National Institute on Drug Abuse
Advancing Addiction Science

Research Report
Revised July 2012

HIV/AIDS Research Report

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HIV/AIDS Research Report

Letter from the Director

Human immunodeficiency virus (HIV) — the virus that causes acquired immune deficiency syndrome (AIDS) — has been with us for three decades now. Today, an entire generation of young adults has never known a world without HIV/AIDS.

Initially characterized by relatively localized outbreaks and then reaching pandemic proportions, the explosive spread of HIV is being reined in by the advent of highly active antiretroviral therapy (HAART) and preventative strategies. And yet, in the United States alone, approximately 50,000 people are newly diagnosed each year — and one in five people living with HIV are unaware they are infected.

Scientific discoveries are moving us closer to envisioning an AIDS-free generation as we continue to take steps toward ending this disease. Improving access to drug abuse treatment; increasing condom use and male circumcision; preventing mother-to-child transmission; implementing syringe-exchange programs combined with HIV risk-reduction strategies; achieving wider distribution of antiretroviral therapies; and scaling up HIV screening to identify infected people early and link them to care are proven strategies toward reaching this goal. New research in basic HIV biology is also providing clues as to how we might successfully purge the pockets of latent virus in HIV-infected persons and thereby achieve a true cure for the HIV/AIDS epidemic.

This Research Report is designed to highlight the state of the science and to raise awareness of the link between HIV/AIDS and drug abuse — not just injection drug use but drug abuse in general. People who are high on drugs or alcohol are more likely to have unsafe sex that might expose them to HIV and other infectious diseases. In some populations, HIV prevalence is converging among injection and noninjection drug users, suggesting that the risky behavior associated with drug abuse in general

is fueling the sustained spread of the virus. For this reason, drug abuse treatment *is* HIV prevention.

As the following pages demonstrate, NIDA's multifaceted approach continues to reveal more about the pivotal role of drug abuse in the spread of HIV and to inform effective strategies to prevent and treat it.

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse

What is HIV/AIDS?

Human immunodeficiency virus (HIV) is the virus that causes acquired immune deficiency syndrome (AIDS) and is transmitted through contact with infected blood and bodily fluids. Such contact can occur through unprotected sex, through sharing of needles or other drug injection equipment, through mother-to-child transmission during pregnancy or breast-feeding, and through receipt of infected blood transfusions and plasma products during medical care in some parts of the world. There is currently no cure for HIV/AIDS. Once an individual contracts HIV, he or she has it for life.

HIV infects immune cells in the body called CD4 positive (CD4+) T cells, which are essential for fighting infections. HIV converts these cells into "factories" that produce more of the HIV virus to infect other healthy cells, eventually destroying the CD4+ cells. An infected person may look and feel fine for many years and may not even be aware of the infection. However, as the individual loses CD4+ cells and the immune system weakens, he or she becomes more vulnerable to illnesses and other infections. Physicians make an AIDS diagnosis when a patient has one or more of these illnesses and a CD4+ cell count of less than 200. Treatment for HIV typically involves highly active antiretroviral therapy, better known as HAART.

What Is HAART?

HAART is a customized combination of different classes of medications that a physician prescribes based on such factors as the patient's viral load (how much virus is in the blood), the particular strain

of the virus, the CD4+ cell count, and other considerations (e.g., disease symptoms). Because HAART cannot rid the body of HIV, it must be taken every day for life. HAART can control viral load, delaying or preventing the onset of symptoms or progression to AIDS, thereby prolonging survival in people infected with HIV. HAART has been in use since 1996 and has changed what was once a fatal diagnosis into a chronically managed disease.[1]

How Is HIV Detected?

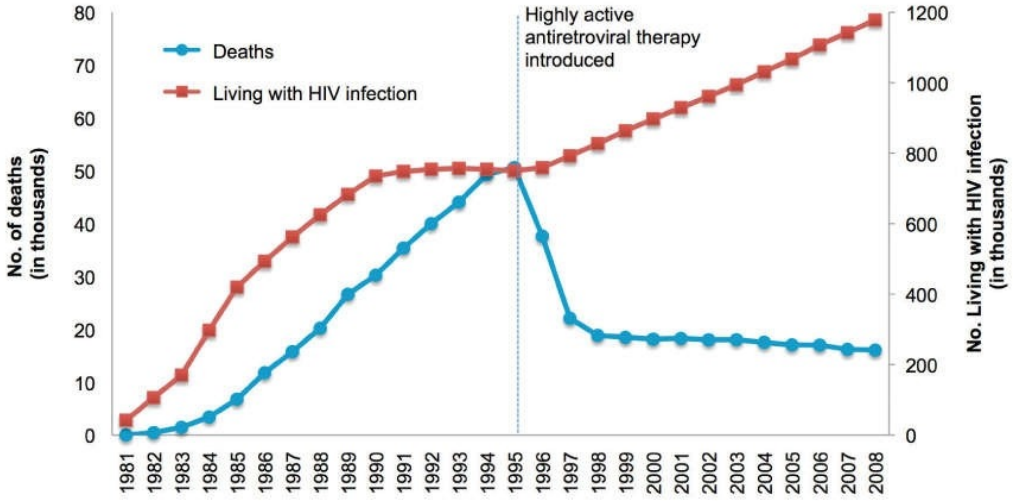
When a person contracts HIV, his or her immune system produces antibodies, which are proteins that recognize the virus. The most commonly used HIV tests detect the presence of these antibodies. There are rapid tests that can provide results in 20 minutes[2], but it usually takes 6–8 weeks after someone has been exposed to the virus for enough HIV antibodies to accumulate for accurate detection through testing (although improved HIV tests are now reducing this window to 2 weeks). This period represents one of the most dangerous for HIV transmission, since a person can receive a negative test result and yet be highly infectious, capable of rapidly spreading the virus through unsafe behaviors. The Centers for Disease Control and Prevention (CDC) now recommends that HIV testing be provided to anyone 13–64 years old as part of routine medical care and that this screening be performed annually for anyone at high risk for HIV infection (e.g., drug abusers, men who have sex with men, and sex workers). NIDA is collaborating with the Substance Abuse and Mental Health Services Administration (SAMHSA) and others to expand rapid HIV testing to drug treatment facilities to better identify HIV infections and to more efficiently engage patients in comprehensive treatment for both drug addiction and HIV infection.

How Does Drug Abuse Affect the HIV Epidemic?

Drug abuse and addiction have been inextricably linked with HIV/AIDS since the beginning of the epidemic. While intravenous drug use is well known in this regard, less recognized is the role that drug abuse plays more generally in the spread of HIV by increasing the likelihood of high-risk sex with infected partners.[3] The intoxicating effects of many drugs can alter judgment and inhibition and lead people to engage in impulsive and unsafe behaviors. Also, people who are abusing or addicted to

drugs may engage in sexually risky behaviors to obtain drugs or money for drugs. Nearly one-quarter of AIDS cases stem from intravenous drug use, and one in four people living with HIV/AIDS in the period of 2005–2009 reported use of alcohol or drugs to an extent that required treatment.[4]

Estimated Persons Living with HIV Infection (Diagnosed and Undiagnosed)† and Estimated AIDS Deaths Among Adults and Adolescents — United States, 1981–2008



Source: Centers for Disease Control and Prevention

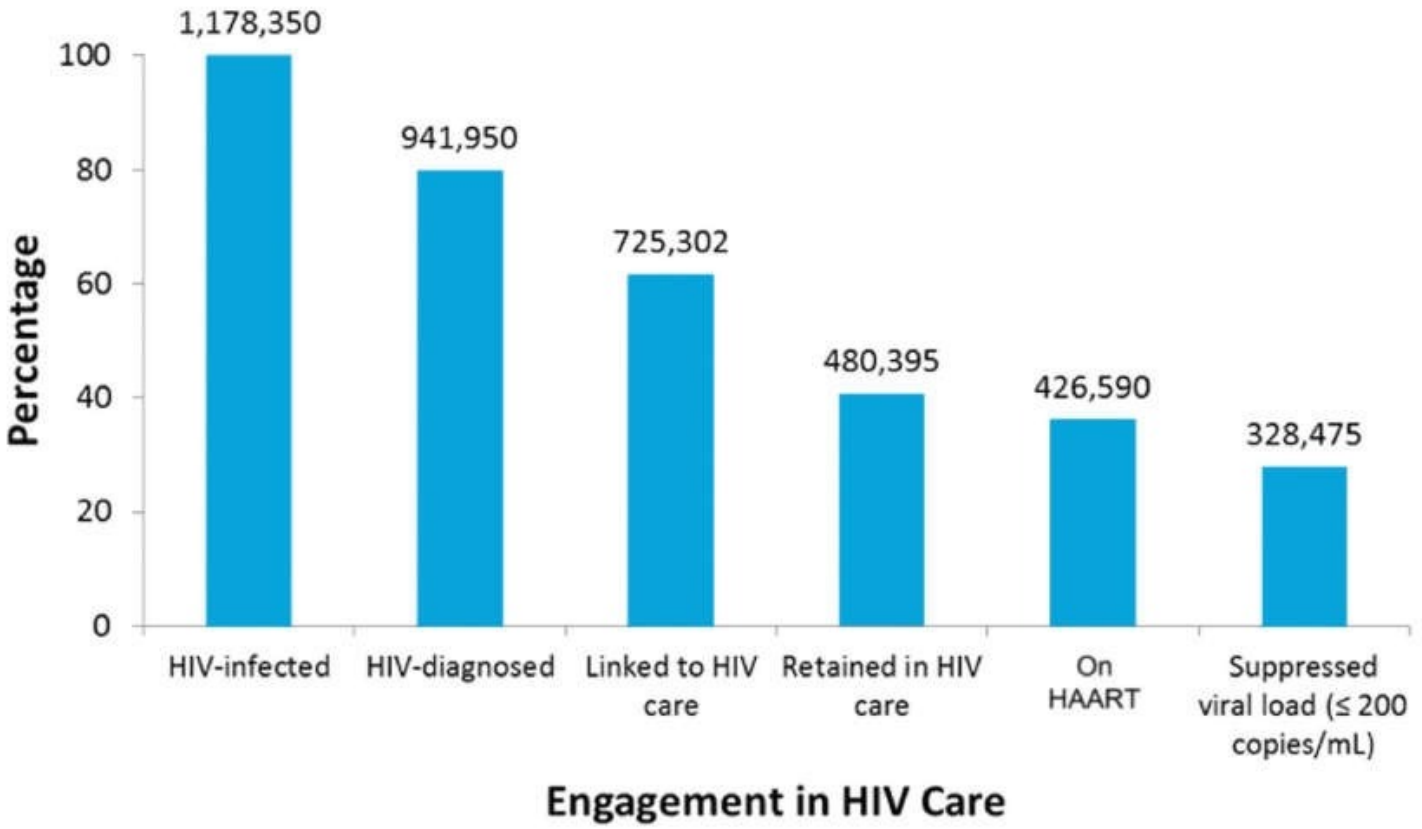
*Estimates were obtained by statistically adjusting the national HIV surveillance data reported through June 2010 for reporting delays, but not for incomplete reporting.
†HIV prevalence were estimated based on national HIV surveillance data for adults and adolescents (aged ?13 years at diagnosis) reported through June 2010 using extended back-calculation. See text description

Drug abuse and addiction can also worsen the progression of HIV and its consequences, especially in the brain. For example, in animal studies, methamphetamine increased the amount of HIV virus present in the brain;[5] and in human studies, HIV caused greater neuronal injury and cognitive impairment in methamphetamine abusers compared to non-drug users.[6,7]

What Is the Scope of HIV/AIDS in the United States?

The Centers for Disease Control and Prevention (CDC) estimates that 1.2 million people are infected with HIV in the United States and that 1 in 5 (20 percent) are unaware that they are infected. In 2010, over 47,000 people were newly diagnosed with HIV, the majority of whom were men. HIV infection is over-represented in the African-American community: African-Americans make up almost one-half of the newly diagnosed cases, followed by Whites and Hispanics.

Number and Percentage of HIV-infected Persons Engaged at Each Stage of HIV Care



Source: Centers for Disease Control and Prevention, MMWR 2011, 60(47):1618-1623.

Effective treatments have dramatically decreased the number of deaths from AIDS since the peak years of the epidemic (1993–1998); however, more than 17,000 people still died from AIDS-related illnesses in 2009. In fact, even among those diagnosed with HIV, a substantial proportion do not receive proper care or remain in treatment (see figure).[8] Additionally, the trend of people living longer with HIV presents new, long-term healthcare challenges for this population.

How Has the HIV/AIDS Epidemic Changed Over the Past 30 Years?

CDC data reveal notable shifts in the HIV epidemic in the United States, with a higher proportion of new infections today occurring among young men who have sex with men (MSM), racial/ethnic minorities, and women. Early in the HIV/AIDS epidemic, infections emerged mainly among White, urban MSM, or male injection drug users (IDUs). However, over the past 30 years, the boundaries between groups at greater and lesser risk for contracting the virus have been dissolving. From 2005 to 2008, estimated HIV diagnoses increased approximately 17 percent among MSM, particularly minority MSM. Risky sexual behavior linked to substance abuse exacerbates this trend, a specific example being the link between risky sexual behavior and methamphetamine abuse.[9]

How Drug Abuse Contributes to HIV Transmission:

- Injection drug use: sharing needles or other equipment with an infected person.
- Sexual Contact:
  - Unprotected sex due to intoxication, which can impair judgment and decisionmaking and reduce inhibitions
  - Unprotected sex with an infected IDU
  - Transactional sex to obtain drugs or money for drugs

Although HAART has transformed the face of HIV/AIDS in this country and around the world, it has also altered the consequences of HIV infection. While new diagnoses of HIV-associated infections and some neurological complications, such as HIV dementia, have decreased since the treatment's introduction,[1] other medical complications have increased. For example, individuals receiving HAART therapy are more vulnerable to developing diabetes, hypertension, and chronic kidney disease.[10] HIV+ patients also have lower bone mineral density,[11] which HAART can amplify by contributing to bone loss, resulting in fractures. Some individual medications that are included in HAART can be toxic to the liver, especially in older individuals, for whom liver function may already be declining due to the natural aging process; this can lead to liver disease.[12]

Another unintended consequence of effective HAART therapy is the development of complacency. Because HAART reduces viral load, some patients mistakenly believe that they do not need to adhere strictly to the treatment regimen or that reduced viral load means elimination of transmission risk.[13-15] This belief can, in turn, lead to a resumption of unsafe sex and drug abuse practices.[16] These and other unhealthy behaviors, such as smoking cigarettes, diminish the benefit achieved with HAART therapy. For example, cigarette smoking among HIV+ individuals is 2–3 times higher than in the general population. HIV-infected smokers are unusually susceptible to respiratory complications, chronic obstructive pulmonary disease, lung cancer, cardiovascular disease, and suppressed immune function.[17]

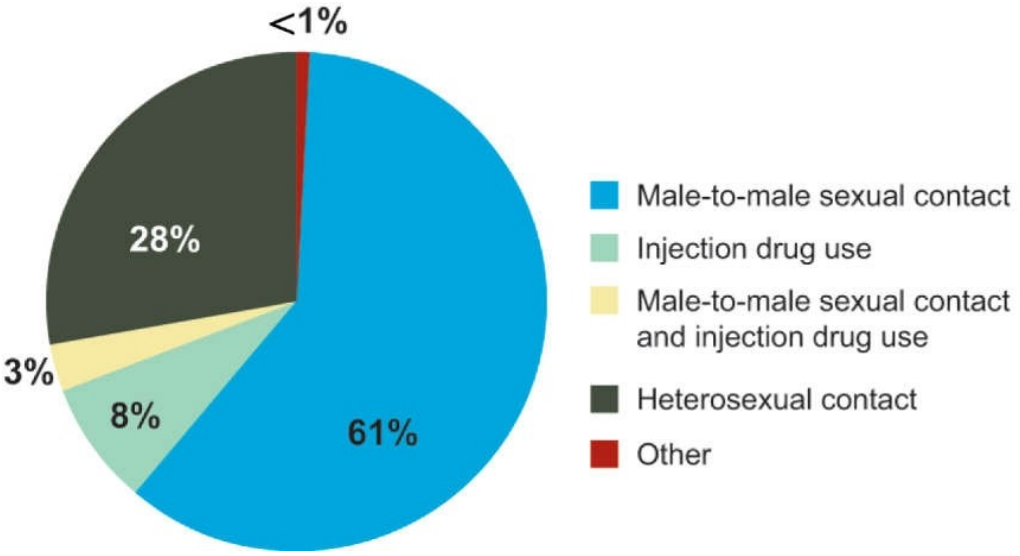
Who Is at Risk for HIV Infection and Which Populations Are Most Affected?

Anyone can contract HIV, and while IDUs are at great risk because of practices related to their drug use, anyone who engages in unsafe sex (e.g., unprotected sex with an infected partner) could be exposed to HIV infection. However, while all groups are affected by HIV, some are more vulnerable than others, as summarized below.

Men Who Have Sex with Men

Gay or bisexual MSM are the most severely affected population. MSM account for just a small fraction (2 percent) of the total U.S. population, yet nearly two-thirds of all new infections occurred within this group in 2009, and one-half of all people living with HIV in 2008 were MSM. MSM within ethnic minority populations are at greatest risk (see "*Ethnic Minorities*," below).

Diagnosis of HIV Infection among Adults and Adolescents, by Transmission Category (2010)*



Source: Centers for Disease Control and Prevention

**These transmission categories do not distinguish infections resulting from non-injection drug use (e.g., sexual behavior resulting from drug or alcohol intoxication).* See text description

Injection Drug Users

Injection drug use has long been associated directly or indirectly with approximately one-third of AIDS cases in the United States. The fact that IDUs made up only 8 percent of new HIV infections in 2010 versus 23 percent in 1994–2000 demonstrates the progress made in HIV prevention and treatment within this population. Still, much work remains; while there may be fewer new infections among IDUs, in 2009, nearly one-half of those who were HIV+ were unaware they were infected.[18]

Hepatitis C and Co-Infection with HIV

Hepatitis C virus (HCV), a leading cause of liver disease, is highly prevalent among injection drug users and often co-occurs with HIV. In the United States, an estimated 3.2 million people are chronically infected with HCV,[22] with injection drug use being the main driver. Nearly one-quarter of HIV patients and over one-half (50–80 percent) of IDUs are infected with both viruses. Chronic HCV and HIV co-infection results in an accelerated progression to end-stage liver disease, with HCV infection being a leading cause of non–AIDS-related deaths among HIV+ individuals.

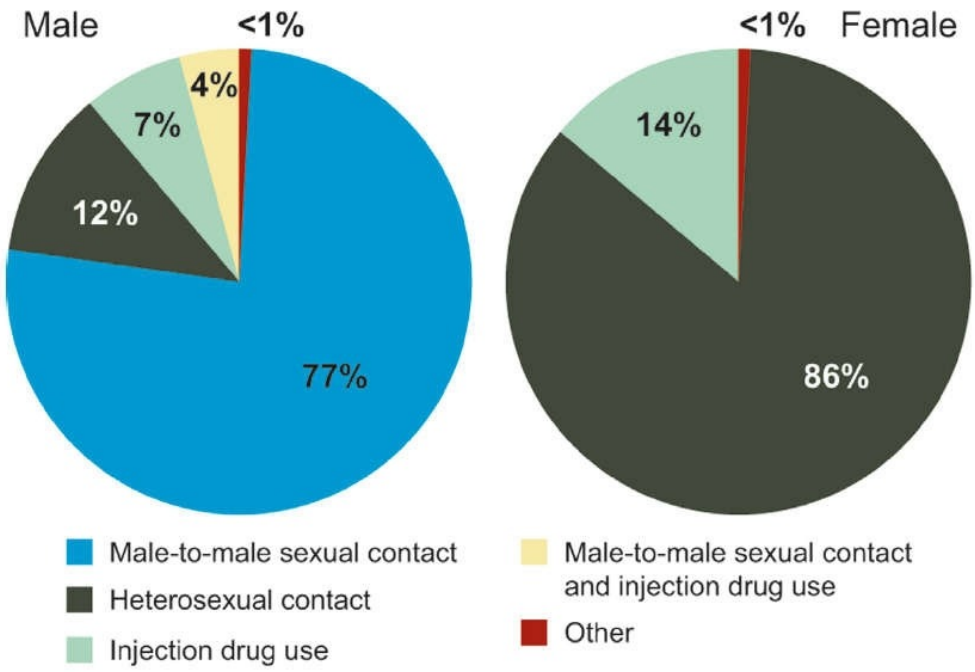
Injection drug use, HIV, and HCV create a complicated tapestry of ailments that present a variety of challenges to healthcare providers. Although HAART medications can effectively treat people infected with HIV, HAART provides only modest benefit for co-occurring HCV. HCV infection, like HIV infection, can be successfully managed if detected early. The newer HCV medications boceprevir and telaprevir — approved by the U.S. Food and Drug Administration (FDA) in 2011 — increase cure rates and decrease treatment length when combined with standard HCV drug regimens,[23] but they must be carefully coordinated with HAART for those co-infected. The added burden of drug addiction further complicates treatment regimens.

Women

Heterosexual contact with an HIV+ partner accounted for over one-quarter of all new infections in 2010 and is the main way that women contract the virus (see figure), especially within ethnic minority communities. Regional variations of HIV incidence in women have changed over time. In the early years of the epidemic, incidence in women predominated in the Northeast, but infection rates and mortality have been steadily increasing in the southern United States.[19] Although injection drug use has declined as a means of HIV transmission over recent years, it is still responsible for 14 percent of HIV diagnoses in women. A recent study conducted by the Massachusetts Department of Public

Health reported 40 percent of White women contracted HIV through injection drug use.[20] Another factor contributing to HIV disease in women is trauma. Trauma resulting from sexual or physical abuse experienced during childhood or adulthood is increasingly associated with rising prevalence of HIV infection and poor health outcomes in HIV+ women.[21] Comprehensive HIV treatment regimens that include mental health services are critical for this population.

Diagnosis of HIV Infection among Adults and Adolescents, by Sex and Transmission Category (2010)



Source: Centers for Disease Control and Prevention

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Ethnic Minorities

HIV surveillance data show that the rates of new HIV infection are disproportionately highest within ethnic minority populations. African- Americans account for a higher proportion of HIV infections than any other population at all stages of the disease from initial infection to death (see text box). Moreover, specific minority subgroups are at particular risk. Nearly two-thirds (64 percent) of new HIV infections among MSM occurred in minority men (Black/African-American, Hispanic/Latino, Asian/Pacific

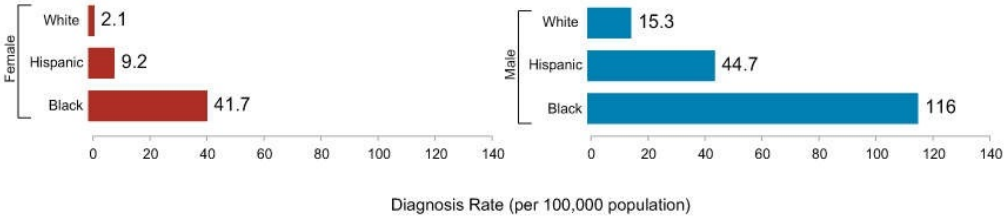
Islanders, and Native American/ Hawaiian). In addition, young minority men (13–24 years old) had the greatest increase (53 percent) of HIV infections of all groups studied between the years 2006 and 2009, occurring predominantly in the South.

The Hispanic population accounted for 1 in 5 new HIV infections in the United States in 2009 — a rate 3 times that of the White community. A number of factors contribute to the high levels of HIV infection within this community, including the country of birth. For example, there is a substantially larger proportion of HIV infections attributed to injection drug use for Hispanic men born in Puerto Rico than anywhere else. Such differences underscore the need for interventions that are socially and culturally tailored for specific populations.

Youth

Young people are also at risk for HIV infection. Approximately 9,800 people aged 13–24 were diagnosed with HIV in 2010, representing 20 percent of newly diagnosed cases, with the highest rate occurring among those aged 20–24. Particular HIV risk behaviors within this age group include sexual experimentation and drug abuse, which are often influenced by strong peer group relationships. Compounding this vulnerability is “generational forgetting”: Studies show that today’s youth may be less likely to perceive the dangers associated with HIV than are older Americans, who witnessed a higher AIDS mortality rate associated with the rapid progression from HIV to AIDS in the early years of the epidemic.

Graph of Estimated Rate of HIV Diagnosis by Gender and Race/Ethnicity (2010)



Source: Centers for Disease Control and Prevention

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Older People

Sixteen (16) percent of new diagnoses of HIV infection in the United States in 2010 occurred among individuals over the age of 50, and this number has been increasing for the past 11 years.[26] Some older persons do not believe they are at risk and thus engage in unsafe sexual practices. The problem is further exacerbated by healthcare professionals who underestimate the vulnerability of this population.

The growing number of people contracting HIV later in life, combined with the prolonged survival made possible by HAART, has contributed to an increasing number of people over the age of 50 living with HIV. This trend will continue, and by 2015, the over-50 population is predicted to represent one-half of all HIV/AIDS cases.[27] The aging population presents a variety of treatment challenges. Older adults progress more rapidly to AIDS, have a greater number of age-related comorbidities (e.g., cardiovascular disease, limited mobility), and report smaller support networks than their younger counterparts.[28]

Criminal Justice System

Young people are also at risk for HIV infection.

The criminal justice system is burdened with a significant population of HIV-infected individuals that can be 2 to 5 times larger than that in the surrounding community.[29] An estimated 1 in 7 HIV+ individuals living in the United States passes through this system each year.[30] The criminal justice system is also burdened with significant substance abuse, with about one-half of Federal and State prisoners meeting the criteria for drug dependence or abuse.[31] Yet, few offenders are screened for HIV,[32] or receive treatment for substance abuse and other mental illness while incarcerated. This situation is further exacerbated upon reentry when released offenders often lack health insurance and fail to be linked to continuing treatment programs within the community. NIDA is helping to address these challenges by researching the best ways to identify and help prisoners get treatment for both drug addiction and HIV while incarcerated and in the community after release.

The Differential HIV Experience of African-Americans

While African-Americans make up 12 percent of the U.S. population, they accounted for 46 percent of new HIV infections in 2010, substantially higher than the rate for Whites or Hispanics. The majority of these were men (70 percent); however, African-American women also have a high rate of HIV diagnosis — nearly 20 times that of White women (see figure). More disheartening is that 1 in 16 African-American men and 1 in 32 African-American women will eventually be diagnosed with HIV.

The causes of this HIV health disparity are complex. HIV infection prevalence is higher and more broadly represented in the African- American community compared to the White population; thus African-Americans are at increased risk of infection simply by choosing intimate partners within their own ethnic communities.[24] Additionally, African-American communities experience high rates of other sexually transmitted infections, and some of these infections can significantly increase the risk of contracting HIV. African-Americans also tend to be diagnosed at later stages in the disease and therefore begin therapy later, increasing the length of time of their infectivity. Once engaged in HAART, African-Americans are more likely to discontinue therapy prematurely,[25] risking resurgence of HIV infectivity and further health complications.

> To address these disparities, NIDA is encouraging research that expands and coordinates prevention and treatment strategies across Federal agencies and within communities to more effectively identify persons at risk and link them to the help they need. Additional efforts are being made to promote healthy lifestyle choices, safe sexual practices, and HIV and substance abuse treatment adherence in a way that is culturally relevant for the African-American community.

How Can HIV Be Prevented and Treated in Drug-Using Populations?

Cumulative research has shown that drug addiction treatment, community-based outreach, testing, and linkage to care for HIV and other infections are the most effective ways to reduce HIV transmission among drug-abusing individuals. Combined pharmacological and behavioral treatments for drug abuse have a demonstrated impact on HIV risk behaviors and incidence of HIV infection.[33] For example, recent research showed that when behavioral therapies were combined with methadone treatment, approximately one-half of study participants who reported injection drug use at the outset of the study reported no such use at the end of the study, and over 90 percent of all participants reported no needle sharing.[34] Drug treatment programs also serve an important role in providing current information on HIV and related diseases, counseling and testing services, and referrals for medical and social services.

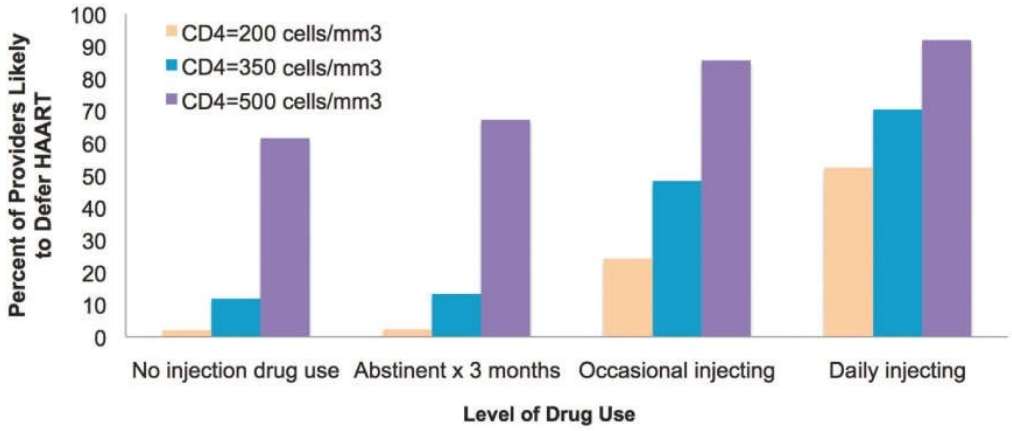
NIDA is also investing in research to identify the most effective strategies to treat HIV among drug users. The mistaken belief that IDUs are unlikely to benefit from HAART because of their chaotic lifestyles has resulted in delays in delivering HIV treatments to drug abusing populations, or even withholding of those treatments — dramatically compromising the quality of life for these individuals and their partners (see figure). This further burdens the healthcare community, leaving unchecked illness within this population.[35] These misperceptions have been refuted by a recent study showing no difference in survival between IDUs and non-IDUs receiving HAART.[36]

Moreover, treatment of drug addiction may actually improve adherence to HIV treatment. Studies show, for example, that treating opioid addiction with buprenorphine or methadone improves both adherence to HAART and the quality of care in HIV+ individuals with a history of opioid abuse.[37,38] These studies confirm that drug addiction should not be a barrier to HIV treatment and that treatment of both conditions is both necessary and effective.

Opportunities to Improve HIV Prevention and Treatment:

- Make HIV testing a routine part of healthcare.
- Initiate HAART therapy early to decrease HIV viral load and reduce infectivity.
- Establish a continuum of care to improve linkage to substance abuse and HIV treatment within the criminal justice system and upon prisoner reentry.
- Improve rates of testing and treatment among African-Americans, MSM, and other groups disproportionately impacted by the epidemic.

HIV+ IDUs Are Less Likely to Receive HAART Treatment than Non-IDUs



See text description

NIDA-funded research is also investigating new technologies to make adherence easier, more accessible, and relevant to targeted audiences. For example, text-messaging and other smartphone applications are being tested to help HIV+ youth improve adherence to HAART treatment. Culturally sensitive and gender-specific Web sites are also under development, designed to provide information to vulnerable populations to help modify risky behaviors, prevent infection, and build social support networks.

Finally, since treatment of co-occurring drug addiction and HIV infection may involve the use of multiple medications, there can be a risk of drug interactions that can decrease the effectiveness of either or both treatments. For instance, when methadone is administered to treat heroin and other opioid addictions along with certain antiretroviral medications (ARVs) that are components of HAART therapy, the concentration of methadone in the blood is significantly decreased,[39] potentially compromising its effectiveness. Newer medications are now available to address these issues. Specifically, buprenorphine — a medication approved for the treatment of opioid addiction in 2002 — does not display the same cross-reactivity with the majority of ARVs and is thus a better choice for HIV+ patients who require treatment for both. [40, 41]

How Do We Implement HIV Prevention on a Broad Scale?

Early detection and treatment prevents transmission of HIV and improves health outcomes for those infected. Research indicates that routine HIV screening in healthcare settings among populations with a prevalence rate as low as 1 percent is as cost effective as screening for other conditions such as breast cancer and high blood pressure. These findings suggest that HIV screening can lower healthcare costs by preventing highrisk practices and decreasing virus transmission.[42]

More recently, scientists demonstrated[43] that providing early HAART therapy to the HIV-infected partner of a heterosexual couple was 96 percent successful in preventing the spread of the virus to the uninfected partner. In fact, early initiation of HAART has been shown to be pivotal in reducing viral load and HIV incidence at the population level.[44, 45] Capitalizing on these and other findings, researchers and clinicians have been testing and promoting the **Seek, Test, Treat, and Retain** approach to identify high-risk populations (Seek) including substance abusers and those in the criminal justice system; test them for HIV (Test); initiate HAART for those who test positive (Treat); and provide the necessary support to help these individuals remain in treatment (Retain, e.g., linking criminal offenders to treatment upon their return to the community). These findings show great promise for preventing the spread of HIV and improving outcomes for those already infected, but studies are now needed to determine the most effective ways to scale up these interventions, especially in the most vulnerable populations.

Summary

NIDA-funded research is also investigating new technologies to make adherence easier, more accessible, and relevant to targeted audiences.

While the need continues for more research, the scientific and medical communities are poised to move forward in developing and disseminating effective HIV prevention and treatment approaches. Three key principles underlie NIDA's strategy: (1) drug abuse and HIV are linked in ways that extend beyond injection drug use; (2) drug abuse and HIV remain intertwined epidemics in the United States and around the world — therefore, drug abuse treatment *is* HIV prevention; and (3) the **Seek, Test, Treat, and Retain** approach, especially when implemented in high-risk populations or settings, stands to decrease viral load and HIV incidence at a population level, improving outcomes for all. Our mission now is to implement these evidence-based strategies so that we can attain our goal of an "AIDS-free generation."

Glossary

Acquired Immune Deficiency Syndrome (AIDS): The most severe manifestation of infection with HIV. An AIDS diagnosis is based on the presence of clinical symptoms, a patient's HIV viral load, and a CD4+ T cell count at or below 200 cells per microliter in the presence of HIV infection. Persons living with AIDS often have infections of the lungs, brain, eyes, and other organs, and they frequently suffer debilitating weight loss, diarrhea, and a type of cancer called Kaposi's sarcoma.

Addiction: A chronic, relapsing disease characterized by compulsive drug seeking and abuse despite adverse consequences. It is associated with longlasting changes in the brain.

Antiretroviral Drugs: Medications used to kill or inhibit the multiplication of retroviruses such as HIV.

Behavioral Treatments: A set of treatments that focus on modifying thinking, motivation, coping mechanisms, and choices made by individuals.

CD4+ T Cells: A type of cell involved in protecting against viral, fungal, and protozoal infections. These cells normally stimulate the immune response, signaling other cells in the immune system to perform their special functions. Also known as helper T cells, they are destroyed or disabled during

HIV infection.

Cultural Relevancy: The ability of an intended audience to view an intervention as applicable to their life circumstances.

Generational Forgetting: Term to describe when knowledge of adverse consequences experienced by a particular generation or population is lost by a younger cohort. In this report, it refers to the diminished view of the dangers of HIV/AIDS among those ages 25 and younger.

Highly Active Antiretroviral Therapy (HAART): A combination of three or more antiretroviral drugs used in the treatment of HIV infection and AIDS.

Hepatitis C Virus (HCV): A virus that causes liver inflammation and disease. Hepatitis is a general term for liver damage and hepatitis C is the most common type of hepatitis found among those with HIV.

Human Immunodeficiency Virus (HIV): The virus that causes AIDS.

Injection Drug Use (IDU): Act of administering drugs directly into a vein using a hypodermic needle and syringe. Injection drug users (IDUs) are individuals that abuse drugs in this way.

Opioid: A compound or drug that binds to receptors in the brain involved in the control of pain and other functions (e.g., morphine, heroin, oxycodone, hydrocodone).

Pharmacological Treatment: Treatment using medications.

Seek, Test, Treat, and Retain (STTR): A research-based model of care that aims to expand HIV testing and reduce viral load and HIV transmission through initiating HAART therapy in HIV+ individuals. This approach reaches out to high-risk groups who have not been recently tested (Seek), engages them in HIV testing (Test), initiates and monitors HAART for those testing positive (Treat), and retains patients in care (Retain).

Viral Load: The quantity of HIV RNA (ribonucleic acid) in the blood. Research indicates that viral load is a better predictor of the risk of HIV disease progression than the CD4+ cell count. The lower the viral load, the longer the time to AIDS diagnosis and the longer the survival time. Viral load testing for

HIV infection is used to determine when to initiate or change therapy.

References

1. Palella, F.J., Jr., et al., *Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators.* N Engl J Med, 1998. 338(13): p. 853-60.
2. Greenwald, J.L., et al., *A rapid review of rapid HIV antibody tests.* Curr Infect Dis Rep, 2006. 8(2): p. 125-31.
3. King, K.M., et al., *Co-occurrence of Sexual Risk Behaviors and Substance Use Across Emerging Adulthood: Evidence for State- and Trait-level Associations.* Addiction, 2012.
4. The NSDUH Report: *HIV/AIDS and Substance Use,* 2010, Substance Abuse and Mental Health Services Administration: Rockville, MD.
5. Marcondes, M.C., et al., *Methamphetamine increases brain viral load and activates natural killer cells in simian immunodeficiency virus-infected monkeys.* Am J Pathol, 2010. 177(1): p. 355-61.
6. Langford, D., et al., *Patterns of selective neuronal damage in methamphetamine-user AIDS patients.* J Acquir Immune Defic Syndr, 2003. 34(5): p. 467-74.
7. Rippeth, J.D., et al., *Methamphetamine dependence increases risk of neuropsychological impairment in HIV infected persons.* J Int Neuropsychol Soc, 2004. 10(1): p. 1-14.
8. Cohen, S.M., et al., *Vital Signs: HIV Prevention Through Care and Treatment - United States, in Morbidity and Mortality Weekly Report* 2011, Centers for Disease Control and Prevention. p. 1618-1623.
9. Degenhardt, L., et al., *Meth/ amphetamine use and associated HIV: Implications for global policy and public health. Int J Drug Policy,* 2010. 21(5): p. 347-58.
10. Phair, J. and F. Palella, *Renal disease in HIV-infected individuals.* Curr Opin HIV AIDS, 2011. 6(4): p. 285-9.
11. Mallon, P.W., *HIV and bone mineral density.* Curr Opin Infect Dis, 2010. 23(1): p. 1-8.
12. Falade-Nwulia, O. and C.L. Thio, *Liver disease, HIV and aging.* Sex Health, 2011. 8(4): p. 512-20.
13. Dukers, N.H., et al., *Sexual risk behaviour relates to the virological and immunological improvements during highly active antiretroviral therapy in HIV-1 infection.* AIDS, 2001. 15(3): p.

369-78.

14. Vanable, P.A., et al., *Impact of combination therapies on HIV risk perceptions and sexual risk among HIV-positive and HIV-negative gay and bisexual men.* Health Psychol, 2000. 19(2): p. 134-45.
15. Boily, M.C., et al., *Changes in the transmission dynamics of the HIV epidemic after the wide-scale use of antiretroviral therapy could explain increases in sexually transmitted infections: results from mathematical models.* Sex Transm Dis, 2004. 31(2): p. 100-13.
16. Tun, W., et al., *Attitudes toward HIV treatments influence unsafe sexual and injection practices among injecting drug users.* AIDS, 2003. 17(13): p. 1953-62.
17. Rahmanian, S., et al., *Cigarette smoking in the HIV-infected population.* Proc Am Thorac Soc, 2011. 8(3): p. 313-9.
18. Wejnert, C., et al., *HIV Infection and HIVAssociated Behaviors Among Injecting Drug Users - 20 Cities, United States, 2009, in Morbidity and Mortality Weekly Report* 2012, Centers for Disease Control and Prevention. p. 133-138.
19. Stone, V.E., *HIV/AIDS in Women and Racial/ Ethnic Minorities in the U.S.* Curr Infect Dis Rep, 2012. 14(1): p. 53-60.
20. *Intersecting Risks:HIV Infection Among Heterosexual W*omen and Men in Massachusetts, 2010, Bureau of Infectious Disease, Office of HIV/AIDS.
21. Machtinger, E.L., et al., *Psychological Trauma and PTSD in HIV-Positive Women: A Meta-Analysis.* AIDS Behav, 2012.
22. Armstrong, G.L., et al., *The prevalence of hepatitis C virus infection in the United States, 1999 through 2002.* Ann Intern Med, 2006. 144(10): p. 705-14.
23. Ghany, M.G., et al., *An update on treatment of genotype 1 chronic hepatitis C virus infection: 2011 practice guideline by the American Association for the Study of Liver Diseases.* Hepatology, 2011. 54(4): p. 1433-44.
24. Hallfors, D.D., et al., *Sexual and drug behavior patterns and HIV and STD racial disparities: the need for new directions.* Am J Public Health, 2007. 97(1): p. 125-32.
25. Currier, J., et al., *Sex-based outcomes of darunavir-ritonavir therapy: a single-group trial.* Ann Intern Med, 2010. 153(6): p. 349-57.
26. Althoff, K.N., et al., *CD4 count at presentation for HIV care in the United States and Canada: are those over 50 years more likely to have a delayed presentation?* AIDS Res Ther, 2010. 7: p. 45.

27. Smith, G., *HIV Over Fifty: Exploring the New Threat, in Special Committee on Aging, U.S. Senate* 2005, U.S. Government Printing Office: Washington, D.C. p. 1.

28. Doyle, K., et al., *Aging, Prospective Memory, and Health-Related Quality of Life in HIV Infection.* AIDS Behav, 2012.

29. Maruschak, L.M., *Bureau of Justice Statistics: HIV in Prisons, 2007-2008,* 2010, U.S. Department of Justice.

30. Spaulding, A.C., et al., *HIV/AIDS among inmates of and releasees from US correctional facilities, 2006: declining share of epidemic but persistent public health opportunity.* PLoS One, 2009. 4(11): p. e7558.

31. Mumola, C.J. and J.C. Karber, *Special Report: Drug Use and Dependence, State and Federal Prisoners,* 2004, 2007, U.S. Department of Justice.

32. Beckwith, C.G., et al., *Opportunities to diagnose, treat, and prevent HIV in the criminal justice system.* J Acquir Immune Defic Syndr, 2010. 55 Suppl 1: p. S49-55.

33. Metzger, D.S., H. Navaline, and G.E. Woody, *Drug abuse treatment as AIDS prevention.* Public Health Rep, 1998. 113 Suppl 1: p. 97-106.

34. Schroeder, J.R., et al., *Changes in HIV risk behaviors among patients receiving combined pharmacological and behavioral interventions for heroin and cocaine dependence.* Addict Behav, 2006. 31(5): p. 868-79.

35. Westergaard, R.P., et al., *Provider and cliniclevel correlates of deferring antiretroviral therapy for people who inject drugs: a survey of North American HIV providers.* J Int AIDS Soc, 2012. 15: p. 10.

36. Wood, E., et al., *Highly active antiretroviral therapy and survival in HIV-infected injection drug users.* JAMA, 2008. 300(5): p. 550-4.

37. Roux, P., et al., *The impact of methadone or buprenorphine treatment and ongoing injection on highly active antiretroviral therapy (HAART) adherence: evidence from the MANIF2000 cohort study.* Addiction, 2008. 103(11): p. 1828-36.

38. Korthuis, P.T., et al., *Improving adherence to HIV quality of care indicators in persons with opioid dependence: the role of buprenorphine.* J Acquir Immune Defic Syndr, 2011. 56 Suppl 1: p. S83-90.

39. McCance-Katz, E.F., *Treatment of opioid dependence and coinfection with HIV and hepatitis C virus in opioid-dependent patients: the importance of drug interactions between opioids and antiretroviral agents.* Clin Infect Dis, 2005. 41 Suppl 1: p. S89-95.

40. McCance-Katz, E.F. and T.W. Mandell, *Drug interactions of clinical importance with methadone and buprenorphine.* Am J Addict, 2010. 19(1): p. 2-3.

41. Carrieri, M.P., et al., *Use of buprenorphine in HIV-infected injection drug users: negligible impact on virologic response to HAART. The Manif-2000 Study Group.* Drug Alcohol Depend, 2000. 60(1): p. 51-4.

42. Sanders, G.D., et al., *Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy.* N Engl J Med, 2005. 352(6): p. 570-85.

43. Cohen, M.S., et al., Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med, 2011. 365(6): p. 493-505.

44. Montaner, J.S., et al., Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. Lancet, 2010. 376(9740): p. 532-9.

45. Kirk, G., et al., *Decline in Community Viral Load Strongly Associated with Declining HIV Incidence among IDU, in 18th Conference on Retroviruses and Opportunistic Infections* 2011: Boston, MA.