have led to renewed optimism toward HIV prevention. Among the arsenal of HIV prevention strategies, treatment as prevention has had the greatest impact on reducing HIV transmission.

The landmark HPTN 052 study showed a 96% reduction in transmission from early initiation of anti-retroviral therapy.<sup>2</sup> Sustained virologic suppression in genital secretions and blood reduce on onward spread through sexual contact. Given that two-thirds of infections are transmitted from those unaware of their status, treatment as prevention has the potential to have population-level impact.<sup>3</sup>

Some studies have identified community viral load, an aggregate of individual viral loads in HIV infected persons living in a community, as a biologic indicator of the effectiveness of anti-retroviral treatment and prevention.<sup>4</sup> Communities that experience high viral loads may also experience high rates of HIV incidence.

Currently 60% of youth do not know they are HIV infected. Youth fare worse along the HIV care continuum when compared to adults. Thirty percent of adults achieve virologic suppression compared to only 11% of youth.<sup>5,6</sup> This stark reality underscores the need for intensified efforts to reach undiagnosed youth. Efforts such as expanded testing and prompt follow up and treatment may help slow the spread of HIV.

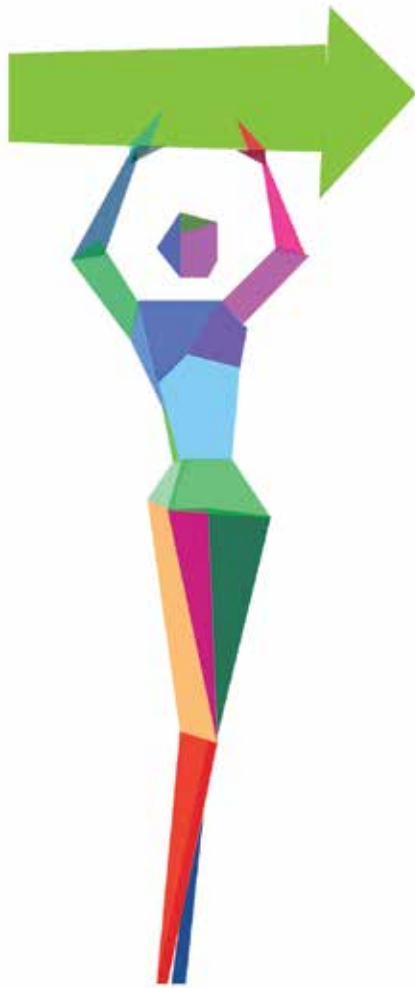
### Responsive Providers Key

It is important that providers are clinically responsive to the needs of young people. Poor health literacy and negative experiences with the health care system may deter youth from seeking care. Many experience difficulty navigating the cantankerous maze of people, places, and information in the health care system. They may also have difficulties expressing their needs and lack confidence in their own health care choices.

It is important that providers engage youth in care in a respectful and non-judgmental manner. It is also important that they are responsive to ethnic diversity, which goes beyond awareness and sensitivity to patients. It necessitates understanding the health issues and behaviors through the cultural lens of the youth, and incorporation of racial and cultural factors in planning and implementation of health care delivery.

Treatment as prevention of HIV has also been used to reduce perinatal transmission of HIV. It has resulted in a greater than 90% reduction in perinatal infections.<sup>7</sup> Despite immense success with this prevention strategy, perinatal infections continue to occur—sporadically in the US and at reduced but still high levels in the developing world. Lack of appropriate prenatal care and access to ART, treatment interruptions, substance abuse, and untreated mental health issues among mothers all contribute to this problem.

Addressing the social determinants that cause these issues will be important to eliminating perinatal infections in this country. HIV infected women are having children at higher rates today than in the past. HIV infected women of child bearing age should receive preconception counseling that specifically addresses conception planning, and PrEP for non-infected partners if they are seeking pregnancy. They should also be offered contraception to prevent unintended pregnancy.



**Condoms are an inexpensive, effective method for preventing HIV, sexually transmitted infections, and pregnancy, yet barriers to access and use remain.**

### Prevention

More recently, HIV Pre-exposure prophylaxis (PrEP) has gained traction as a highly effective method at preventing HIV infection. Non HIV infected individuals can take a daily pill, tenofovir-emtricitabine, to dramatically reduce their risk of becoming HIV infected. PrEP has a proven 42-90% efficacy in preventing HIV acquisition, and recent “real world” studies of demonstrate similar efficacy with consistent use.<sup>9,10</sup>

PrEP has not yet been approved by the FDA for use in prevention by individuals under the age of 18, however the use of tenofovir-emtricitabine is approved for treatment of HIV infected adolescents. PrEP, like other medicines can be prescribed for off-label use and should be considered on a case-by-case basis for high risk adolescents under the age of 18. HIV post-exposure prophylaxis (PEP) is another prevention method that involves initiation of a four-week course of anti-retroviral medications within 72 hours after possible or actual exposure to HIV.

Other biomedical pre exposure prevention strategies are in various stages of development. Intravaginal microbicides infused with antiretrovirals have shown some, albeit inconsistent, promise as a prevention method in women. Alternative drug formulations of PrEP are being developed which include mucosally absorbed and injectable forms. There are also ongoing clinical trials evaluating the efficacy of vaginal rings infused with combination contraception and antiretrovirals to prevent pregnancy and HIV infection including a current Microbicide Trials Network safety study of adolescents using a dapivirine-infused ring.

Sexual behavior change initiatives, such as condom use during sex, are also important tools in preventing HIV. Condomless sex is a major risk factor for HIV, but remains common among adolescents. Forty percent of adolescents did not use a condom during their most recent sexual intercourse.<sup>11</sup>

Behavior change processes around condom use are complex and pose many challenges to young people. It involves having knowledge of HIV disease, but also being at a place of psychosocial maturity and comfort with one's sexuality and sexual orientation that allows for sound decision making around sexual health. External forces such as social inclusion and cultural norms regarding homophobia and transphobia also negatively and positively reinforce condom use.

Condoms are an inexpensive, effective method for preventing HIV, sexually transmitted infections, and pregnancy, yet barriers to access and use remain.

Condom promotions campaigns in schools, clinics, and other institutions where young people congregate are instrumental in HIV prevention. They provide free and readily available condoms to reduce the financial and logistical barriers to use. Giving condoms to youth does not pose a threat to their sexual health. In deference to the opinions of



**Poor health literacy and negative experiences with the health care system may deter youth from seeking care. Many experience difficulty navigating the cantankerous maze of people, places, and information in the health care system.**

### Diagnosis Revolution

Improvements in HIV testing technologies have resulted in earlier detection of HIV and improved identification of acute infections.

The most current modality, the fourth generation HIV immunoassay, can diagnose HIV within 10–14 days post-infection, ten days earlier than the third generation assay. The key difference in these tests is the ability to detect the p24 antigen, an HIV envelope protein, and virologic material during acute infection.

During the acute period, patients may exhibit clinical symptoms that mimic a viral syndrome and have extremely high levels of virus in their blood and genital secretions. The rate of HIV transmission during acute infection is 26 times as high compared to chronic infection.<sup>8</sup> Current recommendations call for prompt treatment of patients with acute HIV infection. The rationales for immediate treatment include reduction in infectivity and severity of acute disease, slower disease progression rates, reduction in the size of viral reservoir, a decreased rate of viral mutation through suppression of viral replication and thus preservation of immune function. The Western blot is no longer used as a confirmatory test due the high false negative rate during seroconversion period and slower turn-around time.

many, studies show that these campaigns do not encourage earlier initiation of sex or increase promiscuity.<sup>12</sup>

Young people may also experience power imbalances in their sexual relationships, limiting their ability to negotiate condoms with sexual partners. Effective condom promotion campaigns should also focus on condom negotiation skills. Developing the language around condom use should take into consideration cultural factors and relationship dynamics.<sup>13</sup>

## Harm Reduction Strategies

Harm reduction strategies also have played an important role in behavior strategies aimed at youth. They focus on reducing risk associated with normative adolescent risk taking behavior.

This includes onset and frequency of sexual activity, condom use, and concurrent sex and drug or alcohol use. Comprehensive sexual education programs in schools and communities have proven to be effective at delaying the onset of sex, reducing the number of partners, and increasing condom use.<sup>14</sup> Abstinence only programs have proven to be ineffective in these same measures.

Young people need accurate and comprehensive information and harm reduction counseling about sex in order to make informed decisions to protect themselves. Providers present in the lives of adolescents should screen for risk taking behaviors and use principles of motivational interviewing to assess risk in a non-judgmental manner.<sup>15</sup> Additionally, utilization of social marketing and digital tools can be used to access youth in mediums where they are more likely to access information.

## Scourge of Stigma

HIV stigma remains a powerful opposing force to HIV prevention and may deter youth from seeking health care and getting tested for HIV. It is a powerful determinant to the success of HIV engagement and treatment. Stigma remains a key reason why youth are reluctant to get tested, disclose their HIV status, seek care, and adhere to antiretrovirals.<sup>16</sup>

HIV infected gay, bisexual, and transgender youth, those who trade their bodies for money or goods, and those viewed as sexually promiscuous are key youth populations that are heavily stigmatized.

Fear coupled with disapproval of behaviors, and lack of education around HIV can perpetuate stigma. Family stigma can lead to rejection from the support systems and also lead to, physical, or verbal abuse. This can be a major barrier for seeking care in youth who rely on families for financial and social support for their livelihoods. Internalized stigma may result in feelings of disempowerment, and can instill fear and avoidance of HIV infection or the need to get tested. Institutional stigma can play out in the form of employment discrimination or judgment loaded interactions with health care workers.

The goal of HIV stigma prevention strategies among youth is to reduce barriers to accessing HIV testing and treatment

services as well as mitigate possible exclusion from social networks.<sup>17</sup> This includes assistance with disclosure to loved ones, supportive mental health counseling and messages of empowerment and self-determination. It also includes working to change discriminatory laws and practices that perpetuate stigmatization of HIV infected individuals at an institutional level.

## Addressing Structural Barriers

Biomedical and behavioral interventions for HIV prevention are very important, especially when used in combination. However, failing to address the structural barriers that feed disparities in HIV infection threaten to undermine the progress made toward reducing incidence.

African Americans and Hispanic-Latinos disproportionately bear the burdens of HIV disease. African-Americans of all age distributions make up nearly half of new HIV infections in the United States and have the highest rates of AIDS at diagnosis.<sup>18</sup> Youth of color, particularly gay and bisexual men, are heavily affected by HIV. Black (58%) and Hispanic-Latino (21%) gay and bisexual youth made up 79% of new infections among youth ages 13 to 24 in 2013.<sup>19</sup>

Popular culture erroneously justifies these disparities by focusing on sexual promiscuity. However studies show increased risk despite even or fewer risk taking behaviors compared to whites.<sup>20</sup> The mass media has also suggested that Black men may act as a “bisexual bridge” between the gay and straight communities, but there has been little evidence to support this hypothesis.

Several linked issues contribute to higher risk of infection among youth of color, with racism as the most significant contributor. A history of oppression in this country, with roots spanning back to institutionalized enslavement, has far reaching consequences in the present day. Educational and employment inequities fuel the high rates of poverty among African American and Hispanic-Latino youth.<sup>21</sup>

Residential segregation is an example of how poverty acts as a powerful social determinant of health. It concentrates vulnerable populations along racial and socio-economic lines within impoverished communities. Poverty can in turn determine access to education, housing and health care. Economically stressed communities tend to have poorer access to health care services.<sup>22</sup> With respect to HIV infection, these individuals are often diagnosed later in their disease process, which may increase community viral load. The acute and chronic stress that stems from racism and resource disparities also have profound impacts on HIV health outcomes.

Poverty also heavily influences sexual behavior among youth and can amplify HIV risk. It is closely associated with higher rates of coerced sex, rape, and unprotected sex in exchange for monetary incentives, food, or clothing. It also contributes to substance use, unstable relationships, and sexual decision making focused on short term gain. In the 2009-2010 school year, Black and Latino students comprised 70% of the arrests

**The goal of HIV stigma prevention strategies among youth is to reduce barriers to accessing HIV testing and treatment services as well as mitigate possible exclusion from social networks.**





**Residential segregation is an example of how poverty acts as a powerful social determinant of health. It concentrates vulnerable populations along racial and socio-economic lines within impoverished communities.**



made in school. Harsh school punishments from suspensions and arrests have resulted in higher numbers of youth of color coming into contact with law enforcement at earlier ages.<sup>23</sup> Once in prison, youth may experience higher risk of HIV due to increase prevalence in prison, and poor access to condoms and testing services.<sup>24</sup>

Complex, racially distinctive sexual networks also may play a role in concentrating the epidemic within communities of color. A young person of color from a poor community with high community viral load and/or high HIV prevalence has a greater chance of contracting HIV with every sexual act than their counterpart in an affluent community with lower community viral load.

Mass incarceration of adults and youth of color further concentrates social networks within their communities. Youth of color also live with the threat of incarceration and racial profiling by law enforcement in school and in their communities. Black youth face higher rates of juvenile incarceration and often receive longer sentences for similar crimes compared to their white counterparts. Social determinants of health have a profound impact on communities of color and are cumulative over the lifespan. These powerful forces may be more reliable predictors of HIV risk and outcomes in that youth are more likely to come contact with HIV disease within their communities.

## Saving Lives—and Dollars

As we move toward our goal of zero incidence, it is important to focus on prevention and away from the crisis based interventions that defined treatment strategies in the past. Prevention saves health care dollars.

Preventing one case of HIV saves the system \$230,000.<sup>25</sup> Prevention also saves families from anguish due to lost loved ones, and loss of income and parentage due to AIDS. It also saves a generation of youth from the fear of navigating sexual relationships under the threat of HIV disease. More importantly, it saves a generation of youth from the fear of navigating sexual relationships under the threat of HIV disease. **HIV**

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She provides HIV and primary care to patients from underserved communities, ethnic and racial minorities, gender minorities, and individuals negatively affected by social determinants of health. She has worked extensively with HIV positive youth and HIV negative high-risk youth in clinical and community based settings. Her work also centers around HIV prevention, and bio-psycho-social models of development and behavior change in high risk populations.

# Small Talks in HIV Prevention

## Cases from the Clinic

### EDITOR'S NOTE:

These two case studies describe how teachable moments and "small talks" can help patients living with HIV adopt safer sexual behaviors

### An unexpected STI symptom signals change in one patient's sexual activities

PETER SHALIT, MD, PhD, AAHIVS

**L**uis is a 44-year-old gay man who was diagnosed with HIV four years ago. At diagnosis he expressed feelings of guilt and shame at becoming infected, and stated he was planning to be celibate "indefinitely" because he felt "contaminated" and was no longer interested in being intimate with other men.

I started Luis on a simple NNRTI-based ART regimen. He was conscientious about taking his medication, and we were able to reduce his follow-up visits to every six months. At each visit, I asked Luis about his sexual activities, and he continued to stick to his "vows of celibacy." At his most recent visit, however, he complained about a painful canker sore inside his cheek that had been bothering him for the past two weeks. On examination, the sore in his left gingiva measured 1.5 cm.

As usual I asked Luis about his sexual activities. He told me that he had started attending some "Positive for Positive" sex parties and had regained his comfort and self-confidence in having sex again. He discovered sex clubs, saying that after his long period of celibacy he felt like "a kid in a candy store." He told me that men he met at the clubs did not discuss their HIV status, nor did they encourage condom use. Luis's renewed sexual activities included receptive and insertive anal sex, mutual oral sex, and mutual rimming (oral/anal contact).

I told Luis I was concerned that the oral lesion inside his cheek might be syphilis. He was skeptical. This was an important teachable moment for him, an opportunity to offer information that would encourage a positive change in his current sexual behavior.

I explained that resuming an active sex life raised some important health issues for him, as well as for his sex partners. For example, oral ulceration increases risk of acquisition and transmission of HIV infection. It also was possible that some of Luis's sex partners were sero-negative, putting them at risk of acquiring HIV or for Luis acquiring another STD. Also, while Luis's NNRTI regimen was effective in suppressing his virus, NNRTIs are known to have a low barrier to resistance. He could possibly acquire an HIV superinfection from an HIV-positive sex partner whose virus was resistant to one or more NNRTIs.

Because we had a well-established, trusting relationship, Luis felt free to ask questions and listened closely to the answers. He agreed to STD screening.

The following day the rapid plasma regain test came back 1:8, confirming a diagnosis of syphilis. When Luis returned for treatment with intramuscular penicillin he said he felt "punished" for becoming sexually active, and he intended to return to his celibate life.

Luis' statement created an opportunity to engage in a non-judgmental, positive discussion about safer sex. I assured Luis that it was possible for him to have a healthy, rewarding sex life while reducing risk. We discussed the importance of routinely using condoms during sex to protect his health as well as to prevent transmitting HIV to others. We agreed to twice-yearly STI screening and talked about the relative risk of sexual contact in anonymous hookup sites vs. sex with men he has gotten to know first. We also set safer sex goals that he could begin to incorporate into his life.

Our brief conversations about safer sexual behavior continued and evolved during each of Luis' follow up visits. In addition, I referred Luis to a counselor familiar with gay men's issues to help alleviate his feelings of guilt and encourage his self-esteem.

### PrEP "small talk" for an HIV discordant couple

JAMES L. RAPER, PhD, CRNP, JD, FAANP, FAAN, FIDSA

**D**uring a routine six-month primary/HIV return visit with Marcus, a 24-year-old African American man with a history of having sex with other men, I had the opportunity to discuss pre-exposure prophylaxis (PrEP), which is one of the key areas of focus in the newly updated U.S. National HIV/AIDS Strategy (<https://aids.gov/federal-resources/national-hiv-aids-strategy/nhas-update.pdf>) for those at high risk of acquiring HIV.

I've been providing care to Marcus since he was diagnosed with HIV at age 19. He's been in good health for five years while taking fixed-dose (EFV/FTC/TDF), with a current >600 CD4+ cell count and a viral load (vRNA) <20 copies). During my sexual risk assessment our dialog went something like this:

Raper: "When was the last time you had sex?"

Marcus: "Two days ago with my boyfriend."

Raper: "New boyfriend. That's exciting! When did you meet?"

Marcus: "I've known him for a couple of years, but we just started being together about four months ago. John moved in with me last month."



Raper: "That's great. What are you guys doing to be safe? Using condoms? Are you monogamous?"

Marcus: "You know, I'm undetectable."

Raper, "Is he HIV-positive too?"

Marcus: "He's not infected. We went together and got all the VD tests at the health department. He knows I've got HIV and that I take my medicine every day. I planned to bring him with me today, but he had to work."

Raper: "I'm glad you went to the health department for STI & HIV screening. I'm really glad John is not infected and that you guys want to keep it that way. The fact that you take your HIV-medicine and that you have a suppressed viral load is really great. I call that a twofer, because you get the health benefits of viral suppression and reduce the risk of HIV transmission to John."

"While the risk is seriously reduced with your undetectable viral load blood test, if it's all right with you, I'd like to tell you about some other things that you should know and consider."

Marcus: "Sure, Doc. Tell me."

Raper: "Research suggests that taking antiretroviral therapy as prescribed and having an undetectable viral load may greatly reduce, but not eliminate, the risk of transmitting HIV to sex partners. The amount of HIV present in other body fluids may not be undetectable all the time. Some HIV medications are more effective at fighting HIV in blood than in genital fluids. Viral load can also be higher in genital fluids because of the presence of other sexually transmitted infections (STIs).

"The fact is that people with a generally undetectable viral load may have occasional and brief viral load increases into the detectable range. These 'viral blips' can occur even when a person is taking HIV medicine. The impact of 'viral blips' on transmission of HIV is unknown. If HIV becomes resistant to medications, the viral load can increase.

"STIs can increase an HIV-positive person's viral load. Some STIs can

cause sores or ulcers in the genital area that create an entry or exit point for HIV. Even without a sore, STIs can increase the risk of transmission."

Marcus: "We've got a closed relationship."

Raper: "I understand; I also understand that sometimes things can change. Right?"

Marcus: "So, what do you suggest?"

Raper: "I tell all my HIV-positive patients who are in a relationship with someone who is HIV-negative, or of unknown status, that it is important for them to consider all the available prevention strategies and act with the mutually acceptable strategies to prevent transmission of HIV. Let's review what we know:

**1. Use condoms consistently and correctly.**

**2. The HIV-positive partner should stay on treatment.** HIV-medicine reduces the amount of HIV virus (viral load) in blood and body fluids. HIV-medicine can keep people with HIV healthy for many years, and greatly reduce the chance of transmitting HIV to sex partners if taken consistently and correctly.

**3. Choose less risky sexual behaviors.** Oral sex is much less risky than anal sex. Anal sex is the highest-risk sexual activity for HIV transmission. Insertive anal sex (topping) is less risky for getting HIV than receptive anal sex (bottoming). Non-penetrating sexual activities that do not involve the potential exchange of body fluids carry little to no risk for transmitting HIV (e.g., frottage & touching).

**4. Pre-exposure prophylaxis (PrEP), taking HIV medicine daily to prevent HIV infection.** PrEP should be considered for the HIV-negative partner. PrEP is meant to be used consistently, as a pill taken every day, and to be used with other prevention options such as condoms. We have a PrEP clinic here if John is interested."

Marcus: "OK, Doc, I'll talk with John about all of this."

Raper: "Great. I'm happy for you guys. I would be happy to meet and discuss the issues again with you and John. Until then, keep up the good work on taking your medication and think about the prevention strategies we just discussed."

**HIV**



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# Help Patients Jump the “Prior Authorization” Insurance Hurdle

## EDITOR'S NOTE:

The following opinion piece was written by Dr. Joseph McGowan, chair of the New York/New Jersey Chapter, to bring attention to the challenging issues practitioners experience regarding utilization management. We are pleased to report this article appeared in *Newsweek*, bringing national attention to the problem.

**H**IV/AIDS RESEARCHERS JUST MADE A BREAKTHROUGH DISCOVERY—patients who start taking anti-HIV medications as soon as they learn they're infected are over 50% less likely to develop full-blown AIDS than patients who delay treatment.<sup>1</sup> Quick access to medications saves lives. But profit-focused insurers are impeding that access through a bureaucratic process known as “prior authorization,” which endangers patients' health by forcing them to wait days or weeks for their prescriber-approved medicines. Lawmakers must overhaul the prior authorization process to ensure that patients and their care providers—not insurance companies—decide the best course of treatment.

Health insurance plans currently restrict patients to a certain set of covered medications. If a patient's provider prescribes a drug not covered under a plan, the patient can seek “prior authorization” from her insurance company to take the medicine.

Too often, insurance companies deliberately make the prior authorization process difficult and time-consuming to prevent patients from accessing costly, but lifesaving, medicines.

Each insurance plan has its own set of covered drugs, prior authorization process, and criteria for approval. Those drugs and criteria change frequently. That means clinicians and support staff—who generally conduct the prior authorization appeal on behalf of their patients—waste significant time navigating insurance bureaucracies. The average medical practice spends 20 hours every week helping patients with the prior authorization process, according to a *Health Affairs* study.<sup>2</sup>

That wasted, uncompensated time costs doctors and nurses money. The typical medical practice loses up to \$85,000 each year dealing with prior authorizations and other insurance bureaucracy.<sup>3</sup> Healthcare providers inevitably pass these costs on to patients in the form of higher prices.

The purposefully complicated prior authorization process doesn't just cost patients money. It also may cost them their health—and in some cases, their lives. About seven in 10 physicians report that the average prior authorization request takes several days to process.<sup>4</sup> During that time, sick patients go without their doctor-recommended treatments.

Sometimes patients are kept waiting far longer to receive their doctor recommended, FDA approved medications. Ten percent of physicians experience average wait times longer than a week when requesting a medication on behalf of their patients.<sup>5</sup> One healthcare provider related the story of a cancer patient who “died before he ever received prior authorization. It took weeks.”<sup>6</sup>

**Too often, insurance companies deliberately make the prior authorization process difficult and time-consuming to prevent patients from accessing costly, but lifesaving, medicines.**

As medical director of one of the largest AIDS treatment centers in New York, I've seen firsthand how drawn-out prior authorization appeals harm patients with serious chronic diseases like HIV/AIDS. HIV treatment is evolving rapidly—no “one size fits all” treatment is appropriate.

Patients living with HIV can keep the disease suppressed for decades—but only if they strictly follow their prescription regimen. Patients who miss just 5% of their doses can suffer a spike in their viral loads, according to a study published in the *American Journal of Managed Care*.<sup>7</sup>

Higher viral loads sicken patients, increase the risk of spreading HIV to others, and even enable the virus to adapt and become resistant to treatment.<sup>8</sup> In short, HIV can spiral out of control in a matter of days or weeks, while patients wait for insurers to approve their prior-authorization request.

In addition to prior authorization hurdles, many plans use “step therapy,” which requires patients to try older, less expensive—but less effective—medications and become sicker before the plan approves a physician's originally prescribed regimen.

Recognizing the cost saving role of Prior Authorization, it might be best to exempt certain classes of therapy that require individualized care plans (such as HIV, Hepatitis C, or mental health medications) from the process.

Lawmakers must crack down on prior-authorization processes



designed to prevent timely access to lifesaving drugs. To save money and enable patients to start their treatments on time, all insurers should be required to use the same standardized prior authorization process and forms. To streamline the authorization process, insurers should provide clinicians and patients with a clearly defined number to call or website to access. That will stop insurers from dragging out authorization requests by constantly transferring doctors from one customer service representative to another.

Insurers must also respond to prior authorization requests within a set time limit. Providers must realize that if the insurance company fails to respond promptly, the prescribed medicine wins an automatic authorization. Better awareness and enforcement of this system will prevent insurers from stringing patients out for weeks on end. The convoluted prior authorization process makes it more difficult for patients to access the medicines their providers prescribe. Reforming the process would rein in abusive insurer practices and ensure better health care for sick Americans.

**HIV**

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BY ELIZABETH DOHERTY, MD, MS and  
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## NEW GUIDELINES

# Cervical Cancer Screening in Women with HIV/AIDS

**A**LTHOUGH USED SINCE THE 1940s TO SCREEN WOMEN FOR CERVICAL CANCER, the traditional Pap smear has relatively low sensitivity (55–60%) as a diagnostic test. However, its capability as a diagnostic tool increases when repeated over time. With a better understanding of the natural history of cervical cancer and the availability of testing for Human Papilloma Virus (HPV), the oncogenic virus responsible for cervical cancer, the recommended time interval between Pap smears was extended in 2012 from yearly to every three to five years. This recommendation was supported by the American Cancer Society, American Congress of Obstetrics and Gynecology, and the U.S. Preventive Services Task Force. In addition, these organizations agreed Pap testing is NOT recommended before age 21 years.<sup>1,2</sup> However, these recommendations did not apply to women with HIV disease.

Given the higher prevalence of cervical disease, more rapid progression and less regression of pre-cancerous lesions, and overall greater risk of cervical cancer in the setting of HIV (especially in women with low CD4 cell counts), annual Pap smears continued to be recommended for women living with HIV. Moreover, there has been no consensus regarding HPV co-testing in the context of managing Pap smears in the population of HIV-infected women.

Fortunately, recent studies have shown that less frequent cervical cancer screenings do NOT increase morbidity or mortality among women living with HIV. A key point is that cervical dysplasia from HPV infection often resolves without intervention in younger women, regardless of their HIV status. As a result, screening and management recommendations are now similar to women without HIV. The most recent CDC/DHHS guidelines reflect this newer data.<sup>3</sup>



SHUTTERSTOCK



### Women living with HIV Aged <30 years

Cervical cancer screening with cytology should begin at the time of diagnosis with HIV for women at age 21. For women less than age 21, (regardless of whether HIV infection was from vertical or horizontal transmission), cervical cancer screening should begin within one year of the onset of sexual activity or at the age of 21, whichever comes first. If the first Pap smear is normal, cytology should be repeated in 6-12 months. **After three consecutive normal Pap smears, women with HIV can space cervical cancer screening to every three years.** Routine co-testing for HPV is NOT recommended. However, reflex HPV testing is recommended to help stratify management when cytology shows atypical squamous cells (ASC-US). If HPV testing is negative, then repeat Pap in 6-12 months is acceptable, but if HPV testing is positive, then the next step should be colposcopy. Repeat cytology should be followed by colposcopy for any cytology results equal to or more advanced than ASC-US, as well as the continued presence of HPV.

### Women living with HIV Aged ≥30 years

For women > 30 years old, cervical cancer screening with cytology should begin at the time of diagnosis with HIV. Unlike for women less than age 30, co-testing with HPV is acceptable and when negative, the screening interval can be extended.

If cytology alone is performed, the recommendations are the same as for younger women. That is, after three consecutive normal Pap smears, women over age 30 can space cancer screening to every three years. When HPV co-testing is available, and both cytology and HPV are negative, co-testing for HPV can also be repeated in three years. If cytology is normal and HPV is positive, co-testing should be repeated in 12 months. Lastly, if either cytology is abnormal OR HPV-testing is positive, colposcopy should be performed. When HPV types 16 or 18 are detected, (due to their highly oncogenic nature), the guidelines recommend colposcopy rather than repeat co-testing in 12 months.

Abnormal cytology without HPV co-testing is managed the same as for women less than age 30. When cytology shows ASC-US, management should be stratified based on reflex HPV result. When HPV testing is positive, the patient should undergo colposcopy. When HPV negative, cytology with reflex HPV testing can be repeated in 6-12 months. Any cytology results equal to or more advanced than ASC-US, as well as continued presence of HPV, should go to colposcopy. The ACS, ACOG, and USPSTF guidelines note that women

Table 1. CDC/DHHS Guidelines for cervical cancer screening among women living with HIV (Ref. #3)			
Age in Years	<21	21–29	≥30
Begin Screening	Within 1 year of onset of sexual activity	At HIV Diagnosis	
Cytology only (Pap smear)	↓ Repeat yearly ↓ If normal x 3, repeat every 3 years		↓ Repeat yearly ↓ If normal x 3, repeat every 3 years
OR			
Co-testing (Pap smear & HIV)	Reflex HPV testing only with ASCUS		↓ If normal x 1, repeat every 3 years

without HIV can stop routine Pap tests at 65 years of age. However, there is NO recommendation for an upper age limit to stop cervical cancer screening for women living with HIV.

### Women living with HIV who have had a hysterectomy

It is important to establish if the woman has had a total hysterectomy or, much less commonly, a supra-cervical hysterectomy. Women with a supra-cervical hysterectomy should continue to have routine cervical cancer screenings based on their age. For women who have had a total hysterectomy for benign disease (e.g. fibromas, severe dysfunctional uterine bleeding, etc), continued routine screening of the vaginal cuff is **NOT** recommended. If the total hysterectomy was done for high-grade CIN, adenocarcinoma in situ or invasive cervical cancer, annual vaginal cuff Pap smears are recommended. **HIV**

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# When to Initiate Antiretroviral Therapy in HIV and Aging

**EDITOR'S NOTE:** The American Academy of HIV Medicine (AAHIVM), the American Geriatrics Society (AGS) and the ACRIA released the first clinical treatment strategies for managing older HIV patients: *The HIV and Aging Consensus Project: Recommended Treatment Strategies for Clinicians Managing Older Patients with HIV* in the fall of 2011. The following chapter was updated August 16, 2015.

- Antiretroviral therapy should be initiated in all patients over the age of 50, regardless of CD4 count
- Providers must be aware of possible increases in drug-drug interactions when prescribing ART to older patients

Multiple cohort studies involving untreated HIV-infected persons have established that older persons have a more rapid progression to AIDS and shortened survival when compared with younger persons.<sup>1,2,3,4</sup> For HIV-infected persons older than 50, sparse data exist from randomized, controlled antiretroviral therapy clinical trials, as most randomized therapy trials have excluded persons older than 50 or 60. A retrospective analysis of 253 patients 50 years of age or older found antiretroviral therapy substantially improved survival rates.

Several large retrospective studies have clearly shown delayed and diminished CD4 cell recovery after starting antiretroviral therapy in older HIV-infected patients when compared with younger age groups.<sup>6,7,8,9</sup> Studies have shown conflicting results with respect to virologic responses in older versus younger<sup>7,10,11,12</sup> with the most comprehensive study showing no significant difference in virologic responses based in older versus younger adults.<sup>8</sup>

The major antiretroviral therapy guidelines that most influences clinical practice in the United States—the Department of Health and Human Services (DHHS) Panel guidelines<sup>13</sup>—now recommends initiating antiretroviral therapy in all persons infected with HIV. The recommendation to use antiretroviral therapy in all HIV-infected persons is based on reducing the risk of disease progression and decreasing the risk of HIV transmission. Data from several large cohort studies have strongly suggested a survival advantage with initiation of antiretroviral therapy earlier in the course of HIV disease.<sup>14,15</sup>

In addition, growing evidence suggests that uncontrolled HIV infection produces a “chronic inflammatory state” associated with an increased risk of developing cardiovascular disease<sup>1</sup> and non-AIDS malignancies,<sup>16</sup> and CD4 counts below 500 are associated with higher cardiovascular risk,<sup>17</sup> and risk for

non-AIDS malignancies.<sup>18</sup> The rationale for recommending antiretroviral therapy for the prevention of HIV transmission is based on several recent studies, most notably the landmark HPTN 052 trial that showed a greater than 95% reduction in HIV transmission in HIV serodiscordant couples when the HIV-infected partner received antiretroviral therapy.<sup>19</sup>

The 2013 DHHS Antiretroviral Therapy guidelines specifically addressed the use of antiretroviral therapy for persons 50 and older, recommending initiating antiretroviral therapy in all persons older than 50 years of age regardless of CD4 cell count, primarily because, when compared with younger patients, these older HIV infected individuals have increased risk for non-AIDS related complications and they have diminished CD4 cell count recovery in response to antiretroviral therapy.<sup>13</sup>

Further, the DHHS guidelines emphasized that older individuals potentially have increased risk for HIV transmission or acquisition, for several reasons, including (1) alterations reduced mucosal and immunologic defenses may occur with post-menopausal atrophic vaginitis, (2) older individuals have less incentive to use of condoms given the lack of need for pregnancy prevention, and (3) persons older than 50 have lower frequency of HIV screening given their perceived low risk for HIV infection.<sup>20</sup>

The use of antiretroviral therapy in older HIV-infected patients presents several challenges, predominantly due to the increased prevalence of non-HIV-related comorbid medical conditions, such as hyperlipidemia, hypertension, diabetes, and coronary artery disease.<sup>21</sup> In addition, older patients may have age-related changes in body composition that can alter medication volume of distribution and influence drug pharmacokinetics. Compared with younger patients, older patients are more likely to be taking multiple medications not related to HIV and thus increasing the likelihood for drug-drug interactions. Further, several studies have shown older HIV-infected patients have increased risk for developing drug-related toxicity, including hyperglycemia, elevated creatinine, and unfavorable alterations in lipid profile.<sup>7</sup> **HIV**



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